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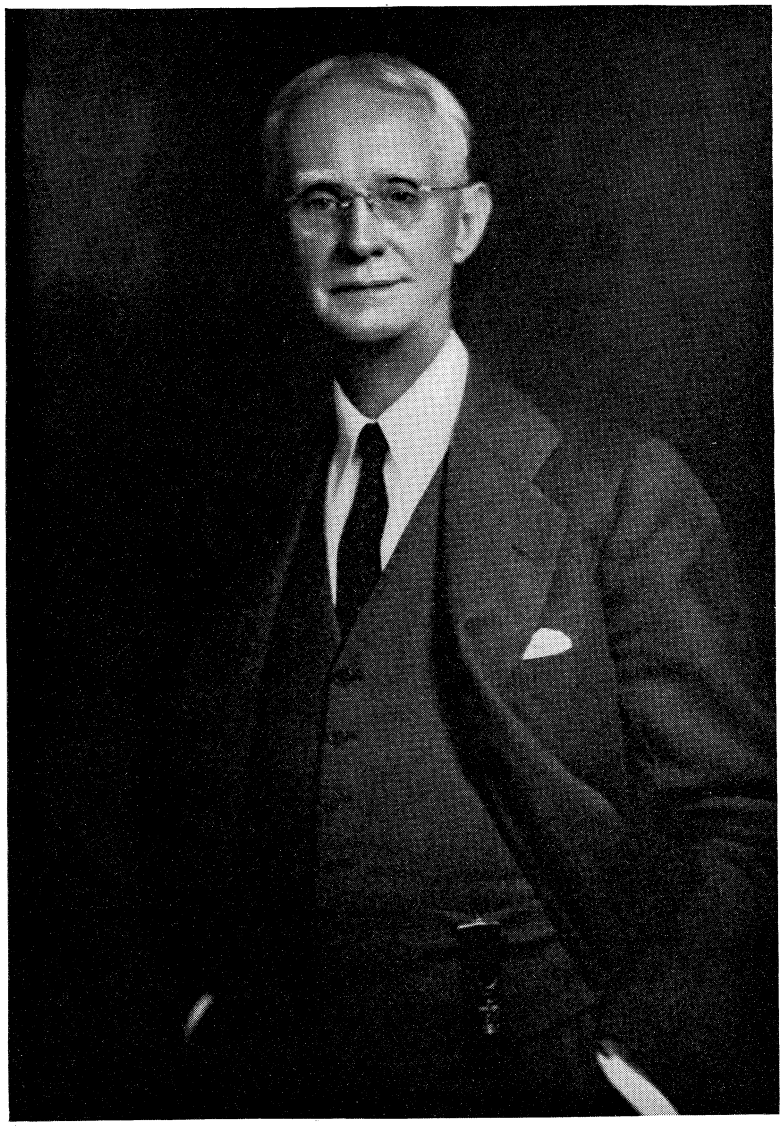

Charles Holmes Herty

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CHARLES HOLMES HERTY

1867–1938

BY FRANK K. CAMERON

Charles Holmes Herty was born December 4, 1867, at Milledgeville, Georgia. His father, Bernard Richard Herty, was born in Milledgeville in 1844, the son of James Herty, a substantial citizen. Bernard Herty enlisted in the Confederate army at the age of 17 years and rose to the rank of Captain. After the war, he returned to Milledgeville to become the leading druggist of the region. Charles Herty's boyhood ambition, to be a druggist also, remained with him to his university days at Baltimore. He and a younger sister were orphaned at an early age, both parents dying before he was 11 years old. Left in somewhat straitened circumstances, Herty always acknowledged gratefully the particular care of an aunt, Miss Florence I. Holmes of Athens, Georgia, who survives him.

Surrounded by relatives and family friends, his boyhood was a happy one. He grew up keenly interested (and successful) in outdoor sports and games, the interest being maintained throughout his life. Graduating from the local school, the Georgia Military Academy, he went to the State University at Athens, taking a Ph.B. in 1886. He entered the Johns Hopkins University in the fall. It was a period of intense intellectual activity at that institution, with a relatively large body of graduate students and few undergraduates. The graduates almost completely dominated the extrascholastic activities and Herty was soon active in them, particularly in glee club and baseball. He was easily the most popular and best loved student of his time. He justified his extracurricular activities because he had now abandoned his ambitions to be a druggist in favor of a teaching career in chemistry and wished to have an appeal to his prospective students, independent of scholastic ability. In 1890 he attained his Ph.D. His dissertation entitled, "The Double Halides of Lead and the Alkali Metals," was a sound piece of work and he returned to a study of double halides later. At this time neither Gibbs' Principle, the phase rule, nor modern techniques were available for guidance. People spoke vaguely of molecular compounds as distinct from atomic compounds and suspected that persistent work in the field would give a clue to the meaning of the also vague concept of valency.

Herty became Assistant Chemist of the Georgia State Experiment Station in 1890 and a year later, 1891, instructor at the State University. He was advanced to Adjunct Professor in 1894 and held the appointment until 1902. In 1895 he married Miss Sophie Schaller of Athens and in 1899 real-

ized a long-time desire by going to Berlin with his wife and two young children. After a year in Berlin listening to Witt and Körner, he went to Zürich to renew his interest in valency by studying with Werner. Returning to Georgia in 1901, he made contact with the U. S. Bureau of Forestry, for Witt's caustic criticism of American methods of obtaining turpentine rankled in his memory and was confirmed by visits to the pine belt. The Naval Stores industry was languishing. Herty was concerned with possibilities for restoring it. His invention of the now universally used cup and accompanying technique was revolutionary, the old boxing method being quite abandoned, with a saving of many millions of dollars. In 1902 he became a regular member of the Forestry Bureau's staff, remaining to 1904. During the years 1904–05 he was with the Chattanooga Pottery Company in connection with the manufacture of his cup.

Financial security now attained, Herty welcomed a return to academic work with the call to head the Department of Chemistry at the University of North Carolina. He was a successful teacher, logical, persuasive and with a never-flagging enthusiasm. Venable and Baskerville had done noteworthy research on the rare earths, and Alvin S. Wheeler had started his long series of investigations on pine oils. Promptly Herty returned to a study of the double halides of platinum and potassium, going on to study the halides and thiocyanates of mercury and lead. While with Werner he had published on the cobalt-ammonia chlorides and he returned for a while to the study of coördination numbers. The reaction of ammonia with ethylphospho-platinic chloride was studied and the compound previouly found by Rosenheim was shown to have a formula strictly in accord with the Werner theory. This publication marked the culmination of Herty's contribution to theoretical or pure chemistry. Henceforward, all his interest in chemistry was as a means for improving the material conditions of people: specifically, to develop industry. He had been writing about turpentine, along the lines he developed in Bulletin No. 40 of the U. S. Bureau of Forestry, which became a classic in the literature of turpentine; and, in 1908, the same year in which his paper on coördination numbers appeared, he reported studies on pine products. He found little change in the optical properties of samples of turpentine gathered throughout the year; the turpentine from the black pine, *Pinus serotinus*, is little used, but was found to be rich in limonene and to absorb more oxygen than the turpentine from the common source, *Pinus heterophylla*. These were followed in the next few years by furher studies of pine products, cotton seed oil, soaps, leather, etc. Of particular interest is the paper delivered before the Eighth International Congress of Applied Chemistry on "The Past, Present and Future of the Naval Stores Industry," and his efforts to obtain isoprene from turpentine. He showed pinene and not dipentene to be the source. Herty served as Dean of the School of Applied Science at the University of North Carolina, 1908–11.

In 1915 Herty was president of the American Chemical Society. An important accomplishment in his administration was the census of American Chemists. In his first presidential address, at New Orleans, he called attention to the resources of the South in raw materials and man power. At Seattle he called attention to the need of more research to supply deficiencies created by the World War, and for coöperation between University laboratories and industry. He suggested acquisition of governmental supplies of raw materials and strong tariff protection. Again President in 1916, in his address in New York he stressed the importance of financial support to make the teaching of chemistry more attractive to competent instructors, the necessity of better training of students going into industry, the desirability of government stores of raw materials, investigation of fuel and potash resources, tariff protection of new American industries, and popularizing chemistry with the laity. In 1916, the A. C. S. News Service was inaugurated. Herty had become accustomed to a much wider audience than the University and was ready to accept the editor's chair in 1917 when expansion of the activities of the American Chemical Society brought a full-time editorship for the *Journal of Industrial and Engineering Chemistry*. He remained with the *Journal* for five years, making it the foremost in its field, and a monument to his talents.

Starting with the motto "Coöperation," a trenchant pen soon showed he could be otherwise than gentle and suave when occasion warranted, and editorials on a wide range of subjects had far-reaching effects on the American industry, particularly in the manufacture of dyes. It is impracticable to cite, much less discuss, the list of subjects. It was the strenuous post-war period. Chemi-

cal education policies, protective tariffs, stimulation of the manufacture of synthetic organic substances, the organization of the Chemical Warfare Service owe much to his incisive and logical editorials. During the war settlement period, September, 1919, he was sent abroad by President Wilson to arrange for the purchase of impounded dyestuffs. This led to the organization of the Textile Alliance for the protection of American purchasers and forming of a domestic dye industry. From it has come the Textile Foundation with its valuable support of research with the funds then accumulated.

In 1921, yielding to the plea that he was, definitely, the best equipped man for the place, he gave up his editorship to become president of the Synthetic Organic Chemical Manufacturers Association, a new organization he had been vigorously advocating. His familiarity with technical procedures coupled with highly developed national gifts were very successful in persuading federal legislation. He retained this position until 1926. His interest in questions of public import was undiminished and it was at this period that he took every practicable occasion to urge studies of synthetic and natural remedial agents for internal medicine, and to further the activities which finally led to the passage of the Ransdell bill, in 1930, assuring the establishment of the National Institute of Health. It was their mutual conviction of the need for a coöperative alignment of medicine and chemistry that brought Herty and Francis P. Garvan together about 1918 and led to that association so important for the coming years. In 1926, feeling that his personal task had been accomplished with the secure establishment of the dye and pharmaceutical industry in the United States, he retired from his administrative duties. He became advisor to the Chemical Foundation, and for two years was engaged in the promotion of research in chemotherapy. Still retaining a connection with the Chemical Foundation, he opened a consulting office in New York in 1928 and maintained it until 1935. His major effort was to direct attention of financial interests to the industrial possibilities of the South Atlantic States with their great resources in raw materials. The Naval Stores industry was prominently in mind and, inevitably, consideration of other uses of the huge cover of pines on the Atlantic littoral. The subject was not entirely new to American chemists. The possibilities of removing the resins yielding a raw material suitable for alcohol or cellulose products had been studied but without practical outcome. A considerable and growing production of Kraft paper existed.

Herty maintained that the secretion of turpentine and resins being a protective device of nature, young pines should be relatively free of them, and the wood as suitable for pulping as spruce or other commercially used woods. He found the resin content of young slash pine to be less than one per cent., comparing favorably in this respect with spruce. Moreover, pine makes a relatively rapid growth and at four to eight years of age compares favorably with spruce of perhaps fifty or sixty years growth. He maintained, further, that pine naturally reseeded itself and given favorable conditions would come in spontaneously in cut-over lands, thus assuring a continuing pine stand without cultivation. Other observers maintain there is a natural cycle of tree growth, hardwood following pine, and left to itself a long period elapses before pines again are the dominant growth. No one doubts, however, that with cultivation, pines will follow pine, and at moderate costs. To obtain consideration of industrialists and financiers, laboratory experimentation and pilot-plant demonstration were needed. These facilities became possible in 1931 with a grant of fifty thousand dollars from the Chemical Foundation, supplemented by twenty thousand a year for five years from the State of Georgia, and substantial support from the city of Savannah. Dr. Herty had been appointed director of research for paper and pulp of the Georgia State Department of Forestry and the Chemical Foundation equipped the establishment known as the Savannah Pulp and Paper Laboratory. In a few years it was shown that the slash and other pines of the South yielded a fine grade of white newsprint. On March 31, 1933, the *Soperton News*, a weekly, was printed on paper made by Herty. In October, 1933, with three refrigerator cars loaded with pulp and transported to Thorold, Canada, a carload of entirely satisfactory news-print was procured, without any untoward incident. Nine newspapers of Georgia used it in their editions of November 20. And this *tour de force* was followed in 1936 by organization of a company by Southern capital for the erection of a plant near Lufkin, Texas, and the manufacture of newsprint. Over a dozen plants for production of cellulose products from pine have recently been added to those al-

ready operating in the Southeast. Some of them frankly admit Herty's influence in bringing them into existence.

The Savannah laboratory has produced high-grade alpha-cellulose which has been made into rayon, and is now investigating the practicability of utilizing in this way gum tupelo and other southern trees as well as pines. Now known as the Herty Foundation Laboratory, it is hoped that means will be found to establish it on a permanent basis, because of its obviously great value to Southern industry, as well as the most fitting of monuments to Herty.

Following the formation of the concept of farm chemurgy by Dr. William J. Hale, in close association with Dr. Herty the Farm Chemurgic Council came into existence, largely because of financial support by the Chemical Foundation and more perhaps because of the enthusiastic support of the late Francis P. Garvan. By reason of the nature of his work with pines, Herty inevitably took a leading part in this work. His addresses and exhibits were striking features at all annual meetings. Chemurgic problems in general including dry alcohol, sweet potato starch and conservation policies, particularly fire control, found frequent and forceful references in a long series of addresses and magazine articles. He continued to answer calls to public service and by presidential appointment was associated with General Hugh Johnson in the early work of the NRA.

Busy with his varied interests, a tired heart rebelled. In July, 1938, he went to a Savannah hospital. After three weeks he seemed to be making a complete recovery. On July 28, it is reported that he ate a good breakfast, and chatted with some early visitor. A few hours later the end came to the long, useful and happy life. He was seventy years of age.

He is survived by his sons Dr. Charles Holmes Herty, Jr., of Bethlehem, Pa., member of the American Chemical Society and a recognized authority on the chemisty of steel making, and Frank Bernard Herty of Brooklyn, N. Y.; his daughter, Miss Sophie Dorothea Herty, of Savannah, Ga., well known plant physiologist; a sister, Mrs. W. D. Hooper of Athens, Ga.; an aunt, Miss Florence Holmes of Athens, Ga.; many relatives and a host of friends. Mrs. Herty died in 1929. His private charities were many. While a vestryman at Chapel Hill, he devised a pension system for retiring clergy; operating successfully in the diocese, the Episcopal Church used it as a model in 1917. He died a vestryman of St. John's, Savannah.

Aside from his professional work, his main interest was always in field sports. He is credited with introducing football to the South when he was on the faculty of the University of Georgia, and he served as Director of Athletics while at the University of North Carolina. On his many trips about the country he rarely missed an opportunity to attend a game of baseball. Adept at the traps in his younger years, he was always keenly interested in the hunting of upland game. He was an expert billiardist.

A recital of Herty's contributions, as here attempted, falls far short of a complete description of his many services, indirect as well as direct, to the cause of chemistry and industry in America. These services must await the perspective of time for adequate evaluation. But his memory long will remain green as it already bids fair to beome a tradition. We can be grateful that he lived and that, as contemporaries in the American Chemical Society, we have shared in some measure in his distinguished merits.

Herty received the medal of the American Institute of Chemists in 1932. In 1934 he received a medal from the Herty Society organized in his honor by the Georgia State College for Women at Milledgeville, in a roster of distinguished scientific workers. He was the Edgar Fahs Smith lecturer at the University of Pennsylvania for 1937 and the Joseph W. Richards Memorial Lecturer before the Electrochemical Society in 1938. Fellow of the American Association for the Advancement of Science, he was a member of the Institute of Chemists, Society of Foresters, the Forestry Association, Institute of Chemical Engineers, the Society of Chemical Industry, the Electrochemical Society, the Society of Engineering Education, the Philosophical Society, the Franklin Institute, the London Chemical Society, the Société de Chimie Industrielle and the Société Chimique de France.

Herty held the Sc.D. from Colgate and Oglethorpe, the Doctor of Chemistry from Pittsburgh. He was made an LL.D. by the University of Georgia in 1928, by the University of North Carolina in 1934, by the University of Florida in 1937, and by Duke University in 1938.

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[CONTRIBUTION FROM THE RESEARCH LABORATORY OF PHYSICAL CHEMISTRY, LAFAYETTE COLLEGE, AND FROM THE RESEARCH LABORATORY OF PHYSICAL CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, NO. 420]

Relation Between Fluidity, Temperature and Chemical Constitution of Pure Liquids

BY E. C. BINGHAM AND S. D. STOOKEY

In a recent report[1] on the results of a general survey of the field of viscosity, the fact is made evident that there is so far apparently no simple equation expressing accurately a direct relationship between viscosity of liquids and temperature. With regard to the form of equations evidently considered best by the investigating committee, the statement is made (1): "As to the influence of temperature, it has been found that the characteristic decrease of the viscosity of a liquid with rising temperature can, with a fair amount of approximation, be described by the exponential formula $\eta = Ae^{B/RT}$."

Also, the committee makes the following statement (1): "In the homologous series of the aliphatic hydrocarbons, alcohols, fatty acids, etc., an increase of the viscosity generally seems to take place with the number of CH_2— groups of the chains, although even a merely rough proportionality or other regularity appears to be out of the question."

We believe that the equation to be discussed in this paper expresses, in a simple and accurate form, a definite relationship between temperature and viscosity; and that in addition it affords a "well defined regularity" in the viscosity–temperature functions of successive members of a homologous series of liquids.

The equation is

$$\varphi/T = a + bT + \ldots \qquad (1)$$

where φ denotes the fluidity in RHES (reciprocal poise) and T is temperature in degrees absolute.

It will be shown that for liquids whose molecules are not longer than nine or ten carbon atoms, equation (1) expresses the fluidity–temperature relationship very accurately without introducing higher terms.

Also, equation (1) shows a very definite and striking relationship between the fluidity–temperature functions of successive members of a homologous series, which will be discussed in section II. This relationship follows from the fact that the constant a in equation (1) is a function of the homologous series to which the compounds belong, and b a function of the molecular weights of the members of the series; so that an equation may be obtained containing constants which are functions only of the series concerned, and not of individual members of the series.

The modified equation is

$$\varphi/T = A_s + \alpha T 10^{(\beta/M - \gamma/M^2)} \qquad (2)$$

M denoting molecular weight, and α, β and γ being constants.

Equation (2) has been found to be almost as accurate as the simple one, equation (1), and so makes it possible to calculate quite precisely the fluidity of any member of the series (as high in the series as the two-constant form of equation (1) is valid), at any temperature at which the substance is in the liquid state, by the use of only four constants.

This paper will be divided into three sections: section I dealing with the application of equation (1) to individual compounds; section II, with the application of equation (2) to homologous series, and section III, with the anomalous behavior of the aliphatic acids, aliphatic alcohols, and water.

Section I: Application of Equation (1)

Procedure.—The best available viscosity data were used. The data consisted of the absolute viscosities measured at small temperature intervals from 0° to the boiling point of each liquid studied, or to 100°. An attempt was made to choose representative members of as many classes of liquids as possible for which reliable data could be obtained, so that each liquid for which data are given in Table I is typical of several to which the equation may be applied with accuracy. The major part of the viscosity measurements were made by Thorpe and Rodger.[2]

Values of the constants a and b in equation (1) were determined by the method of least squares. The fluidities were then calculated at various temperatures from these constants, and the deviation from the observed fluidities recorded.

Table I gives the values of the constants for a number of compounds, with the standard, or root

(1) Second Report on Viscosity and Plasticity, prepared by the Committee for the Study of Viscosity of the Academy of Sciences at Amsterdam, 1938, pp. 37, 57–58.

(2) F. Thorpe and J. Rodger, *J. Phil. Trans., London*, **185A**, Part II, 397 (1894).

mean square, percentage deviation (% S. D.) of the calculated fluidity from the observed, for each compound.

TABLE I

CONSTANTS a AND b OF EQUATION (1) WITH % STANDARD DEVIATION

All viscosity measurements by Thorpe and Rodger.[2]

Substance	$-a$	b	% S. D.
Hexane	1.0773	0.007311	0.2
Isohexane	1.1315	.007741	.2
Hexine	1.16315	.0082135	.1
Heptyl bromide	0.68091	.003225	.15
Propyl iodide	.5797	.003555	.2
Chloroform	.5989	.004105	.0
Carbon tetrachloride	.8431	.0040765	.3
Ethyl ether	1.1231	.008791	.0
Acetone	0.9133	.006727	.1
Methyl propyl ketone	.9521	.005566	.2
Ethyl sulfide	.8765	.005605	.2
Amyl mercaptan	.8276	.004620	.3
Secondary amyl mercaptan	.8764	.005115	.3
Acetaldehyde	.9317	.008423	.1
Acetic anhydride	.8382	.004146	.1
Ethyl acetate	1.1072	.006368	.1
Bromine	0.3710	.002433	.2
Nitrogen tetroxide	.9018	.005852	.1
Benzene	1.2535	.006070	.0
Toluene	0.9331	.005165	.15
		Av.	0.15

Discussion of Results.—Table I demonstrates that equation (1) is valid for a large number of classes of pure liquids, including straight and branched chain saturated aliphatic hydrocarbons, unsaturated hydrocarbons, aromatic hydrocarbons, alkyl bromides and iodides, ethers, aldehydes, ketones, anhydrides, esters, thioalcohols (normal and secondary), alkyl sulfides, and inorganic liquids, including elements and liquefied gases. The average root mean square deviation of the calculated fluidities from those observed is 0.15% for all the liquids in Table I.

This list does not exhaust the range of applicability of equation (1). The only class of liquids for which it is known to be invalid is the alcohols, which will be discussed in Section III.

Section II: Application of Equation 2

Procedure.—Upon examination of the constants a and b, it became evident that a is practically identical for all members of a non-associated homologous series (as high in the series as equation (1), without introduction of higher terms, is valid). That is, when the ratio φ/T is plotted against the absolute temperature, the straight lines representing the members of the series all converge at the absolute zero of temperature.

Also, it was found that the values of the constant b of equation (1) are an exponential function of the molecular weight within a given series, conforming to the equation

$$b = \alpha 10^{\beta/M - \gamma/M^2} \qquad (3)$$

M being the molecular weight, and α, β and γ constants.

These facts make it possible to express the fluidity–temperature relations of all the members of a series (within the above-stated limits) by means of equation (2) given above.

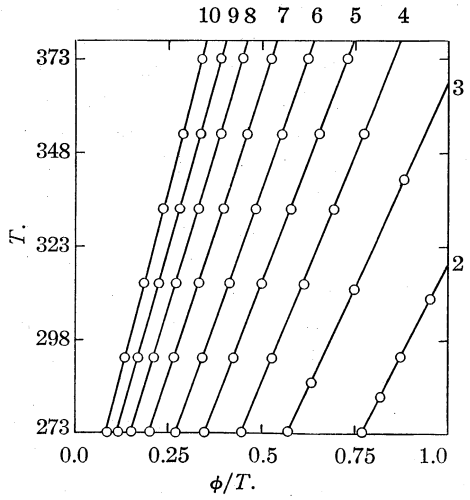

Fig. 1.—Alkyl bromides: φ, fluidity in rhes; T, °K. The numerals denote the number of carbon atoms in the compound.

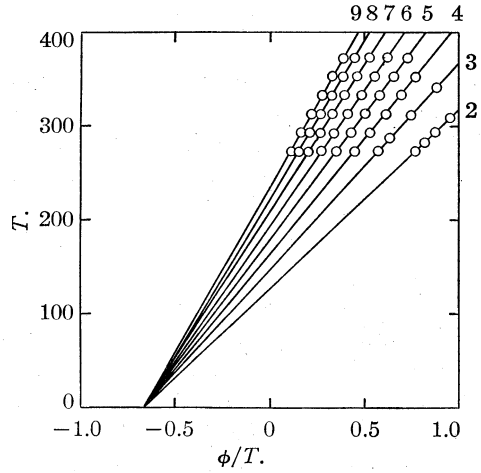

Fig. 2.—Alkyl bromides: curves of Fig. 1 extrapolated to 0°K., showing convergence at absolute zero of the straight lines representing series members.

TABLE II

Alkyl bromides: $\varphi/T = -0.6655 + 0.001252\ T\ 10^{(80.08/M - 1357.6/M^2)}$

Substance	$-a$	b	b'	% S. D. (a, b)	% S. D. (A_s, b')	% S. D. $(A_s, \alpha, \beta, \gamma)$
Ethyl bromide (2)	0.6425	0.005158	0.005238	0.0	0.2	0.4
Propyl bromide (2)	.6880	.004600	.004525	.0	.3	1.6
Butyl bromide (3)	.6255	.003940	.004065	.8	.9	0.9
Amyl bromide (3)	.6921	.003804	.003721	.2	.7	1.6
Hexyl bromide (3)	.6985	.003540	.003437	.3	.9	1.9
Heptyl bromide (3)	.6809	.003225	.003177	.2	.6	0.8
Octyl bromide (3)	.6655	.002980	.002982	.7	.7	0.8
Nonyl bromide (3)	.6311	.002727	.002834	.8	.8	3.5

Alkyl iodides: $\varphi/T = -0.5339 + 0.000162\ T\ 10^{(346.97M - 20759/M^2)}$

Substance	$-a$	b	b'	% S. D. (a, b)	% S. D. (A_s, b')	% S. D. $(A_s, \alpha, \beta, \gamma)$
Methyl iodide (2)	0.50595	0.004112	0.004208	0.1	0.2	0.2
Ethyl iodide (2)	.5160	.003755	.003818	.1	.3	.3
Propyl iodide (2)	.5797	.003555	.003410	.2	.7	.7

Aliphatic n-hydrocarbons: $\varphi/T = -1.0533 + 0.002040\ T\ 10^{(61.97/M - 1229.5/M^2)}$

Substance	$-a$	b	b'	% S. D. (a, b)	% S. D. (A_s, b')	% S. D. $(A_s, \alpha, \beta, \gamma)$
Pentane (2)	1.0708	0.008660	0.008600	0.2	0.2	0.8
Hexane (2)	1.0773	.007311	.007233	.25	.3	1.7
Heptane (2)	1.0894	.006542	.006430	.4	.4	1.1
Octane (2)	1.0581	.005769	.005754	.4	.4	0.9
Nonane (4)	1.0357	.005170	.005225	.3	.6	0.5
Decane (4)	0.98855	.004634	.004837	.8	2.1	2.2

Aliphatic isohydrocarbons: $\varphi/T = -1.1392 + 0.003630\ T\ 10^{(26.76/M - 145.22/M^2)}$

Substance	$-a$	b	b'	% S. D. (a, b)	% S. D. (A_s, b')	% S. D. $(A_s, \alpha, \beta, \gamma)$
Isopentane (2)	1.1850	0.009259	0.009100	0.1	0.2	0.2
Isohexane (2)	1.1315	.007741	.007767	.2	.2	.2
Isoheptane (2)	1.1012	.006826	.006945	.4	.9	.9

n-Mercaptans: $\varphi/T = -0.8014 + 0.001578\ T\ 10^{(63.49/M - 1636.1/M^2)}$

Substance	$-a$	b	b'	% S. D. (a, b)	% S. D. (A_s, b')	% S. D. $(A_s, \alpha, \beta, \gamma)$
Propyl mercaptan (4)	0.8506	0.005778	0.005607	0.0	0.3	0.6
Butyl mercaptan (4)	.8550	.005226	.0050535	.6	.9	1.4
Amyl mercaptan (4)	.8276	.004620	.004538	.3	.7	0.7
Hexyl mercaptan (4)	.8157	.004193	.004149	.3	.5	0.6
Heptyl mercaptan (4)	.7746	.003747	.003831	.5	.6	1.1
Octyl mercaptan (4)	.7617	.003459	.003584	.8	1.8	2.1
Nonyl mercaptan (4)	.7249	.003168	.003408	.7	4.2	5.9

Secondary mercaptans: $\varphi/T = -0.8405 + 0.001361\ T\ 10^{(85.54/M - 2790.3/M^2)}$

Substance	$-a$	b	b'	% S. D. (a, b)	% S. D. (A_s, b')	% S. D. $(A_s, \alpha, \beta, \gamma)$
Propyl mercaptan (4)	1.0997	0.0068355	0.005956	0.1	1.5	1.6
Amyl mercaptan (4)	0.8764	.005115	.004996	.3	0.5	0.7
Hexyl mercaptan (4)	.8781	.004652	.0045345	.4	.9	1.4
Heptyl mercaptan (4)	.8456	.004178	.004161	.6	.7	1.3
Octyl mercaptan (4)	.8167	.003798	.003873	.2	.7	0.8
Nonyl mercaptan (4)	.7856	.003468	.003640	.7	2.3	3.8

The individual values of the constant a were averaged to obtain the series constants "A_s" for each of six aliphatic series: normal hydrocarbons, isohydrocarbons, normal bromides, normal iodides, normal mercaptans, and secondary mercaptans.

The values of b were recalculated from the new series constants, and the fluidities redetermined.

Finally, the constants α, β and γ in equations (2) and (3) were calculated, and the fluidities redetermined with all restrictions, according to equation (2).

Figures 1 and 2 are graphs, φ/T *vs.* T, for a typical series, the alkyl bromides. In Fig. 1, successive lines represent successive members of

(3) A. R. Bayer, Master's Thesis, Lafayette College, 1933.

(4) E. C. Bingham and H. J. Fornwalt, *J. Rheol.*, **1**, 372 (1930).

the series, from ethyl bromide on the right to decyl bromide on the left. The numbers of the lines denote the number of carbon atoms. Figure 2 is identical with Fig. 1 except that the lines are extrapolated to absolute zero and decyl bromide is not represented.

In Table II, a and b are the constants of equation (1); b' is the new value of b calculated from the series constant A_s; and the equations contain all the series constants A_s, $-\alpha$, β and γ of equation (2). The last three columns of Table II contain the percentage standard deviation, or root mean square deviation (denoted by % S. D.) of the calculated fluidities from the observed. The first of the three columns represents the deviation of fluidity calculated from a and b; the second, that calculated from A_s and b'; and the last column, that calculated when equation (2), with all the series constants, is applied.

Figure 3 is a deviation chart, % deviation in fluidity *vs.* temperature for some representative aliphatic bromides.

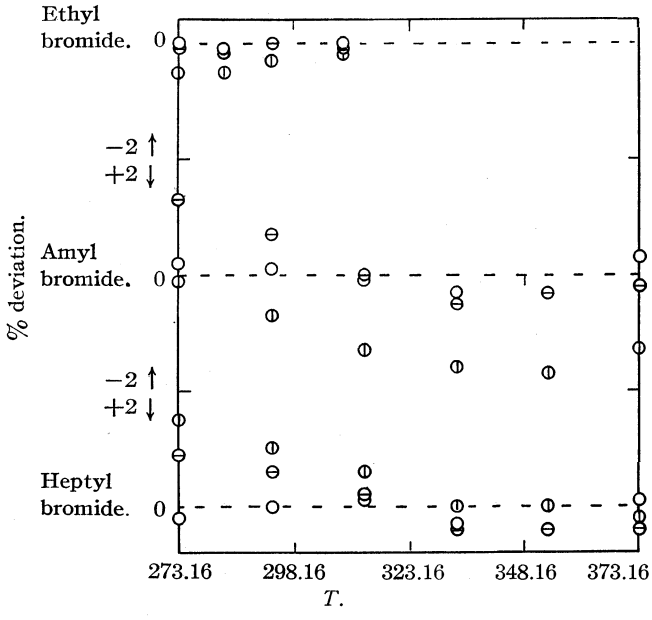

Fig. 3.—Deviation chart. Representative plot of the percentages of deviation of calculated fluidity from observed: open circles represent φ calculated by equation 1; circles with horizontal diameters, φ calculated from a_s (series constant) and b'; circles with vertical diameters, φ calculated by equation 2, with all series constants.

The fluidities of the higher members of the alkyl bromide series have been determined by Bayer[3] and are given at the end of this paper in Table IV.

TABLE IIIA

ALIPHATIC ACIDS (2)

Acid	$-a$	b	% S. D.
Formic	0.90435	0.003737	1.4
Acetic	.8632	.003885	0.45
Propionic	.7224	.003522	.2
Butyric	.7637	.003489	.8

TABLE IIIB

WATER (5)

Temp. range, °C.	$-a$	b	% S. D.
0–25	1.6439	0.0067635	0.3
25–100	1.9149	.007675	
		Max. dev.	0.5

TABLE IV

FLUIDITY OF ALKYL BROMIDES (3)

Bromide	Fluidity in rhes at given temperature, °C. 0.0	20.0	40.0	60.0	80.0	100.0
Butyl	122.0	154.4	192.3	230.8	271.8	321.2
Amyl	94.6	123.9	156.4	192.3	230.6	270.6
Hexyl	73.4	99.1	128.4	161.0	195.5	231.5
Heptyl	54.7	77.5	102.9	131.4	161.8	194.9
Octyl	41.4	61.2	84.0	108.9	136.7	166.5
Nonyl	31.7	48.9	69.2	92.3	117.4	144.5
Decyl	24.3	39.3	75.2	77.7	100.8	125.4

Discussion of Results.—The average standard deviation of the calculated fluidity from the observed, when equation (3) is applied to individual members of the series, is 0.4% for eight alkyl bromides, 0.1% for three alkyl iodides, 0.4% for six *n*-hydrocarbons, 0.2% for three isohydrocarbons, 0.45% for seven *n*-mercaptans, and 0.4% for six secondary mercaptans. The equation fits the data for higher members of the series than those given here with almost equal accuracy, but the percentage deviation increases gradually with increasing molecular weight, due, presumably, not to the increased weight of the molecules (since bromine obeys the equation) but to the effect of the long chains. The curvature is in a direction which shows that for longer molecules the fluidity increases more rapidly at higher temperatures than at low temperatures. Addition of a term of the power series in T of equation (1) corrects for this tendency, if desired.

When the individual values of a are averaged to give a series value A_s, the average standard deviation for bromides is 0.6%, iodides 0.4%, *n*-hydrocarbons 0.7%, isohydrocarbons 0.4%, *n*-mercaptans 1.3%, secondary mercaptans 0.8%.

Applying all restrictions, according to equation

(2), the average standard deviation for *n*-bromides is 1.4%, *n*-iodides 0.4%, *n*-hydrocarbons 1.2%, isohydrocarbons 0.4%, *n*-mercaptans 1.8%, secondary mercaptans 1.1%.

Section III: Anomalous Liquids

Procedure.—The only marked abnormalities noted thus far in the behavior of liquids with regard to equations (1) and (2) occur in compounds which contain a hydroxyl radical. The three abnormal types of liquids are the aliphatic acids, alcohols, and water. Each of the three exhibits a different sort of anomaly.

Table IIIA contains the values of a and b (equation 1) for the first four members of the aliphatic acid series, and the percentage standard deviations. Figure 4 shows the corresponding curves, φ/T *vs.* T, the curves being numbered according to the number of carbon atoms in the compound represented.

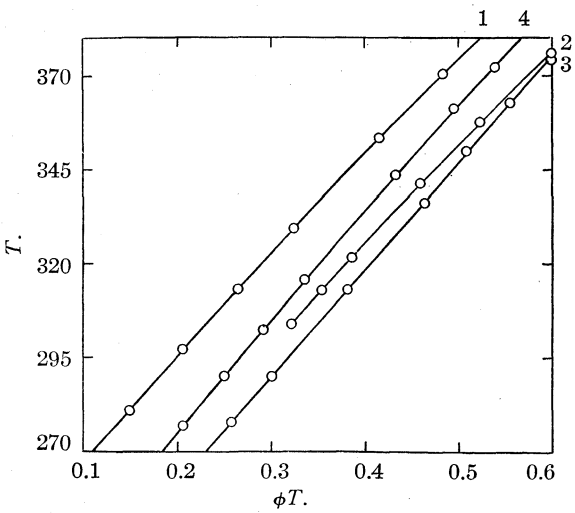

Fig. 4.—Aliphatic acids: the numerals denote the number of carbon atoms in the acids represented: formic, acetic, propionic and butyric. Note contrast between relative positions of curves as compared to Fig. 1.

Table IIIB gives the constants a and b for water; Fig. 5 shows the curve φ/T *vs.* T. The data used are an average of the observations of six observers.[5]

Discussion of Results.—The results show that the aliphatic acids obey equation (1) quite well, the average standard deviation being only 0.7%. In nearly every case, however, there is a definite though slight tendency toward curvature.

(5) E. C. Bingham, "Fluidity and Plasticity," McGraw-Hill Book Co., Inc., New York, N. Y., 1922, p. 339.

On the other hand, comparison of Fig. 4 with Fig. 1 makes very evident the contrast between the apparently random variation of the slopes and positions of the curves for acids, and the regular variation for a typical non-associated series.

The fact that the acids obey equation (1) may be explained by considering that they form nearly stable compounds in their association; for which there is evidence from X-ray measurements.[6]

The slight curvature then is probably caused by the slight instability of the associated liquids.

The φ/T *vs.* T curves of the alcohols all show very decided curvature. This may possibly be caused by the fact that the alcohols, although associated, form unstable compounds, and that the degree of association varies with temperature.

The φ/T *vs.* T curve for water (Fig. 5) is a straight line from 0 to 25°, and from 25 to 100°, curving slightly in the neighborhood of 25°. We have, therefore, applied equation (1) twice, and the two equations reproduce the observed fluidity with a standard deviation of 0.3%, the maximum deviation being 0.5%.

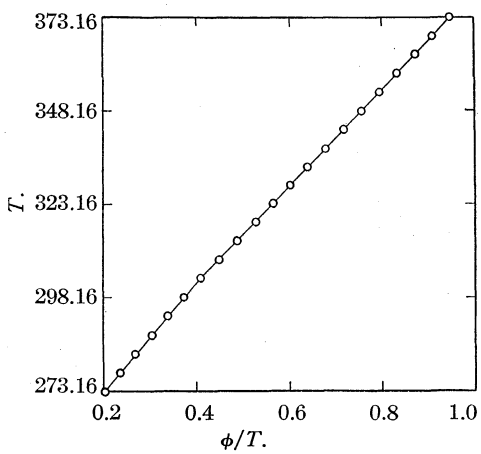

Fig. 5.—Water.

Summary

A simple equation relating fluidity directly to temperature has been shown to fit the data very accurately for a large number of liquids, apparently failing only for alcohols. The equation also shows a definite relation between the viscosity–temperature functions of successive members of a homologous series, making it possible to calculate the viscosity of any member of a non-associated series up to ten carbon atoms at any temperature by means of only four constants.

The fluidities of the aliphatic bromides from

(6) Müller, *J. Chem. Soc.*, **123**, 2054 (1923).

butyl bromide to decyl bromide between 0 and 100° as determined by Bayer, are given.

Note: Equation (1) has been found to apply to some types of solutions as accurately as to pure liquids. Further investigations are being made along this line.

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[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

The Mechanism of Solvolytic Reactions of Organic Halides and the Use of Activity Coefficients in the Equation for a Reaction Velocity

BY PAUL D. BARTLETT

Of the theories about the dependence of reaction velocity in solution upon the solvent, the two which have received the most attention in this century are those of van't Hoff[1] and of Brönsted,[2] later refined by other workers and commonly known, respectively, as the "activity-rate theory" and the "transition-state theory." It is consistent with both theories to regard the activated complex as a molecular species in equilibrium with the reactants. The activity-rate theory then demands that the rate of reaction shall be proportional to the fugacity of the activated complex, while the transition-state theory makes the rate proportional to the concentration of this complex.

For reactants forming nearly ideal solutions below their limits of solubility, the activity-rate theory predicts specific reaction rates inversely proportional to their solubilities in a series of solvents. This prediction was shown by von Halban[3] in 1913 to fall hopelessly short of the facts in the formation of *p*-nitrobenzyltrimethylammonium chloride. Here the introduction of corrections for solubility increased the range of observed velocity constants in eighteen solvents from 9300-fold to over 400,000-fold, when according to the theory it should have rendered the corrected rate independent of solvent.

It has thus long been evident that the activity-rate theory does not possess general validity. Since this is so, the success recently attained by Olson and Halford[4] in reviving this theory and applying it to the calculation of reaction rates in a graded series of methanol–water and ethanol–water mixtures is surprising. The rate of production of hydrogen chloride by *t*-butyl chloride in these series of solvents varies 100-fold for the former and 750-fold for the latter series, and these rates have been calculated in terms of the vapor pressures of the reactants within less than the uncertainty of the data employed in the calculation.

Such agreement cannot be entirely accidental, and from the standpoint of the theory of reaction velocity it is important to try to decide between two possibilities. Either (1) the activity-rate theory is fundamentally true for a solvolytic reaction in mixed solvents, while lacking general validity, or (2) it is not fundamentally true, but represents a useful approximation because of special relationships among the quantities appearing in the equations. It is the purpose of this paper to approach this question by inquiring whether the activity-rate theory fits the data of Olson and Halford uniquely, and to draw such conclusions as may be possible about the factors determining the rate of reaction and the mechanism of this particular reaction.

The liberation of hydrogen chloride from *t*-butyl chloride in these experiments proceeds with the formation of three organic products—*t*-butyl alcohol, methyl *t*-butyl ether, and isobutylene. The reaction is an unfortunate one for testing a kinetic formulation on account of the difficulty in making a convincing demonstration of what is going on. The reaction has been variously designated by Farinacci and Hammett[5] as polymolecular, by Olson and Halford[4] as bimolecular, and by Ingold, Hughes,[6] and their co-workers as unimolecular, depending upon the extent to which attention has been focussed upon the role of the solvent in the rate-determining step. In a recent note[7] the British workers have indicated that the difference between their "unimolecular" and Hammett's "polymolecular" is a matter of language

(1) Van't Hoff, *Vorlesungen*, **1**, 219 (1901).
(2) Brönsted, *Chem. Rev.*, **5**, 269 (1938); also *Z. physik. Chem.*, **115**, 327 (1925).
(3) Von Halban, *ibid.*, **84**, 129 (1913).
(4) Olson and Halford, THIS JOURNAL, **59**, 2644 (1937).
(5) Farinacci and Hammett, *ibid.*, **59**, 2542 (1937).
(6) Bateman, Hughes and Ingold, *J. Chem. Soc.*, 881 (1938).
(7) Bateman, Hughes and Ingold, THIS JOURNAL, **60**, 3080 (1938).

rather than point of view. There remains a difference between the original opinion of Olson and Halford and that of the other workers with regard to the point of attack of the solvent molecule on the chloride. Since the kinetics would be the same regardless of the form of the transition state, we shall postpone discussion of this point.

Olson and Halford[4] (p. 2647) say of their fugacity-rate equation: "This equation is in disagreement with the one obtained from transition state theory by Wynne-Jones and Eyring [*J. Chem. Phys.*, **3**, 492(1935)] unless we assume that the fugacity coefficient of each of the three complexes which we studied remains constant throughout the whole range of experimental conditions. This appears to us highly improbable." Examination of the equations shows that there is actually a less rigid condition than this for the simultaneous perfect applicability of the two equations, owing to the fact that an observed rate is being resolved into two rates governed by different activated complexes. If an approximate equation is used, a fit may under certain conditions be obtained without correctly assigning these contributing rates to their proper transition states. Denoting by k the observed rate constant in terms of mole fractions for the appearance of hydrogen chloride in a solution of *t*-butyl chloride in a mixture of water and alcohol, by f_W, f_A, f_X and f_Y the activity coefficients (expressed as Henry's law constants) of water, alcohol and the transition states involving them, respectively, by f_B the activity coefficient of *t*-butyl chloride, and by M_W and M_A the mole fractions of water and alcohol, and assuming the reaction to occur between one molecule of solvent and one of chloride, the transition-state theory gives the equation

$$k = k_W M_W \frac{f_W f_B}{f_X} + k_A M_A \frac{f_A f_B}{f_Y} \qquad (1)$$

while the activity-rate equation as used by Olson and Halford does not contain the activity coefficients of the transition states

$$k = k'_W M_W f_W f_B + k'_A M_A f_A f_B \qquad (2)$$

The condition that both these equations shall fit the same set of data exactly is found by eliminating k/f_B from Equations (1) and (2)

$$\left(k_W \frac{f_W}{f_X} - k'_W f_W\right) M_W = \left((k'_A f_A - k_A \frac{f_A}{f_Y}\right) M_A$$

This equation may of course be true by both sides being equal to zero, through a constancy of f_X and f_Y, as recognized by Olson and Halford. It may also be true as a result of other modes of dependence of f_X and f_Y upon solvent composition, in which case the quantities k'_W and k'_A will be composite constants. In addition to the functional relationships among the f's which can be seen to satisfy this equation, there are sure to be some others (possibly including the true one) which yield a close enough approximation to the condition of this equation to make both equations (1) and (2) fit the data.

A qualitative consideration of the probable form of the activated complex suggests a simple formulation which, if Equation (1) is correct, might be expected to yield as good an approximation as that of Equation (2). The solubility behavior of an aliphatic chloride is very similar to that of a hydrocarbon, the halogen atom making no characteristic contribution to its solubility in hydroxylic solvents. Any mechanism by which a water or alcohol molecule might attach itself to a *t*-butyl chloride molecule could only have the effect of making it much more alcoholic or aqueous in character. This suggests the provisional assumption that the activity coefficients of the transition states might be sufficiently like those of their hydroxylic components so that the two would approximately cancel, and we might write

$$k = k''_W M_W f_B + k''_A M_A f_B \qquad (3)$$

Like Equation (2), this can be derived from (1) by introducing a somewhat more flexible condition than the one which originally suggested the approximation. Equation (3) follows from (1) if

$$\left(k_W \frac{f_W}{f_X} - k''_W\right) M_W = \left(k_A - k_A \frac{f_A}{f_Y}\right) M_A$$

Equation (3) has been applied to the data of Olson and Halford for the reaction in water–methanol mixtures and the fit compared to that of Equation (2). To make this comparison, we determine the constants k_W and k_A which will give the lowest mean square percentage deviation of the calculated from the experimental rates by both these types of formulation. We assume that the percentage accuracy of the rate constants of Olson and Halford is about the same for the large and small values. To make the mean square percentage deviation a minimum in each case, Equations (2) and (3) are divided through by k and normal equations constructed from the resulting experimental equations. Table I shows the results of this comparison. The fit of Olson and Halford, not using this method, is also included.

TABLE I

Formulation	$(k'_W, k''_W) \times 10^6$	$(k'_A, k''_A) \times 10^6$	% mean deviation	% mean square deviation
O. and H.	0.393	0.0156	3.80	4.61
Least sq. Eq. (2)	0.379	0.01573	4.09	4.48
Least sq. Eq. (3)	11.54	2.07	2.86	3.78

Figure 1 shows this situation graphically. Equations (2) and (3) can be written in the form

$$\frac{a}{b}k'_W + k_A = \frac{k}{b} \qquad (4)$$

and

$$\frac{a'}{b'}k''_W + k''_A = \frac{k}{b'} \qquad (5)$$

wherein $a = M_W f_W f_B$, etc. Equations (4) and (5) demand, respectively, that k/b plotted against a/b, and k/b' against a'/b', should yield straight lines, and from the graphs it is apparent that this is true in both cases.

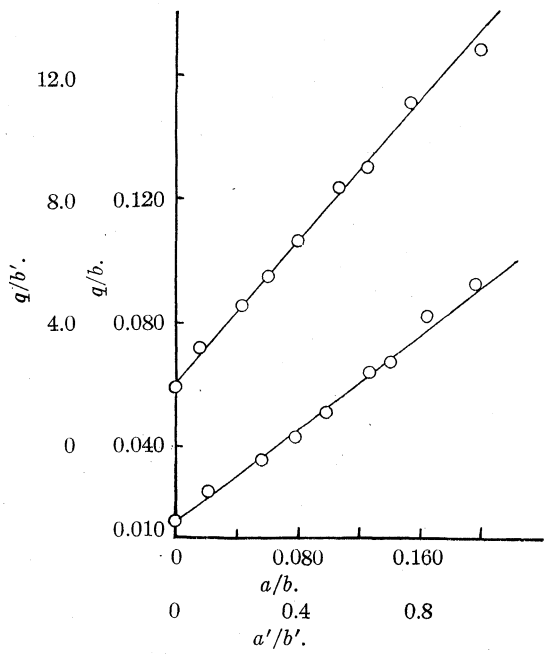


Fig. 1.—Plots of Equation (4) (lower curve) and Equation (5) (upper curve) for the reaction of *t*-butyl chloride with methanol–water mixtures (data of Olson and Halford).

The recalculation by Olson and Halford of Hughes' kinetic data on the solvolysis of *t*-butyl chloride in mixtures of water and ethyl alcohol is impressive for the wide range of velocity which it covers, but the agreement between calculated and observed rates is quite inferior to that in the methanol–water mixtures. The signs of the deviations also suggest a distinct curvature to the points, and the plots of Equations (4) and (5) in Figs. 2 and 3 for the water–ethanol system bear this out. The point at $a/b = 0$, obtained by Olson and Halford by extrapolation of the data of Hughes, is included in this plot but not in the least squares solutions, since it is not an experimental point. One of the points in the plots is so badly out of line that I have carried through the

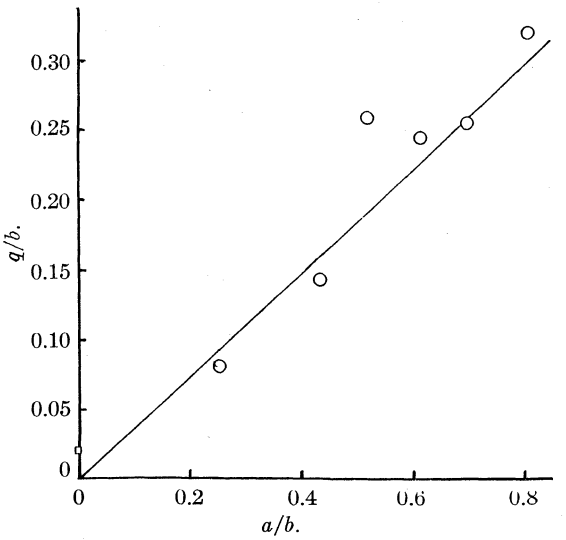


Fig. 2.—Plot of Equation (4) for the reaction of *t*-butyl chloride with ethanol–water mixtures (data of Hughes).

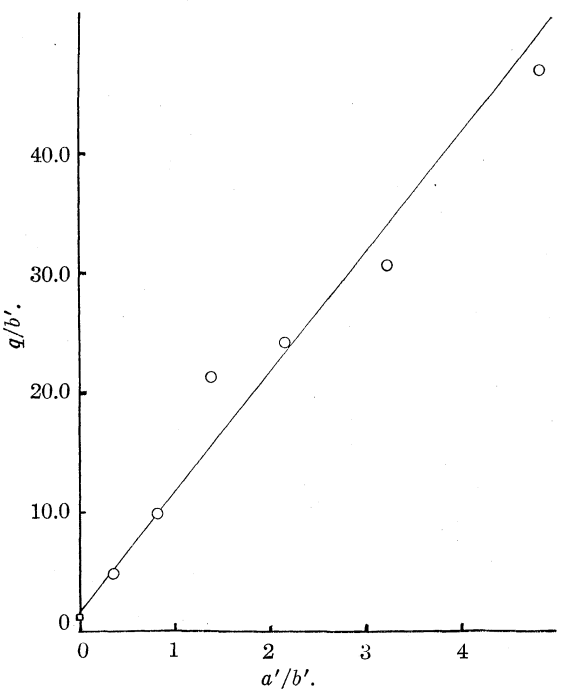


Fig. 3.—Plot of Equation (5) for the reaction of *t*-butyl chloride with ethanol–water mixtures (data of Hughes).

fits both with and without it. The conclusions in both cases are substantially the same.

In this system the Henry's law constants of water vary 79%, and those of alcohol 151%, over the range of solvent composition employed, compared with 27 and 10% in the methanol case. It is therefore to be expected that the two imperfect approximations to the correct formula which we are considering will both fit the facts less well than in the case of water–methanol mixtures. In fact, if we ignore the extrapolated point for pure ethanol, introduced by Olson and Halford, and consider only the experimental points, the best straight line through the points of Equation (4) (the activity equation) intersects the axis of ordinates at a negative value, making $k'_A = -0.0296 \times 10^{-6}$ if we include the suspicious point with the large deviation, and -0.0259×10^{-6} if we reject this point. A negative rate constant is permissible if k' is a composite quantity, but not if it has the fundamental significance attributed to it by Olson and Halford. In such a case, the closest fit that can be made of Equation (4) which has any physical meaning is to assume $k_A = 0$, and that all reaction is due to the water present. Table II shows a comparison of this best allowable fit with the best fit of Equation (5) to the data, both with and without the doubtful point.

TABLE II

No. of points	Formulation	$(k'_W, k''_W) \times 10^6$	$(k'_A, k''_A) \times 10^6$	% mean deviation	% mean sq. dev.
7	O. and H.	0.393	0.021	18.1	24.4
6	Eq. (2)	0.3688	0	11.4	13.91
6	Eq. (3)	10.05	1.63	9.05	10.15
5	Eq. (2)	0.35547	0	8.40	9.00
5	Eq. (3)	9.317	2.029	4.81	5.66

Here again the formulation employing mole fractions of water and alcohol fits the data fully as well as that employing vapor pressures.

Olson and Halford did not test any mechanism involving the participation of more than a single molecule of solvent in the rate-determining step. Since their data are now found to be fitted by different rate equations, it is of interest to see whether they may also be fitted by an equation which postulates three concurrent rate-determining steps in which the chloride collides with two water molecules, a water and an alcohol molecule, or two alcohol molecules. Such an equation would be written

$$k = k'_{WW} p_W^2 f_B + k'_{WA} p_W p_A f_B + k'_{AA} p_A^2 f_B \quad (6)$$

or

$$k = k''_{WW} M_W^2 f_B + k''_{WA} M_W M_A f_B + k''_{AA} M_A^2 f_B \quad (7)$$

depending upon whether vapor pressures or mole fractions of the solvent components were used in the equations. Equation (6) fits the data of Olson and Halford with a root mean square deviation of 3.85% when the following constants are used

$$k'_{WW} = 0.0155 \times 10^{-6}$$
$$k'_{WA} = 0.00299 \times 10^{-6}$$
$$k'_{AA} = 0.000127 \times 10^{-6}$$

Equation (7) fits the same data with a root mean square deviation of 3.12% using the constants

$$k''_{WW} = 9.28 \times 10^{-6}$$
$$k''_{WA} = 14.98 \times 10^{-6}$$
$$k''_{AA} = 2.02 \times 10^{-6}$$

Thus, not only do these data not serve to establish an activity-rate law, but they also afford no proof of the order of the reaction with respect to solvent molecules.

Although the equations using mole fractions seem in general a better approximation than those using vapor pressures, it should be pointed out that all these formulations fit the data better than the accuracy of the data themselves would lead us to expect.[8] Under these circumstances it would appear that errors in the values of f_B (the quantity known with least certainty) must have considerable regularity, if indeed they are as large as supposed. In any event, no weight is to be given to small differences in the fits of different equations.

Table III compares the calculated rates of hydrolysis of *t*-butyl chloride in water–dioxane and water–acetone mixtures by equations (2), (3), (6), and (7).

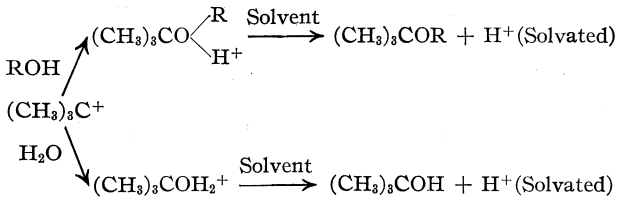
TABLE III

Method of calcn.	Dioxane k	Dioxane % dev.	Acetone k	Acetone % dev.
Observed	644		6.90	
Olson and Halford	745	15.6	11.6	68.1
Equation (2)	720	11.8	11.1	60.8
Equation (3)	927	43.9	9.58	38.8
Equation (6)	581	9.78	8.11	1.73
Equation (7)	404	37.2	2.53	63.3

In a recent paper Bateman, Hughes and Ingold[7] approve the activity formulation of Olson and Halford, but show that the lack of agreement between the predicted and found ratio of alcohol and ether in the products invalidates any idea that

(8) Professor Olson has emphasized in a private communication that the Henry's law constants of *t*-butyl chloride may be in error by as much as 25% or even more.

the solvolysis could be a one-step bimolecular replacement process. This argument stands also if Equation (3) is adopted. The second step of the ionization mechanism of Bateman, Hughes and Ingold



is subject to an activity formulation according to both of the above methods. The data of these authors and of Olson and Halford can be used to test these formulations. The relative amounts of alcohol and ether in the product, so long as the solvent composition remains constant, are supposed to be the result of simple competition between the water and the alcohol in reaction with the *t*-butyl cation. There may be some question of the reversibility of the association step, but it can scarcely be as mobile as the acid–base interchanges among the oxygen-containing compounds, and hence, if, as found by Bateman, Hughes and Ingold, the products resulting from a run are not in equilibrium, the relative forward rates of the association steps between the *t*-butyl ion and the solvent molecules should completely determine the ratio of alcohol and ether in the product. According to the activity-rate theory, the ratio of alcohol to ether in the product should remain proportional to the ratio of vapor pressures of water and alcohol in the solvent. The transition-state theory divides this latter ratio by that of activity coefficients of transition states resembling in appearance the proton alcoholate and etherate in the equation.

In Table IV Column I records the ratio of vapor pressures of water to alcohol in the solvents of Bateman, Hughes and Ingold; II is the ratio of alcohol to ether in the product; and III is the ratio of moles of water to moles of alcohol in the solvent. It is seen that II/I is far from constant as it ought to be according to the activity-rate theory. II/III is more nearly constant, although this would scarcely be demanded by the transition state theory. It may be that no energy of activation is required in the combination of the butyl cation with a water or alcohol molecule, the ion pair representing a plateau of energy from which a change means a direct descent. In this case the near constancy of the ratio II/III would be expected.

TABLE IV

I	II	III	II/I	II/III
	Ethanol–Water Mixtures			
0.611	4.61	2.15	7.5	2.14
.432	2.07	0.808	4.8	2.56
.255	0.90	.359	3.5	2.50
	Methanol–Water Mixtures			
.192	1.53	0.961	8.0	1.59
.099	0.474	.397	4.8	1.19
.0525	.206	.196	3.9	1.05

As has been pointed out repeatedly by Ingold, Hughes, and their collaborators, the two-step nature of the solvolytic process is indicated not alone by the seeming independence of rates and product compositions, but also by the inability of the strongly basic ions, hydroxyl and alkoxyl, to influence the rate of reaction of the secondary and tertiary halides. Any mechanism which allowed a direct attack of a solvent molecule upon the central carbon atom of the halide to take part in the rate-controlling step would be attributing something like a basic function to this solvent molecule and would be at a loss to explain the failure of the far more basic ions to participate in this same manner.

Miss Ethel M. Holmes has given valuable help in these calculations by carrying through the least squares application of Equations (6) and (7) and checking all the other results.

Summary

Evidence of long standing is recalled which shows that the rate of a chemical reaction is not generally proportional to the fugacity of the reactants and to that of the transition state, as apparently found by Olson and Halford for the hydrolysis and alcoholysis of *t*-butyl chloride in mixtures of water and alcohol. A recalculation of their kinetic results and those of Hughes shows that these results are no more consistent with the activity-rate theory than with the Brönsted–Polanyi–Eyring theory of the transition state, supplemented with a not unreasonable assumption about the activity coefficients of the transition states. A special case of the assumed relationship is that the transition state involving water has a water-like activity coefficient and that involving alcohol has an alcohol-like activity coefficient.

This leads to an approximate rate equation in

which vapor pressures of the chloride are used, but mole fractions of water and alcohol. The probability is discussed that the equation of Olson and Halford is, like this, a special approximation and does not represent a fundamental rate law.

Contrary to the conclusions of Olson and Halford, their results do not prove that the hydrolysis and alcoholysis of *t*-butyl chloride in mixed solvents is a bimolecular reaction, for the rates can also be accurately calculated on the assumption of a termolecular transition state by either of the two approximate kinetic equations.

It is shown that the product composition exhibits a dependence on solvent composition which is consistent with the view that the rate-determining step is an ionization, the solvent serving to solvate the anion, and that the solvent components then compete for the cation in rough proportion to their mole fractions.

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The Solvolysis of *t*-Butyl Chloride. Solvolytic Reactions and the Walden Inversion

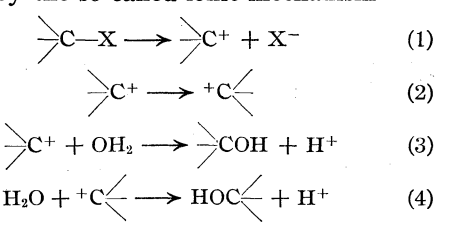
BY SAUL WINSTEIN

A serious problem at the present time is the exact interpretation of first-order solvolytic reactions of organic halides. Ingold and collaborators[1] suppose that these reactions proceed by an ionic mechanism, S_N1

$$RX \xrightarrow{\text{slow}} R^+ + X^-$$
$$R^+ + R'OH \xrightarrow{\text{fast}} ROR' + H^+ \qquad S_N1$$

in which the halide RX ionizes, the cation R^+ reacting rapidly with solvent molecules. Hammett and co-workers[2] believe these solvolytic reactions to be polymolecular, while Olson and Halford[3] and Taylor[4] have presented evidence that they are bimolecular. It is the purpose of the author to present in the following paragraphs evidence and discussion in favor of the polymolecular interpretation of solvolytic reactions of halides and opposed to the ionic mechanism, and to discuss the polymolecular mechanism from the standpoint of the steric results obtained using optically active halides.

Objections to the Ionic Mechanism.—It may be satisfactory for some purposes to speak of solvolytic reactions as involving an ionization with stress placed on the role of solvation in the ionization. But unless solvation is considered explicitly, it is impossible to discuss logically the steric results and product compositions (if mixed solvents are used) from solvolytic reactions of halides. To see this clearly let us formulate the first-order hydrolysis of a halide as involving an ionization of this halide, first without including any mention of solvation in the reaction equations and then allowing for solvation of the organic cation. First let us consider reactions 1–4, which relate to the hydrolysis of a halide molecule by the so-called ionic mechanism



without being explicit about solvation of the organic cation. Reaction 1 represents the ionization process and reaction 2 the process of flattening-out of the cation, permitting it to react to give products with either one of two enantiomorphic configurations, as shown by reactions 3 and 4. One would predict that if the life of the cation were long enough to permit one to speak of the existence of the cation, reaction 2 would be fast enough to give rise to a racemic alcohol from an optically active halide.

Ingold and collaborators[5] explain the usual steric result[2a,6] of solvolytic reactions (predominant inversion with more or less racemization) by the argument that usually X^- will shield R^+ sufficiently so that reaction occurs more easily from the side away from X^- than from the side toward

(1) Gleave, Hughes and Ingold, *J. Chem. Soc.*, 236 (1935).

(2) (a) Steigman and Hammett, THIS JOURNAL, **59**, 2536 (1937); (b) Farinacci and Hammett, *ibid.*, **59**, 2542 (1937).

(3) Olson and Halford, *ibid.*, **59**, 2644 (1937).

(4) Taylor, *J. Chem. Soc.*, 1853 (1937).

(5) Cowdrey, Hughes, Ingold, Masterman and Scott, *ibid.*, 1252 (1937).

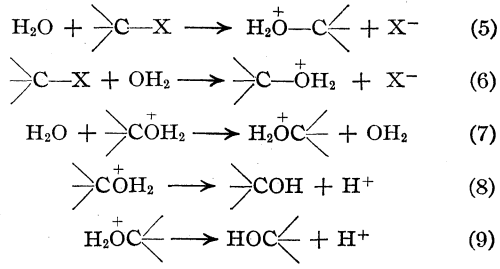
(6) (a) Hughes, Ingold, and Masterman, *ibid.*, 1196 (1937); (b) Hughes, Ingold and Scott, *ibid.*, 1201 (1937).

X^-, so that inversion predominates. In certain cases, such as the solvolysis of α-bromopropionate ion,[7] these workers expect[5] and find complete retention of configuration. It is believed by them that the intermediate zwitterion in this case is stabilized in a pyramidal form and a solvent molecule reacts with it at the place left vacant by bromide ion.

The above arguments do not seem to me to be at all reasonable. It would seem that if ionization were complete enough to permit the reaction to be called unimolecular, then the ion R^+ would be free enough from shielding effects so that a completely racemic product would result from the reaction of R^+ with solvent molecules.

Further, it is my opinion that the correct explanation of the retention of configuration in the first-order solvolysis of α-bromopropionate ion is not that the reaction proceeds by mechanism S_N1 with stabilization of the intermediate zwitter ion, but that instead the carboxylate ion group substitutes for the bromine atom by an intramolecular variety of the usual bimolecular exchange leading to Walden inversion.[8] The formation of the α-lactone is assumed to be the rate-determining step. The α-lactone then rapidly reacts with solvent molecules with a second inversion in the manner of epoxides[9] or β-lactones[10] under some conditions.[11]

If we continue to describe the first-order hydrolysis of a halide as involving an ionization of the halide but now consider solvation explicitly we must admit that only through solvation does the activation energy of such a reaction become low enough to give rise to a reasonable rate for the process of hydrolysis. Thus, as Ogg and Polanyi[12] have pointed out, the hydrate of the carbonium ion and not a bare cation is to be expected from any ionization of a halide in water. Reactions 1–4 are now replaced by 5–9. Reactions 5 and 6 represent the formation of two optically different cation hydrates, depending on the mode of reaction. These cation hydrates we recognize as



oxonium compounds of alcohols. Reaction 2 is replaced by 7, which represents a racemization brought about by a water exchange. Reactions 8 and 9 represent the loss of protons by the oxonium compounds. When the reaction is represented in this way it seems desirable not to speak of an ionization mechanism but rather to regard the solvent as a reactant. One has no reason to suppose that reaction 7 is rapid, so that the steric result of the hydrolysis is determined with the formation of the oxonium compounds. Ogg and Polanyi suggested that ionization goes only by reaction 5, but the considerable racemization accompanying most solvolytic reactions[2a,6] indicates the occurrence of both reactions 5 and 6. How water is able to enter into both reactions 5 and 6 will be seen later.

Hydrolysis and Alcoholysis of *t*-Butyl Chloride.—If, as is discussed above, we regard the solvent as a reactant, further insight into the nature of solvolytic reactions of halides can be gained by studying the solvolyses in mixed solvents. In the case of the first order hydrolysis and alcoholysis of tertiary butyl chloride in mixtures of water with either methyl or ethyl alcohol, considerable data are at hand.[3,13] Olson and Halford[3] have suggested that rates of hydrolysis and alcoholysis of *t*-butyl chloride in binary solvents should be proportional to the fugacities of halide and water or alcohol. Thus the total rate of hydrolysis plus alcoholysis is given by equation 10, where k_m is the measured first-order specific reaction rate constant for the

$$k_m = (k_w p_w + k_a p_a)(p/N)_{RCl} \qquad (10)$$

formation of hydrogen chloride, p_w and p_a are vapor pressures of water and alcohol, respectively, k_w and k_a are constants characteristic of pure water and alcohol, respectively, and $(p/N)_{RCl}$ is the Henry's law constant for the halide in a given solvent. P_A, the mole per cent. of the reaction product which is *t*-butyl alcohol and not its

(7) Cowdrey, Hughes and Ingold, *J. Chem. Soc.*, 1208 (1937).

(8) (a) Olson, *J. Chem. Phys.*, **1**, 418 (1933); (b) Meer and Polanyi, *Z. physik. Chem.*, **19B**, 164 (1932).

(9) Winstein and Lucas, THIS JOURNAL, **61**, 1576 (1939).

(10) Olson and Miller, *ibid.*, **60**, 2687 (1938).

(11) Recently[9] it has been found that 3-bromo-2-butanol reacts with hydrobromic acid with complete retention of configuration. In this case an argument based on stabilization of an intermediate carbonium ion in a pyramidal form is not possible but a role for the bromine atom similar to the role of the negative oxygen in α-bromopropionate ion can be and has been formulated.

(12) Ogg and Polanyi, *Trans. Faraday Soc.*, **31**, 619 (1935).

(13) (a) Hughes, *J. Chem. Soc.*, 255 (1935); (b) Bateman, Hughes and Ingold, *ibid.*, 881 (1938).

alkyl ether, is thus predicted by equation 11

$$P_A = (100/k_m)(k_w p_w)(p/N)_{RCl} \quad (11)$$

Olson and Halford were able to fit exceedingly well the rates of hydrogen chloride formation in water–methyl alcohol and water–ethyl alcohol mixtures with equation 10, k_w being identical in both cases. This same k_w predicted quite well the rates in a water–acetone mixture and a water–dioxane mixture where only *t*-butyl alcohol and no ether results. These facts caused Olson and Halford to conclude that the reaction between *t*-butyl chloride and water or alcohol is bimolecular and not unimolecular.

Olson and Halford neglected to analyze the product of the reaction to see whether the composition agreed with equation 11. Bateman, Hughes, and Ingold[13b] did this and found serious disagreement between observed compositions and those expected from equation 11. These authors felt that this was evidence in favor of the unimolecular (S_N1) mechanism; that is, they assume that solvent plays a significant role in the ionization of the halide but the product composition is given by the inaccessible rate constants for the reactions of R^+ with water or alcohol.

However, the failure of equation 11 to predict the composition of the product does not necessarily indicate that the unimolecular mechanism is the correct one. Alternative explanations are that the solvolysis is not bimolecular but of a higher order or that a fugacity equation such as equation 10 is not applicable. While full justification for the use of fugacity rate expressions is still lacking, nevertheless the suggestion that fugacities should be used instead of concentrations for treating rates in binary solvents where association and solvation occur seems a sensible one. The validity of the use of fugacity rate expressions is assumed in the following discussion.

I have found that equation 12

$$k_m = (k_{w^2} p_w^2 + k_{wa} p_w p_a + k_{a^2} p_a^2)\,(p/N)_{RCl} \quad (12)$$

corresponding to the reaction of tertiary butyl chloride with two solvent molecules, fits the data of Olson and Halford[3] and Hughes[13] as well as equation 10. Here $k_{w^2} p_w^2$ is the term representing reaction involving two water molecules and giving rise to *t*-butyl alcohol, $k_{wa} p_w p_a$ is the term representing reaction with one water molecule and one alcohol molecule and giving rise to either *t*-butyl alcohol or *t*-butyl alkyl ether, and $k_{a^2} p_a^2$ is the term representing reaction with two alcohol molecules and giving rise to ether. The value of k_{w^2} was determined from the data on the water–acetone mixture and the water–dioxane mixture as is shown in Table I, that of k_{a^2} from

TABLE I

DETERMINATION OF k_w FROM DATA ON THE HYDROLYSIS OF *t*-BUTYL CHLORIDE IN ACETONE–WATER AND DIOXANE–WATER MIXTURES[3]

Solvent	Acetone–H_2O	Dioxane–H_2O	Mean
Mole % H_2O	50.3	83.2	
p_w (mm.)	17.8	19.7	
k_m	6.90×10^{-3}	644×10^{-3}	
$(p/N)_{RCl}$ (mm.)	1.65×10^3	96.5×10^3	
$k_{w^2} \times 10^8$	1.319	1.719	1.519
$k_{w^3} \times 10^{10}$	7.41	8.73	8.07
$k_{w^4} \times 10^{11}$	4.16	4.43	4.30

the rate in pure methyl or ethyl alcohol, and that of k_{wa} from the rate in the alcohol solution containing the most water. Tables II and III give a comparison between observed values of k_m and those calculated by Olson and Halford from equation 10 and by the author from equation 12. Values in parentheses are those used in obtaining the constants (k_{wa}, etc.). It is evident that equation 12 fits the data fully as well as equation 10.

In the case of the data in methyl alcohol–water mixtures still another fugacity equation was tried.

$$k_m = (k_{w^3} p_w^3 + k_{w^2 a} p_w^2 p_a + k_{w a^2} p_w p_a^2 + k_{a^3} p_a^3)\,(p/N)_{RCl} \quad (13)$$

It was found that equation 13 fits the data just as well as equation 10 or 12. Equation 13 represents the reaction of *t*-butyl chloride with three solvent molecules, all of water, all of alcohol, or some of each. The value of k_{w^3} was determined from the data on the water–acetone mixture and the water–dioxane mixture as is shown in Table I, and the other constants were evaluated as described for equation 12. Table II lists the values of k_m calculated from equation 13; it is obvious that the equation represents k_m satisfactorily.

Whereas the product compositions were not well predicted by equations 10 and 11, treatment of the data with the aid of equations 12 and 13 leads to satisfactory agreement between predicted and obtained product compositions if one makes reasonable assumptions regarding the terms which lead to a mixture of products. Thus, in the case of equation 12, P_A in the methyl alcohol study is given satisfactorily by equation 14 and

$$P_A = (100/k_m)(k_{w^2} p_w^2 + 0.11\, k_{wa} p_w p_a)\,(p/N)_{RCl} \quad (14)$$

in the ethyl alcohol study by equation 15. On

$$P_A = (100/k_m)(k_{w^2} p_w^2 + 0.01\, k_{wa} p_w p_a)\,(p/N)_{RCl} \quad (15)$$

TABLE II

SUMMARY OF DATA AND CALCULATIONS FOR HYDROLYSIS AND ALCOHOLYSIS OF *t*-BUTYL CHLORIDE IN METHYL ALCOHOL–WATER MIXTURES

I. $k_m = (k_{w^2}p_w^2 + k_{wa}p_wp_a + k_{a^2}p_a^2)\,(p/N)_{RCl}$

$k_{w^2} = 1.52 \times 10^{-8}$ $k_{wa} = 3.15 \times 10^{-9}$ $k_{a^2} = 1.23 \times 10^{-10}$

II. $k_m = (k_{w^3}p_w^3 + k_{w^2a}p_w^2p_a + k_{wa^2}p_wp_a^2 + k_{a^3}p_a^3)\,(p/N)_{RCl}$

$k_{w^3} = 8.07 \times 10^{-10}$ $k_{w^2a} = 1.18 \times 10^{-10}$

$k_{wa^2} = 3.73 \times 10^{-11}$ $k_{a^3} = 9.72 \times 10^{-13}$

Mole % H_2O	p_w mm.	p_a mm.	$(p/N)_{RCl} \times 10^{-3}$	$10^3 k_m$ Obsd. (O. + H.)	$10^3 k_m$ Calculated (O. + H.)[3]	$10^3 k_m$ Calculated (S. W.)(I)	$10^3 k_m$ Calculated (S. W.)(II)
49.7	13.7	70.2	53.5	347	(347)	(347)	(347)
43.2	12.5	76.7	29.8	188	182	182	180
38.3	11.5	81.9	19.8	110	115	115	113
34.6	10.7	84.9	13.8	75.4	76.5	75.7	73.6
28.2	9.10	92.5	8.6	40.7	43.4	42.7	41.3
23.0	7.63	98.0	6.0	25.4	27.2	26.5	(25.4)
17.5	5.92	105	4.1	15.4	16.3	15.8	15.1
7.0	2.46	118	2.1	6.24	5.9	5.7	5.6
0.0	0	126.6	1.48	2.92	(2.92)	(2.92)	(2.92)

TABLE III

SUMMARY OF DATA AND CALCULATIONS FOR HYDROLYSIS AND ALCOHOLYSIS OF *t*-BUTYL CHLORIDE IN ETHYL ALCOHOL–WATER MIXTURES

$k_m = (k_{w^2}p_w^2 + k_{wa}p_wp_a + k_{a^2}p_a^2)\,(p/N)_{RCl}$

$10^8k_{w^2} = 1.52$ $10^9k_{wa} = 2.79$ $10^{10}k_{a^2} = 3.65$

Mole % H_2O	p_w mm.	p_a mm.	$10^{-3}(p/N)_{RCl}$	$10^3 k_m$ Obsd. (Hughes)[13]	$10^3 k_m$ Calculated (O. + H.)[3]	$10^3 k_m$ Calculated (S. W.)
82.9	20.5	25.4	577	4660	4950	(4660)
76.4	19.9	28.6	182	1320	1530	1440
68.4	19.2	31.4	59.2	453	487	453
58.1	17.9	34.5	16.2	145	126	114
44.8	16.6	38.4	6.0	32.9	44.4	39.0
26.2	11.5	45.5	1.68	6.16	9.2	7.1
0.0	0.0	59.0	0.63	0.8	(0.8)	(0.8)

treating the methyl alcohol–water data with equation 13, it turns out that product compositions are given satisfactorily by equation 16.

$$P_A = (100/k_m)(k_{w^3}p_w^3 + 0.61k_{w^2a}\,p_w^2p_a + 0.01\,k_{wa^2}p_wp_a^2)\,(p/N)_{RCl} \quad (16)$$

The comparison between observed[14] values of P_A and those predicted by equations 11, 14, 15 and 16 is shown in Table IV. It is clear that equations 14, 15, and 16 are satisfactory and equation 11 is not.

Thus, if one assumes the validity of rate equations based on fugacities, one obtains evidence that the solvolysis of *t*-butyl chloride in water–alcohol mixtures involves two or more solvent molecules. It is apparent that the data available do not permit a more definite statement to be made; any treatment involving two or more solvent molecules is satisfactory.

(14) In writing down the values of P_A (observed) in Table IV it is necessary to take into account the small amount of olefin produced[13b] in the reaction. In the case of the methyl alcohol–water data Dr. P. D. Bartlett has pointed out to the author that the amount of olefin is proportional to the amount of ether in the reaction product and therefore that the olefin is to be regarded as ether which has been sidetracked. In the case of the ethyl alcohol–water data it would appear that the olefin arises from the sidetracking of both ether and alcohol. A reasonable assumption appears to be that the amount of ether which has been sidetracked amounts to about 40% of the observed ether.

TABLE IV

COMPARISON OF OBSERVED AND CALCULATED PRODUCT COMPOSITIONS FOR THE SOLVOLYSIS OF TERTIARY BUTYL CHLORIDE

I $P_A = (100/k_m)(k_{w^2}p_{w^2} + 0.11\,k_{wa}p_wp_a)(p/N)_{RCl}$ for MeOH + H_2O

$P_A = (100/k_m)(k_{w^2}p_{w^2} + 0.01\,k_{wa}p_wp_a)(p/N)_{RCl}$ for EtOH + H_2O

II $P_A = (100/k_m)(k_{w^3}p_w^3 + 0.61\,k_{w^2a}p_w^2p_a + 0.01\,k_{wa^2}p_wp_a^2)\,(p/N)_{RCl}$ for MeOH + H_2O

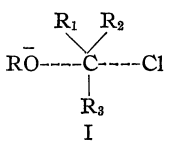
Solvent	Mol % H_2O	P_A = Mol % alcohol in product Obsd.[13]	Calculated (O. + H.)[3]	Calculated I	Calculated II
	49.0	55	83	49	53
MeOH + H_2O	28.4	28	71	31	30
	16.4	14	57	18	14
Mean dev. from P_A (obsd.)			38	4	1
	68.3	78	92	74	
EtOH + H_2O	44.7	62	89	64	
	26.4	43	82	48	
Mean dev. from P_A (obsd.)			27	4	

The Polymolecular Mechanism.—Hammett and co-workers already have proposed,[2] in connection with solvolyses of benzhydryl chloride

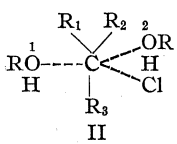
and α-phenylethyl chloride, that solvolytic reaction is a polymolecular one and takes place within a solvation complex. These workers noted that small amounts of water catalyze the alcoholysis of benzhydryl chloride linearly without diverting very much material to benzhydrol, and, also, that small amounts of hydroxylic solvent in acetone are ineffective in hydrolyzing or alcoholyzing benzhydryl chloride. Bateman, Hughes, and Ingold[15] have noted recently that the benzhydryl chloride data of Farinacci and Hammett cannot be treated by equations 10 (but assuming $(p/N)_{RCl}$ is constant) and 11 to predict product compositions and have felt again that the ionic mechanism is indicated. The situation here is similar to that for *t*-butyl chloride. Actually, the data in the case of benzhydryl chloride cover only a narrow range of solvent composition and Henry's law constants for the halide are unknown, so further calculations with vapor pressure rate equations cannot be carried out.

The author agrees essentially with Hammett and co-workers[2] concerning the nature of solvolytic reactions of halides and feels that the difference in steric results obtained from solvolytic reactions and from bimolecular exchanges[8] can be discussed as is done below.

In the case of an ordinary bimolecular substitution of RO^- for Cl^- a transition state[5] such as I is imagined. RO^- is oriented away from the chlorine and clean-cut inversion is the result of reaction through transition state I.



I



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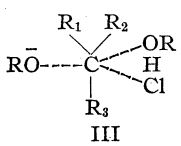
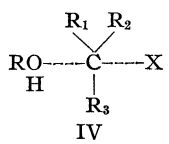


III

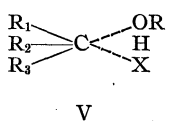
In the case of a solvolytic reaction, let us for the sake of convenience write only two solvent molecules into the transition state II, one in back of the carbon–chlorine dipole and one, due to the tendency toward hydrogen-bond formation to the halogen, on the same side as the chlorine. Products can be obtained from II in two ways, either with inversion, if solvent molecule 1 becomes bonded to the central carbon atom and solvent molecule 2 leaves as part of the solvation sphere of the chloride ion, or with retention of configuration, if solvent molecule 2 becomes bonded to the central carbon atom. From the usual steric results of solvolytic reactions of halides, we would say that solvent molecule 2 competes more or less successfully with solvent molecule 1 for electron donation to the central carbon atom, the predominating process being the one in which solvent molecule 2 leaves as part of the solvation sphere of the chloride ion with solvent molecule 1 becoming bonded to the central carbon atom.

It might be argued that transition state I is an oversimplification and that transition state III should be considered when RO^- replaces a chlorine atom. We see, however, that a solvent molecule would have little success in competition with a negative ion in the same transition state, since a negative ion is a much better electron donator than a solvent molecule. Thus, with reaction going through transition state III we would still expect clean-cut inversion, the solvent molecule always leaving as part of the solvation sphere of the chloride ion.

When a solvolytic reaction is carried out in an inert solvent containing smaller and smaller concentrations of hydroxylic compound, a bimolecular mechanism should be reached. Transition states of the type IV and V seem possible. If the



IV



V

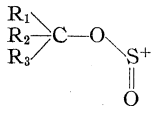
solvent can aid in removing halide ion mechanism IV with inversion is possible. Mechanism V[16] with retention of configuration is possible even when the solvent cannot aid in removing halide ion. Actually, the hydrolysis of *t*-butyl bromide seems to approach a bimolecular mechanism at very low concentrations of water in acetone.[4] More work in this direction and the investigation of the steric result of reactions of this sort under conditions where the mechanism is definitely second-order would serve to yield information about the relative extent of operation of mechanisms IV and V.

Other First-Order Reactions of Halides.—In other first-order reactions of halides more detailed attention should be given to the role of sol-

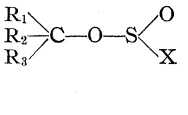
(15) Bateman, Hughes and Ingold, THIS JOURNAL, **60**, 3080 (1938).

(16) Mechanism V has been suggested by Taylor, *J. Chem. Soc.*, 1962 (1937), and is similar to some suggested in other connections.[5]

vent. For example, the conductivity of halides in sulfur dioxide,[17] and the first-order reactions in sulfur dioxide[13b,18] are explained by ionization of the halide. It might be better to remark that sulfur dioxide is a reactant forming a cation–sulfur dioxide ion[19] VI and halide ion, the ion VI undergoing racemization or reaction with reagents.



VI



VII

One recognizes VI as the product obtained by reaction of thionyl halide with one molecule of alcohol and ionization of the remaining halogen atom from the intermediate ester VII. VI can presumably give VII by reaction with halide ion. VII can presumably give halide and sulfur dioxide with or without inversion.[5] In the formation of VI inversion or retention may be the steric result. Thus, only after careful scrutiny of the role of the solvent, sulfur dioxide, may one hope to understand the steric results of reactions in this solvent.

(17) Hückel, "Theoretische Grundlagen der organischen Chemie," Vol. II, Akademische Verlagsgesellschaft m. b. H., Leipzig, 1931, p. 269. See, however, Hughes, Ingold and Scott, *J. Chem. Soc.*, 1271 (1937).

(18) Bergmann and Polanyi, *Naturwissenschaften*, **21**, 378 (1933).

(19) See Waters and Lowry, "Physical Aspects of Organic Chemistry," D. Van Nostrand Co., New York, N. Y., 1937, p. 189.

The author acknowledges with pleasure the help and advice of Dr. Linus Pauling in connection with the ideas presented in this paper and in the preparation of the manuscript.

Summary

A recalculation of the data on the solvolysis of *t*-butyl chloride in alcohol–water mixtures using fugacity rate equations of the type suggested by Olson and Halford shows that the rates and product compositions can be explained assuming that the reaction between *t*-butyl chloride and solvent involves two or more solvent molecules.

The ionic mechanism of Ingold and collaborators for the first-order solvolytic reaction of halides and the explanation of the usual steric result of these reactions on the basis of shielding of the carbonium ion by the ionizing halogen atom is rejected in favor of an interpretation which regards the solvent as a reactant.

The author agrees essentially with Hammett and co-workers on a polymolecular interpretation for solvolytic reactions of halides. The difference in steric results obtained in solvolytic reactions and in exchanges involving attack by negative ions is discussed from the standpoint of possible transition states and competition between different solvent molecules or between a solvent molecule and a negative ion in the transition state.

PASADENA, CALIF. RECEIVED MARCH 25, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

Investigations on the Stereoisomerism of Unsaturated Compounds. IV. The Identification of *cis-trans* Isomers by Rate Studies[1]

BY WILLIAM G. YOUNG, DAVID PRESSMAN AND CHARLES D. CORYELL[2]

Introduction.—The determination of the configuration of *cis-trans* isomers of the ethylene type is a difficult problem in spite of the many modes of approach which have been suggested. None of the generally accepted[3] chemical methods of identification such as ring opening or ring formation, are applicable in all cases and the most reliable physical methods require special equipment which is not available in most laboratories. Consequently, it is particularly desirable to develop chemical methods of establishing the configuration of *cis–trans* isomers which can be applied easily and which will give dependable results.

A study of the rates of reaction of the stereoisomeric ethylene dibromides with potassium iodide in 99% methanol was the most promising method considered. The reaction[4] involved is

$$RCHBrCHBrR' + 3I^- \rightarrow RCH{=}CHR' + I_3^- + 2Br^- \quad (1)$$

for which the rate is first order with respect to

(1) This work was accomplished with the aid of a grant from the Board of Research of the University of California.

(2) Part of this paper was taken from the dissertation submitted by David Pressman in partial fulfilment of the requirements for the degree of Master of Arts, and was presented at the San Diego Meeting of the Pacific Division of the American Association for the Advancement of Science, June, 1938.

(3) Gilman's "Organic Chemistry," Vol. I, John Wiley and Sons, Inc., New York, 1938, p. 370.

(4) Dillon, THIS JOURNAL, **54**, 952 (1932).

both the dibromide and iodide concentrations. It has been shown in the case of two pairs of stereoisomers, fumaric and maleic acids,[5] and *cis*- and *trans*-2-butenes,[6] that the *meso* dibromides (from the *trans* compounds) react more rapidly than the corresponding *d,l*-dibromides (from the *cis* compounds). It is the purpose of this paper to present the experimental results obtained with the dibromides of several more pairs of geometrical stereoisomers in which two hydrogen atoms are adjacent to the double bond, and the other two groups are identical or similar. In every case the dibromide from the *trans* isomer had the larger second-order specific reaction rate constant both at 75° and 60°, and the smaller Arrhenius heat of activation.

Nomenclature.—A convenient nomenclature has been adopted for this work which emphasizes the relationship between the parent unsaturated compound and the product of normal bromine addition (*trans* addition) by naming the product as the dibromide of the parent compound. This nomenclature is especially useful in referring to dibromides of unsymmetrical stereoisomers. *cis*- and *trans*-2-pentenes both give racemic mixtures of 2,3-dibromopentanes which are different from each other. The names *trans*- and *cis*-2-pentene dibromide clearly show this difference by referring to the structure of the parent compound.

Experimental Procedure

Measurement of Reaction Rates

Technique.—The following procedure was used to follow the rate of reaction of the various dibromides with potassium iodide: a solution containing the dibromide, approx. 0.025 molal, and potassium iodide, approx. 0.25 molal, in 99% methanol was prepared at 20°. Eight or ten 20.00-ml. aliquot portions of this solution were then sealed in test-tubes and placed in a thermostat at 75 or 60°. For any given run the temperature was constant to within 0.03°. Tubes were removed at measured intervals and quenched in ice water, broken in an acidified aqueous solution of potassium iodide, and titrated for iodine with 0.015 *N* sodium thiosulfate solution.

Due to the very slight solubility of the *trans*-stilbene dibromide in methanol, it was necessary to use acetone to make a comparison of the isomeric stilbene dibromides. The *trans*-dibromide, 0.003 *M*, liberated iodine from sodium iodide, 0.125 *M*, at an appreciable rate at room temperature and had reacted completely in eighteen hours, whereas the *cis*-dibromide under the same conditions liberated only 5% of the theoretical quantity in eighteen hours.

Calculation of the Rate Constants.—An analysis of equation (1) for the reaction first order with respect to both dibromide and iodide concentrations leads to the following equation connecting initial iodide concentration a, initial dibromide concentration b, fraction φ of the dibromide consumed, and t, time in hours

$$\mathrm{d}\log_{10}\frac{1-3b\varphi/a}{1-\varphi}\Big/\mathrm{d}t=\frac{a-3b}{2.303}k_{\mathrm{obsd.}} \qquad (2)$$

Values of $\log_{10}(1-(3b\varphi/a)/(1-\varphi)$ corresponding to the various samples of a run were plotted as ordinates against the corresponding values of time t, and the best straight line was drawn through the points. The slope of this line was multiplied by the value of $2.303/(a-3b)$ for the run to give $k_{\mathrm{obsd.}}$. This method does not give undue weight to the first analysis made, and the value of k is not affected by the small time necessary to bring the solution to temperature, which would lead to a small positive intercept on the abscissa axis.

As a matter of fact, the best straight lines for many runs did not pass through the origin, but formed small positive intercepts on the ordinate axis. For a given compound, the intercepts for different runs were nearly the same regardless of temperature. Figure 1 is a plot of two runs with *cis*-3-hexene dibromide at 74.90°, which are selected as representative cases showing clearly the existence of the intercept. In a few cases the value of the intercept was uncertain because the measurements had been made within a time interval which was shorter than that used in most runs. In those cases the average intercept obtained with the other runs on the same compound was assumed and the best line was drawn through the points to this assumed intercept. This pro-

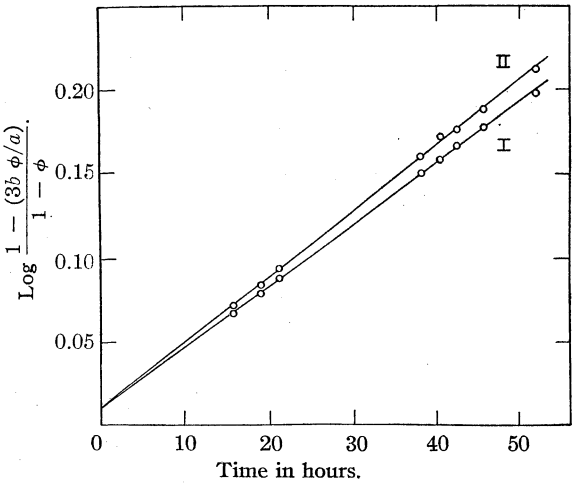


Fig. 1.—Treatment of the runs with *cis*-3-hexene dibromide at 74.90°.

(5) Van Duin, *Rec. trav. chim.*, **43**, 341 (1924); **48**, 345 (1926).
(6) Dillon, Young and Lucas, THIS JOURNAL, **52**, 1953 (1930).

TABLE I

DATA AND CALCULATED VALUES FOR REACTION RATE CONSTANTS AND HEATS OF ACTIVATION

Parent compound	$k_{obsd.}$	Temp., °C.	KI a	Dibromide b	Intercept	k corr.[d]	k corr. KI = 0.25	Av. k	% deviation	Q KI = 0.25
cis-2-Butene	0.0301[a]	74.93	0.233	0.026	0	0.0347	.....	(0.0347)[e]	0	28.60
	.0301[a]	74.93	.227	...	0	.0347	.....			
	.00465[a]	59.72	.228	...	0	.00540	.....	(.00540)[e]	..	
trans-2-Butene	.0562[a]	74.93	.222	.033	0	.0647	.....	(.0647)[e]	..	28.00
	.00902[a]	59.72	.229	...	0	.01046	.....	(.01046)[e]	..	
cis-2-Pentene	.0528	75.00	.232	.020	0.0075	.0564	0.0570	.0570	0.09	26.50
	.0515	74.60	.272	.021	.006	.0576	.0569			
	.00915	59.49	.257	.025	(.009)	.01016	.01012	.01015	.25	
	.00893[c]	59.64	.177	.021	.007	.00976	.01017			
trans-2-Pentene	.0895	75.00	.264	.021	.004	.0956	.0948	.0949	.11	25.68
	.0849	74.60	.244	.022	(.004)	.0947	.0950			
	.01611	59.49	.263	.023	.005	.01786	.01773	.01784	.59	
	.01644[c]	59.64	.249	.021	.003	.01793	.01794			
cis-3-Hexene	.0472[c]	74.90	.244	.022	.010	.05098	.05118	.0508	.72	25.78
	.0469[c]	74.90	.254	.020	.011	.05055	.05045			
	.00843[c]	59.41	.242	.018	,011	.009432	.00947	.00946	.11	
	.00846[c]	59.41	.251	.022	.010	.009465	.00945			
trans-3-Hexene	.1332[c]	74.90	.268	.023	.0065	.1438	.1423	.1437	1.00	24.45
	.1338[c]	74.90	.242	.021	.005	.1444	.1451			
	.02625[c]	59.41	.242	.022	.004	.02927	.02940	.02922	0.64	
	.02596[c]	59.41	.244	.022	.0035	.02895	.02904			
cis-4-Octene	.0982[b]	74.90	.239	.017	(.010)	.1082	.1089	.1078	1.01	25.48
	.0960[b]	74.86	.242	.018	(.010)	.1062	.1067			
	.01862	59.49	.247	.016	(.010)	.02062	.02066	.02055	0.54	
	.01867[c]	59.64	.242	.019	.010	.02035	.02044			
trans-4-Octene	.1239[b]	75.04	.245	.016	.020	.1354	.1358	.1358	..	24.48
	.02544[c]	59.64	.249	.017	.008	.02767	.02768	.02762	0.24	
	.02532[c]	59.64	.250	.019	.007	.02755	.02755			
Maleic acid (*cis*)	1.014[b]	74.90	.259	.021	(.003)	1.116	1.110	1.125	1.29	24.65
	1.033[b]	74.90	.247	.020	.0025	1.137	1.139			
	0.1989[b]	59.45	.238	.020	.003	0.2253	0.2269	0.2257	0.53	
	.1980[b]	59.46	.247	.022	.003	0.2241	.2245			
Fumaric acid (*trans*)	4.195	74.55	.281	.016	−.004	4.668	4.586	4.638	1.11	20.98
	4.250	74.55	.266	.020	−.003	4.730	4.689			
	1.082	59.48	.256	.021	(.000)	1.189	1.185	1.186	0.04	
	1.048	59.48	.199	.023	.001	1.152	1.186			

[a] Natural methanol, rates 7% lower than synthetic methanol I (the standard for this work). [b] Synthetic methanol II, rates 2% lower than on methanol I. [c] Synthetic methanol III, rates same as methanol I. [d] The constants have been corrected for reactivity of solvent, solvent expansion and to the temperatures 75.00 or 60.00°. [e] These calculations were made using the data reported by Dillon;[4] correction has not been made for potassium iodide effect.

cedure gave satisfactory agreement with rate constants calculated from the runs made over longer time intervals. Table I presents the data for all runs made on the compounds to be discussed in this paper. Column 2 lists $k_{obsd.}$ while column 6 lists the intercepts found, with parentheses enclosing assumed values.

In most of the previous work in this field an integrated form of a rate equation has been used. The existence of an ordinate intercept such as was frequently found in this study would lead to calculated constants exhibiting a tendency to fall off. This behavior has been observed by Davis and Heggie,[7] who report that propene dibromide and 1-pentene dibromide give steadily decreasing constants. The data presented by Dillon, Young and Lucas[6] and Dillon[4] gave no evidence of drift in constants.

The intercepts obtained when the data are treated by our method and the drifts obtained by use of an integrated equation may be accounted for chemically on the assumption that with some compounds the reaction starts out abnormally fast

(7) Davis and Heggie, *J. Org. Chem.*, **2**, 470 (1937).

as though catalyzed but very soon becomes normal through destruction of the catalyst. In rare cases this initial liberation of iodine was observable during operations at room temperature.

Effect of Solvent on the Rate Constants.—Due to the fact that the different preparations of 99% methanol exhibited slightly different rates for the same compound, all of the rates involving methanol preparations were corrected to the value they would have exhibited in the first preparation of methanol used in this set of experiments. This was accomplished by comparing the rate constant of a standard substance, some of the original preparation of 1-butene dibromide used by Dillon, Young and Lucas,[6] in the three different solvent preparations used in this work, as suggested by Young and Winstein.[8] The first and third preparations gave identical rate constants while the second preparation gave a rate constant 2% smaller. Accordingly, all of the rate constants determined in solvent II were increased by 2% to afford a comparison with those determined in solvents I and II (see references to column 2, Table I).

Correction of Rate Constants to Standard Temperature.—Since different reactions were studied at slightly different temperatures in the neighborhood of 75.00 and 60.00°, all of the rate constants were corrected to correspond to those temperatures by the use of the experimentally determined temperature coefficients calculated for each compound.

Correction of Rate Constant for Solvent Expansion.—A positive error is made in volume concentrations of substances in methanol at temperatures above 20° due to the thermal expansion of the solvent between the temperature at which the tubes are made up and the temperatures at which the reaction rate is followed. Because the rate constant for a second order reaction has units reciprocal in concentration and time, there is introduced a negative error in the directly calculated values of the rate constant with increasing temperature due to the use of the 20° volume concentrations. Hence a small negative error in the apparent temperature coefficient of the rate constant is introduced. In order to correct for this error the constants at 60° were increased by 4.8% and those at 75° were increased by 6.8% in accord with the measurements[9] on the density of methanol at 20, 60 and 75°. The rate constants corrected for effect of solvent, temperature and alcohol expansion are listed in Table I, column 7.

Correction of Rate Constant for Salt Effect.—Although the reproducibility of the constants listed in column 7 of Table I was fairly satisfactory, there were a few isolated cases with unexpectedly large percentage deviations, in which a high constant seemed to be correlated with high potassium iodide concentration. The data of all pairs of runs in which the iodide concentrations differed by 0.03 *M* or greater are presented in Table II. Column 2 gives the constants from col. 7, Table I, while col. 3 lists the corresponding iodide concentrations. Column 4 shows the percentage increase in the constant associated with the increase in molality of potassium iodide listed in col. 5. Column 6 gives the percentage increase in the constant per mole increase in iodide concentration for each compound, assuming a linear relation between the constant and the iodide concentration. The average increase is 57 ± 6% regardless of the compound or temperature. We have deemed it advisable to correct all of the constants of Table I to a constant iodide concentration (0.25 *M*) before calculating heats of activation (col. 8). These pairs of constants show an average average deviation of 0.55% and a maximum average deviation of 1.3%.

TABLE II

THE EFFECT OF SALT CONCENTRATION ON THE RATE CONSTANTS

Dibromide	*k* corr.	Molal concn. of KI	$\frac{100\,\Delta k}{\text{av. } k}$	Δ KI	$\frac{100\,\Delta k}{k\,\Delta \text{KI}}$
cis-2-Pentene 75°	0.0564	0.232	2.1	0.040	52
	.0576	.272			
cis-2-Pentene 60°	.01016	.257	4.0	.080	50
	.00976	.177			
trans-Crotonic acid[a] 75°	.495	.278	2.0	.029	70
	.485	.249			
trans-Crotonic acid[a] 60°	.1131	.283	6.1	.105	58
	.1064	.178			
Fumaric acid 60°	1.189	.256	3.2	.057	56
	1.152	.199			
Mean (with average deviation)					57 ± 6

[a] Although the study of the *cis*- and *trans*-crotonic acid dibromides is not included in this paper, these data on the *trans* isomer are given to show the consistency of the salt effect with different types of dibromides.

Preparation of Materials

All dibromides used contained the correct percentage of bromine as shown by Carius analyses.

(8) Young and Winstein, THIS JOURNAL, **58**, 102 (1936).

(9) Landolt–Börnstein, "Tabellen," Verlag von Julius Springer, Berlin, 1923, Vol. I, p. 278.

cis- and trans-2-Pentene Dibromides.—These compounds were kindly supplied by Professor H. J. Lucas[10] of the California Institute of Technology.

cis- and trans-3-Hexene Dibromides.—These compounds were prepared by the action of hydrobromic acid on the diacetates of the *meso*-and *d,l*-diethyl glycols.[11] The physical properties of the *cis*-3-hexene dibromide (*d,l*) were b. p. (9 mm.) 80.4–80.6°, d^{25}_4 1.5896, $n^{25}D$ 1.5031, and those of the *trans*-3-hexene dibromide (*meso*) were, b. p. (9 mm.) 79.0–79.2°, d^{25}_4 1.5940, $n^{25}D$ 1.5048.

cis- and trans-4-Octene Dibromides.—The dibromide of *cis*-4-octene was synthesized by Mr. Zene Jasaitis by the action of hydrobromic acid on *meso*-dipropylglycol diacetate[12]: b. p. (4 mm.) 84.0–84.5°, $n^{20}D$ 1.4981, d^{20}_4 1.4569.

trans-4-Octene dibromide was obtained from a mixture of 4,4-dibromooctane and *meso*-3,4-dibromooctane which had been prepared by Mr. Leo Levanas from the racemic dipropylglycol and hydrogen bromide in the presence of zinc bromide.[12] The dibromide mixture was converted into a mixture of octane and *trans*-4-octene by reduction with zinc in alcohol. The hydrocarbon mixture, freed from alcohol, came over through a 30-cm. column of glass helices, at 119–120.3°. This distillate was treated dropwise with bromine at 0°, and the product washed with sodium bisulfite solution and with sodium bicarbonate solution and dried with calcium chloride. Fractionation through a Weston column yielded *n*-octane and a constant-boiling *trans*-4-octene dibromide, b. p. (8 mm.) 103°, $n^{25}D$ 1.4965.

cis- and trans-Stilbene Dibromides.—A mixture of the *cis*- and *trans*-stilbene dibromides was prepared by the action of bromine on freshly distilled stilbene in carbon disulfide in the dark at 0°.[13] The *trans*-stilbene dibromide which separated out was recrystallized twice from benzene, and dried over paraffin in a vacuum. The crystals melted with decomposition at 230–237° (reported m. p. 237°). The *cis*-stilbene dibromide was obtained from the carbon disulfide mother liquor by evaporating the solvent. The residual solid was twice recrystallized from ethanol, yielding a product melting at 109.5–111° (reported m. p. 110°).

Fumaric and Maleic Acid Dibromides.—Fumaric acid was brominated in the presence of water at 100° and the product[14] melted at 270–273° after two recrystallizations from water.

Maleic anhydride and bromine were refluxed at 60–70° for two hours. The colorless reaction mixture was warmed with water, the crystals of fumaric acid dibromide were removed by filtration and the filtrate was concentrated. The first crop of crystals, m. p. 160–162°, was discarded but the second crop which formed after several weeks at room temperature (m. p. 164–167°, reported m. p. 166–167°)[15] was used in this work.

Discussion of Results.—The specific reaction rate constants and the Arrhenius heats of activation for the reactions of the dibromides of several pairs of *cis–trans* isomers with potassium iodide in 99% methanol are listed in cols. 9 and 11 of Table I. In these cases in which the parent unsaturated compounds have two hydrogen atoms adjacent to the double bond and the other two groups are identical or similar the dibromide from the *trans* compound gives a greater rate constant and a smaller heat of activation than the dibromide from the *cis* isomer.[16] It would appear that rate studies of this character offer a valuable method of identifying the isomers of alkene hydrocarbons which cannot be identified readily by the usual methods applied when carboxyl, amino, hydroxyl, etc., groups are present in the molecule. Until data to the contrary are obtained, therefore, it will be assumed that rate constants alone are sufficient for identifying the dibromides from *cis–trans* isomers of the type herein reported. Work on other types of stereoisomeric dibromides now in process should make it possible to establish generalizations regarding the effect of radicals on the rate constants and heats of activation.

The authors are indebted to Professor H. J. Lucas for his generosity in furnishing the *cis*- and *trans*-2-pentenes.

Summary

The reaction of potassium iodide with several pairs of stereoisomeric alkene dibromides in 99% methanol has been investigated at 75 and 60°. A qualitative comparison of *trans*- and *cis*-stilbene dibromides in acetone indicated that the *trans* derivative reacted over a hundred times as rapidly as the *cis* derivative.

In five cases where quantitative comparisons have been made the dibromide from the *trans* parent compound of the type RHC=CHR′ gave a larger rate constant and smaller heat of activation than the dibromide of the *cis* parent compound. The groups R and R′ were identical or similar. Rate studies of this type have been suggested as a means of identifying *cis–trans* isomers.

LOS ANGELES, CALIF. RECEIVED MARCH 1, 1939

(10) For description of these materials, see the article by Lucas and Prater, THIS JOURNAL, **59**, 1682 (1937).

(11) Young, Weiss and Pressman, unpublished work.

(12) Young, Jasaitis and Levanas, *ibid.*, **59**, 403 (1937).

(13) Wislicenus and Seeler, *Ber.*, **28**, 2693 (1895).

(14) Wislicenus, *Ann.*, **272**, 1 (1893).

(15) Michael, *J. prakt. Chem.*, **52**, 289 (1895).

(16) Although Davis and Heggie[7] have pointed out that a reversal of the relative magnitude of rate constants might be observed when the reaction is carried out at different temperatures, it should be noted that the compounds which they cite, the dibromides of ethyl acrylate and maleic acid, do not possess a similarity in structure comparable to that of the stereoisomeric pairs reported in this paper. A study of the action coefficients for these and other reactions which is now almost complete will indicate whether such reversals are ever likely when dealing with stereoisomeric pairs.

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, NO. 696, AND THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

Investigations on the Stereoisomerism of Unsaturated Compounds. V. A Mechanism for the Formation of Butenes from 2,3-Dibromobutanes by the Action of Iodide Ion

BY SAUL WINSTEIN, DAVID PRESSMAN AND WILLIAM G. YOUNG

The reaction of 1,2-dihalides with inorganic iodides to yield unsaturated compounds has been studied from a kinetic standpoint[1] and has been recommended as a method for synthesis of ethylenic compounds.[2] In spite of the considerable attention paid the reaction, the steric result of the elimination of halogen by iodide ion has remained uncertain[1d] until the present time. The question as to whether bromine is eliminated *trans* or *cis* to give pure products or by both of these processes to give a mixed product is of importance from the theoretical standpoint in formulating a mechanism for the reaction and from a practical standpoint for deciding the applicability of the reaction to syntheses of stereoisomeric olefin derivatives. It is the purpose of this paper to show that the removal of bromine from 2,3-dibromobutanes by iodide ion involves almost entirely *trans* elimination at moderate temperatures and that at a higher temperature considerable rearrangement accompanies the reaction. The mechanism of the reaction is discussed on the basis of the experiments presented here and of the previous kinetic results.

The nature of the elimination of bromine from 2,3-dibromobutanes by iodide was investigated by treating pure 2,3-dibromobutanes or a mixture of them with iodide ion either in aqueous propanol at approximately 95° or in diethylene glycol at approximately 200°. The generated butenes were converted to dibromobutanes and analyzed be measuring the rate of reaction of the final dibromide with potassium iodide in methyl alcohol.[1e,3] Table I summarizes the results obtained. Inspection of the table discloses that in propyl alcohol at the lower temperature *meso*-2,3-dibromobutane gives rise to a butene which is 96% *trans*, and *dl*-2,3-dibromobutane gives a butene which is 91% *cis*. Also the ratio of isomers in a mixed dibromide is essentially unchanged by the successive elimination and addition of bromine. These results show that *trans* elimination is by far the predominating reaction. However, in diethylene glycol at the higher temperature *dl*-2,3-dibromobutane gives a butene mixture showing that considerable rearrangement occurs, but even here the elimination is largely *trans*. The small changes in composition of the dibromides at the lower temperature and the considerable change at the higher temperature may be due to the isomerizing effect of the iodine on the butenes[4] or possibly the participation of a mechanism other than the predominating one.

The Mechanism of the Reaction.—The facts that: (a) the elimination of halogen from 1,2-diiodoethane, 1-bromo-2-iodoethane, and 1,2-dibromides, in general, is first order with respect to the dihalide and iodide ion concentrations[1]; (b) elimination of halogen is induced by reducing agents such as iodide ion or zinc; and (c) the elimination of bromine by iodide ion is *trans* suggest a general mechanism (equations (1), (2) and (3)) for the elimination of iodide ion which is in part the reverse of Ogg's[5] negative mechanism for the addition of halogen to the ethylenic linkage.

$$R_1R_2CBr{-}CBrR_3R_4 + I^- \longrightarrow R_1R_2C^-{-}CBrR_3R_4 + IBr \quad (1)$$

$$R_1R_2C^-{-}CBrR_3R_4 \longrightarrow R_1R_2C{=}CR_3R_4 + Br^- \quad (2)$$

$$IBr + 2I^- \longrightarrow I_3^- + Br^- \quad (3)$$

Figure 1 shows graphically the mechanism we propose. Iodide ion attacks and donates elec-

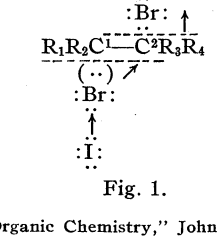


Fig. 1.

(1) (a) Slator, *J. Chem. Soc.*, 1697 (1904); (b) Biilmann, *Rec. trav. chim.*, **36**, 319 (1917); (c) Van Duin, *ibid.*, **43**, 341 (1924); **45**, 345 (1926); (d) **47**, 734 (1928); (e) Dillon, Young and Lucas, THIS JOURNAL, **52**, 1953 (1930); (f) Dillon, *ibid.*, **54**, 952 (1932); (g) Davis and Heggie, *J. Org. Chem.*, **2**, 470 (1938); (h) Young, Pressman and Coryell, THIS JOURNAL, **61**, 1640 (1939).

(2) Hickinbottom, "Reactions of Organic Compounds," Longmans, Green and Co., New York, N. Y., 1936, p. 369.

(3) Young and Winstein, THIS JOURNAL, **58**, 102 (1936).

(4) Gilman, "Organic Chemistry," John Wiley and Sons, Inc., New York, 1938, p. 376.

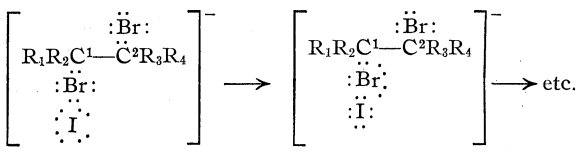
(5) Ogg, THIS JOURNAL, **57**, 2727 (1935).

TABLE I

THE COMPOSITION OF BUTENES RESULTING FROM THE ACTION OF IODIDE ION ON 2,3-DIBROMOBUTANES

No.	Original dibromide K_2	% *dl*	% *meso*	Solvent	Temp., °C.	Final product K_2	% *cis*	% *trans*
1	0.0564	0	100	PrOH	95	0.0554	4	96
2	.0299	100	0	PrOH	95	.0322	91	9
3	.0490	28	72	PrOH	95	.0495	26	74
4	.0298	100	0	$C_4H_{10}O_3$	200	.0394	64	36

trons[6] to one of the bromine atoms of the dibromide giving iodine bromide and the intermediate, $R_1R_2C^-$—$CBrR_3R_4$. The unshared pair of electrons on carbon atom 1 then rapidly attacks the carbon face opposite the remaining bromine atom, freeing bromide ion with inversion of carbon atom C^2. A double bond has thus been formed between carbon atoms C^1 and C^2 and the whole process is then a *trans* elimination of bromine. The iodine bromide formulated as a product immediately reacts with iodide ions to give triiodide and bromide ions.



I

It is thought that the life of the $R_1R_2C^-$—$CBrR_3R_4$ intermediate is exceedingly short, because otherwise reaction with solvent and racemization[7] about carbon atom C^1 would be serious. The decomposition of $R_1R_2C^-$—$CBrR_3R_4$ is thought to occur essentially simultaneously with the breaking of the C—Br bond of carbon atom C^1. Thus, we have here a process quite analogous to the usual bimolecular exchange leading to Walden inversion.[8] In the usual bimolecular exchange involving a negative ion, this ion presents a pair of electrons to an atom, another substituent being expelled with a pair of electrons previously shared. In our process an electron transfer has been brought about but through a longer chain of atoms.

Figure 1 depicts the structure of the 1,2-dibromide as being one with the two bromine atoms *trans* to each other, enabling the electron transfer discussed above to take place. The *trans* configuration with respect to the two bromine atoms is reasonable because this structure may be essentially the normal state of affairs in dihalides[9] or it may tend to be assumed on the approach of the iodide ion.

One might have assumed that the first step in the reaction of iodide ion with a dihalide is a bimolecular exchange of iodide for bromide (with inversion of the carbon atom concerned) with subsequent rapid reaction of the iodobromide. But then for the reaction of the iodobromide with iodide ion only a mechanism such as that proposed by us seems plausible. Thus a total of two Walden inversions would be present in the process and *cis* elimination instead of *trans* elimination would be its result. We feel, therefore, that exchange of iodide for bromide is at most only a subsidiary reaction at low temperatures, but that it may explain part of the deviations from clean-cut *trans* elimination of bromine by iodide ion.

Experimental

Preparation of *meso*-2,3-Dibromobutane.—*trans*-2-Butene was prepared by a modification of the method of Wislicenus, Talbot, Henze and Schmidt[10] in which tiglic acid hydrobromide instead of tiglic acid hydriodide[11] was used.

A solution of 70 g. (0.66 mole) of sodium carbonate in 700 ml. of water was cooled to 0° and added to 60 g. (0.33 mole) of tiglic acid hydrobromide in a flask equipped with a mercury-sealed stirrer and a gas delivery tube. The mixture was warmed slowly. At 30° a slow evolution of gas began. The gas was washed with sodium hydroxide solution, dried with anhydrous calcium chloride and condensed in an ampoule cooled with a solid carbon dioxide–alcohol bath. The temperature of the reaction mixture was raised to 70° over a period of two and one-half hours. The gas evolved at this temperature was soluble in sodium hydroxide and presumably was carbon dioxide. The yield of olefin was 80%. When the reaction was completed in one and one-half hours only 65% yield was obtained. The butene was converted to dibromide by the method previously described.[11]

The tiglic acid hydrobromide was prepared by Mr. Zene Jasaitis by the action of dry hydrogen bromide on a solution of tiglic acid in chloroform.

(6) Professor Linus Pauling has suggested to one of us that perhaps a complex ion, I, is formed which then undergoes the electron transfer to be outlined.

(7) Cowdrey, Hughes, Ingold, Masterman and Scott, *J. Chem. Soc.*, 1257 (1937).

(8) (a) Olson, *J. Chem. Phys.*, **1**, 448 (1933); (b) Meer and Polanyi, *Z. physik. Chem.*, **B19**, 164 (1932).

(9) (a) Beach and Stevenson, *J. Chem. Phys.*, **6**, 635 (1938); (b) Beach and Palmer, *ibid.*, **6**, 639 (1938).

(10) Wislicenus, Talbot, Henze and Schmidt, *Ann.*, **313**, 207 (1909).

(11) Young, Dillon and Lucas, THIS JOURNAL, **51** 2528 (1929).

Preparation of *dl*-2,3-Dibromobutane.—*dl*-2,3-Dibromobutane was prepared from *meso*-2,3-butanediol by the synthesis outlined by Wilson and Lucas.[12]

Reaction of 2,3-Dibromobutanes with Sodium Iodide in Propanol.—Seventy grams (0.46 mole) of sodium iodide was dissolved in a warm mixture of 75 ml. of *n*-propanol and 25 ml. of water. Then 20 g. (0.093 mole) of 2,3-dibromobutane was added. Two liquid phases were present initially but a homogeneous solution resulted upon further heating. The mixture was refluxed gently, the evolved gas being washed with water, dried with calcium chloride and collected in a cold ampoule at −78°. In the reaction flask, iodine was liberated and a white precipitate of sodium bromide formed. After four hours of refluxing, the rate of butene evolution was slow and the reaction was stopped, the apparatus being flushed out with air. The crude yield of hydrocarbon was 87% of the theoretical from *meso*-2,3-dibromobutane, 80% from *dl*-2,3-dibromobutane and 81% from a mixed dibromobutane.

Reaction of 2,3-Dibromobutane with Potassium Iodide in Diethylene Glycol.—Forty grams (0.185 mole) of *dl*-dibromobutane was added dropwise to a hot solution of 80 g. (0.48 mole) of potassium iodide in 300 g. of diethylene glycol. The butene which was evolved continuously during the course of the reaction was washed with a dilute sodium hydroxide solution and dried over anhydrous calcium chloride before being condensed in an ampoule. The temperature of the reaction mixture started at 245° and gradually dropped to 165° at the finish. The yield of butene was 85%.

Analysis of Butene Mixtures.—The butene mixtures were analyzed according to the method previously outlined.[1e] The second order reaction rate constants of the original and final dibromobutanes with potassium iodide in 99% methanol are listed in Table I together with the corresponding compositions of butenes which they represent.

(12) Wilson and Lucas, THIS JOURNAL, **58**, 2396 (1936).

Summary

The elimination of bromine from *dl*- and *meso*-2,3-dibromobutanes by iodide ion has been found to be an almost complete *trans* removal of halogen at moderate temperatures. A mechanism for the process has been proposed. It is thought that iodide ion removes a positive bromine atom and essentially simultaneously with this removal the electron pair which is left unshared by this removal attacks the carbon face opposite the remaining bromine atom forming a double bond and liberating bromide ion.

LOS ANGELES, CALIF. RECEIVED MARCH 14, 1939

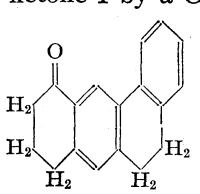
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Syntheses in the 1,2-Benzanthracene and Chrysene Series

BY LOUIS F. FIESER AND WILLIAM S. JOHNSON[1]

Having developed a satisfactory method for the synthesis of pure 8-methyl-1,2-benzanthracene[2] from the keto acid resulting in nearly quantitative yield from the succinoylation of 9,10-dihydrophenanthrene,[3] we have utilized some of the same intermediates for the synthesis of certain other compounds which seemed of interest to the problem of hydrocarbon carcinogenesis.

8-Ethyl-1,2-benzanthracene was prepared from the ketone I by a Grignard reaction followed by



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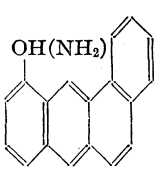


II (III, NH_2)

sulfur dehydrogenation of the low-melting but crystalline tetrahydride obtained on distillation of the resulting carbinol. Like the lower homolog,[2] the completely aromatized hydrocarbon shows a characteristic double melting point when pure. For the preparation of the phenol II, required for comparison with the weakly carcinogenic 3-isomer,[4] the dehydrogenation of 8-keto-hexahydrophenanthrene (I) by the method of Mosettig and Duval[5] using Adams catalyst in naphthalene solution was tried without success. 8-Hydroxy-1,2-benzanthracene, however, can be obtained satisfactorily by dehydrogenation with sulfur,[6] and the phenol was converted into the amine III by the Bucherer reaction.

In view of the enhancement of carcinogenic potency noted with certain combinations of *meso*- and α-methyl groups[4] (5,10-, 5,9-, 9,10-), it seemed important to obtain the di-α-substituted 5,8-dimethyl-1,2-benzanthracene (XII).

(1) Holder of the John Woodruff Simpson Fellowship from Amherst College.

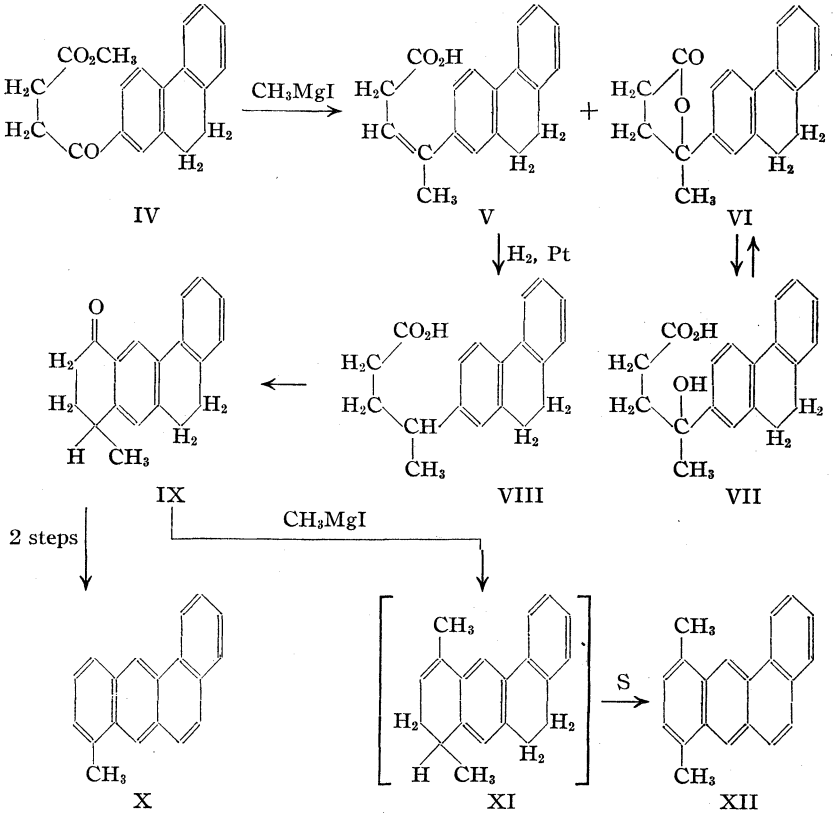
(2) Fieser and Johnson, THIS JOURNAL, **61**, 168 (1939).

(3) Burger and Mosettig, *ibid.*, **59**, 1302 (1937).

(4) For a summary of the data and literature, see Fieser, *Am. J. Cancer*, **34**, 37 (1938).

(5) Mosettig and Duval, THIS JOURNAL, **59**, 367 (1937).

(6) Compare the preparation of 4′-hydroxy-3,4-benzpyrene Fieser, Hershberg, Long and Newman, *ibid.*, **59**, 475 (1937).



The introduction of a methyl group at a point corresponding to the 5-position was accomplished by the action of methylmagnesium iodide on methyl β-(9,10-dihydro-2-phenanthroyl)-propionate (IV). Haworth and co-workers[7] conducted similar reactions with the esters of a number of β-aroylpropionic acids and obtained from the acidic fractions unsaturated acids of the type indicated by formula V. While these acids were obtained in yields up to 50–75%, the neutral fractions apparently were not investigated. In an earlier paper Rupe and Steinbach[8] report the preparation of an unsaturated acid from ethyl β-(*p*-toluyl)-propionate in fair yield, and state, without giving details, that the neutral fraction contained a mixture of unchanged starting material and the ester of the unsaturated acid. They also describe the lactonization of the unsaturated acid with dilute mineral acid. In view of the high yields obtained in the methylation of *o*-aroylbenzoic acids by the procedure[9] of adding Grignard reagent in excess to a suspension of the free keto acid, this method was tried in the present case. When treated with a large excess of methylmagnesium bromide, however, the dihydrophenanthroylpropionic acid was converted largely into an unsaponifiable oil, and the result seemed so unpromising that we turned to the use of the ester. When the ester (IV) was treated with methylmagnesium iodide or bromide in only slight excess and the solution refluxed for about two hours the chief product (64%) was the unsaturated acid V. Material satisfactory for the reduction step but apparently consisting of a mixture of stereoisomers can be obtained easily on one crystallization (53% yield). When the Grignard reaction was moderated by operating at a lower temperature, the yield of the crude unsaturated acid V dropped to 32% and the neutral fraction afforded the corresponding lactone VI in 35% yield. The lactone was isolated from this source in a crystalline condition and it was also prepared by boiling the unsaturated acid with 10% sulfuric acid. By dissolving the lactone in hot alkali and carefully neutralizing the cooled solution the unstable γ-hydroxy acid VII was also isolated in a pure, crystalline condition.

A few attempts were made to reduce the lactone VI with zinc and alkali or by the Clemmen-

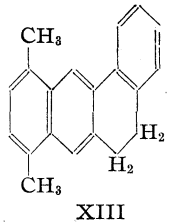
(7) R. D. Haworth and co-workers, *J. Chem. Soc.*, 1784, 2248 (1932); 454, 864 (1934).

(8) Rupe and Steinbach, *Ber.*, **44**, 584 (1911).

(9) Fieser and Newman, THIS JOURNAL, **58**, 2376 (1936).

sen method, but the results were not promising. The easily obtainable unsaturated acid, however, can be hydrogenated smoothly in acetic acid solution to the γ-dihydrophenanthrylvaleric acid VIII. Cyclization to 5-methyl-8-keto-3,4,5,6,7,-8-hexahydro-1,2-benzanthracene (IX) was accomplished most satisfactorily by the action of liquid anhydrous hydrogen fluoride,[10] the pure material being obtained in 81.5% yield. An identical product was obtained in 64% yield by the PCl_5–$AlCl_3$ method in benzene. Cyclization in each case seems to occur exclusively in one direction, and that the product is a benzanthracene rather than a chrysene derivative was established by conversion of the ketone on Clemmensen reduction and dehydrogenation into a hydrocarbon identical with a sample of 5-methyl-1,2-benzanthracene (X) prepared by a different synthesis.[9]

5,8-Dimethyl-1,2-benzanthracene (XII) was prepared from the ketone IX by a Grignard reaction, dehydration of the carbinol, and dehydrogenation with sulfur. Purified through the picrate and by chromatographic adsorption, the dimethyl compound gave evidence from the melting point characteristics of the existence of two polymorphic forms, as noted for other compounds of the 8-series. The intermediate tetrahydride (XI) was not isolated. While the 8-methyl tetrahydride[2] was obtained crystalline in good yield, the oil resulting from the distillation of the carbinol of the 5,8-dimethyl series solidified only partially and the small amount of recrystallized product isolated had the composition of a dihydride. Of the possible structures that of 5,8-dimethyl-3,4-dihydro-1,2-benzanthracene (XIII) is clearly indicated by the



XIII

ultraviolet absorption spectrum (in absolute alcohol) kindly determined by Dr. R. Norman Jones. The curve (Fig. 1) is characteristic of an alkylated β-phenylnaphthalene and is practically identical with that for the similarly constituted 6,7-dihydromethylcholanthrene[11] (dotted line).

(10) Fieser and Hershberg, THIS JOURNAL, **61**, 1272 (1939).
(11) Fieser and Hershberg, *ibid.*, **60**, 940 (1938).

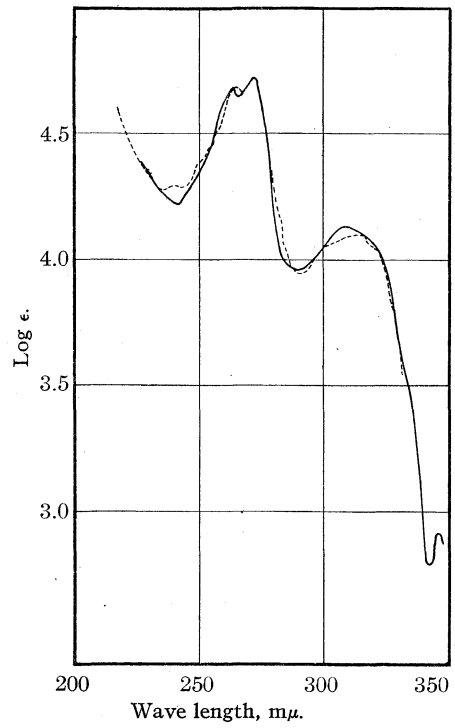
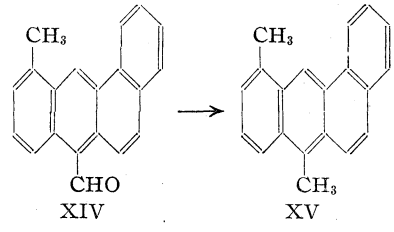


Fig. 1.—Solid line, 5,8-dimethyl-3,4-dihydro-1,2-benzanthracene; dotted line, 6,7-dihydro-20-methylcholanthrene.

Another hydrocarbon of interest for the investigation of the combined influence of *meso*- and α-methyl groups was obtained by condensing 8-methyl-1,2-benzanthracene with methylformanilide and reducing the resulting aldehyde by the Wolff–Kishner method. The dimethyl com-



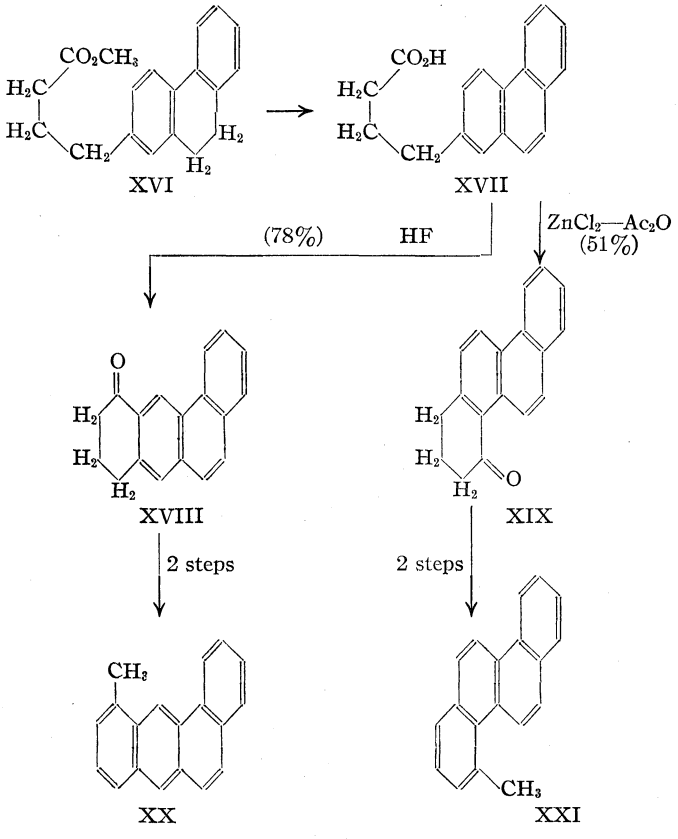
XIV XV

pound is different from the above 5,8-isomer and, since the aldehyde reaction is specific for structures of limited types and is known[12] to give the 10-derivative of 1,2-benzanthracene but to fail with 1,2,5,6-dibenzanthracene, the substance can be regarded with considerable assurance as 8,10-dimethyl-1,2-benzanthracene (XV). Some confirmation of the structure has been obtained by Dr. Jones in a study of the absorption spectra of this and related hydrocarbons which will be reported shortly. The introduction of a 10-methyl group is accompanied by a slight but definite dis-

(12) Fieser and Hartwell, *ibid.*, **60**, 2555 (1938).

placement of the most intense absorption band to longer wave lengths, specific to the *meso* positions.

The starting material for the above work served as well for the synthesis of 4-methylchrysene (XXI), required[13] as a possible model for the highly carcinogenic 3,4-benzpyrene. γ-(9,10-Dihydro-2-phenanthryl)-butyric acid (reduction of IV as acid) was dehydrogenated with sulfur in the form of the ester XVI giving, after saponification, γ-(2-phenanthryl)-butyric acid, XVII. Haworth and Mavin[14] previously prepared this acid from the less accessible 2-acetylphenanthrene and found that on cyclization with 85% sulfuric acid it yielded a mixture of isomeric ketones from which pure 4-keto-1,2,3,4-tetrahydrochrysene (XIX) was isolated in unspecified yield. Our experience was



much the same and the yield of pure XIX, m. p. 125°, was 23%. Ring closure by the hydrogen fluoride procedure[10] gave a high yield of total ketone which consisted almost entirely of the hitherto unknown isomer 8-keto-5,6,7,8-tetrahydro-1,2-benzanthracene (XVIII), m. p. 118°, which was obtained pure in 78% yield. For identification the ketone was converted to 8-methyl-1,2-benzanthracene through a crystalline dihydride. When the acid XVII was cyclized with zinc chloride[15] (0.65 equivalent) in acetic acid-anhydride the distilled and twice crystallized total ketone amounted to 51% and consisted of the pure chrysene derivative XIX. With the ketone available by this convenient process the synthesis of 4-methylchrysene, through a crystalline dihydride, was easily completed.

The sharp contrast in the direction of cyclization with hydrogen fluoride and with zinc chloride is quite striking and of obvious practical significance. The Friedel and Crafts procedure gave mixtures of the two ketones in which the benzanthracene derivative XVIII predominated. This isomer constituted about two-thirds of the total using benzene as the solvent, and a still higher proportion was produced in nitrobenzene solution. These results with γ-(2-phenanthryl)-butyric acid contrast with those reported for the cyclization of β-(2-phenanthryl)-butyric acid[16] and β-(2-phenanthryl)-propionic acid[17] in the Friedel and Crafts reaction and with stannic chloride, for these acids undergo ring closure exclusively at the 1-position.

Experimental Part[18]

8 - Ethyl - 3,4,5,6 - tetrahydro - 1,2 - benzanthracene.—An ethereal solution of 6 g. of 8-keto-3,4,5,6,7,8-hexahydro-1,2-benzanthracene[2] (I) was added with stirring to a cooled Grignard solution from 2 g. of magnesium and 7 g. of ethyl bromide. After refluxing for several hours the product was recovered as usual, heated to effect dehydration, and distilled, b. p. about 185° (1 mm.). The colorless oil (5.55 g., 88.5%) crystallized with difficulty in a solid carbon dioxide bath; a portion purified by several crystallizations from methanol formed large, elongated, highly fluorescent prisms, m. p. 65–67°.

Anal. Calcd. for $C_{20}H_{20}$: C, 92.26; H, 7.74. Found: C, 92.53; H, 7.63.

8-Ethyl-1,2-benzanthracene.—The distilled tetrahydride (1.33 g.) was dehydrogenated by heating with sulfur (0.33 g.) at 210–255° for twenty-five minutes. After very brief heating with a little zinc dust the product was distilled in vacuum, and after decolorizing the yellow oil in ether–alcohol picric acid (1.2 g.) was added. A dark red picrate separated on cooling (1.2 g., m. p. 148.5–149.5°) and an additional quantity (0.25 g.)

(13) Fieser and Seligman, THIS JOURNAL, **60**, 170 (1938).
(14) R. D. Haworth and Mavin, *J. Chem. Soc.*, 1012 (1933).
(15) Fieser and Hershberg, THIS JOURNAL, **59**, 1028 (1937).
(16) E. Bergmann and Hillemann, *Ber.*, **66**, 1302 (1933).
(17) Bachmann and Kloetzel, THIS JOURNAL, **59**, 2207 (1937).
(18) All melting points are corrected.

was obtained on concentration; total yield, 58.5%. Recrystallized from alcohol the picrate formed deep red blades, m. p. 149.5–150°.

Anal.[19] Calcd. for $C_{26}H_{19}O_7N_3$: N, 8.65. Found: N, 8.73.

The picrate (0.7 g.) was decomposed by passing a benzene solution through a tower of alumina; on adding alcohol to the concentrated filtrate the hydrocarbon crystallized in very faintly yellow, glistening needles, m. p. 82–83.5° (0.31 g., 84%). Recrystallization from petroleum ether gave a lower-melting form, m. p. 78–79°, which remelted after solidification at 82.5–83°.

Anal. Calcd. for $C_{20}H_{16}$: C, 93.71; H, 6.29. Found: C, 93.51; H, 6.36.

8-Hydroxy-1,2-benzanthracene was prepared by heating the ketone I (2 g.) with 0.52 g. of sulfur at 230–255° for twenty-seven minutes and distilling the product at the oil pump vacuum. Crystallization from benzene–ligroin gave 1.1 g. of ringlets of small yellow needles, m. p. 138–148°; a second crystallization yielded 0.88 g. (45%) of product, m. p. 149–151°. The further purified phenol formed bright yellow rods, m. p. 151.3–151.8°.

Anal. Calcd. for $C_{18}H_{12}O$: C, 88.50; H, 4.95. Found: C, 88.55; H, 5.21.

The acetate, prepared using pyridine as catalyst, after three crystallizations from ligroin formed light buff colored needles, m. p. 133–133.6°.

Anal. Calcd. for $C_{20}H_{14}O_2$: C, 83.89; H, 4.93. Found: C, 83.86; H, 5.08.

8-Amino-1,2-benzanthracene.—A mixture of 0.5 g. of the hydroxy compound, 2.5 cc. of dioxane, 5 cc. of concentrated ammonia solution, and 2.5 g. of sodium bisulfite in 5 cc. of water was heated in a sealed tube at 190–200° for ten hours. The addition of dilute alkali precipitated a yellow oil which solidified on scratching. This crystallized from benzene–ligroin (Norite) in beautiful, long yellow needles (0.13 g., 26%), m. p. 201.7–202.3° dec. (no change on recrystallization).

Anal.[19] Calcd. for $C_{18}H_{13}N$: N, 5.76. Found: N, 5.49.

Methyl β-(9,10-Dihydro-2-phenanthroyl)-propionate (IV) was prepared by esterification of the keto acid (100 g.) in methanol (1400 cc.) saturated with hydrogen chloride. The ester was washed in ether with soda solution, dried, and distilled, b. p. about 250° (1–2 mm.). One crystallization from methanol gave 88 g. (84%), m. p. 76–78°. A recrystallized sample formed almost colorless prisms, m. p. 77–78°.

Anal. Calcd. for $C_{19}H_{18}O_3$: C, 77.53; H, 6.16. Found: C, 77.65; H, 6.28.

γ-Methyl-γ-(9,10-dihydro-2-phenanthryl)-vinylacetic Acid (V).—The reagent from 3.7 g. of magnesium and 22 g. of methyl iodide in 100 cc. of ether was added with cooling and stirring to a solution of 30 g. of the above ester IV in 500 cc. of benzene. After boiling the mixture under reflux for one and one-half hours the oily intermediate was decomposed with ice and acid. The organic layer was washed with acid and extracted with 10% soda solution. No saponifiable material was found in the neutral fraction. On acidifying the soda solution the unsaturated acid V separated in an almost colorless condition; yield, 18.2 g. (64%). One crystallization from benzene–ligroin gave 15.1 g. (53%) of pale yellow prisms, m. p. 117–125° (mixture of stereoisomers?), suitable for the next step. Eight recrystallizations were required to obtain a sample of the constant m. p. 137–138°, dec. (pale yellow plates).

Anal. Calcd. for $C_{19}H_{18}O_2$: C, 81.98; H, 6.53. Found: C, 82.08; H, 6.41.

γ-(9,10-Dihydro-2-phenanthryl)-γ-valerolactone (VI). (a) **From the Grignard Reaction.**—The ester IV (20 g.) in benzene (75 cc.) was treated with the reagent from 1.8 g. of magnesium and excess methyl bromide and the mixture was warmed gently on the steam-bath for one hour without refluxing. After hydrolysis with 10% sulfuric acid, extraction with soda afforded 4.5 g. (32%) of the crude vinylacetic acid derivative V. Evaporation of the solution containing the neutral fraction gave an oil which largely dissolved in hot alkali. On acidifying the alkaline solution an oil precipitated. This was taken up in ether, and after extracting a small amount of acidic material with soda, drying and evaporating the solution, the lactone VI distilled at about 240° (2 mm.). The colorless distillate was obtained crystalline from ligroin, forming large, colorless prisms, m. p. 60–65°, identical with material prepared in (b); yield, 5 g. (35%).

A second run identical with the above except that the Grignard reaction mixture was refluxed vigorously for two hours gave 9 g. (63%) of the crude vinylacetic acid V and only a small amount of the lactone.

(b) **From the Unsaturated Acid V.**—The crude vinylacetic acid V (4.5 g.) was boiled with 50 cc. of 10% sulfuric acid for four hours and the oily product washed in ether with water and extracted with soda, which removed 2 g. of unchanged acid. After evaporation of the ether the lactone distilled as a colorless oil which slowly crystallized as large, colorless prisms, m. p. 60–68° (1.3 g., 52% based on acid consumed). Further purification gave prisms melting largely at 61.5–63° but giving a clear liquid only at 70°.

Anal. Calcd. for $C_{19}H_{18}O_2$: C, 81.98; H, 6.53. Found: C, 81.91; H, 6.56.

γ-Hydroxy-γ-(9,10-dihydro-2-phenanthryl)-valeric acid (VII) was prepared by acidifying a cooled solution prepared by dissolving the lactone VI in boiling aqueous alkali. The hydroxy acid easily reverts to the lactone, but by careful crystallization from ether it was obtained as small, colorless needles, m. p. 95–97°, dec.

Anal. Calcd. for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80. Found: C, 76.89; H, 6.83.

γ-(9,10-Dihydro-2-phenanthryl)-valeric Acid (VIII).—A solution of 12.1 g. of the vinylacetic acid V in 200 cc. of glacial acetic acid in the presence of Adams catalyst absorbed one mole of hydrogen rapidly at room temperature. The solvent was removed from the filtered solution and the product distilled at about 250° (1 mm.). The saturated acid was obtained in nearly quantitative yield as a colorless oil which set to a glass and, in the course of some time, crystallized. The distilled product was suitable for the next step. A sample of the solid material

(19) Microanalysis by Herbert S. Wight.

when purified by crystallization from ether–petroleum ether formed colorless prisms, m. p. 77.5–78.5°.

Anal. Calcd. for $C_{19}H_{20}O_2$: C, 81.40; H, 7.19. Found: C, 81.16; H, 6.87.

5 - Methyl - 8 - keto - 3,4,5,6,7,8 - hexahydrophenanthrene (IX). (a) Hydrogen Fluoride Procedure.—The valeric acid VIII (11 g.) was treated with 150 g. of chilled liquid anhydrous hydrogen fluoride in a platinum vessel and the solution allowed to stand at room temperature for three hours. After evaporating the reagent, warming the residue with soda solution and cooling, the product solidified. It was washed and dried in benzene and distilled in vacuum, giving a colorless solid. One crystallization from methanol yielded 8.4 g. (81.5%) of flat needles, m. p. 127.2–128.4°; recrystallized, m. p. 127.9–128.4°.

Anal. Calcd. for $C_{19}H_{18}O$: C, 86.98; H, 6.92. Found: C, 86.97; H, 6.83.

(b) **Friedel and Crafts Reaction.**—A mixture of the valeric acid (10 g.) and phosphorus pentachloride (9.5 g.) in 150 cc. of benzene was refluxed for one hour and the solution was cooled and treated under stirring with 9.5 g. of aluminum chloride. After standing two and one-half hours at room temperature and refluxing for one and one-half hours the mixture was poured onto ice and acid and the benzene layer washed and dried. Distillation in vacuum and one crystallization from methanol yielded 6 g. (64%) of colorless needles of the ketone, m. p. 126–127.5°.

5-Methyl-1,2-benzanthracene.—The ketone IX (5.7 g.) was reduced by the Clemmensen–Martin method using 25 g. of amalgamated zinc, 25 cc. of toluene, 1 cc. of glacial acetic acid, 18 cc. of water, and 45 cc. of concentrated hydrochloric acid. Refluxing was continued for forty-eight hours with the addition of a second charge of zinc and a total of 100 cc. of concentrated hydrochloric acid. As the reduction progressed the toluene layer became fluorescent in ultraviolet light. After separation of the layers and extraction with benzene the washed and dried solution was filtered through a tower of alumina to remove any ketone and concentrated. The residual colorless oil (5 g.) was heated with sulfur (1.93 g.) at 200–255° for one hour and the product distilled in vacuum from a pinch of zinc dust and redistilled, giving 2.6 g. (49.5%, from the ketone) of yellowish hydrocarbon, m. p. 140–150°. A 0.25-g. portion treated in alcohol with 0.5 g. of picric acid gave red needles of the **picrate** (0.37 g.), m. p. 164.5–165°; recrystallized from 5% picric acid solution it melted at 165.5–166° (Fieser and Newman,[9] 165.8–166.3°). Recovered by cleavage of the picrate in benzene with an alumina tower, the hydrocarbon crystallized from benzene–alcohol in yellowish plates (0.17 g., 68% from crude hydrocarbon), m. p. 158–159.4°. No depression in m. p. was observed on mixing with an authentic sample of 5-methyl-1,2-benzanthracene,[9] m. p. 158.5–159.1°.

5,8 - Dimethyl - 3,4 - dihydro - 1,2 - benzanthracene (XIII).—The ketone IX (3 g.) in benzene was added with cooling and stirring to the Grignard reagent from 0.55 g. of magnesium and excess methyl chloride. After stirring for one and one-half hours the mixture was refluxed for about two hours. After adding acid the organic layer was washed with dilute acid, water, and sodium chloride solution, dried over sodium sulfate and concentrated. The oil was dehydrated at 250° for one hour and distilled, giving a yellowish oil from which only 0.27 g. of crystalline product, m. p. 75.5–78.5°, separated. Purified by crystallization from alcohol to constant m. p., this formed glistening, colorless needles, m. p. 82.2–82.8°.

Anal. Calcd. for $C_{20}H_{18}$: C, 92.98; H, 7.02. Found: C, 93.07; H, 6.99.

The principal absorption maxima (Fig. 1) are at 271.5 mμ (log ε = 4.72) and 309.0 mμ (log ε = 4.13).

5,8-Dimethyl-1,2-benzanthracene.—The oily hydrocarbon mixture (2 g.) remaining in the above experiment after removal of the crystalline XIII was heated with sulfur (0.49 g.) at 210–215° for twenty minutes, and then for fifteen minutes while raising the temperature to 235°. A yellow product solidified on distillation in vacuum and the color was largely removed by adsorption from benzene on alumina. Addition of alcohol to the concentrated filtrate caused the separation of 0.8 g. of crude hydrocarbon; this was converted into the picrate in benzene–ligroin; yield 1.5 g. (27% from the ketone), m. p. 170–173°. Recrystallized from alcohol the picrate formed dark red needles, m. p. 174.5–175°.

Anal.[20] Calcd. for $C_{26}H_{19}O_7N_3$: N, 8.65. Found: N, 8.82.

The hydrocarbon mother liquor treated with picric acid gave 0.85 g. of light red needles melting at about 114–118° and probably containing incompletely dehydrogenated material.

A sample of purified picrate (0.65 g.) was cleaved in benzene with an alumina tower and on adding alcohol to the concentrated filtrate 0.31 g. of glistening needles of the 5,8-dimethyl compound separated in a pure condition (constant m. p.). The hydrocarbon forms colorless needles melting first at 131.2–131.4°, and remelting at 134.4–134.7°.

Anal. Calcd. for $C_{20}H_{16}$: C, 93.71; H, 6.29. Found: C, 93.59; H, 6.04.

8 - Methyl - 1,2 - benzanthracene - 10 - aldehyde (XIV).—A mixture of 0.79 g. of 8-methyl-1,2-benzanthracene,[2] 0.92 g. of methylformanilide, 0.92 g. of phosphorus oxychloride, and 0.8 cc. of *o*-dichlorobenzene was heated on the steam-bath for two hours and the dark red solution poured into an aqueous solution of 5 g. of sodium acetate. After steam distillation the residual oil was washed and dried in benzene and the product crystallized from benzene–ligroin; the mother liquor on evaporation and addition of alcohol gave 0.3 g. of unchanged hydrocarbon (yellow). The crystallizate was submitted to chromatographic adsorption on alumina. Some unreacted hydrocarbon passed into the filtrate (fluorescence, 0.06 g. collected) and the aldehyde was adsorbed in a bright yellow zone. This was sectioned and eluted with benzene containing a few drops of methanol, and the recovered material was crystallized from benzene–ligroin in yellow needles, m. p. 125–140°. Crystallization from glacial acetic acid gave 0.2 g. (42% based on hydrocarbon consumed), m. p. 145–147°. On further crystallization from benzene–ligroin the aldehyde separated both as large yellow needles, melting at 147.5–148° and remelting

(20) Microanalysis by Lyon Southworth.

at 151.5–152°, and as clusters of fine yellow needles, m. p. 151.5–152°.

Anal.[19] Calcd. for $C_{20}H_{14}O$: C, 88.86; H, 5.22. Found: C, 88.94; H, 5.40.

The hydrazone was obtained by adding 0.5 cc. of hydrazine hydrate to 0.16 g. of aldehyde suspended in 15 cc. of boiling alcohol. After adding a trace of acetic acid the aldehyde dissolved, and presently the hydrazone began to separate as fine, light yellow needles. After boiling for ten minutes and cooling there was obtained 0.15 g. (89%) of product, m. p. 181–181.5°, dec. Recrystallization from alcohol did not change the m. p.

Anal.[19] Calcd. for $C_{20}H_{16}N_2$: N, 9.85. Found: N, 9.71.

8,10-Dimethyl-1,2-benzanthracene was prepared by heating 0.14 g. of the hydrazone with a solution from 0.05 g. of sodium and 2.5 cc. of absolute alcohol in a sealed tube at 195–208° for ten hours. After adding dilute acetic acid the crystalline product was collected. Filtration through alumina in benzene removed a trace of color and the highly fluorescent filtrate when concentrated, diluted with alcohol, and cooled yielded 0.11 g. (87%) of colorless needles, m. p. 145.5–146.5°. Recrystallization from benzene–alcohol did not alter the m. p.

Anal.[19] Calcd. for $C_{20}H_{16}$: C, 93.71; H, 6.29. Found: C, 93.56; H, 6.53.

The **picrate** formed deep red needles from alcohol or benzene–ligroin, m. p. 165.5–166°.

Anal.[19] Calcd. for $C_{20}H_{16}\cdot C_6H_3O_7N_3$: N, 8.65. Found: N, 8.62.

γ-(2-Phenanthryl)-butyric Acid (XVII).—γ-(9,10-Dihydro-2-phenanthryl)-butyric acid[2,3] (33 g.) was esterified by refluxing for four hours with 500 cc. of methanol saturated with hydrogen chloride. After adding water the ester was extracted with ether, washed with soda solution, dried with potassium carbonate, and distilled at about 230° (4–5 mm.) as a colorless liquid; yield 32 g. (92%). For dehydrogenation 31 g. of the ester was heated with 3.6 g. of sulfur at 232–255° for one hour. After adding 2 g. of zinc dust and heating for five minutes longer, distillation at about 240° (4 mm.) gave 28 g. of straw colored oil. This was boiled for one hour with 200 cc. of alcohol containing 7 g. of potassium hydroxide, and on concentrating the solution, adding acetone and cooling, the potassium salt of XVII crystallized in beautiful needles. Washed with acetone, the salt was obtained in a completely colorless condition (22 g.). Acidification of a solution in hot water gave colorless, granular acid, m. p. 131–133°; yield, 17.3 g. (53%). One crystallization from benzene–ligroin gave colorless plates, m. p. 134–135.5° (Haworth and Mavin,[14] 134–135°).

8 - Keto - 5,6,7,8 - tetrahydro - 1,2 - benzanthracene (XVIII).—A mixture of 4.8 g. of γ-(2-phenanthryl)-butyric acid and 100 g. of hydrogen fluoride was allowed to stand overnight and the remaining reagent was largely evaporated on the steam-bath. Soda solution was added and the product extracted with benzene. After washing with saturated sodium chloride solution and drying, the ketone was distilled and crystallized from alcohol (Norite); 3.8 g., m. p. 110–115°. Two more crystallizations from alcohol gave colorless blades, m. p. 117–118°; yield 3.5 g. (78%). On further purification the ketone melted at 117.8–118.5°.

Anal. Calcd. for $C_{18}H_{14}O$: C, 87.77; H, 5.73. Found: C, 87.83; H, 5.94.

8 - Methyl - 5,6 - dihydro - 1,2 - benzanthracene.—The above ketone XVIII (2.5 g.) was treated with methylmagnesium chloride in the usual way and the product dehydrated by distillation in vacuum from a trace of potassium bisulfate. The almost colorless distillate set to a solid (2.3 g., 93%), m. p. 70–76°. A sample for analysis formed glistening, colorless plates from alcohol or from petroleum ether, m. p. 80–80.6° (picrate, m. p. 151–152°, dec.).

Anal. Calcd. for $C_{19}H_{16}$: C, 93.40; H, 6.60. Found: C, 93.71; H, 6.35.

8-Methyl-1,2-benzanthracene was obtained by heating the above dihydride (0.53 g.) with sulfur (0.07 g.) at 205–245° for fifteen minutes, followed by treatment with zinc, distillation, adsorption of colored impurities on alumina, and crystallization from alcohol. There was obtained 0.5 g. (95%) of colorless plates, m. p. 117–118° and remelting at 113.5–114°. This did not depress the m. p. of the sample previously described.[2]

4-Keto-1,2,3,4-tetrahydrochrysene (XIX).—γ-(2-Phenanthryl)-butyric acid (7 g.) was refluxed for seventy minutes with 26 cc. of glacial acetic acid, 17.5 cc. of acetic anhydride, and 2.33 g. of freshly fused zinc chloride. Water was dropped into the hot, dark solution, cautiously at first and then to the point of incipient cloudiness. The crude ketone which crystallized was quite dark; it was washed in benzene with soda solution, water, and salt solution, dried, concentrated and diluted with ligroin. Brownish prisms separated on cooling (4 g.), and distillation at about 245° (3–4 mm.) gave an almost colorless product. On crystallization from benzene–ligroin and then from alcohol the ketone formed colorless prisms or prismatic needles, m. p. 124–125° (Haworth and Mavin,[14] 124–125°); yield 3.3 g. (51%). The purest sample obtained had the m. p. 125–125.5°.

Cyclization of γ-(2-Phenanthryl)-butyric Acid by Other Methods.—(a) On repeating the experiment of Haworth and Mavin[14] (85% sulfuric acid at 100° for fifty minutes), 2 g. of the acid yielded 0.44 g. (23%) of the ketone XIX, m. p. 123–125°.

(b) In another experiment 5 g. of the acid was refluxed in 75 cc. of dry benzene with 5 g. of phosphorus pentachloride, 4.5 g. of aluminum chloride was added after chilling, and after standing overnight the mixture containing a yellow precipitate was refluxed for two and one-half hours. On working up the mixture 0.1 g. of crude starting material was recovered and the distilled neutral fraction on slow crystallization from benzene–ligroin yielded a mixture of blades and prisms. These were largely separated by hand and each substance was separately purified and identified by mixed melting point determination (a mixture of the two ketones gives a marked depression). There was collected 1.65 g. (⅔ of total) of blades of 8-keto-5,6,7,8-tetrahydro-1,2-benzanthracene, m. p. 115–116.5°, and 0.8 g. of prisms of 4-keto-1,2,3,4-tetrahydrochrysene, m. p. 122–125°; total yield 52.5%.

(c) Another variation was to treat the acid (2 g.) in

nitrobenzene (25 cc.) with phosphorus pentachloride (steam-bath) and add a solution of aluminum chloride (1.85 g.) in nitrobenzene (30 cc.) to the solution of the acid chloride under stirring in a salt–ice bath. A mustard colored complex separated. After stirring for five hours in the freezing bath and standing overnight at room temperature the ketonic product was collected in the usual way and the components separated as in (b). The crude 8-ketotetrahydro-1,2-benzanthracene collected amounted to 0.95 g., and 0.1 g. of crude 4-ketotetrahydrochrysene was isolated and identified.

4-Methylchrysene (XXI).—Condensation of the ketone XIX (2.5 g.) with methylmagnesium chloride was conducted as in the examples described above, and vacuum distillation gave 2.23 g. (90%) of solid product suitable for dehydrogenation. This crystallized from alcohol in colorless plates, but the melting point rose steadily on repeating the process, probably as the result of disproportionation. The crude dihydride (1.2 g.) was heated with sulfur (0.16 g.) at 215–245° for thirty minutes, followed by vacuum distillation from a little zinc dust. The yellow solid was sublimed at 190–200° (1–2 mm.) and crystallized from benzene–alcohol (Norite), giving 0.6 g. of colorless plates, m. p. 140–146°. Three crystallizations from benzene–alcohol gave 0.38 g. of highly fluorescent hydrocarbon of the constant m. p. 151–151.5°.

Anal. Calcd. for $C_{19}H_{14}$: C, 94.18; H, 5.82. Found: C, 94.00; H, 5.94.

The material in the mother liquors was converted to the red picrate; 0.25 g., m. p. 132–136°. This substance sublimed nicely at 110–120° (1 mm.), and the sublimate on crystallization from benzene–ligroin separated in either of two forms. One of these appeared as bright red needles which melted at 135–135.5° and remelted at 137.5–138°; the other separated as light orange needles, m. p. 137.5–138°. The orange form changes to the red form on standing in contact with the mother liquor.

Anal.[19] Calcd. for $C_{19}H_{14}\cdot C_6H_3O_7N_3$: N, 8.91. Found: N, 8.88.

A sample of 4-methylchrysene recovered (alumina tower) from the purified picrate melted at 151–151.5° as before and differed from the above sample only in showing a more intense fluorescence, the colorless crystals appearing violet in daylight.

Summary

In extension of previous work 8-keto-3,4,5,6,7,8-hexahydro-1,2-benzanthracene has been employed as an intermediate for the synthesis of the 8-ethyl, 8-hydroxy, and 8-amino derivatives of 1,2-benzanthracene. The 5-methyl and 5,8-dimethyl derivatives of the hydrocarbon have been synthesized from β-(9,10-dihydro-2-phenanthroyl)-propionic acid through the unsaturated acid resulting from the condensation of the ester of the keto acid with methylmagnesium halide. It is shown that this reaction can be conducted in such a way as to yield the lactone as well as the unsaturated acid, and the α-hydroxy acid has also been isolated. Another hydrocarbon of interest for its possible carcinogenic activity has been prepared by conversion of 8-methyl-1,2-benzanthracene into the 10-aldehyde, followed by Wolff–Kishner reduction. 4-Methylchrysene has been synthesized starting with γ-(2-phenanthryl)-butyric acid, conveniently prepared from the product of the succinoylation of 9,10-dihydrophenanthrene. This acid can be cyclized exclusively either to the chrysene derivative, using zinc chloride in acetic acid–anhydride, or to the isomeric ketotetrahydro-1,2-benzanthracene, using liquid hydrogen fluoride. Cyclization with 85% sulfuric acid or by the Friedel and Crafts reaction gives mixtures of the isomers.

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The Synthesis of D-Mannoheptulose, and the Preparation of Some of its Derivatives[1]

BY EDNA M. MONTGOMERY AND C. S. HUDSON

F. B. LaForge reported in 1917 that the avocado (the fruit of *Persea gratissima*, Gaertn.) contains a seven carbon atom ketone sugar in the free state. The ketose was isolated in crystalline form, characterized, and its structure and configuration established as those of D-mannoheptulose.[2] The present paper describes the synthesis of D-mannoheptulose from D-α-mannoheptose (D-manno-D-gala-heptose), a transformation which would be expected to occur because of the configuration assigned to the ketose by LaForge.

The Lobry de Bruyn rearrangement was applied to D-manno-D-gala-heptose under the mild conditions[3] used previously in the synthesis of lactulose from lactose.[4] After equilibrium had

(1) Publication authorized by the Surgeon General, U. S. Public Health Service. Presented in part before the Division of Organic Chemistry at the New York meeting of the American Chemical Society, April 22, 1935.

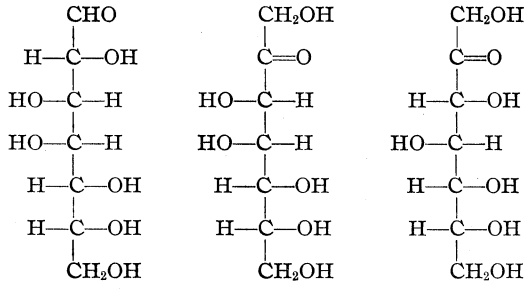
(2) LaForge, *J. Biol. Chem.*, **28**, 511 (1917); Wright, *ibid.*, **28**, 523 (1917).

(3) Wolfrom and Lewis, THIS JOURNAL, **50**, 837 (1928).

(4) Montgomery and Hudson, *ibid.*, **52**, 2101 (1930).

been established, as judged from the constancy of rotation, the aldose components were removed by oxidation with bromine water and subsequent precipitation of the barium aldonates. Crystallization of the ketose portion produced D-mannoheptulose in 25% yield, and D-glucoheptulose[5] in 13% yield. The formation of two ketone sugars from D-manno-D-gala-heptose is not unexpected if we compare this heptose with D-galactose with which it is identical in the configuration of the first four asymmetric carbon atoms, and which it resembles closely in physical and chemical properties. Thus, from the rearrangement of D-galactose with dilute potassium hydroxide, de Bruyn and van Ekenstein[6] were able to isolate not only D-tagatose but also the epimeric ketose, D-sorbose.

The less drastic rearrangement of D-manno-D-gala-heptose in pyridine solution,[7] followed by oxidation of the aldose components, resulted in the recovery of 72% as barium heptonates, and the separation of 21% of pure D-mannoheptulose. No D-glucoheptulose was detected in this case.



D-Manno-D-gala-heptose D-Mannoheptulose D-Glucoheptulose

Glycoside formation with the ketose occurred readily in 0.25 *N* methyl alcoholic hydrochloric acid at room temperature, and a constant rotation[8] of +71.3° was reached in three hours; practically the same rotation was attained when the reaction was carried out at the boiling point of the solution. The product was isolated in 68% yield. From its rotation of +69° in water it is to be designated as α-methyl-D-mannoheptuloside. From the similarity between its rotation and the rotation of the equilibrium solution from which it was obtained, it seems probable that the α-glycoside is formed almost exclusively. In this respect, D-mannoheptulose resembles the configurationally related aldoses, D-mannose and D-lyxose, each of which produces mainly the α-glycoside.

Acetylation of D-mannoheptulose with cold acetic anhydride and pyridine produced a crystalline hexaacetate in an 85% yield. The rotation, +39.0° in chloroform, indicates that it is the α-hexaacetate. Treatment of this acetate with glacial acetic acid saturated with gaseous hydrobromic acid resulted in a crystalline acetobromo-D-mannoheptulose, rotating +104° in chloroform; accordingly, it also is to be designated an α-form. Replacement of the bromine atom through the agency of silver oxide and methyl alcohol yielded a crystalline pentaacetyl-α-methyl-D-mannoheptuloside, rotating +49.5° in chloroform; the same compound is generated by the acetylation of α-methyl-D-mannoheptuloside; deacetylation regenerates the original glycoside. Thus, all the known derivatives of D-mannoheptulose appear as α-forms, and no evidence for a β-form has yet been discovered. The ketose itself shows no mutarotation, and presumably is the pure α-isomer. It is noteworthy that there is no Walden inversion in the passage from the acetobromo compound to the acetylated methylglycoside.

Although D-mannoheptulose is converted to its α-methylglycoside at 20° with the rapidity considered to be characteristic of furanoside formation in the aldose series, nevertheless it seems likely that methyl mannoheptuloside is a pyranoside. Evidence for this belief comes from the data in Table I, in which are compared the rotations of D-mannoheptulose and its derivatives with the rotations of D-mannose and its derivatives, both furanoside and pyranoside. Since the configurations of the asymmetric carbon atoms in the two sugars are identical, it would not be unreasonable to expect a certain similarity in rotations between compounds with the same ring systems. Although the α-mannoheptuloside is formed rapidly at room temperature with acidic methyl alcohol, it also is produced as the principal product when the solution is heated, showing that it is the stable end-product of the reaction and therefore, in all probability, a pyranoside.

Corresponding to the rapid glycoside formation from D-mannoheptulose in methyl alcoholic hydrochloric acid, there is a rapid hydrolysis of the

(5) Austin, THIS JOURNAL, **52**, 2106 (1930).

(6) De Bruyn and van Ekenstein, *Rec. trav. chim.*, **16**, 262 (1897); **19**, 5 (1900).

(7) The method of Danilow, Venus-Danilowa and Schantarovitsch, *Ber.*, **63**, 2269 (1930).

(8) Throughout the article the rotations are specific rotations at 20° for sodium light; *c* designates concentration in grams per 100 cc. of solution.

TABLE I

ROTATIONS[a] OF α-D-MANNOSE, α-D-MANNOHEPTULOSE, AND THEIR DERIVATIVES

	α-D-Mannose			α-D-Mannoheptulose		
	$[\alpha]^{20}D$	Mol. wt.	$[M]^{20}D$	$[\alpha]^{20}D$	Mol. wt.	$[M]^{20}D$
Free sugar	+ 30°[b]	180	5,400	+ 29.2°	210	6,100
Acetate	+ 55.0°[c]	390	21,400	+ 39.0	462	18,000
Acetobromo-	+131.6°[d]	411	54,100	+104	483	50,200
Methylpyranoside	+ 78.6°[e]	194	15,200	+ 69	224	15,400
Methylfuranoside	+113°[f]	194	21,900			
Methylpyranoside acetate	+ 49.1°[g]	362	17,800	+ 49.5	434	21,500
Methylfuranoside acetate	+107°[h]	362	38,700			

[a] Rotations in chloroform, except of the free sugars and glycosides, which are in water. [b] Initial rotation: Levene, *J. Biol. Chem.*, **57**, 333 (1923). [c] Hudson and Dale, THIS JOURNAL, **37**, 1282 (1915). [d] Brauns, *Bur. Standards J. Research*, **7**, 582 (1931). [e] Harris, Hirst and Wood, *J. Chem. Soc.*, 2116 (1932). This value was obtained at 25°. [f] Haworth and Porter, *ibid.*, 650 (1930). [g] Dale, THIS JOURNAL, **46**, 1048 (1924). [h] Haworth, Hirst and Webb, *J. Chem. Soc.*, 656 (1930).

glycoside in dilute aqueous hydrochloric acid. In 0.005 *N* acid at 98°, the hydrolysis constant *k*, expressed in minutes and decimal logarithms, is 0.050. Although this value is very much larger than the constants obtained in the hydrolysis of aldopyranosides, and even for aldofuranosides,[9] yet the recent work of Purves and Hudson[10] has shown that the "glycosides of the keto sugar fructose differ from those of the aldoses in that both ring types possess very nearly the same slight stability toward aqueous acid." A similar conclusion has been reached by Schlubach and Graefe[11] in their study of the sorbosides. In conclusion it may be stated that, although α-methyl-D-mannoheptuloside is hydrolyzed about twice as rapidly as sucrose,[9] a fructofuranoside, no evidence for the size of the ring can be adduced from this behavior.

Experimental

D-Mannoheptulose from D-Manno-D-gala-heptose.—A solution containing 20 g. of D-manno-D-gala-heptose in 200 cc. of 0.05 *N* aqueous barium hydroxide was kept at 35° until the Lobry de Bruyn rearrangement was completed as judged from the changes in rotation. The values observed were +68.6° after fifteen minutes, +49.0° after twenty-four hours, +34.6° after forty-eight hours, and +25.4° (constant) after seventy-two hours. The solution remained clear, and developed only a slight yellow color during the course of five days. At the end of that period sufficient bromine and barium benzoate[12] were added to oxidize the aldehyde sugars to the corresponding aldonic acids; excess bromine, barium, and benzoic acid were removed, and the barium aldonates precipitated with alcohol in the usual way. The filtrate was concentrated *in vacuo* to a sirup which, upon solution in ten volumes of hot methyl alcohol and cooling, deposited 4.2 g. of ketose rotating +60.0° in water. One recrystallization produced 2.6 g. of sugar melting at 170–174° and rotating +66.9° in water (*c*, 2); these data are in accord with the melting point 171–174° and rotation +67.5° in water (*c*, 2.5) reported by Austin for D-glucoheptulose.[5] The combined mother liquors, concentrated in a desiccator over calcium chloride, furnished 6.3 g. of crude ketose, from which was separated 5.1 g. of D-mannoheptulose. The melting point 152° and rotation +29.2° in water (*c*, 2) are in agreement with the values recorded by LaForge.[2] A mixture of the synthetic and natural sugars melted at 152° also. The identification was completed by the "mixed solubility" method;[13] thus, 10 cc. of 80% alcohol at 3° was found to contain 0.3870, 0.3865, and 0.3868 g. from undersaturation, and 0.3860, 0.3862, and 0.3871 g. from supersaturation, of the synthetic, natural, and mixed D-mannoheptuloses, respectively.

The rearrangement of D-manno-D-gala-heptose according to Danilow's procedure was carried out by refluxing a solution of 25 g. of the dried sugar in 250 cc. of pyridine for four and one-half hours. The pyridine was removed by distillation *in vacuo*, and the residue, with rotation +54.5° in water (*c*, 25), treated with bromine and barium benzoate to remove aldehyde sugars as in the preceding experiment. The barium salts weighed 25.3 g., and represented about 72% of the original heptose. From the mother liquor was obtained 5.2 g. of pure, recrystallized D-mannoheptulose melting at 152° and rotating +29.2° in water (*c*, 2).

D-Mannoheptulose from the Avocado.—A number of varieties of avocado were examined but none was found to contain as much ketose as the Trapp variety recommended by LaForge. His procedure was modified somewhat, as follows. The crushed pulp was mixed thoroughly with sufficient 20% ethyl alcohol to make a thin soup, and left overnight. The mixture was heated on a steam-bath until the pulp was well coagulated and then filtered by gravity through folded filters or run through a fruit press. The following morning the filtrate was siphoned from any oil which had collected at the surface of the liquid. The solution was clarified and decolorized by heating to 95° with activated carbon, filtered through carbon, and concentrated *in vacuo* to a thin sirup which was poured into eight volumes of methyl alcohol. The precipitated gum separated in small flakes, showing only a slight reducing action toward Fehling solution. The filtered solution was concentrated *in vacuo* to a thick sirup, which was dissolved in four volumes of methyl alcohol and cooled to 5°. Crystalline perseitol separated first, and was filtered after three hours. The mother liquor, allowed to stand for several days in the ice-box, deposited mannoheptulose contaminated with perseitol. The latter was removed by dissolving each 50-g. portion of the powdered crude sugar in 200 cc. of hot 80% methyl alcohol, and allowing the perseitol to crystallize overnight in the ice-box. The filtered solution was concen-

(9) See for example Haworth and Hirst, *J. Chem. Soc.*, 2625 (1930).
(10) Purves and Hudson, THIS JOURNAL, **59**, 1174 (1937).
(11) Schlubach and Graefe, *Ann.*, **532**, 218 (1937).
(12) Hudson and Isbell, THIS JOURNAL, **51**, 2225 (1929).
(13) Montgomery and Hudson, *ibid.*, **52**, 2105 (1930).

trated *in vacuo;* the sirup, dissolved in methyl alcohol and cooled, deposited practically pure D-mannoheptulose, melting at 152°, and rotating +29.1° in water (*c*, 2). From 21 kg. of pulp, from 36 avocados, there was obtained 315 g. of pure D-mannoheptulose and 75 g. of perseitol, plus 400 g. of non-reducing gum and 310 g. of a final sirup containing 80% solids.

α-Methyl-D-mannoheptuloside.—Glycoside formation occurred readily when a 1% solution of the ketose in absolute methyl alcohol was made 0.25 *N* in hydrogen chloride (see Fig. 1). The rotation, +34.7° after one minute, changed rapidly to +47.5° at the end of four minutes, remained constant during the next three minutes,[14] and then increased slowly to a constant value +71.3° at the end of three hours.[15] The reducing power of the solution was negligible after thirty minutes. An equilibrated solution from 10 g. of ketose was neutralized with silver oxide, the excess silver removed with hydrogen sulfide, and the filtrate concentrated *in vacuo* to a sirup which crystallized after two weeks. The product weighed 7.2 g. It showed no reducing power toward Fehling solution. It is readily soluble in water, methyl alcohol, and ethyl alcohol, sparingly soluble in ethyl acetate, insoluble in ether. Recrystallized from methyl alcohol, as small prisms, it melted at 142°, and showed a constant rotation of +69.0° in water (*c*, 2).

Anal. Calcd. for $C_8H_{16}O_7$: C, 42.83; H, 7.19; OCH_3, 13.84. Found: C, 42.9; H, 7.17; OCH_3, 13.7.

Hydrolysis of α-Methyl-D-mannoheptuloside.—The hydrolysis of a 4.2% solution of the heptuloside in 0.005 *N* aqueous hydrochloric acid at 98° was followed polarimetrically, the samples being cooled rapidly to 20° for measurement. The observed readings, in circular degrees, were +2.82° at zero time, +2.35° after three minutes, +1.72° after ten minutes, +1.43° after fifteen minutes, and a final constant value of +1.17°. The average hydrolysis constant in terms of minutes and decimal logarithms, $k = \frac{1}{t} \log \frac{(r_0 - r_\infty)}{(r - r_\infty)}$, is 0.050. The final reading +1.17°, calculated on the basis of complete hydrolysis, corresponds to a specific rotation of +29.7° as compared with the value +29.2° for the pure mannoheptulose.

D-Mannoheptulose α-Hexaacetate.—The acetylation of 10 g. of pure D-mannoheptulose was accomplished by dissolving the sugar in a mixture of 50 cc. of acetic anhydride and 50 cc. of pyridine at 0°. The solution was kept at that temperature for forty-eight hours, then poured into ice water; the chloroform extract was washed, dried, and concentrated in the usual manner. The resulting sirup crystallized readily. By recrystallization from warm ether there was obtained 18.8 g. (85%) of large prisms, melting at 110°, and rotating +39.0° in chloroform (*c*, 2).

Anal. Calcd. for $C_{19}H_{26}O_{13}$: C, 49.35; H, 5.67; acetyl, 13.00 cc. of 0.1 *N* NaOH per 100 mg. Found: C, 49.26; H, 5.70; acetyl, 13.03 cc.

(14) This plateau may be an indication of extremely rapid furanoside formation, and the subsequent rearrangement to the pyranoside form.

(15) The final rotation for glycoside formation at the boiling point of the solution was +73.5°. Calculated as methylmannoheptuloside, the rotations become +66.9° and 68.9°, respectively.

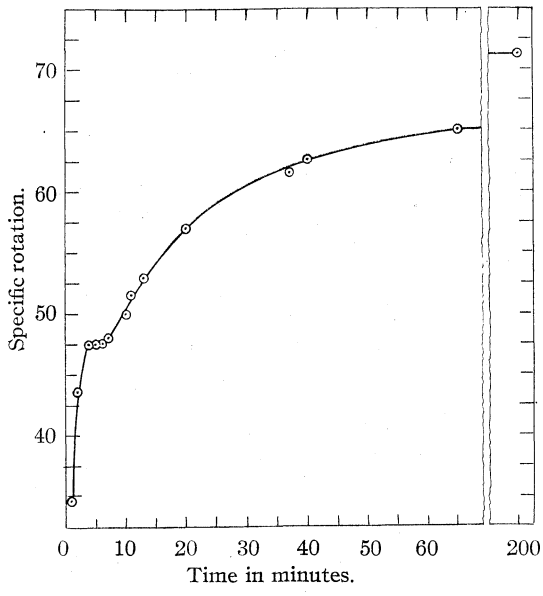


Fig. 1.—Change in rotation of a 1% solution of D-mannoheptulose in 0.25 *N* methyl alcoholic hydrochloric acid at 20°.

α-Acetobromo-D-mannoheptulose.—A paste of 10 g. of crystalline D-mannoheptulose α-hexaacetate and 5 cc. of glacial acetic acid, cooled to 0°, was dissolved at that temperature in 30 cc. of glacial acetic acid which had been saturated previously with gaseous hydrobromic acid. After two hours in an ice-bath the solution was poured into ice water and extracted with chloroform. The chloroform solution was washed, dried, and concentrated *in vacuo;* the resulting sirup, taken up in anhydrous ether, deposited 5.3 g. (50%) of rosets of prisms, melting at 92°. The recrystallized acetobromo-D-mannoheptulose rotated +104.0° in chloroform (*c*, 2).

Anal. Calcd. for $C_{17}H_{23}O_{11}Br$: Br, 16.55. Found: Br, 16.28.

Pentaacetyl-α-methyl-D-mannoheptuloside from α-Methyl-D-mannoheptuloside.—A 3-g. portion of the pure glycoside was acetylated at 0° with a mixture of 30 cc. each of acetic anhydride and pyridine. The product, isolated in the customary manner, weighed 5.3 g. Upon recrystallization from ether it separated in clusters of radiating needle-like prisms melting at 64° and rotating +49.5° in chloroform (*c*, 2). Deacetylation regenerated the original glycoside.

Anal. Calcd. for $C_{18}H_{26}O_{12}$: C, 49.74; H, 6.03; OCH_3, 7.14; acetyl, 11.51 cc. of 0.1 *N* NaOH per 100 mg. Found: C, 49.74; H, 5.90; OCH_3, 7.10; acetyl, 11.48 cc.

Pentaacetyl - α - methyl - D - mannoheptuloside from α-Acetobromo-D-mannoheptulose.—A solution of 4 g. of the pure acetobromo compound in 30 cc. of anhydrous methyl alcohol was shaken with 4 g. of silver oxide for five minutes. The halogen-free filtrate from the silver residues was concentrated *in vacuo* and the sirup dissolved in ether. The 1.5 g. of pentaacetyl-α-methyl-D-mannoheptuloside thus obtained had the same melting point, 64°, and the same rotation, +49.5°, as the sample prepared by acetylation of the α-methyl-D-mannoheptuloside

Summary

1. D-Mannoheptulose has been obtained by the rearrangement of D-α-mannoheptose (D-manno-D-gala-heptose) in dilute barium hydroxide solution, and also in pyridine solution.

2. D-Mannoheptulose α-hexaacetate, α-acetobromo-D-mannoheptulose, α-methyl-D-mannoheptuloside, and pentaacetyl-α-methyl-D-mannoheptuloside have been described.

3. A comparison of the rotations of these mannoheptulose derivatives with the rotations of the corresponding derivatives of D-mannose indicates a pyranoid ring in the mannoheptulose compounds.

4. α-Methyl-D-mannoheptuloside is very readily formed and very readily hydrolyzed; this behavior has been shown not to be inconsistent with the ketopyranoside formulation.

WASHINGTON, D. C. RECEIVED MARCH 27, 1939

[CONTRIBUTION FROM THE POLARIMETRY SECTION, NATIONAL BUREAU OF STANDARDS, AND THE NATIONAL INSTITUTE OF HEALTH, U. S. PUBLIC HEALTH SERVICE]

Relations between Rotatory Power and Structure in the Sugar Group. XXXIII. The Alpha and Beta Methyl Pyranosides of L-Fucose (L-Galactomethylose) and their Triacetates[1]

BY R. C. HOCKETT, F. P. PHELPS AND C. S. HUDSON

In 1925 one of us[2] reported two independent calculations of the specific rotation of α-methyl-L-fucoside, based upon its relationship to α-methyl-D-galactoside and to α-L-fucose, respectively; the values so predicted were −188 and −190. The deviation from the value (−122) that had been observed by Tadokoro and Nakamura[3] was so great that the purity of their product appeared doubtful; its rotation indicated that it might be a mixture of α- and β-forms. We undertook the preparation of the pure forms and soon found that the α-isomer is purified readily by recrystallization; its specific rotation was observed to be −196.9 as the average value of eleven preparations. It was then sought to obtain the pure β-form from the mother liquors of the other; the fractionation proved to be very slow and difficult because the isomers form mixed crystals over a wide range of composition, but it was learned that the β-form is certainly dextrorotatory. In 1930 Votoček and Valentin[4] reported the specific rotation of α-methyl-rhodeoside (α-methyl-D-fucoside) as +190. We then reinvestigated the purification of α-methyl-L-fucoside, confirmed our higher value and prepared the β-methyl-L-fucoside by fractional crystallization from the mother liquors of the α-form, obtaining a product of specific rotation +14, which was not changed by further recrystallization of the substance. In 1932 Minsaas[5] reported the values −197 and +16 for the specific rotations of the α- and β-methyl-L-fucosides, respectively, and Schlubach and Wagenitz[6] found the value −14 for β-methyl-D-fucoside (prepared by synthesis from D-galactose) and −5.9 for its triacetate. It was then discovered[7] that the β-L-fucoside forms a crystalline molecular compound with potassium acetate, but that the α-isomer does not, which enabled us to obtain the β-isomer readily in definite purity; its rotation confirmed the value +14. In 1937 Minsaas[8] reported the preparation of the triacetates of α- and β-methyl-L-fucosides (α-form, m. p. 74°, $[\alpha]^{20}D$ −151; β-form, m. p. 99°, $[\alpha]^{20}D$ +7.0). We have prepared both of these substances and find for the α-form, m. p. 67 and $[\alpha]^{20}D$ −149.7, and for the β-form, m. p. 96–97° and $[\alpha]^{20}D$ +7.1; by deacetylating them we have confirmed the purity of the original fucosides of rotations −197 and +14, respectively. It is evident that the value −197 which Minsaas found for the α-fucoside is substantially correct and that the α-methyl-D-fucoside (rhodeoside) of Votoček (+190) was an impure preparation containing some of the β-isomer. Our data con-

(1) Publication authorized by the Director of the National Bureau of Standards and by the Surgeon General, U. S. Public Health Service. The research was begun in 1926 at the National Bureau of Standards (F. P. P. and C. S. H.) and completed at the National Institute of Health (R.C.H. and C. S. H.). No. XXXII was published in THIS JOURNAL, **61**, 1525 (1939).

(2) Hudson, *ibid.*, **47**, 275 (1925).

(3) Tadokoro and Nakamura, *J. Biochem.* (Japan), **2**, 461 (1923).

(4) Votoček and Valentin, *Coll. Czechoslov. Chem. Commun.*, **2**, 36 (1930).

(5) Minsaas, *Rec. trav. chim.*, **51**, 475 (1932).

(6) Schlubach and Wagenitz, *Ber.*, **65**, 304 (1932).

(7) Watters, Hockett and Hudson, THIS JOURNAL, **56**, 2199 (1934).

(8) Minsaas, *Rec. trav. chim.*, **56**, 623 (1937). On p. 624 the rotations of β-methyl-L-fucoside and its triacetate are recorded as negative, obviously through a misprint because the context shows that the substances are dextrorotatory.

firm Minsaas' rotations except in the case of β-methyl-L-fucoside, for which his value (+16) appears to be about two degrees too large, due doubtless to the smallness of his observed reading (0.41°). The rotational data from our work are recorded in Table I. It is seen that the difference for the methyl fucosides (−37,600) agrees well with values found previously[9] from five other pairs of methyl glycosides; the difference for the acetylated methyl fucosides (−45,150) is decidedly less than would be expected (about −53,500). In an accompanying article[10] it is shown from the oxidation of these fucosides by periodic acid that they are pyranosides and that their alpha and beta classification, which has been made on the basis of their rotations, is correct from the standpoint of the configurations of carbon atom one.

TABLE I

THE ROTATIONS OF THE α- AND β-FORMS OF METHYL-L-FUCOPYRANOSIDE AND THEIR TRIACETATES

Substance	Mol. wt.	$[\alpha]^{20}D$	$[M]D$	Difference
α-Methyl-L-fucopyranoside	178	−197[a]	−35070	−37600
β-Methyl-L-fucopyranoside	178	+ 14.2[a]	+ 2530	
Triacetates of				
α-Methyl-L-fucopyranoside	288	−149.7[b]	−43110	−45150
β-Methyl-L-fucopyranoside	288	+ 7.1[b]	+ 2040	

[a] In water. [b] In chloroform.

Experimental

Preparation of L-Fucose from Seaweed (Hockett and Hudson).[11]—The seaweed (*Ascophyllum nodosum*) is cleaned by soaking it for several days in 3% hydrochloric acid, washing free of chlorides and drying on wire bottomed trays over a radiator until brittle; it is then broken into small pieces and stored.[12] A typical sample lost 12.6% moisture when dried at 110° to constant weight. A kilogram of air-dried seaweed (12.6% moisture) is hydrolyzed by boiling under reflux with 5 liters of 2% sulfuric acid for four hours. The cooled solution is filtered from insoluble material on a large porcelain filter, and the filtrate is neutralized to litmus with 110 g. of calcium carbonate (using a few drops of capryl alcohol to control foaming), followed by the addition of the necessary amount of calcium hydroxide. Seventy grams of decolorizing carbon is added and the mixture allowed to stand overnight. The solids are then removed by decantation and filtration, and the nearly colorless solution is concentrated *in vacuo* to about 2.5 liters, filtered from precipitated calcium sulfate, and further concentrated to 200 cc. Warm methyl alcohol (900 cc.) precipitates a granular material, which is filtered off and washed with three portions, 100 cc. each, of the same solvent. Further impurity is removed by adding 500 cc. of ether to the alcoholic filtrate and filtering again. The solution is now concentrated to a sirup of honey-like consistency, which is dissolved in absolute alcohol to a volume of about 200 cc. At this stage one may proceed to crystallize a portion of the fucose or to prepare the crystalline phenylhydrazone. To follow the first procedure, the 200-cc. solution is reconcentrated to a thick sirup (to reduce the water content), which is then dissolved in about 75 cc. of absolute alcohol and the solution seeded; the yield of crystalline fucose ranges from 13 to 25 g., and the remainder may be recovered from the mother liquor through the phenylhydrazone. To follow the second procedure, there is added to the 200 cc. of alcoholic solution 70 cc. of phenylhydrazine; fucose phenylhydrazone soon crystallizes and the mixture becomes solid. After standing overnight the hydrazone is filtered, washed thrice with absolute alcohol and dried at 50° (wt. 65 to 100 g., corresponding to 43–63 g. of fucose, which represents 5 to 7% of the dry seaweed). The fucose phenylhydrazone is readily converted to the sugar by heating 75 g. of it at 90° for one-half hour with 1800 cc. of water and 36 g. of benzaldehyde, with frequent stirring; an additional 10 g. of benzaldehyde is then added, and the heating and stirring are continued for fifteen minutes. The solution is cooled to 0° and the benzaldehyde hydrazone filtered off through a layer of decolorizing carbon; the filtrate is extracted three times with 100 cc. of chloroform (to remove benzoic acid and excess benzaldehyde) and concentrated to a sirup, which is dissolved in 50 cc. of hot absolute alcohol. Crystallization of fucose begins promptly and is allowed to continue overnight in a refrigerator. The yield of crystalline fucose, after filtration, washing with absolute alcohol and drying at 60° two hours, is about 40 g. The sugar is recrystallized (70% yield) by dissolving in 3 parts of water, concentrating to a sirup *in vacuo* and taking up with 3 volumes of absolute alcohol; the m. p. was 140–141° and the equilibrium $[\alpha]^{20}D$ was −74.9. The rotation of L-fucose, after several recrystallizations to constancy, was $[\alpha]^{20}D$ −76.0. The sugar may also be recrystallized from its solution in absolute methyl alcohol, prepared by refluxing the dry sugar with the solvent. The yield of crystalline fucose from 1 kg. of moisture-free cleaned seaweed through the phenylhydrazone procedure has ranged between 39 and 60 g.

The α- and β-Forms of Methyl-L-fucopyranoside. (a) (Experiments by Phelps).—The fucoside was obtained readily by refluxing 15 g. of fucose for six hours with methyl alcohol containing 1% hydrochloric acid, removing the acid as silver chloride, concentrating *in vacuo* to a sirup and crystallizing from ethyl acetate; yield 7.3 g. After one recrystallization from methyl alcohol and ethyl acetate the plate-like crystals showed $[\alpha]^{20}D$ −197.0 in water. The mother liquor deposited material which proved to be mixed crystals of the α- and β-fucosides. The pure β-form is difficult to obtain from these mixed crystals, but by working with larger quantities and fractionating repeatedly it was finally obtained pure; it showed $[\alpha]^{20}D$ +14.0 ± 0.3 in water (*c*, 4). It crystallizes from methyl or ethyl alcohol and ethyl acetate as long slender almost thread-like needles, which are anhydrous;

(9) Dale and Hudson, THIS JOURNAL, **52**, 2534 (1930).

(10) Maclay, Hann and Hudson, *ibid.*, **61**, 1660 (1939).

(11) These directions follow in general, but with some modifications, those of E. P. Clark, *J. Biol. Chem.*, **54**, 65 (1922).

(12) Grinding the seaweed is not necessary; its dust seems to be harmful to some persons.

from water it forms rather long thick prismatic crystals, which are a monohydrate that is stable in air but which soon becomes anhydrous in a desiccator over lime, passing to a white powder.

(b) (**Experiments by Hockett**).—α-Methyl-L-fucoside, prepared by refluxing fucose with 1% hydrochloric acid in methanol for twelve hours and isolated as described above, was recrystallized from methanol–ethyl acetate to constant properties readily. The pure substance shows m. p. 154° (corr.) and $[\alpha]^{20}D$ −197.1 (*c*, 3.42; 4-dm. tube); a sample which was prepared by deacetylation of its purified triacetate (described below) showed the rotation −197.0 (*c*, 4.16; 4-dm. tube). Analyses for carbon, hydrogen and methoxyl gave the expected values (the substance has been analyzed by previous investigators). The mother liquor from the α-form was treated in absolute alcoholic solution with double the theoretical quantity of dried potassium acetate (CH_3COOK) dissolved in absolute alcohol; silky needles of the 1:1 molecular compound of the β-fucoside separated at once and they were recrystallized from hot absolute alcohol. The β-fucoside was obtained by preparing its triacetate from this molecular compound (as described below) and deacetylating the triacetate with barium methylate, the over-all yield of the two steps being nearly quantitative. The pure β-L-fucoside showed m. p. 121–123° and $[\alpha]^{20}D$ +14.2 (*c*, 3.9; 4-dm. tube) in water.

The α- and β-Forms of Triacetyl-methyl-L-fucopyranoside.—Two grams of the pure α-fucoside was acetylated by heating for thirty minutes on the steam-bath with 12 cc. of acetic anhydride and 6 cc. of pyridine, followed by isolation according to standard procedure; yield 85%. The substance was recrystallized from hot water; a further recrystallization from aqueous methyl alcohol did not change its rotation, which was $[\alpha]^{23}D$ −149.1 (*c*, 0.9) in chloroform (Phelps). The pure α-fucoside was also acetylated by heating with 5 parts of acetic anhydride and one-quarter part of fused sodium acetate; the triacetate was isolated by standard procedure and recrystallized from absolute alcohol, as brilliant plates, which gave the correct analyses (previously reported by Minsaas) for methoxyl, acetyl, carbon and hydrogen, melted at 67° and showed $[\alpha]^{20}D$ −149.7 (*c*, 1.8) in chloroform (Hockett). The β-methyl-L-fucoside triacetate was prepared by heating 5 g. of its pure potassium acetate compound for one hour on the steam-bath with 20 cc. of acetic anhydride, and isolating the substance through standard procedure (yield, quantitative); by recrystallization from absolute alcohol, from which it separates in clear tablets, it is readily brought to constant properties, m. p. 96–97° and $[\alpha]^{20}D$ +7.1 (*c*, 4.5; 4-dm. tube) in chloroform (Hockett). Its analysis showed the correct values for carbon, hydrogen, methoxyl and acetyl, confirming Minsaas' reported analysis for the substance.

Summary

The α- and β-methylpyranosides of L-fucose (L-galacto-methylose) and their triacetates, previously reported by Minsaas, have been reprepared and their purity carefully controlled. The results confirm Minsaas' rotations except in the case of β-methyl-L-fucoside, the rotation of which is found to be +14.2 instead of +16.0. Some modifications of E. P. Clark's directions for preparing crystalline fucose from seaweed are presented. The difference of rotations of the glycosides shows the normal value; the difference for their triacetates is decidedly lower than would be expected.

WASHINGTON, D. C. RECEIVED APRIL 3, 1939

[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF HEALTH, U. S. PUBLIC HEALTH SERVICE]

The Cleavage of the Carbon Chains of Some Methyl Aldohexomethylo-pyranosides by Oxidation with Periodic Acid[1]

BY W. DAYTON MACLAY, RAYMOND M. HANN AND C. S. HUDSON

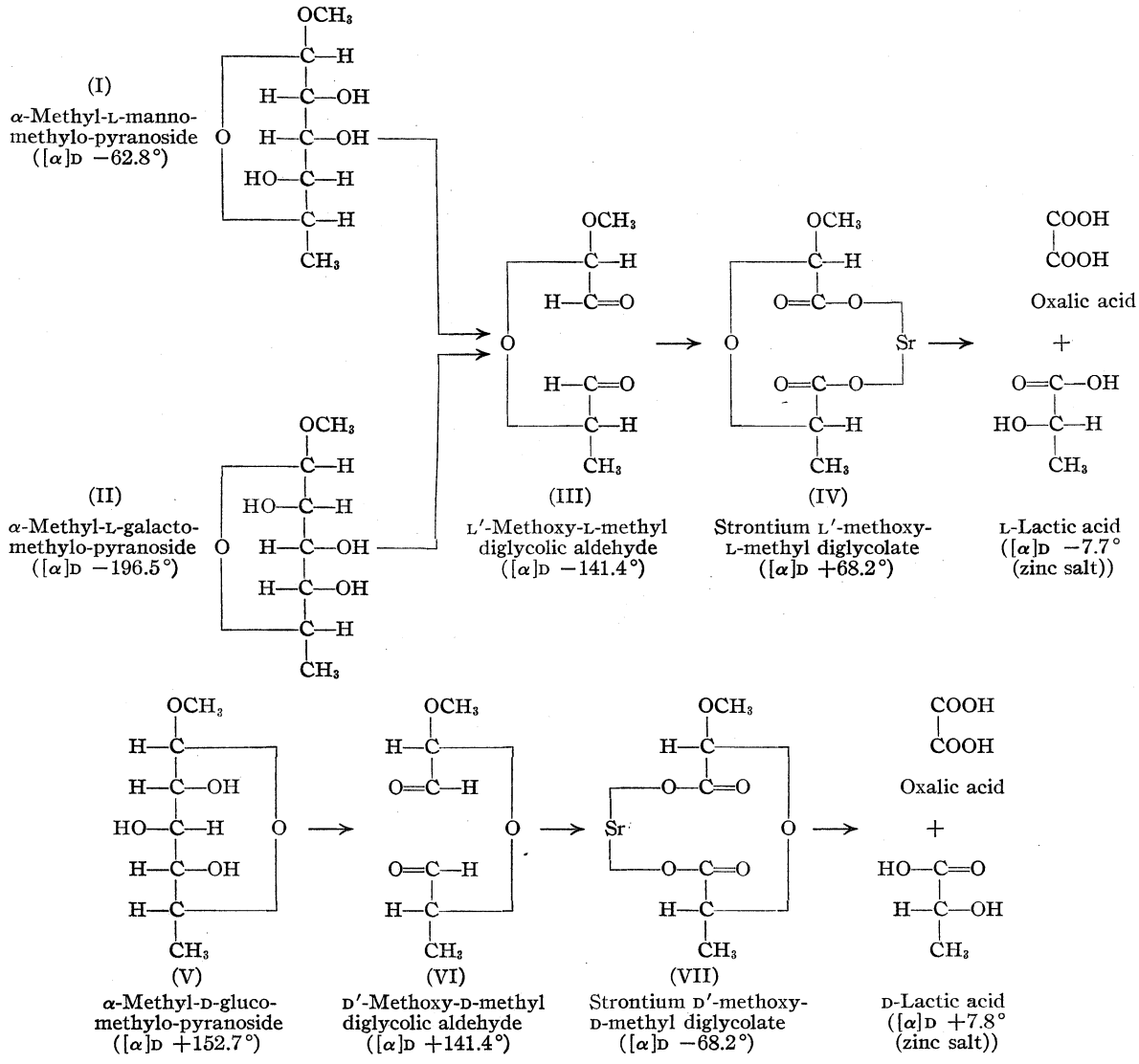
Jackson and Hudson[2] have described the crystalline dialdehyde (III) that results from the oxidation of α-methyl-L-mannomethylo-pyranoside[3] (I) with periodic acid. We have now obtained this same dialdehyde by the similar oxidation of α-methyl-L-galactomethylo-pyranoside (II), and by oxidation of this dialdehyde with bromine water in the presence of strontium carbonate have obtained the crystalline strontium salt of the corresponding dibasic acid (IV). In like manner it has been found that the periodic acid oxidation of α-methyl-D-glucomethylo-pyranoside (V) yields the crystalline enantiomorphous dialdehyde (VI), from which in turn has been prepared the crystalline strontium salt of the corresponding dibasic acid (VII), the enantiomorph of (IV). The hydrolysis of the dibasic acid formed from the strontium salt (IV) yields L-lactic acid[4] in optical

(1) Publication authorized by the Surgeon General, U. S. Public Health Service.

(2) Jackson and Hudson, THIS JOURNAL, **59**, 994 (1937).

(3) We use the nomenclature for methyl pentoses that was suggested by Votoček: L-mannomethylose = L-rhamnose, L-galactomethylose = L-fucose, D-glucomethylose = D-isorhamnose (syn. D-epirhamnose). The D and L symbols refer throughout to configuration.

(4) In the case of the optically active lactic acids and their zinc salts the L-lactic acid is dextrorotatory and its zinc L-lactate levorotatory, while the D-lactic acid is levorotatory and its zinc D-lactate dextrorotatory. D-Lactic acid has the configuration $CH_3—\overset{H}{\underset{OH}{C}}—COOH$.

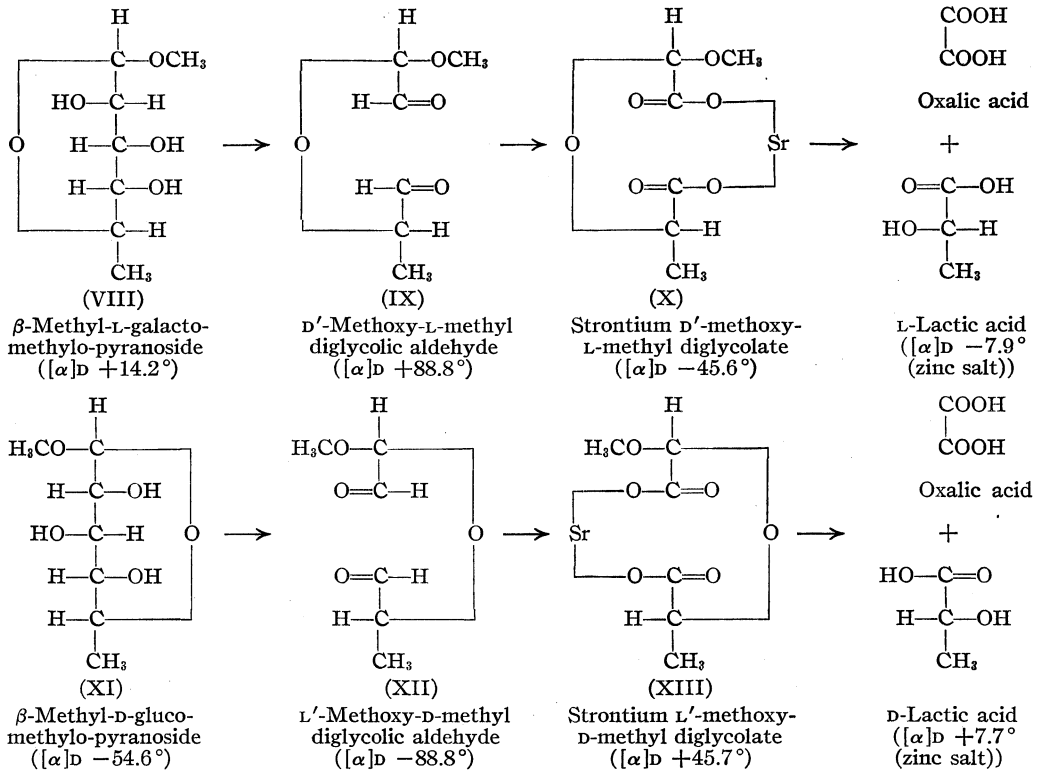


purity, and like treatment of the dibasic acid formed from the strontium salt (VII) yields D-lactic acid. The presence of lactic acid proves that all of these glycosides are pyranosides, and the correlation of the enantiomorphous forms of lactic acid with the known sugar configurations of Fischer proves the configurations of the lactic acids. We believe that this is the most simple and direct way of bringing the lactic acids into Fischer's system of configurations; it supplements the recent proof[2] of the configurations of the forms of glyceric acid that was obtained from the oxidation of the methyl-aldohexopyranosides with periodic acid. The results also prove that the two methylosides, α-methyl-L-mannomethyloside and α-methyl-L-galactomethyloside, have the same configuration for carbon atom one, enantiomorphous to the configuration for carbon atom one in α-methyl-D-glucomethyloside, both configurations having been designated alpha (*i. e.*, α-L- and α-D, respectively) in the past from rotatory considerations. The preparation of α-methyl-D-glucomethylo-pyranoside from α-methyl-D-gluco-pyranoside, by Helferich, Klein and Schafer[5] and by Compton[6] (see experimental part) furnishes the structural proof of the alpha classification of the three methylo-pyranosides.

The oxidation of β-methyl-L-galactomethylo-pyranoside (VIII) with periodic acid has yielded a new dialdehyde (IX) which is also crystalline and passes on bromine oxidation to a new dibasic acid, the strontium salt (X) of which

(5) Helferich, Klein and Schafer, *Ber.*, **59**, 84 (1926); *Ann.*, **447**, 19 (1926).

(6) Compton, THIS JOURNAL, **60**, 398 (1938).

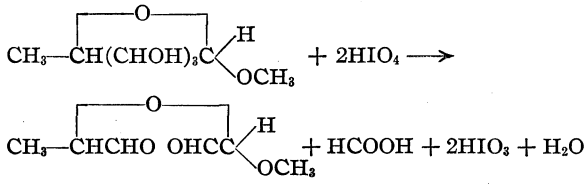


is crystalline. The similar oxidation of β-methyl-D-glucomethylo-pyranoside (XI) has yielded in crystalline state the dialdehyde (XII), which is the enantiomorph of (IX), and the strontium salt (XIII), which is the enantiomorph of (X). Hydrolysis of the dibasic acid of (X) yields L-lactic acid and that of the acid of (XIII) yields D-lactic acid. The two β-glycosides are therefore pyranosides and possess enantiomorphous configurations for carbon atom one, which are the opposites of the configurations for the corresponding α-glycosides. Since β-methyl-D-glucomethylo-pyranoside has been correlated as regards carbon atom one with β-methyl-D-glucoside,[7] the present results prove that the customary α- and β-designations of these methylosides are correct from the stereo-structural standpoint. It is also evident from the rotatory data of column 3, Table III, and Fig. 1 that these methylosides are pure substances, no one of them being a crystalline molecular combination of α- and β-forms.[8]

The four crystalline dialdehydes (two enantiomorphous pairs) and the four corresponding crystalline strontium salts are reference substances which can be employed to learn the ring structure and the α- or β-classification of any methyl pyranoside of the remaining aldohexomethyloses or of any methyl furanoside of the aldopentomethyloses.

The rotational relationships of the aldohexomethylo-pyranosides and their products of oxidation are shown in Table I.

The oxidation of these aldohexomethylo-pyranosides by periodic acid is practically quantitative, one mole of the glycoside consuming 2 moles of periodic acid according to the reaction equation



The distinction between a pyranoside and a furanoside probably can be made very readily in the aldohexomethylose series, since a mole of the pyranoside consumes 2 moles of periodic acid and generates one mole of formic acid, but a mole of the furanoside can be expected to consume only one mole of the acid and produce no formic acid.

It has been known in the past from methylation data[9] and some correlations that three of the

(7) Fischer and Zach, *Ber.*, **45**, 3761 (1912).

(8) *Cf.* Jackson and Hudson, THIS JOURNAL, **61**, 959 (1939).

(9) Hirst and Macbeth, *J. Chem. Soc.*, 22 (1926); Charlton, Haworth and Peat, *ibid.*, 89 (1926), and refs. 5, 6 and 7.

TABLE I

PRODUCTS OF OXIDATION OF THE ALDOHEXOMETHYLO-PYRANOSIDES

Substance	Methyl glycoside $[\alpha]^{20}D$	Dialdehyde (monohydrate)[a] $[\alpha]^{20}D$	Dibasic acid[b] $[\alpha]^{20}D$	Strontium salt[c] $[\alpha]^{20}D$	Resulting zinc lactate[d] $[\alpha]^{20}D$
α-Methyl-L-galactomethylo-pyranoside	−196.5°	−141.4°	−23.3°	+68.2°	−7.7°
α-Methyl-D-glucomethylo-pyranoside	+152.7°	+141.4°	+23.5°	−68.2°	+7.8°
β-Methyl-L-galactomethylo-pyranoside	+14.2°	+ 88.8°	−41.6°	−45.6°	−7.9°
β-Methyl-D-glucomethylo-pyranoside	− 54.6°	− 88.8°	+41.9°	+45.7°	+7.7°

[a] See Table III, note (a). [b] Determined by liberating the acid (c, 0.92–1.05) from its pure, anhydrous strontium salt with an equivalent of hydrochloric acid. [c] See Table IV, note *a*. [d] See Table V, note *a*.

substances here studied (α-methyl-L-mannomethylo-pyranoside and α- and β-methyl-D-glucomethylo-pyranosides) are pyranosides; the present work confirms these ring allocations, extends the proof of the pyranoside structure to the two other glycosides (α- and β-methyl-L-galactomethylo-pyranosides) and proves the α- and β-classification by structural correlation.

We are indebted to Dr. A. E. Knauf for preparing the α- and β-methyl-D-glucomethylosides used in the present investigation. We also express our appreciation to Dr. W. T. Haskins for performing the micro-analyses in connection with this work.

Experimental

Preparation of the Methyl Aldohexomethylo-pyranosides.—The α- and β-methyl-L-galactomethylo-pyranosides were prepared from L-galactomethylose and methyl alcohol containing 1.5% of dry hydrochloric acid gas according to Hockett, Phelps and Hudson.[10] The α-methyloside melted at 157–158° (corr.) and rotated −196.5 ± 0.5°[11] in water, and the β-isomer melted at 122° (corr.) and rotated +14.2° in water.

The α-methyl-D-glucomethylo-pyranoside was obtained by deacetylation of its triacetate, which was prepared by Compton's[6] procedure of tosylation and acetylation of α-methyl-D-glucopyranoside and subsequent iodination and reduction of the terminal carbon atom. The purified triacetate melted at 78–79° (corr.) and rotated +153.4° in chloroform, in good agreement with Compton's values of 77–78° and +153.6°; Helferich, Klein and Schafer[5] reported a melting point of 75° and a rotation of +159.2° in chloroform for the triacetate, which they prepared by reduction of α-methyl-6-bromo-gluco-pyranoside triacetate. Pure α-methyl-D-glucomethylo-pyranoside was found to melt at 98–99°, in agreement with Helferich and his co-workers; the rotation, which apparently has not been recorded, was found to be +152.7° (c, 1.75; l, 4) in water.

The β-methyl-D-glucomethylo-pyranoside was prepared from levoglucosan by way of levoglucosan triacetate, 1,6-dibromo-glucose triacetate, β-methyl-6-bromo-glucoside triacetate and β-methyl-D-glucomethyloside triacetate followed by deacetylation. The purified substance melted at 131–132° (corr.) and rotated −54.6° in water, in agreement with the values of 131–132° and −55.1° reported by Fischer and Zach.[7]

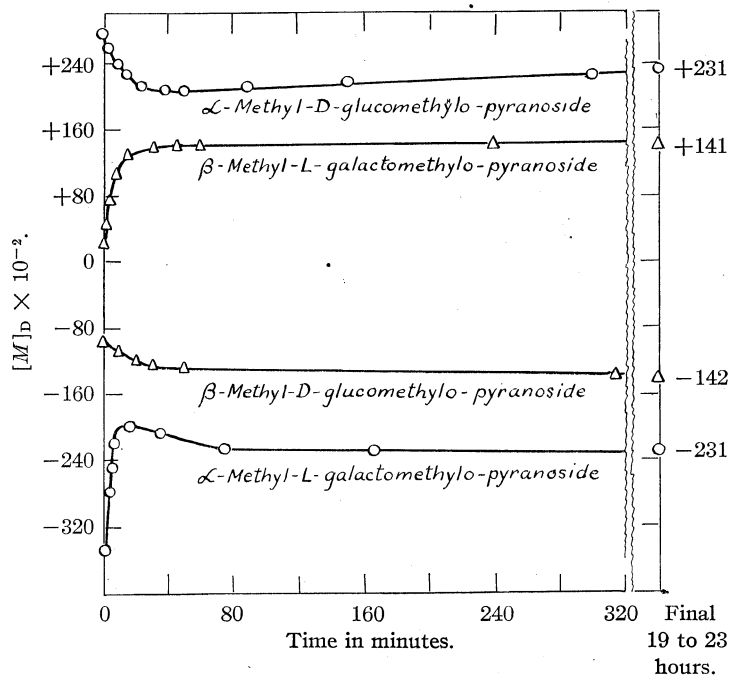


Fig. 1.—Rotatory changes during the oxidation of the methyl aldohexomethylo-pyranosides.

Rotatory Changes during the Oxidation of the Methyl Aldohexomethylo-pyranosides.—To a solution of 0.25 g. of the methyloside in 20 cc. of water was added 4.83 cc. of 0.610 M periodic acid (2.1 molecular equivalents). As quickly as possible the solution was diluted to 25 cc., thoroughly shaken, transferred to a 4-dm. tube and the rotatory changes observed. The solution was kept in a 20° room during the course of the reaction. The rotatory changes during the oxidation are recorded in Table II, and shown in Fig. 1. When the rotation of the solution had become constant, 5 cc. of it was analyzed for periodic acid.[12] The results showed that one mole of the aldohexomethylo-pyranosides (in the order listed in Table II)

(10) Hockett, Phelps and Hudson, THIS JOURNAL, **61**, 1658 (1939).

(11) Unless otherwise stated all rotations are constant specific rotations at 20° for sodium light.

(12) Fleury and Lange, *J. pharm. chim.*, [8] **17**, 107 (1933).

had consumed 1.99, 1.98, 1.99 and 1.99 moles, respectively, of periodic acid. This conforms with the equation previously stated.

TABLE II

ROTATORY CHANGES DURING THE OXIDATION OF THE METHYL HEXOMETHYLO-PYRANOSIDES TO DIALDEHYDES

α-Methyl-L-galactomethylo-pyranoside		α-Methyl-D-glucomethylo-pyranoside		β-Methyl-L-galactomethylo-pyranoside		β-Methyl-D-glucomethylo-pyranoside	
Time[a]	$[M]_D \times 10^{-2}$[b]	Time	$[M]_D \times 10^{-2}$[b]	Time	$[M]_D \times 10^{-2}$[b]	Time	$[M]_D \times 10^{-2}$[b]
0	−350[c]	0	+272[c]	0	+ 25.3[c]	0	− 97.3[c]
3	−281	2	+265	2	+ 46.3	2	− 99.1
4	−252	4	+258	4	+ 75.5	4	−102
5	−238	7	+247	6	+ 94.0	6	−106
6	−218	10	+238	8	+108	9	−110
8	−205	15	+225	10	+116	12	−113
10	−199	25	+213	12	+121	15	−116
12	−199	40	+209	15	+126	19	−118
15	−200	45	+208	20	+133	25	−122
25	−203	50	+209.	30	+138	30	−123
35	−208	90	+214	45	+140	40	−126
75	−226	150	+219	60	+141	50	−129
165	−228	300	+227	240	+141	315	−138
19	−231	22	+231	23	+141	22	−142
hrs.		hrs.		hrs.		hrs.	

[a] Minutes after addition of the periodic acid. [b] Although the solutions were kept in a 20° room throughout the course of the reactions, there were temperature changes in the solutions due to the heat evolved in the oxidation reactions. [c] Calculated from the specific rotations in water of the methyl hexomethylo-pyranosides (mol. wt. 178.1) in the order listed: −196.5 ± 0.5°, +152.7°, +14.2°, −54.6°.

Isolation of the Dialdehydes.—The oxidation of β-methyl-D-glucomethylo-pyranoside and the subsequent isolation of crystalline L′-methoxy-D-methyl diglycolic aldehyde will be described as typical of the procedures used in the oxidation of the four glycosides and the isolation of the corresponding dialdehydes. To a solution of 5.0 g. of pure β-methyl-D-glucomethylo-pyranoside in 148 cc. of water in a 250-cc. volumetric flask was added 99.1 cc. of 0.595 *M* periodic acid (2.1 molecular equivalents). The solution was kept in a 20° room for eighteen hours; it was then made up exactly to 250 cc. with water and its rotatory power determined, which was found to be in agreement with the end-value recorded in Table II for the oxidation of this glycoside. The solution was neutralized to methyl red with a 10% solution of hot strontium hydroxide, and the strontium iodate and periodate salts that precipitated were filtered and washed with water. One gram of strontium carbonate was added and the solution concentrated *in vacuo* to 100 cc. in a water-bath at 50–60°. The strontium carbonate was filtered off and the concentration continued to dryness, partial crystallization of the dialdehyde taking place. The dry residue was extracted with two 50-cc. and two 25-cc. volumes of absolute ethanol, complete extraction being confirmed by the absence of optical activity of an aqueous solution of the crystalline salts remaining after the extraction. The alcoholic extract was concentrated *in vacuo* to a dry sirup which was dissolved in 20 cc. of ether; after shaking for a few minutes, crystals of the dialdehyde began to separate. Twenty-five cubic centimeters of petroleum ether was then added and on standing at room temperature for sixteen hours 2.55 g. of crystalline dialdehyde was obtained. The mother liquor was concentrated to dryness and dissolved in 8 cc. of ethyl acetate, yielding an additional 1.0 g. of crystals. The yield of crystalline product was 3.55 g. (77%) and the rotation of the mother liquor indicated an over-all yield of 95%. Recrystallized from 5 parts of ethyl acetate the L′-methoxy-D-methyl diglycolic aldehyde monohydrate separates in the form of long needles melting at 101–102° (corr.) and rotating −88.8° (*c*, 0.71; *l*, 4) in water.

The four crystalline dialdehydes resulting from the oxidation of their respective parent glycosides form two sets of enantiomorphs. Not only are the properties of the members of each enantiomorphous pair similar in nature, as would be expected of course, but a marked similarity is also found in the properties of the two pairs. Thus, the melting points are nearly the same and the four compounds are readily crystallizable from 5 parts of ethyl acetate or by dissolving them in 10 parts of ether and adding an equal volume of petroleum ether, separating from these solvents as needle-like crystals. Analysis of each of the compounds corresponds to the monohydrate and on heating at 65° over anhydrone in a vacuum (Hyvac pump) they readily sublime without loss of water, which therefore is to be regarded as water of constitution. The yields of crystalline products were 70–80% with overall yields of 90–95%. The rotations, melting points and analyses of these dialdehydes are listed in Table III. The crystallization of the four dialdehydes presents the first opportunity to test an assumption which was made by Jackson and Hudson[2] that the rotation of the non-crystallizable dialdehydes from the periodic acid oxidation of alpha methyl mannopyranoside, etc., is closely given by the constant end rotation of the oxidized solution. In the present case the specific rotations of the dialdehyde monohydrates (mol. wt. 164), as found from the constant end rotations of Table II, are ±23100/164 = ±140.9 and ±14150/164 = ±86.3, in satisfactory agreement with the data of Table III.

Oxidation of the Dialdehydes.—The oxidation of L′-methoxy-D-methyl diglycolic aldehyde to L′-methoxy-D-methyl diglycolic acid and the isolation of the latter in the form of its strontium salt will be described as typical of the technique employed in the oxidation of the four diglycolic aldehydes.

To 10.0 g. of L′-methoxy-D-methyl diglycolic aldehyde monohydrate in 800 cc. of water was added 80 g. of strontium carbonate and 10 cc. of bromine. The oxidation mixture was shaken intermittently for two hours and allowed to stand for an additional fifteen hours. The excess bromine was removed by aeration, the strontium carbonate filtered off and the bromide ions precipitated by shaking with 80 g. of silver carbonate. The silver ions were removed with hydrogen sulfide and the excess hydrogen sulfide by aeration. The solution was concentrated *in vacuo* in a water-bath at 60–70° to a volume of 40 cc. A volume of 40 cc. of absolute ethanol was added and the crystallization of the strontium salt began in a few minutes. After standing in a refrigerator for sixteen hours 11.6 g. of strontium L′-methoxy-D-methyl diglycolate had separated and an additional 0.9 g. was obtained by concentrating the mother liquor to 15 cc. and adding ethanol to saturation; total yield, 12.5 g.

TABLE III

ROTATIONS, MELTING POINTS AND ANALYSES OF THE DIALDEHYDES

Methylo-pyranoside oxidized	Diglycolic aldehyde formed	$[\alpha]^{20}D$[a] (monohydrate)	M. p., °C.	$C_6H_{10}O_4 \cdot H_2O$ C (Calcd. 43.88)	H 7.37	OCH_3 18.91)
α-Methyl-L-galacto-	L′-Methoxy-L-methyl-	−141.4°	98–99.5	43.83	7.56	18.89
α-Methyl-D-gluco-	D′-Methoxy-D-methyl-	+141.4°	98–99	43.83	7.54	18.98
β-Methyl-L-galacto-	D′-Methoxy-L-methyl-	+ 88.8°	100–101	43.78	7.22	18.91
β-Methyl-D-gluco-	L′-Methoxy-D-methyl-	− 88.8°	101–102	44.02	7.31	19.07
α-Methyl-L-manno-	L′-Methoxy-L-methyl-[b]	−143°[c]	101–102	43.88	7.22	18.89

[a] (*c*, 0.77–1.03; *l*, 4) in water. [b] Jackson and Hudson, ref. 2. [c] (*c*, 0.42; *l*, 2) in water.

TABLE IV

ROTATIONS AND ANALYSES OF THE ANHYDROUS STRONTIUM SALTS

Diglycolic aldehyde oxidized	Strontium-diglycolate formed	$[\alpha]^{20}D$[a]	$C_6H_8O_6Sr$ C (Calcd. 27.30	H 3.06	OCH_3 11.76	Sr 33.23)
L′-Methoxy-L-methyl-	L′-Methoxy-L-methyl-	+68.2°	27.29	3.20	11.66	33.24
D′-Methoxy-D-methyl-	D′-Methoxy-D-methyl-	−68.2°	27.45	3.25	11.81	33.33
D′-Methoxy-L-methyl-	D′-Methoxy-L-methyl-	−45.6°	27.37	3.25	11.60	33.03
L′-Methoxy-D-methyl-	L′-Methoxy-D-methyl-	+45.7°	27.20	3.18	11.93	33.06

[a] (*c*, 1.2–1.5; *l*, 4) in water.

(80%). The compound may be recrystallized in a yield of 80% by dissolving in 10 parts of water and adding a like volume of warm 95% ethanol, separating in the form of plate-like crystals rotating +45.7° (*c*, 1.3; *l*, 4) in water. Strontium L′-methoxy-D-methyl diglycolate and its enantiomorph, strontium-D′-methoxy-L-methyl diglycolate, crystallize in the anhydrous form while strontium L′-methoxy-L-methyl diglycolate and its enantiomorph, strontium D′-methoxy-D-methyl diglycolate, when recrystallized by dissolving in 4 parts of warm water and adding 5 parts of warm 95% ethanol, separate in the form of hydrated rhomboid crystals. Although the latter two salts, after being air-dried at room temperature for forty-eight to seventy-two hours, give reproducible specific rotations of +56.3 and −56.2°, respectively, analyses show the substances to contain a small amount of ethyl alcohol in addition to water of hydration. The salts become anhydrous and free of alcohol on heating *in vacuo* (Hyvac pump) over anhydrone at 138° for six hours. The yields of crystalline strontium salts from the oxidations were 80–90%. Rotatory and analytical data concerning them are listed in Table IV.

Hydrolysis of the Acids from the Strontium Salts.—To a solution of 11.2 g. of strontium L′-methoxy-D-methyl diglycolate in 272 cc. of water was added 42.26 cc. of 2.01 *N* sulfuric acid to balance exactly the strontium ions. A volume of 314 cc. of 95% ethanol was added and after standing for eighteen hours the strontium sulfate was filtered off and washed with 50% ethanol. The filtrate was concentrated *in vacuo* to 50 cc. and diluted with 50 cc. of 95% ethanol. The mixture was filtered and the filtrate concentrated to a thick sirup. The sirup was dissolved in 20 cc. of water and reconcentrated to dryness to remove alcohol. The L′-methoxy-D-methyl diglycolic acid sirup was dissolved in 100 cc. of water and heated on a steam-bath for three hours, the rotatory power of the solution becoming constant at the end of two hours. The hydrolyzed solution was diluted to 275 cc., 4 cc. of bromine was added and the reaction mixture allowed to stand for forty-eight hours. The excess bromine was removed by aeration and the oxalic acid precipitated as barium oxalate by neutralizing the solution to phenolphthalein with 0.45 *N* barium hydroxide. The dried barium oxalate (5.0 g., yield 52%) was dissolved in hot dilute hydrochloric acid and the barium ions precipitated with sulfuric acid. On concentration of the filtrate to a small volume the oxalic acid dihydrate crystallized. After recrystallization from water the oxalic acid was identified by its m. p. and its titration with alkali.

The filtrate from the barium oxalate precipitate was balanced with sulfuric acid to remove the barium ions and then shaken with 50 g. of silver carbonate to remove the bromide ions. The silver was removed by precipitation with hydrogen sulfide and the hydrogen sulfide by aeration. The solution was concentrated to 250 cc. and boiled for three minutes with 3 g. of zinc hydroxide. The excess zinc hydroxide was filtered off and the filtrate concentrated *in vacuo* at 60° to a volume of 20 cc. On standing for sixteen hours, 3.2 g. of zinc D-lactate dihydrate separated (yield 59%). Recrystallized from 4 parts of water the zinc D-lactate separated in the form of needle-like crystals and rotated +7.7° (*c*, 3.2; *l*, 4) in water.

Each of the other three strontium salts was treated in the same manner; in each case oxalic acid and an optically active form of zinc lactate were isolated in like yields. The rotations and analyses of the zinc lactates isolated are listed in Table V.

Zinc D-Lactate from Morphine D-Lactate.—The zinc lactates prepared from the four strontium salts exhibited larger rotations (see Table V) than those recorded by Irvine[13] ($[\alpha]D_{15}$ +6.84° (*c*, 5.6) for zinc D-lactate; $[\alpha]D_{20}$ −6.83° (*c*, 7) for zinc L-lactate) for the same compounds which were obtained from racemic lactic acid by resolution with morphine. In order to further establish the rotational values for the optically active zinc lactates a sample of the D-salt was prepared from pure morphine D-lactate. A quantity of morphine D-lactate prepared according to the directions of Irvine[13] was furnished the authors by Dr. E. L. Jackson. Recrystallized twice from 4 parts of 50% ethanol, morphine D-lactate rotates

(13) Irvine, *J. Chem. Soc.*, **89**, 935 (1906).

TABLE V

ROTATIONS AND ANALYSES OF ZINC LACTATES FROM THE STRONTIUM SALTS

Strontium diglycolate	Zinc lactate isolated	$[\alpha]^{20}D^{a}$	$C_6H_{10}O_6Zn \cdot 2H_2O$ C (Calcd. 25.75	H 5.05	Zn 23.39)
L′-Methoxy-L-methyl-	Zinc L-lactate	−7.7°	25.66	5.06	23.30
D′-Methoxy-D-methyl-	Zinc D-lactate	+7.8°	25.73	5.10	23.54
D′-Methoxy-L-methyl-	Zinc L-lactate	−7.9°	25.66	5.12	23.31
L′-Methoxy-D-methyl-	Zinc D-lactate	+7.7°	25.75	5.16	23.56

[a] (*c*, 3.0–3.8; *l*, 4) in water.

−92.2° (*c*, 5.0) in water, in good agreement with the value of −91.8° (*c*, 5) reported by Irvine for this substance. In order to eliminate the possibility of partial racemization by conversion of the D-lactic acid into its calcium salt as done by Irvine, the morphine D-lactate was decomposed and the resultant D-lactic acid isolated according to the directions of Freudenberg and Rhino.[14] To a solution of 9.7 g. of pure morphine D-lactate in 100 cc. of water was added 5 cc. of concentrated ammonium hydroxide. The precipitated morphine was filtered and the filtrate made acid to congo red by the addition of 7.2 cc. of 5.85 *N* sulfuric acid. The solution was then extracted successively with twenty 100-cc. and a like number of 50-cc. volumes of ether. The ethereal extracts were combined, concentrated to a dry sirup and the zinc D-lactate prepared and isolated in a yield of 1.2 g. in the same manner as the zinc lactates obtained from the strontium salts. Recrystallized from 4 parts of water, the zinc D-lactate rotated +7.9° (*c*, 3.2; *l*, 4) in water, in good agreement with the rotational values of the zinc D-lactates obtained from the strontium salts. The specific rotation was the same in a concentration of 5.2.

Summary

The oxidation of α-methyl-L-galactomethylo-pyranoside with periodic acid yields the same crystalline dialdehyde as Jackson and Hudson obtained from the oxidation of α-methyl-L-mannomethylo-pyranoside by the same reagent. A crystalline enantiomorphous dialdehyde is obtained from the periodic acid oxidation of α-methyl-D-glucomethylo-pyranoside. These two dialdehydes, on oxidation by bromine water in the presence of strontium carbonate, form crystalline enantiomorphous strontium salts, derivatives of L′-methoxy-L-methyl diglycolic and D′-methoxy-D-methyl diglycolic acids, respectively. Hydrolysis of these dibasic acids yields L-lactic acid from the former and D-lactic acid from the latter, proving these aldohexomethylosides to be pyranosides and establishing the configurations of the lactic acids through correlation with the known sugar configurations of Fischer. The designation of these three glycosides as α-forms, based in the past upon rotatory considerations, is now proved conclusively through their oxidation by periodic acid.

In like manner, the periodic acid oxidation of β-methyl-L-galactomethylo-pyranoside and β-methyl-D-glucomethylo-pyranoside yields two crystalline enantiomorphous dialdehydes which, in turn, yield two crystalline strontium salts, derivatives of D′-methoxy-L-methyl diglycolic and L′-methoxy-D-methyl diglycolic acids, respectively. Hydrolysis of these dibasic acids yields L-lactic acid from the former and D-lactic acid from the latter, proving the two β-aldohexomethylosides to be pyranosides and their designation as β-forms to be correct from the stereostructural standpoint.

Rotatory data of the oxidation of the four aldohexomethylo-pyranosides show them to be pure substances and not crystalline molecular combinations of α- and β-forms.

The four crystalline dialdehydes and the four corresponding crystalline strontium salts are reference substances which can be employed to learn the ring structure and the α- or β-classification of any methyl pyranoside of the remaining aldohexomethyloses or of any methyl furanoside of the aldopentomethyloses.

(14) Freudenberg and Rhino, *Ber.*, **57**, 1551 (1924).

WASHINGTON, D. C. RECEIVED APRIL 3, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, NO. 191]

The Oxidation of Certain Glycosides by Lead Tetraacetate[1]

BY R. C. HOCKETT AND W. S. MCCLENAHAN[2]

In a previous paper[3] we stated that a number of methyl pyranosides, when dissolved in certain non-aqueous solvents, rapidly consume two molecular equivalents of lead tetraacetate. Evidence was presented that the two stages of the oxidation are (1) cleavage of a carbon–carbon bond between two adjacent, free carbinol groups with formation of a dialdehyde (II) and (2) subsequent elimination of one carbon atom to produce a second dialdehyde (IV).

Since the pyranosides all contain three adjacent unprotected carbinol groups (I), there are obviously two alternative positions in each compound at which the initial cleavage may occur. The isolated final products of the reaction do not, of course, by their structure provide any information regarding the position of initial attack (IV). Criegee,[4] however, has accumulated considerable evidence to the effect that *cis* glycols are oxidized more rapidly than *trans* glycols. Among the glycosides under investigation there may exist three possible types of configuration since the three carbinol groups inside the ring may be considered as forming two overlapping pairs: these types may be designated *cis–cis*, *cis–trans* (I), or *trans–trans*. No compounds of the first type were available during this study, but several *cis–trans* and *trans–trans* glycosides have been investigated. If Criegee's observation with respect to rates of oxidation is of general application it would be predicted that all those glycosides which contain no *cis* glycol configuration would consume their first mole of lead tetraacetate less rapidly than those which contain at least one *cis* pair of hydroxyls.[5] This relation has been verified in all the cases studied. Figure 1 shows a significant gap between the curve representing the oxidation of the slowest *cis–trans* glycoside (α-methyl-1-fucopyranoside) and that of the fastest *trans–trans* glycoside (β-methyl-*d*-xylopyranoside). The correlation between configurations and rates suggests that the *cis* positions are those initially attacked.

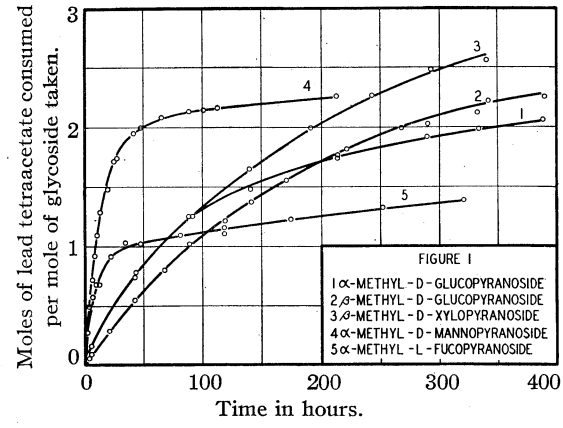


Fig. 1.

The second objective of the present study was to discover what effect upon the rates of oxidation would result from changing the substituent upon the reducing group from methyl to benzyl. In the two cases examined (α-methyl- and α-benzyl-fructofuranoside, β-methyl- and β-benzyl-fructopyranoside,[6(a)] this alteration in structure was found to have very little effect (Fig. 2).

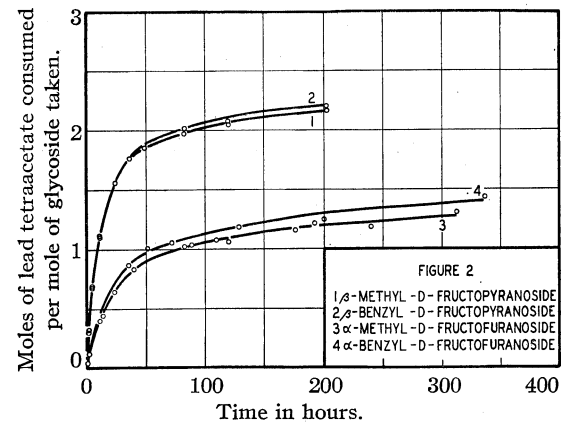


Fig. 2.

(1) This paper was read before the Division of Organic Chemistry at the meeting of the American Chemical Society in Milwaukee, Wisconsin, September, 1938.

(2) The material presented in this paper is taken from a thesis submitted by W. S. McClenahan to the Graduate School of the Massachusetts Institute of Technology in partial fulfilment of the requirements for the degree of Doctor of Philosophy in June, 1938. Mr. McClenahan was Louis Francisco Verges Fellow in Chemistry in 1936–1937 and 1937–1938.

(3) THIS JOURNAL, **60**, 2061 (1938).

(4) Criegee, (a) *Ber.*, **64**, 260 (1931); (b) *ibid.*, **65**, 1770 (1932); (c) *Ann.*, **507**, 159 (1933).

(5) Similar considerations have been employed by Freudenberg and Rogers, THIS JOURNAL, **59**, 1602 (1937), in establishing the configurations of the anhydrohexitols, styracitol and polygalitol.

(6) (a) Purves and Hudson, THIS JOURNAL, **59**, 49, 1170 (1937); (b) Pacsu, *ibid.*, **57**, 745 (1935).

A third objective was to learn whether reversing the configuration of the groups about the reducing carbon would alter the oxidation rates. In the few cases where an α- and β-pair were available for testing, their curves belonged to the same family (Figs. 3 and 4).

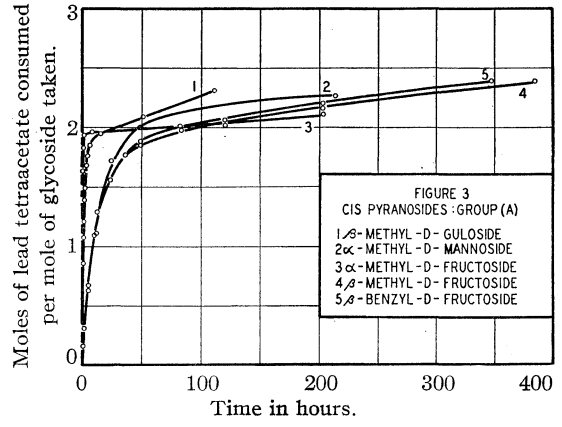


Fig. 3.

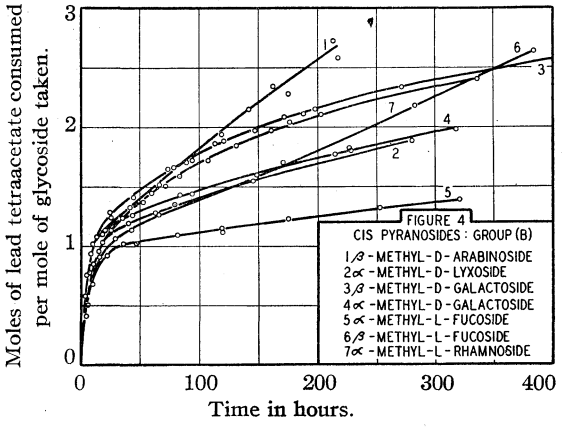
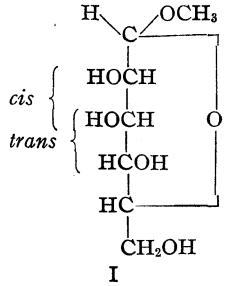


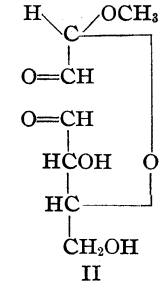
Fig. 4.

The fourth objective was to gain some information concerning the rates of consumption of the second mole of oxidant. The observation of Criegee[7] that glycerol consumes two moles of lead tetraacetate is presumptive evidence that hydroxyaldehydes are attacked by this reagent since glycolaldehyde should be the product of oxidation by the first mole. We found experimentally that the *cis* glycosides studied can be divided sharply into two groups according to whether (A) (Fig. 3) the consumption of oxidant slows down significantly only after the absorption of two moles or whether (B) (Fig. 4) it slows down after use of one mole. It has been found possible to correlate these differences by means of a simple hypothesis. All the glycosides of the first type (A) are so constituted that after initial fission at the *cis* glycol position, the resulting product would be a γ-hydroxyaldehyde (*e. g.*, II). According to the observations of Helferich,[8] hydroxyaldehydes of this nature readily form cyclic hemiacetals; such rearrangement would produce a five-membered ring structure (III) containing a new pair of adjacent carbinol groups which presumably would be attacked readily by the oxidant.[9] The glycosides of the first type (A) are so constituted that after initial fission at the *cis* glycol position, the resulting product would be a γ-hydroxyaldehyde (*e. g.*, II). According to the observations of Helferich,[8] hydroxyaldehydes of this nature readily form cyclic hemiacetals; such rearrangement would produce a five-membered ring structure (III) containing a new pair of adjacent carbinol groups which presumably would be attacked readily by the oxidant.[9] The glycosides of the first type (A) are so constituted that after initial fission at the *cis* glycol position, the resulting product would be a γ-hydroxyaldehyde (*e. g.*, II). According to the observations of Helferich,[8] hydroxyaldehydes of this nature readily form cyclic hemiacetals; such rearrangement would produce a five-membered ring structure (III) containing a new pair of adjacent carbinol groups which presumably would be attacked readily by the oxidant.[9] The gly-

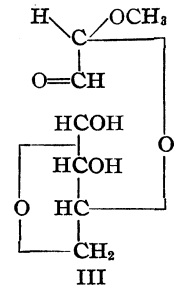


I

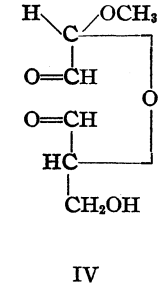
α-Methyl-*d*-manno-pyranoside



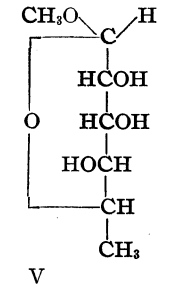
II



III

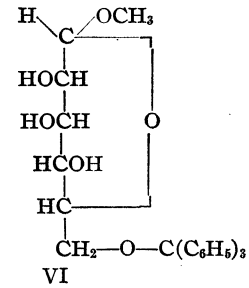


IV



V

α-Methyl-*l*-rhamno-pyranoside



VI

6-Trityl-α-methyl-*d*-mannopyranoside

(7) Criegee, *Ann.*, **495**, 211 (1932).

(8) Helferich, *Ber.*, **64**, 104 (1931).

(9) (a) More exactly, the dialdehyde probably would be in equilibrium with two cyclic hemiacetals in which the new glycol groups would be *cis* and *trans*, respectively. Criegee[4b,c] has shown that *cis* glycols in a five-membered ring system frequently are oxidized very rapidly; the concentration of the *cis* form would tend to maintain itself through a shift in the equilibrium.

(b) Oxidation of such a hemiacetal should yield a formic acid ester similar to that formulated by Felton and Freudenberg, THIS JOURNAL, **57**, 1637 (1935).

(c) A similar hypothesis was advanced by Criegee[7] to explain why α-methyl-mannofuranoside and 1-mannono-γ-lactone produced little formaldehyde when oxidized by lead tetraacetate. In these cases, if initial fission occurs between carbons two and three, cyclic hemiacetal formation would destroy the remaining glycol structure and *prevent* further oxidation (VII, VIII and IX).

cosides of type (B) if initially cleaved at the *cis* position yield products whose structures are unfavorable to hemiacetal formation (unless bimolecularly) and hence may be expected to react further less readily.

The most striking case of this difference is represented by the pair: α-methyl-*d*-mannopyranoside (I) and α-methyl-*l*-rhamnopyranoside (V). These substances would be enantiomorphs save for the lack of oxygen on carbon six of the latter. The former rapidly consumes *two* moles of lead tetraacetate while the latter, although initially attacked at nearly the same rate, slows down a great deal after use of one mole. To gain additional evidence concerning the function of the sixth hydroxyl in promoting the second stage of the reaction, through hemiacetalization, the behavior of 6-trityl-α-methyl-*d*-mannoside (VI) was studied. It was first ascertained that this substituent was stable toward the reaction medium (glacial acetic acid) and then it was found that the rate of oxidation closely paralleled that of the methyl rhamnoside (Fig. 5).

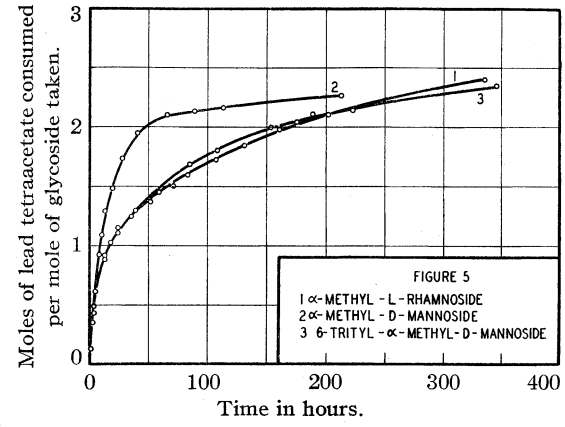
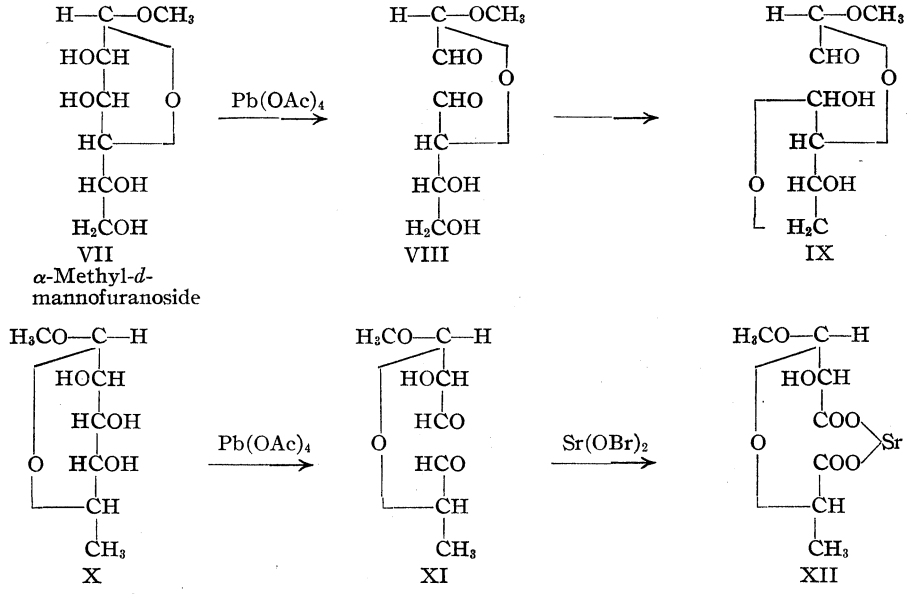


Fig. 5.

previous publication.[3] There was isolated, as its strontium salt, a dibasic acid which seems to contain all the original carbon of the glycoside and therefore probably is represented correctly by formula XII.

The consumption of only one mole of oxidant by this glycoside would have suggested the presence of a furanoside structure but for the rate of this reaction which is characteristic of a *cis*-hydroxyl pair. That α-methyl-*d*-fucoside (−197°) is a pyranoside has been established beyond question by Maclay, Hann and Hudson[11] through oxidation by periodic acid. Hence the very low rate of attack of the dialdehyde initially formed appears attributable to the unfavorable structure



It was also noted from the rate curve that α-methyl-*l*-fucoside (of rotation[10] −197°) is only slowly attacked after oxidation by one mole of oxidant. A sample of this glycoside was therefore treated with an equimolar quantity of lead tetraacetate by the technique described in the

(10) All rotations stated in this paper refer to specific rotations of sodium light at 20°.

(11) Maclay, Hann and Hudson, THIS JOURNAL, **61**, 1660 (1939).

of this substance in accordance with the hypothesis given. The data obtained for several miscellaneous compounds are illustrated in Fig. 6. From this it appears that the oxygen bridge in fructose is stable even after cleavage of the carbon chain has occurred.

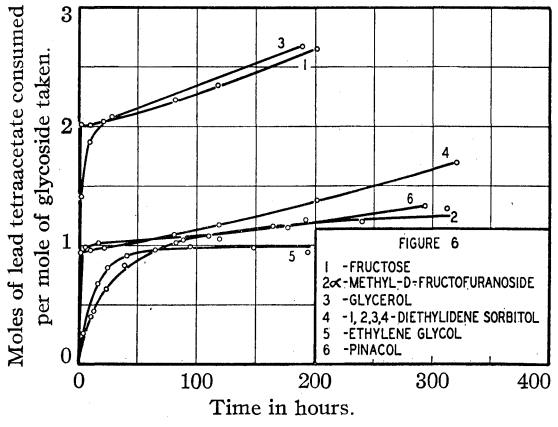


Fig. 6.

In the rate studies the molar concentrations of the glycosides were uniform throughout. A ratio of six and one-half moles of oxidant to one of glycoside was used. That this was virtually equivalent to an infinite excess is indicated by the observation that doubling the ratio in certain cases caused practically no change in rate.

We wish cordially to thank Professor C. B. Purves of this Laboratory for the fructosides employed, Dr. H. S. Isbell of the National Bureau of Standards for samples of α- and β-methyl-*d*-gulopyranosides, and Dr. Paul Arthur, Jr., of this Laboratory for valuable suggestions in the interpretation of the data.

Experimental

Standard Lead Tetraacetate Solution.—The salt prepared as previously described[3] was recrystallized from glacial acetic acid and was made up to a normality of 0.1315 in aldehyde-free acetic acid (29 g. per liter) by dissolving the requisite weight in hot acid, pouring the solution into cool acid and filtering the mixture. The solution was standardized under the conditions used in the rate determinations. It was found to deteriorate gradually over a period of several months.

Rate Determinations.—To 49 cc. of aldehyde-free acetic acid in a 100-cc. glass-stoppered volumetric flask was added 0.0005 mole (0.001 equivalent) of the dry glycoside which had been purified until its rotation agreed with recorded values. Warming on the steam-bath was necessary in a few cases. After cooling the solution to 20°, the time was noted and 50 cc. of standard lead tetraacetate solution at 20° was added from a pipet. The mixture was made up rapidly to 100 cc., mixed and placed in a constant temperature room maintained at 20–21°. At noted intervals, 10-cc. samples were withdrawn and run into 20 cc. of aqueous buffer solution containing 20 g. of reagent sodium or potassium iodide and 250 g. of sodium acetate per liter; the liberated iodine[12] was titrated with 0.02 *N* sodium thiosulfate solution.

The method was employed successfully upon as little as 0.000125 mole (24 mg.) of glycoside by making proportionate reductions in all the quantities given above.

α-Methyl-*l*-rhamnopyranoside.—A 3-g. sample of triacetyl-α-methyl-*l*-rhamnopyranoside melting at 86–87° (corr.), showing a rotation of −54.65° in acetylene tetrachloride (*c*, 3.2112; *l*, 4) and −60.34° in chloroform (*c*, 3.2100; *l*, 4) was deacetylated with barium methylate.[13] The concentration of the resulting aqueous solution was calculated from its optical rotation, the solvent was removed by distillation under reduced pressure and remaining traces of water by several redistillations in the presence of glacial acetic acid. The sirup was made up to 250 cc. with acetic acid and aliquots containing 0.0005 mole of methyl rhamnoside were withdrawn for oxidation experiments.

6 - Trityl - α - methyl - *d* - mannopyranoside.—This substance, prepared by the method of Watters, Hockett and Hudson,[14] who also proved the structure, rotated +22.1 (*c*, 1.4680; *l*, 2; $CHCl_3$) after drying to constant weight *in vacuo* at 65°.

α- and β-Methyl-*l*-fucosides.—Fucose, extracted from *Ascophyllum nodosum*, was converted to the glycosides as described by Hockett, Phelps and Hudson,[15] using precipitation with potassium acetate to separate the β-isomer from the predominating α-form.[16]

Oxidation of α-Methyl-*l*-fucopyranoside.—Two grams (0.011 mole) of the fucoside was oxidized in 150 cc. of chloroform with 5 g. (0.011 mole) of lead tetraacetate according to the method previously described.[3] After removing lead and acetic acid, the rotation of an aqueous solution was observed, and a specific rotation of approximately −80° was calculated assuming that the oxidation had been complete and that only one product had been formed. A titration by the Cajori[17] method revealed that approximately two equivalents of aldehyde had been formed per mole of lead tetraacetate consumed. In a two-stage oxidation, the same quantity of aldehyde would be produced by two moles of oxidant. After oxidation with strontium hypobromite, 2.5 g. (71%) of very fine crystals of a strontium salt was obtained. The rotation was unchanged by recrystallization after a value of +29.80° in water (*c*, 0.6924; *l*, 4) was reached. The free acid liberated by an equivalent quantity of hydrochloric acid rotated −13.2° (*c*, 0.2650; *l*, 4); after adding 3 drops more of concd. hydrochloric acid, −16.8°.

(12) An experiment was made which indicated that the aldehydes formed in the oxidation of the glycosides probably do not react appreciably with the liberated iodine in the *acid* solution: 5-cc. of standard lead tetraacetate solution was added to a mixture of 5 cc. of acetic acid and 20 cc. of buffer solution. Then 0.5 g. of glucose was added. After five minutes, the titer with sodium thiosulfate was found to be the same as with a blank.

(13) Isbell, *Bur. Standards J. Research*, **5**, 1185 (1930).

(14) Watters, Hockett and Hudson, THIS JOURNAL, **61**, 1528 (1939).

(15) Hockett, Phelps and Hudson, *ibid.*, **61**, 1658 (1939).

(16) Watters, Hockett and Hudson, *ibid.*, **56**, 2199 (1934).

(17) Cajori, *J. Biol. Chem.*, **54**, 622 (1922).

Anal. Calcd. for $C_7H_{10}O_7Sr \cdot 2H_2O$: H_2O, 10.93. Found: loss in wt. at 105°, *in vacuo*, 10.18, 11.0. Calcd. for $C_7H_{10}O_7Sr$: Sr, 29.84. Found: 29.40, 29.25. Calcd. for $C_6H_8O_6Sr$: Sr, 33.23.[18]

Summary

1. The rates of oxidation of a number of glycosides by lead tetraacetate in glacial acetic acid have been measured.

2. All the glycosides which contain a *cis* glycol structure consumed the first mole of lead tetraacetate much more rapidly than those which contain only *trans* glycol structures, suggesting that the initial attack is at the *cis* position when such is present.

3. In two cases, substitution of benzyl for methyl on the first carbon has no effect upon the oxidation rates.

4. In several cases, α- and β-isomers have been found to show a general similarity in the oxidation experiments.

5. The glycosides containing glycol structures have been separated by experimental study into two groups: (A) those which consume a second mole of oxidant with a speed comparable to that at which the first is consumed, and those (B) which consume the second mole at a distinctly lower rate, and a hypothesis has been proposed to explain this difference.

6. The substitution of a trityl radical at carbon six of α-methyl-*d*-mannopyranoside is shown to shift this glycoside from group (A) to group (B) in accord with the prediction of the hypothesis.

7. α-Methyl-*l*-fucoside (−197°) has been oxidized by one mole of lead tetraacetate in chloroform solution and by strontium hypobromite to a dibasic acid containing all the carbon of the original substance.

CAMBRIDGE, MASS. RECEIVED APRIL 5, 1939

(18) The physical properties of our salt also differ markedly from those of the strontium salt obtained by Maclay and Hudson (ref. 11) which contains one carbinol group less.

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY OF PRINCETON UNIVERSITY]

Glycofuranosides and Thioglycofuranosides. VI. Preparation of Dimethyl Acetal and Methylfuranosides from *d*-Fructosediethylmercaptal

BY EUGENE PACSU

In a preliminary communication[1] it was reported that the application of the furanoside synthesis developed[2] in this Laboratory to *d*-fructosediethylmercaptal had resulted in the unexpected formation of *d*-fructosedimethylacetal. This was the second observed case where a sugar acetal had been formed from a starting material that contained all of its hydroxyl groups unprotected, the first case being that of the *l*-rhamnosedimethylacetal.[2e] The starting material, fructosediethylmercaptal, could not be obtained directly from fructose and mercaptan. Since Emil Fischer showed[3] that his general method for the preparation of sugar mercaptals had failed in the case of fructose and sorbose, it appeared as though the ketose mercaptals could not exist at all. However, Brigl and Schinle found[4] that the benzoyl analog of pentaacetyl-*keto*-fructose, for which the open-chain structure with a free carbonyl group was previously established[5] by Pacsu and Rich, gave readily a mercaptal derivative on treatment of the substance with ethyl mercaptan and dry hydrogen chloride. Subsequently, Wolfrom and Thompson reported[6] the formation of pentaacetyl fructosediethylmercaptal from pentaacetyl-*keto*-fructose and ethyl mercaptan in the presence of zinc chloride. From the acetylated mercaptal, on deacetylation with ammonia in methyl alcoholic solution, the authors obtained fructosediethylmercaptal in about 78% yield. It has now been found that the yield of the latter compound can be increased almost to that required by the theory, if the deacetylation be carried out at room temperature in methyl alcoholic solution in the presence of a small quantity of barium methylate.

The reaction between sugar mercaptals and mercuric chloride in neutral alcoholic solution was hitherto believed[2b] only to proceed through the following two stages

(1) Pacsu, THIS JOURNAL, **60**, 2277 (1938).

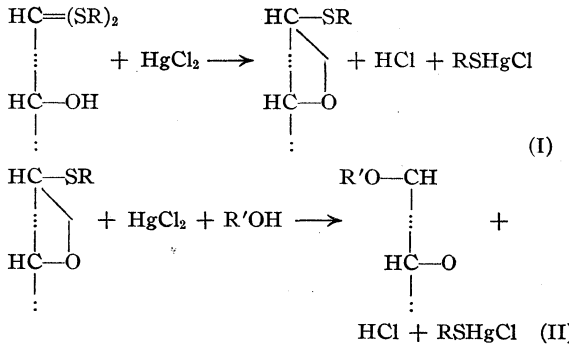
(2) (a) Pacsu and Green, *ibid.*, **58**, 1823 (1936); (b) Green and Pacsu, *ibid.*, **59**, 1205 (1937); (c) Green and Pacsu, *ibid.*, **59**, 2569 (1937); (d) Green and Pacsu, *ibid.*, **60**, 2056 (1938); (e) Green and Pacsu, *ibid.*, **60**, 2288 (1938); (f) Pacsu and Scattergood, *ibid.*, **61**, 534 (1939).

(3) Fischer, *Ber.*, **27**, 673 (1894).

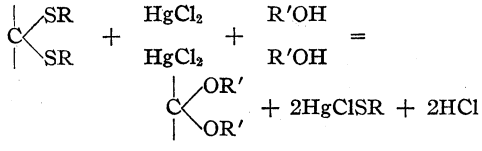
(4) Brigl and Schinle, *ibid.*, **66**, 325 (1933).

(5) Pacsu and Rich, THIS JOURNAL, **54**, 1697 (1932); **55**, 3018 (1933).

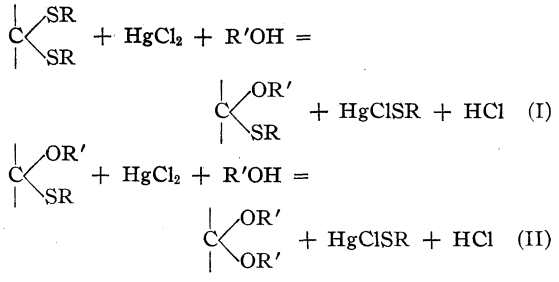
(6) Wolfrom and Thompson, *ibid.*, **56**, 880 (1934).



Usually, the final products of the reaction were found to be the more negative rotating forms of the furanosides admixed to a much smaller quantity of the diastereomers. Only in the case of glucose mercaptals was it possible to isolate the intermediate thiofuranosides, because the latter type of compounds, with the exception of the thioglucofuranosides, evidently reacted faster with mercuric chloride than the sugar mercaptals themselves. However, the reaction between *l*-rhamnose ethylmercaptal and methyl alcoholic mercuric chloride was shown recently[2e] to give rise to rhamnosedimethylacetal beside a large quantity of a sirupy product which undoubtedly was a mixture of the methyl rhamnofuranosides. Now it has been found that fructose ethylmercaptal reacts with mercuric chloride in methyl alcohol to yield almost exclusively the dimethylacetal, provided that the reaction is carried out at a very low temperature (−80°). In the formation of dimethylacetals the reaction must have proceeded either directly, according to the following general equation

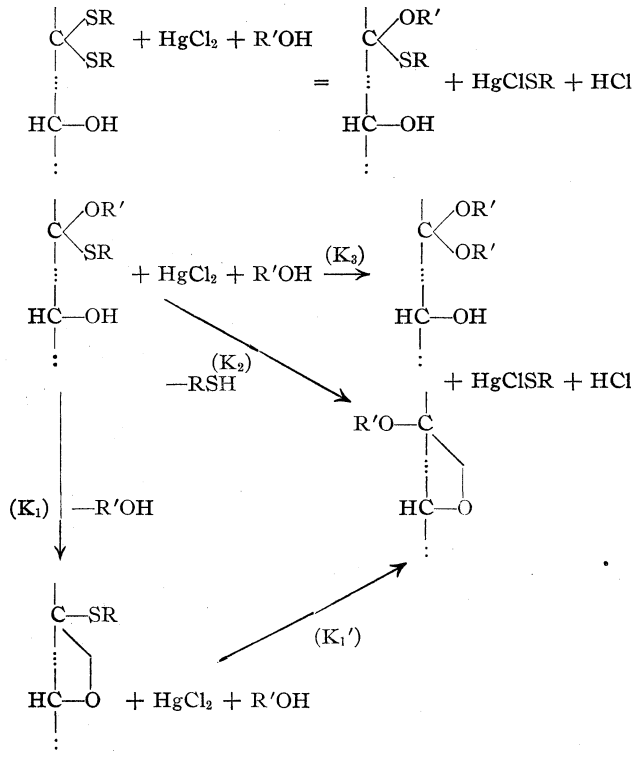


or in two stages, through the mixed acetal, as follows



Since it has not been possible to isolate the postulated intermediate product, the mixed acetal, it is to be concluded that if the dimethylacetal formation took place indirectly, according to the latter equations, then the velocity of the second stage of the reaction must have been very much faster than that of the first phase of the process. In the light of this interpretation the acetal formation in either direct or indirect way from a mercaptal appears to be a distinct reaction, which, depending upon unknown factors, may or may not occur as a side-reaction accompanying the usual conversion of the sugar mercaptals into furanosides and thiofuranosides.

However, it should be pointed out that it is entirely possible to consider all the observed products of the reaction, namely, thioglycofuranosides, glycofuranosides and acetals as being derived from one common intermediate, the mixed acetal. This view is best illustrated by the following diagram



According to this conception, the mixed acetal may undergo three distinct transformations: (1) loss of one mole of alcohol results in the formation of thioglycosides (K_1) which usually react further (K_1') to give rise to furanosides; (2) intramolecular loss (K_2) of one mole of mercaptan

yields furanosides; (3) intermolecular loss (K_3) of one mole of mercaptan produces acetals. Of course, the yields of the final product or products will depend upon the relative rates of the single stages. Until the mixed acetal can be isolated and the rates of its different transformations studied, this interpretation appears to be the most plausible for the mechanism of the complex reaction of sugar mercaptals with alcoholic mercuric chloride.

By the preparation of fructosedimethylacetal, it became quite definite that Purves and Hudson's[7] "gamma-methylfructoside (a)" is not identical with this acetal. From the results of analysis of gamma-methylfructoside mixtures by means of invertase the authors concluded that the constituent hydrolyzed by invertase and fermented by yeast must have a specific rotation of $-52 \pm 2°$, calculated for a true methylfructoside of molecular weight 194. Since this "gamma-methylfructoside (a)" has never been isolated and analyzed in substance, it could have represented the acetal, the hemiacetal or the β-methylfructofuranoside. In fact, its specific rotation ($-54°$) if calculated for a dimethyl acetal of molecular weight 226, becomes $-46.3°$, whereas the crystalline fructosedimethylacetal was found to have $[\alpha]^{20}D$ $-46.5°$. It was, therefore, of great interest to investigate the behavior of the crystalline acetal toward invertase and yeast.

On the addition of a powerful invertase solution the rotation of the crystalline acetal was found to remain unchanged for several hours in an unbuffered solution and dropped very slowly in a solution buffered to *p*H 4.5. Under identical conditions the same invertase solution hydrolyzed 75.7% of a 1.28% sucrose solution at *p*H 4.5 in thirty minutes. Furthermore, it partially hydrolyzed in thirty-five minutes the gamma-methylfructoside mixture prepared according to Purves and Hudson,[7a] the time of hydrolysis and final rotation being practically the same as those reported by the authors. The negative action of the invertase solution on the acetal was not due to inactivation, since the mixture rapidly inverted sucrose or hydrolyzed the gamma-methylfructoside mixture. The very slow change of rotation observed in the acetal-enzyme solution at *p*H 4.5 subsequently was found to be caused by the slow hydrolysis of the acetal due to the hydrogen ions, since it also occurred in the absence of invertase.

(7) Purves and Hudson, (a) THIS JOURNAL, **56**, 702 (1934); (b) **56**, 708 (1934).

Experiments carried out in fermentation saccharimeters showed that the acetal was fermented by yeast in distilled water, as measured by the volume of the carbon dioxide generated, about four times slower (twenty-three hours) than sucrose under identical conditions (six hours). However, yeast was without any effect on the acetal in a citric acid–disodium phosphate buffer solution of *p*H 7, while sucrose reacted in about twenty hours under similar conditions. When the hydrogen-ion concentration of the former solution was afterward adjusted to *p*H 5.6, a very slow fermentation began, the carbon dioxide generation reaching the end in about one week. These results clearly indicated that the action of yeast on the acetal in an unbuffered solution was due to the fermentation of fructose liberated from the acetal by the acid content of the yeast and that it was not a genuine enzymotic effect. They also suggested that the acetal must be extremely sensitive toward acid, a fact which subsequently was found to be the case, since the substance was hydrolyzed at room temperature in a 0.08 *N* hydrochloric acid within two minutes, and in a 0.00089 *N* acid in about six hours.

In a preliminary experiment carried out in anhydrous methyl alcoholic solution containing 0.84% hydrogen chloride, the specific rotation of the acetal was found to change in one hour from the initial rotation of $-63°$ to a dextrorotatory maximum of 14° calculated for methylfructoside. This transformation followed a unimolecular course with the velocity constant of $10^4 K = 347 \pm 20$. After the point of maximum rotation had been reached the rotation diminished very slowly, but the solution was still non-reducing. A detailed study is being made of the behavior of the acetal in acid media to discover the nature of substances present in the equilibrium mixture.

The reaction between fructose diethylmercaptal and methyl alcoholic chloride does not always give rise to the acetal exclusively. The acetal was found to be the single product only when the temperature had been kept very low during the reaction. At 0° or at higher temperature the reaction also proceeded in other directions and, beside the acetal, it gave rise to a considerable amount of a non-reducing, sirupy mixture. On systematic extractions with acetone and ethyl acetate, this mixture was finally separated into a crystalline product and a liquid fraction. The former was identified as the "crystalline gamma-

methylfructoside" of Purves and Hudson,[7b] showing the correct m. p. 69° and $[\alpha]^{20}D$ 93.0° in water solution. The liquid fraction has not yet been obtained in sufficient purity, but its specific rotation and especially the fact that invertase hydrolyzes it rapidly, lend support to the view that it represents the assumed "gamma-methylfructoside (a)" of Purves and Hudson. Attempts are being made to obtain this interesting substance in pure form.

Experimental

Preparation of *d*-Fructosediethylmercaptal.—Pentaacetyl-*keto*-fructose prepared according to Cramer and Pacsu[8] was converted into its ethyl mercaptal by the procedure of Wolfrom and Thompson.[6] The deacetylation was best carried out in small portions and the crude products obtained were united and recrystallized from methyl alcohol and ether. In a typical experiment 0.5 cc. 0.33 *N* barium methylate solution, prepared by refluxing barium oxide in anhydrous methyl alcohol for thirty minutes, was added to 5 g. of the acetylated mercaptal dissolved in 15 cc. of anhydrous methyl alcohol. After sixteen to twenty hours of standing at room temperature, one drop of the solution remained clear on addition of water, indicating that the reaction was completed. The residue obtained from the solution was crystallized from a small amount of methyl alcohol containing twice the volume of ether; yield, almost quantitative; m. p. and specific rotation in methyl alcohol agreed with the values given by Wolfrom and Thompson. The specific rotation of the mercaptal in water solution was found to be $[\alpha]^{20}D$ 16.5°; $[\alpha]^{20}_{6568}$ 12.9°; $[\alpha]^{20}_{5463}$ 20.2°; $[\alpha]^{20}_{61}$ 27.4° (*c*, 2.174).

Preparation of *d*-Fructosedimethylacetal.—To 11.4 g. of the mercaptal in 100 cc. of anhydrous methyl alcohol 17 g. of yellow mercuric oxide was added in a three-necked flask equipped with a mercury-sealed mechanical stirrer, a separatory funnel and a reflux condenser. The apparatus was placed in a Dewar flask containing an acetone–carbon dioxide mixture and the flask was immersed in an ice–salt bath. Under vigorous stirring a solution of 21.8 g. of mercuric chloride (2 moles) in 60 cc. of anhydrous methyl alcohol was added in about fifteen minutes to the mercaptal through the separatory funnel. After seventeen hours of continuous stirring at the freezing mixture's temperature, a filtered sample failed to produce $HgCl\text{-}SC_2H_5$ precipitate on heating, an indication that the reaction was completed. Then the reaction mixture was filtered and 5 cc. of pyridine was added to the filtrate for the removal of the excess of mercuric chloride. After two hours' standing at 0° the solution was filtered from the mercuric chloride–pyridine precipitate and evaporated *in vacuo* to a sirup. In order to remove the last traces of the pyridine salt the sirup was dissolved in ice cold water and the solution filtered with carbon. The filtrate was then made alkaline to phenolphthalein with a few drops of dilute alkali and evaporated *in vacuo* to a sirup. This was dissolved in methyl alcohol, filtered with carbon, if necessary, and the solution evaporated under diminished pressure to a colorless, non-reducing sirup, which gradually changed into a mass of diamond-shaped crystals. The substance crystallized from hot *n*-propyl alcohol in beautifully developed prisms. After a final recrystallization from absolute ethyl alcohol it had m. p. 107–108°; $[\alpha]^{20}D$ −45.6°; $[\alpha]^{20}_{6563}$ −35.6° and $[\alpha]^{20}_{5463}$ −53.6° in water solution (0.2977 g. of substance, 10 cc. of solution; 2-dm. tube; rotations, 2.71, 2.12 and 3.19° to the left, respectively); yield, 7 g. In methyl alcohol solution the acetal had $[\alpha]^{20}D$ −63.0°, $[\alpha]^{20}_{6563}$ −50.0° and $[\alpha]^{20}_{5463}$ −76.1° (*c*, 1.15).

Anal. Calcd. for $C_8H_{18}O_7$: OCH_3, 27.4. Found: OCH_3, 27.1.

Preparation of Pentaacetyl *d*-Fructosedimethylacetal.—One gram of the acetal was acetylated at 100° with acetic anhydride containing 5% of anhydrous sodium acetate. After the solution was evaporated *in vacuo*, a sirupy residue was obtained which, on addition of water, changed at once into crystals. On recrystallization from absolute alcohol, the substance was obtained in well-developed prisms with m. p. 109° and $[\alpha]^{20}D$ 0° in chloroform solution. In an acetyl estimation 0.1453 g. of the compound required 16.4 cc. of 0.1 *N* sodium hydroxide solution. The value calculated for the hydrolysis of five acetyl groups is 16.6.

Action of Methyl Alcoholic Mercuric Chloride on *d*-Fructosediethylmercaptal at 0° and Higher Temperature.—The experiment described for the preparation of fructosedimethylacetal was repeated with the modification that the apparatus was kept in ice cold water and the mercuric chloride solution was added to the mercaptal in about two hours. After eighteen hours of continuous stirring at 0° the reaction mixture was worked up in the usual manner. There was obtained 6.3 g. of a sirupy material which, on seeding with acetal crystals, gradually changed into a crystalline mass. Crystallization from *n*-propyl alcohol yielded 1.8 g. of pure acetal.

In another experiment the mercuric oxide was added to the methyl alcoholic mercuric chloride solution which was kept boiling gently. Then the mercaptal solution was added drop by drop in one hour to the mixture which was refluxed for an additional hour. After standing at room temperature for several days, the sirupy product obtained from this experiment changed into a partly crystalline mass, from which about 2 g. of pure acetal was isolated by crystallization from *n*-propyl alcohol.

From the residue of the united mother liquors of the crystalline acetal obtained in these two experiments a non-reducing, sirupy product with $[\alpha]^{20}D$ 6.4 was isolated by extraction with hot ethyl acetate and evaporation of the solution. This product was separated by treatment with hot acetone into an acetone-soluble (sp. rot. +14°) and an acetone-insoluble (−15.7°) fraction. From the +14° fraction hot ethyl acetate dissolved a portion which had +35°, while the part insoluble in ethyl acetate deposited from its acetone solution a small quantity of the crystalline acetal. Then the +35° and the −15.7° fractions were united and extracted with hot ethyl acetate giving a solution (A) and an insoluble sirup (B). Solution (A) was cooled to 0° and, after it had cleared up, it was decanted from an insoluble sirup. On prolonged standing at room temperature the solution deposited a small amount of crystalline acetal, which was removed by filtration. In

(8) Cramer and Pacsu, THIS JOURNAL, **59**, 1148 (1937).

the filtrate, on standing at room temperature, well-shaped, pointed prisms commenced to form which, after recrystallization from methyl alcohol containing a little amyl alcohol, had m. p. 69° and $[\alpha]^{20}D$ 92.8° in water solution. The substance was, therefore, identical with Purves and Hudson's "crystalline gamma-methylfructoside." The ethyl acetate-insoluble substance (B) was again extracted with hot ethyl acetate and the aqueous solution of the insoluble portion was tested with invertase solution. The initial rotation (−35.2°) of the nonreducing solution then dropped rapidly to −64.4° and the solution became strongly reducing. The substance, therefore, must represent the "gamma-methylfructoside (a)" postulated by Purves and Hudson.

Acknowledgment is made to Dr. C. S. Hudson for the invertase samples used in this investigation. The author also wishes to thank Messrs. Walter J. Kauzmann and E. Justin Wilson, Jr., for their helpful assistance in the experimental work.

Summary

1. *d*-Fructosediethylmercaptal reacted at −80° with methyl alcoholic mercuric chloride to give crystalline *d*-fructosedimethylacetal in excellent yield.

2. The same reaction when carried out at 0° or higher temperature gave rise to a partly crystalline material, from which, beside the acetal, the "crystalline gamma-methylfructoside" of Purves and Hudson was isolated. Another constituent obtained from the mixture represented the "gamma-methylfructoside (a)," whose presence in the liquid gamma-methylfructoside mixtures was postulated by the same authors. This substance was hydrolyzed rapidly by invertase.

3. The apparent reaction of the acetal with invertase and yeast was found to be due to the hydrolyzing effect of the acidic media rather than to a genuine enzymotic effect. In solutions buffered to *p*H 7 the action of both invertase and yeast was found to be completely negative.

4. A new mechanism for the reaction of sugar mercaptals with alcoholic mercuric chloride was suggested.

5. Crystalline pentaacetyl *d*-fructosedimethylacetal was prepared.

PRINCETON, NEW JERSEY RECEIVED APRIL 6, 1939

[A COMMUNICATION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Hydrogenation of Hydroxyamides

BY JAMES D. D'IANNI[1] AND HOMER ADKINS

The multiplicity of reactions that may occur when a hydroxyamide reacts with hydrogen under the influence of copper chromite[2] made it seem desirable to investigate rather carefully the nature of the products in the hydrogenation of representative compounds of this type.[3] Oeda failed to obtain amino alcohols by the hydrogenation of α-hydroxyamides.[4]

Monohydroxy Amides.—Five hydroxyamides, in which hydroxyl was in the α, β, γ, δ or ε position with respect to the N-pentamethylenecarbonamido or —C(O)NC_5H_{10} group, were submitted to hydrogenation over copper chromite. The detailed results are given in Table I. A typical reaction was

$$CH_3CHOH(CH_2)_2C(O)NC_5H_{10} \longrightarrow CH_3CHOH(CH_2)_2CH_2NC_5H_{10} + H_2O$$

The yields of the corresponding hydroxyamines were as follows: α, 51%, β, 0%, γ, 79%, δ, 76%, ε, 60%.

In the case of the β-hydroxybutyramide the chief product was N-*n*-butylpiperidine in 78% yield, formed according to the reaction

$$CH_3CHOHCH_2C(O)NC_5H_{10} \longrightarrow CH_3(CH_2)_2CH_2NC_5H_{10} + 2H_2O$$

This reaction is in accord with the well-established labilizing effect toward hydrogenolysis of nitrogen or oxygen substituents in the β-position with respect to each other.[5] A 4% yield of propylpiperidine from a lactamide was also isolated and presumably was formed by the same type of reaction.

Evidence for another type of hydrogenolysis

(1) This investigation was carried out in part while Dr. D'Ianni was a teaching assistant of the University and in part while he was a Procter and Gamble Fellow in 1937–1938.

(2) Groger first prepared the compound $CuCr_2O_4$ which he called copper chromite [Groger, *Z. anorg. Chem.*, **58**, 412 (1908); **76**, 30 (1912). When this compound was first reported by Connor, Folkers and Adkins as a catalyst for hydrogenation (for references on its early use see Adkins, *Ind. Eng. Chem., News Ed.*, **15**, 548 (1937)], it was referred to by the same name. In later papers from this Laboratory the catalyst has been called "copper-chromium oxide," since in some cases, a change in composition occurred during the course of a hydrogenation. However, W. A. Lazier and others prefer the use of the more convenient term, copper chromite (Lazier, U. S. Patents 1,746,782, 1,746,783 (1930), 1,964,000 (1934)).

(3) For references to earlier work by Wojcik, Paden, Sauer and Adkins see THIS JOURNAL, **60**, 402 (1938).

(4) Oeda, *Bull. Chem. Soc. Japan*, **12**, 121–127, 377–381 (1937).

(5) Adkins, "Reactions of Hydrogen, etc.," University of Wisconsin Press, Madison, 1937, p. 88.

TABLE I

HYDROGENATION OF AMIDES[a]

Amide	G. catalyst (moles amide)	%	% yield of products
N-Pentamethylenelactamide	6 $CuCr_2O_4$ (0.2)	51	1-Piperidinopropanol-2
		10	1,2-Di-piperidinopropane
		10	Propanediol-1,2
		10	Piperidine
		4	N-*n*-Propylpiperidine
	3 Ni(R) (0.1)	27	1-Piperidinopropanol-2
		18	Propanediol-1,2
		38	Piperidine
		23	Unchanged amide
N-Pentamethylene-β-hydroxy butyramide	3 $CuCr_2O_4$ (0.1)	78	N-*n*-Butylpiperidine
		12	Piperidine
	3 Ni(R) (0.1)	86	N-Pentamethylenebutyramide
		12	Piperidine
N-Pentamethylene-γ-hydroxy valeramide	4 $CuCr_2O_4$ (0.1)	79	5-Piperidinopentanol-2
		6	1,4-Dipiperidinopentane
		7	Piperidine
	5 Ni(R) (0.15)	15	5-Piperidinopentanol-2
		58	γ-Valerolactone
		44	Piperidine
		18	Unchanged amide
N-Pentamethylene-Δ-hydroxy caproamide	4 $CuCr_2O_4$ (0.1)	76	6-Piperidinohexanol-2
		14	1,4-Dipiperidinohexane
		4	Piperidine
	3 Ni(R) (0.1)	34	6-Piperidinohexanol-2
		29	Piperidine
		15	Δ-Caprolactone
		14	Unchanged amide
N-Pentamethylene-ε-hydroxy heptanoamide	2 $CuCr_2O_4$ (0.05)	60	7-Piperidinoheptanol-2
		26	Heptanediol-1,6
		14	1,6-Dipiperidinoheptane
		9	Piperidine
N-Pentamethylene caproamide	3 Ni(R) (0.1)	83	Unchanged amide
		7	Piperidine
		5	Hexanol-1
		6	N-*n*-Hexylpiperidine
Di-N-*n*-amylmalamide	16 $CuCr_2O_4$ (0.4)	32	N-*n*-Amylpyrrolidone
		30	Di-*n*-amylamine
		14	N-*n*-Amylsuccinimide
		12	Di-N-*n*-amylsuccinamide
		9	N-*n*-Amylpyrrolidine
		7	*n*-Amylamine
Di-N-*n*-amyltartaramide	15 $CuCr_2O_4$ (0.25)	20	Di-*n*-amylamine
		11	N-*n*-Amylpyrrolidine
		8	*n*-Amylamine
2,2-Dimethyl-5-phenyl-4-oxazolidone	5 $CuCr_2O_4$ (0.15)	35	Mandelamide
		29	Phenylethylene glycol
		3	Phenethyl alcohol
		47	Diisopropylamine (as hydrochloride)

[a] The hydrogenations were made at 225° with the nickel catalyst and at 250–260° for copper chromite, except for the oxazolidone, for which 210–215° was used. The hydrogenations were made in dioxane solution (0.1 mole of amide, 40 ml. of dioxane), the time of reaction for nickel being five to eight hours and with copper chromite one to four hours.

was found in the glycols from each of the five amides, *i. e.*

$$CH_3CHOHC(O)NC_5H_{10} \longrightarrow CH_3CHOHCH_2OH + C_5H_{10}NH$$

Piperidine was isolated from each of the reaction mixtures and the glycol was isolated from the products of two of the amides. It is possible that this type of hydrogenolysis is the primary reaction with all the amides and that the hydroxyamine is actually formed by the interaction of the amine and the glycol, *i. e.*

$$CH_3CHOHCH_2OH + C_5H_{10}NH \longrightarrow CH_3CHOHCH_2NC_5H_{10} + H_2O$$

There exist no data, so far as we know, which show conclusively the course of the reaction or reactions by which an amine is formed from an amide.

Diamines were isolated in yields of 6 to 14% from the products of three amides. These presumably were formed by a reaction similar to that given just above.

$$CH_3CHOHCH_2NC_5H_{10} + C_5H_{20}NH \longrightarrow CH_3CH(NC_5H_{10})CH_2NC_5H_{10} + H_2O$$

Raney nickel, as compared to copper chromite, is relatively inactive for the hydrogenation of amides to amines. A fair comparison between the catalysts has not been made, as copper chromite has been used at 250 to 260° while Raney nickel has been used at 225°. Raney nickel in one case brought about a rather violent reaction between dioxane and hydrogen at 250° so that we have since hesitated to run hydrogenations with Raney nickel in dioxane above 225°. However, even at 225° Raney nickel has induced a considerable hydrogenation of the hydroxyamides. The yields of amino alcohols were in three cases 15, 27 and 34%, as compared with 79, 51 and 76% when copper chromite was used with the same amides at 250°. In each of the cases with Raney nickel, considerable amounts of unchanged amide remained in the reaction mixture, even after periods of reaction two or three times as long as required for complete hydrogenation with copper chromite.

The greater ease of hydrogenation over nickel of hydroxyamides, as compared with amides containing no hydroxyl group, is shown by the fact that 83% of the caproamide and only 14% of the Δ-hydroxycaproamide were recovered after each was hydrogenated for eight hours. A similar difference in the rate of reaction of the amides over copper chromite does not exist.

The real value of Raney nickel in the hydrogenation of amides is indicated by the result of its use with the β-hydroxyamide. The hydroxyl group was removed and the amide group was unchanged, *i. e.*

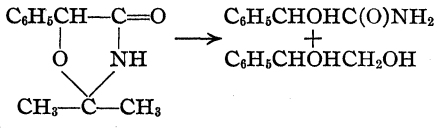
$$CH_3CHOHCH_2C(O)NC_5H_{10} \longrightarrow CH_3CH_2CH_2C(O)NC_5H_{10} + H_2O$$

The butyramide was obtained in 86% yield while with copper chromite, as noted above, the amide group was also hydrogenated and butylpiperidine obtained in 78% yield.

Another difference between the products isolated from a hydrogenation over nickel as compared with those over copper chromite, is the presence of lactones from the γ- and Δ-hydroxyamides. This may be due to the longer period of heating necessary with nickel or to the activity of copper chromite for the hydrogenation of lactones to glycols.

Hydroxy Diamides.—Hydrogenation of N-amylmalamides and N-amyltartaramides over copper chromite gave a mixture. Six products were isolated from the malamide while only three of the many formed were isolated from the tartaramide. The general course of the reactions is rather clearly indicated by the products from the malamide. The first step is apparently the loss of the hydroxy group to give a succinamide. The latter then goes to a succinimide, a pyrrolidone and a pyrrolidine, as reported by Paden,[6] with incidental formation of amyl- and diamylamines.

The hydrogenation of the cyclic amide, 2,2-dimethyl-5-phenyl-4-oxazolidone, over copper chromite gave interesting results, for the oxazolidone ring was cleaved at three different linkages, *i. e.*



Mandelamide and the glycol were formed in similar amounts, the latter was in part converted to phenethyl alcohol. Almost one-half of the isopropyl groups were recovered as diisopropylamine.

An amide derived from a tetrahydroxy acid such as mucic acid offers the possibility of many different reactions involving hydrogenation and hydrogenolysis. Twelve different products have actually been characterized, as listed in Table II. Attempts were made in early experiments to hydrogenate the compound with Raney nickel at 175–200° and with copper chromite at 225–235°. Acetylpiperidine, 1,4-dipiperidinobutane and piperidine were isolated from these experiments. The weight of these three products obtained from 34 g. of the amide was 7 g. after hydrogenation for ten hours over Raney nickel or 8 g. after four to five hours over copper chromite. Since the larger share of the products so obtained could not be separated or characterized, subsequent hydrogenations were made at 250° for five hours over copper chromite.

(6) Paden and Adkins, THIS JOURNAL, **58**, 2487 (1936).

TABLE II

PRODUCTS FROM DI-N-PENTAMETHYLENE MUCAMIDE

	Products	G.[a]	B. p. °C.	Mm.	$n^{25}D$
I	Piperidine	23	105–110	740	1.4368
II	N-Ethylpiperidine	10	125–135	740	1.4413
III	N-*n*-Butylpiperidine	7.5	165–175	740	1.4474
IV	2-Piperidinoethanol-1	7	70–80	8	1.4602
V	N-Acetylpiperidine	4.2	80–95	8	1.4682
VI	1,2-Di-piperidinoethane	12	110–120	8	1.4786
VII	6-Piperidinohexanol-1	11.5	125–135	8	1.4820
VIII	1,4-Di-piperidinobutane	44	140–150	8	1.4846
IX	1,6-Di-piperidinohexane	12.5	113–123	1	1.4859
X	1,6-Di-piperidinohexanol-2	22	127–137	1	1.4924
XI	1,6-Di-piperidinohexanediol-2,5	16	150–160	1	1.4990
XII	Di-N-pentamethyleneadipamide	11	160–170	1	1.5021

[a] These figures represent the weights of the various fractions obtained from the products of the hydrogenation of 1 mole of the amide (344 g.). As shown in the experimental part these figures do not represent pure compounds. Ninety-nine grams of water was formed. The intermediate fractions and mechanical losses during fractionation amounted to 77 g. The hydrogenations were made at 250–260° under 200–350 atm. during periods of five hours each using 40 g. of copper chromite with 0.5 mole of amide dissolved in 400 ml. of dioxane. One mole of amide took up 6.5 moles of hydrogen.

A reasonable scheme for the formation of the various products identified is given in Fig. 1. The formulas of two hypothetical intermediates not isolated are indicated in brackets.

The carbon chain of mucamide is broken between carbon atoms 2 and 3. In no case was a product isolated which contained an uneven number of carbon atoms from the acid radical. That is to say, rupture did not occur between carbons 1 and 2, or 3 and 4. This is a striking fact for in the hydrogenolysis of sugars the change occurs very largely between carbons 3 and 4, with small amounts of one and two carbon fragments.[7] The yield of products (0.24 mole) containing two carbon atoms was almost exactly equal to the yield of products containing four carbon atoms (0.25 mole). The yield of products (0.29 mole) containing the uncleaved chain of six carbon atoms was a little greater than the yield of cleavage products of either of the two types.

As a result of hydrogenolysis between carbon

(7) Zartman and Adkins, THIS JOURNAL, **55**, 4559 (1933). *Cf.* for example Horst and Balle, German Patent 624,443, January 21, 1936.

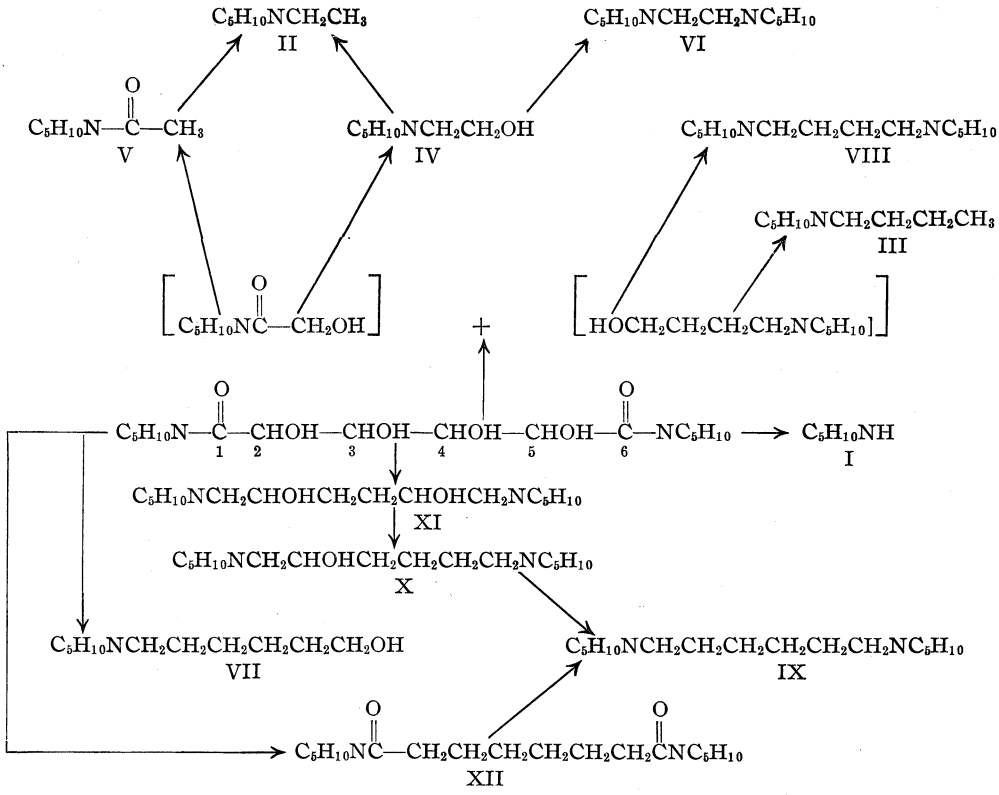


Fig. 1.—Hydrogenolysis of N-pentamethylenemucamide.

atoms 2 and 3 of the mucamide, acetylpiperidine, V, ethylpiperidine, II, and β-hydroxylethylpiperidine, IV, would be formed readily by hydrogenation. The reaction of IV with piperidine would give dipiperidinoethane, VI. Piperidine, I, as has been shown above, is a normal product of the hydrogenolysis of pentamethylene substituted amides. The fragment containing carbon atoms 3, 4, 5 and 6 would by similar transformations give butylpiperidine, III, and dipiperidinobutane, VIII. The compounds listed as VII to XII inclusive would result from the hydrogenolysis of oxygen or piperidino groups from the six carbon chain of the amide. There is no conclusive evidence for the position of the hydroxyl groups shown in XI and X. The hydroxyls are believed to be situated as shown for these are the positions in which hydroxyl groups are most stable toward hydrogenolysis.[5] Compounds would not be expected in which hydroxyl groups were beta to each other or to an amino group. Hydroxyls would therefore be found on carbon atoms 2 and (or) 5.

Experimental Part

The hydrogenations usually were made either in a vessel having a void of 270 ml. or one having a void of 1880 ml. The preparation of catalysts and procedure have been previously described.[5]

The separation of products was based upon fractional distillation of the products. In most cases a "modified Widmer" column having a spiral 15 cm. in length with 12 turns of the helix was used.[8] Spirals with greater or less pitch in the helix were occasionally advantageous. The usual rate of fractionation was 6 to 9 g. per hour, the conduct of the fractionation being as previously described.[8] In general it has been found advantageous to make a rough separation of the products into fractions boiling over 20 or 30° and then carefully fractionate the fractions so obtained. This was particularly important in separating the products from the mucamide.

Amines distilling over with dioxane were recovered as hydrochlorides and in most cases were then converted to the free amines and again fractionated. The same procedure was used for separating amines from glycols or amides having similar boiling points. Amines were characterized by boiling points, neutral equivalents and the formation of solid derivatives (see Table III). In a few cases it was not feasible to separate the components in the quantity of a mixture available. In these cases the proportion of the components of a mixture was estimated from the results of titration with acid, and the presence of each component established by the formation of solid derivatives.

Many of the compounds referred to in this paper have not hitherto been described in the literature. The ana-

(8) Martha E. Smith and Adkins, THIS JOURNAL, **60**, 657 (1938).

lytical data and certain physical properties for thirty such compounds are given in Table III.

Certain derivatives have been described previously: 1-piperidinopropanol-2, b. p. 67–68° (7 mm.), $n^{25}D$ 1.4586, and its methiodide, m. p. 147° (from dry ethanol–ether);[9] 1,2-dipiperidinopropane, b. p. 120–123° (7 mm.);[10] picrate of N-*n*-butylpiperidine, m. p. 132–133°;[11] 3,5-dinitrobenzoate of hexanol-1, m. p. 59–60°;[12] picrate of N-*n*-hexylpiperidine, m. p. 108–109° (from ethanol);[13] N-*n*-amylpyrrolidine, b. p. 76–82° (25 mm.), and its picrate, m. p. 119–120° (from ethanol);[14] chloroplatinate of N-*n*-amylpyrrolidine, m. p. 150° (from ethanol);[15] hydrochloride of diisopropylamine, m. p. 209–211°;[16] phenylethylene glycol, b. p. 115–125° (1 mm.), m. p. 69–70° (from benzene), dibenzoate of phenylethylene glycol, m. p. 95–96° (from dilute alcohol);[17] α-naphthylurethan of phenethyl alcohol, m. p. 118–119° (from petroleum ether).[18]

N-*n*-Butylpiperidine (3 g., b. p. 165–175° at 740 mm.) was prepared by the hydrogenation of N-pentamethylenebutyramide (4.7 g.) in 15 ml. of dioxane, with copper chromite at 260° under 300 atm. within one hundred minutes. 7-Piperidinoheptanol-2 (1.2 g.) and 1,6-dipiperidinoheptane (1.1 g., b. p. 127–130°) were obtained by hydrogenating N-pentamethylene-ε-hydroxyheptanoamide (3 g.) with piperidine (2.6 g.) in 14 ml. of dioxane and 1 g. of copper chromite at 260° for 4.3 hours under 300 atm. The picrate of the diamine (m. p. 203–205° dec.) (from ethanol) was made. 1,4-Dipiperidinopentane (1.4 g., b. p. 118–119° at 1 mm., $n^{25}D$ 1.4806) was obtained by heating 5-piperidinopentanol-2 (2.0 g.) with piperidine (1.7 g.) in 10 ml. of dioxane and 1 g. of copper chromite for three and one-half hours at 250° under a pressure of 150 atm. of hydrogen. The picrate, m. p. 168–169° (from ethanol), as well as those given above were used for comparison and mixed melting points.

The fractions listed in Table II were characterized and estimated as follows: I. The neut. equiv. was 98 (calcd. 85). Piperidine was characterized by its addition product with carbon bisulfide, m. p. 170°. II. The neut. equiv. was 110 (calcd. 113) and the amine gave a picrate, m. p. 173–174°, which showed no lowering when the compound was mixed with an authentic sample.[19] III. The neut. equiv. was 156 (calcd. 141) with a picrate of m. p. 130–131°. IV. The neut. equiv. was 154 (calcd. 129) and the compound gave a hydrochloride of the benzoate, m. p. 173–174° (from absolute alcohol–ether), which was compared with an authentic sample.[20,21] The amine could not be separated by fractionation from the acetylpiperidine with which it formed a constant boiling mixture. The separation was made after acidifying the mixture with hydrochloric acid using congo red as an indicator. The amide, acid and water were then evaporated under 10 to 20 mm., the amine recovered from the salt showed a b. p. of 69–70° (9 mm.), $n^{25}D$ 1.4700. V. As indicated above acetylpiperidine could not be separated by fractionation from piperidinoethanol. Fraction V contained about 20% of the amine. The purest sample of the amide had a b. p. 90–91° (8 mm.), $n^{25}D$ 1.4775, and was characterized by hydrolysis to piperidine and acetic acid which were characterized in the usual way. VI. The neutral equivalent indicated that this fraction was quite impure, *i. e.*, 147 compared with 98. The dipiperidinoethane was converted into its methiodide, m. p. 246°, a hydrochloride of the correct analysis, m. p. over 323°,[22] and a picrate, m. p. 225–227° (dec.), were also obtained.[23] VII. The fraction showed the correct analysis for nitrogen and approximately the correct neutral equivalent (181 compared with 185). Solid derivatives could not be obtained. VIII. A sample purified from this fraction had a b. p. 98–99° (1 mm.) and $n^{25}D$ 1.4826, and neut. equiv. of 114 (calcd. 112). A hydrochloride, m. p. 309°, was compared with an authentic sample. The m. p. of picrate was 185–186° (from alcohol).[24] IX. A sample purified from this fraction had a b. p. 114–118° (1 mm.), $n^{25}D$ 1.4859 and a neut. equiv. of 131 (calcd. 126). The methiodide, m. p. 250–253°, showed the correct analysis.[25] X. A sample purified from this fraction, b. p. 125–130° (1 mm.), $n^{25}D$ 1.4949, showed a high neut. equiv. (150 as compared with 134), but gave 1.04 and 1.09 moles of methane in a Zerevitinoff analysis. A picrate, m. p. 138–139°, and a hydrochloride, m. p. 189–191°, were obtained. XI. The neutral equivalent of this fraction indicated the presence of a neutral compound to the extent of 30%. This impurity was presumably dipentamethyleneadipamide. The fraction was therefore hydrogenated in dioxane at 250° over copper chromite. The product, b. p. 150–160° (1 mm.), $n^{25}D$ 1.4943, showed a neut. equiv. of 148 (calcd. 142) and gave a dipicrate, m. p. 170–173° (from alcohol). There was also obtained 1,6-dipiperidinohexane. b. p. 110–120° (1 mm.), resulting from the hydrogenation of the dipentamethyleneadipamide. XII. This fraction was approximately equal parts amide and the glycol of XI, so that it was hydrogenated as above and the resulting 1,6-dipiperidinohexane characterized as the dimethiodide, m. p. 250–253° (from alcohol and ether).

Preparation of Esters.—Diethyl mucate,[26] m. p. 167–168° after one recrystallization from ethanol, was obtained in yields of 76 to 90% through the reaction of mucic acid (50 g.) and dry ethanol (800 ml.). Hydrogen chloride was passed in for three to four hours, the mixture refluxed with stirring, filtered hot and the ester allowed to crystallize out. The higher yields were obtained using four times the quantities selected above, and making allowance for the recovered acid.

Diethyl tartrate (b. p. 150–155° at 13 mm.)[27] in yields of 55 to 67% was made similarly except that the product was distilled.

(9) Laun, *Ber.*, **17**, 680 (1884).
(10) Aschan, *ibid.*, **32**, 991 (1899).
(11) Von Braun, *ibid.*, **40**, 3930 (1907).
(12) Malone and Reid, THIS JOURNAL, **51**, 3424 (1929).
(13) Von Braun and Buckman, *Ber.*, **64**, 2615 (1931).
(14) Von Braun, *ibid.*, **49**, 2641 (1916).
(15) Ochiai and Tsuda, *ibid.*, **67**, 1011 (1934).
(16) Skita and Keil, *ibid.*, **61**, 1457 (1928).
(17) Zincke, *Ann.*, **216**, 295 (1883).
(18) Bickel and French, THIS JOURNAL, **48**, 747 (1926).
(19) Evans, *J. Chem. Soc.*, **71**, 524 (1897).
(20) Von Braun, Braunsdorf and Rath, *Ber.*, **55**, 1674 (1922).
(21) Pyman, *J. Chem. Soc.*, **93**, 1801 (1908).
(22) Brühl, *Ber.*, **4**, 740 (1871).
(23) Knorr, Hörlein and Roth, *ibid.*, **38**, 3139 (1905).
(24) Bruno Wojcik, Ph.D. Thesis, Wisconsin, 1934.
(25) Von Braun, *Ber.*, **43**, 2862 (1910).
(26) Fischer and Speirer, *ibid.*, **28**, 3254 (1895).
(27) Anschütz, *ibid.*, **18**, 1399 (1885).

TABLE III

ANALYTICAL DATA ON PREVIOUSLY UNREPORTED COMPOUNDS

Compound	Formula	$n^{25}D$	B. p. or m. p. °C.	Mm.	Analyses, % Calcd.	Found
N-Pentamethylene lactamide	$C_8H_{15}NO_2$	1.4850	105–108	2	8.92 N	8.78
			128–129	7		
N-Pentamethylene-β-hydroxybutyramide	$C_9H_{17}NO_2$	1.5065	118–123	7	8.19 N	8.35
			84–88	1		
N-Pentamethyl-Δ-hydroxycaproamide	$C_{11}H_{21}NO_2$	1.4910	135–140	1	7.04 N	7.07
N-Pentamethylene-ε-hydroxyheptanoamide	$C_{12}H_{23}NO_2$	1.4857	145–148	0.5	6.57 N	6.53
Di-N-*n*-amyl malamide	$C_{14}H_{28}N_2O_3$		146		10.29 N	10.45
Di-N-*n*-amyl tartaramide	$C_{14}H_{28}N_2O_4$		194–195		9.72 N	9.84
Di-N-*n*-amyl succinamide	$C_{14}H_{28}N_2O_2$		180–181		10.94 N	11.16
N-Pentamethylene butyramide	$C_9H_{17}NO$	1.4750	105–109	7	9.03 N	8.92
Di-N-pentamethylene mucamide	$C_{16}H_{28}N_2O_6$		231 (dec.)		8.14 N	8.03
1,2-Di-piperidinopropane dipicrate	$C_{25}H_{32}N_8O_{14}$		171–172		16.77 N	16.72
5-Piperidino-pentanol-2	$C_{10}H_{21}NO$	1.4698	107	6	8.19 N	8.15
5-Piperidino-pentanol-2 picrate	$C_{16}H_{24}N_4O_8$		97–98		14.00 N	14.22
1,4-Di-piperidinopentane	$C_{15}H_{30}N_2$	1.4806	118–119	1	11.76 N	11.70
1,4-Di-piperidinopentane dipicrate	$C_{27}H_{36}N_8O_{14}$		168–169		16.09 N	16.13
6-Piperidino-hexanol-2	$C_{11}H_{23}NO$	1.4720	123–125	7	7.57 N	7.76
6-Piperidino-hexanol-2 picrate	$C_{17}H_{26}N_4O_8$		86–89		13.53 N	13.55
1,5-Di-piperidinohexane	$C_{16}H_{32}N_2$	1.4810	122–123	0.5	11.11 N	10.91
1,5-Di-piperidinohexane dipicrate	$C_{28}H_{38}N_8O_{14}$		166–167		15.78 N	15.89
7-Piperidino-heptanol-2	$C_{12}H_{25}NO$	1.4729	105–106	1	7.04 N	6.88
7-Piperidino-heptanol-2 picrate	$C_{18}H_{28}N_4O_8$		62–64		13.08 N	12.98
1,6-Di-piperidinoheptane	$C_{17}H_{34}N_2$	1.4808	127–130	1	10.53 N	10.37
1,6-Di-piperidinoheptane dipicrate	$C_{29}H_{40}N_8O_{14}$		203–205 (dec.)		15.47 N	15.62
1,4-Di-piperidinobutane dipicrate	$C_{26}H_{34}N_8O_{14}$		185–186		16.42 N	16.52
1,6-Di-piperidino-hexanol-2	$C_{16}H_{32}N_2O$	1.4949	125–130	1	10.45 N	10.38
1,6-Di-piperidino-hexanol-2 dipicrate	$C_{28}H_{38}N_8O_{15}$		138–139		15.43 N	15.65
1,6-Di-piperidino-hexanol-2 dihydrochloride	$C_{16}H_{34}N_2OCl_2$		189–191		20.82 Cl	20.6
1,6-Di-piperidino-hexanediol-2,5	$C_{16}H_{32}N_2O_2$	1.4943	150–160	1	9.86 N	9.81
N-Pentamethylene β-(β′-hydroxybutyryl)-hydroxybutyramide	$C_{13}H_{23}NO_4$	1.4896	105–110	1	5.45 N	5.97
N-Pentamethylene α-(α′-hydroxyisobutyryl)-hydroxy-isobutyramide	$C_{13}H_{23}NO_4$	1.4651	108–108.5	1	5.45 N	5.43
1,6-Di-piperidino-hexanediol-2,5 dipicrate	$C_{28}H_{38}N_8O_{16}$		170–173		15.09 N	15.24

Diethyl malate[28] (471 g., b. p. 120–130° at 13 mm. from 500 g. acid) was prepared similarly except that about 60% of the volume of the alcohol used was distilled off, replaced with dry ethanol and the esterification repeated.

Ethyl lactate (80 g., b. p. 83–84° at 50 mm.) was made through the reaction of dry ethanol (500 ml.), lactic acid (250 g. of 85% acid) in carbon tetrachloride (250 ml.) for twenty-four hours using an automatic separator which returned the heavier liquid to the flask. Additional ethanol was added and the refluxing continued as long as water was formed.

Ethyl β-hydroxybutyrate (b. p. 64–65° at 7 mm.), ethyl γ-hydroxyvalerate (b. p. 55–60° at 0.5 mm.), ethyl ε-hydroxyheptoate (b. p. 89–91.5° at 0.5 mm., $n^{25}D$ 1.4309) and Δ-caprolactone (b. p. 95–97° at 8 mm., $n^{25}D$ 1.4470) were made by the hydrogenation in ethanol of the corresponding keto esters.[29] Copper chromite at 150° was used for acetoacetic ester while Raney nickel at 125–130° was used in the other cases.

Ethyl ε-ketoheptoate (18 g., b. p. 110–113° at 7 mm., $n^{25}D$ 1.4385) was prepared by the hydrolysis of α-acetyl-Δ-cyanovaleric ester (33.5 g.) during eight hours of refluxing with 20% hydrochloric acid (175 ml.). The solution was cooled, saturated with ammonium sulfate, extracted nine times with ether, the solution dried over anhydrous sodium sulfate and the ether distilled. The residue was taken up in 200 ml. of dry ethanol and filtered. The crude acid was esterified in 100 ml. of carbon tetrachloride for twelve hours using an automatic separator, and the ester separated by fractionation.

The α-acetyl-Δ-cyanovaleric ester (b. p. 85–91° at 1 mm.) used in the above preparation was prepared as by Derick and Hess[30] but the yields were about one-fourth that reported by these investigators.

Ethyl Δ-ketocaproate[31] (161 g., b. p. 98–99° at 9 mm.) was made from α-acetylglutaric ester (274 g.) by refluxing with 500 ml. of 4 *N* hydrochloric acid for nine to ten hours. The Δ-ketocaproic acid (142 g., b. p. 103–107° at 1 mm.) obtained by fractionation was esterified in 250 ml. of ethanol and 125 ml. of carbon tetrachloride for six hours as in the preparation of the ethyl ε-ketoheptoate.

Preparation of Amides.—The N-pentamethylene amides of β-hydroxybutyric and ε-hydroxyheptanoic acids were made in 60% yields by heating the corresponding

(28) Wislicenus, *Ber.*, **25**, 2448 (1892).

(29) Connor, Cramer and Adkins, THIS JOURNAL, **52**, 5192 (1930

(30) Derick and Hess, *ibid.*, **40**, 547 (1918).

(31) Isbell, Wojcik and Adkins, *ibid.*, **54**, 3685 (1932).

ethyl esters (0.5 mole) with piperidine (1.0 mole) for four hours at 200° under hydrogen. N-Pentamethylene-Δ-hydroxycaproamide was made in the same way in 86% yield except that caprolactone was used instead of an ethyl ester. The b. p. and refractive index of the pentamethylene β-hydroxybutyramide are b. p. 118–123° (7 mm.), and $n^{25}D$ 1.5065, and not as previously given.[32]

N-Pentamethylene lactamide, di-N-*n*-amyl malamide, and di-N-*n*-amyl tartaramide were made by refluxing the ethyl ester of the acid (0.5 mole) with a 10% excess of piperidine or amylamine. The yields of the lactamide were 70 to 80% after twenty hours, 87% after three hours for the malamide and 98% after five hours for the tartaramide. The amides were recrystallized from dilute alcohol.

Di-N-pentamethylene mucamide (m. p. 231 dec.) was obtained in quantitative yield by gently heating and stirring a mixture of diethyl mucate (57 g.) with piperidine (40 g.) for a few minutes. The product was washed with ether and alcohol but was not recrystallized.

N-Pentamethylene caproamide (b. p. 95–99° at 1 mm., $n^{25}D$ 1.4725) was made in 81% yield by heating caproic acid (29 g.) and piperidine (21 g.) in dioxane (48 ml.) for three hours at 250° under hydrogen.

Attempts to distil N-pentamethylene-γ-hydroxy-valeramide (prepared by the reaction for four hours of 72 g. of the ester and 85 g. of piperidine at 200° under hydrogen) gave caprolactone. Therefore the crude amide was subjected to hydrogenation without purification.

2,2-Dimethyl-5-phenyl-4-oxazolidone (80 g., m. p. 127°) was obtained by the reaction of mandelamide (160 g.) with acetone (600 ml.).[33] The product was refluxed with Raney nickel in ethanol for thirty minutes and then crystallized from ethanol.

Refluxing ethyl β-hydroxybutyrate (100 g.) for four hours with piperidine (77 g.) gave only 19 g. of the desired amide. There was also obtained 46 g. of a compound, b. p. 105–110° at 1 mm., $n^{25}D$ 1.4896, which gave the correct analysis for N-pentamethylene-β-(β′-hydroxybutyryl)-hydroxybutyramide. Similarly when ethyl α-hydroxyisobutyrate (132 g.) was heated, for four hours at 200° under hydrogen, with piperidine (170 g.) the desired amide was not obtained. Instead a compound (56 g.), b. p. 108° at 1 mm., $n^{25}D$ 1.4651, was obtained which showed the correct analysis for N-pentamethylene-α-(α′-hydroxyisobutyryl)-hydroxyisobutyramide. The formation of these products is analogous to those formed in the hydrogenation of β-keto esters in the absence of a solvent.[29]

(32) Wojcik and Adkins, THIS JOURNAL, **56**, 2423 (1934).

(33) Fischer, *et al.*, *Ber.*, **65B**, 1032 (1932).

Summary

Various N-pentamethylene amides having a hydroxyl group in the α, β, γ, δ or ε position have been submitted to hydrogenation over copper chromite. The corresponding amino alcohols have been obtained in yields of 51 to 79%, except from the amide having the hydroxyl group in the β-position, in which case the hydroxyl group was eliminated and the chief product was the alkylpiperidine. Glycols and diamines were also obtained in low yields from certain of the hydroxy amides.

Raney nickel catalyzed the same types of reaction with hydroxyamides as did copper chromite. However, reaction was not so rapid and the yields of piperidino alcohols were much lower than with copper chromite.

Raney nickel with $CH_3CHOHCH_2C(O)NC_5H_{10}$ gave the amide $CH_3CH_2CH_2C(O)NC_5H_{10}$ while copper chromite also catalyzed the hydrogenation of the carbonyl group giving the amine $CH_3CH_2CH_2CH_2NC_5H_{10}$.

The action of hydrogen over copper chromite upon di-N-pentamethylene mucamide gave twelve products as listed in Table II. It is a striking fact that cleavage of the six carbon chain occurred exclusively between carbon atoms 2 and 3 and never between carbon atoms 3 and 4, as in the hydrogenolysis of the six carbon sugars and the corresponding alcohols.

The hydrogenolysis of amides derived from malic, tartaric and mandelic acids has also been studied.

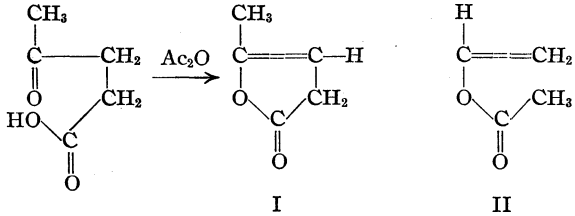
MADISON, WISCONSIN RECEIVED MARCH 9, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

The Structure of Vinyl Polymers. III.[1] The Polymer from α-Angelica Lactone

BY C. S. MARVEL AND CHARLES L. LEVESQUE[2]

α-Angelica lactone (I), readily prepared by the action of acetic anhydride on levulinic acid,[3] may be regarded as a disubstituted vinyl acetate (II)



I II

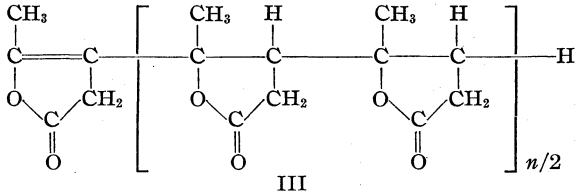
type. Such esters, with terminal substituents on the vinyl group, do not polymerize readily, but it seemed possible that the strain due to the lactone ring structure might activate the double bond in this case. Although peroxides, the usual catalysts for vinyl polymerization, are ineffective, α-angelica lactone is easily polymerized by the boron fluoride–ether complex. The product is a tacky, dark red solid. Attempts to remove the color have been unsuccessful.

Long irradiation of α-angelica lactone with ultraviolet light also produces a polymer. Although less highly colored than the product obtained by the use of boron fluoride, it is also of lower molecular weight, since it shows an appreciable cold flow. Only the polymer formed by the boron fluoride catalyst was used in the investigations reported below.

Cryoscopic determinations in benzophenone and bromine titration of the residual double bonds gave values of 800–900 for the average molecular weight of the polymer. This corresponds to a chain of eight to nine units. The relatively low value of the molecular weight, and the presence of one double bond per molecule indicate a stepwise polymerization related to the Friedel–Crafts reaction, rather than the chain mechanism frequently encountered in other vinyl polymerizations. The double bond is probably in a terminal unit.

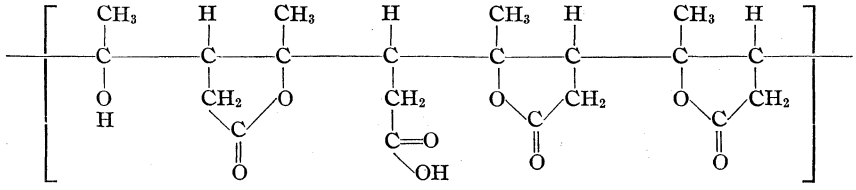
Most of the lactone groups are retained in the polymer, since it dissolves only slowly in aqueous sodium hydroxide, reacts with ammonia to produce a polylactam, and with phenyllithium to give a polyalcohol. As is frequently the case with polymers, the two latter reactions do not proceed to completion. Analysis indicates that in the lactam, 80%, and in the alcohol, 90% of the carbonyl groups have undergone reaction.

Analyses of the original polymer demonstrated that approximately every fourth lactone unit had added a molecule of water. If a "head to tail" structure (III, $n = 7$ or 8) is assumed for the polymer, this result is readily explained.



III

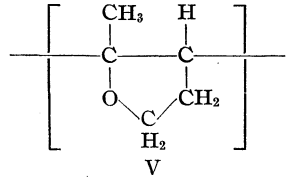
Boron fluoride is a *trans* esterification catalyst, and a *trans* esterification of a polymer such as III would result in the liberation of some hydroxyl and carboxyl groups. Since *trans* esterification is a random reaction certain of these groups will become isolated (IV).



IV

Since this reaction would tend to approach equilibrium, the number of unesterified groups cannot be calculated by Flory's statistical method.[4] The value found, however, is quite consistent with the "head to tail" formulation.

When an attempt was made to hydrogenate the lactone units to tetrahydrofuran units (V) at 250°



V

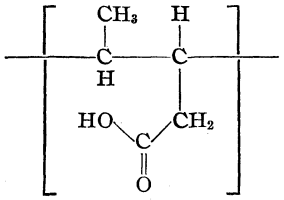
(1) For the second communication in this series, see Marvel and Denoon, THIS JOURNAL, **60**, 1045 (1938).

(2) Du Pont Fellow in Chemistry.

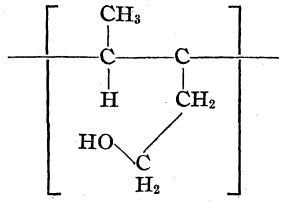
(3) Gilmour, *J. Chem. Soc.*, **105**, 753 (1914).

(4) Flory, THIS JOURNAL, **61**, 1518 (1939).

and 400 atm. over copper–chromium oxide,[5] the amount of hydrogen absorbed was nearly twice that calculated for this reaction alone. The polymeric material isolated weighed only 70% as much as the starting material, and had a much lower average molecular weight. Analysis of this product showed that reactions other than simple hydrogenation of the carbonyl groups had occurred. These facts also pointed to the "head to tail" structure (III), since this structure contains the grouping –O–C–C–C–O. It has been shown[6] that in this group, common to 1,3-glycols and their ethers, 1,3-diketones, β-keto esters, etc., the carbon–oxygen bonds and the carbon–carbon bonds are especially sensitive to cleavage by hydrogen at high pressure and temperature over copper–chromium oxide. Under the conditions used in our reduction experiment, in addition to tetrahydrofuran units (V), the polymer III would also produce units of VI and VII,



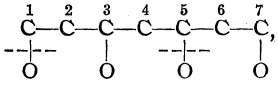
VI



VII

formed by hydrogenolysis of the carbon–oxygen bond both before and after reduction of the carbonyl group. The analytical results may be explained on the basis that a mixture of these structural units (V, VI and VII) is produced. Hydrogenolysis of the carbon–carbon bonds would account for the lower molecular weight, and the losses.

To test this hypothesis, the original polymer was treated with hydrogen at 175° and 400 atm. over copper–chromium oxide. From certain of the data of Connor and Adkins,[6] it seemed possible that at this temperature, cleavage of the carbon–oxygen bonds might take place to a much greater extent than cleavage of the carbon–carbon bonds. It is obvious that the former cleavage can never be quantitative. In the group



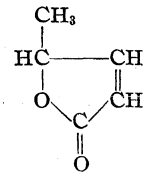
for example, cleavage of the bonds, as indicated at carbon atoms 1 and 5, would destroy the 1,3-glycol character of the carbon–oxygen bond at carbon atom 3. Hence this bond would not cleave. Applying the methods of Flory,[4] and assuming no carbon–carbon cleavage, it may be calculated that for a 1,3-type polymer of n units, the following relation holds

$$S_n = \frac{2}{n}\left(1 + \frac{3}{3} + \frac{4}{3} + \frac{5}{3} + \cdots \frac{n}{3}\right) = \frac{n+1}{3}$$

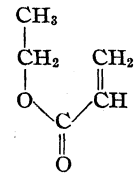
S_n is the number of carbon–oxygen bonds per molecule not cleaved. For an octamer $S_8 = 3$. Hence only 62.5% of the carbon–oxygen bonds should be cleaved, and the polymer will take up 0.625 molecule of hydrogen per unit. Since there is also one double bond for every eight units, another 0.125 molecule of hydrogen per unit will be taken up, making the total amount of hydrogen absorbed 0.75 molecule per unit.

This figure agrees satisfactorily with the experimental result. The polymer absorbed 0.84 ± 0.05 molecule of hydrogen per unit to give a quantitative yield of a polyacid. The analysis of the material obtained agreed with that calculated on the assumptions above, and a determination of the molecular weight showed that little carbon–carbon cleavage had taken place.

We have considered the possibility that isomerization of the α-form to β-angelica lactone (VIII)[7] might have taken place before polymerization. This β-lactone is a substituted ethyl acrylate (IX) type. However, neither of the two

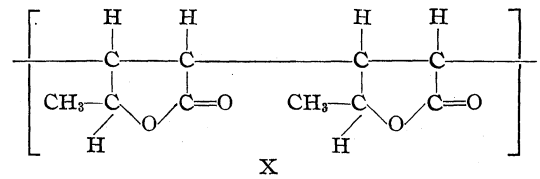


VIII

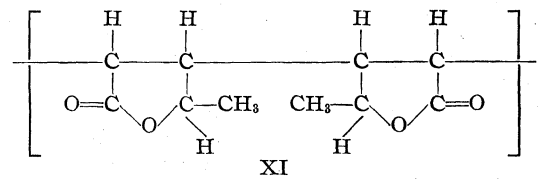


IX

possible structures for a β-angelica lactone polymer (X, XI) would have the 1,3-glycol grouping



X



XI

which has been shown to be present in our polymer.

(5) Connor, Folkers and Adkins, THIS JOURNAL, **54**, 1138 (1932).
(6) Connor and Adkins, *ibid.*, **54**, 4678 (1932).
(7) Thiele, Tischbein and Lossow, *Ann.*, **319**, 188 (1901); Auwers, *Ber.*, **56**, 1672 (1923).

From these data, the polymer produced from α-angelica lactone is a polylactone having a "head to tail" structure, and containing about 25% free carboxyl and hydroxyl groups (IV).

Experimental

Polymerization of α-Angelica Lactone by the Boron Fluoride–Ether Complex.—To a solution of 15 g. of α-angelica lactone[3] in 40 cc. of carbon disulfide was added 0.4 cc. of the boron fluoride–ether complex. The solution was refluxed gently for five hours. The colorless supernatant layer was decanted from the viscous red polymer layer which was then washed by decantation with several portions of ether, and freed of volatile matter by heating slowly (one and a half hours) to 80° at 2 mm. There remained 14.7 g. of a dark red solid, tacky, but showing no cold flow. It was readily soluble in acetone, dioxane, cellosolve, ethyl alcohol and butyl alcohol, slowly soluble in aqueous sodium hydroxide, insoluble in water, ether, benzene and ligroin.

Mol. wt. (benzophenone): 845. Bromine titration: 3.030 g. of polymer in ethanol–chloroform required 17.3 cc. of 0.214 *N* bromine in carbon tetrachloride; eq. wt., 818. The polymer may also be prepared in ether solution, though in lower yields.

Anal. Calcd. for $(C_6H_8O_2)_4 \cdot H_2O$: C, 58.4; H, 6.40. Found: C, 58.17, 58.19, 58.38; H, 6.64, 6.89, 6.56.

Polymerization of α-Angelica Lactone by Ultraviolet Light.—Five cubic centimeters of α-angelica lactone in a quartz test-tube was irradiated for two weeks with light from a mercury vapor arc. At the end of this time, the lactone had polymerized to a very viscous orange liquid. The liquid had the same solubility characteristics as the boron fluoride catalyzed polymer.

Poly-α-angelica Lactam.—A solution of 6.0 g. of polylactone in 50 cc. of dioxane was placed in a glass-lined steel bomb, cooled in dry-ice, and 20 cc. of liquid ammonia added. The bomb was sealed, and heated at 150–160° for three hours, then allowed to cool to room temperature overnight. The glass liner containing the reaction mixture was removed, the supernatant liquid decanted and the precipitated polymer washed with dioxane and ligroin. After drying *in vacuo* over concentrated sulfuric acid 4.0 g. of brittle, red-brown solid remained. It was readily soluble in water.

Anal. Found: N, 11.59.

Assuming the free carboxyl groups (IV) are converted to ammonium salt groups, this analysis shows that 84% of the lactone groups have been converted to lactam groups.

Reaction of Polylactone with Phenyllithium.—A solution of phenyllithium in ether was prepared under nitrogen from 2.3 g. of lithium and 25 g. of bromobenzene, and the ether displaced by toluene. To this was added a solution of 6.0 g. of the polylactone in a mixture of 50 cc. of dimethyl ether of ethylene glycol and 50 cc. of toluene. Heat was evolved and a reddish-brown, flocculent precipitate formed. The mixture was stirred and heated on a steam cone for sixteen hours then 50 cc. of water was added cautiously and steam passed through the mixture for two hours to remove solvents and diphenyl. Fifteen cubic centimeters of concentrated hydrochloric acid was added, and the steam distillation continued for one hour. The hot polymer, which had collected as a heavy, oily liquid, was thoroughly washed with several portions of hot water. After cooling, and drying *in vacuo* over sulfuric acid, 10.0 g. of plastic, chocolate brown solid remained. It was soluble in alcohol, and insoluble in aqueous sodium hydroxide.

Anal. Calcd. for $C_{17}H_{18}O_2$: C, 80.2; H, 7.14. Found: C, 78.15; H, 6.85.

Hydrogenation of the Polymer at 250°.—A solution of 10 g. of the polylactone in 135 cc. of butanol was twice refluxed over Raney nickel, and filtered into a 280-cc. steel bomb. Five grams of copper–chromium oxide catalyst[5] was added and the bomb filled with hydrogen at 3325 lb. (222 atm.) and 25°. After shaking at 250° for ten and a half hours, the pressure drop (after cooling) was 900 ± 20 pounds, equivalent to 3.92 ± 0.05 moles of hydrogen per mole of polymer unit. The reaction mixture was filtered, centrifuged, and the solvent removed *in vacuo* in a stream of nitrogen. The residual liquid was washed into an evaporating dish with a little alcohol and, after drying *in vacuo* over sulfuric acid, left 7 g. of a light brown, viscous liquid.

Anal. Calcd. for C_5H_8O: C, 71.5; H, 9.6; $C_5H_{10}O$: C, 69.8; H, 11.8; $C_5H_8O_2$: C, 60.0; H, 8.06. Found: C, 67.54; H, 9.94; mol. wt. (benzophenone), 351.

Hydrogenation of the Polylactone at 175°.—Fourteen and eight-tenths grams of polymer was dissolved in 140 cc. of dioxane which previously had been treated with hydrogen and copper–chromium oxide. The solution was twice refluxed over Raney nickel and then filtered into a 280-cc. steel bomb containing 5.0 g. of copper–chromium oxide. Hydrogen at 4100 lb. (273 atm.) and 25° was admitted and the bomb shaken at 175° until absorption of hydrogen ceased (twenty hours). The pressure drop (cold) was 320 ± 20 pounds, equivalent to 0.84 ± 0.05 mole of hydrogen per mole of polymer unit. The product was isolated as before, giving 15.1 g. of a very viscous brown polymer, insoluble in water, but readily soluble in aqueous sodium bicarbonate.

Anal. Calcd. for 75% $C_5H_8O_2$ + 25% $C_5H_6O_2$: C, 60.31; H, 7.58. Found: C, 60.20; H, 7.24; mol. wt. (benzophenone), 767.

Summary

The polymer prepared by the action of boron fluoride–ether complex on α-angelica lactone has been shown to be a polylactone having the "head to tail" structure.

URBANA, ILLINOIS RECEIVED APRIL 15, 1939

[CONTRIBUTION FROM THE METCALF CHEMICAL LABORATORY OF BROWN UNIVERSITY]

The Preparation and Reactions of Some Triphenyllead Derivatives

BY LAURENCE S. FOSTER, WILLIAM M. DIX AND IRVING J. GRUNTFEST

Introduction

By taking advantage of the reducing properties of solutions of the alkali metals in liquid ammonia and related solvents, it is possible to prepare some types of organo-metallic compounds which elude preparation in any other way. The method has had striking success in studying the organo-metallic compounds of the elements in Group 4B of the periodic table.[1] Until very recently no work on lead compounds from this viewpoint had been reported,[2] and the purpose of this investigation was to extend the earlier studies to the triphenyllead derivatives.[3]

In all of their properties the triphenyllead derivatives are found to follow the trends observed with the corresponding derivatives of the other elements in Group 4B. In passing from lead to carbon, the strength of the bond between the phenyl group and the metallic element becomes continually greater and, except for carbon, the same is true of the metal-to-metal bond in the dimeric form of the "free group." The high degree of dissociation of hexaphenylethane is decidedly abnormal, but the apparent partial dissociation of hexaphenyldilead, $(C_6H_5)_3Pb—Pb(C_6H_5)_3$, observed in dilute benzene solutions, is not unexpected.

The halides of triphenyllead and triphenyltin are stable in liquid ammonia, but those of the germanium and silicon derivatives are irreversibly and completely ammonolyzed. Triphenylmethyl halides undergo partial ammonolysis, but the reaction is reversible and the compounds may be used in preparations in ammonia without much side reaction.

With all of the Group 4B elements, the alkali metal salts of the triphenyl derivatives are stable in liquid ammonia at $-33.4°$. There is, however, a marked deepening of the color of their solutions in proceeding from lead to carbon. A solution of sodium triphenylplumbide, $NaPb(C_6H_5)_3$, is colorless when dilute and pale yellow when concentrated, but a solution of potassium triphenylmethide, $KC(C_6H_5)_3$, is an intense red even when dilute. The solutions of the corresponding salts of the intervening metals are intermediate in color. In these salts the triphenylmetal anion becomes progressively more electronegative in the same order When, for example, sodium triphenylgermanide is allowed to react with an ammonium salt, the anion, $(C_6H_5)_3Ge^{1-}$, takes on a proton and triphenylgermane is precipitated. This reaction is characteristic of the entire group with the exception of the lead analog. No hydride is formed when ammonium bromide is added to a solution of sodium triphenylplumbide in ammonia, but the solution appears to contain ammonium triphenylplumbide as a highly ionized salt. Evidently the triphenylplumbide ion, $(C_6H_5)_3Pb^{1-}$, is not basic enough to remove the proton from the ammonium ion, and the normal group reaction is not observed, even in the presence of great excess of ammonium salt.

Experimental

Preparation of Tetraphenyllead.—The method followed was that of Gilman and Robinson,[4] in which carefully dried lead dichloride is allowed to react with phenylmagnesium bromide, but with the substitution of xylene for benzene to increase the temperature of refluxing. The yields were sometimes as high as 81% (based upon the amount of lead dichloride used) but the results were not uniform.

Preparation of Triphenyllead Chloride.—Dry hydrogen chloride was passed into a solution of tetraphenyllead in chloroform, according to the method of Gilman and Robinson,[5] and the yield of 75% of the theoretical agreed with their observations.

Preparation[6] and Purification of Triphenyllead Iodide.—The preparation of triphenyllead chloride is not entirely satisfactory, so the iodide was investigated. It was found that it could be made easily and in addition the iodide proved to be a superior reagent for the syntheses undertaken. A solution of iodine in chloroform was stirred vigorously into a suspension of an equivalent quantity of tetraphenyllead in chloroform. The solvent and the iodobenzene formed in the reaction were removed by vacuum distillation at 100°. The yellow crystalline residue was extracted with methyl alcohol to separate the product from the diphenyllead diiodide also formed and from the unreacted tetraphenyllead. Crude triphenyllead iodide

(1) A review of some of this work is given by Kraus, *J. Chem. Ed.*, **8**, 2130 (1931).

(2) Calingaert and Soroos, *J. Org. Chem.*, **2**, 535 (1938).

(3) Many of the results reported here confirm the findings of Gilman and Bailie in a contribution which appeared after this manuscript was submitted to the Editor; THIS JOURNAL, **61**, 731 (1939).

(4) Gilman and Robinson, THIS JOURNAL, **49**, 2315 (1927).

(5) Gilman and Robinson, *ibid.*, **51**, 3112 (1929).

(6) The preparation was carried out by H. I. Boynton as a part of a senior research problem, 1933.

was crystallized from the extract in an amount representing 97% of the theoretical yield. Even after several recrystallizations, the product still had a light yellow color, and melted over a range from 138° to 141°.[7] It was found that the colored impurity could be removed by dissolving the iodide in ether and allowing the solution to stand over metallic sodium or silver for two days. From the ether, pure white crystals of the iodide were recovered which melted sharply at 142° (uncorr.).[8]

Preparation of Hexaphenyldilead (Triphenyllead).—Krause and Reissaus[7b] (p. 894) prepared hexaphenyldilead by the reaction of phenylmagnesium bromide and lead dichloride in absolute ether, where it is an intermediate product in the formation of tetraphenyllead. Austin[9] reported that it is isolated as a by-product of the reaction between phenyllithium and lead dichloride, when the mixture is not heated to too high a temperature. It may be prepared most simply and practically quantitatively by reducing triphenyllead iodide by means of an equivalent amount of sodium in dry liquid ammonia. After the reaction is completed and the ammonia has evaporated, the residue is extracted with chloroform, filtered and concentrated by distillation until the solution is nearly saturated. Cold ethyl alcohol is added to precipitate the hexaphenyldilead. It is recrystallized in the same way, *i. e.*, from chloroform solution by the addition of ethyl alcohol. The amount of the purified product is above 90% of the theoretical yield.

Use of Tetrasodium Nonaplumbide, Na_4Pb_9, as a Reducing Agent.—If triphenyllead chloride is used in place of the iodide in the preparation of triphenyllead, the reaction does not proceed so smoothly, evidently due to the lower solubility of the chloride in ammonia. It was found feasible, however, to carry out the reduction of the chloride by means of tetrasodium nonaplumbide, Na_4Pb_9,[10] which evidently is a much weaker reducing agent than sodium and permits the reduction to proceed without cleavage of phenyl groups from the triphenyllead radical. The equations for the reactions involved in the preparation of hexaphenyldilead by means of this reducing agent are

$$9PbCl_2 + 22Na = Na_4Pb_9 + 18NaCl$$
$$Na_4Pb_9 + 4(C_6H_5)_3PbCl = 2[(C_6H_5)_3Pb]_2 + 4NaCl + 9Pb$$

Lead dichloride is placed in a reaction tube immersed in a bath of liquid ammonia at −33.4°. When ammonia is condensed upon the lead halide, it swells tremendously, due to the formation of ammines,[11] and partly dissolves. Sodium is added in several pieces. The tetrasodium nonaplumbide formed is soluble and the solution is practically opaque. Triphenyllead chloride in powdered form is added slowly from an attached tube and hexaphenyldilead precipitates. The color of the solution disappears and a curdy mass (Pb) rapidly settles to the bottom of the tube. After the ammonia has evaporated, hexaphenyldilead is extracted from the residue and recrystallized. The yield of the purified product is above 90% of the theoretical.

Properties of Hexaphenyldilead. (a) **Stability.**—Krause and Reissaus[7b] report that when it is heated, hexaphenyldilead decomposes at 155° with the deposition of lead and finally melts at 225°, the melting point of tetraphenyllead. We have observed that different samples vary in their behavior. One exploded at 173°, turned black and melted at 225°. Frequently the blackening appears at 170°. If the determination is carried out very slowly in an open sample tube, no blackening is observed, due to the oxidation of the deposited lead, but melting occurs invariably at 225°. If the sample tube is evacuated, decomposition may occur from 5 to 10° below 170° but the blackening is always observed. The characteristic pyrolytic behavior may be used in confirming the identity of the material.

Hexaphenyldilead becomes yellow and infusible when kept for six months in a loosely corked, colorless bottle in the normal illumination of the laboratory, but samples have been kept for five years in the dark without change. From a solution of hexaphenyldilead in alcohol, kept for two months in the dark, the substance was recovered without change in its properties, but when it was dissolved in benzene, it underwent reaction, especially if the solution was kept warm. These observations are not entirely compatible with those of Krause and Reissaus, and may explain the anomalous molecular weight data discussed in a later section.

(b) **Solubility.**—Hexaphenyldilead is very soluble in carbon tetrachloride and chloroform, moderately soluble in benzene and acetone, and very slightly soluble in liquid ammonia, methyl and ethyl alcohols, ethyl ether and petroleum ether. It is insoluble in water.

(c) **Molecular Weight.**—Krause and Reissaus[7b] present evidence to show that hexaphenyldilead is highly dissociated into the monomeric form in dilute solutions in benzene. Three cryoscopic determinations made at different concentrations confirm their findings. At the concentrations stated below, expressed in grams of hexaphenyldilead per 1000 g. of benzene, the apparent molecular weight is seen to be less than 876, the theoretical value for the dimer: 9.53 g., 768; 18.71 g., 773; and 29.94 g., 791. While in both these results and those of Krause and Reissaus there is a steady rise in molecular weight with concentration increase, no mass action constant could be calculated for either set of data. At present it is not possible to offer any explanation for the observations.

Preparation of Sodium Triphenylplumbide.—This substance may be made in ammonia solution by reducing triphenyllead chloride or iodide or hexaphenyldilead by means of sodium or tetrasodium nonaplumbide. To prepare the pure salt, however, the reaction between sodium and hexaphenyldilead must be adopted. Due to side reactions, finely divided lead may appear as a precipitate, but if great care is exercised to prevent the concentration of sodium from becoming high at any time, not enough lead is formed to lower the yield appreciably. If the temperature is allowed to rise as the ammonia evaporates ammonolysis occurs, yielding unknown products. By removing the ammonia under reduced pressure at −33.4° or lower, the salt crystallizes from a faintly yellow saturated solution as a solid with a rather intense lemon-yellow color. The color

(7) (a) Grüttner, *Ber.*, **51**, 1301 (1918); (b) Krause and Reissaus, *ibid.*, **55**, 897 (1922).

(8) The method was checked by M. A. Dicesaro, who obtained a yield of 87.7% of the purified product on a 10-g. run.

(9) Austin, THIS JOURNAL, **54**, 3726 (1932).

(10) Smyth, THIS JOURNAL, **39**, 1299 (1917); Kraus, *ibid.*, **44**, 1229 (1922); Zintl, Goubeau and Dullenkopf, *Z. physik. Chem.*, **154**, 1 (1931); Zintl and Harder, *ibid.*, **154**, 47 (1931).

(11) Biltz and Fischer, *Z. anorg. allgem. Chem.*, **124**, 230 (1922).

fades as the residual ammonia is withdrawn, and the dry, cream-colored salt formed is stable at room temperature.

Preparation of Triphenylethyllead.—Since the properties of triphenylethyllead had been established previously,[12] its preparation was undertaken to demonstrate the existence of the triphenylplumbide ion in the ammonia solution of the sodium salt. An excess of ethyl bromide was admitted to the reaction vessel and white crystals of triphenylethyllead were precipitated. A pure product was obtained by dissolving the crude material in a small quantity of ethyl ether, adding about twice the quantity of methyl alcohol and evaporating the solution *in vacuo* at room temperature. The material precipitated in white curds, which when dried *in vacuo* formed a fine white powder. The melting point was 39° and molecular weight determinations and analyses for lead identified it as triphenylethyllead. It is very soluble in ether, acetone, carbon tetrachloride and petroleum ether, less soluble in methyl alcohol and only very slightly soluble in ammonia.

Ammonium Triphenylplumbide.—When an ammonium salt,[13] in equivalent amount, is added to a liquid ammonia solution of sodium triphenylplumbide, no reaction is observed. If a small excess is added, no change in appearance of the solution is apparent, but in the presence of great excess, complete destruction of the triphenylplumbide radical results, accompanied by the separation of metallic lead in large, heavy, black curds and the production of benzene.

When the solution containing sodium and ammonium triphenylplumbides is evaporated at low temperatures under reduced pressure, crystals do not appear until it has become very concentrated and no indication of reaction between the ammonium ion and the triphenylplumbide ion is detectable. If ethyl bromide is added to the dilute solution, a white precipitate of triphenylethyllead separates, indicating that the triphenylplumbide ion remains unchanged. Ammonium triphenylplumbide appears to be stable and very soluble in liquid ammonia at −33.4°.

Reaction of Sodium Triphenylplumbide with Methylene Chloride.—Sodium triphenylplumbide, freed of ammonia at −33.4°, was allowed to react with an excess of dry methylene chloride. The salt dissolved at first to form a yellow solution, but the color gradually faded, due presumably to reaction. A soft, waxy solid of indefinite melting point and soluble in petroleum ether was isolated from the product. A single molecular weight determination gave a value of 640, suggesting that the product might contain two triphenyllead radicals, comparable to the product of the reaction of sodium triphenylgermanide with methylene chloride.[14] No similar product was detected, however, when the reaction was carried out in liquid ammonia solution. Since no pure, well characterized product could be obtained, this reaction was not investigated further.

Summary

1. Methods for the preparation of tetraphenyllead, triphenyllead iodide, hexaphenyldilead, sodium triphenylplumbide and triphenylethyllead are described and some of the reactions and properties of these compounds are recorded.

2. Use is made of tetrasodium nonaplumbide, Na_4Pb_9, as a mild reducing agent in liquid ammonia solutions.

3. The existence of ammonium triphenylplumbide as a fairly stable and soluble salt in liquid ammonia has been indicated, but triphenylplumbane does not appear to be formed.

(12) Krause and Schmitz, *Ber.*, **52**, 2150 (1919); Krause and Schlöttig, *ibid.*, **58**, 430 (1925).

(13) Compressed tablets (5 grain) of ammonium bromide, supplied by Burroughs, Wellcome and Co., New York, serve as a very satisfactory source of ammonium ions.

(14) Kraus and Nutting, THIS JOURNAL, **54**, 1622 (1932).

PROVIDENCE, R. I. RECEIVED JANUARY 27, 1939

[CONTRIBUTION FROM THE METCALF CHEMICAL LABORATORY OF BROWN UNIVERSITY]

Ammino Compounds of Triphenyllead Chloride

BY LAURENCE S. FOSTER, IRVING J. GRUNTFEST AND LINTON A. FLUCK

When ammonia is condensed upon crystalline triphenyllead chloride at the boiling point of liquid ammonia, the volume of the solid increases greatly, indicating that a reaction occurs. It has been shown that a series of ammino compounds exists, none of which is stable at room temperature. Two methods have been employed in an attempt to establish the composition of the solid phases: in the first, method I, which was entirely volumetric, the amount of ammonia which was added or withdrawn from the reaction chamber was measured by means of a gas buret; and in the second, method II, the gas buret was used to make small, definite adjustments in the amount of ammonia in the system, but the composition of the phase under investigation was determined by decomposing it and absorbing and weighing the ammonia evolved. Method I was found to be useful for a preliminary exploration of the system, but since the errors in the volume measurements were cumulative, it did not prove to be entirely satisfactory. Method II was used in determining the composition of the highest ammino compound only, and had the advantage that it was much more rapid.

Using the volumetric method (I), two runs

were carried out, each taking about three months, due to the slowness with which equilibrium is established between the solid phases. The results were not in very good agreement, and from the data it was not possible to determine the ratio of the number of moles of ammonia per mole of triphenyllead chloride with an error of less than 10%. The results are shown graphically in Fig. 1, where the equilibrium pressures are plotted against the number of moles of ammonia per mole of triphenyllead chloride present in the condensed phase. There are indications of the existence of at least four ammino compounds which have the following approximate compositions

Vapor pressure, mm.	400	160	100	50
Moles NH_3	9.65	2.7	1.8	1.3

The vertical line in the graph, corresponding to 9.72 moles of ammonia, was drawn from the data obtained using method II. The existence of a metastable compound with a vapor pressure of 415 mm. is suggested, but its composition was not established.

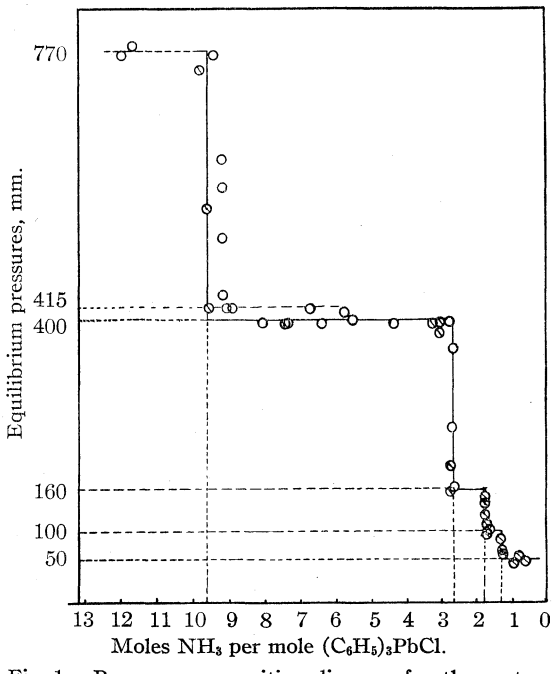


Fig. 1.—Pressure–composition diagram for the system $(C_6H_5)_3PbCl$–NH_3 at −33.4°.

Due to the uncertainties of the results, it was decided to repeat part of the work, focusing the attention upon the compound containing the largest amount of ammonia, since it could be prepared readily in equilibrium with the saturated solution and analyzed conveniently by the use of method II. The experiments were performed independently by two operators who used different equipment and different preparations of triphenyllead chloride. The results of eight experiments gave an average composition of 9.72 moles of ammonia per mole of triphenyllead chloride, and the deviations of the individual results from the mean were less than 1%. The composition for this single compound is in fair agreement, thus, with that obtained through the use of the first method.

While it is not usual for the numbers of molecules in complex ammino compounds to be so far from a ratio of small whole numbers, it appears that the tentative conclusion must be drawn that with triphenyllead chloride the ratio of the number of moles of ammonia per mole of chloride, in the highest complex, has a value of about 29 to 3 or 68 to 7. Additional information concerning the structure will be needed before a formula can be assigned. The experimental data for the other ammino compounds are so inaccurate that no statement concerning their compositions is justified at this time.

Few studies have been made of the compounds formed between organo-metallic substances and neutral molecules, like those described here. In the index of the treatise by Krause and von Grosse,[1] out of the 6000 organo-metallic compounds listed only two dozen ammino or similar complex derivatives are catalogued, and none of them show any irregularities. It may be noted, however, that Biltz and Fischer[2] found that several ammino compounds are formed by the lead dihalides, the compositions of some of which do not correspond to ratios of small whole numbers; *e. g.*, $4PbCl_2 \cdot 13NH_3$ and $2PbCl_2 \cdot 11NH_3$. They postulated that these compounds consist of mixtures of simpler ammines, but until structure determinations have been made the question as to their formulas also remains unanswered.

Experimental

Preparation of Triphenyllead Chloride.—The starting material was tetraphenyllead and it was converted to triphenyllead chloride by the method of Gilman and Robinson.[3] The samples used were shown to be pure by the melting point, 206°, and by analysis for chlorine. The material is stable toward ammonia; the weights and melt-

(1) Krause and von Grosse, "Die Chemie der metall-organischen Verbindungen," Berlin, 1937.

(2) Biltz and Fischer, *Z. anorg. allgem. Chem.*, **124**, 230 (1922).

(3) Gilman and Robinson, THIS JOURNAL, **51**, 3112 (1929).

ing points of the samples remained unaltered, even though the outward appearance was considerably changed during the formation and decomposition of the complexes. Triphenyllead chloride is stable toward air and atmospheric moisture.

Apparatus and Procedure.—The sample of triphenyllead chloride was sealed in a "Pyrex" glass bulb (vol., 17 ml.) attached to a long stem of capillary tubing, a stopcock and one part of a ground joint. The reaction bulb thus could be removed from the system and weighed. It was cooled to −33.4° in a bath of liquid ammonia. In addition to connections to the source of purified and redistilled ammonia and to a "Hyvac" vacuum pump, the remaining apparatus consisted of a mercury manometer; a removable bulb, similar to the reaction bulb, holding anhydrous calcium chloride for absorbing and weighing the ammonia evolved upon decomposition of the compounds; and a jacketed gas-measuring buret[4] equipped with a Pettersson compensator set for 760 mm. and 0°,[5] so that the number of moles of gaseous ammonia added or withdrawn from the reaction vessel could be determined without laborious calculations. The volumes of the connecting tubes were determined so that it was possible to compute at any time, from the total amount of ammonia in the system, the amount of ammonia held in the condensed phase.

Since the vapor pressures of the solid compounds were found not to vary appreciably with small temperature fluctuations, no attempt was made to maintain the boiling point of the bath ammonia at a strictly constant temperature. The vapor pressure of the saturated solution of triphenyllead chloride, on the other hand, did vary considerably with temperature, and it seemed advisable, prior to recording significant vapor pressure values, to replace the ammonia in the bath with a fresh supply and to allow it to evaporate against a definite pressure, to ensure that the temperature was −33.4°.

Sufficient ammonia was condensed in the reaction tube to form a saturated solution of triphenyllead chloride in equilibrium with the highest ammino complex. After the crystals had been allowed to remain in contact with the solution for several days, ammonia was withdrawn, either in measured quantities by means of the gas buret (method I) or more rapidly by means of the vacuum pump (method II). In either case, when the sample was nearly dry the remaining excess ammonia was taken off slowly by means of the buret, and when it was established that the dry salt was in equilibrium with the vapor, the pressure was recorded and the composition of the complex compound was determined.

Using method I, additional ammonia was removed in known decrements and the system was allowed to return to equilibrium after each removal. In this way the equilibrium pressure–composition diagram, shown in Fig. 1, was arrived at.

In method II, once the ammino compound was formed, in the manner just described, it was decomposed by allowing it to warm to room temperature and the ammonia evolved was absorbed in the weighing tube containing calcium chloride, cooled to −33.4°. By subtracting the amount of ammonia computed to be in the gas phase in the reaction bulb, at −33.4°, the amount of ammonia held in the solid phase was obtained. The data are given in Table I, expressed in moles of reactants.

TABLE I

COMPOSITION OF THE HIGHEST AMMINO COMPOUND OF TRIPHENYLLEAD CHLORIDE FORMED AT −33.4° (BY METHOD II)

Moles of $(C_6H_5)_3PbCl$	Moles of NH_3	Ratio of moles NH_3 to moles $(C_6H_5)_3PbCl$
0.003163	0.03107	9.82
	.03064	9.69
	.03063	9.68
.002558	.02495	9.75
.002079	.02030	9.76
	.02021	9.72
	.02021	9.72
	.02017	9.70
	Av.	9.72

TABLE II

EQUILIBRIUM PRESSURES OF THE AMMINO COMPOUNDS OF TRIPHENYLLEAD CHLORIDE

Compound	Vapor pressure, mm. At start	At equilib.	Time elapsed
400 mm.	410	401.5	18 hrs.
compound	379	399.8	4 days
	386.5	397.5	2 days
	394	399	1 day
	396	400	1 day
	418	408	3 days
	Accepted pressure	400	
160 mm.	154	158.5	1 day
compound	236	161	1 day
	Accepted pressure	160	
100 mm.	202	96.5	1 day
compound	91.3	98	1 day
	149.5	101.5	1 day
	Accepted pressure	100	
50 mm.	93	55.5	1 day
compound	74	50.5	1 day
	119	65.2	1 day
	104	57.5	1 day
	Accepted pressure	50	
Metastable	755	416	1 day
415 mm.	411.5	417.5	12 hrs.
compound	375	415.2	17 hrs.
	442	413	1 day
	403.5	417	20 hrs.
	357	415	1 day
	462	417	1 day
	Accepted pressure	415	
Possible 38 mm.	80	38	1 day
compound	18.5	37	1 day
	Accepted pressure	38	

(4) The apparatus was somewhat similar to that described by Friedrichs, *Z. anorg. allgem. Chem.*, **116**, 141 (1921).

(5) Pettersson, *Z. anal. Chem.*, **25**, 467 (1886); *cf.* Dennis, "Gas Analysis." The Macmillan Co., New York, N. Y., 1929, page 95.

In Table II the data are given from which the values of the equilibrium pressures were estimated. It will be noted that in most cases it was possible to approach the equilibrium from both sides.

Summary

The compounds formed between ammonia and triphenyllead chloride have been investigated and their vapor pressures measured at −33.4°. Several compounds were detected, but the composition of only one was determined accurately. In this compound the number of moles of ammonia per mole of triphenyllead chloride cannot be expressed as the ratio of small whole numbers.

PROVIDENCE, R. I. RECEIVED JANUARY 27, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE INSTITUTE OF TECHNOLOGY, UNIVERSITY OF MINNESOTA]

The Standardization of Strong Oxidizing Agents with Potassium Iodide by the Acetone Method

BY I. M. KOLTHOFF AND H. A. LAITINEN

Lewis[1] attributes the low results obtained by us[2] in the standardization of potassium permanganate with pure potassium iodide by the acetone method of Berg[3] to the use of too low an acidity. The acidity used in our work was 0.9 *N*, while Berg used 2.0–2.5 *N* with potassium iodate as the oxidant. According to his comments the most suitable acidity seems to vary with the oxidant which is being standardized. In order to determine whether our low results were caused by too low an acidity, we have extended our experiments over a range of varying concentrations of acid. The same sample of pure potassium iodide as described previously[2] was used. An accurately weighed amount of the pure iodide was dissolved in water, 50 ml. of acetone, water and varying amounts of 9 *M* sulfuric acid were added to make a volume of 200 ml. One tenth normal potassium permanganate, standardized by the accurate method previously described, was added from a weight buret to within about 1% of the end-point (40 to 50 ml.) and the titration was then finished with 0.01 *N* permanganate which was added from an ordinary buret. The results were found to be independent of the acidity when the initial sulfuric acid concentration lay between 0.5 and 4 *N*. The results were always low, but depended upon the speed with which the 0.01 *N* permanganate was added in the immediate vicinity of the end-point. When it was added at a rate of about ten seconds per drop the results were 1.0%, low; on the other hand, if the permanganate was added rapidly until the color change persisted for thirty seconds, the results were 0.2% low. The speed of addition of the permanganate up to 0.5% before the equivalence point did not affect the results. Apparently, the low results have to be attributed to the fact that part of the 0.01 *N* permanganate added in the immediate vicinity of the end-point reacts with the acetone and the iodoacetone and is withdrawn from reaction with iodide. If the titration was carried out and finished with 0.1 *N* permanganate, which was added either from a weight or a volume buret, the results were found to be close to the theoretical value but always slightly low. This is evident from the experiments reported in Table I which were carried out at varying acidity. In all these experiments 25 ml. of acetone was used in an initial volume of 100 ml.

TABLE I

STANDARDIZATION OF 0.1 *N* PERMANGANATE WITH POTASSIUM IODIDE BY BERG'S METHOD. THEORETICAL VOLUME OF PERMANGANATE 47.70 ML.

Initial normality of H_2SO_4	0.25	0.5	1.0	2.0	3.0	4.0
0.1 *N* permanganate used	[a]	47.69[b]	47.68[b]	47.67	47.62	47.63
Error, %		−0.02	−0.04	−0.06	−0.16	−0.14

[a] Reaction velocity too small to allow titration.
[b] Average of two to three titrations.

Under the specified conditions the titration yields excellent results, particularly when the initial acidity is between 0.5 and 2 *N* and the titration is carried out with 0.1 *N* permanganate. It was found that the amount of acetone in the initial volume of 100 ml. could be changed between 10 and 50 ml. without changing the results

(1) D. Lewis, THIS JOURNAL, **59**, 1401 (1937).
(2) I. M. Kolthoff, H. A. Laitinen and J. J. Lingane, *ibid.*, **59**, 429 (1937).
(3) R. Berg, *Z. anal. Chem.*, **69**, 369 (1926).

more than 0.05%. From the practical point of view the use of the following procedure for the standardization of 0.1 *N* permanganate is to be preferred over the standardization with sodium oxalate.

Procedure for the Standardization of 0.1 *N* Permanganate (and 0.1 *N* Ceric Sulfate).—Weigh out approximately 0.35 g. of pure potassium iodide, dissolve in 75 ml. of water, add 5 ml. of 18 *N* sulfuric acid, 3 drops of 0.025 *N* ferrous phenanthroline sulfate solution and 20 to 25 ml. of C. P. acetone. Mix and titrate with 0.1 *N* permanganate until the end-point color change from red to practically colorless persists for thirty seconds.

In his experiments, Lewis used a C. P. Mallinckrodt product of potassium iodide and found results which agreed within 0.1 to 0.2% with the normality obtained with sodium oxalate. Using our precise methods[2] we determine the purity of a C. P. Mallinckrodt product of potassium iodide. After drying at 250° we found a potassium iodide content of 99.94% as compared to 100.00% for our pure product. Thus, for most practical purposes the standardization can be made with the dried Mallinckrodt product.

A limitation of the method is that the procedure described gives low normalities in the standardization of 0.01 *N* permanganate. Under the most favorable conditions (fast titration close to the end-point), the results were found to be 0.8 to 1% low.

The experiments described above were repeated with ceric sulfate. The results obtained were strictly comparable with those obtained with permanganate. The procedure given for the standardization of 0.1 *N* permanganate gives equally good results in the standardization of 0.1 *N* ceric sulfate, but again yields 0.8 to 1% low results in the standardization of 0.01 *N* ceric sulfate.

A separate investigation has been made of the cause of the low results obtained in the slow titrations with 0.01 *N* permanganate in the vicinity of the end-point. In the following experiments 5 ml. of 0.1 *N* permanganate was added to a mixture of 25 ml. of C. P. acetone in 100 ml. of dilute sulfuric acid. After standing for fifteen minutes at room temperature, the excess of permanganate was determined by adding an excess of standard iodide and titrating with 0.1 *N* permanganate according to the procedure described above. From the results given in Table II it is evident that the amount of permanganate which has reacted is proportional to the acidity of the solution.

TABLE II

REACTION OF PERMANGANATE WITH ACETONE IN ACID MEDIUM AFTER FIFTEEN MINUTES

Sulfuric acid, *N*	0.5	1.0	2.0	3.0	4.0
MnO_4^- reduced, %	17	34	70	98	100

Since the reduction of the permanganate may be attributed to impurities in the acetone, we have repeated the experiments with purified samples. The original C. P. sample was refluxed for several hours with an excess of permanganate and distilled. In other experiments the original sample was purified by making the sodium iodide addition compound from which the purified product was obtained by distillation.[4] The purified products behaved similarly to the original sample. Particularly immediately after addition of the permanganate the reaction velocity was found to be relatively great, the relative rate being greater with 0.01 *N* than with 0.1 *N* permanganate. A few figures given in Table III illustrate the behavior. The latter only partly accounts for the low results obtained in slowly titrating with 0.01 *N* permanganate near the end-point. Part of the error must be attributed to the fact that the presence of iodo-acetone increases the rate of reduction of permanganate. This rate was found to increase with increasing concentrations of iodoacetone.

The conditions under which the experiments of Table III were carried out were chosen so as to correspond closely to those in the neighborhood of the end-point in the titration. To a solution of 25 ml. of acetone in 140 ml. of 1.3 *N* sulfuric acid were added the indicated reagents and 2.90 ml. of permanganate. After various periods of standing at room temperature the amount of permanganate left was determined as described before.

TABLE III

RATE OF REACTION OF PERMANGANATE WITH ACETONE UNDER VARYING CONDITIONS

Concentration of Manganous sulfate, *M*	Iodo-acetone, *M*	Normality of permanganate	Permanganate reduced in % after 1	5	15	30 min.
		0.1	12[a]		36[a]	50[a]
					32[c]	44[c]
0.0065	0.013	.1	22[a]		85[a]	90[a]
		.01	36[a]	50[b]		
.0065	.013	.01	40[a]	100[a]		
			25[b]	99[b]		
.00065		.01	43[a]	57[a]		

[a] Unpurified C. P. acetone. [b] Purified by the sodium iodide addition compound. [c] Purified by refluxing and distilling from neutral permanganate.

Acknowledgment.—We wish to express our appreciation to the Graduate School of the University of Minnesota for a grant which enabled us to carry out this investigation.

Summary

1. A simple procedure is given for the standardization of 0.1 *N* permanganate and 0.1 *N* ceric sulfate by Berg's method using potassium iodide as a primary standard.

2. The method gives 0.8 to 1% low results in the standardization of 0.01 *N* solutions.

3. Low results are shown to be due to a reduction of the oxidizing agent by the acetone and the iodoacetone in the close neighborhood of the end-point.

MINNEAPOLIS, MINN. RECEIVED APRIL 13, 1939

(4) K. Shipsey and E. A. Werner, *J. Chem. Soc.*, **103**, 1255 (1913); H. L. Lochte, W. A. Noyes and J. R. Bailey, THIS JOURNAL, **44**, 2563 (1922).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

The Action of Liquid Ammonia Solutions of Sodium, Potassium, and Potassium Amide upon Bismuth Oxyiodide[1]

BY GEORGE W. WATT[2] AND W. CONARD FERNELIUS

The successful removal of halogen from organic combination and the reduction of inorganic halides by the action of the alkali and alkaline earth metals in liquid ammonia solution[3] suggests the possibility of obtaining sub-oxides of certain metals by the reduction of oxyhalides such as bismuth oxyiodide, BiOI. The experiments described below, however, show that the compound is reduced completely in that both iodine and oxygen are removed by the alkali metal. It might be expected that the amide ion, NH_2^-, would be more selective, since it has been shown to be a mild reducing agent.[4] However, KNH_2 undergoes simple metathesis to form $BiONH_2$.

Experimental

The Action of Sodium and Potassium in Liquid Ammonia on Bismuth Oxyiodide

When 0.500 g. of bismuth oxyiodide (Merck C. P.) was treated with a solution of sodium or potassium (0–25°) in liquid ammonia,[5] the light red color of the oxyhalide was discharged immediately, the solid phase changed to a grayish-black color, and a small amount of a somewhat flocculent white precipitate appeared. A blue color, indicative of an excess of alkali metal, persisted for a short time when it was replaced either by a pale yellow color (3 equivalents of potassium) or by violet colors (all other cases). In every instance a small and variable amount of a water-insoluble gas (hydrogen) was formed during the reaction.

Upon completion of the reaction, the insoluble reaction product was washed with liquid ammonia until colorless washings were obtained, or until the intensity of the color of the washings showed no visible decrease upon repeated washing. The solvent was then allowed to evaporate and the tube was opened for analysis.

Data relevant to these reactions are presented in Table I. The values representing analyses are the average of two or more determinations.

TABLE I

Expt.	Alkali metal	Alkali metal used, g.	Analysis of insol. reaction product: Sample, g.	Found, %: Bi	Alkali metal	N	%I[a] recovered from washings
			Three equivalents alkali metal				
2	K	0.333	0.5888	82.7	12.2	0.6	97.4[b]
3	K	.333	.6834	84.8	8.6	.5	97.7[b]
1	Na	.196	.5912	73.7	18.4	...	...
4	Na	.196	.3840	73.1	18.6	.5	100
			Six equivalents alkali metal				
5	K	0.666	0.7270	68.1	26.6	.3	99.2
8	K	.666	.6640	63.4	28.9	Trace	99.2
6	Na	.392	.6512	63.3	29.3	Trace	99.5
9	Na	.392	.9136	62.5	30.2	0.6	99.4

[a] Based on iodine used as BiOI. [b] Some iodine inadvertently lost prior to analysis.

Discussion

The data of Table I indicate that the following reactions are involved

$$BiOI + 3M \longrightarrow Bi + MI + M_2O \quad (1)$$
$$2NH_3 + 2M \longrightarrow 2MNH_2 + H_2 \quad (2)$$
$$M_2O + NH_3 \longrightarrow MOH + MNH_2 \quad (3)$$
$$3M + Bi \longrightarrow M_3Bi \text{ (insoluble)} \quad (4)$$
$$M_3Bi + xBi \longrightarrow M_3Bi{\cdot}Bi_x \text{ (soluble)} \quad (5)$$

The analyses of the washings for iodide ion show clearly that ammonia solutions of sodium and potassium quantitatively remove the iodine from bismuth oxyiodide (reaction 1). The evolution of hydrogen accompanying the reduction is due to the reaction between the metal and solvent, probably catalyzed by the liberated bismuth metal (reaction 2). The occurrence of reactions 2 and 3 accounts for the appearance of nitrogen (as MNH_2) in the washings.

Alkali monoxides (indicated in reaction 1) are not stable in liquid ammonia but are ammonolyzed to hydroxides (reaction 3),[6] thereby ex-

(1) Original manuscript received April 29, 1935.

(2) Present address: Department of Chemistry, The University of Texas, Austin, Texas.

(3) For primary references see: W. C. Fernelius and G. W. Watt, *Chem. Rev.*, **20**, 211–213, 226–232 (1937).

(4) F. W. Bergstrom and W. C. Fernelius, *ibid.*, **12**, 77 (1933).

(5) For technique see E. C. Franklin, "The Nitrogen System of Compounds," A. C. S. Monograph, 1935, pp. 317–330; W. C. Johnson and W. C. Fernelius, *J. Chem. Ed.*, **6**, 447–450 (1929).

(6) C. A. Kraus and E. F. Whyte, THIS JOURNAL, **48**, 1781 (1926). For similar reactions of Rb_2O and Cs_2O see: E. Rengade, *Compt. rend.*, **140**, 1536 (1905); *Bull. soc. chim.*, [3] **35**, 775 (1906); *Ann. chim. phys.*, [8] **11**, 348 (1907).

plaining the white precipitate observed. Further, the analysis of the insoluble products indicates the presence of alkali hydroxide.

The composition of the insoluble products depends upon the nature of the alkali metal and the number of equivalents used. The pale yellow color (KNH_2) of the ammonia solution at the end of the reaction with three equivalents of potassium as well as the analytical data indicate that no insoluble bismuthide was formed. If the potassium in the insoluble product is assumed to be in the form of potassium hydroxide (in expt. 2, 12.2% potassium corresponds to 17.5% potassium hydroxide, the total analysis (100.8%) accounts for all of the sample.

When three equivalents of sodium are used, the color of the washings indicates the presence of bismuthides (reactions 4 and 5) which are sufficiently soluble to impart intense colors to the liquid ammonia.[7] The presence of an insoluble bismuthide is indicated by the following considerations. If all of the sodium in the insoluble products is assumed to be in the form of sodium hydroxide, the total of the analysis is several per cent. above 100 (expt. 4, 18.6% Na is equivalent to 32.3% sodium hydroxide and the total then equals 105.9%).[8]

When six equivalents of sodium or potassium are used, the solutions above the solids are strongly colored (violet for potassium and blue-violet for sodium). These colors grow less intense but persist throughout the washing process. The amount of bismuth present in the washings and the amount of alkali metal in the insoluble products are greater for the experiments involving six equivalents of alkali metal. A simple calculation shows that all of the alkali metal cannot be present as hydroxide (in expt. 6, 29.3% sodium is equivalent to 50.9% sodium hydroxide, and the total of the analysis would be 114.2%; in expt. 5, 26.6% potassium is equivalent to 38.2% potassium hydroxide, and the total of the analysis would be 106.6%). These data show that with excess alkali metal, bismuthides are formed and that the tendency to form bismuthides is greater for sodium than for potassium.

(7) E. Zintl, J. Goubeau and W. Dullenkopf, *Z. physik. Chem.*, **A154**, 1–46 (1931), give the following data: Na_3Bi, insoluble black solid; Na_3Bi_3, deep violet solution in liquid ammonia; Na_3Bi_5, brown solution.

(8) While it might be argued that the use of *exactly* three equivalents of sodium would lead to the production of metallic bismuth only, such a situation would be difficult to realize experimentally because in each reaction there is a variable quantity of alkali metal converted to amide by reaction with the solvent.

Experimental

The Action of Potassium Amide in Liquid Ammonia on Bismuth Oxyiodide

Preliminary experiments showed that bismuth oxyiodide reacts with a molar equivalent of potassium amide in liquid ammonia at or near room temperature to form a very dark red solid which decomposes slowly in the presence of liquid ammonia with liberation of elementary bismuth and which explodes violently when exposed to the air. When an excess of potassium amide is used, an identical product is obtained.

One-half gram of bismuth oxyiodide was brought into reaction with the potassium amide from 0.32 g. (large excess) of potassium. After standing for one hour, during which there was no further change, the ammonia solution was decanted and the solid (dark red with traces of black) was washed free of ammonia-soluble impurities. The ammonia was allowed to escape, the tube sealed off, evacuated, and the insoluble reaction product hydrolyzed *in vacuo* by the vapors from dilute hydrochloric acid. A clear solution and a small amount of a black insoluble solid (Bi) resulted.

Anal. Found (independent experiments), N, 5.7, 5.8. Calcd. for $BiONH_2$: N, 5.80; for BiN, N, 6.28. Analysis of the washings for iodine gave values of 99.8 and 99.7% (based on the weight of iodine in the BiOI used), thus showing conclusively that the oxyiodide was quantitatively dehalogenated.

Discussion

In view of the similarity of the properties of the product described above with those of bismuth nitride, BiN,[9] one might suspect that the following reaction had occurred

$$BiOI + KNH_2 \longrightarrow BiN + KI + H_2O$$

Water thus formed, however, would lead to the production of white ammonia-insoluble potassium hydroxide by interaction with the excess potassium amide

$$KNH_2 + H_2O \longrightarrow KOH + NH_3$$

There was no evidence whatever of the appearance of potassium hydroxide among the products of the reactions under consideration. Furthermore, the analyses for nitrogen show that the product must be bismuth oxyamide rather than bismuth nitride. Accordingly, the reaction must be one of simple metathesis

$$BiOI + KNH_2 \longrightarrow BiONH_2 + KI$$

Summary

1. Bismuth oxyiodide is reduced by liquid ammonia solutions of sodium and potassium at room temperature in accordance with the equation $BiOI + 3M + NH_3 \longrightarrow Bi + MI + MOH + MNH_2$.

2. With excess alkali metal, bismuthides are formed.

3. The reaction between potassium amide

(9) E. C. Franklin, THIS JOURNAL, **27**, 847 (1905).

and bismuth oxyiodide in liquid ammonia at room temperature may be represented by the equation $BiOI + KNH_2 \longrightarrow BiONH_2 + KI$.

COLUMBUS, OHIO RECEIVED MAY 1, 1939

[CONTRIBUTION FROM THE AVERY LABORATORY OF CHEMISTRY OF THE UNIVERSITY OF NEBRASKA]

The Ternary System: Ethyl Alcohol, Toluene and Water at 25°

BY E. ROGER WASHBURN, ALBERT E. BEGUIN AND ORVILLE C. BECKORD

In order to have solubility and distribution data for this system at 25° to compare with the systems already studied[1] and others which are soon to be described, it has been found necessary to carry out this investigation. Ormandy and Craven[2] and Tarasenkov and Poloznintzeva[3] have studied this system but their studies did not include determinations of the distribution of alcohol between the toluene-rich and water-rich layers or refractive indices of the saturated solutions, and the temperatures at which they worked were not those at which our earlier studies have been made.

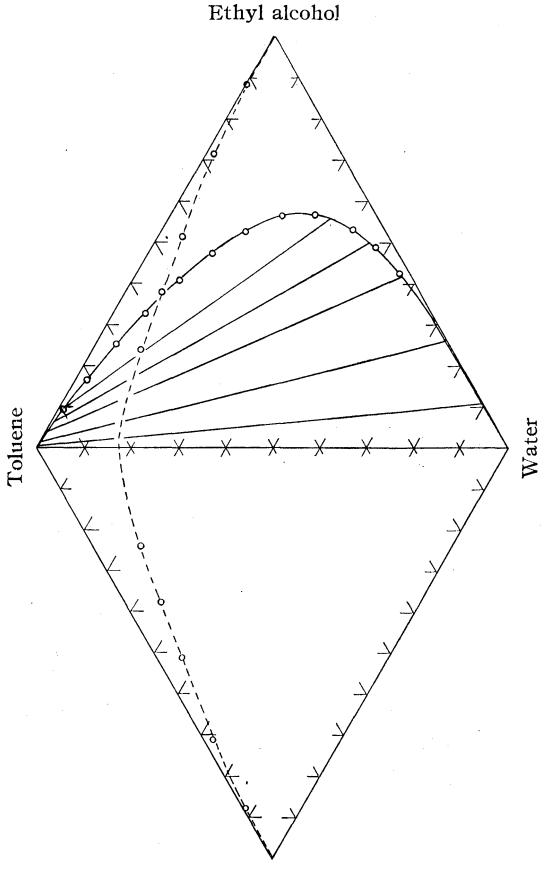


Fig. 1.—Solubility and conjugation curves at 25.0°.

Materials.—Carefully purified water was used. It was distilled from alkaline permanganate and collected while hot. A commercial grade of absolute ethyl alcohol was refluxed over lime for many hours and carefully fractionated. Its specific gravity d^{25}_4 was 0.7851 ± 0.0001, while its refractive index $n^{25}D$ was 1.35940 ± 0.00001.

Toluene of "analytical reagent grade" was dried over sodium and fractionated. This material had a specific gravity d^{25}_4 of 0.8608 ± 0.0002 and an index of refraction

TABLE I

SOLUBILITIES AND REFRACTIVE INDICES AT 25.0°

Wt. % toluene	Wt. % alcohol	Wt. % water	Refractive index
*89.84	9.36	0.81	1.4779
85.54	13.04	1.42	1.4719
*81.13	16.74	2.13	1.4660
76.33	20.66	3.01	1.4595
*70.46	25.29	4.25	1.4520
*60.61	32.66	6.73	1.4381
*49.26	40.83	9.91	1.4233
*39.40	47.37	13.23	1.4108
*29.52	52.89	17.59	1.3980
24.67	54.96	20.37	1.3920
*19.96	56.42	23.62	1.3860
17.66	56.76	25.58	1.3830
*12.94	56.66	30.39	1.3770
9.41	55.46	35.12	1.3720
* 6.37	53.04	40.59	1.3679
5.33	51.78	42.89	1.3660
* 3.72	48.89	47.39	1.3630
* 1.75	42.48	55.76	1.3585
	Toluene saturated with water		1.4923
	Water saturated with toluene		1.3320

TABLE II

REFRACTIVE INDICES AND CONCENTRATIONS OF ALCOHOL IN CONJUGATE SOLUTIONS AT 25.0°

Water-rich layer		Toluene-rich layer		
Refractive index	Wt. % alcohol	Refractive index	Wt. % alcohol	Distribution ratio
*1.3389	11.0	1.4920	0.2	0.02
1.3440	19.2	1.4912	.7	.04
*1.3480	25.7	1.4903	1.3	.05
1.3540	35.2	1.4882	2.7	.08
*1.3581	41.7	1.4850	4.7	.11
1.3616	46.9	1.4841	5.3	.11
*1.3641	50.0	1.4822	6.5	.13
1.3683	53.3	1.4796	8.2	.15
*1.3724	55.6	1.4778	9.4	.17

(1) E. R. Washburn and others, THIS JOURNAL, **53**, 3237 (1931); **54**, 4217 (1932); **56**, 361 (1934); **57**, 303 (1935); **59**, 2076 (1937).
(2) Ormandy and Craven, *J. Inst. Petroleum Tech.*, **7**, 325 (1921).
(3) Tarasenkov and Poloznintzeva, *J. Gen. Chem.* (U. S. S. R.), **2**, 84 (1932).

$n^{25}D$ of 1.49371 ± 0.00001. Although this specific gravity is almost identical with that listed in the "International Critical Tables,"[4] we have reason to believe that the value is a little too low for toluene of highest purity. A small portion of what we believe to be a more nearly pure toluene was used in part of the work. It had a specific gravity d^{25}_4 of 0.86221 ± 0.00003 and a refractive index of 1.49375 ± 0.00003. We were not able to detect any difference in the solubility results obtained with the two grades of toluene.

Procedure.—The solubility curve was determined at 25.0 ± 0.1° in a constant temperature bath by a titration method not greatly different from that previously described.[1] The refractive indices were measured with an Abbe refractometer at the same temperature. An immersion refractometer was used in obtaining the constants for the pure liquids. Large scale curves were plotted for the refractive indices *versus* concentration of each of the three components in the saturated solutions. These curves were used in determining the composition of the conjugate solutions formed when alcohol in insufficient amounts to bring about homogeneity was added to two liquid phase mixtures of water and toluene. Samples were removed from each of the layers, after equilibrium had been reached, for the determination of refractive index. The results are given in Tables I and II. The values marked with a (*) were used in plotting the solubility curve with its tie lines as shown in Fig. 1. The conjugation curve (4) (p. 398), is also indicated. Its intersection with the solubility curve locates the plait point.

(4) "International Critical Tables," Vol. III, p. 29.

Summary

The solubility curve for the ternary system ethyl alcohol, toluene and water has been determined at 25.0°. The refractive indices of the saturated solutions have been recorded. The compositions of various conjugate solutions throughout a large range of concentrations have been measured.

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[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

Molecular Freedom and Melting in Alkyl Halides

BY WILLIAM O. BAKER AND CHARLES P. SMYTH

In the course of an investigation relating the structure of organic molecules to their rotational mobility in the solid state, dielectric constant and apparent conductance measurements over a range of temperature and frequency were made on liquid and solid *i*-propyl and *n*-amyl bromides. The crystalline phases were also examined with the polarizing microscope. The *n*-amyl bromide molecule was chosen as less rod-like than long chain compounds,[1] but more anisotropic than the *i*-amyl, *i*-butyl and *i*-propyl derivatives. The latter was selected as intermediate in symmetry between the nearly spherical *t*-butyl halides[2] and the isobromides.[3]

The dielectric measurements with a capacity bridge involved the general procedure previously employed.[4] The usual precautions of pumping off dissolved gases from the liquids, and of slow freezing to reduce void formation, were observed. Temperatures were determined with a platinum resistance thermometer. A small unsilvered dewar tube with a liquid air cooling device was mounted on the microscope stage for observations between crossed nicols.

Purifications of Materials

Final purification was fractionation through a packed jacketed 80 × 2 cm. Pyrex column with still head equipped for variable reflux ratio. Boiling points were measured with Anschütz type short range thermometers calibrated by the Bureau of Standards, and the surface for liquid–vapor equilibrium to give true boiling temperatures was increased by use of a mercury well in the column top. Refractive indices were determined with a Pulfrich refractometer.

***i*-Propyl Bromide.**—Material from the Eastman Kodak Co., dried over pure calcium bromide for several weeks, was twice fractionally distilled; b. p. 59.5°; f. p. −90.8°; $n^{20.0}D$ 1.42476. "International Critical Tables" values are: b. p. 59.6°; $n^{20}D$ 1.4251, while Skau and McCullough[5] give b. p. 59.41° and f. p. −90.0°. As with the *i*-amyl bromide, the absence of Maxwell-Wagner interfacial polarization on freezing and the low apparent specific conductance values for the liquid assured purity.

***i*-Amyl Bromide.**—The Eastman product was dried over calcium bromide for two weeks and twice fractionated; b. p. 128.6°; m. p. −88.7°; $n^{20.0}D$ 1.44455; "International Critical Tables" values are: b. p. 127.9°; $n^{20.0}D$ 1.4444; whereas Skau and McCullough[5] gave b. p. 129.6°, m. p. −87.9°, and Deese[6] reports m. p. −88.0°.

Experimental Results

The dielectric constants, ϵ, and specific conductances k (ohm^{-1} cm.$^{-1}$) form Table I, in which, also, the temperatures are given in the first column, and the appropriate frequencies in kilocycles are indicated for the other data. Many measurements at intermediate temperatures have

(1) Baker and Smyth, THIS JOURNAL, **60**, 1229 (1938).
(2) Forthcoming publication.
(3) Baker and Smyth, THIS JOURNAL, **61**, in press (1939).
(4) Smyth and Hitchcock, *ibid.*, **54**, 4631 (1932); **55**, 1830 (1933).
(5) Skau and McCullough, *ibid.*, **57**, 2439 (1935).
(6) Deese, *ibid.*, **53**, 3673 (1931).

TABLE I

i-C_3H_7Br

Kc. t, °C.	50	5	0.5	50	5	0.5	50	5	0.5
	ϵ			$k \times 10^{10}$			ϵ''		
Cooling									
− 85.6	16.07	16.07	16.08	60.2	47.3	46.2	0.22	1.71	16.7
− 90.6	16.52	16.58	16.59	58.7	41.0	40.2	.21	1.48	14.5
− 94.6	16.89	16.94	16.93	52.0	35.5	35.0	.19	1.29	12.7
− 97.2	17.09	17.16	17.17	50.3	35.3	34.3	.18	1.28	12.4
−100.9	17.47	17.53	17.50	45.2	30.2	29.5	.16	1.10	10.7
− 90.1	3.80	3.78	4.22	32.9	21.5	15.0	.12	0.78	5.5
− 90.4	3.52	3.63	4.09	33.5	19.6	13.8	.12	.71	5.0
− 91.8	3.39	3.53	3.85	31.8	17.7	12.0	.12	.64	4.4
−100.7	3.12	3.26	3.64	40.2	11.5	7.8	.15	.42	2.8
−103.5	3.06	3.20	3.55	43.5	10.0	6.3	.16	.36	2.3
−122.0	2.77	2.91	3.18	19.6	8.1	4.2	.07	.29	1.5
−127.2	2.72	2.77	2.97	7.1	4.2	2.2	.03	.15	0.8
−130.5	2.69	2.70	2.83	3.5	2.2	1.7	.01	.08	..
−132.7	2.68	2.68	2.74	...	1.9	1.4	..	.07	0.6
−156.8	2.61	2.61	2.60	3.5	0.5	0.6	..	..	..
−184.6	2.54	2.52	2.54	...	...	...	..	..	..
Warming									
−138.7	2.61	2.59	2.59	3.5	0.8	0.8	0.01	0.03	0.3
−128.3	2.62	2.65	2.80	3.5	1.2	1.5	.01	.04	.5
−125.7	2.63	2.69	2.88	8.9	3.8	1.5	.03	.14	.5
−119.3	2.66	2.87	3.03	17.7	6.2	2.0	.06	.22	.7
−115.2	2.71	2.98	3.14	35.2	6.7	2.9	.13	.24	1.1
−112.5	2.73	3.06	3.63	45.2	14.2	7.2	.16	.52	2.6
−108.7	2.81	3.13	3.79	55.4	14.9	7.2	.20	.54	2.6
−106.8	2.93	3.08	3.34						

i-C_3H_7Br

Kc. t, °C.	50	5	0.5	50	5	0.5	50	5	0.5
	ϵ			$k \times 10^{-10}$			ϵ''		
−101.5	2.98	3.28	4.02	53.6	17.7	8.0	0.19	0.64	2.9
− 94.7	3.21	3.58	4.49	45.2	21.7	9.5	.16	.79	3.4
− 92.4	3.53	4.01	5.07	46.8	25.7	13.2	.17	.94	4.8
− 91.3	4.13	4.58	5.93	52.0	35.2	19.6	.19	1.2	7.1
− 91.0	4.69	5.13	6.63	55.4	42.1	26.6	.20	1.5	9.7
− 90.8	5.10	5.60	7.64	52.0	46.3	34.8	.19	1.6	12.6
− 90.7	5.69	6.16	8.22	62.0	52.0	39.5	.22	1.9	14.3
− 90.7	6.28	6.74	8.29	65.3	57.0	48.6	.24	2.1	17.5
− 90.3	14.57	15.38	15.86	117.4	126.9	126.9	.42	4.6	45.7
− 85.9	16.16	16.17	16.05	106.0	101.7	102.0	.38	3.7	36.7
− 81.8	15.79	15.80	15.82	119.0	113.5	113.0	.43		

n-$C_5H_{11}Br$

Kc. t, °C.	50	5	0.5	50	5	0.5
	ϵ			$k \times 10^{10}$		
Cooling (1)						
− 38.3	7.86	7.87	7.87	19.6	17.0	17.0
− 45.7	8.12	8.11	8.13	17.7	16.3	16.2
− 59.7	8.59	8.60	8.60	14.2	12.4	12.5
− 61.2	8.66	8.66	8.68	12.4	11.5	11.5
− 71.1	9.06	9.07	9.07	10.6	8.4	8.5
− 85.8	9.70	9.70	9.70	5.3	4.2	4.2
− 88.8	9.85	9.86	9.86	5.3	3.5	3.5
− 90.3	9.91	9.93	9.93	5.3	3.2	3.2
− 93.1	10.00	10.06	10.00	3.5	2.6	2.6
− 97.4	9.45	8.81		1.7	1.8	
− 96.6			8.42			1.8
− 96.2	8.14	7.73	7.38	1.7	1.7	1.7
− 95.9	6.97	6.67	6.42	1.7	1.7	1.7
− 95.6	6.18	5.70	5.33	1.7	1.7	1.6
− 95.3	4.95	4.53	4.28	1.7	1.6	1.5
− 95.2	3.79	3.62	3.52	1.7	1.5	1.5
− 95.6	3.40	3.27	3.15	1.7	1.5	1.2
− 96.9	3.14	3.07			0.9	
− 98.4			2.92			0.9
−105.0	2.68	2.68	2.67		.8	.8
−109.4	2.67	2.65	2.62		.6	.7
−111.6	2.62	2.62	2.60		.5	.7
−121.8	2.60	2.59	2.59			
−128.2	2.58	2.58	2.58			
−134.6	2.58	2.58	2.58			
−173.0	2.47	2.47	2.45			

n-$C_5H_{11}Br$

Kc. t, °C.	50	5	0.5	50	5	0.5
	ϵ			$k \times 10^{10}$		
Cooling (2)						
− 85.4	9.66	9.68	9.66	5.3	4.0	4.0
− 95.5	10.21	10.21	10.18	3.5	1.9	1.9
− 95.8	9.72			3.5		
− 95.2		8.94			1.9	
− 94.8			8.45			1.9
− 93.9	7.11			1.7		
− 93.6	4.38			1.7		
− 93.7	3.63			1.7		
− 93.7	3.14			1.7		
− 93.8	2.96			1.7		
− 94.0	2.90			1.7		
− 94.2	2.87			1.7		
− 94.5	2.80			1.7		
− 95.0	2.76			1.7		
− 96.7	2.69					
− 98.2	2.65	2.63			0.8	
−101.3			2.55			
−105.1	2.58					
−108.7	2.56					
−111.9	2.55					
−115.2	2.54					
Warming						
− 97.5	2.67	2.66	2.66		0.8	0.8
− 92.4	2.80	2.81	2.80		.9	.9
− 90.6	2.96	2.96	2.96		1.0	1.1
− 90.4	2.99	3.01	2.99		1.0	1.0
− 90.2	3.06	3.07	3.05		1.1	1.1
− 90.0	3.12	3.13	3.12		1.1	1.1
− 89.6	3.25	3.27	3.26		1.2	1.4
− 89.2	3.58	3.60	3.59		1.4	1.4
− 88.9	4.01	4.05	4.04		1.6	1.6
− 88.6	4.73	4.84	4.83		1.7	1.7
− 88.5	5.93	6.03	6.01	1.7	2.0	2.0
− 88.4	6.67	6.76	6.75	1.7	2.0	2.4
− 88.4	7.45	7.64	7.70	1.7	2.4	2.5
− 88.4	8.76	9.06	9.13	2.5	2.6	2.7
− 88.3	9.71	9.77	9.77	3.5	3.2	3.2
− 88.2	9.74	9.75	9.74	3.5	3.2	3.2
− 87.3	9.71	9.72	9.71	5.3	3.3	3.3
− 85.0	9.67	9.67	9.65	5.3	3.6	3.8
− 83.3	9.58	9.59	9.57	3.8	4.2	4.2

been omitted, but those given are often selected from different runs to demonstrate reproducibility. The imaginary part of the dielectric constant $\epsilon'' = 1.8 \times 10^9\ k/f$, in which f, the frequency in kilocycles, is given for *i*-propyl bromide. The apparent values of ϵ'' just below the freezing point are too high because of a certain amount of direct current conductance. In the dielectric constant values for amyl bromide between 97.4 and 96.9°, the apparent decrease with decreasing frequency arises from the fact that the readings were taken in the order of decreasing frequency. Although the temperature changed by less than 0.01° during the readings at the three frequencies, the rapid crystallization with consequent setting of the dipoles caused a decrease in dielectric constant which was not influenced by the frequency.

Discussion of Results

Figure 1 represents the general immobilizing of the dipoles of *i*-propyl bromide upon freezing, after

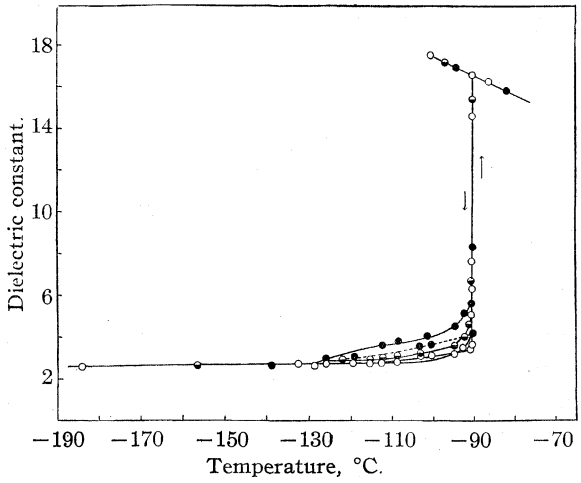


Fig. 1.—Temperature dependence of the dielectric constant of *i*-propyl bromide. (Filled circles represent values at 0.5 kc., half-filled circles values at 5 kc., and hollow circles values at 50 kc.)

slight supercooling, with hindered rotational freedom extending to about −131°. Below this temperature, dispersion has disappeared, and the dielectric constant is nearly the square of the refractive index, as electron polarization alone would require. The polarizing microscope shows pronounced double refraction in the crystals, hence anisotropy, on solidification, so the rotation is probably not about all axes. The cubic, or, occasionally, the hexagonal, class is characteristic of molecular crystals in which rotational molecular freedom comparable to that in the liquid obtains.[2,7] The sharp reduction of the dielectric constant at the freezing point suggests that rotation around any axis perpendicular to the C–Br line ceases at this temperature, while the gradual fall of the dielectric constant accompanied by anomalous dispersion from this temperature down to about −131° indicates the possibility of a decreasing hindered rotation about this axis or one nearly parallel to it, a behavior undetectable in many structures.

Although beginning at the same temperature as that at which it ends on cooling, the dispersion is more pronounced on warming, and a coöperative loosening, like rotational premelting, may occur.[1,8,9] Inspection of Table I confirms the idea of hindered rotation with no transition in that the dielectric loss as indicated by ϵ'' shows only a steady decline after solidification.

The *i*-propyl bromide molecule is sufficiently symmetrical to pack with an economy of free volume in the liquid, but its anisotropic lattice implies that the liquid arrangement is not of cubic-packed spheres. Hence, some supercooling is expected,[3] but soon, on cooling, the thermodynamic potential, probably with the aid of short relaxation times, is able to effect crystallization with free energy diminution, unlike the cases of the more anisotropic *i*-butyl and *i*-amyl compounds. Further, standard theories that supercooling proceeds in the complete absence of nuclei are supported by the exact continuity of the supercooled ϵ curve with that for the liquid in Fig. 1. Minute crystallites would cause a sharp change in the dielectric constant.[4,10]

Figure 2 shows the dielectric behavior of *n*-amyl bromide on cooling and warming. Like diethyl ether,[11,12] it evidently possesses a monotropic transition resulting in a low temperature form which melts at −88.7°, about 5.9° higher than the phase which first apears on freezing. This transformation had appeared in thermal studies on *n*-amyl bromide[6] for, about 25° below the melting point, the calorimeter was found suddenly to heat up 5° against a 10° shield gradient. Skau and McCullough[5] confirmed the presence of two forms, an unstable one melting at −94.6° (a value close to −94.5°, our higher freezing point indicated on Fig. 2), and a stable one melting at −87.9°. They quote Simon[13] as reporting a

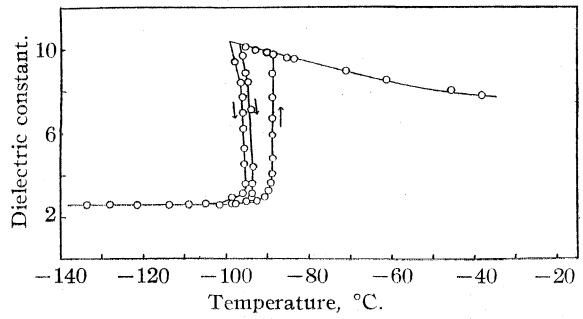


Fig. 2.—Temperature dependence of the dielectric constant of *n*-amyl bromide.

freezing point of −95.25°, a value close to the lower freezing temperature, −95.9°, on Fig. 2. The dielectric measurements, tracing the mechanical behavior of the polar molecules, reveal that, although their anisotropy prevents much supercooling, crystallization either does not pro-

(7) Smyth, *Chem. Rev.*, **19**, 329 (1936).
(8) A. Ubbelohde, *Trans. Faraday Soc.*, **34**, 282, 292 (1938).
(9) A. Müller, *Proc. Roy. Soc.* (London), **A158**, 403 (1937).
(10) J. Errera, *Phys. Z. der Sowietunion*, **3**, 443 (1933).
(11) Huettig and Smyth, THIS JOURNAL, **57**, 1523 (1935).
(12) McNeight and Smyth, *ibid.*, **58**, 1718 (1936).
(13) Simon, *Bull. soc. chim. Belg.*, **38**, 47 (1929).

ceed rapidly enough, or does not release sufficient latent heat, completely to return the system to a "true" freezing point. This would seem to explain the divergent data of previous investigators, for the freezing point will appear to vary with the bath gradient.

Many polymorphic transitions involving only anisotropic lattices, as the polarizing microscope showed both forms of *n*-amyl bromide to be, are found to involve rotational freedom about at least one molecular axis.[1] However, Fig. 2 resembles similar data for diethyl ether[12] in indicating, after occasional orientation just below the freezing point has ceased, that only electronic and atomic polarizations are contributing to the dielectric constant. An X-ray analysis of the transformation would seem desirable, as discovery of a mode of motion not involving librations in the rearrangement of a molecular lattice might result.

Optical examination gave direct evidence of the transition. The initial crystals were strongly anisotropic, but the double refraction increased when a given sample was held at a low temperature. When the sample was frozen, cooled briefly about 30° below the melting point, and then allowed to warm up quite rapidly, sharp melting of the unstable form was first observed. However, distributed through the liquid were tabular, strongly doubly-refracting crystals which did not themselves melt until a distinctly higher temperature. The latter were the so-called stable form. On prolonged standing at low temperature, the transformation was complete, and only one melting process was observed under the microscope.

The observation that *i*-propyl bromide melted at nearly the same temperature as *n*-amyl bromide, and about 20° higher than *n*-propyl bromide, coupled with data from other work,[2,3] led to examination of the melting properties of simple alkyl halides. The mono-halides, and especially the bromides, were chiefly considered, because they have closely similar polarizabilities and permanent moments, obey Trouton's rule well as shown by available data,[14] and exhibit no extensive liquid association. They should thus have comparable behavior in condensed phases. Also, the dimensions of the molecules should be little altered by interchanges of methyl and bromo groups, since the same method of measurement yields 2.0 and 1.9 Å., respectively, for their radii.[15] Even a chlorine atom with radius of 1.65 Å. approximates the methyl group in size. Hence, it is not surprising that the relationships noted below apply to the isomeric hydrocarbons as well as to the isomeric halides.

Writers on the theories of fusion and of liquids have considered the thermodynamic and statistical changes accompanying melting.[16-18] Hirschfelder, Stevenson and Eyring explained the low entropies of fusion of substances which gained non-translational degrees of freedom in the solid state (as by rotational transitions) as arising from the communal sharing of free volume possible on liquefaction. They have shown that if complete communal sharing immediately occurs,[19] the entropy of fusion, ΔS_f, should be 2 e. u. for a substance already possessed of rotational freedom, as found for *t*-butyl chloride.

Relationships among the entropies of fusion of structurally similar compounds also have been sought,[20-22] but without definite reference to structure. Melting points are often regarded as constitutive properties of organic compounds[23] and an empirical equation connecting them with molecular weights has been suggested.[24] The linear relation between number of C atoms and melting points for odd or even members, respectively, of an homologous series, has been long known,[23] and it has been observed without explanation that isomers often deviate from such straight lines.

Thermal and viscosity data are listed in Table II, under the headings m. p., melting point; ΔS_f, entropy of fusion; t. p., transition point; ΔS_t, entropy of transition; $\Delta t°_{liq.}$, liquid interval under normal conditions, in degrees; $\Delta E_{vis.}$, the activation energy for viscous flow, in calories per mole; and $\Delta E_{vap.}$, the energy of vaporization in calories per mole.

Figure 3 demonstrates, as shown by the data of Table II, that nearly spherical molecules, which have rotational transitions in the solid, melt far

(14) Landolt–Börnstein, "Tabellen."

(15) Stuart, "Molekülstruktur," Verlag von Julius Springer, Berlin, 1934, p. 48.

(16) Herzfeld and Mayer, *Phys. Rev.*, **46**, 995 (1934).

(17) Frenkel, Todes and Ismailow, *Acta Phys.-Chim. U. R. S. S.*, **1**, 97 (1934); Frenkel, *ibid.*, **4**, 341 (1936).

(18) Hirschfelder, Stevenson and Eyring, *J. Chem. Phys.*, **5**, 896 (1937).

(19) For other cases see Gurney and Mott, *Trans. Faraday Soc.*, **35**, 364 (1939).

(20) Walden, *Z. Elektrochem.*, **14**, 713 (1908).

(21) Kordes, *Z. anorg. allgem. Chem.*, **160**, 67 (1927).

(22) Clusius, *Z. Elektrochem.*, **39**, 598 (1933).

(23) Gilman, "Treatise on Organic Chemistry," John Wiley & Sons, Inc., New York, N. Y., 1938, Chap. 20.

(24) Austin, THIS JOURNAL, **52**, 1049 (1930).

TABLE II

Substance	M. p., °K.	ΔS_f	T. p., °K.	ΔS_t	$\Delta t°_{liq.}$	$\Delta E_{vis.}$ cal./mole	$\Delta E_{vap.}/\Delta E_{vis.}$
CH_3Br	180.1				96.2		
C_2H_5Br	155.1	9.03			156.0		
n-C_3H_7Br	163.1	9.56			181.0	1770	
i-C_3H_7Br	184.1				148.4	1770	3.5
n-C_4H_9Br	160.4	13.5			214.3		
i-C_4H_9Br	155.1	(3.87)[a]	231.7[b]	low	209.6	1990	3.5
t-C_4H_9Br	255.4	low	208.9	high	90.9	2680	2.4
n-$C_5H_{11}Br$	185.1	18.6			216.7		
i-$C_5H_{11}Br$	161.1				232.6	1760	4.3
n-$C_6H_{13}Br$	188.1	23.0			241.0		
CCl_4	250.3	2.30	255.5	4.79	99.9	2500	2.7
t-C_4H_9Cl	248.5	2.0	219.3[b]		75.2	2490	2.4
CBr_4	366.7	0.79	319.4	1.68	95.9		
C_2Cl_6[c]	459.9	4.3	344.2	7.3	0		
$C(CH_3)_4$	253.1				29.5		
$C_2(CH_3)_6$	377.1	4.51	148.1	3.24	2.8		
$(CH_3)_3CCH:CH_2$[d]	158.4	1.65	124.9	8.32	155.9		
$(CH_3)_2CH(CH_2)_3CH_3$	154.0	13.8			209.1		
$CH_3CH_2CH(C_2H_5)CH_2CH_3$	154.3	14.7			212.1		
$CH_3C(CH_3)_2(CH_2)_2CH_3$	148.1	9.5			204.5		
$(CH_3)_2CHCH_2CH(CH_3)_2$	152.5	10.5			204.2		
$CH_3CH_2C(CH_3)_2CH_2CH_3$	138.2	12.2			221.0		
$(CH_3)_3CHC(CH_3)_3$	247.7	2.14	121.0	4.69	106.3		

[a] Value probably low because of glass formation; Timmermans, *Bull. soc. chim. Belg.*, **44**, 17 (1935). [b] Baker and Smyth, to be published. [c] Parijs, *Z. anorg. allgem. Chem.*, **226**, 424 (1936). [d] Kennedy, Shomate and Parks, THIS JOURNAL, **60**, 1507 (1938); b. p.'s from Edgar, Calingaert and Marker, *ibid.*, **51**, 1483 (1929); Huffman, Parks and Thomas, *ibid.*, **52**, 3241 (1930).

above the "normal" temperature, as t-butyl bromide melts at 255.4°K., 95° above n-butyl bromide. Further, those molecules of somewhat lower symmetry, which can still acquire some rotational freedom before melting, like that found above for i-propyl bromide, will still melt significantly higher and with correspondingly lower entropies of fusion than their non-rotating isomers. This agrees with the position of i-propyl bromide on Fig. 3, and, conversely, the normal location of the n-amyl bromide point confirms the dielectric results in deciding against rotational freedom in the solid.

The abnormal positions of methyl chloride and bromide probably do not mean exceptional librational freedom, although rotation about the C–X axis would not be detected by dielectric measurements, which, for methyl bromide, yield a solid state polarization only slightly higher than the molecular refraction.[25] However, the methyl halide lattices contain a high concentration of dipoles, and might be expected to have greater lattice energies than the higher homologs, in which the dipoles are diluted by the hydrocarbon residues.

(25) Morgan and Lowry, *J. Phys. Chem.*, **34**, 2385 (1930).

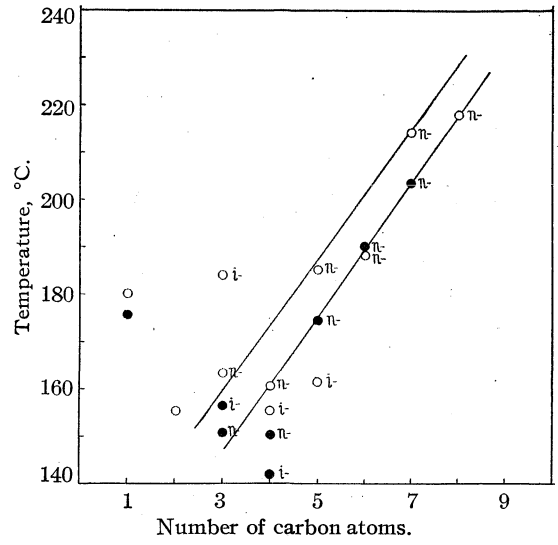


Fig. 3.—Graph of melting point against number of carbon atoms in alkyl chlorides and bromides. (Filled circles ● represent chlorides, hollow circles ○ bromides.)

The following proposals indicate agreement between the thermodynamic and mechanical interpretations of melting properties. The trend toward equilibrium in a system under given conditions involves an increase in entropy while maintaining the minimum free energy feasible.

At a given temperature, a solid can acquire entropy with small change of free energy by going over into the liquid, so melting occurs, and, at a still higher temperature, the boiling point, complete transition to the gas, the most disordered and hence highest entropy state of all, takes place. If, however, the symmetry of a molecule is such that its interaction with neighbors in a lattice does not vary much with its orientation, thermal agitation may give it sufficient kinetic energy to acquire, by means of a polymorphic transition, or simply a gradual loosening, a degree of rotational freedom approaching that in the liquid. A satisfying degree of disorder or increase in entropy has been introduced, and the actual melting can be economically postponed to a higher temperature, when the tendency to increase the entropy still further, by gaining translational freedom, finally causes liquefaction. That a lattice whose molecules possess orientational freedom should have a reduced entropy of fusion is shown in another way by

$$\Delta S_t = R \ln (W_l/W_s)$$

where W_l = number of ways of realizing the liquid state, W_s = number of ways of realizing the solid state; the order of magnitude is given by a W_l/W_s ratio of 2 in which $R \ln 2 = \sim 1.4$ cal./mole/°,[26] for example.

From their approximate obedience to Trouton's rule, most normal liquids are found to have the same entropy of vaporization at their boiling points. Hence, from the above argument, one would expect those molecules which gain extra entropy in the solid, and thus melt higher than is normal, to have liquid ranges much shorter than similar but less symmetrical molecules behaving normally in the solid. This is borne out in Table II, where *n*-butyl bromide has a liquid range of 214° and *t*-butyl bromide is a liquid for only 91°. Striking examples of very symmetrical molecules with solid transitions, that gain so little entropy on melting that they go over into the vapor almost immediately, are hexamethylethane, with 2.8° of liquid interval, and hexachloroethane, which, like iodine, forms no liquid under normal conditions. X-Ray studies have shown the onset of rotational freedom in these two molecules,[27,28] as their non-polarity precludes dielectric investigation. The recorded ΔS_f of hexachloroethane, which would be the entropy change on sublimation less that of vaporization, is little more than half the entropy of transition, so a vanishingly small liquid range is suggested.

i-Butyl and *i*-amyl bromides, which vitrified readily, appear on Fig. 3 to melt too low, possibly because of the efficiency of their packing in the liquid as indicated by glass formation. However, since the dielectric studies showed that the molecules could not rotate in the crystalline solids,[3] it would appear that the conditions of a small change in internal energy accompanied by a large, desirable entropy increase would lower the melting temperature.

The *t*-butylethylene data are included to provide another example besides carbon tetrabromide of an entropy of fusion less than the 2 units to be expected from communal volume sharing. Although its liquid range 160° is greater than those of the alkyl halides which have transitions, it is still a bit shorter than that of the unbranched butylethylene.

Data for six of the isomeric heptanes, at the bottom of Table II, further illustrate the generalizations. As the symmetry of the molecule finally reaches the maximum possible in 2,2,3-trimethylbutane, the melting point rises from a normal one around 150 to 247.7°K., and, correspondingly, the liquid interval drops from an average of over 200 to 106.3°. Parks and Huffman[29] observed that increased branching in a paraffin hydrocarbon leads to a marked decrease in ΔS_f. This behavior is understandable in the light of the present results, where the additional symmetry to be derived from branching may produce librational freedom in the solid.

The applicability of the explanation of the melting point variation among isomers may be further examined in the camphor compounds. Camphor has a rotational transition in the solid state,[30,31] and is a symmetrical molecule, as may be seen from kinetic theory models. If it is made unsymmetrical and the solid transition thus eliminated by moving the two methyl groups from the inner bridge to the outer ring, fenchone results, which should, by the above concept, have a lower melting point and a longer liquid interval than camphor. This is well confirmed by the comparison: α-camphor, m. p. 451.8°K., liquid interval, 30.4°; fenchone, m. p. 278.1°K., liquid in-

(26) Oldham and Ubbelohde, *Trans. Faraday Soc.*, **35**, 328 (1939).
(27) West, *Z. Krist.*, **A88**, 195 (1934).
(28) Finbak, *C. A.*, **32**, 1996 (1938); *Tids. Kjemi Bergvesen*, **17**, No. 9 (1937).
(29) Parks and Huffman, *Ind. Eng. Chem.*, **23**, 1138 (1931).
(30) Yager and Morgan, THIS JOURNAL, **57**, 2071 (1935).
(31) White and Morgan, *ibid.*, **57**, 2078 (1935).

terval, 188°. Similar considerations may be extended through the camphor series, where other rotational transitions are known.[30,31] Hence, the size of the molecules involved would not seem to limit the validity of the principle.

An independent index of the symmetry a molecule is likely to exhibit in condensed phases, and hence of its properties arising therefrom, comes from an examination of the activation energy of viscous flow, interpreted by the modern theory of viscosity.[32,33] Eyring has shown that to make a hole the size of a molecule in a liquid requires the same energy as to vaporize the molecule. Further, the mechanism of viscous flow involves an activation process which, apparently, requires extra volume, on the part of the flowing molecules, perhaps that swept out by a rotating couple. For nearly spherical molecules, this needed free volume is about one-third the size of a molecule, that is, the ratio $\Delta E_{\text{vap.}}/\Delta E_{\text{vis.}}$ is 2.5 to 3.[33] For rod-like molecules, however, the flow process seemingly goes in the most economical way, say by the couple's rotation about an axis parallel to the chain axes. Then, the $\Delta E_{\text{vap.}}/\Delta E_{\text{vis.}}$ ratio is about 4,[32] as rods rotating by each other require relatively less extra volume than spheres. This idea agrees with the independent calculations of the activation energies for orientation of *i*-butyl and *i*-amyl bromides.[3] The activation energies for viscous flow listed in Table II were calculated from the data in the Landolt–Börnstein "Tabellen." Perfectly straight lines for the plots of log η against $1/T$ were obtained. The $\Delta E_{\text{vap.}}$ values are from $\Delta H_{\text{vap.}} - (pV)_{\text{vap.}}$. The ratios are very approximate, but are consistent with the rest of the scheme in showing that a molecule which requires a large fraction of the energy of vaporization for the process of viscous flow will, in general, have a sufficiently symmetrical force field to gain vibrational degrees of freedom in the solid, and hence exhibit a reduced ΔS_{f}. An alternative method of statement is that molecules whose force fields interact nearly equally in all orientations with those of surrounding molecules in condensed phases will have no preferred arrangements in the flow process, and $\Delta E_{\text{vap.}}/\Delta E_{\text{vis.}}$ will be 2.5 to 3. However, molecules whose interaction potentials vary greatly with orientation will possess $\Delta E_{\text{vap.}}/\Delta E_{\text{vis.}}$ ratios of 4 or more indicating definite relative positions during flow, and, further, will be unlikely to show rotational freedom in the solid. Exceptions to this latter class are certain of the long chain compounds,[1] but, here, the mode of motion in the solid, about one axis only, is very like that found to be easiest in the flow process.

It may thus be concluded from fusion data, coupled with dielectric and crystallographic results, that members of a homologous aliphatic series (including isomers) melting above the normal temperatures indicated by the graph of melting point against number of carbon atoms have gained entropy by rotational freedom in the solid. Hence, since fewer than the normal degrees of freedom are gained on fusion, these compounds will have abnormally short liquid intervals. Viscosity results agree with the other structural data in assigning this behavior to symmetrical molecules.

(32) Eyring, *J. Chem. Phys.*, **4**, 283 (1936).
(33) Ewell and Eyring, *ibid.*, **5**, 726 (1937).

Summary

Dielectric constant and dipole loss measurements over a range of temperature and frequency on liquid and solid *i*-propyl bromide reveal a small hindered rotational freedom of the molecules in the anisotropic molecular lattice over a 40° interval below the freezing point. Similar studies on *n*-amyl bromide show that its already-known monotropic transition, which results in a melting point (−88.7°) 5.9° higher than the freezing point, does not involve detectable rotational freedom. These results, together with measurements on *t*-butyl halides as well as other data in the literature, lead to a correlation of the melting points, heats and entropies of fusion, and liquid intervals of alkyl halides with the shapes and mobilities of their molecules in the crystals.

PRINCETON, N. J. RECEIVED APRIL 3, 1939

[CONTRIBUTION FROM THE GEORGE HERBERT JONES CHEMICAL LABORATORY OF THE UNIVERSITY OF CHICAGO]

Energy Relations in Transformations from Three to Two-Dimensional Systems. I. The Latent Heat and Entropy of Spreading of Myristic and Pentadecylic Acids

BY WILLIAM D. HARKINS AND G. C. NUTTING

1. Introduction. Heats of Spreading and Freezing

By the application of a Clapeyron equation in the form

$$\Delta H = \lambda_{S \rightarrow F} = T(\partial f/\partial T)(a_F - a_S) \qquad (1)$$

it is possible to determine the latent heat of spreading $\lambda_{S \rightarrow F}$ of a solid S to form a film F upon an aqueous subsolution. Here f is the film pressure at equilibrium between the crystals and the film and a the area of the surface involved. In practice a_S may be made sufficiently small to be negligible.

Since the values of the temperature required to give the same molecular area at equilibrium in a monolayer of either the 14 or the 15 carbon atom acid are not very different, it is apparent that the differences in the latent heats of spreading, at any given value of a_F, are almost entirely determined by the value $\partial f/\partial T$ of the slope of the f, T curve.

Values of these slopes have been determined by Cary and Rideal,[1] who find $\partial f/\partial T$ to be practically the same for both myristic and pentadecylic acid, that is the f, T curves are parallel, which is not in agreement with our data as presented later. The values of the latent heats of solidification or "settling" of these acids have been determined by King and Garner,[2] and these are, in kcal. per mole, 10.7 for the even (14 C) and 10.30 for the odd (15 C) acid if the solid is in the α-form. The transformation $\alpha \rightarrow \beta$ of the odd acid evolves 1.20 kcal. per mole in addition.

Thus the tightness of binding of the molecules of the even (14 C) acid may be said to be 10.7 kcal. per mole greater in the crystals than in the three dimensional liquid, while for the odd (15 C) acid the value is 10.3 or 11.5 as has been stated. The effects of the small changes of volume are neglected.

All of the monolayers formed by these two acids are liquids in the ranges of T, f, and a considered here. They may be classified as: I, Liquid, condensed; II, Liquid, intermediate (or transition); and III, Liquid, expanded.

(1) A. Cary and E. W. Rideal, *Proc. Roy. Soc.* (London), **A109**, 328 (1925).

(2) Annie M. King and M. E. Garner, *J. Chem. Soc.*, 578 (1931).

In these liquid monolayers the energy of molecular binding may be assumed to be greater than in the three dimensional liquid on the basis of the orientation theory, which assumes intimate contact between the carboxyl groups and water molecules, both of which have powerful dipoles. On the basis of the reasoning given above the energy added as heat (Q_F) to produce a spreading of the material from the crystals over the surface of the liquid should for any of the solids be less than the heat of melting (Q_M), or (1) $Q_F < Q_M$.

2. Apparatus and Methods.—The film balance used for the measurement of film pressure, an improved form of that described by Harkins and Myers,[3] was of the general Adam–Jessop type, and was built in such a way as to give a high degree of accuracy in the measurements. For the determination of $\partial f/\partial T$ it is essential to have more accurate temperature control. The use of an air thermostat alone is not sufficient to determine closely enough the temperature of the film. The trough of stainless steel used to contain the subsolution was 80 × 25 × 0.5 cm. with the bottom of the trough hollow, and water from a thermostat was circulated through the shallow reservoir in this bottom, so that the subsolution came rapidly to the thermostat temperature. Water from the thermostat was also circulated through the top of the metal box which inclosed the trough and underneath the trough, and the box was surrounded by an air thermostat.

In performing the experiments, two or three hundred small crystals of fatty acid, supplied by Drs. E. E. Reid and Jane D. Meyer, were placed on a clean surface of 0.01 N sulfuric acid and the temperature of the air and the subsolution were equalized. Temperatures were read by means of thermocouples placed just above and just below the film-covered surface. The air within the film balance case was kept saturated with water vapor. This precaution was necessary for two reasons. At the higher temperatures if the air is not kept saturated, evaporation is rapid and the level of the subsolution in the film trough drops considerably in the course of an experiment, which introduces a proportionate error in the film pressures. Also rapid evaporation produces in the film-covered surface a temperature lower (by an unknown amount) than that measured with the thermocouples. The area included between the float and barrier of the film balance, which was available for spreading, was about 100 sq. cm. The criterion of equilibrium was constancy of film pressure within 0.1 dyne per cm. for ten to fifteen minutes. Attainment of equilibrium below 20° required about two hours but the time became rapidly less as the temperature was raised.

Since a considerable number of investigators

(3) W. D. Harkins and R. J. Myers, *J. Chem. Phys.*, **4**, 716 (1936).

TABLE I

LATENT HEAT OF SPREADING OF MYRISTIC AND PENTADECYLIC ACIDS ON AN AQUEOUS SUBSOLUTION OF *p*H 2

Acid	Area per molecule at equilib. press., sq. Å.	T, °C.	Equilib. press., dynes per cm.	Entropy (s), ergs per molecule per degree $\times 10^{-16}$	Entropy (S), cal. per mole per degree	Latent heat of spreading (λ), kcal. per mole	Internal latent heat (λi), kcal. per mole	State of film
Myristic	22.3	12.5	9.8	14.7	21.3	6.07	5.79	Condensed
$(\partial f/\partial T = 0.662)$	23.4	14.8	11.4	15.4	22.3	6.46	6.08	Intermediate
	23.6	9.5	7.7	15.5	22.5	6.40	6.13	Condensed
$(\lambda_{S \rightarrow L} = 10.7$ kcal. per mole)	25.7	16.6	12.5	16.9	24.5	7.14	6.69	Intermediate
	28.4	25.0	18.1	18.7	27.1	8.12	7.38	Expanded
	28.9	21.7	15.9	19.0	27.6	8.17	7.51	Expanded
Pentadecylic	20.9	25.0	20.6	10.8	15.7	4.67	4.17	Condensed
$(\partial f/\partial T = 0.517)$	21.2	21.7	18.8	11.0	15.9	4.68	4.11	Condensed
$(\lambda_{S_\alpha \rightarrow L} = 10.3)$	21.5	17.9	16.9	11.1	16.1	4.68	4.06	Condensed
$(\lambda_{S_\beta \rightarrow L} = 11.5)$								

have used the ring method in an attempt to determine the surface tension of a subsolution covered with an insoluble film, and since this method was applied by Cary and Rideal to determine the pressures of films in equilibrium with crystals of myristic, pentadecylic, and other acids, it is important to point out why this method fails. The film pressure is given by the equation

$$f = \gamma_S - \gamma_F$$

where γ_S is the surface tension of the clean surface of the subsolution, and γ_F the value when the film is present. However, at least with rings of the size in use, the ring method does not measure γ_F. This is due to the fact that, in order to meet the conditions of the theory of the method, the ring must be pulled completely from the liquid, and the maximum pull exerted gives the surface tension. Now at the instant when the maximum pull is exerted, the area of the surface inside the ring is much greater than when the surface is plane. Thus unless crystals of the solid are kept on the surface inside the ring, the surface tension found will be higher than the true tension for the film. The film pressure as determined will thus be too low; much too low if the film is initially condensed, considerably if expanded, and not very much if the film is in the intermediate (transition) state just above the pressure of the transition Intermediate → Expanded. Even if crystals are present inside the ring the time which elapses during the pulling of the ring from the surface is often insufficient to give equilibrium. In addition the weight of the crystals must be negligible or the method is inaccurate.

Values of the variable correction factor, which is essential if the pull on the ring is to be transformed into a surface tension, had not been determined at the time of Cary and Rideal's work. The corrections cannot now be made because of insufficient data on the dimensions of the ring which they used.

The Wilhelmy method, used as a film balance in the form recommended by Harkins and Anderson,[4] should give fully as accurate results as those which we report in this paper, and this method is much more adaptable if temperatures much higher than 45° are to be used.

3. Latent Heat and Entropy of Spreading of Monolayers

For myristic acid the magnitude of the slope $\partial f/\partial T$ as taken from Fig. 1 was found to be 0.662, while pentadecylic acid exhibited a much smaller value (0.517), or the difference between the two is 27% of the latter magnitude. The corresponding slopes found by Cary and Rideal are 0.568 and 0.552, so their work fails to exhibit a difference between the slopes.

The values of the entropy and of the latent heat of spreading are given in Table I. Pressure–area measurements on myristic and pentadecylic acids at several temperatures have been reported in another paper.[5] The areas given in Column 2 of Table I have been taken from the data of that paper for pressures read from the curves of Fig. 1. The relation between the latent heat and the molecular area of the film in equilibrium with the solid, is exhibited in Fig. 2, and is seen to be nearly linear. The complete relationship involves a three dimensional plot, since the temperature is also involved. The entropy of spreading increases with the molecular area, that is, with

(4) W. D. Harkins and T. F. Anderson, THIS JOURNAL, **59**, 2189 (1937).

(5) G. C. Nutting and W. D. Harkins, *ibid.*, **61**, 1180 (1939).

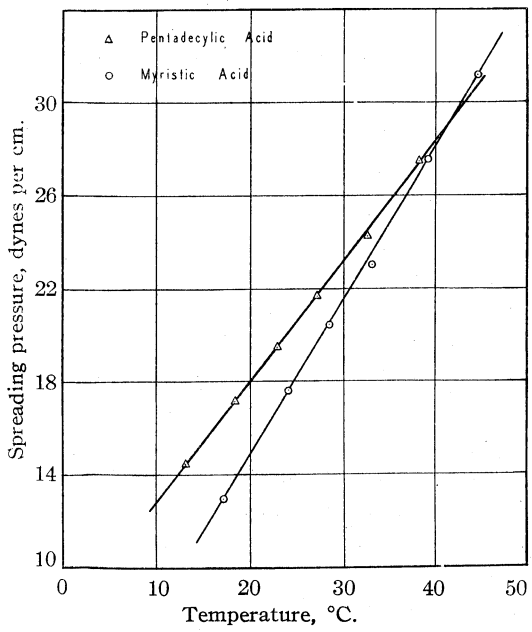


Fig. 1.—Equilibrium spreading pressures of crystals of myristic and pentadecylic acid on an aqueous subsolution at pH 2.

the two dimensional "dilution" of the film. This is similar to the relation found in the vaporization of a liquid, since the entropy of vaporization increases as the concentration of the equilibrium vapor decreases.

The latent heat of spreading involves a work term $\int f\,da$ and, if this is subtracted, the internal latent heat is obtained. This gives the increment in molecular energy (λ_i) involved. Thus

$$\Delta E = \Delta H - W = \lambda_i = \lambda - f(a_F - a_S) = \left(T\frac{\partial f}{\partial T} - f\right)(a_F - a_S) \quad (2)$$

The values for myristic acid given in Column 9 of the table show that λ_i in calories per mole changes from 5800 at an area of 22.3 to 7500 at an area of 28.9 sq. Å. per molecule.

The entropy of spreading is found to vary from 14.5 to 19 $\times 10^{-16}$ ergs per degree per molecule for myristic acid at areas from 22.3 to 28.9 sq. Å. per molecule. This would give, if a linear extrapolation is justified, about 26 $\times 10^{-16}$ ergs per molecule per degree at 40° . With pentadecylic acid the entropy is about 11 at an area of 21 in the above units. These values may be compared with those for the entropy of vaporization of a normal liquid which follows Hildebrand's relation. Thus, for example, the values are 15.7 ergs per degree per molecule if the concentration of the vapor is 0.0201

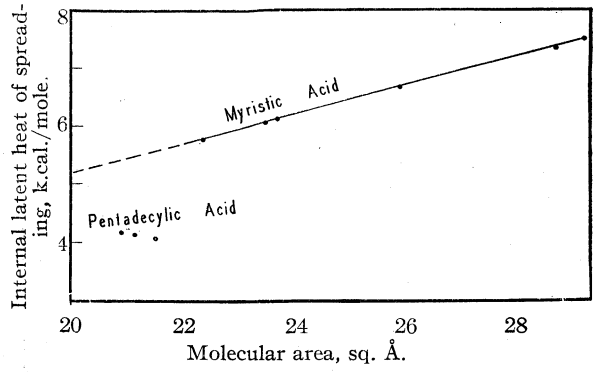


Fig. 2.—Internal latent heat of transformation from three-dimensional crystals to two-dimensional films on an aqueous subsolution at pH 2. The values for pentadecylic acid are in such a limited range of areas that the slope is uncertain, but it is certain that the values increase with molecular area as in the case of myristic acid.

mole per liter,[6] and 18.8 if the concentration is 0.00507. These have been chosen at concentrations of the vapor which are associated with entropy values of the same order as those for spreading as cited above. From the rate at which the heat of spreading increases with the temperature it seems that at the melting point the value must still be below the heat of fusion. This means that the spreading of the material from a liquid lens gives off heat instead of absorbing it.

4. Summary

1. By the use of the equation $\Delta h = \lambda_{S \rightarrow F} = T(\partial f/\partial T)_a\,(a_F - a_S)$, the latent heats of spreading of crystals of myristic and pentadecylic acid to form a monolayer on 0.01 N sulfuric acid have been determined. The measurements involved are the determination of the pressures of the film in equilibrium with the crystals at various temperatures, and that of the molecular area at each temperature and pressure.

2. The latent heats of spreading for myristic acid are found to increase with molecular area in an almost linear way, and rise from 6020 cal. per mole at 22.1 sq. Å. per molecule to 8060 cal. per mole at 28.7 sq. Å. The corresponding increase of entropy is from 14.5 to 18.9 $\times 10^{-16}$ ergs per degree per molecule.

3. The latent heat of spreading is of the order of a thousand calories per mole less for pentadecylic (15 C) than for myristic (14 C) acid.

CHICAGO, ILLINOIS RECEIVED APRIL 7, 1939

(6) W. D. Harkins, *Proc. Nat. Acad. Sci.*, **5**, 152 (1919).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF MAINE]

A New Synthesis of Acetals of Chloroacetaldehyde and Bromoacetaldehyde

BY EDWARD M. FILACHIONE[1]

A variety of methods for the preparation of the acetals of chloroacetaldehyde and of bromoacetaldehyde has been reported. These may be summarized briefly as follows: (a) chlorination of ethyl alcohol[2,3]; (b) the reaction of the α,β-dihalogenated ethyl ether with sodium ethylate[4-7] or with ethyl alcohol[8]; (c) halogenation of the acetal[9] preferably in the presence of calcium carbonate[10-12] or sodium ethylate[13] and (d) the halogenation of paraldehyde followed by treatment with ethyl alcohol.[14-16]

Except for the process mentioned in the patent literature,[13] the yields, where reported, were not highly satisfactory. A synthetic method from a readily available starting material, easily carried out, and resulting in good yields was the purpose of the present work.

There is described in the patent literature[17] the addition of halogens to vinyl acetate yielding α,β-dihaloethyl acetate.

$$CH_2{=}CH{-}O{-}COCH_3 + X_2 \longrightarrow CH_2(X){-}CH(X){-}OCOCH_3$$

An inspection of this dihalide shows that it contains a very reactive halogen atom as well as an ester grouping that should undergo alcoholysis almost completely. Hence it is reasonable to expect the halogen and the acetoxy group to be replaced by alkoxyl groups merely by treatment with the alcohol.

Such was found to be the case. Vinyl acetate dibromide was prepared by the addition of bromine to vinyl acetate. This was then mixed with ethyl alcohol. On standing they reacted and bromoacetal was formed. Ethyl acetate and hydrogen bromide were also among the products. In actual practice it was found more efficient to pass the halogen into a solution of vinyl acetate in the alcohol. The addition of halogen to the double bond is so rapid that halogenation of the alcohol is not extensive.

In any mechanism written, undoubtedly the first step is addition of halogen to the double bond.

$$CH_2{=}CH{-}OAc + X_2 \longrightarrow CH_2(X){-}CH(X){-}OAc \qquad (1)$$

The acetal may result from this by several paths which may be indicated as follows

$$CH_2(X){-}CH(X){-}OAc + C_2H_5OH \overset{HX}{\rightleftharpoons} CH_2(X){-}CH(X){-}OH + C_2H_5OAc \qquad (2)$$

$$CH_2(X){-}CH(X){-}OH \rightleftharpoons CH_2(X){-}CHO + HX$$

$$CH_2(X){-}CHO + 2C_2H_5OH \overset{HX}{\rightleftharpoons} CH_2(X){-}CH(OC_2H_5)_2 + H_2O \qquad (3)$$

or the following may represent the course of reaction

$$CH_2(X){-}CH(X){-}OAc + C_2H_5OH \rightleftharpoons CH_2(X){-}CH(OC_2H_5){-}OAc + HX \qquad (2a)$$

$$CH_2(X){-}CH(OC_2H_5){-}OAc + 2C_2H_5OH \overset{HX}{\rightleftharpoons} CH_2(X){-}CH(OC_2H_5)_2 + C_2H_5OAc + H_2O \qquad (3a)$$

Reactions (2) and (3) are slow and do not occur at the low temperature of the halogen addition. By using methyl alcohol in place of ethyl alcohol, the methyl haloacetal is formed.

Experimental

Purification of Vinyl Acetate.—The practical grade vinyl acetate (purchased from Eastman Kodak Co.) was distilled and the fraction boiling at 69–71° was collected. Distillation gives an anhydrous ester since the water comes

(1) Present address: Cornell University, Ithaca, N. Y.
(2) Lieben, *Ann.*, **104**, 114 (1857).
(3) Fritsch, *ibid.*, **279**, 300 (1894).
(4) Lieben, *ibid.*, **146**, 193 (1868).
(5) Wislicenus, *ibid.*, **192**, 112 (1878).
(6) Natterer, *Monatsh.*, **3**, 444 (1882).
(7) Kluger, *ibid.*, **26**, 881 (1905).
(8) Paternò and Mazzara, *Gazz. chim. ital.*, **3**, 254 (1873).
(9) Pinner, *Ber.*, **5**, 149 (1872).
(10) E. Fischer and Landsteiner, *ibid.*, **25**, 2551 (1892).
(11) Willstätter, *ibid.*, **35**, 602 (1902).
(12) J. v. Braun, *ibid.*, **35**, 3388 (1902).
(13) German Patent 639,507 (1936); *C. A.*, **31**, 3940 (1937).
(14) Freundler, *Bull. soc. chim.*, [4] **1**, 70 (1907); Freundler and Ledru, *ibid.*, [4] **1**, 73 (1907).
(15) Späth, *Monatsh.*, **36**, 4 (1915).
(16) Rotbart, *Ann. chim.*, [11] **1**, 506 (1934).
(17) British Patent 325,115 (1929); *C. A.*, **24**, 3800 (1930).

over in the first portion. Care was taken not to distill to dryness in case peroxides were present.

Synthesis of the Acetals

Ethyl Chloroacetal.—A solution of 43 g. (0.5 mole) of vinyl acetate in 150 cc. (2.5 mole) of absolute ethyl alcohol was placed in a 3-necked flask and the flask immersed in a crock containing dry ice–acetone cooling mixture. The flask, where exposed to light, was wrapped with black cloth. Accompanied by vigorous stirring, a stream of dry chlorine, flowing at the rate of 0.4 g. per minute, was bubbled into the solution for ninety minutes, *i. e.*, till the theoretical amount had been added. The mixture was next allowed to warm to room temperature and then stand overnight. It was then poured into an equal volume of iced water, and the ethyl chloroacetal, which separated as an oil, was taken up with ether. The ether solution was washed twice with cold water, then with sodium bicarbonate solution until the ether layer showed no acid reaction to moist litmus, then washed once more with cold water, and finally dried with anhydrous calcium chloride. The ether was removed by distillation from a water-bath, and the residual ethyl chloroacetal was fractionated *in vacuo*. The yield was 62 g. (83% yield) of ethyl chloroacetal boiling at 53–54° (16 mm.); d^{20}_{20} 1.017; $n^{20}D$ 1.4171; M_D 37.7 (calculated 38.1); Cl, 23.38 (theoretical 23.23).

Further proof of the identity of this compound was obtained by hydrolysis. Ethyl alcohol was identified in the hydrolyzate through its 3,5-dinitrobenzoate, m. p. 92°. Chloroacetaldehyde was identified in the hydrolyzate by oxidation with hydrogen peroxide to chloroacetic acid, m. p. 60°.

An experiment identical to the above except that the chlorine was passed in at a higher temperature (−10 to −5°) resulted in a 70% yield of ethyl chloroacetal.

Methyl Chloroacetal.—This preparation was carried out exactly as above. From 86 g. (1 mole) of vinyl acetate in 200 cc. (5 moles) of methyl alcohol, there resulted 66 g. (53% yield) of methyl chloroacetal boiling at 124.5–126.5° (atmospheric pressure); d^{20}_{20} 1.094; $n^{20}_{20}D$ 1.4150; M_D 28.5 (calcd. 28.8).

Anal. Calcd. for $C_4H_9O_2Cl$: Cl, 28.48. Found: Cl, 28.47.

Hydrolysis of this acetal gave an hydrolyzate in which methyl alcohol was shown to be present by isolation of its 3,5-dinitrobenzoate, m. p. 106°. Hydrolysis followed by oxidation with hydrogen peroxide gave chloroacetic acid, m. p. 62°, showing the presence of chloroacetaldehyde.

Ethyl Bromoacetal.—Air was passed over the surface of 12.5 cc. (0.25 mole) of bromine, and the bromine laden stream of air was led into a solution of 21.5 g. (0.25 mole) of vinyl acetate in 75 cc. (1.3 moles) of absolute ethyl alcohol. During this addition (one and one-half hours) the solution was stirred. Cooling was effected by a freezing mixture (about −10°). The resulting solution was worked up exactly as above. The yield was 33 g., or 68% of the theoretical, of ethyl bromoacetal boiling at 62–63° (15 mm.); d^{20}_{20} 1.276; $n^{20}D$ 1.4395; M_D 40.7 (calcd. 41.0).

Another experiment similar to the above except that liquid bromine was added dropwise to the ethyl alcohol solution of vinyl acetate gave a 58% yield of ethyl bromoacetal. This substance is a good lachrymator.

This acetal was characterized as above. Hydrolysis gave ethyl alcohol, identified through its 3,5-dinitrobenzoate, and bromoacetaldehyde, identified by oxidation with hydrogen peroxide to bromoacetic acid, m. p. 45°.

Methyl Bromoacetal.—A solution of 64.5 g. (0.75 mole) of vinyl acetate in 150 cc. (3.7 moles) of methyl alcohol was cooled in a dry ice–acetone mixture. To this was added, with stirring, a solution of 120 g. (38.5 cc., 0.75 mole) of bromine in 100 cc. of chloroform. (It was necessary to use a solution of bromine since liquid bromine solidified in the stem of the dropping funnel.) The addition required two hours, during which time the reaction mixture remained below −40°. The resulting solution was worked up as the others. Thus there was obtained 59 g. (a yield of 46%) of methyl bromoacetal boiling at 48–51° (18 mm.); d^{20}_{20} 1.467; $n^{20}D$ 1.4475; M_D 30.8 (calcd. 31.7). This compound is also lachrymatory.

As in the above cases, this acetal was characterized by its products of hydrolysis. These were shown to be methyl alcohol and bromoacetaldehyde.

Summary

A new synthesis of acetals of chloroacetaldehyde and bromoacetaldehyde has been investigated. The addition of chlorine to vinyl acetate in the presence of ethyl alcohol or in the presence of methyl alcohol resulted in good yields of the acetals, ethyl chloroacetal and methyl chloroacetal, respectively. Similarly, addition of bromine to vinyl acetate in the presence of methyl or ethyl alcohol formed the corresponding bromoacetals. The yields of the ethyl haloacetals were considerably higher than the yields of the corresponding methyl haloacetals.

As for the mechanism, undoubtedly the halogen first adds to the vinyl acetate, resulting in the α,β-dihaloethyl acetate, which subsequently reacts with the alcohol present in the mixture, giving rise to the acetal of the α-haloacetaldehyde.

ORONO, MAINE RECEIVED APRIL 24, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF HARVARD AND STANFORD UNIVERSITIES]

Saponins and Sapogenins. X. The Isolation of Gitogenin from Chlorogalum Pomeridianum

BY C. R. NOLLER, L. H. GOODSON AND MARTIN SYNERHOLM

In a recent paper Marker and Rohrmann[1] state that they "have isolated from the acid hydrolysis extracts of *Chlorogalum pomeridianum* in addition to chlorogenin and tigogenin a substance which appears to be identical with gitogenin." This interest of other workers in *Chlorogalum* as a source of steroid sapogenins prompts us to report the observations in regard to their isolation which we have made since our original publication.[2]

Hydrolysis of the alcoholic extracts of the ground bulbs or of the partially purified saponins followed by separation of the sapogenins by crystallization always has yielded an intermediate fraction melting between 230 and 255° which could be made to melt over the comparatively narrow range of 235–240°.[3] Oxidation of this material with Kiliani's mixture[7] gave an acid fraction which appeared to be identical with gitogenic acid. Three possibilities seemed likely: (1) that the material was a molecular compound of chlorogenin and tigogenin, the gitogenic acid being formed by oxidation of the latter; (2) that it was a new sapogenin which also gave gitogenic acid on oxidation; (3) that it contained gitogenin possibly as a molecular compound with chlorogenin or tigogenin. Melting point determinations of mixtures of pure tigogenin and chlorogenin eliminated the first possibility as shown in Fig. 1.[4] Moreover, an analysis checked almost exactly for the composition $C_{27}H_{44}O_4$. This could result from an equimolar mixture of tigogenin, $C_{27}H_{44}O_3$, and a trihydroxy compound, $C_{27}H_{44}O_5$, or from a mixture of the isomeric substances gitogenin and chlorogenin.

Further attempts to separate the mixture by crystallization of the sapogenins were without encouraging results. While the material crystallized well from benzene, carbon tetrachloride, ethylene chloride, and dioxane, there was no more evidence that a separation was taking place than when crystallized from methyl, ethyl or isopropyl alcohol. Separation was effected readily, however, after conversion to the benzoates or acetates. The mixed esters were extracted with ether in which one isomer is much more soluble than the other and this was followed by systematic crystallization of the two portions to constant melting point. The less soluble benzoate, its saponification product and the acetate had melting points almost identical with those of authentic samples of gitogenin dibenzoate, gitogenin and gitogenin diacetate.[5] Mixtures of the corresponding compounds gave slight but definitely observable depressions or elevations over that for the components even when present in the same bath, which, until a satisfactory explanation is found, is a disturbing fact. The specific rotations, however, of the two sapogenins and of their acetates were identical within experimental error and in spite of the melting behavior of the mixtures we feel certain that the two sapogenins are identical.

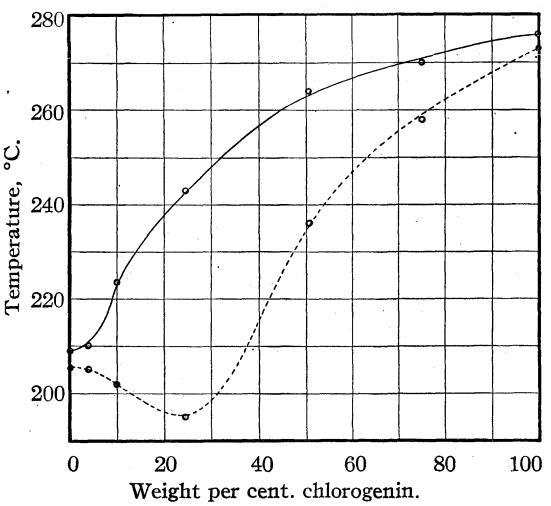


Fig. 1.—Melting point diagram for mixtures of tigogenin and chlorogenin.[4]

The more soluble benzoate, its saponification product and the acetate proved to have the same

(1) Marker and Rohrmann, THIS JOURNAL, **61**, 946 (1939).

(2) Liang and Noller, *ibid.*, **57**, 525 (1935).

(3) McMillan, Thesis, Stanford University, 1937, p. 40.

(4) In all of the melting point diagrams, the dotted curve represents the temperature at which the mixture first wets the walls of the capillary tube while the solid line gives the temperature at which the melt is entirely clear. In Figs. 1 and 3 the melting point diagram indicates that the components form a continuous series of solid solutions with the melting point passing through a minimum. The fact that the temperature at which the melt is clear does not pass through a minimum as does the softening point is probably caused by the system not being in equilibrium.

(5) The authors are greatly indebted to Dr. W. A. Jacobs of the Rockefeller Institute for Medical Research for a generous sample of gitogenin from *Digitalis* leaves.

melting points, respectively, as chlorogenin dibenzoate, chlorogenin and chlorogenin diacetate and the specific rotations of the sapogenins were identical within experimental error. Here again the mixture of the benzoates and of the acetates melted slightly lower than either component, while the mixture of the sapogenins melted higher. The fact that these phenomena occur with the chlorogenin fraction of the mixture supports our belief that they do not indicate non-identity and that the other component is indeed gitogenin.

The melting point curve for mixtures of gitogenin and chlorogenin given in Fig. 2 shows that the two components do not form a continuous series of solid solutions, but form a eutectic. This

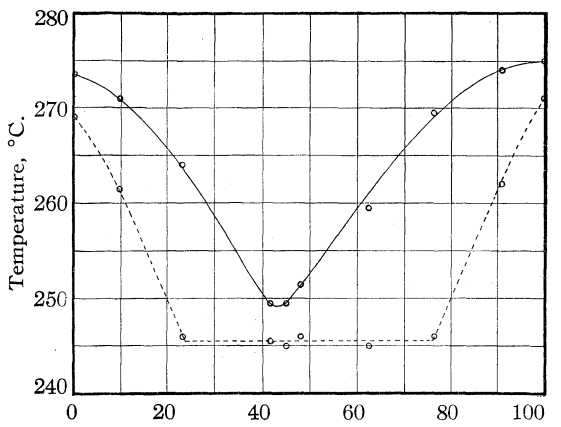


Fig. 2.—Melting point diagram for mixtures of gitogenin and chlorogenin.[4]

eutectic is the cause of the relatively sharp melting point of approximately equimolar quantities of gitogenin and chlorogenin. Apparently the solubility of the gitogenin and chlorogenin in the solvents used is practically identical and the solubility of the eutectic mixture is greater than that of either of the pure components with the result that with an excess of chlorogenin, crystallization leads to a separation of pure chlorogenin and the eutectic. One discrepancy in this explanation is the fact that the melting point of 235–240° commonly encountered in isolating the sapogenins is about 10° lower than that of the eutectic as determined by the mixed melting point curves. It is possible that the natural mixture contains some tigogenin which may lower the melting point of the eutectic.

Figure 3 gives the melting point diagram of mixtures of tigogenin and gitogenin which is very similar to Fig. 1 except that the lowering of the softening point of tigogenin by gitogenin is less than in the case of tigogenin and chlorogenin.

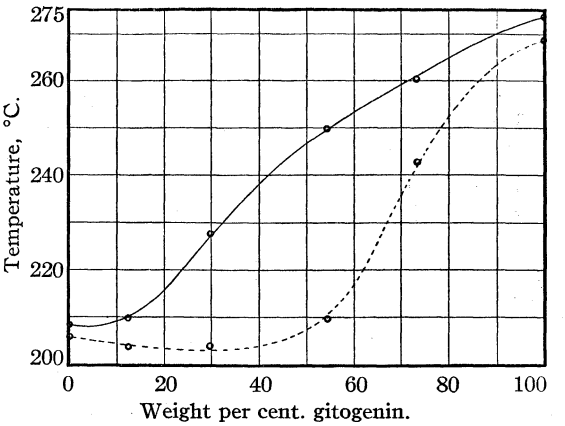


Fig. 3.—Melting point diagram for mixtures of tigogenin and gitogenin.[4]

The general procedure for the isolation of the sapogenins has been improved considerably over the method originally published[2] and our present procedure is recorded in the experimental part. The identity of tigogenin from *Chlorogalum* with that from *Digitalis* has been confirmed further by conversion into tigogenin acetate, tigogenone, tigogenone oxime, the C_{22} lactone acetate obtained by oxidation and the C_{22} hydroxy lactone, the melting points of which all checked with those recorded in the literature for derivatives of tigogenin isolated from *Digitalis purpurea* or *Digitalis lanata*.

Experimental

Isolation of the Mixed Sapogenins.—Several hundred pounds of bulbs of *Chlorogalum pomeridianum* from which the outer husks had been removed were put through a power food grinder at the San José plant of the California Prune and Apricot Growers Association. The resultant mash was mixed thoroughly with about an equal volume of methyl alcohol to act as a preservative and the saponin extracted as opportunity and facilities permitted. Addition of the methyl alcohol caused a thickening of the mash presumably due to a precipitation of plant gums by the alcohol. For isolating the saponins the mixture of ground bulb and methyl alcohol was pressed in a cider press. The expressed liquid yielded very little sapogenin on hydrolysis so that it was hardly profitable to work it up other than to recover the methyl alcohol. The press cake was extracted in 12-liter flasks with boiling methyl alcohol, the hot solution filtered and allowed to cool overnight. The saponins which separated were filtered and stored moist in tightly stoppered wide-mouthed bottles. The extraction with hot methyl alcohol was repeated until no saponin separated on standing overnight. Each of the mother liquors was concentrated and additional crops of saponin were obtained.

For hydrolysis a saturated solution of the saponins in hot methyl alcohol was prepared and an equal volume of 10% aqueous hydrochloric acid added. A flocculent precipitate formed which after twelve hours of refluxing became crystalline and was filtered. The advantage of using the saponins which have been isolated as above rather than the crude extracts is that about half the time is required for hydrolysis, and the hydrolysis product is light colored and almost pure sapogenins, very little residue being left after exhaustive extraction with hot carbon tetrachloride.

It was found that a partial separation of the sapogenins could be obtained in the next step, the extraction of the crude hydrolysis product with carbon tetrachloride. Extraction was carried out in Soxhlet extractors until a copious crop of crystals had formed in the boiling flask. These were filtered and the extraction continued and crops removed until no more sapogenin separated. The carbon tetrachloride was then concentrated and successive crops of crystals removed. The melting point of each crop was taken and the various crops combined into three groups: those melting below 230°, those melting between 230 and 245° and those melting above 245°.

Isolation of Tigogenin.—The combined fractions melting below 230° were extracted in a Soxhlet extractor with a petroleum hexane fraction (Viking Distributing Company, b. p. 60–70°), separating crops of crystals until the rate of extraction is relatively slow. The crops melting up to 220° could be purified readily by several crystallizations from isopropyl alcohol when they melted at 203–208°. Concentration of the hexane mother liquors gave material melting as low as 180–186°. This low melting point was found to be caused by the presence of a non-crystallizable oil. The melting point of these fractions readily could be brought to that of tigogenin by one crystallization from hexane, in which the oil is very soluble, followed by recrystallization from isopropyl alcohol.

A special effort was made to obtain a sample of tigogenin of maximum purity. A sample that had been purified by crystallization from isopropyl alcohol was converted to the acetate by means of acetic anhydride and pyridine. After two crystallizations from ethyl alcohol the acetate melted at 202–208° while Jacobs and Fleck[6] report 200–202°. Saponification of the acetate and two crystallizations from isopropyl alcohol brought the melting point of tigogenin to 206.5–209° which could not be raised nor the range narrowed by subsequent recrystallizations. This value compares favorably with the 206.5–210° previously reported.[2]

Oxidation of a less pure sample of tigogenin, m. p. 199–204°, gave tigogenone which after two crystallizations from acetone melted at 203–205°. This was converted to the oxime, which after three crystallizations from acetone melted at 256–258°.

Isolation of Chlorogenin.—The crude fractions melting above 245° readily gave pure chlorogenin by repeated crystallization from methyl alcohol. The purest sample of chlorogenin that we have obtained was prepared by crystallizing a product, m. p. 270–275°, once from methyl alcohol, twice from dioxane and twice from methyl alcohol, after which it melted at 273–276°. No change in the melting point was observed during the last three crystallizations.

(6) Jacobs and Fleck, *J. Biol. Chem.*, **88**, 546 (1930).

Separation of Gitogenin and Chlorogenin.—All attempts to separate the crude fraction melting between 230 and 245° into its components by crystallization or partial extraction with hot solvents failed. The solvents tried were benzene, dioxane, ethylene dichloride, carbon tetrachloride, methyl alcohol and 95% ethyl alcohol. While there were minor changes in the melting point, such as spreading or narrowing of the range, successive crops of the dissolved and undissolved portions would melt at so nearly the same temperatures that no practical separation could be made.

A fraction having the narrow melting range of 235–239° occasionally was obtained, usually when using carbon tetrachloride as a solvent. Five grams of this fraction on oxidation at room temperature by the procedure of Kiliani and Merk[7] gave 4 g. of crude oxidation product. This was extracted with cold benzene, giving 1.5 g. of insoluble material. The benzene extract after washing with 10% sodium carbonate solution and evaporation of the benzene gave 0.72 g. of neutral product. The sodium carbonate extracts on acidification gave 1.3 g. of acidic material. The benzene insoluble material was completely soluble in sodium carbonate solution. This behavior on oxidation is in marked contrast to that of chlorogenin[8] which yields very little acidic material. The benzene insoluble acid was crystallized eight times from glacial acetic acid, the melting point then remaining constant at 243–245°. Windaus and Schneckenburger[9] report the melting point of gitogenic acid as 242–243° and Jacobs and Simpson[10] as 244° with preliminary sintering.

The remainder of the sapogenin sample, m. p. 235–239°, was recrystallized for analysis.

Anal. Calcd. for $C_{27}H_{44}O_4$: C, 74.96; H, 10.25. Found: C, 74.77; H, 10.24.

The separation of the mixture was first effected through the benzoates. A mixture of 9 g. of material, m. p. 230–240°, 17 g. of benzoyl chloride, 9.5 g. of pyridine and 500 cc. of benzene was refluxed for fifteen minutes, allowed to stand at room temperature for three hours and the benzene distilled from a steam-bath until a sirup remained. The residue was rubbed up with 6 *N* hydrochloric acid and then three times with 25-cc. portions of 80% ethyl alcohol, decanting from the residue. The product is still pasty at this point but, on the addition of 25 cc. of ether, a portion goes into solution leaving a solid which can be filtered. The undissolved portion weighed 4 g. and melted at 211–227°. It was only slightly soluble in hot methyl alcohol, 95% ethyl alcohol or hexane, very soluble in dioxane and could be crystallized from isopropyl alcohol, ethyl acetate or acetone. After two crystallizations from each of the last three solvents, the product melted at 223–228°.

Anal. Calcd. for $C_{41}H_{52}O_6$: C, 76.84; H, 8.18. Found: C, 76.89; H, 8.22.

A mixture with an equal amount of gitogenin benzoate, m. p. 223–227°, melted at 222–227°. All three samples were placed at the same time in a Hershberg[11] apparatus so that the lowering though slight was definitely observable. The specific rotation for the dibenzoate isolated from the

(7) Kiliani and Merk, *Ber.*, **34**, 3564 (1901).
(8) Noller, THIS JOURNAL, **59**, 1092 (1937).
(9) Windaus and Schneckenburger, *Ber.*, **46**, 2628 (1913).
(10) Jacobs and Simpson, *J. Biol. Chem.*, **110**, 429 (1935).
(11) Hershberg, *Ind. Eng. Chem., Anal. Ed.*, **8**, 312 (1936)

mixture was $[\alpha]^{25}D$ −75.9° in pyridine. The sample of gitogenin benzoate available was not sufficiently large for a determination of its rotation.

The dibenzoate was saponified by refluxing 1.8 g. with 0.8 g. of potassium hydroxide in 60 cc. of ethyl alcohol for three hours. The sapogenin was precipitated by the addition of water and crystallized twice from 95% ethyl alcohol and three times from 90% ethyl alcohol, when it melted at 269–274°. A recrystallized sample of gitogenin melted at 270–274.5° and a mixture of equal amounts of the two preparations melted at 271–275°. Here again all three tubes were in the same melting point bath. The specific rotation for the sample from *Chlorogalum* was $[\alpha]^{25}D$ −61.3° in pyridine, while that for gitogenin was $[\alpha]^{25}D$ −60.9°.

The sapogenin was converted to the diacetate by heating 0.2 g. with 1 cc. of acetic anhydride and 1 cc. of pyridine on the steam-bath for two hours and allowing to stand overnight. After precipitation with water the product was crystallized from methyl alcohol when it melted at 239–244°. This sample was not used for determination of the specific rotation or a mixed melting point with gitogenin diacetate, the sample obtained below from the acetylation of the mixed sapogenins being used for this purpose.

The filtrate from the above ether extraction of the crude benzoate gave on evaporation an oil which partially solidified on cooling. On rubbing up with 25 cc. of 80% ethyl alcohol, the mass solidified sufficiently to be pulverized and filtered. The product, which weighed 8 g. and melted at 130–165°, probably contained considerable benzoic acid. Two crystallizations from isopropyl alcohol and one from ethyl acetate raised the melting point to 180–197° and two more crystallizations from acetone brought it to 196–203.5°.

Anal. Calcd. for $C_{41}H_{52}O_6$: C, 76.84; H, 8.18. Found: C, 76.72; H. 8.27.

When mixed with an equal amount of chlorogenin dibenzoate, m. p. 203.5–207.5°, the melting point was 195.5–205.5°, a slight but noticeable depression.

Saponification gave the sapogenin which after two crystallizations from methyl alcohol melted at 268–274°. A mixture with an equal part of chlorogenin, m. p. 268–275°, melted at 269–276°, a slight but definite elevation. The specific rotation of the sapogenin was $[\alpha]^{25}D$ −47.7° in dioxane while that for pure chlorogenin was $[\alpha]^{25}D$ −46.3°.

Conversion to the acetate by acetic anhydride and pyridine and crystallization from methyl alcohol gave a product, m. p. 154–156°. A mixture with an equal part of chlorogenin diacetate, m. p. 153.5–156.5°, melted at 152.5–155°.

The extreme solubility of chlorogenin diacetate and the slight solubility of gitogenin diacetate in hot methyl alcohol suggested that the mixture could be separated more conveniently through the acetates. A mixture of 10 g. of the mixed sapogenins, m. p. 230–245°, with 50 cc. of acetic anhydride and 80 cc. of pyridine was heated on a hot-plate until completely homogeneous and then allowed to stand overnight. Decomposition with an excess of water and filtering gave 11.5 g. of air-dried product. This was rubbed up with 50 cc. of ether and filtered. The air-dried insoluble portion weighed 5 g. and melted at 225–235°. It was recrystallized five times from methanol when it melted at 239–243°. No change in melting point took place during the last two crystallizations. A mixture with a sample of gitogenin, m. p. 239–243°, melted at the same temperature as far as measurement with the thermometer indicated, although the mixture appeared to shrink just before the individual samples and was definitely clear before them. The specific rotation of the acetate separated from the mixture was $[\alpha]^{25}D$ −80.2° in pyridine compared with −80.7° for an authentic sample of gitogenin diacetate.

The ether extract contained the chlorogenin diacetate contaminated by a small amount of gitogenin diacetate which was difficult to remove by crystallization because of its insolubility. This is true also when separating through the benzoates and the best procedure is to saponify the partially purified esters and continue the purification by crystallization of the chlorogenin.

Determination of Melting Point Diagrams for Mixtures.—The fact that some decomposition takes place at the melting point and that only limited amounts of material were available made it necessary to mix the components mechanically and to take the melting points in capillary tubes. Only slightly more material was weighed out than was necessary to fill the capillary tube in order to ensure adequate mixing. The data used in Fig. 1 were obtained on samples carefully mixed mechanically with a small spatula. It was later found more convenient to dissolve the sample in a few drops of dioxane, allow the solvent to evaporate and to grind the residue with a spatula, this method being used for the data of Fig. 2 and Fig. 3. Melting points in this and the previously recorded work were taken in a Hershberg melting point apparatus[11] with completely immersed calibrated Anschütz thermometers having 0.2° scale divisions. The points of the lower curves are the temperatures at which the sample first wet the sides of the capillary tubes while those of the upper curves represent the temperatures at which the melts were completely clear. The rate of rise of temperature was less than 1° per minute in the neighborhood of the melting point. In spite of the precautions taken it is obvious that this procedure could not be expected to give more than roughly quantitative results.

Summary

1. An improved procedure is given for the isolation of steroid sapogenins from *Chlorogalum pomeridianum*.

2. Besides the previously reported tigogenin and chlorogenin a third sapogenin has been isolated which has been shown beyond reasonable doubt to be identical with gitogenin from *Digitalis* in spite of an unexplainable behavior of mixed melting point determinations.

3. Melting point diagrams for mixtures of tigogenin and chlorogenin and for tigogenin and gitogenin indicate that these pairs form a continuous series of solid solutions, while mixtures of gitogenin and chlorogenin form a eutectic at approximately 42% gitogenin.

CAMBRIDGE, MASS. RECEIVED APRIL 21, 1939

[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY OF THE UNIVERSITY OF CHICAGO]

The Peroxide Effect in the Addition of Reagents to Unsaturated Compounds. XX. The Addition of Hydrogen Bromide to 2-Butyne and 2-Bromo-2-butene

BY CHEVES WALLING,[1] M. S. KHARASCH AND F. R. MAYO

Since the report in 1933 of the reversal by certain catalysts, notably oxygen and organic peroxides, of the direction of addition of hydrogen bromide to olefins,[2] investigation in this Laboratory and elsewhere has disclosed some thirty olefins which undergo such a reversal of the direction of addition.[3] In all of these, addition occurs to a terminal double bond, while with a number of other olefins with non-terminal double bonds, no such reversal has been observed. Accordingly, it has become of increasing interest to know whether the presence of a terminal double bond is essential for this phenomenon.

The addition of the second of two molecules of hydrogen bromide to 2-butyne[4] appeared as a likely subject for investigation for two reasons. In the first place, the unsymmetrical distribution of substituents about the double bond in 2-bromo-2-butene would be expected to yield only one product of normal addition. Secondly, it has been observed in this Laboratory that halogen atoms attached to a molecule favor abnormal addition by retarding the normal reaction.

Addition of hydrogen bromide was carried out under the conditions specified in Table I, 5.4 g. of butyne being used in every instance. In the experiments marked "vacuum" the usual technique developed in this Laboratory was employed,[2] with evacuation to a pressure of 10^{-4} to 10^{-5} mm. After addition, the reaction mixture was first distilled at 5–10 mm. directly from the tubes in which the reaction took place into a trap at −80°, and the yield was determined at this point. In the case of additions in pentane the solvent was evaporated before distillation, while in experiments carried out in acetic acid the products were washed with water. All products were then distilled at 30 mm. in a Podbielniak column, and the index of the main fraction was taken. The first few drops of distillate and material which did not distill were rejected, but loss by this method rarely exceeded 2 g.

(1) Du Pont Fellow, 1938–1939.

(2) Kharasch and Mayo, THIS JOURNAL, **55**, 2468 (1933).

(3) See Kharasch, Engelmann and Mayo, *J. Org. Chem.*, **2**, 288 (1937), for references to the subject.

(4) As the product of the addition of one molecule of hydrogen bromide to 2-butyne is necessarily 2-bromo-2-butene under all conditions, no necessity of isolating this intermediate arises. There is no reason to expect that the *cis* and *trans* isomers would give rise to different products (see ref. 7).

Experimental Part

2-Butyne was prepared from sodium acetylide, sodamide, and dimethyl sulfate in liquid ammonia by the method of Bried and Hennion[5] except that the reaction was carried out in a flask cooled in a bath of solid carbon dioxide and acetone. In this way the temperature of the reaction mixture was held at −70 to −60° during the addition of the dimethyl sulfate. The products were distilled through water to remove ammonia, and collected in a vessel cooled in ice water. Loss of product from the receiver was prevented by a trap maintained at −80°. With the use of a 2-liter flask containing about 1 liter of ammonia, 2 moles of sodium acetylide and other reagents in proportion could be handled with ease. The product was fractionated through a Podbielniak column. The yield from four moles of sodium acetylide was 88 g. (41%) of 2-butyne; b. p. 27.0–4° (754 mm.); m. p. −28° to −27°; $n^{20}D$ 1.3920.

Identification of Products.—Analysis was by index of refraction, checked by the boiling range of the products. The wide difference in index and boiling point of the two products makes the analyses certain to at least 5%. The most probable index of 2,2-dibromobutane was determined as $n^{20}D$ 1.5015 by measurements, after another fractionation, on the combined products of the experiments showing normal addition. The material was definitely identified by conversion to the 2,4-dinitrophenylhydrazone of methyl ethyl ketone (m. p. 111–112°; melting point of mixture with known sample 111–112°). The racemic 2,3-dibromobutane was identified by boiling point and index of refraction.

As the meso and racemic forms of 2,3-dibromobutane have different indices of refraction ($n^{20}D$ 1.5116 and 1.5147, respectively),[6] the question naturally arises as to whether variations in the index of the abnormal products are due to variations in the ratios of the isomeric 2,3-dibromobutanes or to the presence of small quantities of 2,2-dibromobutane. To answer this question, the products of all experiments giving the abnormal product were combined and carefully fractionated through a Podbielniak column.[7] While the first portion had an index of 1.5108, indicating it to be largely 2,2-dibromobutane, the remaining 80% had an index of 1.5145–7. Thus, the abnormal product appears to be entirely the racemic isomer, and the percentages of normal and abnormal product are calculated on this basis.

Discussion of Results

The results of our experiments are summarized in Table I. It will be noted that under most con-

(5) Bried and Hennion, THIS JOURNAL, **59**, 1310 (1937).

(6) Dillon, Young and Lucas, *ibid.*, **52**, 1953 (1930).

(7) Podbielniak, *Ind. Eng. Chem., Anal. Ed.*, **5**, 119 (1933).

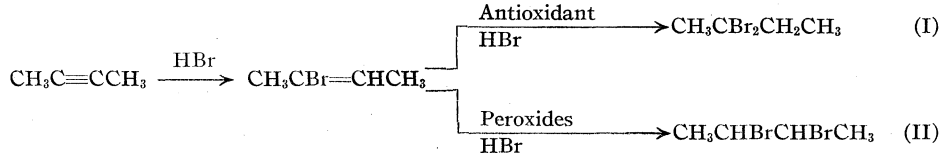
TABLE I

ADDITION OF HYDROGEN BROMIDE TO 2-BUTYNE

Expt.	Conditions of addition: Mol. HBr[a]	Temp., °C.	Time, hr.	Substance Added	Mol.[a]	Vacuum technique	Product[e]: Yield, %	B. p. (30 mm.) °C.	$n^{20}D$	% 2,2-dibromide
III	2.4	20	2	Catechol	0.04	(+)	60[d]	52	1.5022	95
V	2.0	20	12	Diphenylamine	.02	(+)	60[b,d]	30–53	1.4947	(100)
VI	2.2	20	2	Diphenylamine	.02	(+)	65[d]	51–52	1.5012	100
IV	3.0	−80	12	$FeBr_3$	.01	(−)	50[d]	51	1.5018	98
XI	2.4	20	22	.....	...	(−)	75	51–53	1.5013	100
X	2.4	20	22	Acetic acid	2.0	(+)	85	51–53	1.5012	100
II	2.5	20	12	Acetic acid[c]	2.00	(−)	98	62	1.5139	6
VII	2.5	20	2	Acetic acid[c]	2.0	(−)	95	62–63	1.5132	11
VIII	2.6	20	5	Ascaridole	0.04	(−)	90	51–60	1.5022	95
I	2.6	20	24	Ascaridole	.03	(−)	100	52–64	1.5070	58
IX	2.4	20	4	Ascaridole	.04	(−)	85	62–65	1.5134	10
				Pentane	6.0					
XII	2.5	20	12	Ascaridole	.04	(−)	90	62–64.5	1.5142	4
				Pentane	6.0					

[a] In moles per mole of 2-butyne. [b] Considerable 2-bromo-2-butene in product. [c] Sample of 2-butyne employed gave very strong test for peroxide. [d] Not including 10–20% of dark, non-volatile material obtained. [e] Indices used in analysis: 2,2-dibromobutane, $n^{20}D$ 1.5015; racemic 2,3-dibromobutane $n^{20}D$ 1.5147.

ditions described in Table I the product is exclusively normal, namely, 2,2-dibromobutane,[8] and that even the addition of 3 mole per cent. of ascaridole fails to reverse the addition completely. However, when the normal addition is retarded by dilution with pentane, the product is almost exclusively abnormal. In acetic acid solution, addition is normal (expt. X) except when the 2-butyne has a high peroxide content (expts. II and VII).



The discovery of a case of abnormal addition to a non-terminal double bond considerably increases the number of compounds which may be expected to undergo this reaction. In fact, it now seems likely that, with certain exceptions, abnormal addition to any ethylenic bond may be observed. The exceptions appear to be as follows. (1) Compounds in which symmetrical substitution by groups of the same order of electronegativity results in a double bond of low polarity. Compounds such as 2-pentene[9] and 9-undecenoic acid[10] give an equimolecular mixture of two addition products in the presence or absence of peroxides, and it cannot be determined whether or not reversal takes place. A border-line case is that of 2-bromopropene, which gives a 2:1 mixture on normal addition and a single product in the presence of oxygen or peroxides.[3] (2) Compounds in which double bonds are conjugated with carboxyl and similar groups. (3) Compounds for which abnormal addition is masked by a very rapid normal reaction. All known cases of failure to obtain a reversal of the direction of addition of hydrogen bromide in the presence of peroxides seem to fall into one of these three classes.

The effect of a rapid normal addition in the abnormal reaction is clearly demonstrated in the case of 2-butyne. Here, the normal reaction is comparatively rapid (almost complete in two hours at 0°), with the result that only upon dilution does the abnormal reaction become important. The abnormal reaction, being presumably a chain reaction,[3] is not retarded greatly by dilution with an inert solvent.

The principle of preferential retardation of the normal reaction by dilution appears to be a valuable tool, and it is now being employed in this Laboratory in attempts to detect abnormal addition in the addition of hydrogen bromide to several olefins which show a rapid normal reaction.

Summary

1. 2-Butyne adds hydrogen bromide in the

(8) This is the product reported by Wislicenus and Hölz, *Ann.*, **250**, 232 (1889).

(9) Kharasch, Walling and Mayo, THIS JOURNAL, **61**, 1559 (1939).

(10) Abraham, Mowat and Smith, *J. Chem. Soc.*, 948 (1937).

absence of oxygen and peroxides to give 2,2-dibromobutane.

2. Under the influence of peroxide catalysis racemic 2,3-dibromobutane is obtained. This product is most easily obtained by retarding the normal reaction through dilution with an inert solvent.

CHICAGO, ILLINOIS RECEIVED APRIL 20, 1939

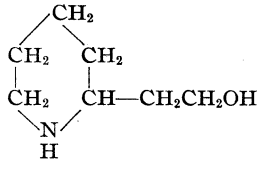
[CONTRIBUTION FROM THE RESEARCH LABORATORY OF THE MALTBIE CHEMICAL CO.]

Local Anesthetics from β-(2-Piperidyl)-ethanol

BY L. A. WALTER AND RUSSEL J. FOSBINDER

The recent publication of Tullock and MacElvain[1] on anesthetics derived from α-picoline prompts submission of the following paper.

A series of substituted benzoic esters of β-



(2-piperidyl)-ethanol was prepared by refluxing one equivalent of the hydrochloride of the amino alcohol with one equivalent of acid chloride in dry chloroform. The amino ester hydrochlorides were purified by crystallization from absolute alcohol or from absolute alcohol–ether mixture. The N-phenylurethan and the cinnamate were prepared similarly from phenyl isocyanate and cinnamoyl chloride, respectively. The hydrochlorides of the nitro esters were reduced to the amino compounds with platinum and hydrogen in glacial acetic acid.

Pure β-(2-pyridyl)-ethanol is best prepared by heating α-picoline with twice its weight of 40% formaldehyde in a sealed tube at 120° for sixteen to twenty hours. The mixture is then fractionally distilled at a pressure sufficiently reduced so that the temperature of the mixture never rises above 130°. The yields are only 15 to 20% but the product is not contaminated with the β-(2-pyridyl)-allyl alcohol which is formed by dehydration of β-(2-pyridyl)-propylene glycol at higher temperatures. Some of the latter compound is formed from two moles of formaldehyde and one of picoline even at 120°.

The pyridyl alcohol was reduced to the piperidyl alcohol with sodium and absolute alcohol.[2]

The properties of the compounds are recorded in the following table. They are all nicely crystalline and non-hygroscopic without exception.

TABLE I

	β-(2-Piperidyl)-ethanol ester hydrochloride	Formula	M. p., °C., corr.	Analyses, %Cl Calcd.	Found
I	Benzoate	$C_{14}H_{20}O_2NCl$	189–191[a]	13.14	13.08
II	*p*-Nitrobenzoate	$C_{14}H_{19}O_4N_2Cl$	209–210	11.26	11.15
III	*m*-Nitrobenzoate	$C_{14}H_{19}O_4N_2Cl$	170–172	11.26	10.96
IV	*o*-Nitrobenzoate	$C_{14}H_{19}O_4N_2Cl$	148–150	11.26	11.46
V	*p*-Aminobenzoate	$C_{14}H_{21}O_2N_2Cl$	249–251	12.44	12.20
VI	*m*-Aminobenzoate	$C_{14}H_{21}O_2N_2Cl$	177–180	12.44	12.28
VII	*o*-Aminobenzoate	$C_{14}H_{21}O_2N_2Cl$	209–211	12.44	12.30
VIII	*p*-Ethoxy, *m*-nitrobenzoate	$C_{16}H_{23}O_5N_2Cl$	150–155	9.87	10.21
IX	*p*-Ethoxy, *m*-aminobenzoate	$C_{16}H_{25}O_3N_2Cl$	173–175	10.78	10.61
X	*p*-Ethoxybenzoate	$C_{16}H_{24}O_3NCl$	146–148	11.29	11.44
XI	Cinnamate	$C_{16}H_{22}O_2NCl$	180–182	11.98	11.95
XII	N-Phenylurethan	$C_{14}H_{21}O_2N_2Cl$	200–202	12.44	12.54

[a] Ladenburg, *Ann.*, **301**, 124 (1898), gives m. p. 182–183°.

TABLE II

Compound	Duration of anesthesia rabbit cornea, min., 2% solution	Subcutaneous toxicity to mice M. L. D. 50% mg./kg.
I	6	85
V	47	20
VI	27	87
VII	100	23
IX	10	..
X	15	..
XI	0	..
XII	9	40
Cocaine	56	10

(1) Tullock and MacElvain, THIS JOURNAL, **61**, 961 (1939).

(2) Marvel and Shelton, *ibid.*, **51**, 915 (1929).

Their action as topical anesthetics is shown in Table II.

However, such data alone does not necessarily give a true idea of relative anesthetic usefulness. The compounds have been subject to extensive pharmacologic investigation the results of which will be published elsewhere.

Several members of a similar series of esters have been prepared from β-(2-piperidyl)-propanol, γ-(2-piperidyl)-propanol, and (2-piperidyl)-isopropanol. The last two alcohols are prepared readily from the corresponding pyridine compounds, which, in turn, are easily prepared in 40% yields by treating lithium picolyl with ethylene oxide, and with acetaldehyde, respectively. This will be the subject of a future communication.

Summary

A series of substituted benzoic esters of β-(2-piperidyl)-ethanol hydrochloride has been prepared and their local anesthetic properties determined.

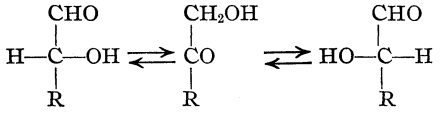
NEWARK, N. J. RECEIVED APRIL 17, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY AND FROM THE CHEMICAL LABORATORY OF MCGILL UNIVERSITY]

The Rearrangement of α-Hydroxy Carbonyl Compounds

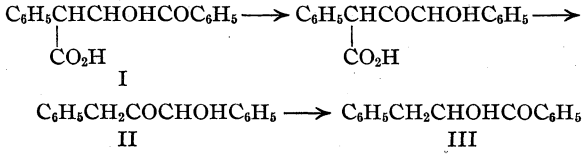
BY PHILIP G. STEVENS

The first case of the rearrangement of α-hydroxy carbonyl compounds was that studied by Lobry de Bruyn,[1] wherein glucose, fructose, and mannose were shown to be in equilibrium with one another in alkaline solutions. The essential change is a shift of the carbonyl and hydroxyl groups, presumably through a dienol intermediate

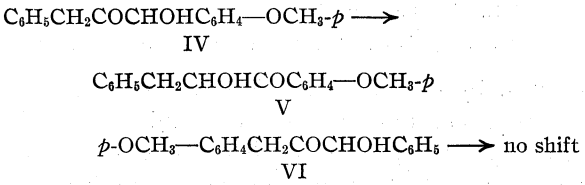


Wohl[2] found that in all probability the same equilibrium existed between certain trioses, namely, glyceric aldehyde and dihydroxyacetone, because in alkaline solutions both compounds yielded the same β-acrose. This view was supported later by Fischer's discovery[3] that glyceric aldehyde could be converted into dihydroxyacetone by mere boiling with pyridine. Still later a similar shift of the carbonyl and hydroxyl groups has been reported by Shoppee[4] with highly substituted cyclic α-hydroxy ketones.

More recently Kohler and Kimball[5] observed the same shift in alkaline media with derivatives of diphenylpropane. Thus α-phenyl-β-hydroxy-β-benzoylpropionic acid I with alkalies lost carbon dioxide spontaneously, forming α-hydroxy-dibenzyl ketone II; and this in turn could be converted to its isomer α-hydroxy-benzylacetophenone III. The conversion of II into III convinced them that the mechanism of the formation of II from I involved a similar shift



Later Kohler and Leers[6] found the same shift in the *p*-methoxy substituted series. The position of the substitute was, however, of importance, for while both mono-*p*-methoxy-substituted acids formed hydroxy ketones corresponding to II, only one of these would undergo further shift to that corresponding to III



Although neither III, V, nor VI was altered by further treatment with alkalies, Kohler and Kimball believed that an equilibrium existed between the two isomers, but offered no evidence as proof, for in no case was the shift —CH_2—CHOH—CO— → CH_2—CO—CHOH— observed.

This paper deals with the observation of such a reverse shift with the *p*-chloro analog of IV

(1) Lobry de Bruyn, *Ber.*, **28**, 3078 (1895).
(2) Wohl, *Ber.*, **33**, 3095 (1900).
(3) Fischer, *ibid.*, **60**, 479 (1927).
(4) Shoppee, *J. Chem. Soc.*, 1662 (1928).
(5) Kohler and Kimball, THIS JOURNAL, **56**, 729 (1934).
(6) Kohler and Leers, *ibid.*, **56**, 981 (1934).

$C_6H_5CH_2CHOHCOC_6H_4Cl\text{-}p$ ⟶
VII
$C_6H_5CH_2COCHOHC_6H_4Cl\text{-}p$
VIII

Henze[7] likewise observed a reverse shift in a similar system in the presence of sodium ethylate, but did not report the existence of an equilibrium between the two substances

$CH_3COCH_2CHOHCOC_6H_5$ ⟶ $CH_3COCH_2COCHOHC_6H_5$

If these intramolecular shifts are to be classed with that of Lobry de Bruyn, it is essential to establish the existence of an equilibrium in alkaline media between the two isomeric hydroxy ketones. This it has been possible to do in the case of VII and VIII, for each has been transformed into the other by means of weak alkali. The reaction should then be written VII ⇄ VIII.

It is quite likely then that all α-hydroxy carbonyl compounds are in equilibrium with their dismutation isomers, and that the failure to observe this equilibrium may be due merely to the position of the equilibrium being almost entirely on one side or the other—or due to the unfavorable physical or chemical properties of one of the isomers, making its isolation difficult.

The establishment of this equilibrium lends support to the new mechanism recently advanced by Hibbert[8] for the formation of lignin from guaiacol and pyruvic aldehyde. This system is closely related to that reported in this paper, and hence it is quite probable that an equilibrium actually exists

$CH_3COCHO + C_6H_4(OH)(OCH_3)$ ⟶
$CH_3COCHOHC_6H_3(OH\text{-}p)(OCH_3\text{-}m)$ ⇄
$CH_3CHOHCOC_6H_3(OH\text{-}p)(OCH_3\text{-}m)$ ⟶ lignin

The mechanism of the interconversion of these hydroxy carbonyl compounds very probably involves a dienol intermediate. This is consistent with the existence of an equilibrium, since alkaline media favor enolization. Acid media being proton donors likewise favor enolization, and should also cause an equilibrium to be established. Favorsky[9] has shown already that similar interconversions occur under the influence of acids, and hence it is probable that here, too, an equilibrium exists between the two isomeric substances.

In the work here, it unfortunately was impossible to determine the position of the equilibrium between VII and VIII, because of the unstable character of both isomers, as well as the unfavorable physical properties of one of them, VII.

The sensitive character of VIII for example was shown by its behavior with strong alkalies, whereby large amounts of oxidation and reduction products appeared. These would be expected if a dienol intermediate were formed, since dienols are peculiarly active hydrogen donors.[10] The following scheme, in part suggested earlier by Kohler and Kimball, indicates a possible course of the reaction with strong alkalies

$C_6H_5CH_2COCHOHC_6H_4Cl\text{-}p$ (VIII) ⇄ $(C_6H_5CH_2C(OH)=C(OH)C_6H_4Cl\text{-}p)$ ⇄ $C_6H_5CH_2CHOHCOC_6H_4Cl\text{-}p$ (VII)

Oxidation and reduction

$(C_6H_5CH_2COCOC_6H_4Cl\text{-}p) + (C_6H_5CH_2CH_2COC_6H_4Cl\text{-}p)$ not isolated

Cleavage: $p\text{-}ClC_6H_4CO_2H$

Benzilic acid rearrangement: $C_6H_5CH_2C(OH)(C_6H_4Cl\text{-}p)(CO_2H)$

This work was done under the direction of Professor Kohler, in partial fulfilment for the degree of Doctor of Philosophy, Harvard University, 1929. Some time before his death, Professor Kohler kindly gave the author permission to publish the work independently.

Experimental Part

α-Hydroxy-*p*-chlorobenzyl Benzyl Ketone, VIII.—This α-hydroxy ketone was prepared both from α-phenyl-

(7) Henze, *Z. physiol. Chem.*, **232**, 117 (1935).
(8) Hibbert, THIS JOURNAL, **61**, 725 (1939).
(9) Favorsky, *Bull. soc. chim.*, **39**, 215 (1925).
(10) Szent-Györgyi, *Ber.*, **72A**, 53 (1939); compare Fuson and Corse, THIS JOURNAL, **61**, 975 (1939).

β-hydroxy-*p*-chlorobenzoylpropionic acid, previously reported by Kohler and Shohan,[11] and by synthesis from *p*-chlorobenzaldehyde cyanhydrin and benzylmagnesium chloride. The ketone crystallized from 95% alcohol as needles, melting at 125.5–126°.

Anal. Calcd. for $C_{15}H_{13}O_2Cl$: C, 69.1; H, 5.0. Found: C, 69.0; H, 5.0.

Action of Alkalies on the α-Hydroxy Ketone, VIII.—In contrast to the α-hydroxy ketones II and IV, this ketone yielded with strong alkalies non-crystallizing oils, from which only secondary products could be isolated, namely, *p*-chlorobenzoic acid, and α-hydroxy-α-*p*-chlorophenyl-β-phenylpropionic acid. These acids result from cleavage and benzilic acid rearrangement respectively, of the intermediate α-diketone, formed presumably from the dienol intermediate by intermolecular oxidation and reduction. The latter acid crystallized from ether and ligroin, and melted at 201–202° with decomposition.

Anal. Calcd. for $C_{15}H_{13}O_3Cl$: C, 65.1; H, 4.7. Found: C, 64.9; H, 4.9.

It was further identified by synthesis from α-phenyl-α'-*p*-chlorobenzoylethylene oxide by means of alkalies according to the method of Bodforss[12] and Jörlander,[13,14] and also by oxidation with sodium dichromate in acetic acid to *p*-chlorodesoxybenzoin. This ketone crystallized from ligroin as plates melting at 104.5–105.2°.

Anal. Calcd. for $C_{14}H_{11}OCl$: C, 72.9; H, 4.8. Found: C, 73.2; H, 4.7.

This difference in reaction between these α-hydroxy ketones is probably due to the much greater solubility of the isomeric ketone VII. It was only by using weak alkalies that it was possible to isolate VII, and then only with difficulty and in very poor yields. Five grams of VIII was dissolved in 75 cc. of hot 95% alcohol; 50 cc. of water was added, and an excess of solid sodium carbonate. The solution turned orange at once. After thirty minutes of boiling, the solution was made faintly acid, and then evaporated to one-half its volume. On cooling 2.7 g. of VIII precipitated unchanged. The filtrate was evaporated further until it become cloudy, and was then allowed to stand overnight. The oil which had precipitated was now extracted with chloroform and ligroin mixture. More water was then added, precipitating more oil (about 0.2 g.). This finally crystallized on standing for four days at 0°, and melted at 39–42°. A mixed melting point with the isomeric ketone VII, m. p. 43–44°, was 41–44°.

Benzyl-*p*-chloroacetophenone.—This saturated ketone, prepared easily by reduction of benzal-*p*-chloroacetophenone with Adams platinum oxide catalyst in methyl alcohol solution, crystallized from ligroin as plates, melting at 75–76°.

Anal. Calcd. for $C_{15}H_{13}OCl$: C, 73.2; H, 5.3. Found: C, 72.5; H, 5.0.

Benzyl-α-bromo-*p*-chloroacetophenone.—The ketone brominated easily in chloroform solution, yielding a crystalline α-bromo ketone, melting at 92–93°.

Anal. Calcd. for $C_{15}H_{12}OClBr$: C, 55.6; H, 3.7. Found: C, 55.6; H, 3.9.

Benzyl-α-hydroxy-*p*-chloroacetophenone, VII.—Seventeen grams of the bromo ketone was dissolved in 500 cc. of hot 95% alcohol, and water was added until the boiling solution just remained clear. Then 4.2 g. of sodium bicarbonate was added, and the mixture boiled for 40 minutes. The solution became yellowish. On cooling, 3.3 g. of the bromide precipitated unchanged, and was filtered out. The filtrate was poured into water, extracted with ether, and dried. Addition of ligroin deposited an oil which slowly crystallized at −10–15°. Thus 3.7 g. of the hydroxy ketone was obtained, which after several recrystallizations from chloroform and ligroin melted at 43–44°. The ketone was very soluble in all solvents save ligroin and water, and is far more soluble than its isomer VIII.

Anal. Calcd. for $C_{15}H_{13}O_2Cl$: C, 69.1; H, 5.0. Found: C, 69.0; H, 5.3.

Action of Alkalies on the α-Hydroxy Ketone, VII.—One-fifth gram of VII was dissolved in 10 cc. of 95% alcohol. An excess of sodium carbonate was now added, and the mixture boiled for one hour. The solution was then neutralized, and the volume reduced to 5 cc. On cooling, the isomeric α-hydroxy ketone VIII crystallized out pure, melting at 125–126°, and identified by comparison with an authentic sample.

Summary

1. Two isomeric α-hydroxy ketones, derived from *sym*-diphenylpropane, have been shown to be in equilibrium in alkaline solution.

2. The presence of this equilibrium lends support to Hibbert's theory of lignin formation.

CAMBRIDGE, MASSACHUSETTS
MONTREAL, CANADA RECEIVED APRIL 3, 1939

(11) Kohler and Shohan, THIS JOURNAL, **48**, 2425 (1926).
(12) Bodforss, *Ber.*, **49**, 2795 (1916).
(13) Jörlander, *ibid.*, **50**, 406 (1917).
(14) Ref. 5, p. 731.

[CONTRIBUTION FROM THE RESEARCH LABORATORIES DIVISION OF THE GENERAL MOTORS CORP.]

The Isomerization of Cyclohexane and Methylcyclopentane[1]

BY A. L. GLASEBROOK AND W. G. LOVELL

Recently Montgomery, McAteer, and Franke[2] reported a reversible isomerization of the butanes occurring in the presence of aluminum bromide. Since the isomerization was unaccompanied by side reactions, it offered a method for experimentally determining the equilibrium constant.

In view of Montgomery's success, we decided to study the reversible isomerization of cyclohexane and methylcyclopentane reported by Nenitzescu and Cantuniari.[3] These investigators found cyclohexane or methylcyclopentane to rearrange in the presence of moisture-containing aluminum chloride to give an equilibrium mixture containing approximately 22% methyl cyclopentane. In addition, a small amount of saturated hydrocarbon, suspected to be *n*-hexane, was produced. Other investigators have not found the reaction products of aluminum chloride and cyclohexane to be as simple as reported by Nenitzescu. In addition to methylcyclopentane, Zelinsky[4] also reports dimethylcyclobutane as one of the reaction products. Ipatieff and Komarewsky[5] also found methylcyclopentane among the reaction products of cyclohexane and aluminum chloride, but 34% of the reaction products boiled higher than cyclohexane and consisted of 34% dimethylcyclohexane and 66% of a mixture containing dicyclohexyl and dimethyldicyclopentyl. These experiments, however, were carried out in closed autoclaves at 150°, and represent quite severe conditions.

In general, our results at lower temperatures confirm the findings of Nenitzescu. The anhydrous aluminum chloride was inert toward the hydrocarbons and the addition of water or hydrogen chloride was required to effect reaction. The reactions were remarkably clean, and the gas and tar which usually characterize the action of aluminum chloride on hydrocarbons were completely absent, even in experiments lasting as long as seven weeks. Also, the aluminum chloride remained clean and powdery and only a slight discoloration occurred. However, when aluminum bromide was substituted for aluminum chloride, a tarry lower layer was formed and isobutane was evolved.

Distillation of relatively large amounts of the reaction products in an 80-plate column showed them to consist almost exclusively of a mixture of cyclohexane and methylcyclopentane; refractive index measurements of the initial distillate and distillation residue indicated only traces of other products to be present. Fractionation of 15 liters of cyclohexane–aluminum chloride reaction product indicated that not more than about 5% of the cyclohexane reacting is consumed in side reactions which accompany the isomerization. Branched chain hexanes, methylcyclohexane, 1,3-dimethylcyclohexane, dicyclohexyl, and dimethyldicyclopentyl are the probable products of the side reactions.

Since isomerization appeared to be practically the sole reaction, experimental determination of the equilibrium constant and the effect of temperature on it were next studied. Experiments were carried over the temperature range 25 to 77.4° (boiling temperature) at 10° intervals, in which the equilibrium was approached from both sides. The course of the reaction was followed by the change in the refractive index. The data obtained are shown in Table I and Fig. 1.

TABLE I

EQUILIBRIUM CONCENTRATIONS OF METHYLCYCLOPENTANE

Reaction temp., °C.	Approach to equilibrium from cyclohexane side $n^{20}D$	Approach to equilibrium from cyclohexane side Mole % methylcyclopentane	Approach to equilibrium from methylpentane side $n^{20}D$	Approach to equilibrium from methylpentane side Mole % methylcyclopentane	Average mole % methylcyclopentane
25	1.4242	11.70	1.4239	13.30	12.5
35	1.4238	13.95	1.4236	15.00	14.5
45	1.4234	16.15	1.4234	16.15	16.2
55	1.4229	18.95	1.4228	19.50	19.2
65	1.4225	21.10	1.4224	21.70	21.4
77.4	1.4217	25.60	1.4217	25.60	25.6

Assuming the cyclohexane–methylcyclopentane solutions to be ideal, the data of Table I were used to calculate the equilibrium constant and ΔF°, by means of the equation $\Delta F^\circ = -RT \ln K$ for the

(1) Presented before the Symposium on the Role of Catalysis in Petroleum Chemistry held by the Petroleum Division at the Baltimore meeting of the American Chemical Society, April 3–7, 1939.

(2) Montgomery, McAteer and Franke, THIS JOURNAL, **59**, 1768 (1937).

(3) Nenitzescu and Cantuniari, *Ber.*, **66**, 1097 (1933); see, also, Aschan, *Ann.*, **324**, 1 (1902); Grignard and Stratford, *Compt. rend.*, **178**, 2149 (1924).

(4) Zelinsky and Turowa-Pollak, *Ber.*, **65**, 1171 (1932).

(5) Ipatieff and Komarewsky, THIS JOURNAL, **56**, 1926 (1934).

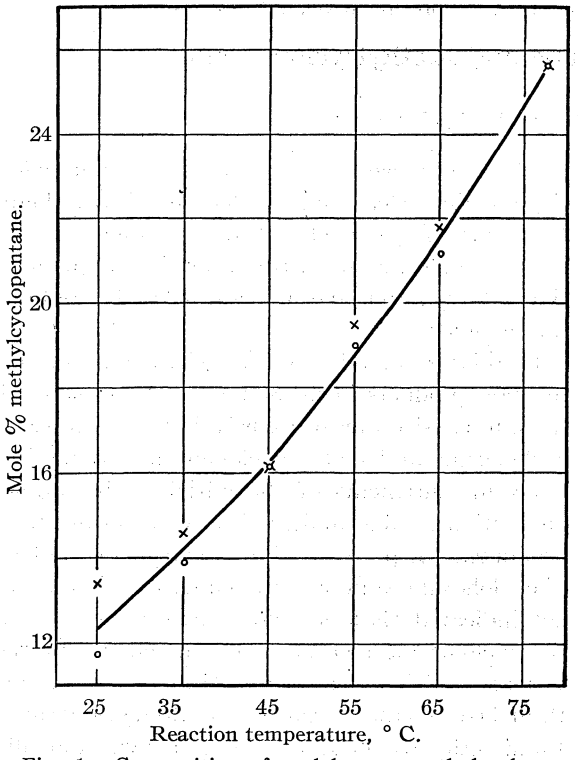


Fig. 1.—Composition of cyclohexane–methylcyclopentane equilibrium mixtures. X, Equilibrium approached from methylcyclopentane side; O, Equilibrium approached from cyclohexane side.

liquid phase reaction: cyclohexane → methylcyclopentane. These results are shown in Table II.

TABLE II

EQUILIBRIUM BETWEEN CYCLOHEXANE AND METHYLCYCLOPENTANE

Reaction temp., °C.	K	$\Delta F°$
25	0.143	1150
35	.170	1085
45	.193	1040
55	.238	936
65	.272	875
77.4	.344	743

The values of $\Delta F°$ and K were used to calculate the heat of reaction and the entropy change. The heat of reaction was calculated by the use of the van't Hoff equation, $d(-R \ln K)/d(1/T) = \Delta H$, and the entropy change calculated from the equation $\Delta F = \Delta H - T\Delta S$. The thermodynamic constants obtained from the equilibrium measurements are summarized in Table III and compared with the results of Parks.[6]

(6) Parks and Huffman, "The Free Energies of Some Organic Compounds," A. C. S. Monograph Series No. 60, The Chemical Catalog Co., New York, 1932; Huffman, Parks and Barmore, THIS JOURNAL, **53**, 3876 (1931); Parks, Huffman, and Thomas, *ibid.*, **52**, 1032 (1930); Parks, paper presented at the Washington meeting of the Am. Chem. Soc., 1933.

TABLE III

THERMODYNAMIC CONSTANTS FOR THE REACTION: CYCLOHEXANE (liq., 25°) ⟶ METHYLCYCLOPENTANE (liq., 25°)

	Calcd. from equilibrium measurements	Calcd. from third law by Parks
ΔH, cal.	3510	−1100
ΔS, e. u.	7.9	10
$\Delta F°$, cal.	1150	−4100

With the exception of ΔS, the constants obtained by the different methods are in rather poor agreement. Parks' value for ΔH is based on earlier work[7] on the heats of combustion of the two hydrocarbons. The combustion data, particularly that of methylcyclopentane, are rather uncertain and considering the magnitudes of the heats of combustion, it is probable that their small difference, or ΔH, contains considerable error. With Parks' method of calculation any error in ΔH is, of course, carried over to $\Delta F°$.

Experimental

Materials and Analytical Methods.—The cyclohexane used in the experiments for the identification of the reaction products was a C. P. grade manufactured by the Eastman Kodak Company. Distillation of this material indicated a negligible quantity of higher-boiling impurity. The cyclohexane used for the study of the equilibrium constants was a constant boiling fraction distilled from the Eastman Kodak Company material and had a refractive index of 1.4262 at 20°. The methylcyclopentane was prepared by the action of aluminum chloride on cyclohexane. Only the constant boiling fraction having a refractive index of 1.4100 at 20° was used. Baker C. P. anhydrous aluminum chloride was used throughout without further purification. The aluminum bromide was prepared by the action of bromine on aluminum.

Unless otherwise stated, the fractionating column used throughout this work was a spiral-packed, vacuum-jacketed, automatic recording and controlled column having 80 theoretical plates and a low holdup (40 cc.).

A series of methylcyclopentane–cyclohexane mixtures were prepared and the refractive indices determined with an Abbe–Zeiss refractometer, with temperature control within 0.2° by an independent cooling and circulating system. A plot of the data given in Table IV was used to obtain refractive index analyses.

TABLE IV

REFRACTIVE INDICES OF METHYL CYCLOPENTANE–CYCLOHEXANE MIXTURES

Mole % methylcyclopentane	7.19	13.26	19.89	24.91	29.95	35.01
$n^{20}D$	1.4250	1.4238	1.4227	1.4219	1.4210	1.4200

The Action of Aluminum Chloride on Methylcyclopentane.—For a quantitative experiment, 750 cc. of methylcyclopentane, 150 g. of anhydrous aluminum chloride, and 5 cc. of water were placed in a 2-liter flask equipped with a reflux condenser connected to a gas receiver. The

(7) Kharasch, *Bur. Stds. J. Research*, **2**, 374 (1929).

reaction mixture was boiled for three hours, the reaction flask was then cooled, the liquid decanted, and washed with water. Tar and gas were not formed in this experiment. After drying, 650 cc. of product remained, indicating a loss of 100 cc. Absorption of the liquid by the aluminum chloride and the drying agent probably accounts for the principal part of the loss, washing and handling account for the remainder. The dried product had a refractive index of 1.4220 at 20°, which, according to the data of Table IV, indicates the presence of 24.0 mole % methylcyclopentane.

For the distillation analysis, 600 cc. of the product was used. The distillation curve obtained is shown in Fig. 2. Altogether 536.8 cc. was distilled, leaving a residue of 58 cc. with a refractive index of 1.4282 at 20°, indicating that part of the residue consisted of material boiling higher than cyclohexane. The first 11 cc. of distillate also had a refractive index 0.0022 lower than pure methylcyclopentane. However, the products of the side reactions are relatively small in quantity and the mixture can be considered as consisting solely of methylcyclopentane and cyclohexane. The distillation curve shows 151.5 cc. methylcyclopentane and 448.5 cc. cyclohexane. Converting to mole % gives 24.6 mole % methylcyclopentane, a figure which compares favorably with the 24.0 mole % found by refractive index measurements.

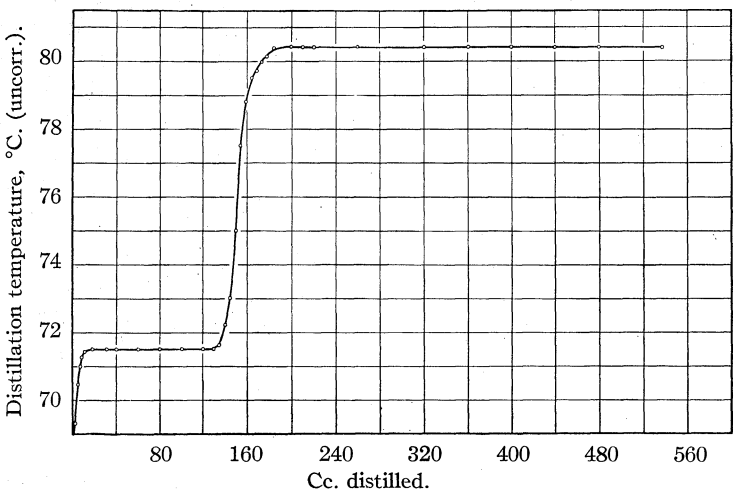


Fig. 2.—Distillation of 600 cc. methylcyclopentane–aluminum chloride reaction mixture. Distillation residue, 58 cc.

The Action of Aluminum Chloride on Cyclohexane.—Preliminary experiments indicated similarity between the cyclohexane–aluminum chloride and methylcyclopentane–aluminum chloride reactions. The addition of water to the anhydrous aluminum chloride was found to be necessary to promote reaction and the reaction products were free of tar and gas.

A quantitative experiment was made to discover the reaction products and to test the feasibility of using refractive index measurements as a method of analysis: 1500 cc. of cyclohexane, 300 g. of aluminum chloride, and 6.5 cc. of water were boiled for three hours in the same apparatus as used in the methylcyclopentane experiment. The reaction product was then cooled, the clear liquid decanted, washed, and dried; 1270 cc. of dried material was recovered having a refractive index of 1.4225 at 20°. The data of Table IV show this to be equivalent to 21.0 mole % methylcyclopentane. Distillation of 1200 cc. of this material gave a curve similar to that shown in Fig. 2, and showed the mixture to contain 250 cc. of methylcyclopentane and 950 cc. of cyclohexane. These volumes correspond to 20.2 mole % methylcyclopentane which compares favorably with the 21.0 mole % found by refractive index measurements. In this distillation, the first 30 cc. of distillate had a refractive index of 1.4087 at 20° and the 508 cc. of residue had a refractive index of 1.4266 at 20°, indicating that side reactions had occurred to a slight extent.

The products and extent of the side reactions were determined in a similar type of experiment in which a total of approximately 15 l. of cyclohexane was treated with aluminum chloride. Distillation in an 80-plate column gave 2.5 l. of pure methylcyclopentane, 50 cc. of material boiling below methylcyclopentane, and 97 cc. of material boiling above cyclohexane. Redistillation of the lower boiling material in a 28-plate column and refractive index measurements suggested the presence of only paraffinic constituents. The bulk of the material distilled in one plateau at 61°. The $n^{20}D$ of this material was 1.3756, and it was probably a mixture of isomeric hexanes; however, the small amount did not allow complete separation. No trace of *n*-hexane could be detected. Redistillation of the higher boiling material revealed three plateaus: 20 cc. boiled at 99.5°, 25 cc. at 119.5°, and 30 cc. from 208 to 220°. The 99.5° material is probably methylcyclohexane, although the refractive index of 1.4212 at 20° is somewhat low. The 119.5° material had a refractive index of 1.4237 and is probably 1,3-dimethylcyclohexane, since a product with these constants has been identified as such by Ipatieff.[5] The material boiling from 208 to 220° and having a refractive index of 1.4680 to 1.4703 undoubtedly consists of dimethyldicyclopentyl and dicyclohexyl, as reported by Ipatieff[5] and Nenitzescu.[8] On the basis of this experiment, not more than about 5% of the cyclohexane reacting is consumed in side reactions which accompany the isomerization.

The Action of Aluminum Bromide on Cyclohexane.—Previous work[9] with paraffins suggested that aluminum bromide could be substituted advantageously for the chloride. However, when the bromide was used with cyclohexane, tar formation and gas evolution resulted. Also, appreciable quantities of paraffins boiling lower than methylcyclopentane were formed. Isobutane, isopentane, and the isomeric hexanes were among the reaction products.

The Cyclohexane–Methylcyclopentane Equilibrium.—The apparatus used in these experiments consisted of a 200-cc. reaction flask fitted with a reflux condenser. The top of the condenser connected to a drying tube, the other end of which was open to the atmosphere. The reaction

(8) Nenitzescu and Ionescu, *Ann.*, **491**, 189 (1931).

(9) Glasebrook, Phillips and Lovell, THIS JOURNAL, **58**, 1944 (1936).

flasks were immersed in a constant temperature bath which maintained the temperature within 0.5°.

Although experiments had shown the equilibrium to be independent of catalyst concentration, nevertheless, uniform quantities, consisting of 100 cc. of hydrocarbon, 30 g. of aluminum chloride, and 1 cc. of water, were used in each experiment. At each temperature studied, simultaneous experiments were made to approach the equilibrium from both sides.

In the preliminary experiments it was also noted that the reaction undergoes an induction period. If the aluminum chloride, water, and hydrocarbon are mixed and allowed to stand at room temperature, refractive index measurements indicate very little reaction, even after several days of standing. If, however, the reaction mixture was heated to boiling, reaction started within fifteen minutes. In view of this fact, the reaction flasks were always boiled for a few minutes after the reactants were mixed to initiate the reaction. Samples were withdrawn at the end of the boiling period, and refractive index measurements made to make certain that the reaction mixtures were still far removed from the probable equilibrium. The reaction flasks then were placed in the constant temperature bath. Periodically, samples of the reaction mixture were withdrawn by inserting a glass tube down through the reflux condenser. The samples immediately were washed, dried, and analyzed by means of refractive index measurements. The reactions were continued until the refractive indices reached and maintained a constant value. Constant values were reached in about two hours at the boiling point, but three or four weeks were required at the lower temperatures.

The data obtained are presented in Table I.

Summary

1. The reaction of cyclohexane or methylcyclopentane in the presence of anhydrous aluminum chloride promoted by water results in an equilibrium mixture consisting principally of the two hydrocarbons. In the case of cyclohexane, the side reactions amount to approximately 5% based on the quantity of cyclohexane isomerized.

2. The equilibrium constants for the isomerization reaction have been determined at 10° intervals from 25° to the boiling temperature (77.4°).

3. From these data, values of the free energy change, heat of reaction, and entropy change for the isomerization reaction have been computed and compared with values calculated from heat capacity data.

DETROIT, MICHIGAN RECEIVED MARCH 8, 1939

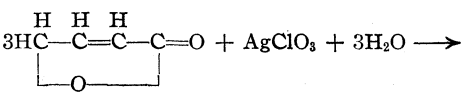
[CONTRIBUTION FROM THE KENT AND GEORGE HERBERT JONES LABORATORIES, UNIVERSITY OF CHICAGO]

The Reduction of *dl*-Erythronic Lactone to *dl*-Erythrose[1]

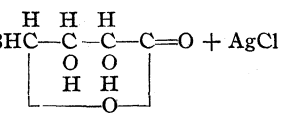
BY J. W. E. GLATTFELD AND B. D. KRIBBEN

For some years past, work on the preparation and study of the eleven C_4-saccharinic acids has been carried on in these Laboratories.[2] The work, which is now completed, was done in order to provide data on the constants and properties of these acids that might be useful in detecting them in, and separating them from, reaction mixtures produced by the action of alkalies on the tetroses.

The next step in the program is the synthesis of the *dl*-tetroses themselves. A source of one of these tetroses, *dl*-erythrose, has been found in *dl*-erythronic lactone which is prepared by the oxidation of the lactone of γ-hydroxy-isocrotonic acid, obtained as a by-product in the synthesis of one of the C_4-saccharinic acids.[3] The oxidation is achieved with osmium tetroxide-activated silver chlorate[4] according to the equation



Lactone of γ-hydroxy-isocrotonic acid



dl-Erythronic lactone

Some success has been attained in the conversion of the *dl*-erythronic lactone so obtained into *dl*-erythrose. This paper gives an account of the work.

The optically active forms of the aldotetroses seem to be fairly well known, the constants of the threoses[5] resting, perhaps, on a somewhat firmer

(1) This article is condensed from a dissertation presented by B. D. Kribben in partial fulfilment of the requirements for the degree of Doctor of Philosophy in the University of Chicago.

(2) Glattfeld and co-workers, THIS JOURNAL, **42**, 2314 (1920); **43**, 2675 (1921); **47**, 1742 (1925); **49**, 2309 (1927); **53**, 3164 (1931); **55**, 1114 (1933); **55**, 3663 (1933); **60**, 415 (1938).

(3) Glattfeld, Leavell, Spieth and Hutton, *ibid.*, **53**, 3164 (1931).

(4) (a) Hilmeyer Cohen, Ph.D. dissertation, University of Chicago, 1928; (b) Géza Braun, THIS JOURNAL, **51**, 235 (1929).

(5) Hockett, Deulofeu, Sedoff and Mendive, *ibid.*, **60**, 278 (1938).

basis than those of the erythroses.[6] As far as the authors are aware there is found in the literature only one report of the isolation of these sugars in the racemic form.[6a]

Two previous attempts to reduce *dl*-erythronic lactone to *dl*-erythrose in this Laboratory proved to be unsuccessful. Hutton[7] tried sodium and other amalgams and reported a maximum yield of 2.5% of the aldehyde. Miss Stack[8] attempted the reduction of both the lactone and the butyl ester, with hydrogen in the presence of platinum black. At both high and low pressures she obtained 60–70% yields of erythritol and found no evidence of aldehyde formation. These results indicate: (a) the rate of reduction of the aldehyde to erythritol is so much faster than the rate of formation of the aldehyde, that the concentration of the latter in the mixture is always very small; or (b) that, under the conditions of the experiment, the formation of the aldehyde is not a step in the mechanism by which the alcohol is formed. The former assumption seems the more probable in view of the high reactivity of the furanose type of aldose in general.

A more circuitous method of reducing sugar acids to aldehydes has been reported recently by Cook and Major.[9] They prepared pentaacetylgluconic acid, converted it to the acid chloride and successfully reduced the latter to pentaacetylglucose by means of hydrogen in the presence of palladinized barium sulfate according to the procedure of Rosenmund.[10] The yield was almost quantitative. Mochel[11] and Straitiff[12] have recently applied this procedure to the reduction of two of the C_4-saccharinic acids to the corresponding aldehydes and the method showed promise of being adaptable to the reduction of *dl*-erythronic lactone to *dl*-erythrose.

The first step to be accomplished was the preparation of *dl*-triacetyl-erythronic acid. Nef[13] had prepared the diacetyl and dibenzoyl derivatives of *dl*-erythronic lactone, the former as a sirup and the latter as a crystalline solid. During the course of the work herewith reported, the diacetyl lactone was obtained in almost quantitative yield as a crystalline solid which melted at 52.0–52.5°. It was hoped that, by the use of catalysts or higher temperatures, the lactone bond could be opened during acetylation and the triacetyl acid obtained. The use of acetic anhydride with pyridine, zinc chloride and hydrochloric acid as catalysts in the acetylation procedures did not bring this about. This failure showed that it would be necessary to break the bond previous to acetylation attempts, if the triacetyl acid was to be obtained. The simplest method for breaking the lactone bond proved to be conversion to a salt.

The calcium salt was prepared according to the method of Snoddy[14] but attempts to acetylate it proved unsuccessful. The sodium and potassium salts were then prepared. Attempts to crystallize these salts from water were unsuccessful. However, when the lactone was dissolved in absolute methyl alcohol and the solution treated with alcoholic alkali at low temperatures, white crystalline products were obtained. The sodium salt was very hygroscopic; the potassium salt much less so.

The sodium salt reacted with acetylating agents with great violence but the potassium salt was acetylated smoothly at low temperatures by means of acetyl chloride. Potassium chloride precipitated during the reaction with the potassium salt. After removal of this salt and the excess acetyl chloride, followed by concentration of the solution, there remained an almost colorless sirup that could neither be distilled without decomposition nor induced to crystallize. The neutralization equivalent of this sirup indicated that it was composed to a large extent of the triacetylated *dl*-erythronic acid. This conclusion was confirmed by the preparation and analysis of the calcium salt. The triacetylated acid, upon treatment with highly purified thionyl chloride, was converted into the acid chloride. It is interesting to note that some workers[11] have reported difficulties in the preparation of the acid chlorides by means of thionyl chloride and have, therefore, preferred phosphorus pentachloride as the chlorinating agent. These difficulties were encountered in this work, when a supposedly pure commercial grade of thionyl chloride was used. However, carefully purified thionyl chloride proved to be satisfactory.

The reduction of the triacetyl acid chloride was

(6) Felton and Freudenberg, THIS JOURNAL, **57**, 1637 (1935).
(6a) Ruff, *Ber.*, **34**, 1365 (1901).
(7) Donald Hutton, Ph.D. dissertation, University of Chicago, 1930.
(8) Glattfeld and Stack, THIS JOURNAL, **59**, 753 (1937).
(9) Cook and Major, *ibid.*, **58**, 2410 (1936).
(10) Rosenmund, *Ber.*, **51**, 585 (1918).
(11) Glattfeld and Mochel, THIS JOURNAL, **60**, 1011 (1938).
(12) Glattfeld and Straitiff, *ibid.*, **60**, 1384 (1938).
(13) Nef, *Ann.*, **357**, 250 (1907).
(14) Snoddy, S.M. dissertation, University of Chicago, 1934.

carried out in a manner prescribed by Rosenmund.[10] Hydrogen was bubbled into a xylene solution of the acid chloride in which was suspended palladinized barium sulfate. After a short induction period, the evolution of hydrogen chloride began, and the reaction proceeded smoothly until it was about 85% completed when the rate became extremely slow. The course of the reaction was followed by determination of the amount of volatile acid and chloride entrained by the excess hydrogen as it bubbled through the reaction mixture (see Experimental Part). Both the acid and chloride were determined because it was found that hydrogen chloride was not the only volatile acid produced and the true extent of the reduction could be ascertained only by the determination of the chloride content of the effluent gases. The results of these analyses are given in the table below.

TABLE I

REDUCTION OF THE ACID CHLORIDE

Acid chloride 30.0 g.
Pd–$BaSO_4$ catalyst 2.0 g.
Dry xylene 100.0 cc.

Time, min.	*N* NaOH consumed, cc.	*N* $AgNO_3$ consumed, cc.	Redn. calcd. from NaOH consumed, %	Redn. calcd. from $AgNO_3$ consumed %
5	0.83	..	0.77	..
8	1.66	..	1.55	..
10	2.50	..	2.32	..
14	4.99	..	4.65	..
19	8.31	..	7.72	..
24	12.5	..	11.6	..
43	24.9	21.9	23.2	20.4
60	37.4	32.2	35.9	29.3
79	49.9	43.0	46.5	40.2
102	62.4	54.0	58.1	50.4
118	70.6	61.4	66.0	57.2
147	83.1	72.5	77.5	67.5
172	91.5	..	85.5	..
187	95.8	..	89.1	..
204	100.0	87.5	93.7	81.5
231	104.0	90.8	96.8	84.3
275	108.2	93.0	100.7	87.5
Calcd.	107.2	107.2		

After removal of the catalyst and the xylene, the reaction mixture was fractionated at reduced pressure. The analysis of the main fraction which boiled at 126–129° at 2 mm. showed that reduction of the acid chloride to the aldehyde had been accomplished but that a diacetyl- instead of a triacetyl-erythrose had been produced. This unexpected result was verified by the preparation and analysis of the 2,4-dinitrophenylhydrazine derivative of the product. The compound produced was apparently the dinitrophenylhydrazone of neither triacetyl- nor diacetyl-erythrose. It contained 45.70% of carbon and 14.82% nitrogen instead of the 45.07% carbon and 13.15% nitrogen which are theoretical for the dinitrophenylhydrazone of triacetyl-erythrose and the 43.75% carbon and 14.58% nitrogen which are theoretical for the dinitrophenylhydrazone of diacetyl-erythrose. While these results are not close enough to either set of figures to prove the identity of the compound, they do indicate that one acetyl group was lost either in the reduction step or the subsequent fractionation. That this loss took place in the reduction step is indicated by the fact that acetaldehyde was present in the alkali solutions through which the hydrogen was passed after it left the reaction flask.

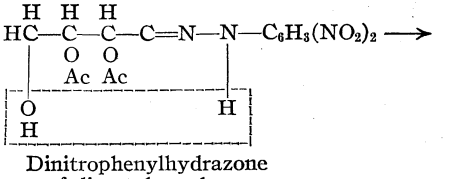
But the loss of one acetyl group and replacement by a hydrogen atom alone would not give a product of the correct composition for an analysis such as was obtained for this dinitrophenylhydrazine derivative. This change together with the loss of one molecule of water, however, would do so as the data in the following table show. The agreement in the nitrogen figure is not good but, because of the difficulties

THE DINITROPHENYLHYDRAZINE DERIVATIVE

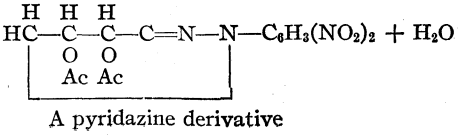
	A Triacetyl-dinitro-phenyl-hydrazone $C_{16}H_{18}N_4O_{10}$	B Diacetyl-dinitro-phenyl-hydrazone $C_{14}H_{16}N_4O_8$	B-H_2O $C_{14}H_{14}N_4O_9$	Found
C	45.07	43.75	45.90	45.70
H	4.22	4.17	3.83	3.62
N	13.15	14.58	15.30	14.82

inherent in nitrogen determinations by the combustion method in compounds of this type, the low figure obtained is perhaps not surprising.

The structure of the compound under discussion has not been determined. Mr. E. M. May of this Laboratory has suggested that the loss of a molecule of water might have occurred as indicated.



Dinitrophenylhydrazone of diacetyl-erythrose



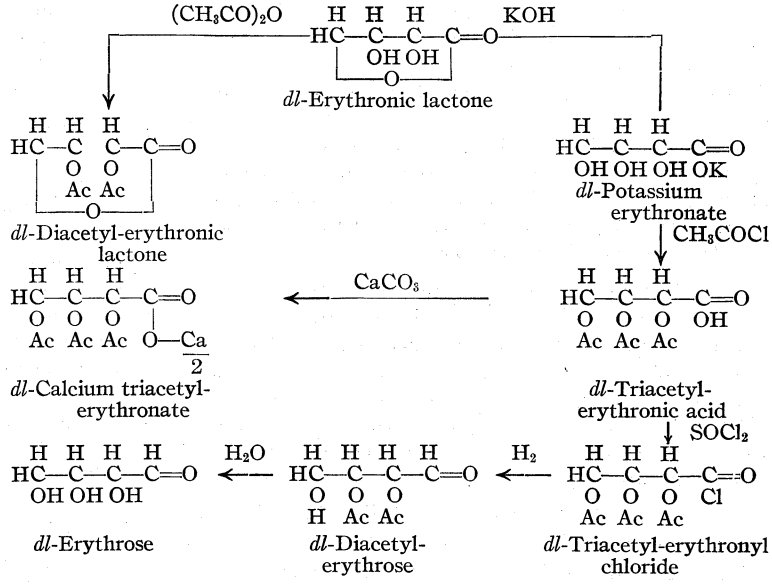
A pyridazine derivative

The structure indicated has been accepted tentatively. An attempt to prepare a derivative of the diacetyl-erythrose with phenylhydrazine resulted in the formation of an oil that could not be crystallized.

The hydrolysis of the diacetyl-erythrose was accomplished by warming a mixture of it with an equal volume of water to 70° and holding the mixture at that temperature until the compound had dissolved. If either alkali or acid was added or if the temperature was raised to hasten the reaction, the solution rapidly turned brown. The acetic acid formed during the hydrolysis was removed to a large extent by repeated extraction with chloroform. The distribution coefficient for acetic acid in chloroform–water mixtures is unfavorable to removal of acetic acid by this process at low concentrations of acetic acid and the separation was not very complete. Evaporation of the extracted solution at reduced pressure over phosphorus pentoxide left a light yellow sirup. Attempts to crystallize this product from methyl and ethyl alcohols proved to be unsuccessful. The sirup reduced cold Fehling's solution and, upon condensation with phenylhydrazine in the usual manner, gave a small yield of an osazone which, after recrystallization from benzene, melted at 162–165°. Fischer,[15] who prepared *dl*-erythrosazone by treatment with phenylhydrazine of a reaction mixture obtained by the oxidation of erythritol, reports a melting range of 166–168°.

The chart scheme summarizes the work reported in this paper beginning with the starting product *dl*-erythronic lactone. It shows the compounds new to the literature that were prepared in the course of the work and indicates how they were prepared.

NEW PRODUCTS FROM *dl*-ERYTHRONIC LACTONE



Experimental Part

Preparation of *dl*-Diacetyl-erythronic Lactone.—Seventy-five grams of freshly-distilled acetic anhydride was poured into a Claisen flask. Dry hydrogen chloride was passed into the liquid until an increase in weight of 2 g. was observed. The flask was stoppered and fitted with a calcium chloride tube at the side-arm. The contents were cooled in ice and, when a temperature of 0° was attained, 20 g. of *dl*-erythronic lactone was added. The mixture was shaken intermittently and allowed to warm to about 20°. After the lactone had dissolved, the solution was allowed to stand at room temperature for three hours. The excess acetic anhydride was removed by distillation under reduced pressure finally at 100°, the temperature of the bath raised to 200° and the residue fractionated. The major portion distilled between 172–176° at 9–10 mm. Upon standing this fraction slowly crystallized; yield 31.5 g., 93% of the theoretical, calculated as the diacetyl-lactone.

The crude material melted at 47–50°. After two recrystallizations from hot water the melting point of the product was found to be 52.5–53°.

Anal. Calcd. for diacetyl-erythronic lactone, $C_8H_{10}O_6$: C, 47.50; H, 4.98; neut. equiv., 67.3. Found: C, 47.48; H, 5.06; neut. equiv., 67.5.

In the preparation of the diacetyl lactone, acetyl chloride may be substituted for the acetic anhydride–hydrogen chloride solution with equivalent yields. The pure product obtained by either method is an odorless, white, stable, crystalline material. It is readily soluble in alcohol and ether and may be recrystallized from water. A water solution of the diacetyl lactone slowly develops the odor of acetic acid.

The use of other catalysts such as zinc chloride, sodium acetate, or pyridine did not cause the opening of the lactone bond. In every case, the only product recovered was the diacetyl lactone. The presence of these catalysts made the recovery of the diacetyl derivative more difficult.

The Preparation of *dl*-Potassium Erythronate.—A solution of 118 g. (1 mole) of *dl*-erythronic lactone in 350 cc. of methyl alcohol was poured into a large evaporating dish and cooled to 5°. Fifty-six and one-tenth grams (1 mole) of pure potassium hydroxide dissolved in 400 cc. of methyl alcohol was added slowly to the lactone solution, with constant stirring, and at such a rate that the temperature of the solution did not rise above 10°. After all the

(15) Fischer, *Ber.*, **20**, 1090 (1887).

alkali had been added a gummy precipitate began to separate. The gum was triturated in the solution until it hardened to a cake. After about two hours the precipitation seemed to be complete. Most of the reaction solution was decanted, the cake was loosened from the sides of the dish and ground to a paste in the presence of a small amount of the solution. The paste was transferred to a Büchner funnel, the solid washed thoroughly with methyl alcohol, and dried in a vacuum desiccator: yield 132 g. of a stable white crystalline powder, 76% of the theoretical calculated as potassium erythronate.

Anal. Calcd. for $C_4H_7O_5K$: C, 27.56; H, 4.05; K, 22.45. Found: C, 27.76; H, 4.03; K, 22.47.

The Preparation of *dl*-Sodium Erythronate.—This salt was prepared in exactly the same manner as the potassium salt. The yield in the case of this salt was lower, about 60%. The product was a very hygroscopic white powder. Unless it was kept in a desiccator it soon turned into a greenish-brown sirup.

Anal. Calcd. for $C_4H_7O_5Na$: C, 30.38; H, 4.43; Na, 14.46. Found: C, 30.52; H, 4.48; Na, 14.37.

The Preparation of *dl*-Triacetyl-erythronic Acid (hereinafter called the triacetyl acid).—To 245 g. of freshly distilled acetyl chloride in a wide-mouthed Erlenmeyer flask was added, in small portions, 100 g. of potassium erythronate. Hydrogen chloride was evolved copiously and time was allowed between additions for the foam to subside. After all the potassium salt had been added and the evolution of hydrogen chloride had practically ceased, the flask was attached to a reflux condenser and the reaction mixture was heated on a boiling water-bath for one hour. At this point the mixture was a viscous sirup in which the potassium chloride was held in colloidal suspension. Addition to the sirup of six volumes of dry ether caused the coagulation and precipitation of the salt. The precipitate was removed by filtration and the filtrate treated with 2 g. of activated carbon. After removal of the carbon, the ether solution was evaporated at reduced pressure to a viscous, almost colorless sirup. The sirup was moderately soluble in water, quite soluble in ether and alcohol, and insoluble in chloroform, ligroin, and benzene. It did not crystallize from any of these solvents: yield 128 g., or 74%.

Anal. Calcd. for the triacetyl acid, $C_{10}H_{14}O_8$: neut. equiv., 65.5. Found: neut. equiv., 66.1.

Attempts to distil the sirup at 2 mm. resulted in rapid decomposition. A small fraction was recovered between 156–160° and later identified as the diacetyl lactone. Acetic anhydride was shown to be present in the distillate. Most of the material in the distilling flask was converted into a black tar.

The Preparation of *dl*-Calcium Triacetyl-erythronate.—Fifteen grams of the triacetyl acid dissolved in 40 cc. of 80% methyl alcohol was warmed to 40° and 2 g. of calcium carbonate added. After the evolution of carbon dioxide had ceased the solution was cooled, the precipitate was allowed to settle, and the supernatant liquid decanted. The precipitate was dried on a water-bath and thoroughly washed with ether to remove any unchanged acid. The precipitate was then treated with 50 cc. of water and the excess calcium carbonate removed by filtration. The calcium salt in the filtrate was again precipitated by the addition of 50 cc. of methyl alcohol. The precipitate was removed by filtration, washed with ether, and dried over phosphorus pentoxide; yield 6.3 g. or 37%. The product was a stable white powder moderately soluble in water.

Anal. Calcd. for calcium triacetyl-erythronate $C_{20}H_{26}O_{16}Ca$: C, 42.66; H, 4.62; Ca, 7.13. Found: C, 42.60; H, 4.66; Ca, 7.21.

The Preparation of *dl*-Triacetyl-erythronyl Chloride.—Twenty-five grams of the triacetyl acid and 25 g. of purified thionyl chloride (see below) were mixed and the mixture allowed to stand overnight in a flask fitted with a reflux condenser and protected from atmospheric moisture with a calcium chloride tube. The following day the mixture was refluxed on a water-bath until the evolution of hydrogen chloride had practically ceased (about four hours). Very cold water was circulated through the reflux condenser to prevent the loss of thionyl chloride. The residue was distilled at reduced pressure. The main fraction boiled between 115–130° at 2 mm. This fraction was again distilled at 2 mm. and from it there was obtained 21 g. of a mobile colorless liquid which boiled at 114–116°; a 79% yield calculated as triacetyl acid chloride. The substance fumed in moist air and possessed a sharp odor similar to that of hydrogen chloride.

Anal. Calcd. for the triacetyl acid chloride, $C_{10}H_{13}O_7Cl$: C, 42.77; H, 4.67; Cl, 12.64; neut. equiv., 55.9. Found: C, 42.77; H, 4.43; Cl, 12.77; neut. equiv., 56.1.

The Purification of Thionyl Chloride.[16,17]—Two hundred grams of thionyl chloride was mixed with 30 g. of quinoline and distilled through a Schneider column. The fraction which boiled at 74–78° was mixed with 30 g. of boiled linseed oil and again distilled through the Schneider column. The fraction which boiled at 75–76° was colorless and remained so when kept in the dark. It was this fraction which was used in the preparation of the acid chloride.

The Reduction of *dl*-Triacetyl-erythronyl Chloride.—Thirty grams of the acid chloride was dissolved in 100 cc. of dry xylene and 2 g. of palladinized barium sulfate (5% Pd) catalyst added.[18] The flask which contained the solution was attached to a reflux condenser and the mixture was heated to 135° in an oil-bath. Hydrogen, purified and dried by passage through 5% solutions of silver nitrate and potassium permanganate, then through concentrated sulfuric acid and copper gauze at dull red heat and finally through soda lime and phosphorus pentoxide, was introduced into the solution at such a rate as to keep the catalyst in uniform suspension. After a few minutes the evolution of hydrogen chloride began and proceeded smoothly, gradually lessening as the reaction approached completion. The effluent gases from the reflux condenser were conducted into a solution which contained a known amount of alkali and a few drops of phenolphthalein. When the alkali solution changed color, the effluent gases were conducted immediately into another solution of known alkali content. By noting the time at each color change and consequently the time required for the production of a known quantity of hydrogen chloride, both the rate and extent of the reduc-

(16) H. Meyer and R. Turnau, *Monatsh.*, **28**, 153 (1907).

(17) H. Meyer and K. Schlegl, *ibid.*, **34**, 569 (1913).

(18) Gattermann and Wieland, "Laboratory Methods of Organic Chemistry," 22d edition, The Macmillan Co., New York, N. Y., 1934, pp. 369–370.

tion of the acid chloride were followed (see Table I). The chloride in these solutions was estimated by titration with a normal solution of silver nitrate with dichlorofluorescein as the indicator. The chloride content of the solutions, calculated as hydrogen chloride, did not account for all of the acid present. Attempts were made to identify this additional volatile acid but they were unsuccessful. It was noticed that the solutions used for the estimation of the chloride had a distinct odor of acetaldehyde. This aldehyde probably was produced by the reduction of the acetyl group that was lost from the triacetyl acid chloride during the reduction process (see analysis below). When the chloride determination indicated that the reduction was 85% complete, the rate of reaction had become very slow and the reduction was discontinued in order to prevent thermal decomposition of the product obtained.

The xylene was removed by the introduction of the reaction solution dropwise into a small Claisen flask, evacuated to 10 mm. and heated to 100°. Attempts to distil the reaction mixture at reduced pressure in the ordinary manner caused so much foaming that serious mechanical loss resulted. The residue was fractionated at 2 mm. A small fraction which distilled between 114–120° proved to be unchanged acid chloride. The main fraction distilled between 125–140°. A second fractionation of this portion yielded 14.5 g. of a mobile, colorless liquid which boiled at 126–129° at 2 mm., a yield of 20% calculated as diacetyl-erythrose. The product possessed a mild aromatic odor and gave no test for chloride. It quickly reduced boiling Fehling's solution.

Anal. Calcd. for diacetyl-erythrose, $C_8H_{12}O_6$: C, 47.03; H, 5.92; neut. equiv., 102. Found: C, 47.20; H, 5.80; neut. equiv., 99.3.

The Reaction of *dl*-Diacetyl-erythrose with 2,4-Dinitrophenylhydrazine.—Two grams of the diacetyl-erythrose was dissolved in 50 cc. of a saturated solution of 2,4-dinitrophenylhydrazine in ethyl alcohol and the mixture was boiled for two minutes. Upon the addition of 5 drops of concentrated hydrochloric acid the solution immediately turned from orange to bright yellow. The solution was stored overnight in the icebox during which time a crop of bright yellow, needle-like crystals formed; yield 0.3 g. These were removed by filtration and recrystallized twice from a small quantity of methyl alcohol; m. p. 172–173°. Further recrystallization did not raise the melting point.

Anal. Calcd. for $C_{14}H_{14}N_4O_8$ (see above): C, 45.90; H, 3.83; N, 15.30. Found: C, 45.70; H, 3.62; N, 14.82.

The Hydrolysis of *dl*-Diacetyl-erythrose.—A mixture of 10 g. of the diacetyl-erythrose and 10 cc. of water was heated to 70° and held at that temperature until all the aldehyde had dissolved. The solution was extracted with ten 10-cc. portions of chloroform to remove the acetic acid formed during the hydrolysis. It was then evaporated over phosphorus pentoxide in a vacuum desiccator to a light colored viscous sirup; yield 2.4 g. or 41%. The odor of acetic acid was still quite noticeable in the sirup but attempts to remove it by further extraction with chloroform were unsuccessful. The sirup readily reduced cold Fehling's solution.

Preparation of *dl*-Erythrose Phenylosazone.—To a solution of 2 g. of the sirupy *dl*-erythrose in 3 cc. of 95% ethyl alcohol were added 2 g. of freshly-distilled phenylhydrazine and 2 g. of glacial acetic acid. The solution was allowed to stand in the dark for twelve hours. During this time a small quantity of brownish-yellow crystals had formed. They were separated by filtration and recrystallized from benzene; m. p. 162–165°.

Summary

1. *dl*-Diacetyl-erythronic lactone was prepared in almost quantitative yield by the acetylation of the lactone. It was a crystalline solid which melted at 52.5–53°. It has been reported heretofore only as a sirup.

2. The potassium and sodium salts of *dl*-erythronic acid as well as *dl*-triacetyl-erythronic acid and its calcium salt are reported for the first time.

3. Triacetyl-erythronic acid was converted into the corresponding acid chloride in high yield. This acid chloride was reduced according to the method of Rosenmund as modified by Cook and Major. Diacetyl-erythrose, instead of the expected triacetyl-erythrose, was obtained.

4. A crystalline product was obtained by the action of 2,4-dinitrophenylhydrazine upon the *dl*-diacetyl-erythrose. The analytical data showed that two molecules of water had been eliminated in the course of the reaction and the compound has been characterized tentatively as a pyridazine derivative.

5. *dl*-Diacetyl-erythrose was hydrolyzed to *dl*-erythrose, which was recovered as a light yellow sirup.

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Heats of Combustion of Some Mono- and Disaccharides

BY THEODORE H. CLARKE[1,2] AND GEBHARD STEGEMAN

A program has been instituted at this Laboratory for obtaining the thermal data on compounds of physiological interest. Studies are being carried out on carbohydrates and glycerides, and in this paper are presented the combustion data on six carbohydrates.

Method and Apparatus.—Since the proposed course of study will involve only liquids and solids, the "bomb calorimeter" method has been adopted. The determinations were made isothermally, that is, the rise in temperature of the calorimeter is observed while the temperature of the jacket is kept constant.

The calorimeter system was patterned after that of Dickinson.[3] A hollow removable head was so arranged that the calorimeter could be surrounded completely by a well-stirred water-bath kept constant to within ±0.002°. Two ball-bearing mounted stirrers driven by constant speed motors were employed to circulate the water in the jacket and to pump water through the head. The jacket also was provided with a cooling coil for use in warm weather. The calorimeter proper had a stirrer mounted in a side-tube and connected by means of a hard rubber connector to a shaft extending through the head. This stirrer was driven by a belt to the main stirrer shaft.

An "Emerson double-valved bomb" of 516-ml. capacity was used throughout the investigation. Gold-plated electrodes with threaded binding posts, gold-plated crucible support, and gold-plated inner linings for the bomb were employed to eliminate any corrosion. The material to be burned was placed in a platinum cup.

The temperature measuring system consisted of a Bureau of Standards calibrated platinum resistance thermometer, a White double potentiometer, and a type H. S. galvanometer, all supplied by Leeds and Northrup Co. A shunt of seventy ohms was placed across the galvanometer which then had a sensitivity of 0.000005 ohm (0.00005 C) per 0.1 mm. deflection and was quite stable. The galvanometer was used as a deflection instrument.

Burgess–Parr oxygen bomb fuse wire was used to ignite the sample. As the same length of wire and the same source of energy for its ignition were used throughout all the determinations, the heat evolved by the ignition of the wire was included in the heat equivalent of the calorimeter. As in general sugars tend to melt rather than to ignite, a small disk of filter paper was placed on top of the sample to start the combustion. Whatman's No. 42 ashless filter paper, kept in a constant humidity container, having a determined heat of combustion of 3999.2 cal./g. was used. The error for the size of filter paper disk was less than 0.1 cal.

The mass of the calorimeter and water was determined to ±0.05 g. by means of a large capacity balance having a sensitivity of ±0.01 g. The mass of the sample was determined to ±0.00002 g. by means of a good analytical balance. Weighings were made on both arms of the balance to eliminate any differences in the arms of the balance.

The bomb was first evacuated and then filled with commercial oxygen to a pressure of 30 atm.; 3 g. of water was placed in the bomb for each determination.

Units.—The unit of energy used throughout this paper is the defined conventional calorie which has been derived from the international joule by the factor 1 cal. = 4.1833 int. j.[4,5] The unit of mass is the "gram true mass" which is derived from the mass in air against gold-plated brass weights by the use of a suitable conversion factor.

Errors.—In the calculation of the precision of these determinations the procedure proposed by Rossini[5] has been used. The errors are defined: "assigned error" on the standardizing substance, ± e%; error on the standardization or "calibration error" ± c%; error on the actual determination or "reaction error," ± b%; and the final precision error, ± p. e.%. This procedure gives an error larger than the usual "probable error" but as Rossini states, "it seems better because it yields an 'error' which is conservative and reasonable."

Calibration of the Calorimeter

The energy equivalent of the calorimeter was determined by burning benzoic acid (sample No. 39e) supplied by the Bureau of Standards. Benzoic acid has been chosen as the primary standard for combustion calorimetry and the value for the isothermal heat of combustion of this sample is given as 26.419 international kilojoules per gram mass.[6] In Table I are presented a series of values of the energy equivalent of the calorimeter as determined from the heat of combustion of benzoic acid.[7] It was not always possible to obtain complete combustion of benzoic acid, but in the cases where carbon appeared it was present in such small quantities as to be impossible to weigh. Any uncertainty due to this effect appears to be within the experimental error.

From the results in Table I, the energy equivalent of the calorimeter has been assigned the value of 2769.1 ± 0.3 cal. per °C. at 25°.

(1) From a thesis submitted by T. H. Clarke in partial fulfilment of the requirements for the degree of Doctor of Philosophy, June, 1939.

(2) This work was made possible by a grant from the Buhl Foundation, Pittsburgh, Penna.

(3) Dickinson, *Bull. Bur. Standards*, **11**, 243 (1915).

(4) Technical News Bull. Bur. of Standards, No. 156 (1930).

(5) Rossini, *Chem. Rev.*, **18**, 252 (1936).

(6) Jessup and Green, *Bur. Standards J. Research*, **13**, 491 (1934).

(7) It was felt desirable from the way that the measurements were made to carry one more figure than the exact number of completely significant figures and to express the final results to the correct number of significant figures.

TABLE I

CALIBRATION WITH BENZOIC ACID

ΔR, corr. rise, ohms	Δt, corr. rise, °C.	Total heat evolved, cal.	True mass	Corr. Fe + HNO_3	Energy equivalent, cal./°C.	Δ	$(\Delta)^2$
0.355297	3.3305	9223.44	1.46048	1.59	2768.91	0.19	0.0361
.333560	3.3132	9176.08	1.45298	1.08	2769.23	− .13	.0169
.330492	3.2828	9092.33	1.43972	2.13	2769.04	.06	.0036
.329841	3.2763	9071.75	1.43646	1.13	2768.90	.20	.0400
.335990	3.3374	9243.64	1.46368	1.74	2769.19	− .09	.0081
.328920	3.2672	9049.64	1.43296	1.74	2769.31	− .21	.0441

$M = 2769.1_0$ cal. °C.$^{-1}$

Errors: e = ±0.007%, c = ±0.005%, p. e. = ±0.009% (±0.3 cal.)

TABLE II

TABLE ON PREPARATION

Sample	Source	Filtrations	Pptg. medium	Time in medium, days	Washing medium	Drying temp., °C.	Drying time, days over "Drierite"
α-Lactose monohydrate	B	1	40% alcohol	10	Cold abs. ether	50	10
α-*d*-Galactose	E	6	60% alcohol	4	Cold abs. ether	45	7
α-*d*-Galactose	P	3	60% alcohol	4	Cold abs. ether	45	8
β-*d*-Levulose	E	3	80% alcohol	5	Cold abs. alc.	45	8
β-*d*-Levulose	P	5	80% alcohol	5	Cold abs. alc.	45	8
β-Maltose monohydrate	E	3	60% alcohol	5	Cold abs. ether	50	8
β-Maltose monohydrate	P	4	60% alcohol	5	Cold abs. ether	50	8
l-Sorbose	U. S. D. A.	1	H_2O	..	Cold water	47	8
l-Sorbose	Pf	1	H_2O	..	Cold water	47	8
β-Lactose	E	1	H_2O	..	Cold water	100	7

B = Borden Research Laboratory.[9] E = Eastman Kodak Co. P = Pfanstiehl Chemical Co. Pf = Pfizer Chemical Co.[9] U. S. D. A. = United States Department of Agriculture.[9]

TABLE III

COMPARISON OF OPTICAL VALUES

All values measured $[\alpha]^0_{20}$

Sample	Source	Values determined Initial	Values determined Final	Hudson's values Initial	Hudson's values Final
β-Lactose	E	35.0	55.0	35.2	55.3
β-*d*-Levulose	P	−132.6	− 92.3	−133.0	− 92.5
β-*d*-Levulose	E	−132.4	− 92.3		
β-Maltose monohydrate	E	111.9	131.0	112.0	131.0
β-Maltose monohydrate	P	112.0	131.1		
α-Lactose monohydrate	B	89.0	55.0	90.0	55.3
α-*d*-Galactose	E	143.9	80.3	144.0	80.5
α-*d*-Galactose	P	144.0	80.0		
l-Sorbose	Pf	...	− 43.2	...	− 43.1
l-Sorbose	U. S. D. A.	...	− 43.1	...	− 43.1

Preparation of Samples

As the procedure developed was somewhat similar in the case of all the sugars investigated, only a general discussion of the method will be given and the specific conditions for each sample tabulated at the end of this discussion (Table II). The sugar under investigation was dissolved in sufficient water to make a fluid liquid and filtered through best grade filter paper to remove any carbon, silica, etc., carried through from the manufacturer's filters. The water was then evaporated under vacuum (in order to avoid heating the sample in excess of 35–40°) until the amount of water remaining equaled the water necessary to form the aqueous fraction of the water–ethyl alcohol mixture used for recrystallization of a single isomeric form. The sample was allowed to stand for a given period of time in contact with this alcohol solution to ensure that only one isomer was present in the solid phase. This is the procedure developed by Hudson.[8] The sam-

(8) Hudson and Yanovsky, THIS JOURNAL, **39**, 1013 (1917).

(9) α-Lactose monohydrate was secured through the courtesy of Borden Research Laboratory, Bainbridge, N. Y.; *l*-sorbose through the courtesy of Charles Pfizer Chemical Co., N. Y.; and *l*-sorbose through the courtesy of J. J. Stubbs, Bureau of Chemistry and Soils, United States Department of Agriculture.

TABLE IV

THE COMBUSTION DATA

		ΔR corr. rise, ohms	Δt corr. rise, °C.	Total heat evolved, cal.	Corr. filter paper, cal.	Corr. Fe + HNO_3	True mass	$-\Delta U_B/M$ cal. $g.^{-1}$	Δ
l-Sorbose	Pf	0.320854	3.1870	8825.11	147.37	1.64	2.32944	3724.54	−0.10
l-Sorbose	Pf	.324333	3.2216	8920.93	156.45	1.56	2.35222	3725.38	− .94
l-Sorbose	Pf	.323577	3.2141	8900.16	147.37	1.49	2.34992	3724.08	.36
l-Sorbose	U. S. D. A.	.308256	3.0619	8478.70	87.90	1.09	2.25247	3724.67	− .23
l-Sorbose	U. S. D. A.	.308848	3.0678	8495.04	91.34	1.09	2.25647	3723.91	.53
l-Sorbose	U. S. D. A.	.307795	3.0573	8465.97	88.06	1.17	2.24929	3724.17	.27
l-Sorbose	U. S. D. A.	.308226	3.0616	8477.88	87.66	0.06	2.25278	3724.36	.08
								Mean = 3724.4_4 cal. $g.^{-1}$	
Errors: e = ±0.007%, c = ±0.005%, b = ±0.010%, p. e. = ±0.013% (±0.5 cal.)									
β-d-Levulose	P	0.317635	3.1551	8736.79	93.02	..	2.31598	3732.29	−0.03
β-d-Levulose	P	.308538	3.0646	8486.18	92.02	1.02	2.24877	3732.32	− .06
β-d-Levulose	P	.305090	3.0305	8391.76	79.82	0.87	2.22683	3732.24	.02
β-d-Levulose	E	.306549	3.0454	8433.02	78.62	1.12	2.23774	3732.91	− .65
β-d-Levulose	E	.308278	3.0621	8479.26	94.82	1.37	2.24645	3731.70	.56
β-d-Levulose	E	.317229	3.1510	8625.43	90.14	1.20	2.31346	3732.11	.15
								Mean = 3732.2_6 cal. $g.^{-1}$	
Errors: e = ±0.007%, c = ±0.005%, b = ±0.009%, p. e. = ±0.012% (±0.5 cal.)									
α-d-Galactose	E	0.316599	3.1448	8708.27	95.70	1.06	2.32459	3704.53	0.30
α-d-Galactose	E	.306756	3.0470	8437.45	89.58	1.20	2.25270	3705.18	− .35
α-d-Galactose	P	.307239	3.0518	8450.74	88.26	1.17	2.25659	3705.29	− .46
α-d-Galactose	P	.304659	3.0262	8379.85	91.98	1.26	2.23719	3704.03	.80
α-d-Galactose	E′	.305088	3.0304	8391.48	89.74	1.17	2.24032	3705.08	− .25
								Mean = 3704.8_3 cal. $g.^{-1}$	
Errors: e = ±0.007%, c = ±0.005%, b = ±0.013%, p. e. = ±0.015% (±0.6 cal.)									
β-Lactose	E	0.318287	3.1615	8754.51	...	1.39	2.22567	3932.80	0.08
β-Lactose	E	.315229	3.1312	8670.60	...	1.22	2.20458	3932.44	.28
β-Lactose	E′	.313892	3.1179	8633.78	...	1.36	2.19499	3932.78	− .06
β-Lactose	E′	.314856	3.1275	8660.36	...	1.29	2.20186	3932.62	.10
β-Lactose	E″	.289556	2.8762	7964.49	...	0.94	2.02429	3932.77	− .05
β-Lactose	E″	.290500	2.8855	7990.24	...	2.06	2.03112	3932.89	− .17
								Mean = 3932.7_2 cal. $g.^{-1}$	
Errors: e = ±0.007%, c = ±0.005%, b = ±0.004%, p. e. = ±0.009% (±0.4 cal.)									
β-Maltose monohydrate	E	0.314177	3.1207	8641.53	115.54	1.28	2.25660	3777.68	0.10
β-Maltose monohydrate	E	.312056	3.0996	8583.10	121.17	1.17	2.23927	3778.36	− .58
β-Maltose monohydrate	E	.311066	3.0898	8555.96	115.18	1.17	2.23410	3777.64	.14
β-Maltose monohydrate	P	.311426	3.0934	8565.93	119.38	1.36	2.23524	3778.20	− .42
β-Maltose monohydrate	P	.311772	3.0968	8575.34	117.78	1.34	2.23851	3777.61	.17
β-Maltose monohydrate	P	.307546	3.0548	8459.04	120.25	1.20	2.20703	3777.74	.04
β-Maltose monohydrate	P	.311504	3.0942	8568.15	120.37	1.28	2.23606	3777.40	.38
β-Maltose monohydrate	P	.311017	3.0893	8554.58	116.17	1.29	2.23346	3777.60	.18
								Mean = 3777.7_8 cal. $g.^{-1}$	
Errors: e = ±0.007%, c = ±0.005%, b = ±0.006%, p. e. = ±0.010% (±0.4 cal.)									
α-Lactose monohydrate	B	0.306716	3.0466	8436.34	104.54	14.97	2.21134	3760.99	0.59
α-Lactose monohydrate	B	.310056	3.0797	8527.99	120.41	1.44	2.23431	3762.30	− .72
α-Lactose monohydrate	B	.310256	3.0818	8533.87	112.78	3.21	2.23733	3762.47	− .89
α-Lactose monohydrate	B′	.311070	3.0900	8556.58	118.46	1.44	2.24353	3760.45	1.13
α-Lactose monohydrate	B′	.310333	3.0825	8535.75	116.26	1.31	2.23743	3762.43	−0.85
α-Lactose monohydrate	B′	.310236	3.0816	8533.32	119.98	1.42	2.23670	3760.86	.72
α-Lactose monohydrate	B″	.305216	3.0317	8395.08	84.42	1.21	2.20877	3762.02	− .44
α-Lactose monohydrate	B″	.296546	2.9456	8156.66	77.86	1.08	2.14768	3761.13	.45
								Mean = 3761.5_8 cal. $g.^{-1}$	
Errors: e = ±0.007%, c = ±0.005%, b = ±0.015%, p. e. = ±0.017% (±0.6 cal.)									

ple was then filtered, washed with a suitable medium, vacuum dried over "Drierite" and stored over calcium chloride for some time before usage. This procedure was used for *α*-lactose monohy-

TABLE V

SUMMARY OF DERIVED DATA[a]

	Mol. wt.	$-\Delta U_B$ kcal. mole^{-1}	$-\Delta U_R$ kcal. mole^{-1}	$-\Delta H^\circ_{298.16}$ kcal. mole^{-1}	$-\Delta H_R$ kcal. mole^{-1}
l-Sorbose	180.157	670.98 ± 0.09	670.30 ± 0.09	303.80	309.13
β-*d*-Levulose	180.157	672.39 ± 0.08	671.70 ± 0.08	302.38	307.71
α-*d*-Galactose	180.157	667.45 ± 0.10	666.76 ± 0.10	307.33	312.66
β-Lactose	342.298	1346.16 ± 0.12	1345.47 ± 0.12	534.38	544.16
β-Maltose monohydrate	360.314	1361.19 ± 0.13	1360.50 ± 0.13	587.68	598.35
α-Lactose monohydrate	360.314	1355.35 ± 0.23	1354.66 ± 0.23	593.52	604.19
Sucrose[3]	342.298	1349.68	1348.99	530.87	540.65
α-*d*-Glucose[13]	180.154	670.17 ± 0.07	669.58 ± 0.13	305.73	311.06
α-*d*-Glucose hydrate[13]	198.169	667.37 ± 0.12	666.73 ± 0.18	376.90	383.12

[a] All thermal values are for 25°C. See text for explanation of symbols.

drate, α-*d*-galactose, β-*d*-levulose, β-maltose monohydrate. β-Lactose and *l*-sorbose were treated similarly with the exception of the alcohol treatment.

The number of filtrations varied with the sample and are tabulated. The pressure varied between 1–3 mm. Samples were kept for ten to fourteen days over calcium chloride, were bottled and stored over calcium chloride while being used.

As standards of purity of the samples used, the following criteria were adopted: agreement in optical rotation values with those of Hudson and others and the checking of results on samples from different sources or in some cases the checking of results on samples from the same source secured from different batches. In this way it is believed that the possibility of error caused by poor samples has been practically eliminated.

Heats of Combustion.—In Table IV the experimental results of the combustions on these six compounds are listed with the errors stated as discussed earlier in this paper.

Calculated Values.—In addition to the results in Table IV we have calculated the value of $-\Delta U_B$, the heat evolved in the bomb process in kcal. per gram formula weight; $-\Delta U_R$, the decrease in energy for the chemical reaction at the standard state as defined by Washburn[10]; and $-\Delta H^\circ_{298.16}$, the heat of formation of the compound from the elements by the use of −68,318.1[11] and −94,029.8 cal.[12] for the heats of formation of water and carbon dioxide. A summary of the derived values is given in Table V.

(10) Washburn, *Bur. Standards J. Research*, **10**, 543 (1933), equations 2 and 81.

(11) Rossini, private communication.

(12) Rossini and Jessup, *J. Research Bur. Standards*, **21**, 1491 (1938).

(13) Huffman and Fox, THIS JOURNAL, **60**, 1403 (1938).

Discussion of Results

The values determined here along with those on sucrose[3] and glucose[13] complete the combustion data on the three physiologically most important disaccharides (maltose, lactose, sucrose) and their component monosaccharides (levulose, galactose, glucose). Investigations on the specific heats of these compounds are being carried on in this Laboratory and the values for the free energy of formation of these sugars will be reported at a future date.

The assignment of the precision errors to our measurements is a mathematical process without assumptions, but a statement of the limits of accuracy involves factors difficult to evaluate. Optical rotation as a criterion of purity is not extremely accurate; but by its use and the method of checking samples from different sources and batches, it is believed that the absolute errors due to purity of sample have been nearly eliminated. A conservative estimate might place the accuracy error as 0.025–0.035%.

No error is stated for the value of $-\Delta H^\circ_{292.16}$ as this would involve the errors on the determination of the heats of formation of water and carbon dioxide. Since in the comparison of values the influence of the errors on water and carbon dioxide would be constant, the uncertainties are probably those of the heats of combustion of the compounds.

Galactose was burned by Stohmann[14] and anhydrous lactose by Stohmann,[14] and by Karrer and Fioroni,[15] whose results are higher by several tenths of one per cent. than the values here reported. The reported values for the hydrated form of lactose[14,16,17] and maltose[14,16] lie as much

(14) Stohmann and Langbein, *J. prakt. Chem.*, [2] **45**, 305 (1892).

(15) Karrer and Fioroni, *Ber.*, **55B**, 2854 (1922).

(16) Emery and Benedict, *Am. J. Physiol.*, **28**, 310 (1911).

(17) Van Rechenberg, *J. prakt. Chem.*, [2] **22**, 11 (1880).

as 1% lower than our values. The authors believe, however, that due to the higher precision attainable today, preparation of the samples by the method of Hudson,[8] and carefully controlled drying conditions, the reported values are worthy of consideration.

Summary

1. A brief description of a precise calorimetric system for measuring heats of combustion and the standardization of the apparatus with a precision of 0.009% have been presented.

2. The heats of combustion, reduced to the standard state $-\Delta U_R$, are reported as: *l*-sorbose, −670.30; *β*-*d*-levulose, −671.70; *α*-*d*-galactose, −666.76; *β*-lactose, −1345.47; *β*-maltose monohydrate, −1360.50; *α*-lactose monohydrate, −1354.66 kcal. per mole for the constant pressure process at 25°.

3. A comparison of these results with older values in the literature shows discrepancies of from 0.1–1%.

PITTSBURGH, PENNA. RECEIVED APRIL 21, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES, THE OHIO STATE UNIVERSITY]

Equilibria of Mercuric Oxide in Solutions of Dilute Nitric Acid. Evidence for Stepwise Dissociation of Bases

BY A. B. GARRETT AND W. W. HOWELL

Equilibrium data for mercuric oxide in alkali[1] showed no minimum in the mercuric oxide–alkali graph and showed only a very low degree of dissociation for mercuric hydroxide as an acid. This paper presents equilibrium data in *acid* solutions; such data make possible the determination of (1) the position of minimum solubility of mercuric hydroxide, (2) the equilibrium constants of mercuric hydroxide as a base, and (3) the direct evidence for stepwise dissociation of bases. In addition to this, these data, together with the equilibrium data of mercuric oxide in alkali, give the complete record of the behavior of mercuric oxide in dilute solutions of nitric acid and sodium hydroxide.

Procedure.—The general procedure in the determination of the solubility of mercuric oxide in acid was similar to that described by Garrett and Hirschler.[1] The red mercuric oxide used was prepared by the calcination of mercuric nitrate which had been prepared from especially purified mercury and nitric acid. The yellow mercuric oxide was Merck Reagent Quality Mercuric Oxide. The nitric acid was C. P. quality acid. Conductivity water was used for all solutions. All preparations were made in an atmosphere of nitrogen. The temperature was 25.00 ± 0.02°.

The equilibrium periods, sedimentation periods, method of filtration, and determination of the mercury content of the samples were the same as those described by Garrett and Hirschler.[1]

(1) Garrett and Hirschler, THIS JOURNAL, **60**, 299 (1938).

The concentration of acid was determined by preparing the samples with standard solutions of the acid used. The acidity was corrected for the amount of acid used to react with the oxide. The *p*H value of each of the solutions was determined (after equilibrium was established) by means of a glass electrode.

The Data.—The data are given in Tables I and II and in Figs. 1, 2, 3, and 4. All of the data are expressed in moles of mercuric oxide and moles of acid per 1000 g. of water. In most of these data is given the average value of a pair of samples one of which approached equilibrium from undersaturation (u) and the other from supersaturation (s). Several samples, for which the mate was lost, are marked (u) or (s) to indicate the approach to equilibrium.

The data were calculated on the assumption of the following reactions

$$HgO + H_2O \rightleftharpoons Hg(OH)_2 \quad (1)$$

$$HgO + H^+ \rightleftharpoons Hg(OH)^+ \quad (2)$$

$$K_2 = \frac{m_{Hg(OH)^+}\gamma_{Hg(OH)^+}}{m_{H^+}\gamma_{H^+}}$$

$$HgO + 2H^+ \rightleftharpoons Hg^{++} + H_2O \quad (3)$$

$$K_3 = \frac{m_{Hg^{++}}\gamma_{Hg^{++}}}{m^2_{H^+}\gamma^2_{H^+}}\, a_{H_2O}$$

The acidity of the standard solutions of which the samples were made was corrected for the acid used in reactions indicated in equations (2) and (3). The curvature of the mercuric oxide–acid graph (Figs. 1, 3, and 4) indicates that reaction (3) is appreciable. While no direct method is

TABLE I

THE SOLUBILITY OF YELLOW MERCURIC OXIDE IN NITRIC ACID

Moles HNO_3/1000 g. H_2O as samples were made up	Moles HNO_3/1000 g. H_2O corr. for $Hg(OH)^+$ and Hg^{++} from values of K_2 = 0.17 and K_3 = 53	Moles HNO_3/1000 g. H_2O from glass electrode data (glass electrode value of H^+ divided by γ_{HNO_3})	Moles HgO/1000 g. H_2O
5.00×10^{-5}	4.0×10^{-5}	3.2×10^{-5}	2.43×10^{-4}
1.00×10^{-4}	1.2×10^{-4}	5.5×10^{-5}	2.57×10^{-4}
2.00×10^{-4}	1.7×10^{-4}	9.5×10^{-5}	2.67×10^{-4}
4.00×10^{-4}	4.0×10^{-4}	2.9×10^{-4}	3.11×10^{-4}
6.00×10^{-4}	5.0×10^{-4}	4.0×10^{-4}	3.35×10^{-4}
8.00×10^{-4}	6.9×10^{-4}	1.5×10^{-3}	3.80×10^{-4}
1.03×10^{-3}	8.2×10^{-4}		4.15×10^{-4}
2.00×10^{-3}	1.5×10^{-3}	1.1×10^{-3}	6.08×10^{-4}
4.00×10^{-3}	2.8×10^{-3}	3.8×10^{-3}	12.1×10^{-4}
6.00×10^{-3}	3.8×10^{-3}		18.3×10^{-4}
8.00×10^{-3}	4.4×10^{-3}		23.2×10^{-4}
1.06×10^{-2}			30.0×10^{-4}
1.56×10^{-2}			50.5×10^{-4}
2.00×10^{-2}	8.4×10^{-3}	8.1×10^{-3}	65.5×10^{-4}
2.00×10^{-2}			68.0×10^{-4}
3.00×10^{-2}			111×10^{-4}
3.00×10^{-2}			108×10^{-4}
4.00×10^{-2}			173×10^{-4}
4.00×10^{-2}			169×10^{-4}
5.00×10^{-2}		1.0×10^{-2}	217×10^{-4}
5.85×10^{-2}		1.0×10^{-2}	236×10^{-4}
6.00×10^{-2}			253×10^{-4}
6.34×10^{-2}		1.4×10^{-2}	262×10^{-4}
6.83×10^{-2}		1.3×10^{-2}	299×10^{-4}
7.00×10^{-2}			312×10^{-4}
7.03×10^{-2}		1.3×10^{-2}	312×10^{-4}
7.22×10^{-2}		1.3×10^{-2}	329×10^{-4}
7.43×10^{-2}		1.3×10^{-2}	333×10^{-4}
7.61×10^{-2}		1.3×10^{-2}	349×10^{-4}
7.80×10^{-2}		1.2×10^{-2}	362×10^{-4}
9.76×10^{-2}		1.6×10^{-2}	449×10^{-4}
1.17×10^{-1}		1.4×10^{-2}	536×10^{-4}
1.37×10^{-1}			638×10^{-4}
1.40×10^{-1}		1.8×10^{-2}	596×10^{-4}
1.56×10^{-1}		2.3×10^{-2}	718×10^{-4}
1.60×10^{-1}		1.9×10^{-2}	662×10^{-4}

readily available to determine $m_{Hg^{++}}$ it can be determined together with the $m_{Hg(OH)^+}$ by a method of approximation with the aid of a relationship of activity coefficients similar to that derived for the dissociation of copper hydroxide.[2] Assuming that the total solubility of the mercuric oxide (S_{HgO}) is expressed by the equation

$$S_{HgO} = m_{Hg(OH)_2} + m_{Hg(OH)^+} + m_{Hg^{++}} \qquad (4)$$

where $m_{Hg(OH)_2}$ is the undissociated mercuric hydroxide (essentially water solubility since $Hg(OH)_2$ is only slightly dissociated[1])

$$m_{Hg(OH)^+} = K_2 \frac{m_{H^+}\gamma_{H^+}}{\gamma_{Hg(OH)^+}}$$

(2) Johnston and McDowell, THIS JOURNAL, **58**, 2009 (1936). The use of this relationship is necessary here since $\gamma_{Hg^{++}}$ has not been determined. An alternative procedure at this point would be to use the value of the activity coefficient for an ion similar to Hg^{++}. A probable choice would be $\gamma_{Pb^{++}}$ from the data of $\gamma_{Pb(NO_3)_2}$ given by Randall and Vanselow, *ibid.*, **46**, 2448 (1924).

TABLE II

THE SOLUBILITY OF RED MERCURIC OXIDE IN NITRIC ACID

Moles HNO_3/1000 g. H_2O as samples were made up	Moles HNO_3/1000 g. H_2O corr. for $Hg(OH)^+$ and Hg^{++} from values of K_2 and K_3	Moles HNO_3/1000 g. H_2O from glass electrode data (glass electrode value of H^+ divided by γ_{HNO_3})	Moles HgO/1000 g. H_2O
1.00×10^{-4}	3.8×10^{-4}	1.4×10^{-4}	2.98×10^{-4}
2.00×10^{-4}	4.6×10^{-4}	0.7×10^{-4}	3.14×10^{-4}
3.00×10^{-4}	2.8×10^{-4}	1.4×10^{-4}	2.77×10^{-4} (u)
5.00×10^{-4}	6.1×10^{-4}	3.0×10^{-4}	3.48×10^{-4} (s)
7.00×10^{-4}	6.6×10^{-4}	3.8×10^{-4}	3.56×10^{-4}
9.00×10^{-4}	8.1×10^{-4}	4.8×10^{-4}	4.02×10^{-4} (u)
2.00×10^{-3}	1.5×10^{-3}	2.5×10^{-3}	6.32×10^{-4}
3.00×10^{-3}	2.2×10^{-3}	1.9×10^{-3}	9.17×10^{-4}
5.00×10^{-3}	3.2×10^{-3}	3.8×10^{-3}	14.2×10^{-4}
7.00×10^{-3}	4.0×10^{-3}	4.1×10^{-3}	20.2×10^{-4}
9.00×10^{-3}	5.0×10^{-3}	5.0×10^{-3}	27.9×10^{-4}
2.00×10^{-2}	8.3×10^{-3}	7.3×10^{-3}	64.2×10^{-4} (s)

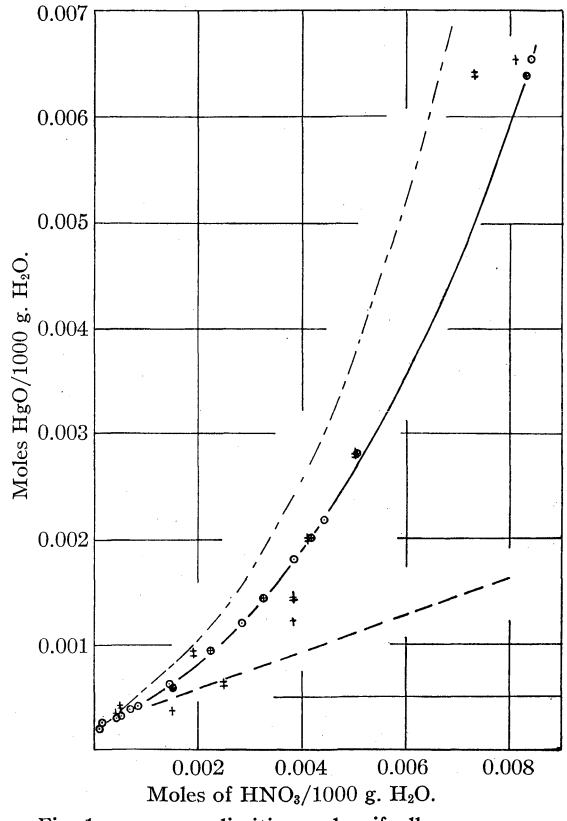


Fig. 1.— — - —, limiting value if all mercury were in the form Hg^{++} as indicated by equation (3); — — —, amount of $Hg(OH)^+$ present; ‡†, glass electrode values; ⊙, calculated values from K_2 and K_3.

and

$$m_{Hg^{++}} = K_3 \frac{m^2_{H^+}\gamma^2_{H^+}}{\gamma_{Hg^{++}}} \times \frac{1}{a_{H_2O}}$$

Then

$$S_{HgO} = m_{Hg(OH)_2} + K_2 \frac{m_{H^+}\gamma_{H^+}}{\gamma_{Hg(OH)^+}} + K_3 \frac{m^2_{H^+}\gamma^2_{H^+}}{\gamma_{Hg^{++}}} \times \frac{1}{a_{H_2O}} \quad (5)$$

which can be simplified to the following equation with the aid of the relationship of activity coefficients referred to above and also assuming $\gamma_{H^+}/\gamma_{Hg(OH)^+} = 1$ at low and moderate values of the ionic strength.

$$S_{HgO} = m_{Hg(OH)_2} + K_2 m_{H^+} + K_3 m^2_{H^+} \left(\frac{1}{\gamma^2_{HNO_3}}\right)\left(\frac{1}{a_{H_2O}}\right) \quad (6)$$

The terms in parentheses (equation 6) can be evaluated from reliable data[3] and from Raoult's law, respectively.

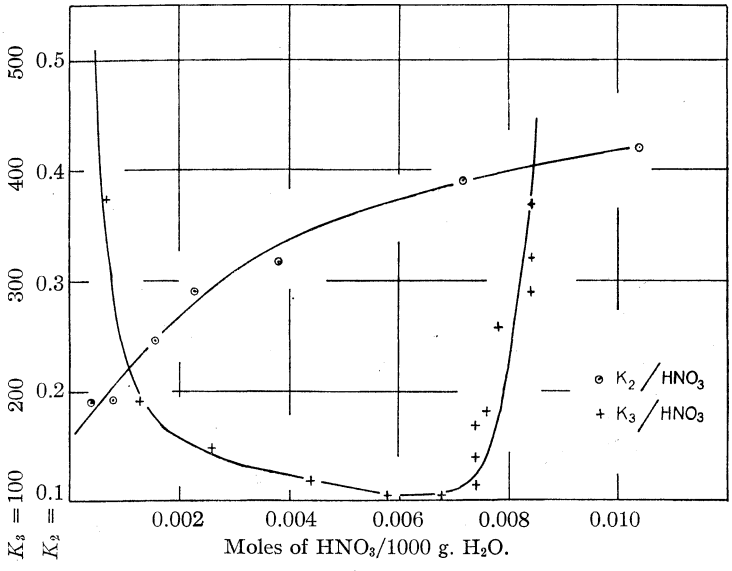


Fig. 2.

The values of K_2 and K_3 were first determined by assuming as first approximation that reactions (2) and (3) proceed to the same extent; the acid concentrations were corrected for the amount used in the reactions with HgO; K_2 and K_3 were then evaluated by solution of simultaneous equations (using equation 6). This procedure was repeated until constant values of K_2 and K_3 were obtained. As a critical test of this method, this whole procedure was again repeated on the assumption that reaction (2) was the only effective reaction and the value of the acidity was corrected accordingly. This method gave approximately the same values of K_2 and K_3 as the first procedure.

An indication of the limiting value of K_2 and K_3 was obtained by the independent calculation of K_2 and K_3 assuming, in the calculation of K_2, that reaction (3) did not take place, and, in the calculation of K_3, that reaction (2) did not take place. These values of K_2 and K_3 were then plotted against the concentration of acid (see Fig. 2). It is obvious that at low concentrations the ratio of K_2/m_{HNO_3} should be constant. Extrapolation of the K_2/m_{HNO_3} graph indicates a value of $K_2 > 0.1$ and < 0.2 at $m_{HNO_3} = 0$. This justifies the magnitude of the value of $K_2 = 0.17$ determined by the method of approximations described above. The value of K_3 could not be determined graphically as readily as that of K_2 due to an apparent theoretical buffering action occurring at approximately $m_{HNO_3} = 0.008$ (see Fig. 2). This graph does indicate the limits of acid concentration through which the value of K_2 and K_3 can be calculated reliably; furthermore, it suggests a limiting value in the magnitude of 100 for K_3 which is in agreement with the value of $K_3 = 53$ from the method of approximations. Additional information given by Fig. 2 is the fact that the drift in the values of K_2 and K_3 indicates clearly that neither reaction (2) alone nor reaction (3) alone is sufficient to account for the solubility of mercuric oxide in nitric acid. The alternative is that the dissociation of mercuric hydroxide must be a stepwise dissociation process; such a process was suggested by Kolthoff,[4] who observed from data in cell reactions that "Wanneer nu de dissociatie van het kwikhydroxyde totaal volgens folgende vergelijking plaats had: $Hg(OH)_2 = Hg^{++} + 2OH^-$, zou $[Hg^{++}] = {}^1/_2[OH^-]$ zijn.

"Uit de genoemde waarden blijkt daarentegen, dat $[Hg^{++}]$ veel kleiner is, en dat de dissociatie, die wel is waar zeer gering is, hoofdzakelijk a.v. plaats heeft: $Hg(OH)_2 = Hg(OH)^+ + OH^-$."

"If now the total dissociation of $Hg(OH)_2$ took place according to the following equation $Hg(OH)_2 \rightleftarrows Hg^{++} + 2OH^-$ then $[Hg^{++}]$ should be equal to ${}^1/_2(OH)^-$ but from the values given it is evident on the other hand that the Hg^{++} is much

(3) Abel, Redlich and Lengyel, *Z. physik. Chem.*, **132**, 189 (1928).

(4) Kolthoff, *Chem. Weekblad*, **14**, 1016 (1917).

smaller and that the dissociation, which is probably very small, takes place chiefly as follows

$$Hg(OH)_2 \rightleftharpoons Hg(OH)^+ + OH^-$$

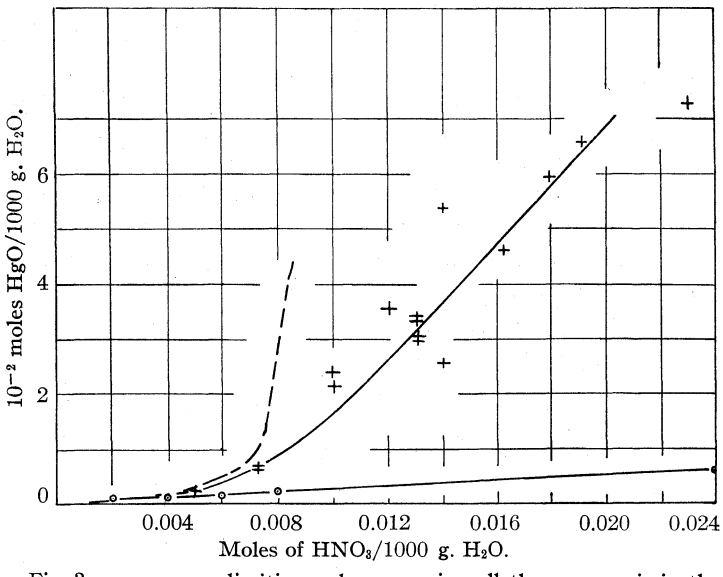


Fig. 3.— — — — , limiting value assuming all the mercury is in the form of Hg^{++} [see equation (3)]; +, glass electrode values; ⊙, values from concentration of standard acid with which the samples were made up.

Our method of treatment of the data, however, gives *direct* evidence of a stepwise dissociation process for bases. Figure 1 shows the agreement between the calculated values of nitric acid and those measured by means of the glass electrode. This graph also shows the limiting value of m_{HgO}/m_{HNO_3} assuming that all of the mercuric oxide may be in the form Hg^{++}. Figure 3 gives a similar comparison of this limiting value with that obtained by glass electrode measurements at higher concentrations. These graphs (Figs. 1 and 3) are direct evidence of the fact that mercuric hydroxide dissociates in a stepwise manner.

The calculated values of nitric acid (calculated from K_2 and K_3) show excellent agreement with the glass electrode values to m_{HNO_3} = 0.008 (see Fig. 1). Efforts to obtain values of K_2 and K_3 to fit the curve above this value were fruitless. This may be due to too small a value of K_3—however, a larger value of K_3 disturbed the agreement of the data at the low concentration where the limiting law would be most applicable. It may well be assumed that above $m_{HNO_3} = 0.008$ the solubility of the mercuric oxide becomes so high that the activity coefficient relationship[2] used to simplify the expression for K_3 is no longer valid; also the assumption that the ratio $\gamma_{H^+}/\gamma_{Hg(OH)^+} = 1$ may not be valid in this high solubility range. If, however, the lack of fit is due to an incorrect value of K_3, it can be observed here that the value of K_3 *could not* be greater than 100 nor less than 53. We believe the former reason is the more probable explanation.[5]

The values of K_2 and K_3 can be converted to the respective ion products and ionization constants by the use of the ion product of water and the value of $a_{Hg(OH)_2} = 2.4 \times 10^{-4}$ (see Ref. 1), and will give the following values for the reactions

$$Hg(OH)_2 \rightleftharpoons Hg(OH)^+ + OH^- \quad (4)$$
$$K_4 = a_{Hg(OH)^+} a_{OH^-} = 1.7 \times 10^{-15}$$

and

$$K_4' = \frac{a_{Hg(OH)^+} a_{OH^-}}{a_{Hg(OH)_2}} = 7.1 \times 10^{-12}$$

and

$$Hg(OH)_2 \rightleftharpoons Hg^{++} + 2OH^- \quad (5)$$
$$K_5 = a_{Hg^{++}} a_{OH^-}^2 = 5.3 \times 10^{-27}$$

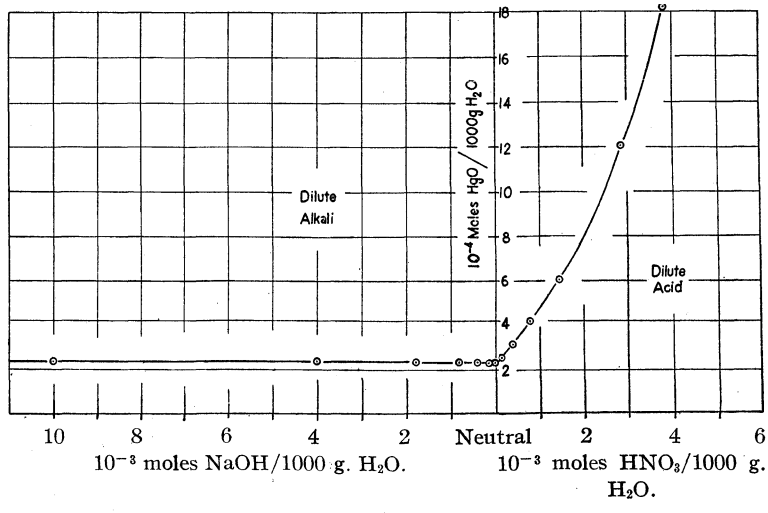


Fig. 4.

and

$$K_5' = \frac{a_{Hg^{++}} a_{OH^-}^2}{a_{Hg(OH)_2}} = 2.2 \times 10^{-23}$$

(5) Another possible explanation is that another equilibrium may be involved in addition to those considered here. This is possible due to the notoriously unpredictable characteristics of mercury compounds. The more probable explanation, however, lies in the uncertainty of the value of the activity coefficients.

The corresponding values calculated by Kolthoff at 18° are

$$K_4' = 5.35 \times 10^{-11}$$
$$K_5' = 7.38 \times 10^{-23}$$

An interesting fact with respect to mercuric oxide is that the position of minimum solubility appears to be that in water solution (see Fig. 4 which includes data given by Garrett and Hirschler[1]). This is to be expected since Kolthoff has indicated that the *p*H of water solutions of mercuric oxide at 18° is approximately 7.2. It is also to be observed that the value[1] of K_6 for the reaction

$$H_2HgO_2 \rightleftharpoons H^+ + HHgO_2^- \qquad (6)$$

is

$$K_6 = 1.4 \times 10^{-15}$$

and the ion product is 3.4×10^{-19}; while the value of K_4' for the reaction

$$Hg(OH)_2 = Hg(OH)^+ + OH^- \qquad (4)$$

is

$$K' = 7.1 \times 10^{-12}$$

and the ion product is 1.7×10^{-15}. The similar magnitude of K_4' and K_6 and of the ion products of these two reactions is further evidence of a nearly neutral hydroxide and therefore one which would be expected to give its minimum solubility at approximately *p*H = 7. In fact both the m_{H^+} and the m_{OH^-} contributed by the mercuric hydroxide are less than the concentration of these ions produced by water; however, the $m_{OH^-} > m_{H^+}$. This indicates the minimum solubility might be expected to be slightly on the basic side. These very low values of m_{H^+} and m_{OH^-} contributed by the dissociation of mercuric hydroxide serve to explain the fact that the conductivity of aqueous solutions of mercuric oxide is about that of the solvent itself.

The character of the solid phase was established by analysis for the nitrate ion and for the mercury content, respectively. This was particularly necessary at the high acid concentration where one might expect basic salt formation. The solid phase was separated from the mother liquor by filtration; it was washed quickly in the filter crucible with two small portions of water to remove adsorbed nitric acid and analyzed with standard potassium iodide solution. All samples except one analyzed to mercuric oxide and gave negative nitrate tests.

Summary

The solubility of mercuric oxide has been determined in nitric acid solutions ranging from 0.00005 to 0.16 molal. The constants for the dissociation of mercuric hydroxide have been evaluated from these data. The values of these constants are in good agreement with the fact that mercuric hydroxide solutions have a very low conductivity and give a *p*H value of approximately 7. They are also in agreement with similar constants obtained from e. m. f. measurements (Kolthoff). The data indicate that the minimum solubility is in water solutions, that mercuric hydroxide dissociates in a stepwise manner, and that the H^+ and OH^- contributed by mercuric hydroxide in water solution are less than those contributed by the solvent.

COLUMBUS, OHIO RECEIVED APRIL 26, 1939

[CONTRIBUTION FROM RESEARCH LABORATORIES, SHAWINIGAN CHEMICALS, LTD.]

The Viscosity Function. II.[1] Viscosity and Constitution

BY ERNEST P. IRANY

The graphical method of analyzing viscosity data by means of functional viscosity scales has revealed a great number of general regularities in the dependency of viscosity on temperature, volume (ideal dilution) and pressure. One may reasonably expect some relation between viscosity and chemical constitution to be derivable by the same or analogous means.

However, before this can be attempted it is important to realize the difficulties arising from the uncertainty which still surrounds the concepts to be dealt with. We are not yet able to define the liquid state or to recognize the real meaning of constitution within it. Molecules, as described by their chemical formula, exist in gases but not in the crystal lattices of solid bodies; all that can be said about liquids is that their molecules must be in some intermediate condition: neither as mobile and independent as in gases nor as fixed and diffused as in solids. Precisely what

(1) The first paper on the subject appeared in THIS JOURNAL, **60**, 2106 (1938).

the physical units of liquid constitution are—single molecules, more or less permanent and more or less well-defined groups of molecules, or even some kind of organized structure—remains a matter of speculation.

Association, Intermolecular Forces.—When considering the existence in liquids of units composed of several molecules or molecular structures of some kind, strong binding forces must be assumed. The problem of viscosity now divides itself, for, should viscosity be correlated with the intensity of these intermolecular forces or with the association of molecular volumes which they may bring about? The forces as well as the volumes partake of constitution, whatever it be.

This distinction is very decisive for the approach to the problem of constitutional viscosity. Most modern authorities still prefer to connect viscosity with variously defined additive volumes or weights which are held to be a property of certain atoms or atomic groups. Often the disregard of the intermolecular forces is very explicitly stated.[2] However, as shown in the following, volume or weight association of the physical units does not as such provide a valid interpretation of constitutive viscosity.

Association Factors.—The paraffin hydrocarbons are known to be "non-polar" or "non-associated"—in their case the controversial aspects of constitution are absent. They are available in a very long and unbroken series of homologs and, as a matter of course, they are always chosen as the first objects of study in the verification of a new rule of constitutional additivity. It is mostly very easy to show regular increments in no matter what terms, but agreement usually fails as soon as the new formula is applied to other types of liquids which, presumably, are more "polar" or "associated." If the latter view is adhered to, agreement with facts may be enforced by specifying "association factors" which are supposed to denote a bodily enlargement of the molecular unit. These factors disagree widely, depending on their source; whether they possess real significance or whether they merely reflect the inadequacy of the original premises can only be decided by independent evidence.

Such proof can be found in the viscosity–temperature functions of polar as well as non-polar liquids of various types. If represented in the functional ϕ scale, all appear as perfectly straight lines. This accord in linearity can only mean that all liquids except some, such as the lower alcohols and fatty acids, are either non-associated or that their state of association is entirely independent of temperature. The suggested association factors are fractional numbers, indicating the liquids to be mixtures of several species of multiple molecular size; that such equilibria should be unaffected by large temperature changes is, however, barely conceivable. Hence: *The association factors as deduced from empirical rules of constitutionally additive viscosity are not real; most liquids are not associated and the rules thus amended are wrong.*

If, then, association of molecules does not suffice to explain liquid constitution in its relation to viscosity, the whole basis must be altered. The intermolecular forces must be included in the concept of constitution, without implying that they actually cause associative combinations. These forces, the resultants of equilibria within the molecules, cannot be computed—least of all as mere sums of some atomic constants. However, where variable association occurs, it can be recognized by the graphical method of functional scales; it reveals itself in deviations from linearity.

The Equation of the Liquid State.—The explicit mathematical or graphical statement of nature and physical behavior of a liquid would be its equation of state. Without argument on its exact form, it may be said that this basic function correlates the three variables of condition—volume, pressure and temperature; it must contain general constants and also various specific material constants—parameters in which the nature of the substance, in other words, its constitutive elements, are expressed. Among the latter the regularities must be detected which govern viscosity.

The three viscosity functions (that of volume (dilution), that of temperature and that of pressure) are, in combination, a complete expression of the equation of state in parameter form. The functional scales employed in the graphical method of generalization are common to all normal liquids and, hence, embody the general constants of the equation of state; the individually descriptive constants must appear as intercepts or gradients of the straight lines which record and distinguish the function of each substance. The

(2) Bingham, "Fluidity and Plasticity," 1922, p. 148, etc.; McLeod, *Trans. Faraday Soc.*, **21**, 151 (1925); Staudinger and Heuer, *Ber.*, **63**, 222 (1930).

question now arises as to how many of these constitutive elements of viscosity are necessary and sufficient.

Number of Material Factors.—One given viscosity measurement determines one point in each of the three functional diagrams; in order to determine a line, another point must be given in each figure—which brings the total to four (Fig. 1). However, two of the functional scales—that of ideal mixture (volume) and that of temperature—are identical; in other words, volume and temperature are of the same relevance with respect to constitution. (The temperature function may be considered a special case of dilution, *i. e.*, with a solvent of no viscosity or a void.) Accordingly, the number of independent constitutional factors reduces from four to three.

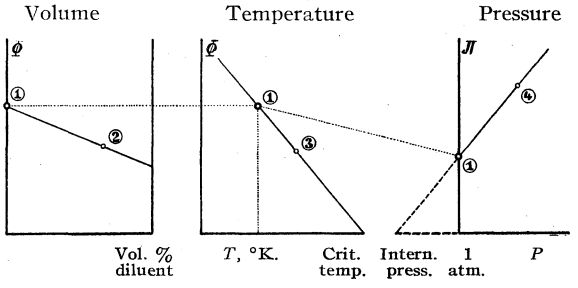


Fig. 1.—Constitutive parameters of the viscosity functions.

The viscosity of liquids is not appreciably affected by pressures of several atmospheres. It is entirely correct to assume that, ordinarily, viscosity measurements are compared under strictly "corresponding" conditions with regard to pressure—at the external pressure nil. This dispenses with another material constant, leaving only two. Further simplification is not possible. Hence: *No rule of constitutive viscosity can be generally valid unless it postulates two independent parameters of different computation.*

To recognize the necessity of two constitutional constants is one step, but to define them in such a way that they become additive in terms of atomic values is another, far more difficult one, which cannot be attempted here. This problem is most complex with the most simple chemical compounds because among them every structural difference is large enough to obscure all physical relationship. Additive increments can only be expected in certain series of homologous substances in which the intermolecular forces are either negligible or constant for all members: for example, (a) homologous series of non-polar substances, (b) polymer-homologous series of substances which are composed of a large and variable number of identical polar groupings.

The former are represented by the normal paraffin hydrocarbons, the latter by various polyvinyl derivatives. In both cases one of the two constitutive parameters becomes a serial constant; the other is, therefore, uniquely descriptive of the individual member and additive in any terms of structure, such as molecular volume, molecular weight, number of constituent groupings, degree of polymerization—all of which become synonymous. It must be kept in mind, however, that this final simplification applies only within series of the above description; the absence of this limitation is the common error which invalidates the numerous single-parameter rules of additive viscosity and the supplementary association factors.

Paraffin Hydrocarbons.—If the viscosities are plotted in ϕ scale against reduced absolute temperatures, T/Θ,[1] (Fig. 9) the lines of the members of this series coincide almost completely. Hence, $\phi = CT/\Theta$, where C is a serial constant, and Θ, the critical temperature, appears as the constitutive parameter. The problem resolves to that of the critical temperature and its additivity; reversely, the critical temperature of a hydrocarbon can be computed from a single viscosity measurement. That the whole series—though not absolutely "non-polar"—is distinguished by very weak intermolecular forces which are the same for each member, can be proved in the functional viscosity–pressure diagram (II scale); the extrapolated internal pressures have a constant value of about 1200 kg./cm.^{2} (Fig. 11[1]).

Polymer Homologs.—Since most of these substances are high-molecular colloids, the distinction by critical temperatures is meaningless; the constitutive parameters must be defined

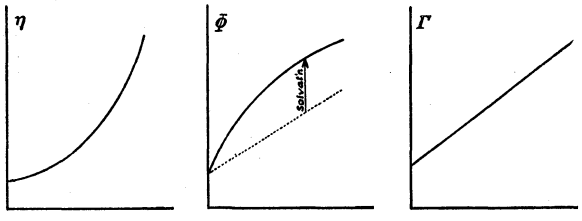


Fig. 2.—Polyvinyl acetate solution.

through the viscosity–concentration function of solutions. The series of polyvinyl acetates may serve as an example.

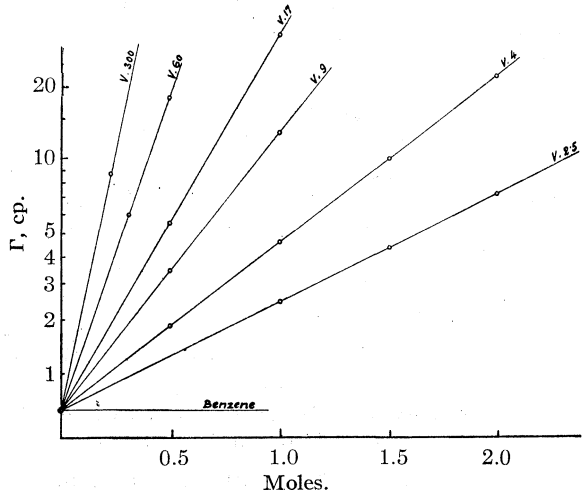


Fig. 3.—Polyvinyl acetates, benzene solutions.

If the viscosities of polyvinyl acetate solutions are plotted in ϕ scale against concentration, no straight lines appear, but curves whose trend indicates strong associative or solvating effects between solute and solvents of various description (Fig. 2). Since all polyvinyl acetates consist of regularly repeated identical groupings, the disposition of their intermolecular forces must be the same and characteristic of the whole series. The polar effects which cause the deviations from linearity in the ϕ scale diagram can, therefore, be expressed as a single serial constant which may be incorporated into the viscosity scale. This can be done by the same graphical method as that applied in the construction of the ϕ scale itself (Fig. 2[1]), except that in the present case not an "ideal" mixture but, specifically, a polyvinyl acetate solution is used as a standard. The resulting viscosity scale Γ embodies the serial polarity as well as the concentration effects of *all* polyvinyl acetates in a given solvent, *e. g.*, benzene (Fig. 3). The lines shown in the diagram are perfectly straight and differ only in their gradients; the latter represent the individual constitutive parameter—the degree of polymerization.[3]

Analogous viscosity scales can be constructed for other solvents, such as ethyl acetate, butyl acetate, pyridine, dioxane, chloroform, tetrachloroethane, acetic acid. In each case accurate linearity for polyvinyl acetates of every degree of polymerization is obtained. These scales are, by precept, specific for each solvent. However, it is most significant that, actually, a majority of them have been found one and the same. It must be concluded that all solvents of this group induce the same state of solvation, that they respond to a certain normal polarity of the solute, revealing a characteristic regularity in the associative tendencies of polyvinyl acetates.

If the gradients of the lines in the various diagrams represent, as concluded, the respective degrees of polymerization, they should appear in proportions fixed by the nature of the samples. That this is true with the greatest precision is

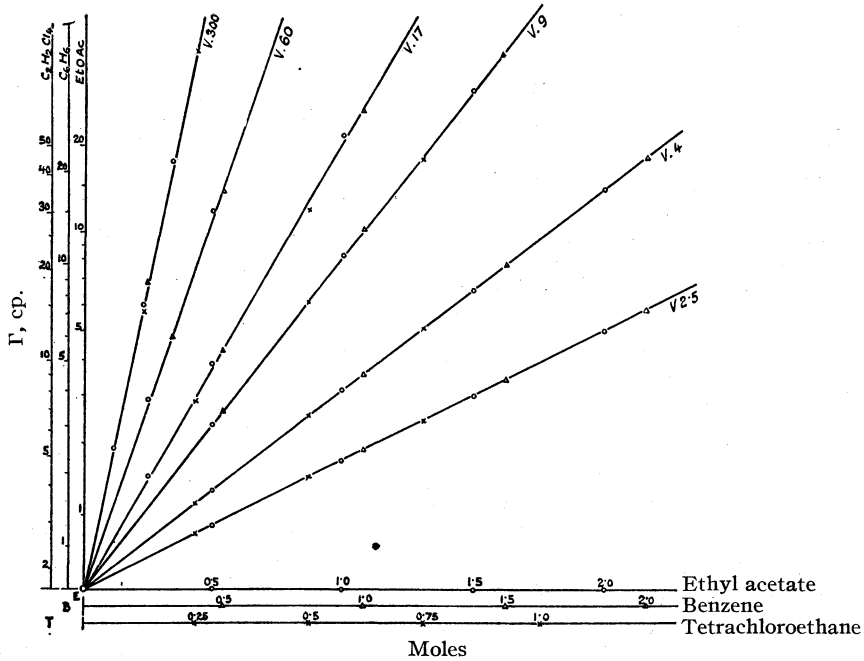


Fig. 4.—Polyvinyl acetates (Gelva).

(3) Polyvinyl acetates ("Gelva," manufactured by Shawinigan Chemicals, Ltd.) are mixtures of high and low polymers over a wide range. The mean degree of polymerization is indicated in the figures by "V ..." which is the viscosity of the sample in one-molar (86 g./l.) benzene solution at 20°.

shown in Fig. 4, where the viscosities of one specimen ("V.4") in three solvents, *viz.*, ethyl acetate, benzene and tetrachloroethane, are plotted on the same straight line. The origin of this line represents the viscosities of the respective pure solvents, and the scales are adjusted accordingly. As a result, the lines of the three solutions of each sample coincide; the complete Γ diagrams of ethyl acetate, benzene and tetrachloroethane solutions of polyvinyl acetates register exactly when superimposed. Hence, the gradients are independent of the solvent but descriptive of the solute.

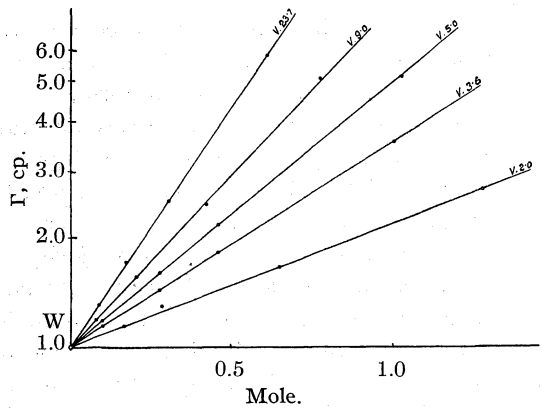


Fig. 5.—Polyvinyl alcohols in water.

That the same regularities exist in the solutions of all true polymer homologs can be shown by many other examples, such as the water-soluble polyvinyl alcohols (Fig. 5),[4] the polyisobutylenes (Fig. 6),[5] various cellulose derivatives (Fig. 7). All these substances give linear concentration functions in their own characteristic viscosity scales which compensate for association and solvation effects common to all members. In some series these effects are absent; they, therefore, appear linear in the ideal ϕ scale. Examples of these are indene resins, toluene sulfonamide resins, colophony, chlorinated diphenyl resins, etc. (Fig. 8). In order to illustrate the deviations of the specific Γ scales from ideality, an ideal mixture is plotted in the diagrams which appears strongly curved in all cases except Fig. 8.

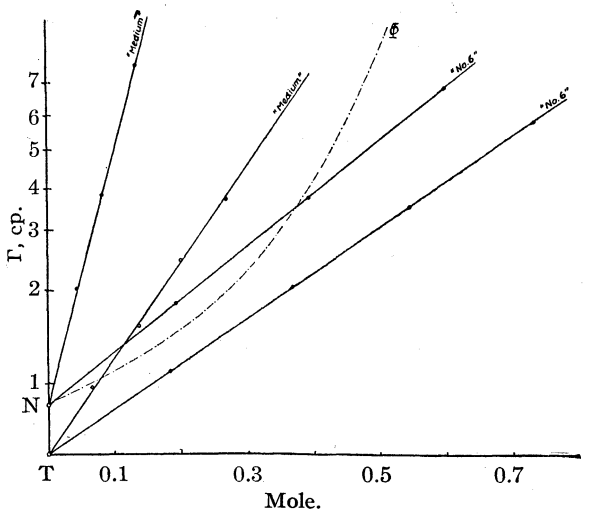


Fig. 6.—Poly-butylenes ("Vistanex") in V. M. naphtha (N) and in toluene (T).

Molecular Weights.—That the gradients of the lines in the Γ diagrams appear in the proportions of the molecular weights of the solutes can be made clear by analogy to Staudinger's "viscosity law."[6] The latter is based upon a formula by Einstein[7] which expresses the viscous resistance in an ideal case—that of spherical, rigid and non-polar particles dispersed in a viscous liquid—but without assumption of mutual attractions. Because of the disregard of the latter, the formula is not applicable to real solutions, but under

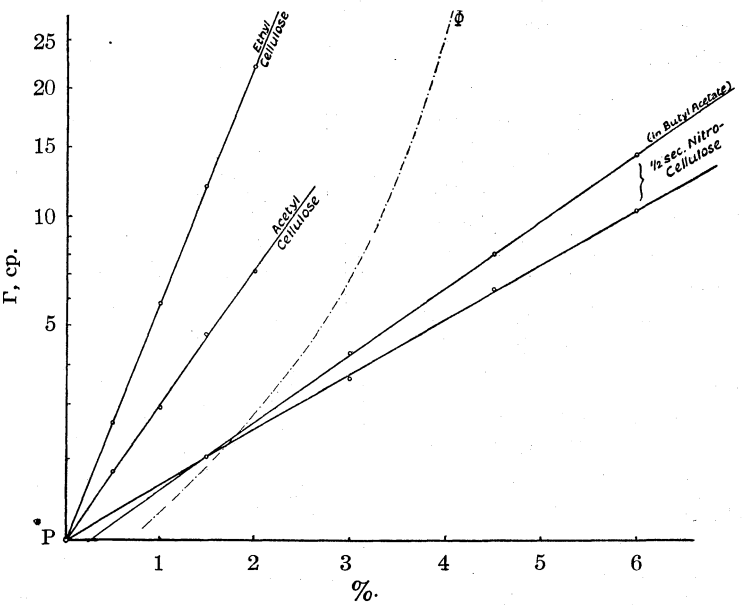


Fig. 7.—Cellulose derivatives in pyridine.

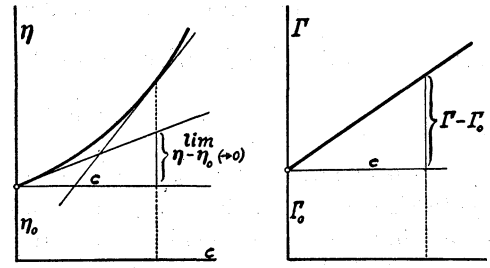
(4) "Solvar" (Shawinigan Chemicals, Ltd.).
(5) "Vistanex" (Advance Solvents & Chemical Corp.).
(6) Staudinger, "Die hochmolekularen Verbindungen," Verlag J. Springer, Berlin, 1932.
(7) Einstein, *Ann. Physik*, **19**, 289 (1906).

the limitation of minimum concentration, Staudinger transformed it into

$$\eta_{sp} = \lim_{c=0} \frac{\eta - \eta_0}{\eta_0} = K_m Mc \qquad \lim_{c=0} \frac{\eta - \eta_0}{c} = (\eta_0 K_m) M$$

where η_{sp} is termed "specific viscosity," K_m is a constant valid for a given polymer-homologous series in a given solvent, M the molecular weight and c the concentration.

In a diagram where absolute viscosity is plotted against concentration, the term $(\eta - \eta_0)/c$ appears as the gradient of the curve in the vicinity of the origin (Fig. 9). The same figure, drawn in Γ parallel to the viscosity axis, the intercepts on it are in proportion of the molecular weights of the solutes, or, more correctly, their individual constitutive parameters which may be expressed equally well in terms of molecular weights, volumes, chain lengths, number of constituent units, etc.



Staudinger's law. Gamma function.

Fig. 9.—Molecular weight of polymer homologs.

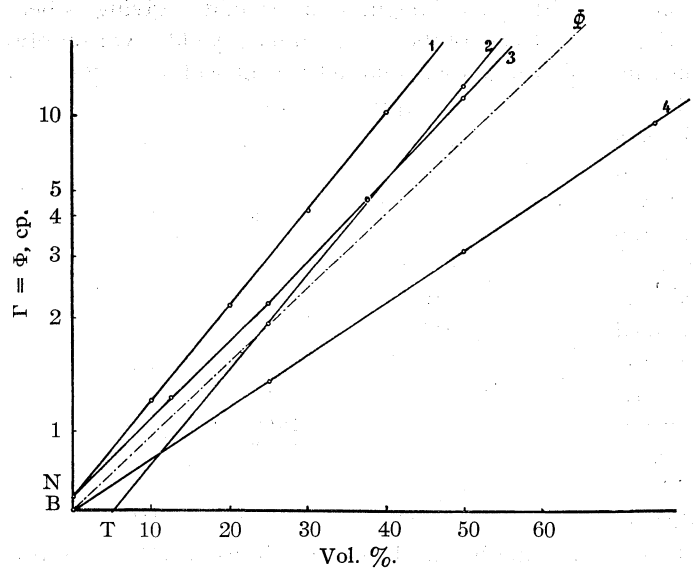


Fig. 8.—No solvation: 1, indene resin (Nevindene) in butyl acetate; 2, toluene sulfonamide resin (Santolite MHP) in toluene; 3, rosin in butyl acetate; 4, chlorinated diphenyl (Aroclor) in V. M. naphtha.

scale, represents the curve as a straight line of constant gradient; there is no need to limit the rule to low concentrations. Accepting the reasoning that led from Einstein's formula to that of Staudinger as substantially correct, the substitution of Γ for η would, according to definition, compensate for the effects of intermolecular forces at *any* concentration

$$\Gamma_{sp} = \frac{\Gamma - \Gamma_0}{\Gamma_0} = K_m Mc$$

Γ_{sp}/c, now to be termed "specific viscosity function," is the gradient of the straight line in the Γ diagram. In other words, if a line is drawn

Summary

Graphical analysis of viscosity data shows that most pure chemical compounds are unassociated in the liquid state. The association factors which, while derived from empirical rules of constitutionally additive viscosity, are necessary to uphold their validity, have no meaning.

It can be proved that the general viscosity function contains not less than two independent constitutive parameters. It therefore appears impossible to specify single atomic constants supposed to be additive in terms of viscosity.

The best approach to the problem is not through the study of the most simple chemical compounds, but that of truly polymer-homologous series of high-molecular substances. In the latter case, one parameter, expressing the polar character common to all members of the series, is constant and the second parameter becomes constitutionally additive. This has been proved by graphical evidence on various such series.

The method of analysis is an extension of the principle of the functional viscosity scales reported in a preceding paper to which reference is made.

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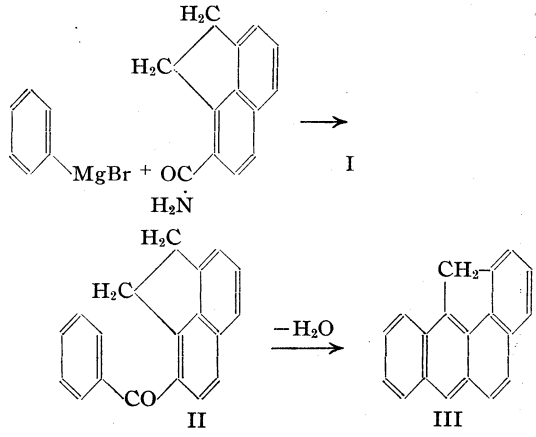
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Synthesis of 1′,9-Methylene-1,2-benzanthracene and Related Hydrocarbons

BY LOUIS F. FIESER AND JAMES CASON[1]

It seemed of interest for a number of reasons to synthesize 1′,9-methylene-1,2-benzanthracene (III) and investigate its chemical properties and possible biological actions. Like the as yet unknown[2] 1′,9-dimethyl compound, the hydrocarbon may constitute a simplified model of the highly reactive and powerfully carcinogenic 3,4-benzpyrene, and the presence of a methylene group at the meso position 9 may confer upon the substance some of the special properties of the cholanthrenes[3] or of 8,9-dimethylene-1,2-benzanthracene.[4] It is also interesting to learn whether the 1′,9-methylene derivative, considered as a simple alkylated 1,2-benzanthracene, is associated in biological properties with the moderately carcinogenic[3] 9-methyl compound[5] or with the inactive[3] 1′-methyl derivative.[2,6] While 1′,9-methylene-1,2,5,6-dibenzanthracene[7] gives a moderate yield of tumors in mice only after a very extended induction period,[3] the relationship between the inactive 9,10-dimethyl-1,2,5,6-dibenzanthracene[8] and the highly potent 9,10-dimethyl-1,2-benzanthracene[9] suggests that the simpler 1′,9-methylene compound is well worthy of investigation.

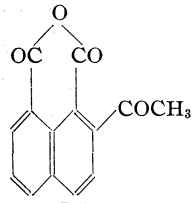
One possible route to the desired hydrocarbon involved the synthesis and pyrolysis of 1-benzoylacenaphthene (II). A small quantity of this ketone was obtained in preliminary work by M. E. Gross from 3-acenaphthylmagnesium iodide and benzonitrile, but this route was temporarily abandoned because of the difficulty of obtaining adequate quantities of the required 3-iodoacenaphthene from the rather inaccessible 3-nitro compound (literature, ref. 7). The situation is considerably altered, however, by the recent observation that 3-acetoacenaphthene can be prepared very easily by the acetylation of the hydrocarbon in the presence of anhydrous hydrogen fluoride.[10] In a large-scale preparation the yield of satisfactory 3-isomer was 29%, and the hypohalite oxidation to 3-acenaphthoic acid proceeded very smoothly. In one trial the Friedel and Crafts condensation of the acid chloride with benzene took an abnormal course and gave a sparingly soluble yellow product. The amide (I), obtainable from the acid with little loss, condensed very smoothly if slowly with phenylmagnesium bromide, giving 1-benzoylacenaphthene (II) in 95% yield. On pyrolysis the ketone suffered loss of water at 425° and



1′,9-methylene-1,2-benzanthracene (III) was isolated in a satisfactory condition in 13% yield. The Elbs reaction proceeds about as expected, the difficulty of ring closure into a benzenoid nucleus being offset by the favorable utilization of a methylene group of an alicyclic ring. The hydrocarbon (m. p. 123°) has a faint greenish-yellow color which was retained on purification through the picrate, by chromatographic adsorption, and treatment with maleic anhydride. Like methylcholanthrene and 3,4-benzpyrene, and in contrast to 1′,9-methylene-1,2,5,6-dibenzanthracene, it couples rapidly (deep color in five minutes) with *p*-nitrobenzenediazonium chloride in acetic acid solution.[11] The hydrocarbon is attacked rather readily by lead tetraacetate and apparently is converted into a mixture of products. The condensation with methylformanilide was tried with unpromising results, for at 0° a part of the material was recovered unchanged and a part converted into tars.

(1) Research Fellow on funds from the National Cancer Institute.
(2) Fieser and Seligman, THIS JOURNAL, **60**, 170 (1938).
(3) Review paper: Fieser, *Am. J. Cancer*, **34**, 37 (1938).
(4) Fieser and Seligman, THIS JOURNAL, **57**, 2174 (1935).
(5) Newman, *ibid.*, **59**, 1003 (1937); Cook, Robinson and Goulder, *J. Chem. Soc.*, 393 (1937).
(6) Cook and Robinson, *ibid.*, 505 (1938).
(7) Fieser and Hershberg, THIS JOURNAL, **57**, 1681 (1935).
(8) Cook, *J. Chem. Soc.*, 489 (1931); Akin and Bogert, THIS JOURNAL, **59**, 1564 (1937).
(9) Bachmann and Chemerda, *ibid.*, **60**, 1023 (1938); Newman, *ibid.*, **60**, 1141 (1938).
(10) Fieser and Hershberg, *ibid.*, **61**, 1272 (1939).
(11) Fieser and Campbell, *ibid.*, **60**, 1142 (1938).

In preparing the starting material some further study was made of the reaction between acenaphthene and acetic acid in the presence of hydrogen fluoride. The yield and the ratio of isomers was the same when acetyl chloride was used in place of the free acid. It was ascertained also that neither 1- nor 3-acetoacenaphthene suffers rearrangement under the conditions of the acylation. 3-Acetoacenaphthene picrate was found to exist in two polymorphic forms of the same melting point, one separating as orange prisms and the other appearing as yellow needles. 1-Acetoacenaphthene was converted into two new reference compounds of the naphthalene series. Oxidation with sodium dichromate in acetic acid solution gave 2-aceto-1,8-naphthalic anhydride (IV), and



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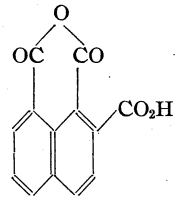
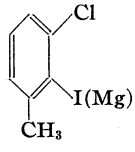


V

oxidation of 1-acenaphthoic acid by the same method gave 2-carboxy-1,8-naphthalic anhydride (V).

Some further synthetic experiments may be reported. A satisfactory procedure was worked out for the preparation of 2-iodo-3-chlorotoluene (VI) from 2-iodo-3-nitrotoluene and attempts were made to condense the Grignard reagent from the dihalide with β-acetonaphthalene, in the hope of



VI

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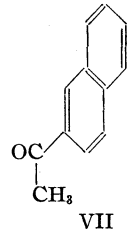
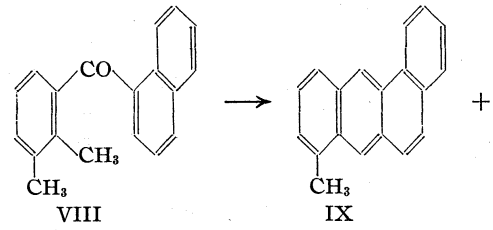


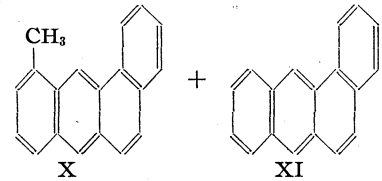
VII

obtaining a ketone which might be convertible into 5,10-dimethyl-1,2-benzanthracene[12] by the synthetic method employed for the 3,9-isomer.[13] The reaction proceeded very poorly and the small amount of product obtained after dehydration contained considerably less than the expected amount of chlorine and could not be hydrogenated. Condensation with β-naphthonitrile also gave poor results, and the difficulty is thus attributable to the hindered character of the more reactive halogen substituent, and perhaps to the opportunity for some interaction with the *o*-chloro atom.

As a possible route to the known 5-methyl-1,2-benzanthracene,[12,14,15,16] *vic.*-*o*-xylyl α-naphthyl ketone (VIII) was synthesized from *vic.*-cyano-*o*-xylene and α-naphthylmagnesium bromide and submitted to pyrolysis at 425–430°. There was

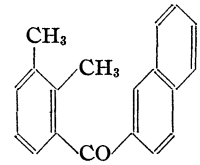


VIII IX

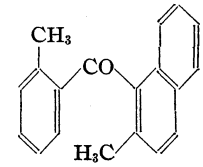


X XI

obtained a mixture of hydrocarbons found to contain the 5-methyl compound IX, the 8-methyl isomer[17] X, and 1,2-benzanthracene (XI). The formation of 8-methyl-1,2-benzanthracene evidently is the result of a rearrangement, presumably involving the migration of the xyloyl group of the ketone VIII from the α- to the β-position in the naphthalene nucleus, as postulated for the formation of 1,2,5,6-dibenzanthracene on pyrolysis of 1-(α-naphthoyl)-2-methylnaphthalene.[18] The isomeric *vic.*-*o*-xylyl β-naphthyl ketone (XII) was prepared for comparison and pyrolyzed.



XII



XIII

The hydrocarbon mixture resulting in fairly good yield was found to consist in large part of 8-methyl-1,2-benzanthracene, identified as the quinone, and no 1,2-benzanthracene was noted. Because of the difficulty of isolating a pure product from the mixture, this is not a practical preparative method. The observation that a methyl group is in part retained at position 8 is of interest because of the contrasting result obtained by

(12) Fieser and Newman, THIS JOURNAL, **58**, 2376 (1936).
(13) Fieser and Seligman, *ibid.*, **61**, 136 (1939).
(14) Cook, *J. Chem. Soc.*, 1591 (1932).
(15) Bachmann and Wilds, THIS JOURNAL, **60**, 624 (1938).
(16) Fieser and Johnson, *ibid.*, **61**, 1647 (1939).
(17) (a) Fieser and Johnson, *ibid.*, **61**, 168 (1939); (b) Cook and Iball, *J. Chem. Soc.*, 270 (1939).
(18) Cook, *ibid.*, 487 (1931).

Cook[18] on pyrolysis of 1-*o*-toluyl-2-methylnaphthalene (XIII). With this ketone, where ring closure involved condensation into a benzenoid nucleus, the sole product was 1,2-benzanthracene. With the isomer XII, in which the more reactive naphthalene nucleus is involved in the cyclization, the pyrolysis proceeds more smoothly, for the second methyl group is largely retained. This is in line with the high yield of 1,2-benzanthracene from *o*-tolyl β-naphthyl ketone,[19] in contrast to the low yield from the isomeric 1-benzoyl-2-methylnaphthalene.[20] The observation that methyl groups in the α-positions 5 and 8 of the benzanthracene system withstand to some extent the drastic conditions of the Elbs reaction substantiates previous comments[21] on the subject.

Experimental Part[22]

1-Acetoacenaphthene was prepared as described[10] from 154 g. of powdered acenaphthene, 65 g. of acetic acid, and 750 g. of anhydrous hydrogen fluoride, allowed to stand in a copper flask for forty-eight hours with occasional stirring. After adding soda solution and benzene, filtering, separating the green benzene layer and distilling, there was obtained 182 g. of total ketone, b. p. 193–195° at 8 mm. Successive crystallizations of the top fraction from 400 cc., 500 cc., and 650 cc. of methanol gave 53 g. of the 1-isomer, m. p. 104–105°, and 4.5 g. more of the pure material was obtained from the final mother liquor; yield 29%.

When acetyl chloride (added slowly) was used in place of acetic acid neither the total yield nor the ratio of isomers was affected. To test the stability of the ketone under the conditions of the acylation, 5 g. of 1-acetoacenaphthene was treated with 200 g. of anhydrous hydrogen fluoride and the solution allowed to stand for forty-two hours. The recovered and distilled product on crystallization from methanol gave 4 g. of starting material, m. p. 104.5–105°, and 0.6 g. of the corresponding picrate, m. p. 114–114.5°, was obtained from the mother liquor.

The picrate crystallized from methanol as light yellow needles, m. p. 114.5–115°.

Anal. Calcd. for $C_{20}H_{15}O_8N_3$: N, 9.88. Found: N, 9.97.

The trinitrobenzene derivative, which is considerably less soluble, formed bright yellow plates from alcohol, m. p. 113.5–114°.

Anal. Calcd. for $C_{20}H_{15}O_7N_3$: N, 10.27. Found: N, 10.12.

3-Acetoacenaphthene was separated as the picrate from the mother liquors from the first two crystallizations of the 1-isomer. After several crystallizations from methanol a total of 39 g. of satisfactory product, m. p. 97–97.5°, was collected. Treated with ammonia, this afforded 16 g. of 3-acetoacenaphthene, m. p. 69–69.5°; after melting and freezing several times the polymorphic form, m. p. 56.5–57.5°, was obtained. The 3-ketone (5 g.) was recovered unchanged (4 g., m. p. 69.2–69.6°) after standing for forty-two hours in hydrogen fluoride solution.

The picrate was found to exist both in the orange-prism form previously described[10] and in the form of long, fine, yellow needles of the same m. p. If the yellow modification is introduced to a bath preheated to 93° it melts at once, but when heated gradually the m. p. is 97–97.5°. The orange picrate separates as cubic or elongated prisms when crystallization occurs at or above room temperature, while the **yellow picrate** crystallizes from a colder, more dilute solution. The transition temperature seems to be about 20–25°. If the temperature is lowered after the orange form has started to separate, yellow needles are deposited from the same solution. The picrates are interconvertible and yield the same ketone.

Anal. (yellow picrate). Calcd. for $C_{20}H_{15}O_8N_3$: N, 9.88. Found: N, 9.75.

2-Aceto-1,8-naphthalic Anhydride (IV).—A mixture of 1 g. of 1-acetoacenaphthene and 8 g. of sodium dichromate in 20 cc. of acetic acid was heated at 55–65° for one hour, boiled for three minutes, and poured (cold) into 100 cc. of water. The tan precipitate was crystallized twice from acetic acid containing a few drops of acetic anhydride (Norite), giving 90 mg. of almost colorless, diamond-shaped plates of the constant m. p. 219–219.3°.

Anal. Calcd. for $C_{14}H_8O_4$: C, 70.00; H, 3.38. Found: C, 69.86; H, 3.54.

1-Acenaphthoic Acid.[10]—A stirred solution of 15 g. of 1-acetoacenaphthene in 300 cc. of dioxane (purified with sodium) was treated in the course of twenty minutes with a hypochlorite solution[23] from 48 g. of HTH, 34 g. of potassium carbonate, 9.6 g. of potassium hydroxide, and 300 cc. of water. After an initial exothermic reaction (to 75°), the temperature was maintained at 60° with stirring for one-half hour (one hour for a 50-g. run). Excess reagent was destroyed with bisulfite, the solution was cooled, diluted with 1 l. of water, filtered from a slight sediment, and acidified. The precipitate was coagulated by boiling, collected and washed; yield, 14.5 g. (95.5%), m. p. 254–256°. No further purification is required for the following reactions.

2-Carboxy-1,8-naphthalic Anhydride (V).—To a solution of 1 g. of 1-acenaphthoic acid in 30 cc. of acetic acid at 90°, 6 g. of sodium dichromate was added gradually at such a rate as to maintain a temperature of 90–95°. After forty minutes at this temperature and boiling for five minutes the solution was poured into 100 cc. of water containing 10 cc. of concentrated hydrochloric acid. After boiling for a few minutes and cooling, the product slowly separated as light yellow crystals (260 mg.). Two crystallizations from acetic acid containing a little acetic anhydride gave colorless plates melting constantly at 297.5–298.5°.

Anal. Calcd. for $C_{13}H_6O_5$: C, 64.46; H, 2.48. Found: C, 64.48; H, 2.65.

The methyl ester, prepared with diazomethane in ether

(19) Bachmann, *J. Org. Chem.*, **1**, 347 (1938); Fieser and Hershberg, THIS JOURNAL, **59**, 2502 (1937).

(20) Fieser and Dietz, *Ber.*, **62**, 1827 (1929).

(21) Fieser and Peters, THIS JOURNAL, **54**, 3742 (1932).

(22) All melting points are corrected. Microanalyses by Lyon Southworth.

(23) Newman and Holmes, *Org. Syntheses*, **17**, 65 (1937).

suspension, crystallized from acetic acid–anhydride as small, nearly colorless plates, m. p. 191–192°.

Anal. Calcd. for $C_{14}H_8O_5$: C, 65.63; H, 3.15. Found: C, 65.80; H, 3.29.

1-Acenaphthoyl Chloride.—The precipitated acid (1 g.) was refluxed with purified thionyl chloride (2 cc.) for two hours, the excess reagent evaporated at reduced pressure, and the solidified residue crystallized from benzene–ligroin (Norite). This gave tan needles, m. p. 109.5–110.5°; yield 0.85 g. (82%). A recrystallized sample melted at 110–111°.

Anal. Calcd. for $C_{13}H_9OCl$: C, 72.02; H, 4.20. Found: C, 71.85; H, 4.40.

When a good grade of commercial thionyl chloride was used without purification with quinoline and linseed oil, both the acid chloride and the amide obtained from it contained impurities which persisted after numerous crystallizations.

On treatment of the acid chloride (3.8 g.) in benzene (30 cc.) with aluminum chloride (2.9 g.) at the refluxing temperature there was obtained a yellow substance which is not altered by prolonged boiling with dilute acid, is sparingly soluble in organic solvents, decomposes above 200°, and leaves an ash on ignition.

1-Acenaphthamide.—The crude acid chloride from 12 g. of 1-acenaphthoic acid was dissolved in 150 cc. of warm dioxane and the solution was added rapidly to 120 cc. of well-stirred, cold, concentrated aqueous ammonia solution. After thirty minutes 500 cc. of water was added, and after stirring for fifteen minutes longer the precipitated amide was collected. The yield of light tan powder melting at 219–222° and suitable for the Grignard reaction was 12 g. (quantitative). A sample recrystallized from alcohol formed colorless, short needles, m. p. 227–228° (constant).

Anal. Calcd. for $C_{13}H_{11}ON$: N, 7.11. Found: N, 6.96.

1-Benzoylacenaphthene.—Ten grams of the solid, precipitated amide was added to the Grignard reagent from 5.1 g. of magnesium and 32 g. of bromobenzene in 200 cc. of ether and the mixture was refluxed with stirring for seventy-two hours. The complex, which separated as a solid, was decomposed with ice (50 g.) and concentrated hydrochloric acid (25 cc.), giving the ketimine hydrochloride as a light yellow solid insoluble in either the water or ether layer. The ether was evaporated and after adding 35 cc. each of concentrated hydrochloric acid, glacial acetic acid and toluene the mixture was refluxed two hours for hydrolysis. The toluene layer was separated, washed with water and bicarbonate solution, dried and distilled. The ketone distilled as a light yellow oil, b. p. 210–215° at 1 mm., which crystallized at once on cooling. The yield of distilled material suitable for pyrolysis was 12.4 g. (95%). A sample crystallized for analysis from methanol formed colorless needles, m. p. 91.5–92°.

Anal. Calcd. for $C_{19}H_{14}O_4$: C, 88.34; H, 5.46. Found: C, 88.02; H, 5.48.

The ketone was also prepared by M. E. Gross starting with 1-nitroacenaphthene (19.8% yield in the nitration), through the amine (88%) and iodide (yield about 45%, in two experiments the material completely decomposed on vacuum distillation). The condensation of benzonitrile with the lithium derivative was tried without success; with the Grignard reagent the yield of distilled ketone was 15%. A purified sample melted at 93–94°, uncorr. (found: C, 88.23; H, 5.32).

1′,9-Methylene-1,2-benzanthracene.—A 9.9-g. charge of distilled 1-benzoylacenaphthene was heated in a bath at 420–425° for forty minutes and the hydrocarbon distilled at 1 mm. and a bath temperature of 250–350°. The solidified distillate was dissolved in 100 cc. of alcohol, 3.5 g. of picric acid was added, and after concentrating to a volume of about 50 cc. there separated on slow cooling 2.75 g. of dark red picrate. A solution of this in 40 cc. of benzene was put through a tower of alumina and the hydrocarbon, which showed a bright blue fluorescence in ultraviolet light, was washed through until a lighter blue fluorescent zone reached the bottom of the tower. The benzene was evaporated and the hydrocarbon was crystallized from 50 cc. of alcohol, giving light yellow plates, m. p. 121.5–122°; yield, 1.2 g. (12.9%). After three further crystallizations the hydrocarbon (0.85 g.) melted at 122.5–123°; a sample which had been crystallized repeatedly as the trinitrobenzene derivative melted at 122.7–123.1°. The purified material (plates) has a faint fluorescent greenish-yellow color not removed by purification as above, crystallization of the picrate, chromatographic adsorption, or treatment with maleic anhydride.

Anal. Calcd. for $C_{19}H_{12}$: C, 94.96; H, 5.04. Found: C, 94.92; H, 5.08.

The **picrate** crystallizes from alcohol in the presence of excess picric acid as dark red needles, m. p. 141.5–142°.

Anal. Calcd. for $C_{25}H_{15}O_7N_3$: N, 8.95. Found: N, 8.51.

The **trinitrobenzene derivative** separates from alcohol in bright orange needles, m. p. 162.5–163°.

Anal. Calcd. for $C_{25}H_{15}O_6N_3$: N, 9.27. Found: N, 9.21.

2-Iodo-3-chlorotoluene.—**2-Iodo-*m*-toluidine** was prepared by the hydrogenation of 2-iodo-3-nitrotoluene (30 g.) in acetic acid (100 cc.) in the presence of Adams catalyst (0.3 g.), absorption being complete in ten hours. The filtered solution was treated with 20 cc. of 12 *N* sulfuric acid and 1 l. of ether and the precipitated salt collected (35.5 g., 94%). For conversion to the amine this salt was dissolved by warming in 400 cc. of water containing 4 cc. of 12 *N* sulfuric acid, the solution was filtered from a little dark material (colorless filtrate), and neutralized carefully at 0° with cold ammonium hydroxide. The amine separated in a colorless, crystalline condition, m. p. 40–40.6° (compare 41–42°[24]); yield 21.7 g. (82% from the nitro compound).

For conversion to the iodochlorotoluene it is best to omit isolation of the amine or its salt. The acetic acid solution from the hydrogenation of 20 g. of the nitro compound was diluted with 290 cc. of water and 58 cc. of concentrated hydrochloric acid and cooled to −5° with stirring. To the resulting suspension of the hydrochloride a cooled solution of 6.3 g. of sodium nitrite in 35 cc. of water was added all at once. After stirring for thirty

(24) Wheeler and Liddle, *Am. Chem. J.*, **42**, 452 (1909).

minutes below 0°, 10 g. of urea was added; after twenty minutes more the cold (unfiltered) solution was added to a stirred solution of 9.1 g. of cuprous chloride in 43 cc. of concentrated hydrochloric acid and 11 cc. of water. The complex began to decompose at once, and a dark oil began to separate. After stirring for one-half hour below 0° and for one hour longer after removal from the cooling bath, the mixture was steam distilled. The heavy oil, which distilled slowly, was extracted with ether, washed with alkali, acid, and water, dried and distilled. This gave a nearly colorless oil, b. p. 123–125° at 14 mm.; yield 14.3 g. (74.5%, from the nitro compound). The product solidified at about 24° and melted at 25.5–26.5°; recrystallized from methanol it formed colorless plates, m. p. 27.3–27.6°.

Anal. Calcd. for C_7H_6ClI: C, 33.28; H, 2.38. Found: C, 33.02; H, 2.64.

Long and Dains[25] report the preparation of the dihalide as a yellow oil which darkened on standing and solidified at −26°.

The dihalide formed a Grignard reagent readily, but no acid was obtained on attempted carbonation with solid carbon dioxide. From the reaction with β-acetonaphthalene there was obtained after dehydration a small yield (30%) of product which contained only about three-quarters of the expected amount of halogen and which could not be hydrogenated in the presence of Adams catalyst in acetic acid or, at high pressure, using copper chromite or Raney nickel. The reaction with β-naphthonitrile also gave a low yield (30%) of non-homogeneous oil.

***vic.*-Cyano-*o*-xylene.**—*vic.*-*o*-Xylidine was prepared (first experiments by T. G. Webber, Jr.) by reduction of the nitro compound with iron and water according to James, Snell and Weissberger,[26] but in better yield (91.5%; b. p. 98–100° at 11 mm., 118–119° at 25 mm.). Catalytic reduction also proceeded smoothly (92%) but was less convenient. The amine (20 g.) in water (140 cc.) and concentrated hydrochloric acid (54 cc.) was diazotized at −5° with sodium nitrite (13.7 g.) in water (85 cc.), the solution was neutralized with solid sodium carbonate, and the dark solution was added to a cold solution prepared from 29 g. of sodium cyanide and 20 g. of cuprous chloride in 130 cc. of water. A dark yellow complex separated and began to decompose on allowing the mixture to come to room temperature. After steam distillation the nitrile was extracted with ether, washed with alkali and water, dried and distilled, giving a colorless oil, b. p. 105–107° at 11 mm.; yield 8.6 g. (40%). Brunner, Hofer and Stein[27] obtained about the same yield by a different procedure.

***vic.*-*o*-Xylyl α-Naphthyl Ketone (VIII)** was prepared by adding 5.5 g. of *vic.*-cyano-*o*-xylene in 35 cc. of benzene to the reagent from 10.5 g. of α-bromonaphthalene and 1.3 g. of magnesium in 40 cc. of ether and 10 cc. of benzene. After most of the ether had been distilled, the mixture was refluxed with stirring overnight. After adding 40 g. of ice and 20 cc. of concentrated hydrochloric acid and removing the solvent with steam, 30 cc. more hydrochloric acid was added together with 30 cc. of acetic acid and 40 cc. of toluene. After refluxing for six hours the collected product distilled, after a fore-run containing naphthalene, as a viscous yellow oil, b. p. 190–195° at 1 mm.; yield 9.7 g. (89%). The ketone was not obtained crystalline.

Anal. Calcd. for $C_{19}H_{16}O$: C, 87.66; H, 6.19. Found: C, 88.24; H, 6.18.

Pyrolysis of VIII.—In one experiment 2.2 g. of *vic.*-*o*-xylyl α-naphthyl ketone was heated with 0.25 g. of zinc dust at 425–430° for two hours. Distillation at 1 mm. gave 1 g. of crystalline yellow solid, and after a prolonged process of fractionation of the hydrocarbon from alcohol and of its picrate from benzene–hexane there was obtained 10 mg. of **5-methyl-1,2-benzanthracene,** m. p. 154–156°. A mixture with a known sample[12] melted at 156–158°; there was a large depression on admixture with 1,2-benzanthracene.

In another experiment, conducted as above except that no zinc dust was used, there was isolated a small quantity of **1,2-benzanthracene,** m. p. 154–157°, mixed m. p. 155–157°. A picrate fraction (1 g., m. p. 153–154°) which had been crystallized repeatedly from alcohol and then put through an adsorption tower in benzene gave a hydrocarbon mixture melting below 125° and apparently containing 8-methyl-1,2-benzanthracene. Since a pure product could not be isolated, the material was oxidized to the quinone as described by Fieser and Johnson.[17a] The yellow zone in the tower was eluted with benzene–methanol, and the material was fractionally crystallized from acetone. One fraction was obtained as long, light yellow needles of **8-methyl-1,2-benzanthraquinone,** m. p. 194.5–196°, mixed m. p. 195–196° (sample, ref. 17a). Another small fraction formed fluffy yellow needles, m. p. 171–172.5°, and probably was 5-methyl-1,2-benzanthraquinone.

***vic.*-*o*-Xylyl β-naphthyl ketone (XII)** was obtained as described for the isomer in 87% yield as a yellow oil which slowly solidified. A sample crystallized several times from methanol formed colorless prisms, m. p. 62–63°.

Anal. Calcd. for $C_{19}H_{16}O$: C, 87.66; H, 6.19. Found: C, 87.93; H, 6.19.

Pyrolysis of XII.—Pyrolysis of 2.6 g. of the β-naphthyl ketone with 0.5 g. of zinc dust at 420–425° for one and one-half hours gave 1.8 g. of distilled product. No pure hydrocarbon could be isolated by crystallization as the hydrocarbon, picrate, or trinitrobenzene derivative; the best sample of hydrocarbon melted at 110–112°, and a mixture with 8-methyl-1,2-benzanthracene[17a] melted at 114–116°. A 1 1-g. sample of hydrocarbon mixture, m. p. 98–108°, was oxidized to the quinone and after adsorption on alumina and crystallization from acetone there was obtained 45 mg. of **8-methyl-1,2-benzanthraquinone,** m. p. 196–196.5°, and 130 mg., m. p. 192–195°. This showed no depression with an authentic sample.[17a] The amount of this quinone was about three-quarters of that obtained from the pure hydrocarbon by Fieser and Johnson.[17a] The mother liquors contained another quinone which was not isolated in a pure condition but which melted at 162–164° and showed a large depression when mixed with 1,2-benzanthraquinone.

(25) Long and Dains, *Kansas Univ. Science Bull.*, **9**, 208 (1930).

(26) James, Snell and Weissberger, THIS JOURNAL, **60**, 2085 (1938).

(27) Brunner, Hofer and Stein, *Monatsh.*, **63**, 92 (1933).

Summary

1-Benzoylacenaphthene, obtained conveniently from the available 1-aceto compound by a phenyl Grignard reaction on the corresponding amide, gives 1′,9-methylene-1,2-benzanthracene on pyrolysis in 13% yield.

Further data are given on the preparation of 1-acetoacenaphthene by the hydrogen fluoride procedure and on the characterization and oxidation of the ketone.

A study of the pyrolysis of *vic.-o*-xylyl α- and β-naphthyl ketones shows that methyl groups in the α-positions 5 and 8 of the 1,2-benzanthracene molecule withstand to some extent the conditions of the Elbs reaction but that with the α-naphthyl isomer there appears to be both migration of the aroyl group and partial elimination of the methyl substituent.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, OREGON STATE COLLEGE]

Diffusion Velocity and Molecular Weight. I. The Limits of Validity of the Stokes–Einstein Diffusion Equation

BY LEO FRIEDMAN AND PAUL G. CARPENTER[1]

Considerable interest has been evidenced in recent years in the use of diffusion velocity studies as a means of determining molecular weights.[2–4] Some results have been obtained that are in excellent agreement with results yielded by other methods.[3] On the other hand, the results of Northrop and Anson on hemoglobin[2,5] have been discouraging, as were the results of one of the authors on gelatin (to be reported in a later paper of this series).

In the use of diffusion velocity as a means of determining molecular weights, too little attention has been paid to the concentration of the diffusate. Since the Stokes–Einstein diffusion equation makes no provision for change in concentration and is derived on the assumption of free diffusion, it would appear that the diffusion coefficient to be used for the calculation of molecular weight should be determined at infinite dilution.

In a classical paper on this subject Sutherland[6] made an effort to apply the Stokes–Sutherland–Einstein equation to the evaluation from diffusion data of the molecular weights of a number of non-electrolytes ranging in molecular weight from methyl alcohol to raffinose. Undoubtedly his failure to obtain closer agreement between diffusion data and molecular weight was due to inaccuracy of data available at that time. In this paper he also gives a general empirical equation for use as the molecular weight becomes small.

Attempt to Evaluate Molecular Weights of Non-Electrolytes from their Diffusion Coefficients.—Examination of the diffusion data for non-electrolytes to be found in the "International Critical Tables" shows that the diffusion coefficient varies considerably with the concentration of the diffusate. Calculations of the molecular weights of these non-electrolytes have been made by use of the Stokes–Einstein diffusion equation

$$D = \frac{RT}{N}\frac{1}{6\pi\eta r}$$

combined with the relationship

$$M = {}^4/_3\pi r^3 dN$$

Results of several of these calculations are given in Table I. In the case of each non-electrolyte, the last value of the diffusion coefficient labeled 0 concentration has been calculated from the molecular weight of the substance. It is to be observed in each case that the value so obtained is not unreasonable when compared with the experimental values reported in the "International Critical Tables."

If the results of Table I are represented graphically by plotting the diffusion coefficient against the square root of the concentration of the diffusate, it is possible to draw a straight line from the theoretically calculated diffusion coefficient through the experimental points taken from the

(1) Present address: Willamette University, Salem, Oregon.
(2) J. H. Northrop and M. L. Anson, *J. Gen. Physiol.*, **12**, 543 (1929).
(3) J. W. McBain and T. S. Liu, THIS JOURNAL, **53**, 59 (1931).
(4) J. W. McBain, C. R. Dawson and H. A. Barker, *ibid.*, **56**, 1021 (1934).
(5) M. L. Anson and J. H. Northrop, *J. Gen. Physiol.*, **29**, 575 (1937).
(6) W. Sutherland, *Phil. Mag.*, [6] **9**, 781 (1905).

TABLE I

MOLECULAR WEIGHT CALCULATIONS FROM DIFFUSION COEFFICIENTS

C_0	$10^5 D$ cm.²/sec.	Calcd. mol. wt.
	Mannitol at 10°	
0.5	0.39 ± 0.02	242
.25	.40 ± .02	224
.125	.42 ± .02	194
0[a]	.432	182
	Lactose at 10°	
0.2	0.32 ± 0.02	459
0.1	.32 ± .02	459
0[a]	.353	342
	Lactose at 20°	
0.2	0.41 ± 0.02	531
0.1	.43 ± .02	460
0[a]	.475	342
	Maltose at 10°	
0.5	0.29 ± 0.01	623
.25	.31 ± .02	510
.01	.32 ± .02	463
0[a]	.354	342
	Maltose at 20°	
0.5	0.38 ± 0.01	862
.25	.41 ± .02	536
.1	.42 ± .02	499
0[a]	.476	342
	Sucrose at 12°	
2.0	0.25 ± 0.02	1183
1.5	.28 ± .02	842
1.0	.30 ± .02	685
0.5	.325 ± .02	539
0.25	.34 ± .02	471
0.1	.35 ± .02	431
0.075	.355 ± .02	413
0[a]	.381	342
	Sucrose at 14°	
1.0	0.33 ± 0.02	838
0.5	.35 ± .02	702
0.25	.36 ± .02	645
0[a]	.402	342
	Sucrose at 20°	
2.0	0.32 ± 0.02	903
1.0	.38 ± .02	679
0.5	.41 ± .02	540
0.25	.43 ± .02	468
0[a]	.481	342
	Sucrose at 29°	
1.0	0.50 ± 0.02	607
0.5	.53 ± .02	510
0.25	.55 ± .02	448
0[a]	.611	342
	Salicin at 20°	
0.12	0.46 ± 0.03	300
0.06	.49 ± .03	248
0[a]	.494	286

[a] For 0 concentration the value of $10^5 D$ has been calculated from the molecular weight.

"International Critical Tables." When the circles used to represent the experimental values are so drawn that they represent the probable experimental error of each point, the straight line will pass through each circle, although it must be admitted that one could not determine where to draw this line from the experimental points alone. The data in the "International Critical Tables" are too limited to make this possible.

Experimental Studies on the Diffusion of Glucose.—Since the diffusion values found in the "International Critical Tables" are relatively few and are not so exact as can now be obtained with newer methods of studying diffusion, a study of the diffusion velocity of glucose has been made. The apparatus used consisted of glass cells of the type employed by Northrop and Anson,[2] and McBain and his co-workers.[3,4] The experimental procedure used by McBain and co-workers was followed. Because of the extremely low concentrations resulting in the outside solution, this method effectively measures diffusion against water. Cell constants were calculated from the diffusion coefficient of potassium chloride as listed in the "International Critical Tables" from the work of Öholm. The glucose concentrations were measured by determining the amount of potassium iodate needed for complete oxidation of a sample.[7]

All experiments on glucose were carried out at 25° and several determinations of diffusion velocities were made at each concentration. The results of this study are given in Table II, in the third column of which the apparent molecular weight of glucose has been calculated from the diffusion coefficient obtained at each concentration.

(7) R. J. Williams, E. Rohrman and B. E. Christensen, THIS JOURNAL, **59**, 291 (1937).

TABLE II

DIFFUSION OF GLUCOSE AT 25°

Concn.	*D* in cm.²/day	Calcd. mol. wt.
0.60	0.535	237
.50	.539	232
.40	.543	227
.355	.546	223
.30	.550	218
.25	.552	216
.20	.556	211
.10	.566	200
.00 (extrap.)	.586	180

The experimental values are reported graphically in Figs. 1 and 2, in which it is evident that

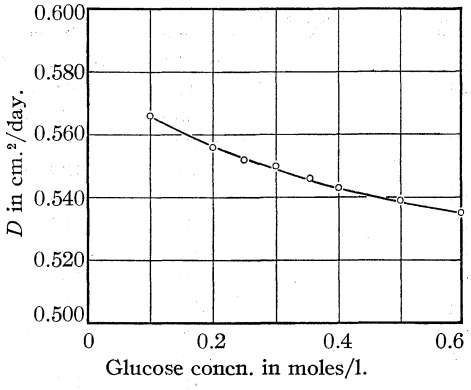

Fig. 1.—Diffusion of glucose at 25°.

when sufficiently accurate diffusion data are obtained, it is possible by plotting diffusion coefficient against square root of the concentration to extrapolate to infinite dilution and thus obtain the value of diffusion coefficient that will yield the correct molecular weight when substituted in the Stokes–Einstein diffusion equation.

Even more striking is the fact that this relationship holds for a substance of molecular weight of 180 whereas most investigators have felt that the Einstein relationship could not be applied to substances of such low molecular weight.

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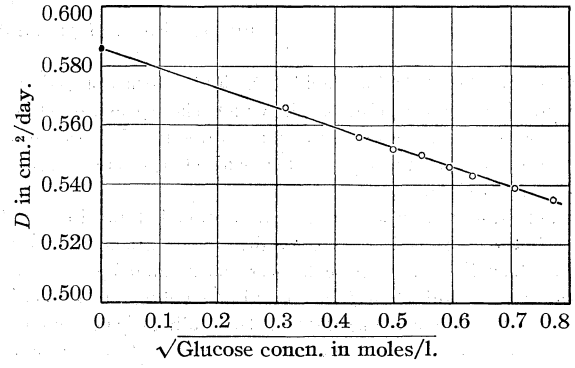

Fig. 2.—Diffusion of glucose at 25°.

Summary

It has been shown that molecular weights of simple non-electrolytes can be calculated from diffusion coefficients determined at infinite dilution, (1) by an examination of the values of diffusion coefficient to be found in the "International Critical Tables," and (2) by experimental study of the diffusion velocity of glucose.

CORVALLIS, OREGON RECEIVED FEBRUARY 20, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, OREGON STATE COLLEGE]

Diffusion Velocity and Molecular Weight. II. The Effect of *p*H upon Particle Size in Gelatin Solutions

BY LEO FRIEDMAN AND KARL KLEMM[1]

Change of hydrogen ion concentration of a gelatin solution brings about marked changes in many of the properties of the solution. In seeking explanations of these changes, some investigators have attributed them to increased or decreased hydration with changing *p*H or to increased or decreased particle size with changing *p*H. Investigators of diffusion of colloidal materials have observed marked changes in diffusion velocity with changing *p*H.[2-4]

Experimental

In order to investigate the effect of *p*H upon particle size in gelatin solutions, diffusion experiments have been carried out using 3% solutions of Eastman Kodak Co. electrodialyzed gelatin, adjusted to various *p*H's by the

(1) Present address: The Paraffine Companies, Inc., Emeryville, Calif.

(2) H. R. Bruins, *Kolloid Z.*, **54**, 265, 272 (1931); **57**, 152 (1931).

(3) J. Lazle and J. Groh, *Biochem. Z.*, **173**, 248 (1926).

(4) J. W. McBain, C. R. Dawson and H. A. Barker, THIS JOURNAL, **56**, 1021 (1934).

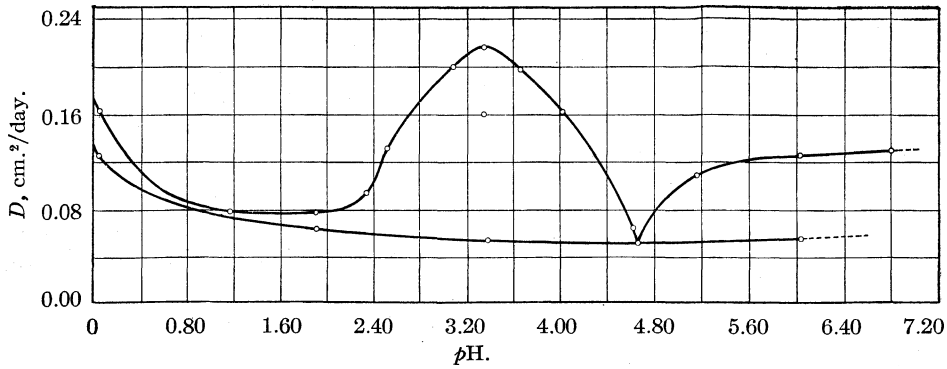

Fig. 1.—Effect of *p*H on diffusion velocity of gelatin.

addition of hydrochloric acid. A similar series of experiments has been carried out in which there was added to the above solutions a sufficient amount of potassium chloride to eliminate the electrical charge effect upon diffusion velocity.[4]

Diffusion coefficients were determined following the method and technique of McBain and co-workers[4,5] with the exceptions that the cells were suspended by a metal rod from a universal joint, making leveling of the cells easier and more certain, and that the sealing of the systems to prevent evaporation between the cell and the outside beaker was improved. Diffusion cells containing fused-in sintered Jena glass membranes (G_4) were used. The cells were calibrated with 0.1 *N* potassium chloride solutions using values from Öholm as listed in the "International Critical Tables." All diffusion measurements were made at 35° and extended over twenty-five hours. Gelatin concentrations after diffusion were determined by the colorimetric micro-method of Koch and McMeekin,[6] with the following modification. After the digestion, the material was diluted to 25 ml. instead of 100 ml., which allowed use of samples containing 0.1 to 0.25 mg. of nitrogen. This permitted shorter diffusion times. All nitrogen determinations were made in quadruplicate.

Since the source of the material and the previous history, especially thermal treatment, have such a marked effect upon the properties of gelatin solutions, these factors were controlled carefully and conditions were duplicated as nearly as possible in all determinations.

The results are given in Table I and are shown graphically in Fig. 1.

TABLE I

Electrolytes added	Concn. KCl, *N*	*p*H soln.	*D*, cm.²/day
HCl		0.054	0.163 ± 0.005
HCl		1.17	.078 ± .003
HCl		1.90	.077 ± .003
HCl		2.33	.093 ± .001
HCl		2.51	.130 ± .002
HCl		3.08	.200 ± .003
HCl		3.34	.216 ± .007
HCl		3.65	.197 ± .008
HCl		4.04	.162 ± .013
HCl		4.60	.064 ± .003
None		4.66	.051 ± .004
NaOH		5.16	.108 ± .003
NaOH		6.03	.125 ± .004
NaOH		6.80	.129 ± .002
HCl + KCl	0.250	0.054	.125 ± .001
HCl + KCl	.100	1.90	.063 ± .001
HCl + KCl	.020	3.35	.160 ± .002
HCl + KCl	.100	3.38	.053 ± .003
NaOH + KCl	.100	6.03	.055 ± .002

Discussion

A study of the two graphs shown in Fig. 1 reveals the cause of the abnormally high values of diffusion coefficient obtained by many investigators of lyophilic systems.[2,3] The lower curve reveals the cause of the large decreases in value of diffusion coefficient frequently found by investigators upon the addition of salts to lyophilic solutions.[2,3] The lower curve also reveals the effect of *p*H upon the aggregation–deaggregation equilibrium of 3% gelatin solution at 35° within the *p*H range of 0.05 to 6.40. Below *p*H 2, the values of *D* indicate a rapid disintegregation or deaggregation of the gelatin micellae, whereas if *p*H is above 2 since *D* remains nearly constant, there is a much smaller change in the particle size in gelatin solutions with changing *p*H. The point at *p*H 3.34, $D = 0.160$, shows that the addition of an insufficient amount of salt to a system of given concentration and *p*H will decrease the value of *D*, but will not reduce it to the minimum value for that *p*H.

An excellent explanation for the shape of the upper curve has been presented by McBain, Dawson, and Barker[4] in discussing their results obtained in the study of the diffusion of egg albumin. The results obtained in this study are an excellent corroboration of their work.

It is quite evident from the above results that any investigations of the diffusion of lyophilic colloidal substances must be carried out at the iso-

(5) McBain and Liu, THIS JOURNAL, **53**, 59 (1931).

(6) Williams, "Introduction to Biochemistry," D. Van Nostrand Co., New York, N. Y., 1931, p. 456.

electric point or the solutions must contain a sufficient amount of salt, if the results are to be used for the calculation of particle size.

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Summary

The effect of *p*H upon diffusion velocity of gelatin solutions has been measured over the *p*H range 0.05 to 6.4.

The effect of added potassium chloride at the various *p*H's upon the diffusion coefficient has been measured.

Results obtained indicate that between *p*H's 2 and 6.4 only a small change in particle size takes place in 3% gelatin solution at 35°, but below *p*H 2, there is a rapid decrease in particle size.

CORVALLIS, OREGON RECEIVED MARCH 7, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, OREGON STATE COLLEGE]

The Effect of Non-electrolytes upon the Time of Setting of Gelatin Gels

BY LEO FRIEDMAN AND W. N. SHEARER[1]

In an earlier investigation[2] a study was made of the effect of non-electrolytes upon diffusion velocity in gelatin gels. Interpretations of the results obtained involved the hypothesis that non-electrolytes present in gelatin gels actually influenced gel structure. With the view to further investigate this possible influence the following study of the setting of gelatin gels was undertaken.

Experimental.—Gelatin solutions containing 25 g. of electrodialyzed calfskin gelatin in 475 ml. of water were made up. The gelatin was first placed in 200 ml. of water in a one-liter flask and permitted to stand for twenty-two hours in a thermostat at 25°, after which 275 ml. of water was added and the solution heated to 55° until the gelatin was dissolved completely. This solution was then cooled to 25° in the thermostat.

Varying amounts of the non-electrolytes to be used were dissolved in enough water to make up 10 g. of solution. These non-electrolyte solutions were then placed in wide-mouthed bottles, approximately 6.3 cm. in diameter, and 90 ml. of the gelatin solution was poured into each bottle. The bottles were placed immediately in the thermostat and tightly stoppered.

In order to determine when the gels had set a penetrometer was used. The penetrometer consisted of a glass tube about 45 cm. long and 8 mm. in diameter sealed and rounded on the end which was used to test the gel. At the other end of the glass tube was fastened a larger glass tube 18 cm. long and 12.5 mm. in diameter. Around the first tube was a coil consisting of 25 loops of steel wire 0.035 mm. in diameter so fastened that the spring resisted the movement of the smaller glass tube into the larger. As an indication that a gel had set the following criterion was followed.

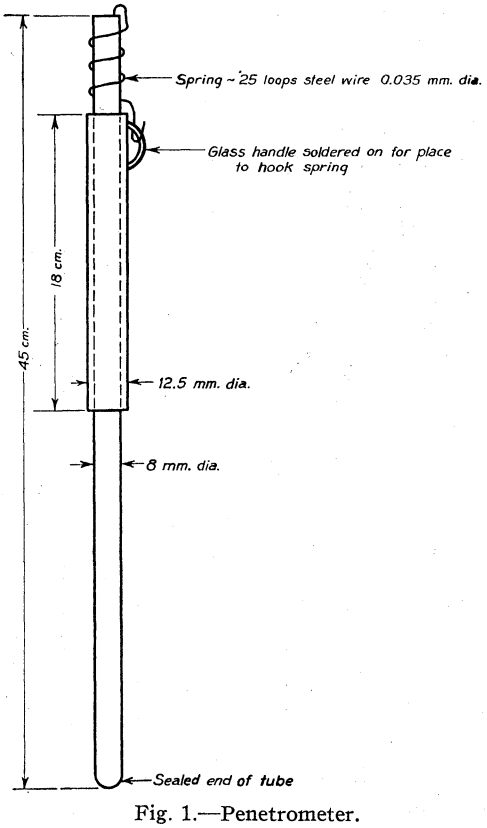


Fig. 1.—Penetrometer.

When a gel had set enough so that the tube would go into the gel far enough to stretch the spring to the 2.6 cm. mark from the starting point without

(1) Present address: Western Waxed Paper Co., North Portland, Oregon.

(2) Leo Friedman and W. N. Shearer, THIS JOURNAL, **56**, 1323 (1934).

TABLE I

EFFECT OF NON-ELECTROLYTES UPON TIME OF SETTING OF GELATIN GELS

Molar concn.	Sucrose at 25° S. T. Min.	Sucrose at 25° % Incr. S. T., %	Urea at 25° S. T. Min.	Urea at 25° % Incr. S. T., %	Levulose at 25° S. T. Min.	Levulose at 25° % Incr. S. T., %	Levulose at 17° S. T. Min.	Levulose at 17° % Incr. S. T., %
0.00	212	....	305	....	185	....	45	....
.01	219	3.3	331	8.5	200	8.1	..	....
.02	243	14.6	351	15.1	204	10.3	49	8.9
.03	232	9.4	359	17.7	201	8.7	..	....
.04	221	4.2	355	16.4	195	5.4	..	....
.05	215	1.4	...	....	175	− 5.4	47	4.4
.06	...	....	318	4.3	...	....	..	....
.10	201	− 5.2	...	....	141	−23.8	42	− 6.7
.20	166	−21.7	235	−22.9	136	−25.5	34	−24.4

breaking the surface of the gel, it was considered to have completely set. This empirical method and home-made penetrometer were found to be very accurate and convenient in testing gels.

Table I gives the results obtained in the study of the time of setting of gelatin gels in the presence of sucrose, urea, and levulose. It is to be noted that up to a concentration of 0.02 to 0.03 molar non-electrolyte setting time was increased, but this effect became less marked at higher concentrations and finally at concentrations of 0.2 molar, setting times had been decreased by more than 20%.

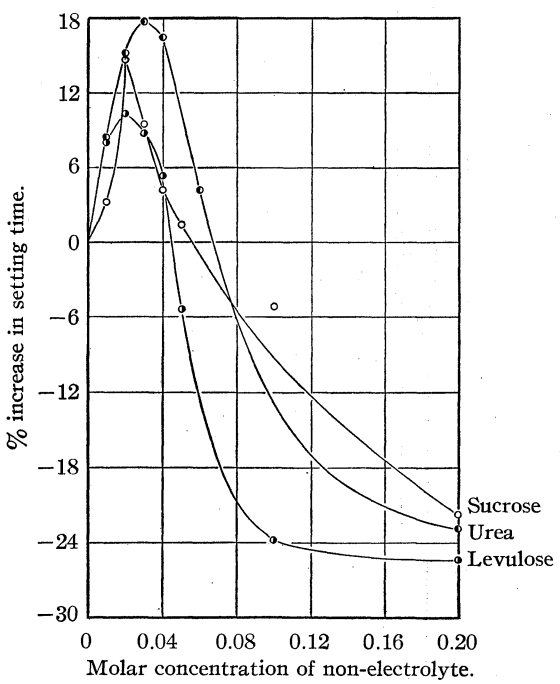


Fig. 2.—Effect of non-electrolytes on setting of gelatin gels.

Discussion

In the investigation of the effect of non-electrolytes upon diffusion velocity in gelatin gels,[2] it was found that low concentrations of non-electrolyte brought about an increase in diffusion velocity, this effect reaching a maximum at concentrations below 0.04 molar. At higher concentrations of non-electrolyte the diffusion velocity was increased less and at concentrations above 0.08 to 0.18 molar for the various non-electrolytes used the diffusion velocity was slower than in the absence of any non-electrolyte. These results were explained by assuming that non-electrolytes influence diffusion in gels in two ways: (1) by increasing the radii of the pores within the gel due to a decrease in the hydration of the solid phase, and (2) by increasing the viscosity of the medium through which diffusion takes place.

As early as 1900, Hardy[3] observed that the rate of setting influenced the structure of gels, and that gels which had been cooled rapidly had a "finer structure." In an earlier investigation by one of the authors[4] on diffusion of non-electrolytes in gelatin gels, it was observed that when gels were set at low temperatures, which results in rapid setting, gels were formed through which diffusion was more rapid than through gels set at higher temperatures.

On the other hand those concentrations of non-electrolytes which through their presence slow down gel formation yield gels through which diffusion is more rapid than through those gels that have set more rapidly due to the presence of higher concentrations of non-electrolytes. When rate of setting is influenced by foreign substances, it appears that slow setting yields gels with a more open structure, since diffusion velocity in gels[2] varied directly with time of setting.

Published with the approval of the Monographs

(3) Hardy, *J. Physiol.*, **24**, 288 (1899); *Proc. Roy. Soc.* (London), **66**, 95 (1900).

(4) Leo Friedman, THIS JOURNAL, **52**, 1305 (1930).

Publications Committee, Oregon State College, as Research Paper No. 18, School of Science, Department of Chemistry.

Summary

A study of the effect of non-electrolytes upon the rate of setting of gelatin gels has been carried out.

Small concentrations of non-electrolytes increase setting time, this effect becoming a maximum at 0.02–0.03 molar.

Concentrations of non-electrolyte exceeding 0.1 molar cause gels to set more rapidly than in the absence of non-electrolytes.

Comparison with results of diffusion experiments leads to the conclusion that the slower setting gels have a more open structure.

CORVALLIS, OREGON RECEIVED MARCH 7, 1939

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

Catalytic Dehydration of C_6–C_8 Aliphatic Alcohols

BY SEYMORE GOLDWASSER AND HUGH S. TAYLOR

An apparatus for the study of vaporized hydrocarbons and its application to the dehydrogenation of cyclooctene were described in a previous paper.[1] In seeking a good source of aliphatic hydrocarbons, it was found that certain alcohols were available in comparatively large quantities. Catalytic dehydration of these alcohols in this same apparatus proved to be an excellent source of alkenes and provided certain information concerning the mechanisms of dehydration and isomerization.

The separation of the pure isomers resulting from the dehydration of an alcohol was accomplished by the use of a modification of the Podbielniak column together with a special head which permits controlled reflux ratio.

Apparatus.—The column proper is shown in Fig. 1. It consists simply of a Pyrex tube, A, 1.5 meters long and 4.5 mm. i.d., flared at both ends to fit in a 1.8-meter long 16-mm. tube, B, which has a 16-mm. ground joint at one end and is ring-sealed at 1 and 2 at both ends. The space between the two tubes is evacuated through a side tube with the column at about 150°, the necessary heat being provided electrically with 12.2 meters of no. 20 chromel wire wound externally. About 6.1 meters of no. 20 chromel are wound spirally on a rod of such size that, when the spiral is stretched to six or seven turns per inch (2.5 cm.), it fits snugly inside the center tube of the column. This is the Podbielniak type packing. It does not allow reflux liquid to run down the column but causes it to travel down in a spiral path. More time is thus afforded for equilibrium to be set up and separation is excellent. The hold-up is small and the amount of liquid reaching the head without flooding is much larger than can be secured with the helical glass packing. A 200° thermometer, C, graduated in tenths of one degree is tied with asbestos directly to the column so that the bulb of the thermometer touches the evacuated jacket about one-third from the bottom. Just above the ground joint and also 1.5 meters up the column are wound asbestos strips so that the column is tightly supported inside a 1.5-meter 35-mm. Pyrex tube.

The head, D, which is described by J. H. Simons,[2] is sealed on just above the outermost insulating jacket and fitted with a thermometer, E, which is calibrated at 0, 56.7 and 100°. This head is a total condensing variable take-off type and has the advantage that it will accurately control reflux ratio, that it allows accurate and direct temperature measurement, and that hot hydrocarbon vapors can in no way come in contact with any contaminating surfaces. It can be adjusted for total return so that, in adjusting the column for operation, there is no loss.

Heating of the liquid is supplied by a small electrical heater, F. Either a 100-cc. or 200-cc. flask, G, with interchangeable ground joints may be used. The receivers are 30 cm. long 12-mm. tubes immersed in an ice-bath so that the outlet tube, H, from the head is at a lower level than the

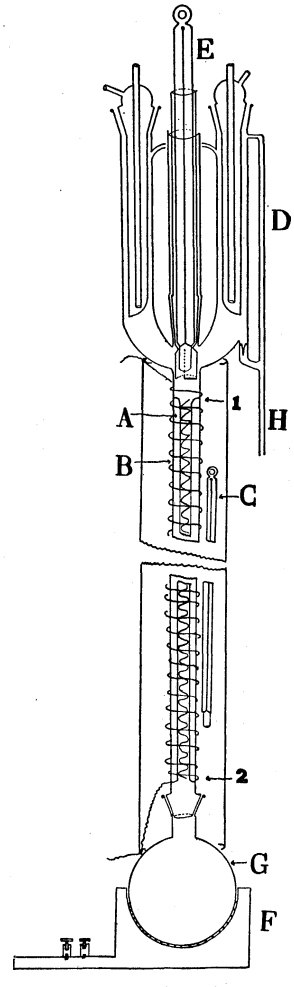


Fig. 1.—Fractionation apparatus.

(1) S. Goldwasser and H. S. Taylor, THIS JOURNAL, **61**, 1260 (1939).

(2) J. H. Simons, *Ind. Eng. Chem., Anal. Ed.*, **10**, 29 (1938).

surface of the ice, eliminating as far as is possible loss from evaporation during a distillation.

The catalytic apparatus used in this study of dehydration is identical with that previously described.[1] When the rate of passage of alcohol was 20 cc. per hour or more, the central buret tube used was 12 mm. o.d.

Materials.—The alcohols used were commercial products supplied by E. I. du Pont de Nemours and Company and by Carbon and Carbide Chemical Corporation. They were purified by careful distillation in the column described. The maximum impurity in any one of the alcohols proved to be about 3%. The heptanol-4 used was synthesized as follows.

A manganous oxide was prepared by passing methanol vapors over manganous carbonate *in situ* at 400°. The temperature was then raised to 450° and butyric acid passed over it. The heptanone-4 formed was separated by fractional distillation. This was then reduced by passing its vapors mixed with hydrogen over a nickel catalyst at 150°. Repetition of passage and distillation gave a pure heptanol-4; sp. gr. d^{20}_4 0.820, refractive index $n^{20}D$ 1.4325, b. p. (760 mm.) 155.4°.

The properties of the other purified alcohols were:

	Sp. gr. d^{20}_4	n_D	B. p., °C. (760 mm.)
Hexanol-1	0.8189	1.4161	156.4
2-Ethylbutanol-1	.8328	1.421	148.9
2,4-Dimethylpentanol-1	.819		157
2,4-Dimethylpentanol-3	.8288	1.4226	140
2-Ethylhexanol-1	.833		184.6

The catalysts used in the investigation were alumina, chromic oxide gel and thoria. Uranium oxide was found to be inactive for dehydration. The preparation of chromic oxide gel has been described previously. Alumina was prepared by precipitating aluminum hydroxide from a 1.5 *N* aluminum nitrate solution with concentrated ammonia, vigorously stirred and filtered on a Büchner funnel. When dried at 100° the particles obtained were glassy, large and non-crumbling. Several other methods were tried for this preparation, including precipitation from dilute solutions and heating before filtration. The method cited proved to be the most convenient in preparation and handling, and also the most active in dehydration. The thoria catalyst used was prepared by the method of Kramer and Reid.[3] It consists of thoria supported on pumice in the proportion 1:3 and is prepared by the ignition of thorium nitrate under carefully controlled conditions.

Procedure.—The procedure for the passage of an alcohol over a catalyst is identical with the procedure described for the dehydrogenation of cycloöctene. It is very convenient to collect the product in a pig of 100-cc. capacity, used only for the alcohols. The liquid condensed separates into two layers, water and hydrocarbon. To determine extent of dehydration, the water layer is drawn off and weighed, and the volume of the hydrocarbon layer measured. The specific gravity of the alcohols is about 0.82, the hydrocarbon about 0.69. For 100 cc. of alcohol dehydrated, there should be 96 cc. of hydrocarbon and 14.1 cc. of water. This method of estimation is quite accurate. The hydrocarbon is then dried over calcium chloride for two hours, then placed over a new batch of calcium chloride in a second flask and allowed to stand for twelve hours. This eliminates any unchanged alcohol as well as water. Traces of water show up as a cloudiness in the first drops refluxing in the fractionation. When this occurs, the column must be opened and dried thoroughly.

For the fractionation of the dry hydrocarbon mixture, the procedure will be described in detail. The mixture is placed in a 200-cc. flask fitted with a ground joint and attached to the column. The heater is placed under the flask and its temperature adjusted so that the liquid will begin to boil in about half an hour. The valve in the head is turned so that all vapors will pass to the non-exit side and the condenser on the other side adjusted so that all condensate will return to the column. The rheostats in series with the heating coil around the vacuum jacket are adjusted from time to time so that the temperature shown by the thermometer in the outer jacket keeps pace exactly with that in the head. The purpose of this and the vacuum jacket is to make the column as adiabatic as possible, so that heat exchange will take place only between the refluxing liquid and the vapors coming up the column. As soon as the column is operating properly, that is, about 30 drops of liquid are returning to the column every five seconds, with no flooding, the condenser on the exit side is adjusted so that one drop is collected in the receiver every five seconds. As the distillation is in progress, a plot is made with the number of drops as the abscissa and the temperature of the head as ordinate. The receiver is changed at the beginning and end of each horizontal part of the curve, there resulting two portions of liquid for each constant boiling fraction, one of a nearly pure hexene isomer, the other of a mixture consisting of the two isomers between the boiling points of which the mixture distils. Total reflux is used for five minutes at the end of each horizontal part in order to make the break sharper. Throughout the distillation, outer jacket temperature must be the same as, or 1° lower than, the temperature of the head. The receivers are of known volume and the amount of each fraction may be ascertained without undue transfer of liquid.

Specific gravities, correct to the third decimal place, and Hanus numbers are taken for each fraction. The Hanus number determination is used to determine the purity of the fraction with respect to non-olefins, and the fraction corresponding to a horizontal part of the curve is then identified by comparison with a table of boiling points and specific gravities of hydrocarbons, as described in the next section. The absolute amount of the various isomers in a mixture is determined by extrapolation of the horizontal and rising parts of the curve. The meeting point of the lines gives the amount of the pure fraction. The slopes of the vertical lines are those of the tangents to the distillation curve at the points of inflection. It must be understood that, even for the fractions corresponding to the horizontal parts of the curve, absolute purity is not obtained. The main constituent of a given fraction is present, however, in amounts greater than 95%. The fractionation, from which the data in Table II are taken, is shown in abbreviated form in Fig. 2, and demonstrates

(3) Kramer and Reid, THIS JOURNAL, **43**, 880 (1921).

the method of extrapolation. The validity of the method was checked by the fractionation of known mixtures, in which case complete substantiation was found.

The amount of the liquid to be placed in the distilling flask was determined by that component of the mixture which was present in smallest amounts, since to get a good flat in the curve required about 0.75 cc. In all cases, 100 cc. of an alcohol or more was dehydrated, and 100 cc. of the dry hydrocarbon mixture fractionated, so that, as a rule, volumes were equal to percentages. In certain cases where material was scarce and the composition of the resultant mixtures was known qualitatively by previous experience, a 20-cc. sample was sufficient, and a 10-cc. sample of a two-component mixture was sometimes sufficient.

Identification of Fractions.—The first satisfactory compilation of the physical properties of pure hydrocarbons has appeared only recently. The compilation was made by G. L. Eaton.[4] The table is comprehensive and lists specific gravities, etc., for every pure hydrocarbon known. No complete tabulation of octene isomers is available.

To illustrate difficulty in identification, the following may be cited. Fractionations continuously gave a cut at 65.6–65.7° and no further cut to 66.2°. There appeared to be no isomer boiling at the lower temperature recorded in the literature. However, one of the isomers of 3-methylpentene-2 was reported as boiling at 65.7–66.2°. By the elimination of the fractions which were known with some certainty, it was decided that the fraction boiling at 65.7° must be 3-methylpentene-2 and further work was carried out on this basis. A paper by van Risseghem,[5] which has appeared recently, in which was described the isolation of several pure hexene isomers identified by chemical means and checked with infrared spectra, records that the isomer variously reported as boiling at 65.7–66.2° is *trans*-3-methylpentene-2 and that its true boiling point is 65.7°. This concordance may be used to emphasize the confidence that may be placed in the fractionations obtained.

While most boiling points reported are uncorrected, transformations of values found at one pressure to another pressure for purposes of comparison are necessary. According to an article on conversion factors in the same treatise,[4] the following facts are found.

B. p. at 760 mm., ° C.	0	50	100	150
Corr. per mm. for b. p. at 760 ± 50 mm.	0.035	0.040	0.046	0.051

Moxt hexene isomers boil in the range 60 to 70°. The correction on a normal day will amount to 0.4°, which is as much as the difference between two isomers to be separated. Pressure variations corresponding to as much as 0.6° have been found in interrupted distillations of a given cut.

With a distillation curve corrected to 760 mm., it was found that the sequence of the fractions together with their boiling points could be correlated readily with the

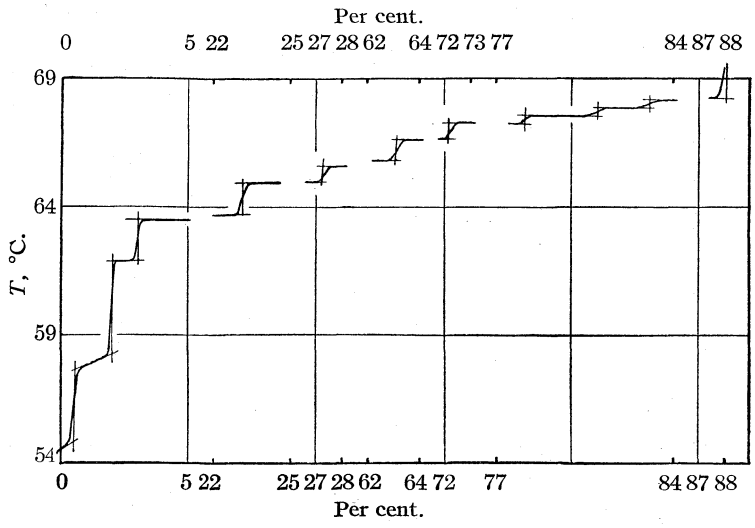


Fig. 2.

boiling point sequence of the isomeric olefins in question. A correlation with specific gravities served as additional check. If the specific gravities fell in the sequence which the fractions required when the identifications were made from the boiling point, identification was assumed to be adequate for the purposes of the present study, a procedure which is common in other work of this type. Accordingly, we have, in the succeeding data, labelled the respective cuts with the name of the alkene having the corresponding boiling point. Substances of a type other than hydrocarbon can confuse identification, but the use of specific gravities eliminates this possibility. In certain cases, where there was a good quantity of isomer available, dibromo derivatives were prepared as a further check. For example, the dibromo derivative prepared from the hexene identified as hexene-1, gave a product: b. p. 77–77.5° (15 mm.) and sp. gr.$^{13.5}_4$ 1.596, whereas the literature shows this derivative to have: b. p. 77–78° (15 mm.) and sp. gr.$^{13.5}_4$ 1.59625.

The possibility of the formation of azeotropic mixtures was considered. In sixty or more fractionations of mixtures of pure hexene isomers, containing every possible combination of such isomers, save one to be mentioned, no fractions were found which did not correspond exactly with tabulated isomers in all properties. Only in one case, with mixtures containing both hexene-1, b. p. 63.5–64.0°, and *trans*-3-methylpentene-2, b. p. 65.7–66.0°, was there evidence for a constant boiling mixture at 65.0°. However, no more than 4% of the total multicomponent mixture came off in this form.

Table Ia was used for the identification of the hexenes. Similar tables, Tables Ib and Ic, were used for the heptenes and the octenes.

Table II shows a typical fractionation. The

(4) G. L. Eaton, "Science of Petroleum," Vol. II, Oxford University Press, Oxford, 1937, p. 1302, etc.

(5) H. van Risseghem, *Bull. soc. chim. Belg.*, **47**, 47 (1938)

percentage data given are deduced from Fig. 2, by the method of extrapolation given. All percentages in the tables following are deduced in a similar manner from the fractionation curves (see Figs. 3–7). The close checks found for the observed and the calculated values of specific gravities and unsaturation attest both the purity and the correctness of method.

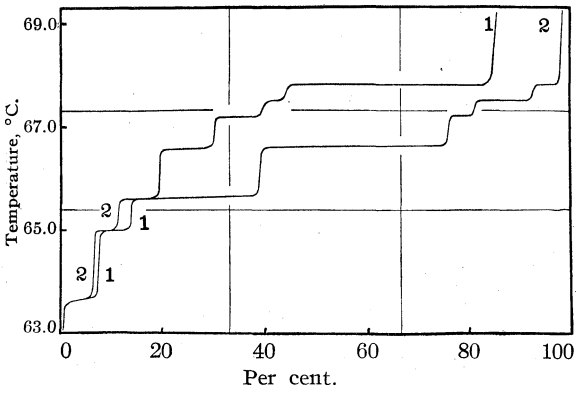


Fig. 3.—Distillation curves of dehydration products on alumina at 398° from 2-ethylbutanol-1: 1, fast speed; 2, slow speed.

Observed B. p., °C.	Sp. gr.$^{20}_4$	Indicated hexene isomer	Lit. data B. p., °C.	Sp. gr.$^{20}_4$
63.5–63.7	0.673	Hexene-1	63.5–63.7	0.6732
65.6–65.8	.694	3-Methylpentene-2-*t*	65.6–65.8	.6940
66.6	.689	2-Ethylbutene-1	66.6	.6897
67.2	.690	2-Methylpentene-2	67.2	.6904
67.5	.720	Hexene-3	67.5	.7190
67.8	.696	3-Methylpentene-2-*c*	67.8	.6956

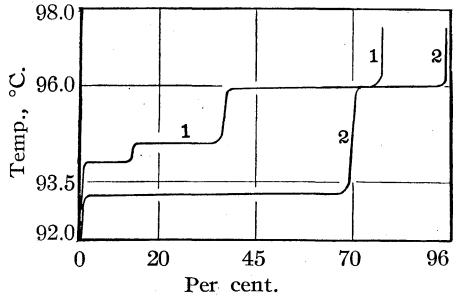


Fig. 4.—Distillation curves of dehydration products on alumina at 398° from heptanol-4: 1, fast speed; 2, slow speed.

Observed B. p., °C.	Sp. gr.$^{20}_4$	Indicated heptene isomer	Lit. data B. p., °C.	Sp. gr.$^{20}_4$
93.1–93.2	0.712	3-Methylhexene-2	93.1–93.3	0.7120
93.9–94.0	.707	2-Ethylpentene-1	93.9–94.3	.7079
94.5–94.6	.709	2-Methylhexene-2	94.4–94.6	.7089
95.8–95.9	.704	Heptene-3	95.8–96.1	.7043

Experimental Results

(A) Effect of Rate on Products of Dehydration.—Purified hexanol-1 was passed over a preparation of alumina at 398°. The rate of

TABLE Ia

Isomeric hexenes	B. p. 760 mm. (range) °C.	Sp. gr.^{20}
3,3-Dimethylbutene-1	41.2	0.6529
4-Methylpentene-1	53.6–53.9	.6646
3-Methylpentene-1	53.6–54.0	.6700
4-Methylpentene-2-*c*	54.2–55.2	.6702
2,3-Dimethylpentene-2	56.0	.6803
4-Methylpentene-2-*t*	57.7–58.5	.6709
2-Methylpentene-1	61.5–62.0	.6817
Hexene-1	63.5–64.1	.6732
3-Methylpentene-2-*t*	65.7–66.2	.6940
2-Ethylbutene-1	66.2–66.7	.6897
2-Methylpentene-2	67.0–67.2	.6904
Hexene-3-*t*	67.3–67.5	.7170
3-Methylpentene-2-*c*	67.6–68.2	.6956
Hexene-2	67.9–68.1	.6813
Hexene-3-*c*	70.0–71.2	.7190
2,3-Dimethylbutene-2	73.0	.7280

TABLE Ib

Isomeric heptenes	B. p. 760 mm. (range) °C.	Sp. gr.$^{20}_4$
4,4-Dimethylpentene-2	76.0	0.6881
3,3-Dimethylpentene-1	76.9	.6961
2,3,3-Trimethylbutene-1	80.0	.707
2,4-Dimethylpentene-1	80.9–81.3	.6937
2,4-Dimethylpentene-2	82.6	.6947
3-Methylhexene-1	84.0	.6953
2,3-Dimethylpentene-1	84.1–84.3	.7054
5-Methylhexene-1	84.7	.6936
4-Methylhexene-2 (1)	85.1–85.6	.6981
5-Methylhexene-2 (1)	85.6–86.1	.7020
3,4-Dimethylpentene-2	86.2–86.4	.7126
2-Methylhexene-3	86.4–86.9	.6942
4-Methylhexene-2 (2)	87.1–87.6	.7007
4-Methylhexene-1	87.2–87.5	.6969
3-Methyl-2-ethylbutene-1	88.7–89.1	.7186
5-Methylhexene-2 (2)	91.1–91.6	.6990
2-Methylhexene-1	91.1–91.5	.7000
3-Methylhexene-2	93.1–93.3	.7120
2-Ethylpentene-1	93.9–94.3	.7079
2-Methylhexene-2	94.4–94.6	.7089
3-Ethylpentene-2	94.8–94.9	.7172
Heptene-1	94.9	.6993
2,3-Dimethylpentene-2	95.1	.719
Heptene-3	95.8–96.1	.7043
Heptene-2	98.1–98.4	.7034

TABLE Ic

Isomeric octenes	B. p. 760 mm. °C.	Sp. gr.$^{20}_4$
5,5-Dimethylhexene-3	100.1	0.7408
2,4,4-Trimethylpentene-1	102.6	.711
2,4,4-Trimethylpentene-2	104.5	.7211
4,4-Dimethylhexene-2	105.6	.7202
6-Methylheptene-1	111.5	.7124
2-Methylheptene-3	120.4	.7314
4-Methylheptene-3	120.4	.724
Octene-1	123	.7155
2-Methylheptene-2	125.2	.816

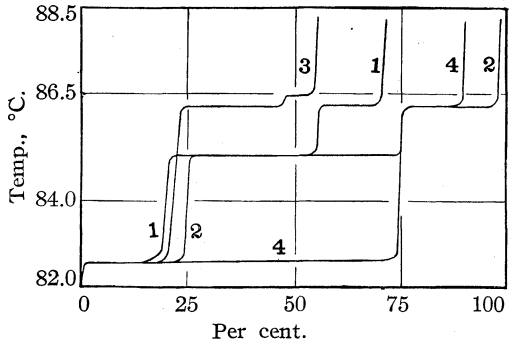


Fig. 5.—Distillation curves of dehydration products on alumina at 398° from 2,4-dimethylpentanol-1: 1, fast speed; 2, slow speed and 2,4-dimethylpentanol-3; 3, fast speed; 4, slow speed.

Observed B. p., °C.	Sp. gr.$^{20}_4$	Indicated heptene isomer	Lit. data B. p., °C.	Sp. gr.$^{20}_4$
82.6	0.695	2,4-Dimethylpentene-2	82.6	0.6947
85.1–85.2	.701	4-Methylhexene-2	85.1–85.6	.7007
86.2–86.3	.712	3,4-Dimethylpentene-2	86.2–86.4	.7126
86.4–86.5	.694	2-Methylhexene-3	86.4–86.9	.6942

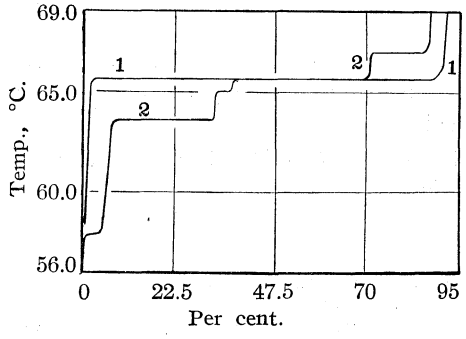


Fig. 6.—Distillation curves of dehydration products on thoria at 398° from hexanol-1: 1, slow speed; 2, fast speed.

Observed B. p., °C.	Sp. gr.$^{20}_4$	Indicated hexene isomer	Lit. data B. p., °C.	Sp. gr.$^{20}_4$
57.8–58.1	0.670	4-Methylpentene-2-*t*	57.7–58.5	0.6709
63.5–63.6	.673	Hexene-1	63.5–63.7	.6732
65.6–65.7	.694	3-Methylpentene-2-*t*	65.6–65.8	.6940
66.6	.689	2-Ethylbutene-1	66.6	.6897

flow was controlled to 1%. The results are recorded in Table III, together with a set of data for a 10% UO_2–90% Al_2O_3 catalyst available from other work.

(1) The first and most obvious thing about Table III is that the primary products are shown to be hexene-1, 2-methylpentene-1, 4-methylpentene-2, and, surprisingly, a small amount of 2-methylpentane. (2) As the rate becomes slower, the actual amount of hexene in the mixture increases at the expense of unchanged hexanol. The hexene-1 in turn decreases and other hexene isomers appear. That this is due to direct

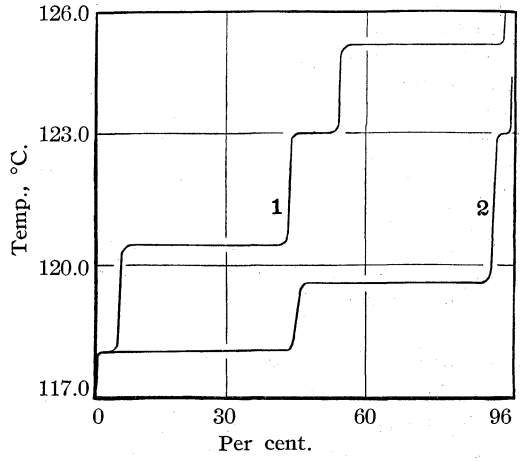


Fig. 7.—Distillation curves of dehydration products on thoria at 398° from 2-ethylhexanol-1: 1, slow speed; 2, fast speed.

Observed B. p., °C.	Sp. gr.$^{20}_4$	Indicated isomer	Lit. data B. p., °C.	Sp. gr.$^{20}_4$
118.1		?		
119.6		?		
120.4	0.724	4-Methylheptene-3	120.4	0.724
123.0	.717	Octene-1	123	.7155
125.0–125.1	.816	2-Methylheptene-2	125.2	.816

TABLE II

DEHYDRATION OF HEXANOL-1 ON ALUMINA, 3.12 CC./HOUR AT 398°

B. p., °C.	Compound	%	Sp. gr. (obsd.)	Sp. gr. (lit.)	Unsaturation (Obsd.)	Unsaturation (Calcd.)
54.6–55.0	4-Methylpentene-2-*c*	0.5	0.670	0.6702		
57.7–58.5	4-Methylpentene-2-*t*	1.5	.671	.6709		
61.9	2-Methylpentene-1	1.1	.682	.6817	0.00391	0.00394
63.5–63.7	Hexene-1	20.0	.673	.6732	.00389	.00390
65.0	Mixture	4.0				
65.6	3-Methylpentene-2-*t*	36.0	.694	.6940	.00399	.00400
66.6	2-Ethylbutene-1	9.0	.689	.6897		
67.2	2-Methylpentene-2	6.0	.690	.6904	.00398	.00399
67.5	Hexene-3	3.0	.720	.7190		
67.8	3-Methylpentene-2-*c*	2.0	.696	.6956		
68.0–68.1	Hexene-2	5.0	.680	.6813		
Over 150	Polymer	12.0	.762			

The micro-pipet used for Hanus no. contained 0.2638 cc.

TABLE III

Products	Rate of passage, in cc./hr./10 g. catalyst, 45.5	22.5	11.2	3.1	3.1 (10% UO_2–90% Al_2O_3)
4-Methylpentene-2-*c*				0.5	
4-Methylpentene-2-*t*	2	2	1.1	1.5	5
2-Methylpentane	1	3	2.0	0.0	0
2-Methylpentene-1	5.5	5	6.1	1.1	8
Hexene-1	49.0	51	66.7	22.0	40
3-Methylpentene-2-*t*			7.1	38.0	28
2-Ethylbutene-1			2.3	9.0	
2-Methylpentene-2				6.0	
Hexene-3				3.0	
3-Methylpentene-2-*c*				2.0	
Hexene-2				5.0	
Polymer	18.0	20	16.0	12.0	17
(Ether in polymer)	(1)	(0.5)	(0)	(0)	
Unchanged hexanol-1	24.0	20	0.0	0.0	
Total	99.5	101	101	100.1	98
Major products, corrected for unchanged hexanol: hexene-1	64	65	66	22	
Major products, corrected for unchanged hexanol: polymer	24	25	16	12	

isomerization of hexene-1 on the alumina surface will be shown in a later paper. The same is the case with 2-methylpentene-2, as is shown in the table. (3) The faster the passage, the more unchanged hexanol and polymer is found. An ether is found in the polymer only in the case of most rapid passage. Slower passage allows any ethers formed to decompose. (4) Correcting for unchanged hexanol, it is seen that the amount of polymer formed is a function of the unchanged hexanol. The amount of hexene formed does not change, but slower rate allows its isomerization. (5) The results found for 10% uranyl on alumina lie between the results from the two slowest rates on pure alumina. This is due to a screening of alumina surface by inactive uranyl, as will be shown.

The polymer discussed is a yellow oily liquid with a boiling range of 200–250°. This and the specific gravity point to a dodecalene. A Hanus number determination corresponds exactly with that calculated for a dodecalene.

(B) Effect of Catalyst on Products of Dehydration.—

TABLE IV

PURIFIED HEXANOL-1 PASSED AT 3.1 CC./HR./10 G. CATALYST AT 398°

Products	Catalyst, % Al_2O_3 (a)	Al_2O_3 (b)	ThO_2	10% UO_2	100% UO_2	Cr_2O_3
4-Methylpentene-2-*c*	0.5	0.5				
4-Methylpentene-2-*t*	1.5	1.5		5		23.4 benz.
2-Methylpentene-1	1.1	1.6		8		37 olef.
Hexene-1	20.0	21.0		40		37.6 sats.
Mixture	4.0	3.5		2		
3-Methylpentene-2-*c*	36.0	35.0	90	28		
2-Ethylbutene-1	9.0	8.5				
2-Methylpentene-2	6.0	6.2				
Hexene-3	3.0	3.2				
3-Methylpentene-2-*t*	2.0	1.8				
Hexene-2	5.0	4.1				
Polymer	12.0	13.0	10	17		
Hexanol					100	

This table yields the following conclusions. (1) Mode of preparation of aluminum oxide does not significantly change dehydration. Four different pure aluminas were tried. (2) Isomerization proceeds much more rapidly on thoria. All intermediate isomers have disappeared. All hexene-1 has isomerized to 3-methylpentene-2. (This will be elaborated in a later paper.) (3) 100% uranium oxide produces no dehydration, either at 400 or at 500°. The catalyst preparation

proved to be active for dehydrogenation, however. No preparation of pure uranium dioxide was found that dehydrated. (4) As was shown in section (A), the 10% uranyl catalyst on alumina gives products which are the same as though a faster rate were used over pure alumina. (5) The reaction with chromic oxide is a different type from the others. Not only is there dehydration but dehydrogenation. Benzene is formed from the hexene-1 and some of the olefins formed are hydrogenated at this comparatively low temperature. Water vapor when mixed with olefin over chromic oxide causes oxidation of the olefin so that considerable carbon dioxide is evolved.

The effect of rise of temperature is slight, except to decrease decomposition. In the case of chromic oxide, however, an increase to 460° gives excellent dehydrogenating conditions. The ma-

TABLE V

EFFECT OF RATE AND CATALYST ON PRODUCTS OF DEHYDRATION

Products	Hexanol-1 f	Hexanol-1 s	2-Ethylbutanol-1 f	2-Ethylbutanol-1 s	Heptanol-4 f	Heptanol-4 s	2,4-Dimethyl pentanol-1 f	2,4-Dimethyl pentanol-1 s	2,4-Dimethyl pentanol-3 f	2,4-Dimethyl pentanol-3 s
				Alumina at 398°						
4-Methylpentene-2-*c*		0.4								
4-Methylpentene-2-*t*	2	1.5								
2-Methylpentene-1	5	1								
Hexene-1	51	22	11	9						
3-Methylpentene-2-*t*		38	9	30						
2-Ethylbutene-1		9	10	37						
2-Methylpentene-2		6	10	5						
Hexene-3		3	4	12						
3-Methylpentene-2-*c*		2	43	5						
Hexene-2		5								
2-Methylhexene-2					22					
Heptene-3					40	25				
2-Ethylpentene-1					15					
3-Methylhexene-2						70				
4-Methylhexene-2							35	49		
2-Methylhexene-3									5	
2,4-Dimethylpentene-2							20	24	17	20
3,4-Dimethylpentene-2							15	24	30	75
Polymer	20	12	4	2	18	5	10	3	8	5
Ether	0.5	0	0.6	0	0	0				
Unchanged	20	0	3	0	5	0	20	0	40	0
Decomposed (off-gas)	0.2	0.5	0.3	0.7	0.2	0.4	0.3	0.6	0.2	0.6

Products	Hexanol-1 f	Hexanol-1 s	Products	2-Ethylhexanol-1 f	2-Ethylhexanol-1 s
	Thoria at 398°				
4-Methylpentene-2-*t*	5		Octene-1	12	2
Hexene-1	30		2-Methylheptene-2	40	
3-Methylpentene-2-*t*	35	90	4-Methylheptene-3	40	
2-Methylpentene-2	15		B. p. 118.1°	5	46
			B. p. 119.6°		46
Polymer	15	10		5	5
Unchanged	0	0		2	0
Decomposed	0.8	1.5		0.4	1.1

Products	320°	380°	Hexanol-1 398°	420°	460°	Heptanol-4 410°	2,4-Dimethyl-pentanol-1 400°
			Cr_2O_3, 3.11 cc./hr./10 g.				
Aromatic		17	25	33	46	40	5
Olefin (liq.)		24	37	51	49	50	20
Saturate		58	38	15	5	10	25
Polymer							50
Unchanged	100 (hexanol-1 unchanged on 100% UO_2 at 400, 500°)						

f = 22.5 cc./hr./10 g. catalyst. s = 3.1 cc./hr./10 g. catalyst.

jor product is benzene, and the saturates drop to 5%. There is no water in the exit gas, it being entirely converted to hydrogen and carbon dioxide.

To determine whether there are analogous effects with change in rate of passage with other alcohols, the primary products of decomposition were determined in the cases of several other alcohols.

Table V gives the percentage decomposition of the hydrocarbon layer resulting from the dehydration of several alcohols at a slow and a rapid rate. Figures 3, 4, 5, 6 and 7 record the distillation curves obtained with the products from the six-, seven- and eight-carbon alcohols indicated. The correlation of the "flats" in the curves and the specific gravities is made with data, for the isomer indicated, obtained from Tables Ia, b, and c. In every case, save for the two unidentified octenes, this correlation leads to the designation of the isomer as given below each curve. It is from such distillation curves that the data in Table V were deduced.

From Table V, it is seen that the following are the primary products of dehydration on alumina gel.

(1) Hexanol-1: hexene-1; 2-methylpentene-1; 4-methylpentene-2.

(2) 2-Ethylbutanol-1: hexene-1; 3-methylpentene-2; 2-ethylbutene-1; 2-methylpentene-2; hexene-3.

(3) Heptanol-4: heptene-3; 2-ethylpentene-1; 2-methylhexene-2.

(4) 2,4-Dimethylpentanol-1: 4-methylhexene-2; 2,4-dimethylpentene-2; 3,4-dimethylpentene-2.

(5) 2,4-Dimethylpentanol-3: 2-methylhexene-3; 2,4-dimethylpentene-2; 3,4-dimethylpentene-2.

(6) 2-Ethylhexanol-1: 2-methylheptene-2; 3-methylheptene-2; 4-methylheptene-4; octene-3.

The only one of these cases in which there is any doubt as to the primary products is that of hexanol-1 on thoria. The fastest rate used still gave 100% dehydration.

Analysis of Results

Production of Oily Polymer.—The polymer is produced in larger quantity at the faster rates. This is the case with both alumina and thoria. As was pointed out in the detailed table of effect of rate of passage on the products of hexanol dehydration, the amount of polymer depends on the amount of hexanol in the vapor. Although the concentration of hexene-1 is as large at 11.2 cc./hour as at 22 cc./hour, the amount of polymer has fallen sharply and there is no hexanol left unchanged. To confirm this, purified hexene-1 was passed over a thoroughly dry alumina. Although every other condition was the same, there was no polymer formed. Water vapor mixed with hexene-1 likewise had no effect. This points definitely to an intermediate in the dehydration reaction which can either polymerize or give olefin. Evaporation without drying shows that the amount of polymer is not changed by calcium chloride used in drying.

Formation of Ethers.—Ethers are known to be very unstable on dehydration catalysts at temperatures over 350°. The presence of an ether was found only in the products from the two most rapid passages of hexanol-1.

Distribution of Products.—Table III in section (A) shows that isomerization occurs as passage of alcohol becomes slower, the olefins having both greater availability of surface and more time on the surface. The straight chain olefin, hexene-1, seems to be the least stable at the temperature and passes to the various isomers tabulated. The other primary products are more stable, 2-methylpentene-2 also tending to disappear, however. This, also, is confirmed by passage of the pure isomer. The isomer 3-methylpentene-2-*trans* seems to be the most stable and the percentage of this increases as the rate decreases further. In the rapid dehydration of 2-ethylbutanol-1 (Table V), 3-methylpentene-2-*cis* appears as the major primary product. In the slower passage the same effects of isomerization appear. Again 2-methylpentene-2 and the straight chain hexene-1 disappear, as does the major product. Again, 3-methylpentene-2-*trans* appears as the major secondary product. In the dehydration of hexanol-1 on thoria, it is evident that both dehydration and isomerization occur much more rapidly than on alumina since, even at the fastest rate, there is no unchanged alcohol and the major products appear to be 3-methylpentene-2 and hexene-1. All the hexene-1 which has isomerized has gone to this 3-methylpentene-2 isomer and at the slower rate there is nothing in addition but polymer.

The three 7-carbon alcohols dehydrated show somewhat similar behavior. Heptene-3, the straight chain major product from heptanol-4, isomerizes to branched chain isomers which in turn give 3-methylhexene-2, while 2-methylhexene-2 goes directly to 3-methylhexene-2-*trans*, as is shown if the pure isomer is passed over alumina at various rates of speed. This is exactly analogous to hexanol-1. The other two 7-carbon

alcohols are different in that there is no straight chain primary product. The migration of a methyl group across a double bond toward the center of the molecule, which is the trend observed above, is prevented for either of two reasons. The length of the hydrocarbon chain is such that either the double bond is one carbon removed from the side chain or migration across the bond makes the side chain no more central. For both 2,4-dimethylpentanol-1 and 2,4-dimethylpentanol-3 the primary and secondary products are the same, the percentages changing with the amount of unchanged alcohol in the vapor.

Amount of Unchanged Alcohol.—From the results on alumina, it would seem that ease of dehydration is in the order:

	2-Ethylbutanol-1	>	heptanol-4	>	hexanol-1	>	2,4-dimethylpentanol-1	>	2,4-dimethylpentanol-3
Unchanged alcohol	*3* (primary)		*5* (secondary)		*20* (primary)		*20* (primary)		*40* (secondary)

where the numbers are the amount of unchanged alcohol resulting from dehydration under comparable conditions.

While it has generally been found that the comparative rates of dehydration of alcohols are in the order primary, secondary, tertiary, this does not hold here.

Discussion.—From the results above, it is possible to derive a mechanism which affords a very convenient picture and proves itself useful in understanding dehydration of higher alcohols.

Mechanism.—Models for the above five alcohols were constructed to scale. To investigate what possible hydrogens could be involved with the hydroxyl group in dehydration, the models were contorted in every way possible. Those hydrogens which could actually touch the oxygen of the hydroxyl group were taken as possibilities. The hydrogens on carbons 3, 4 and 5 of heptanol-4 are inaccessible, but the hydrogens on 1, 2, 6, and 7, are all equally accessible. In hexanol-1, only the hydrogens on carbon 2 are inaccessible, those in fact which are usually supposed to be involved. In the case of 2,4-dimethylpentanol-1 only the hydrogens on carbon 2 are entirely inaccessible. Similarly with the others. Assuming that by elimination of water in these various possible ways, there is formed a sort of activated ring involving 3, 4, 5 or 6 carbons, as the case may be, a series of reactions may be predicted. The predictions are made in the following manner.

Each bond in the hypothetical ring is in turn broken and a free radical intermediate indicated which satisfies its valence requirements internally, giving rise to an olefin. That such predictions are valid is shown by Egloff in his book "Reactions of Pure Hydrocarbons,"[6] in which are enumerated the reactions of many cyclic hydrocarbons under various conditions, together with the products formed. While the reactions of such hydrocarbons at high temperatures may produce a bewildering array of products, such a method of prediction accounts for all in an orderly fashion. The formation of 5- and 6-membered rings in any quantity was early ruled out because catalytic pyrolysis of such substances produces characteristic products: comparatively high boiling homologs of cyclohexene in the case of the 6-membered ring; various gaseous hydrocarbons from the 5-membered ring. Both of these cases could have been detected easily but were found in none of the investigations under discussion.

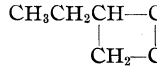
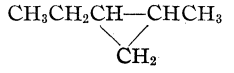
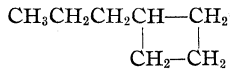
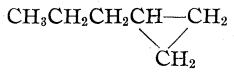
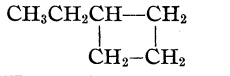
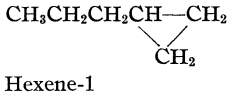
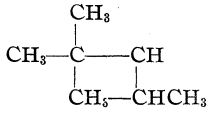
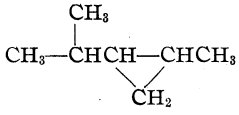
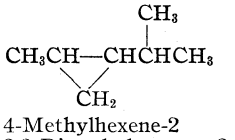
The reason for this non-formation of the larger, more stable, rings may lie in the fact that the alcohols used were too short-chained to allow such rings to be formed except by the reaction of the hydroxyl group with primary hydrogens. The great difference in reactivity between primary and secondary hydrogens is well exemplified by the cyclization of the hydrocarbons on chromic oxide. *n*-Octane, when dehydrogenated on chromic oxide, does not give ethylbenzene as the major product as might be supposed, but according to Moldavski,[7] gives 90% *o*-xylene and only 10% ethylbenzene. This together with the facts that octane is easier to aromaticize than heptane and heptane than hexane means that two secondary hydrogens are removed more easily than one primary and one secondary, while one primary and one secondary are removed more easily than two primary hydrogens.

Forming the hypothetical 4- and 3- membered rings with the five alcohols discussed, certain conclusions result. It will be noted that 2,4-dimethylpentanol-3 does not allow the formation of a 4-membered ring, while 2,4-dimethylpentanol-1 allows two different 3-membered rings,

(6) G. Egloff, "The Reactions of Pure Hydrocarbons," Reinhold Publishing Corp., New York, N. Y., 1937, pp. 689–696.

(7) Moldavski and Kamusher, *Compt. rend. Acad. Sci. U. S. S. R.*, **1**, 355 (1936).

TABLE VI

Alcohol	4-Carbon ring	3-Carbon ring	Found	Hydrogens available 3-Ring *p*	3-Ring *s*	4-Ring *p*	4-Ring *s*	4-Ring *t*
2-Ethylbutanol-1								
	Hexene-2 3-Methylpentene-2	Hexene-3 3-Methylpentene-2 2-Methylpentene-2 2-Ethylbutene-1	Hexene-3 3-Methylpentene-2 2-Methylpentene-2 2-Ethylbutene-1	0	4	6	0	0
Heptanol-4								
	Heptene-3 2-Ethylpentene-1 3-Methylhexene-2	Heptene-3 2-Ethylpentene-1 3-Methylhexene-2 2-Methylhexene-2	Heptene-3 2-Ethylpentene-1 2-Methylhexene-2	0	4	6	0	0
Hexanol-1								
	Hexene-1 2-Ethylbutene-1 3-Methylpentene-2	Hexene-1 2-Methylpentene-1 2-Methylpentene-2	Hexene-1 2-Methylpentene-1 4-Methylpentene-2	0	2	0	2	0
2,4-Dimethylpentanol-1								
	2,2-Dimethylpentene-3 2,4-Dimethylpentene-2	 2,4-Dimethylpentene-2 2,3-Dimethylpentene-3 4-Methylhexene-2	 2,4-Dimethylpentene-2 2,3-Dimethylpentene-3 4-Methylhexene-2	3	2	0	0	1
2,4-Dimethylpentanol-3	Impossible			12	0	0	0	0
		4-Methylhexene-2 2,3-Dimethylpentene-3 2,4-Dimethylpentene-2	2-Methylhexene-3 2,3-Dimethylpentene-3 2,4-Dimethylpentene-2					

only one of which involves a secondary hydrogen, however. It also may be seen that, when only one carbon in the 3- or 4-membered ring is substituted, there are only two scissions which are different; when two carbons are substituted, there are three; if the two substitutions in the 4-membered ring are different, there are three. It will be remembered that if these rings were actually formed, the momentary presence of the oxygen and a hydrogen atom in the ring makes 3- and 4-membered rings into 5- and 6-membered rings, respectively.

While, in general, the products are similar from both types of ring, they are different enough in some cases to allow discrimination. The case of butanol-1 is a good example. The 4-membered ring allows formation only of butene-1 and butene-2. The 3-membered ring allows these two and also isobutene. This latter actually is found as one of the products of dehydration with iodine[8] as catalyst. This also points to the comparative ease of removal of a secondary hydrogen as compared with a primary.

Table VI shows the assumed 3- and 4-membered rings and their products for the five alcohols discussed. Under the alcohol considered are shown the hypothetical 3- and 4-membered rings resulting from dehydration together with the products to be expected from them. The column "Found" gives the primary products actually found. The column "Hydrogens available" indicates the number of hydrogens bound to carbon available for the formation of each ring and the class of hydrogen: primary, secondary and tertiary.

The exact agreement of the primary products found and those predicted from the 3-membered ring is apparent. In hexanol-1, there is one product which is not accounted for in either way, but the 3-membered ring still gives the better agreement. The tabulation of the hydrogens available brings to light an important corollary.

(8) F. C. Whitmore, "Organic Chemistry," D. Van Nostrand Co., New York, N. Y., 1937, p. 40.

Ease of Dehydration.—Under the discussion of the amount of unchanged alcohol, it was shown that the order of ease of dehydration was not that expected. In Table VII are listed the number of hydrogens available in the same order as found for ease of dehydration.

TABLE VII

	2-Ethyl-butanol-1	Hep-tanol-4	Hex-anol-1	2,4-Di-methyl-pentanol-1	2,4-Di-methyl-pentanol-3
Order found	3	5	20	20	40
3 ring, s	4	4	2	2	0
3 ring, p	0	0	0	3	12
4 ring, s	0	0	2	0	0
4 ring, p	6	6	0	0	0

Table VII shows the exact correlation between the number of secondary hydrogens available for the formation of the 3-membered ring by the elimination of water, and the ease of dehydration. The most difficult to dehydrate is 2,4-dimethylpentanol-3, as is shown by the large amount of unchanged alcohol after a passage. There are no hydrogens available except primary ones, in a position for 3-ring formation. At the slower passage, dehydration involving the primary hydrogens takes place, and complete dehydration is made possible by the large number of such hydrogens available.

The products of dehydration as reported by other workers conform to this proposed mechanism of dehydration. To be noted in this connection is the paper by Cramer and Glasebrook[9] which has appeared since the completion of the work in this paper. The dehydration of 2,2-dimethylbutanol-3 was found to give several products, namely, 2,2-dimethylbutene-3, 2,3-dimethylbutene-1 and 2,3-dimethylbutene-2, which are the products to be expected from the mechanism proposed above.

Conclusion

Evidence from three sources thus points to an activated intermediate stage having the configuration corresponding to a 3-membered ring. (1) The most strongly adsorbed substance in the system involved in the dehydration of an alcohol is the alcohol itself, by reason of its hydroxyl group. The formation of larger amounts of polymer when alcohol vapor is present in larger quantities indicates that the alcohol is flushing something from the surface. This substance, which produces olefins if allowed to remain on the surface, may be displaced as polymer by alcohol or, displaced as active intermediate, may polymerize in the vapor phase. The presence of some polymer even at the slowest rates indicates that flushing by alcohol still exists on a portion of the catalyst, probably at the point of entrance to the catalyst. Pure olefin, with or without water vapor, gives no polymer whatsoever on alumina and thoria surfaces.

(2) Ease of dehydration is shown to be correlated with the number of secondary hydrogens on the carbon second from that having the hydroxyl group. The elimination of water in this position causes the formation of an activated intermediate stage with the configuration of a 3-membered ring, and this in turn breaks down.

(3) The products which are predicted from the reactions of pure hydrocarbons, assuming that this activated cyclopropane configuration is formed, correspond exactly with those found to be the actual primary products of dehydration. The effects of various catalysts on the products may be summarized as follows. Alumina tends to break all the bonds of the ring more or less indiscriminately and to give all the products possible. The proportions of the various products give the relative frequency of the various scissions. This fits with other observations that alumina opens bonds in those rings which are strained. Thoria is less general in its action and tends to break one bond selectively. This is illustrated in the alcohols studied by other workers. Chromium oxide introduces the further complication of dehydrogenation. The olefin gives aromatization instead of isomerization, but, in this case, poisoning of the catalyst prevents ready determination of the nature of the olefin products.

Summary

1. An apparatus and a procedure have been described which allow the separation of isomers resulting from the dehydration of an alcohol.

2. The effects of rate of passage and change of catalyst have been investigated and interpreted.

3. Ease of dehydration and structure of the alcohol have been correlated and ease shown to be dependent on the availability of secondary hydrogen atoms on the carbon beta to that with the hydroxyl group.

4. The conclusion is derived that there is an activated intermediate stage in dehydration that has the configuration corresponding to a 3-membered ring.

(9) Cramer and Glasebrook, THIS JOURNAL, **61**, 230 (1939).

PRINCETON, NEW JERSEY RECEIVED MARCH 4, 1939

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

Isomerization of Alkenes on Alumina and Thoria

BY SEYMORE GOLDWASSER AND HUGH S. TAYLOR

Investigation of catalytic dehydration of C_6–C_8 alcohols has shown it to be an excellent method for the production of alkene hydrocarbons for the catalytic study of their vapors.[1] One of the facts brought out by this investigation is that olefins isomerize extensively when allowed to remain in contact with the active surfaces studied. Further work with the purified olefins themselves was thought desirable.

The apparatus for the catalytic studies[2] and for fractionation of the liquid products[1] have been described already. The procedures both for the passage of olefin and the separation and identification of the products were identical with those described. No drying of the hydrocarbons over calcium chloride was necessary, however, in the runs with pure olefins. The olefins used in the study of isomerization were the purified fractions resulting from the dehydrations and the isomerizations themselves. The catalysts used were prepared as previously noted.

Experimental Results.—To determine whether results on different samples of a catalyst can be compared with each other, ten different preparations of pure alumina were made. These were as follows: solutions of aluminum nitrate were prepared in the five strengths—1.5, 1, 0.5, 0.3 and 0.1 *N*. Aluminum hydroxide was precipitated by the addition of 15 *N* ammonia, rapidly and without stirring in the case of the 1.5 *N* aluminum nitrate solution (catalyst a), 0.1 *N* ammonia slowly with rapid stirring in the case of the 0.1 *N* solution of aluminum nitrate (catalyst b). The others were graded between. Two samples of each catalyst were made, one was heated to boiling before filtration, the other filtered and dried at 80° before final drying. The only effect found was on the particle size and appearance of the alumina itself. Isomerization was not affected. The results found for the two most contrasting catalysts are as follows.

TABLE I

Al_2O_3: Temperature 398°, Rate 3.1 cc./hr./10 g.

The runs were in the order hexanol-1 (a), hexene-1 (a), hexanol-1 (b), hexene-1 (b). The catalyst was dried by passing dry nitrogen over it for 12 hours. This was done between hexanol-1 and hexene-1 the first time only. The second time the catalyst was allowed to be wet. Fractionation of products of hexanol-1 dehydration without any drying on calcium chloride show the same proportion of polymer. In this case it is impossible to separate the fractions because of azeotropic mixtures of water and hydrocarbons. The polymer is easily separated, because it has a much higher boiling point.

	Hexanol-1 (a)	Hexanol-1 (b)	Hexene-1 (a)	Hexene-1 (b)
4-Methylpentene-2	2%	2%		
2-Methylpentene-1	1.1	1.5		
Hexene-1	22.0	23.7	5.9	6.3
3-Methylpentene-2-*t*	38.0	36.8	9.8	10.2
2-Ethylbutene-1	9.0	8.5	38.7	38.3
2-Methylpentene-2	6.0	6.2	27.7	27.9
Hexene-3	3.0	3.2	11.3	10.6
3-Methylpentene-2-*c*	2.0	1.8	5.3	5.2
Hexene-2	5.0	4.1		
Polymer	12.0	13.0	0	0

It may be seen that the mode of preparation of the pure alumina catalyst has no appreciable effect on the distribution of products. Catalyst (a) is made up of large glossy translucent chunks; (b) crumbles and is white. To be specially noted is the fact that there is no polymer formed in the runs with pure hexene-1, wet or dry. After two runs, the alumina is jet black from carbonization. This has no effect on the distribution of products. The products are found to be the same immediately after burning off the carbon with oxygen-bearing nitrogen and after ten runs without burning off the carbon.

Comparison of the products of dehydration of hexanol-1 and isomerization of hexene-1 at comparable rates of passage shows that the change of products from the dehydration with increase in rate is the result of progressive isomerization of the primary product hexene-1, and not to a change of mechanism of dehydration. Table II demonstrates this.

Hexene-1 shows the same products at 11.2 cc./hr. as hexanol-1 shows at 3.1; the same holds true for hexene at 22.5 cc. and hexanol-1 at 11.2 cc./hr./10 g. At the higher rates, hexene-1 tends to remain unchanged. The conclusion is that the alcohol is more strongly adsorbed than the olefin so that, at the faster rates, the proportion of material adsorbed changes so that the olefin does not remain on the surface long enough to isomerize.

(1) S. Goldwasser and H. S. Taylor, THIS JOURNAL, **61**, 1751 (1939).
(2) S. Goldwasser and H. S. Taylor, *ibid.*, **61**, 1260 (1939).

At the slower rates, hexene-1 isomerizes more rapidly than the hexene-1 mixed with the alcohol since no surface is taken up by the alcohol or the product water. However, it is clear that the additional isomers produced at the slower rate of passage of alcohol are due to isomerization of the major primary product, hexene-1.

The course of isomerization as related to the structure of the olefin is summarized in Table III.

Analysis of Results.—(1) The first and most obvious conclusion concerning isomerization to be drawn from this table is that the straight chain olefin is the most unstable at these temperatures. Hexene-1 and heptene-1 give a large number of isomers on alumina. No other isomer gives any straight chain substance, however.

(2) On alumina at 398°, equilibrium is not reached from either the 2-methylpentene-2 side or the 3-methylpentene-2 side, since the per-

TABLE II

Alumina at 398°: (a) is hexanol-1, (b) is hexene-1

Rate in cc./hr./10 g. catalyst = Products	45.5 (a)	(b)	22.5 (a)	(b)	11.2 (a)	(b)	3.1 (a)	(b)
4-Methylpentene-2-*c* and -*t*	2		2		1.1		2	
2-Methylpentene-1	5.5		5		6.1		1.1	
Hexene-1	49.0	92	51	89	66.7	24	22	6.3
3-Methylpentene-2-*t*		8		9.2	7.1	36	38	10.2
2-Ethylbutene-1				1.8	2.3	13	9	38.3
2-Methylpentene-2						12	6	27.9
Hexene-3						8	3	10.6
3-Methylpentene-2-*c*						5	2	5.2
Hexene-2						2	5	
Polymer	18	0	20	0	16	0	12	0
Unchanged hexanol	24		20		0		0	

TABLE III

ISOMERIZATION OF OLEFINS AS RELATED TO STRUCTURE, RATE = 3.12 CC./HR./10 G.

Substance	Cat.	*T*, °C.	Products A	B	C	D	E	F	G	H	I	J	K	L	M	N
Hexene-1	Al_2O_3	398	38.3		28		10.2		6.3		11				0	
Heptene-1				5.0		0		70		25		0			0	
Hexene-1	ThO_2	398	5				90								5	
2-Methylpentene-2	Al_2O_3	398			62		35								3	
2-Methylhexene-2				15		42		40							5	
2-Methylpentene-2	ThO_2	398	25		2		70								3	
2-Methylhexene-2				20		3		72							5	
3-Methylpentene-2-*t*	Al_2O_3	398	5		22		70								3	
3-Methylhexene-2-*t*				2		10		82							6	
3-Methylpentene-2-*t*	ThO_2	398	19		7		70								4	
3-Methylhexene-2-*t*				15		2		76							7	
3-Methylpentene-2-*t*	ThO_2	440	30		5		40						16		6	3
3-Methylhexene-2-*t*				20		8		45						11	9	7
3-Methylpentene-2-*t*	Al_2O_3	440	6		8		52						29		3	2
3-Methylhexene-2-*t*				3		5		63						18	7	4
2-Ethylbutene-1	ThO_2	398	26		2		69								3	
2-Ethylpentene-1				21		3		71							5	
2-Methylpentene-2	Cr_2O_3	474	32% benzene, 65% unsatd. 3% satd.													
3-Methylpentene-2-*t*			32%		63%			5%								

A = 2-Ethylbutene-1 C = 2-Methylpentene-2 E = 3-Methylpentene-2-*t*
B = 2-Ethylpentene-1 D = 2-Methylhexene-2 F = 3-Methylhexene-2-*t*
G = Hexene-1 I = Hexene-3 K = 2-Methylpentene-1 M = Polymers
H = Heptene-1 J = Heptene-3 L = 2-Methylhexene-1 N = Isohexane

The primary fractionation data from which Table III, as well as Tables I and II, were constructed are given in Table IV which lists, from a given isomerization of a pure hexene or heptene, the volumes of liquid obtained at each "plateau" with the boiling range indicated.

TABLE IV

YIELDS AND FRACTIONATION DATA OF ISOMERIC HEXENES AND HEPTENES

Substance	Cat.	T, °C.	Volume distilled Total	Plateaus	Inter-mediates	Fractionation data Cc.'s collected in plateaus of indicated boiling range
Hexene-1	Al_2O_3	398	100	95	5	5.9 (63.5–63.6); 9.6 (65.6–65.7); 36.3 (66.6); 26.5 (67.1–.2); 10.4 (67.5–67.6).
Heptene-1			100	94	6	70.5 (91.2–91.3); 4.7 (93.9–94.0); 23.5 (94.9–95.0).
Hexene-1	ThO_2	398	55	53	2	47.7 (65.6–65.7); 2.7 (66.6–66.7); 2.6 (over 150).
2-Methylpentene-2	Al_2O_3	398	70	68	2	23.8 (65.6–65.7); 42.2 (67.1–67.2); 2.2 (over 145).
2-Methylhexene-2			85	82	3	32.8 (93.1–93.2); 12.3 (93.9–94.0); 34.5 (94.4–94.5); 4.1 (over 160).
2-Methylpentene-2	ThO_2	398	91	87	4	61.0 (65.6–65.7); 21.8 (66.6–66.7); 1.7 (67.1–67.2); 2.6 (over 150).
2-Methylhexene-2			79	75	4	54.8 (93.1–93.2); 15.0 (93.9–94.0); 2.2 (94.4–94.5); 3.7 (over 160).
3-Methylpentene-2-*t*	Al_2O_3	398	93	90	3	63.0 (65.6–65.7); 4.5 (66.6–66.7); 19.8 (67.1–67.2); 2.7 (over 150).
3-Methylhexene-2			59	56	3	46.5 (93.1–93.2); 1.1 (93.9–94.0); 5.6 (94.4–94.5); 3.4 (over 160).
3-Methylpentene-2-*t*	ThO_2	398	76	73	3	51.1 (65.6–65.7); 13.9 (66.6–66.7); 5.1 (67.1–67.2); 2.9 (over 150).
3-Methylhexene-2			100	95	5	72.1 (93.1–93.2); 14.2 (93.9–94.0); 1.9 (94.4–94.5); 6.6 (over 160).
3-Methylpentene-2-*t*	ThO_2	440	100	94	6	2.8 (60.1–60.2); 15.0 (61.9–62.0); 37.6 (65.6–65.7); 28.2 (66.6–66.7); 4.7 (67.1–67.2); 5.6 (over 150).
3-Methylhexene-2			89	85	4	5.8 (90.0–90.1); 9.5 (91.1–91.2); 38.3 (93.1–93.2); 17.0 (93.9–94.0); 6.8 (94.4–94.5); 7.7 (over 160).
3-Methylpentene-2-*t*	Al_2O_3	440	93	88	5	1.8 (60.1–60.2); 25.5 (61.9–62.0); 45.8 (65.6–65.7); 5.3 (66.6–66.7); 7.1 (67.1–67.2); 2.6 (over 150).
3-Methylhexene-2			97	91	6	3.6 (90.0–90.1); 16.4 (91.1–91.2); 52.3 (93.1–93.2); 2.7 (93.9–94.0); 4.6 (94.4–94.5); 6.4 (over 160).
2-Ethylbutene-1	ThO_2	398	100	97	3	67.0 (65.6–65.7); 25.3 (66.6–66.7); 2.0 (67.1–67.2); 2.9 (over 150).
2-Ethylpentene-1			90	87	3	61.8 (93.1–93.2); 18.3 (93.9–94.0); 2.6 (94.4–94.5); 4.3 (over 160).

centages of products resulting are not the same from the two isomerizations. The same holds true for 2-methylhexene-2 and 3-methylhexene-2. On thoria, however, the composition of the isomerized liquid is practically the same starting from either the 2- or 3-methyl isomer. Therefore, isomerization is faster on thoria than on alumina. This agrees with the comparative rates of dehydration found for these two catalysts. That there is still some straight chain isomer left after passage over alumina and none over thoria also points to this conclusion. It is also to be noticed that the 7-carbon olefins isomerize slightly faster than the 6-carbon ones, as is evidenced by the fact that the isomers are closer to the composition found on thoria under the same conditions.

(3) The main isomerization observed is the migration of a methyl group across a double bond. The more stable of the two positions is the more centralized one. All 2-methyl compounds give the corresponding 3-methyl compounds in large quantities. The reverse migration occurs only to a small extent.

(4) The isomer 2-ethylbutene-1 is the result of migration, not of a methyl group but of the double bond. The methyl group is in the same relative position as in the stable 3-methylpentene-2. Both 2-ethylbutene-1 and 2-ethylpentene-1 give the same composition of products over thoria as the 2- and the 3-methyl compounds. The similarity in composition of the products from isomerization of all these hydrocarbons indicates a reaction path conforming to a specific pattern.

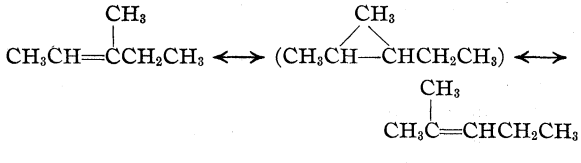
(5) Rise in temperature to 440° causes the double bond to shift to the end of the chain and considerable 2-methylpentene-1 and 2-methylhexene-1 are found. Decomposition has been enough to allow some hydrogenation of olefin. The same is true for both chromium and thorium oxides.

(6) Contrary to the findings concerning the

formation of polymer in the isomerization of a pure straight chain olefin, it is seen here that, while the straight chain olefin does not give any polymer on isomerization, there is some formed in all other cases.

(7) The formation of benzene from the 2-methylpentenes and 3-methylpentenes with chromic oxide catalyst points to the fact that there must be some isomerization to the straight chain taking place with consequent ring closure of the olefin. The only olefin for which any isomerization to the straight chain seems likely is the 2-methylpentene-1 isomer. If only a trace of hexene-1 or hexene-2 is formed from this isomer, benzene is formed immediately on the catalyst and the 2-methylpentene-1:hexene-1 equilibrium is displaced to the straight chain side. The results at 440° on thoria and alumina show the extent to which 2-methylpentene-1 is formed at higher temperatures. The fact that there is only 32% aromatic yield from the methylpentenes as compared with 95 to 100% from the hexenes is evidence of the comparative slowness of the isomerization to straight chain olefins even at the higher temperature of 474°.

Mechanism.—A mechanism which brings together several of the above findings concerning isomerization is, as in the case of the dehydration of alcohols described in a previous paper, the formation of an activated intermediate stage having the configuration corresponding to a 3-membered ring. That is, it is assumed that, on the surface of the catalyst, the following takes place



If this occurs, the products may be predicted exactly as in the case of the alcohols, and are found to agree exactly with those found. The formation of polymer in the isomerization of the branched olefin points to the same type of activated intermediate found with the alcohols. That no compound such as 4-methylpentene-2 is found, as well as that 4-methylpentene-2 and its analogs do not isomerize, indicates that methyl groups migrate across double bonds only under these conditions.

At higher temperatures, where migration of a double bond is found to take place, 2-methylpentene-1 is formed from 2-methylpentene-2 by the same mechanism. The methyl group is again on the inside of the double bond. It is this type of reaction which gives hexene-1 as a product, which then immediately aromaticizes on chromium oxide.

Summary

1. Two different preparations of the same alumina catalyst have been shown to be comparable as to their effects on isomerization of alkenes.

2. Change in distribution of isomers produced with change in rate of passage of an alcohol over a dehydrating catalyst has been shown to be due to isomerization of the olefin products themselves.

3. The products of isomerization at 400° have been determined for several olefins and comparative rates of isomerization on thoria and alumina studied.

4. A mechanism postulating an intermediate 3-carbon ring structure similar to that proposed for the dehydration of alcohols has been found to account for the products of isomerization.

5. The order of stability of some olefins at 400° is as follows: 3-methylpentene-2-*t* > 2-ethylbutene-1 > 3-methylpentene-2-*c* > 2-methylpentene-2 > 2-methylpentene-1 > hexene-1. 3-Methylhexene-2-*t* > 2-ethylpentene-1 > 3-methylhexene-2-*c* > 2-methylhexene-2 > 2-methylhexene-1 > heptene-1.

PRINCETON, NEW JERSEY RECEIVED APRIL 17, 1939

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

Aromatization of Heptane, Heptene and Hexene Isomers on Chromic Oxide

BY SEYMORE GOLDWASSER AND HUGH S. TAYLOR

Aliphatic alcohols containing six to eight carbon atoms have been found to be good sources of various aliphatic alkenes.[1] A convenient mechanism for the interpretation of the course of isomerization of these olefins on active non-dehydrogenating surfaces having been formulated, further work was undertaken on dehydrogenation. The present paper records a study of the effects of structure and rate of passage of hydrocarbons on the reactions involved in ring closure and aromatization.

Apparatus.—The apparatus and procedure were the same as described for the dehydrogenation of cycloöctene.[2] Samples of pure cyclohexene and 1,3-cyclohexadiene were kindly sent us from the Harvard Laboratories. Pure *n*-heptane, sulfur-free, was obtained from the California Chemical Company. All the other materials were prepared by dehydration of alcohols.

Analysis.—Because chromium oxide catalysts poison too quickly to give sufficient material for ready determination of composition by fractionation, a different method of analysis had to be used. Specific gravities and Hanus numbers were first determined for each sample. The spread of physical properties between aromatics and naphthenes, naphthenes and olefins, olefins and saturates, allowed the composition to be calculated fairly well from these determinations alone. The assumption is made that there are no substances present which do not belong to these classes. The compositions found were often checked both by calculation from off-gas volume and composition and from analysis of the liquids by means of dimethyl sulfate and bromination. There was never any disagreement between the various methods of checking. Fractionation of the liquid products from certain catalysts which do not poison over long periods of time gave still another check of the validity of the calculations used.

Experimental Results

Cyclohexene and Cyclohexadiene.—The results obtained are given in Table I.

Cyclohexene is observed to give a quantitative yield of hydrogen at 390° and the evolution of hydrogen ceases completely only below 300°. The cyclohexene continues to give benzene, however, to temperatures as low as 200° by a self reduction–oxidation on the surface. When temperatures below that causing evolution of hydrogen are used, raising the temperature of the catalyst does not cause evolution of hydrogen from fresh cyclohexene, but the value for conversion to benzene remains that of the lowest temperature used. After getting 0.9% benzene at 163°, a rise to 316° gave only 1% as compared with 20% at 305° after revivifying. Revivification by oxidation in the standard manner always restored full activity. It seems therefore that, at lower temperature, the cycloölefin, with a longer life on the surface than at higher temperatures, poisons the catalyst and remains on the surface, possibly as a hydrocarbon fragment desorbable only with difficulty.

TABLE I

Rate: 3.12 cc./hr./15 g. Cr_2O_3 catalyst

Olefin	*T*, °C.	Moles gas per mole olefin (100% H_2)	% benzene	% cyclohexane	% unchanged
Cyclohexene	395	2	100	0	0
Cyclohexene	337	0.5	50	50	0
Cyclohexene	276	0	10.4	20.8	68.8
Cyclohexene	211	0	8.17	16.3	75.5
Cyclohexene	163	0	0.90	1.8	97.2
Cyclohexene	239	0	0.80	1.7	97.2
Cyclohexene	316	0	1.0	1.7	97.3
Revivify for 24 hours					
Cyclohexene	305	0	20	40	39.7
Cyclohexene	175	0	2.3	4.7	93
Cyclohexene	246	0	2.1	4.9	93
Revivify for 24 hours					
Cyclohexene	510	2	100	0	0
Cyclohexadiene	193	0.9	97	3	0
Cyclohexadiene	137	0	43.6	21.8	34.6
Cyclohexadiene	146	0	44	22	35
Cyclohexadiene	95	0	33	17	50
Revivify for 24 hours					
Cyclohexadiene	137	0	48.6	21.3	35.6
Cyclohexadiene	95	0	33	17	50
Cyclohexadiene	193	0	34	18	48
Revivify for 24 hours					
Cyclohexadiene	95	0	33	17	50
Revivify for 24 hours					
Cyclohexadiene	500	1	100	0	0

Non-catalytically at 500°, cyclohexane has been shown to give as products 25% benzene, 40% hydrogen and 22% ethane. In not one of the runs tabulated was there any decomposition. Even at 500°, although the catalyst had never been heated above 490°, the water vapor which must have come off had no effect on the cycloölefin, although it oxidized *n*-heptane and other aliphatic hydrocarbons. Here, with cyclohexene and a dehydrogenating catalyst, the production of ben-

(1) Goldwasser and Taylor, THIS JOURNAL, **61**, 1751 (1939).
(2) Goldwasser and Taylor, *ibid.*, **61**, 1260 (1939).

TABLE II

HEPTANE ON CHROMIC OXIDE GEL

These runs were done in the order indicated and are the values found after twenty minutes. After an hour, poisoning has cut down the conversion from 40–50%. The catalyst was revivified between each run.

Catalyst	T, °C.	Liq. rate cc./hr./15 g.	Contact time, min. (gas)	Off-gas Mol./mol.	Off-gas % H_2	Liquid composition % arom.	Liquid composition % satd.	Liquid composition % unsatd.
Cr_2O_3	468	3	9	3.75	95	100	0	0
Cr_2O_3	468	18	1½	3.03	92	92.3	5.9	1.8
Cr_2O_3	468	9	3	3.77	94	100	0	0
Cr_2O_3	468	3	9	3.75	95	100	0	0
Cr_2O_3	468	27	1	2.75	98	69	25	6
ThO_2	468	3	9	0.05	1	0	97.5	2.5
Al_2O_3	540	3	9	.05	4	0.5	99.1	.3
Al_2O_3 (act.)	540	3	9	.4	42	2	80	18

zene is so rapid that there is little chance for decomposition.

Cyclohexadiene is exactly similar to cyclohexene except that the lowest temperature at which hydrogen evolution occurs is 175° instead of 300°. Rise of temperature gives no hydrogen with new cyclohexadiene as with cyclohexene. At 95°, just a little above the boiling point of benzene, there is still 33% yield of benzene with 17% cyclohexadiene hydrogenated and 50% unchanged. This small yield is not the result of permanent poisoning as is shown by revivification and repetition at the low temperature without any intervening run.

***n*-Heptane.**—The effect of rate on the conversion of *n*-heptane to toluene is shown in Table II.

The fastest rate at which complete conversion to toluene is found is 9 cc. per hour, with the vapor in contact with the catalyst for three minutes. At a rate three times this, conversion in one passage is still 69%.

The results with thoria and pure alumina show the normal amount of unsaturation which accompanies thermal decomposition. There is no aromatization. At 540°, small amounts of aromatic normally appear in thermal decompositions of hydrocarbons. The second alumina cited in the table has a small iron content and is sufficiently dehydrogenating to give some aromatization. The great difference between a dehydrogenating and an isomerizing catalyst is evident. The rate of poisoning or fall in the evolution of hydrogen with time decreases with increase of rate. Anything that decreases the life of an olefin on the active surface decreases the rate of poisoning.

Olefins.—The influence of structure of an olefin on aromatization is shown in Table III, which presents some typical results found with various olefins. After each run there was a ten to twenty-four hour period of revivification, an eight to ten hour reduction period and a four to eight hour period for the flushing of hydrogen from the surface by the use of purified nitrogen as described in the procedure of the first paper in this series. The order of experiment is as listed.

The results obtained may be summarized as follows. (*1*) *Effect of Rate on Conversion of Olefin.*—Heptene-1 at 474° shows complete conversion at the slowest rate tried, but poisoning is more rapid than at high rates. In the experiments at the rapid rate, where poisoning takes place more slowly, a lower rate of aromatization than is the case for heptane is found. This indicates that the olefin is on the surface for a shorter time interval.

(*2*) *Effect of Temperature on Conversion.*—A rise in temperature of 50° doubles the percentage of heptene-1 converted to toluene and causes the time for half-way poisoning to be tripled. The heptene spends less time on the surface and is more readily dehydrogenated at the higher temperature. Aromatics do not poison the catalyst.

The effect of rise of temperature on the amount of conversion of the methylpentene is less marked, although the poisoning changes qualitatively in the same way. This smaller temperature effect reflects the fact that the necessary isomerization does not have as large a temperature coefficient as dehydrogenation, and that the slow process in the over-all reaction to benzene is the isomerization of the branched hexene to the straight chain hexene.

(3) *Effect of Structure on Conversion.*—(a) 7-Carbon olefin: the position of the double bond in the straight chain heptene does not cause any

TABLE III

OLEFINS ON CHROMIC OXIDE GEL

Rate: 3.1 cc./hr./15 g.

The data given are for the first five minutes of the run. The last run carried out was a heptane run in order to make sure that the catalyst had not changed activity during many runs. Several of the above were repeated on fresh catalysts with no change in results. The heptene runs were done in the order tabulated to test reproducibility of results.

Olefin	T, °C.	Moles gas per mole reagent	Liquid sp. gr.	Liquid compn. % arom.	% sat.	% unsat.	Gas compn. % H_2	% sat.	% unsat.	Time ½ poisoned, min.
5-Methylhexene-2	424	2	0.78	50	12	38	31	57	12	10
Heptene-3	350	0	.70	0	5	95				
Heptene-3	420	1.5	.78	48	12	40				10
Heptane (check)	460	2.9	.860	100	0	0	98	1	1	
Heptene-1	424	1	.775	45	13	42	92.3	7	0	10
Heptene-1	398	0.3	.750	36	32	32	15	85	0	Rapid
Heptene-1	474	2.2	.84	90	2	8	89.5	4	6	40
Heptene-1	424	1	.770	44	15	41	91.5	8	0	10
Heptene-1	474	2.1	.839	90	2	8	89	3	8	40
2-Methylpentene-2	474	1.0	.755	32.5	7	60	56	34	10	30
3-Methylpentene-2-*t*	474	1.0	.760	32	5	62	55	38	7	30
2-Ethylbutene-1	474	1.0	.759	32	6	62	57	35	8	30
Octene-1	474	2.57	.849	84	1	15	94	3	3	
Heptene-1 18 cc./hr.	474	1.5	.78	48	1	51	93	5	2	70
Heptene-1 0.5 cc./hr.	474	2.9	.860	98	0	2	99	0	1	10
3-Methylpentene-2-*t*	424	0.6	.780	21	18	61	95	4	1	10
2-Methylpentene-2	424	.83	.735	27	24	49	92	6	2	10
2-Ethylbutene-1	424	.59	.720	20	20	60	93	6	1	10
Heptane (check)	460	3.9	.860	100	0	0	98	0	2	

marked difference in the rate of conversion to an aromatic. The rate is also that of 5-methylhexene. As was seen in the work on isomerization, the branched chain olefin is formed with great rapidity from the straight chain. 5-Methylhexene-2 is readily cyclicized and dehydrogenated. (b) 6-Carbon olefin: unless methylcyclopentane is first formed and then ring enlargement to cyclohexane occurs, any branched chain 6-carbon olefin must isomerize to the straight chain olefin before ring closure takes place. At 474°, the three isomers tried showed identical properties over chromium oxide. There is 32% conversion and the same amount of decomposition and poisoning for each. At 424°, 2-methylpentene-2 shows somewhat the higher rate of conversion to benzene, gas evolution is higher but it is of the same composition. 2-Ethylbutene-1 and 3-methylpentene-2-*t* are equal in conversion and poisoning rates, but are slower than the 2-methylpentene.

(4) *Effect of Structure on Poisoning.*—The slower the conversion to aromatics, the faster the poisoning becomes. Branched chain olefins are found to poison the catalyst more rapidly than straight chain. Again it is seen that increase of life of an olefin on the surface of a catalyst increases the rate of poisoning.

Discussion.—The conclusions to be drawn from the cycloölefin experiments are several. Once a 6-membered ring is formed on chromic oxide catalyst, the ring is not broken again at these temperatures. If the temperature is high enough to dehydrogenate an olefin, or cyclohexane or its homologs, the temperature is already too high to allow the presence of more than minute amounts of cyclohexene and even less cyclohexadiene. When cyclohexene is dehydrogenated, no cyclohexadiene intermediate can be expected to be isolated since, as has been shown, cyclohexadiene yields its hydrogen quantitatively at a temperature 100° below the lowest temperature at which cyclohexene evolves the gas. Indeed, the temperature is 25° below the temperature at which cyclohexene poisons the catalyst so that there is even no disproportionation. Although only a small amount of cyclohexene may be formed in a given reaction, the subsequent reactions to cyclohexadiene and to benzene are so rapid and complete at the higher temperatures, that the total reaction is far displaced and in some cases even 100% conversion is found.

It is evident that, for aromatization of an aliphatic hydrocarbon, dehydrogenating conditions are required which improve the chance that cyclohexene or its homologs may be formed. That there is a small but definite chance of this

happening without any special catalyst is shown by the fact that the same reaction occurs to a small extent in a Pyrex vessel and, as shown, on alumina and thoria. The reaction goes to a larger extent when dehydrogenating conditions are present. Save for the cracking reactions, the conversion of heptane to toluene is quantitative on chromic oxide gel with sufficient contact time.[3]

The data on the aromatization of the olefins agree with the results from isomerization experiments. The 6-carbon branched chain olefins, while giving only 32% aromatics as compared with 90% for the straight chain compound under the same conditions, are all quite similar. It has been shown that isomerization from one branched olefin to another is rapid at this temperature with the methyl group tending to centralize. The reason for the comparatively low yield must be the necessary isomerization to and low concentration of the straight chain olefin. This is further borne out at the lower temperature where isomerization is slower, and the differences of structure of the starting materials have more influence. The 2-methylpentene-2 isomer gives a better conversion to benzene than does either 2-ethylbutene-1 or 3-methylpentene-2-*t*, two isomers which have been shown to be about equal in rate of reaction on an active surface. The reason seems to be that there is one step less to the straight chain from the 2-methyl than from the 3-methyl isomer.

The other properties of the olefins can be summarized similarly. Both liquid and gaseous products show the occurrence of disproportionation at the lower temperatures. As the evolution of hydrogen decreases with decreasing temperature, hydrogenation to saturates begins and poisoning increases. The olefin content of the off-gas at lower temperatures is small and the liquid products have a higher concentration of saturates.

(3) Moldavski and Kamusher, *Bull. Soc. Acad. Sci., U. S. S. R. (N. S.)*, 1936, have shown that *n*-heptane, *n*-octane, and *n*-hexane cyclicize on chromic oxide gel but not on thoria, alumina, uranium oxide, zinc oxide, nickel chromate and floridin. Subsequent work by the present writers will show that cyclization actually does occur on special preparations of uranium oxide which have marked dehydrogenation properties.

Summary

1. The dehydrogenation of cyclohexene and 1,3-cyclohexadiene on chromic oxide gel surfaces has been investigated.

2. The influence of character of catalyst on aromatization has been shown. For the conversion of aliphatic hydrocarbons to aromatic hydrocarbons, a dehydrogenating catalyst must be used.

3. The influence of structure of olefin on poisoning, aromatization and disproportionation has been demonstrated.

4. Conclusions concerning isomerization drawn from these experiments agree with those found on other catalysts.

PRINCETON, NEW JERSEY RECEIVED APRIL 17, 1939

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, NO. 686]

The Electron Diffraction Investigation of the Structure of Benzene, Pyridine, Pyrazine, Butadiene-1,3, Cyclopentadiene, Furan, Pyrrole, and Thiophene

BY V. SCHOMAKER AND L. PAULING

The determination of values of interatomic distances in molecules has been found to provide much information regarding electronic structure, especially in the case of substances which resonate among two or more valence-bond structures. The interpretation of interatomic distances in terms of the types of bonds involved is made with use of an empirical function formulated originally for single bond–double bond resonance of the carbon–carbon bond.[1] There are given in this paper the results of the determination of the configurations of two molecules involving Kekulé resonance, pyridine and pyrazine, of two molecules with conjugated double bonds, butadiene and cyclopentadiene, and of three five-membered heterocyclic molecules, furan, pyrrole, and thiophene, together with the conclusions regarding their electronic structures reached by application of the bond type–interatomic distance function. In addition, because of the improvement in electron diffraction technique since the study of benzene in these Laboratories four years

(1) L. Pauling, L. O. Brockway and J. Y. Beach, THIS JOURNAL, **57**, 2705 (1935); L. Pauling and L. O. Brockway, *ibid.*, **59**, 1223 (1937).

ago[2] and because of its similarity to pyridine and pyrazine, this substance was re-investigated.

Experimental Method.—The diffraction photographs were prepared with the apparatus and technique described by Brockway.[3] Ten or more photographs were made for each substance, the electron wave length used being about 0.0613 Å. and the camera distance 10.83 cm. The values of $s_0 = 4\pi(\sin\theta/2)/\lambda$ given in the tables are averages of the values found by visual measurement of ring diameters for ten or more films.

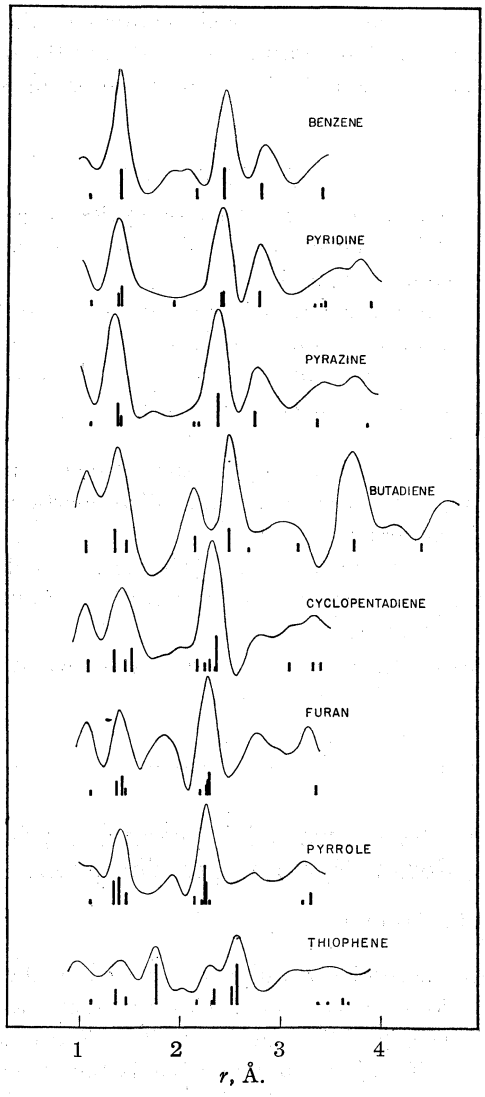


Fig. 1.—Radial distribution curves.

The radial distribution treatment,[4] with refinements soon to be described in THIS JOURNAL, was applied as the first step in the interpretation of the data for each substance. Further selection from among the small range of molecular models compatible with the radial distribution curve for each substance was then made by the usual visual method, involving comparison with simplified theoretical intensity curves for the models under discussion.

The sample of benzene used was prepared by redistilling thiophene-free benzene and rejecting the first and last portions. A similar treatment was given to pyridine (Kahlbaum), pyrrole (Eastman), and thiophene (Eastman). Butadiene was prepared by treating tetrabromobutane in ethyl alcohol solution with granulated zinc and redistilling the product several times. Cyclopentadiene was prepared by distilling dicyclopentadiene; in order that appreciable repolymerization should not take place in the sample the diffraction photographs were made immediately after the distillation (within one hour). Furan was prepared by the decarboxylation of furoic acid and purified by fractional distillation. A sample of pyrazine kindly given us by Professor F. W. Bergstrom was used without further purification.

Benzene, Pyridine, and Pyrazine.—New photographs of benzene were obtained showing four more measurable rings than those used in the

TABLE I

BENZENE

Max.	Min.	I	C_k[a]	s_0	s[b]	s/s_0
1		4	2	3.20	2.89	(0.904)[c]
	2	−10	− 7	4.30	4.19	(0.974)
2		10	14	5.71	5.75	1.006*
	3	− 1	− 2	7.60	7.57	0.996
3		4	11	9.48	9.89	(1.043)
	4	− 1	− 3	10.26	10.92	(1.063)
4		3	11	11.20	11.15	(0.991)
	5	− 7	−27	12.46	12.50	1.003*
5		4	19	13.63	13.89	1.020
	6	− 2	− 9	14.85	...[d]	...
6		2	10	15.98	15.80	0.989
	7	− 5	−23	17.42	17.40	0.999*
7		3	15	18.61	18.84	1.012*
	8	− ½	− 2	20.18	20.29	1.005
8		1½	7	21.30	21.17	0.994
	9	− 2	− 8	22.70	22.20	0.979
9		2	8	23.80	24.00	1.008
10		1	3	(27.0)	...[d]	...

Average	1.002
Average deviation	0.008
(C–C = 1.39 × 1.002 =	1.393 Å.)
(C–H = 1.075 × 1.002 =	1.077 Å.)
C–C = 1.39 ± 0.02 Å	
C–H = 1.08 ± 0.04 Å.	

[a] The coefficients of the terms $(\sin l\, s_k/l\, s_k)$ of the radial distribution function. [b] Calculated for coplanar hexagonal model with C–H = 1.075 Å. and C–C = 1.39 Å. [c] Less reliable values, not included in taking the average, are shown in parentheses. [d] The theoretical curve does not indicate a precisely measurable feature at this point. * In finding the average value of s/s_0, the starred values are given double weight, for we believe them to be more reliable than the others. Doubly weighted values of s/s_0 are similarly indicated in the following tables.

(2) L. Pauling and L. O. Brockway, *J. Chem. Phys.*, **2**, 867 (1934).
(3) L. O. Brockway, *Rev. Modern Phys.*, **8**, 231 (1936).
(4) L. Pauling and L. O. Brockway, THIS JOURNAL, **57**, 2684 (1935).

earlier investigation in these Laboratories. The radial distribution curve calculated with the C and s values of Table I (Fig. 1) shows three principal peaks, at 1.37 Å., 2.43 Å. (= $\sqrt{3} \times$ 1.40 Å.), and 2.83 Å. (= 2 × 1.415 Å.), representing the C–C separations for a regular hexagon with edge about 1.39 Å. The small peaks do not provide reliable information about the C–H bond distance. In order to make an approximate evaluation of this distance, intensity curves were calculated for plane hexagonal models with C–C = 1.39 Å. and C–H varying between 1.00 and 1.18 Å. at intervals of 0.03 Å. These curves (Fig. 2) differ significantly only in the region from the third to the sixth ring. (Note that in the tables a feature of the photographs is for convenience designated by "max." or "min." even though it appears to be a shelf or the inner edge of a shelf, respectively, and that in the text the numbers assigned to the rings correspond to those for maxima in the tables.) The visual intensity estimates for the third and fourth rings have the ratio $^4/_3$; this is not in accordance with the curves with C–H = 1.12 Å. or more, which make the fourth ring as strong as the third. Moreover, the 1.03 curve (as well as the 1.00 curve) shows only a very poorly defined shelf in place of the fourth ring. The 1.06 and 1.09 curves satisfactorily reproduce all of the features observed on the photographs, including the fifth and sixth rings. The quantitative comparison of observed s values with those calculated for C–C′ = 1.39 Å. and C–H = 1.075 Å. (the mean for the 1.06 and 1.09 curves), given in Table I, leads to C–C = 1.393 ± 0.02 Å. and C–H = 1.08 ± 0.04 Å. This value for the C–H distance agrees well with the value C–H = 1.090 ± 0.005 Å. which may be inferred from the C–H stretching frequencies and our knowledge of the relation of these frequencies to C–H bond distances.[5]

Wierl[6] and Pauling and Brockway[2] have previously reported C–C = 1.39 Å. in benzene. Jones[7] has reported the values C–C = 1.40 ± 0.01 Å. and C–H = 1.14 ± 0.01 Å. It seems probable that the latter value is in error.

An intensity curve was calculated also for a plane trigonal model, with C–H = 1.09 Å., C–C = 1.36 and 1.42 Å. alternately around the ring, the angles C–C–C = 120°, and the angles H–C–C = 123 and 117°, corresponding to quite incomplete resonance between the Kekulé structures. This curve is practically indistinguishable from that for the corresponding plane hexagonal model with C–H = 1.09 Å. and C–C = 1.39 Å. The electron diffraction method is accordingly unable to add to the existing theoretical and experimental evidence[8] for complete resonance in the benzene molecule.

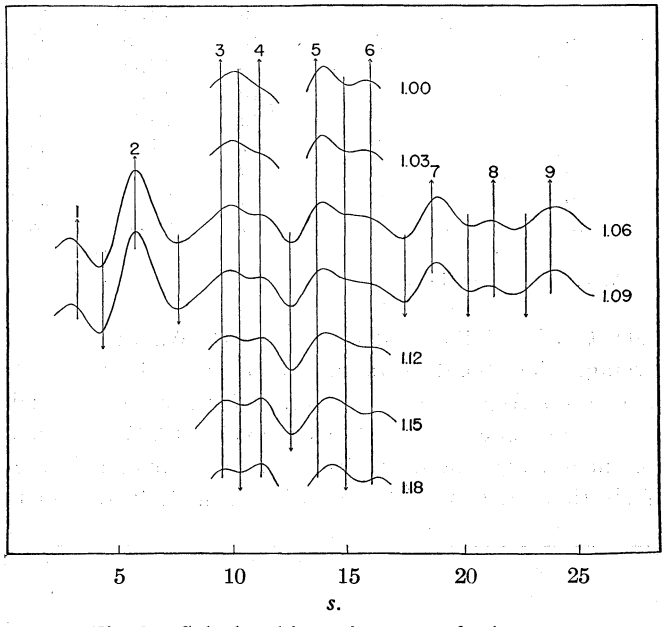


Fig. 2.—Calculated intensity curves for benzene.

The photographs obtained for pyridine and pyrazine are so closely similar to those of benzene as to leave no doubt that the three molecules have nearly identical structures. The radial distribution curve for pyridine (Fig. 1) calculated from the data given in Table II has well-defined peaks at 1.38, 2.39 (= $\sqrt{3} \times$ 1.38), and 2.76 (= 2 × 1.38) Å. The sharpness of the 2.39 peak indicates that the six meta distances in the ring are nearly equal. The calculated intensity curve for the model with C–C = 1.39 Å., C–N = 1.33 Å., C–H = 1.08 Å., the angle C–N–C = 119° and the angles C–C–C = 121°, and having nearly equal "meta" and "para" distances, is shown in Fig. 3. The comparison of s_0 and s values for this model (Table II) leads to the values C–H =

(5) E. Eyster, *J. Chem. Phys.*, **6**, 580 (1938).
(6) R. Wierl, *Ann. Physik*, **8**, 521 (1931).
(7) P. L. F. Jones, *Trans. Faraday Soc.*, **31**, 1036 (1935).
(8) C. K. Ingold, *Proc. Roy. Soc.* (London), **A169**, 149 (1938).

TABLE II

PYRIDINE

Max.	Min.	I	C	s_0	Model I[a] s	Model I[a] s/s_0	Benzene "1.09," "1.39" s	Benzene "1.09," "1.39" s/s_0
1		4	2	3.19	2.99	(0.947)	2.89	(0.906)
	2	−10	− 7	4.37	4.16	(0.952)	4.19	(0.959)
2		10	14	5.69	5.83	1.025*	5.75	1.011*
	3	− 1	− 2	7.58	7.68	1.027	7.57	0.999
3		4	11	9.14	9.94	(1.087)	9.89	(1.082)
	4	− 1	− 3	10.21	10.74	(1.053)	10.92	(1.070)
4		3	11	11.24	11.30	(1.004)	11.15	(0.992)
	5	− 7	−27	12.73	12.75	1.002*	12.50	0.982*
5		4	19	13.88	14.23	1.025	13.89	1.001
	6	− 2	− 9	15.12	15.85	(1.048)	...	...
6		2	10	16.20	16.31	1.007	15.80	0.975
	7	− 5	−23	17.60	17.66	1.003*	17.40	.988*
7		3	15	18.86	19.10	1.013*	18.84	.999*
	8	− 1/2	− 2	20.33	20.60	1.013	20.29	.997
8		1 1/2	7	21.44	21.40	0.997	21.17	.987
	9	− 2	− 8	22.65	22.47	0.992	22.20	.980
9		2	8	23.82	24.27	1.018	24.00	1.007
10		1	3	28.0	28.18	1.007	...	...
					Average	1.011		0.994
					Average deviation	0.009		0.010

[a] Models described in text.

1.09, C–C = 1.405, and C–N = 1.344 Å., with average ring bond distance 1.385 ± 0.01 Å. The comparison with the s values for a regular hexagonal model leads to the same value 1.385 Å. for the average ring bond distance. It seems unlikely that the C–C distance differs from 1.39 Å., and the results accordingly suggest that the C–N distance is about 1.37 ± 0.03 Å.

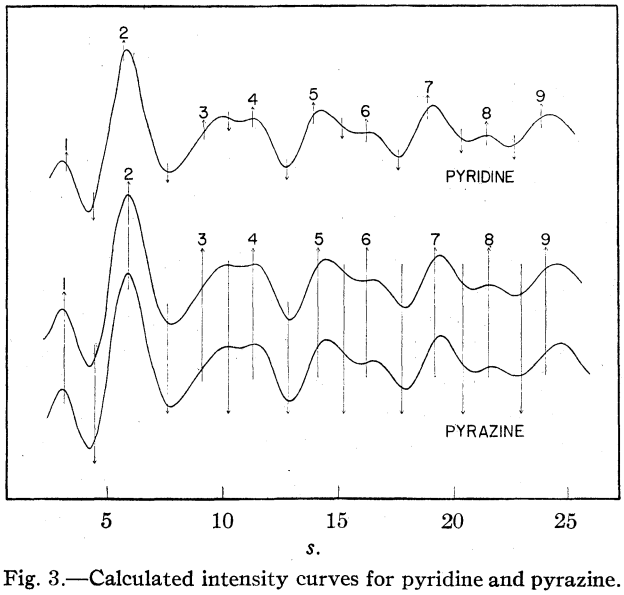


Fig. 3.—Calculated intensity curves for pyridine and pyrazine.

The principal peaks on the radial distribution curve for pyrazine (Fig. 1) lie at 1.36, 2.37 ($= \sqrt{3} \times 1.37$), and 2.76 ($= 2 \times 1.38$ Å.). Intensity curves for model I, with C–C = 1.39 Å., C–N = 1.33 Å., C–H = 1.09 Å., and all ring angles 120°, and for model III, with the same bond distances but with the ring angles at nitrogen 123° and at carbon 118°30′, making the meta distances equal, are shown in Fig. 3. These curves, as well as the benzene curve (representing a regular hexagonal model), agree qualitatively with the photographs. The quantitative comparison for all three leads to the value 1.366 ± 0.01 Å. for the average ring bond distance. With C–C = 1.39 Å., this corresponds to C–N = 1.35 ± 0.02 Å.

Butadiene-1,3 and Cyclopentadiene.—The photographs of butadiene which were obtained are diffuse and were measured only with difficulty, so that the determination of the configuration of the molecule is less precise than usual. Thirteen rings could be seen, with the s_0 and I values given in Table IV. These correspond to the radial distribution curve shown in Fig. 1, with peaks at 1.07, 1.38, 2.12, 2.48, (3.0), 3.71, (4.13), and (4.65) Å., the values in parentheses being unreliable. The carbon–carbon peak at 1.38 Å. represents the mean of the values for the two double bonds and the intervening single bond, which has some double bond character. If the double bonds have about the normal distance 1.34 Å. found in ethylene and allene,[1b,5] the value 1.46 Å. is indicated for the conjugated single bond. The peak

TABLE III

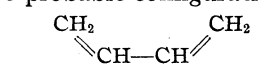
PYRAZINE

	Max.	Min.	I	C_k	s_0	Model I[a] s	Model I[a] s/s_0	Model III s	Model III s/s_0	Benzene "1.09," "1.39"	
	1		4	2	3.09	3.02	(0.977)	3.06	(0.990)	2.90	(0.938)
		2	−10	−10	4.41	4.23	(.959)	4.20	(0.952)	4.19	(.950)
	2		10	16	5.89	5.87	.996*	5.89	1.000*	5.75	.976*
		3	− 2	− 5	7.59	7.77	1.023	7.71	1.016	7.60	1.002
	3		4	12	9.08	10.23	(1.127)	10.24	(1.128)	9.87	(1.087)
		4	− 1/2	− 2	10.20	10.70	(1.049)	10.62	(1.042)	10.90	(1.068)
	4		4	16	11.27	11.37	(1.008)	11.35	(1.007)	11.20	(0.994)
		5	− 7	−31	12.76	12.90	1.012*	12.89	1.011*	12.50	.980*
	5		4	19	14.07	14.43	1.026	14.45	1.027	13.93	.991
		6	− 1	− 4	15.21	16.02	(1.053)	15.92	(1.047)	...[b]	...
Shelf	6		2	10	16.20	16.50	1.018	16.55	1.022	15.80	.975
		7	− 5	−25	17.73	17.90	1.010*	17.95	1.007*	17.40	.982*
	7		3	14	19.16	19.40	1.013*	19.41	1.013*	18.85	.984*
		8	− 1	− 4	20.37	20.85	1.024	20.90	1.026	20.30	.997
	8		1	4	21.51	21.60	1.004	21.70	1.008	21.13	.983
		9	− 2	− 7	22.97	22.70	0.988	22.78	0.992	22.20	.967
	9		2	6	24.04	24.55	1.021	24.65	1.025	24.00	.988
					Average		1.012		1.012		0.984
					Average deviation		0.008		0.008		0.007

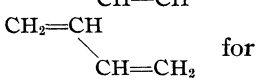
[a] Models described in text. [b] The theoretical curve does not show a measured feature at this point.

at 2.48 Å. corresponds to the 1,3 and 2,4 carbon–carbon distances; this value leads to about 125° for the C=C—C bond angle.

Of the two probable configurations *cis*



and *trans*



for the molecule, the latter is suggested by the presence of a large radial distribution peak at 3.71 Å., which is just the value calculated for the *trans* model. The small radial distribution peak at 3.0 Å. is probably without significance.

The intensity curves I, II, III, and IV of Fig. 4 are calculated for coplanar *trans* models with C–H = 1.06 Å., the angle H—C=C = 115°, and the angle H—C—H = 109.5°. Although these hydrogen parameters are so chosen as to agree as well as possible with minor peaks of the radial distribution function, no great reliance can be placed on them, and indeed it is likely that for this molecule the C–H bond distance is 1.09 Å. The models have the following additional parameters

Model	C=C	C—C	Angle C=C—C
I	1.38 Å.	1.38	126°10′
II	1.36	1.44	124°40′
III	1.34	1.48	123°5′
IV	1.32	1.54	120°10′

The average of the carbon–carbon bond distances has for each model approximately the radial distribution value 1.38 Å. and the angle C=C—C is such as to give the radial distribution value 2.48 Å. for the 1,3- and 2,4-distances. The agreement with the photographs is reasonably satisfactory for curves II and III, but not for I and IV. For example, the relative intensities of rings 9 and 10 are not well reproduced by curve IV, and those of rings 11 and 12 are not given satisfactorily by either curve I or curve IV. The appearance on the photographs of a doublet (rings 6 and 7) rather than a single ring may be due to an inflection in curves II and III in this region; otherwise the agreement is excellent. Curves were also calculated for about ten models differing slightly from these, with no improvement.

It is concluded that the butadiene molecule has the configuration described by the following parameter values: C–H = 1.06 Å. (assumed), C=C = 1.35 ± 0.02 Å., C–C = 1.46 ± 0.03 Å., angle C=C—C = 124 ± 2°. The configuration is probably essentially coplanar and *trans;* the evidence for this view provided by the radial distribution function is not conclusive inasmuch as it is not supported by a strong dependence of the theoretical intensity curves on the relative rotation of the vinyl groups of the butadiene model. The electron diffraction data are not incompatible with a mixture of *cis* and (predominantly) *trans* molecules. However, other experimental evidence (reviewed by Mulliken[9]) together with theoretical

(9) R. S. Mulliken, *J. Chem. Phys.*, **7**, 121 (1939). See, however, **7**, 373 (1939).

considerations[10] indicates that butadiene molecules must be essentially coplanar and *trans*.

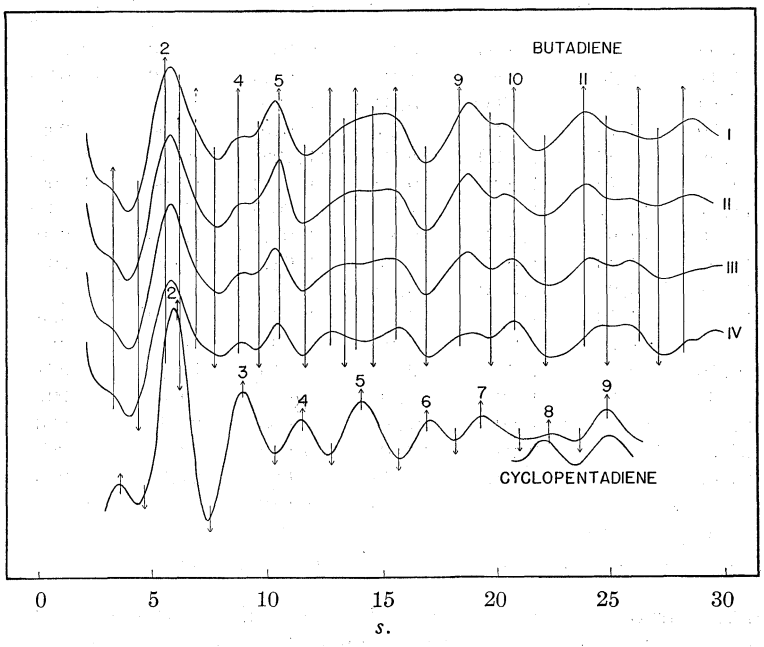
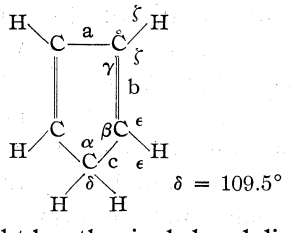


Fig. 4.—Calculated intensity curves for butadiene and cyclopentadiene.

The spectroscopic conclusion of Bartholomé and Karweil[11] that in butadiene there is essentially free rotation about the C–C bond with a barrier not greater than 200 cal./mole is almost certainly incorrect.

Data for the excellent photographs of cyclopentadiene, showing nine rings, are given in Table V. The corresponding radial distribution curve (Fig. 1) has peaks at 1.06, 1.42, and 2.33 Å. The number of parameters determining the structure of this molecule is so great as to prevent their independent evaluation. The molecule



without doubt has the single bond distance *c* equal to about 1.53 Å., as in the cycloparaffins, and the double bond distance *b* equal to about 1.35 Å., as in butadiene. The conjugated single bond *a* is probably about 1.46 Å. Many models with approximately these values for the carbon–carbon distances, with various ring angles, and with C–H = 1.09 Å. were found to give calculated curves showing by their qualitative appearance that $\alpha = 101 \pm \sim 3°$ and leading on quantitative comparison to the value 1.445 ± 0.01 Å. for the average ring bond distance. This is exactly the average of the values suggested above. Assuming the average of the values of *b* and *c* to be reliable, we write C–C = 1.46 ± 0.04 Å. as the value determined for the conjugated double bond. The curve shown in Fig. 4, with *s* values given in Table V, is that for the model with the values *a* = 1.44, *b* = 1.34, and *c* = 1.54 Å., and the angles $\alpha = 101°$, $\beta = 109°$, $\gamma = 110°$. While this curve is slightly better than any of the others we have calculated, it is not possible to base a satisfactory determination of the relative values of the bond distances on the qualitative appearance of the diffraction pattern. The curve gives an excellent representation of the appearance of the photographs except that the fourth minimum of the curve is much too deep relative to the fifth minimum, and the eighth maximum is much too weak. On the films the eighth ring appears to be as strong as the ninth. These discrepancies arise from ignoring the temperature effect,[12] that is, the effect on the diffraction pattern of the variation of the interatomic distances resulting from molecular vibrations. We have found that when probable variations of the various interatomic distances are considered, the slight trouble of the fourth and fifth minima is resolved, as is the greater difficulty of the eighth maximum. This is illustrated for the region of the eighth maximum by the last curve of Fig. 4, which has been plotted for the best cyclopentadiene model (C–C = 1.53, 1.46; C=C = 1.35; $\alpha = 101°$), with the carbon–hydrogen interactions omitted as an approximation to the effect at large diffraction angles of the temperature factor corresponding to the large amplitudes of vibration of the hydrogen atoms.

(10) L. Pauling and J. Sherman, *J. Chem. Phys.*, **1**, 679 (1933); W. G. Penney, *Proc. Roy. Soc.* (London), **A158**, 306 (1937).

(11) E. Bartholomé and J. Karweil, *Z. physik. Chem.*, **B35**, 442 (1937).

(12) L. O. Brockway, *Rev. Modern Phys.*, **8**, 238 (1936). The temperature effect may be somewhat significant also for the other molecules discussed in the paper. Its dominating importance for cyclopentadiene is perhaps coincidental. We expect to investigate this question further.

TABLE IV

BUTADIENE

Max.	Min.	I	C_k	s_0	Model II s	Model II s/s_0	Model III s	Model III s/s_0
	1	− 3	0	2.37	...	(.....)	...	(.....)[a]
1		5	2	3.35	...	(.....)	...	(.....)
	2	−10	− 7	4.47	4.01	(0.897)	4.10	(0.918)
2		15	14	5.62	5.92	(1.053)	5.94	(1.057)
	3	− 1	− 1	6.24	...	(.....)	...	(.....)
3		7	11	6.98	...	(.....)	...	(.....)
	4	− 2	− 4	7.74	7.90	1.020	7.95	1.026
4		4	8	8.79	9.00	1.023	9.05	1.029
	5	− 1	− 2	9.68	9.30	0.961	9.40	0.971
5		6	16	10.56	10.62	1.006*	10.40	.985*
	6	− 4	−11	11.67	11.55	0.990*	11.60	.994*
6		3	10	12.74	...	(.....)	...	(.....)
	7	− 1	− 3	13.33	...	(.....)	...	(.....)
7		3	9	13.82	...	(.....)	...	(.....)
	8	− 2	− 6	14.60	...	(.....)	...	(.....)
8		3	10	15.58	...	(.....)	...	(.....)
	9	− 4	−13	16.90	16.92	1.001*	16.93	1.002*
9		3	10	18.37	18.78	1.022*	18.79	1.022*
	10	− 1	− 3	19.72	19.94	1.011*	19.80	1.004*
10		1	3	20.79	20.40	0.981*	20.72	0.997*
	11	− 2	− 5	22.13	22.00	0.994*	22.35	1.010*
11		2	4	23.88	23.97	1.004*	24.12	1.010*
	12	− 1	− 2	24.87	...	(.....)	...	(.....)
12		1	2	26.26	...	(.....)	...	(.....)
	13	− 1	− 1	27.10	...	(.....)	...	(.....)
13		1	1	28.20	...	(.....)	...	(.....)
					Average	1.001		1.003
					Average deviation	0.012		0.001

[a] The theoretical curve does not have a well-defined maximum or minimum corresponding to the measured ring.

TABLE V

CYCLOPENTADIENE

Max.	Min.	I	C_k	s_0	Model I[a] s	Model I[a] s/s_0
1		28	1	3.66	...	...
	2			4.71	4.45	(0.946)
2		70	14	6.13	6.00	(.979)
	3			7.54	7.46	.990
3		28	15	8.98	9.01	1.003
	4			10.37	10.41	1.004
4		12	11	11.54	11.53	0.999
	5			12.78	12.68	0.992
5		18	24	14.09	14.14	1.003
	6			15.68	15.80	1.007
6		7	12	16.90	17.07	1.009
	7			18.16	18.15	0.999
7		7	13	19.29	19.40	1.006
	8			20.99	21.40	1.019
8		3	5	22.28	22.45	1.007
	9			23.62	23.43	0.992
9		3	5	24.87	24.86	0.999
				Average		1.002
				Average deviation		0.005
				Average ring bond distance		1.443 Å.

[a] Model for which a = 1.44 Å., b = 1.34 Å., c = 1.54 Å., α = 101°.

TABLE VI

FURAN

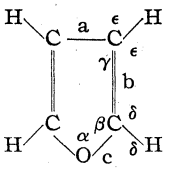
Max.	Min.	I	C_k	s_0	s[a]	s/s_0
	1			2.42	2.52	(0.961)
1		11	0	3.61	3.82	(1.057)
	2			4.78	4.50	(0.941)
2		20	4	6.15	6.07	.987
	3			7.76	7.70	.991
3		12	7	9.13	9.43	(1.032)
	4			10.60	10.75	(1.013)
4		6	15	11.73	11.60	(0.989)
	5			13.16	12.90	(0.980)
5		10	28	14.44	14.56	1.008
	6			16.23	16.30	1.004
6		3	13	17.65	17.73	1.004
	7			18.89	18.55	(0.982)
7		3	15	19.88	19.77	0.994
	8			21.55	21.63	1.003
8		1½	11	23.26	23.20	0.997
	9			24.26	24.57	1.012
9		1½	5	25.46	25.55	1.003
				Average		1.000
				Average deviation		0.0065
				Average ring bond distance		1.395 Å.

[a] Model XIX: C–O = 1.41, C=C = 1.35, C—C = 1.46, α = 105°, β = 110.8°, γ = 106.7°.

Furan, Pyrrole, and Thiophene.—The data for furan (Table VI) lead to a radial distribution curve (Fig. 1) with principal peaks at 1.39 and 2.26 Å., indicating an average ring bond distance

of 1.39 Å. This is substantiated by comparison with calculated intensity curves, which gives 1.395 ± 0.01 Å. for this average.

If the assumption be made that in the molecule



the values of a and b are 1.46 and 1.35 Å., respectively, as in butadiene and cyclopentadiene, it is found that there is excellent qualitative and quantitative agreement between the photographs and models with C–H = 1.09 Å., c = 1.41 ± 0.02 Å., α = 107 ± 4°, β = 109 ± 3°, and γ = 107 ± 2°, as is illustrated for model XIX by Fig. 5 and Table VI. The quantitative agreement is impaired by change in c, and the qualitative agreement by change in α (with corresponding changes in β and γ). It is interesting to note that the value of c is only slightly less than the single bond C–O value, 1.43 Å.

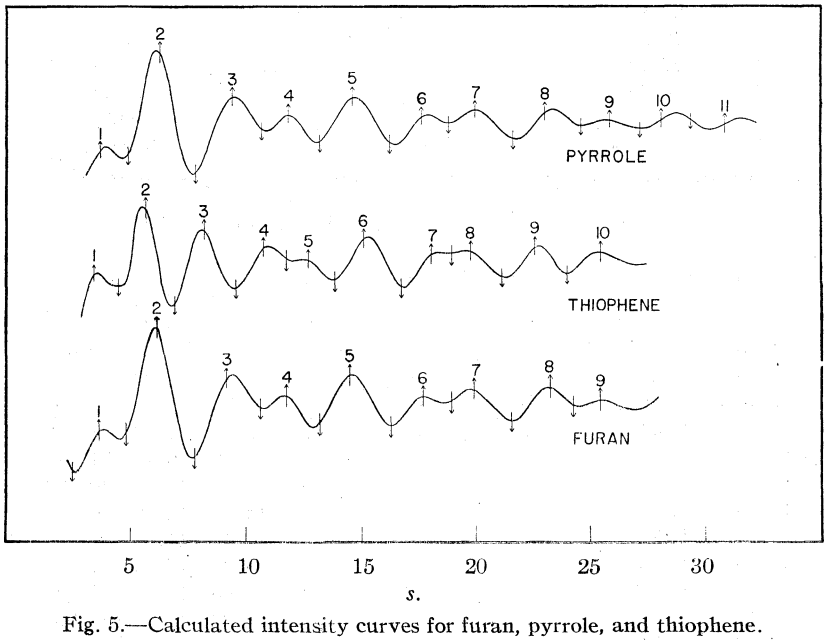


Fig. 5.—Calculated intensity curves for furan, pyrrole, and thiophene.

The curve for model XIX represents the appearance of the photographs very well, except that the sixth and seventh maxima actually appear to be equally strong. Several of the twenty theoretical curves calculated for furan are nearly as satisfactory, and one, for the model with C—O = 1.42, C=C = 1.34, C—C = 1.44, and α = 104°, is somewhat better, the sixth and seventh maxima on it being equally high. This improvement is probably not significant, especially since the temperature effect may here play a role as with cyclopentadiene. We find that it is not possible to determine the relative values of the bond distances in the heterocyclic molecules containing only light atoms within reasonable limits by the qualitative comparison, and we have accordingly assumed appropriate values for C=C and C—C. For any reasonable given set of ring bond distances qualitative agreement is obtained only when the bond angles are so chosen as to make the cross-ring distances equal to within a few hundredths of an ångström unit.

The photographs for pyrrole are very closely similar to those for furan, and lead to the same value, 1.395 ± 0.01 Å., for the average ring bond distance. The radial distribution function shown in Fig. 1 has important sharp peaks at 1.40 and 2.25 Å. With a = 1.46 and b = 1.35 Å., the average ring bond distance leads to c = 1.41 Å., which is 0.06 Å. less than the C–N single bond value. In accordance with the discussion given below, it seems probable that this decrease, indicating double bond character, is accompanied by further decrease in a, and that the values in the molecule are C—H = 1.09 Å. (assumed), a = 1.44 Å. (assumed), b = 1.35 Å. (assumed), and c = 1.42 ± 0.02 Å. The angles have the values α = 105 ± 4°, β = 110 ± 3°, and γ = 108 ± 2°. The agreement of the photographs with a model falling within this range is shown in Fig. 5 and Table VIII. Other models give the same average ring bond distance.

The data from the photographs of thiophene, showing ten rings (Table VIII), lead to the radial distribution curve of Fig. 1, with peaks at 1.40 Å. (C–C), 1.74 Å. (S–C), 2.29 Å. (C–C, meta), and 2.55 Å. (S—C). If the values C—C = 1.44 and C=C = 1.35 Å. be assumed in this molecule, as in pyrrole, the radial distribution curve leads to the configuration with S—C = 1.74 ± 0.03 Å., angle C—S—C = 91 ± 4°, angle S—C=C = 112 ± 3°, and angle C=C—C = 113 ± 3°. The curve calculated for this model (with C—H = 1.09 Å.) agrees very well with the photographs, as shown in Fig. 5 and Table VIII.

Discussion

Pyridine and Pyrazine.—The values found

TABLE VII

PYRROLE

Max.	Min.	I	C_k	s_0	Model I^a s	s/s_0
1		10	0	3.61	...	(...)
	2			4.85	...	(...)
2		30	8	6.26	6.09	0.972
	3			7.79	7.71	0.989
3		12	7	9.36	9.49	1.014
	4			10.62	10.83	1.019
4		5	7	11.79	11.81	1.001
	5			13.12	13.04	0.994
5		10	22	14.53	14.67	1.009
	6			16.18	16.47	1.018
6		4	13	17.54	17.85	1.017
	7			18.72	18.77	1.003
7		4	15	19.93	19.95	1.001
	8			21.60	21.79	1.009
8		4	17	22.98	23.38	1.017
	9			24.57	24.65	1.003
9		1	4	25.82	25.70	0.995
	10			27.14	27.15	1.000
10		2	7	28.07	28.80	(...)
	11			29.34	30.19	(...)
11		1	3	30.81	31.55	(...)
		Average				1.004
		Average deviation				0.010
		Average ring bond distance				1.395 Å.

[a] Model: a = 1.47 Å., b = 1.34 Å., c = 1.40 Å., α = 105°, β = 110°, γ = 106°.

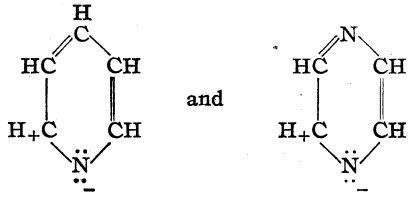
TABLE VIII

THIOPHENE

Max.	Min.	I	C_k	s_0	Model I^a s	s/s_0
1		2	0	3.37	3.53	(1.047)[b]
	2			4.42	4.50	(1.019)
2		10	5	5.64	5.52	(0.978)
	3			6.90	6.80	.986
3		8	9	8.17	8.05	.985
	4			9.53	9.50	.997
4		3	5	10.71	10.92	(1.019)
	5			11.70	12.08	(1.032)
5		1	3	12.63	12.42	(0.983)
	6			13.80	13.78	0.999
6		3	11	15.05	15.30	1.016
	7			16.68	16.82	1.008
7		1	5	17.98	18.30	(1.017)
	8			18.88	18.85	(0.998)
8		1	6	19.71	19.60	(0.994)
	9			21.10	21.30	1.009
9		1	9	22.53	22.79	1.010
	10			23.97	24.04	1.003
10		½	5	25.41	25.33	0.997
				Average		1.001
				Average deviation		0.008

[a] Model described in text. [b] Many of the features of the thiophene photographs are of types known to be difficult to measure. Here the inner rings and the components of the two doublets have been thrown out of the average, since measurements of both types of features are known to be unreliable. The effect of the choice of rings to be thrown out is here somewhat greater than usual and may amount to ±0.005 in s/s_0.

for the C–N Kekulé-type bond distance in pyridine and pyrazine, 1.37 ± 0.03 Å. and 1.35 ± 0.02 Å., respectively, are somewhat larger than the expected value 1.33 Å. for 50% double bond character. It is possible that this is the result of the large electronegativity of the nitrogen atom, leading to significant additional resonance with ionic structures such as



Probably the effect on the C–N distance is greater for pyridine than for pyrazine because in pyridine there are three structures giving the nitrogen atom a negative formal charge and only single bonds, while in pyrazine there are four such structures of which only two affect a given one of the nitrogen atoms. Investigations of the C–N distances in related compounds such as pyridazine, pyrimidine, and cyanuric and cyameluric[13] derivatives would be of interest in this connection.

(13) L. Pauling and J. H. Sturdivant, *Proc. Natl. Acad. Sci.*, **23**, 615 (1937), have discussed the cyanuric and cyameluric derivatives.

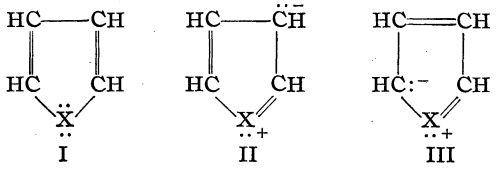
It may be mentioned that this interpretation is in agreement with the deactivating and β directing influence of nitrogen in pyridine and its analogs[14] with respect to substitution reactions.

Butadiene-1,3 and Cyclopentadiene.—The value 1.46 Å. for the single bond between conjugated double bonds in butadiene-1,3 and cyclopentadiene has been discussed already in connection with the values found in other hydrocarbons containing conjugated systems.[15] Penney's[10] predicted value for the conjugated bond in butadiene, 1.43 Å., appears to be a little too low.

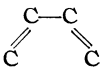
Furan, Pyrrole, and Thiophene.—The carbon–heteroatom distances found in furan, pyrrole, and thiophene correspond to 5 ± 5%, 12 ± 6%, and 17 ± 10% double-bond character, respectively. Resonance of the normal structure I with structures of the types II and III (X = O, NH, S) is assumed to be responsible for this double-bond character, while excited structures characteristic

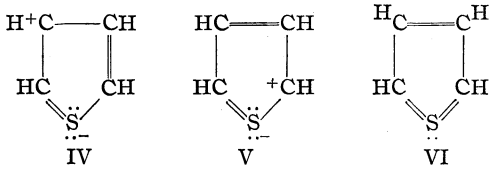
(14) G. W. Wheland and L. Pauling, THIS JOURNAL, **57**, 2086 (1935).

(15) L. Pauling, H. D. Springall, and K. J. Palmer, *ibid.*, **61**, 927 (1939).



I II III

of the conjugated system  together with structures of the type III lead to the shortening of the C—C bond and the lengthening of the C=C bond. The C–C distance is assumed to be 1.46 Å. for furan and 1.44 Å. for pyrrole and thiophene, corresponding approximately to the expected contributions of various structures in these molecules. Besides those already mentioned, we may write for thiophene further reasonably stable structures, of types IV, V, and VI, involving the violation of the octet rule by sulfur, and contributing to the shortening of the C–S and C–C bonds. The



IV V VI

extent of their contribution is discussed below.

It is of interest to compare our results regarding furan, pyrrole, and thiophene with other information about these molecules. First of all, it is understandable that the very electronegative oxygen atom should not like to assume the positive charge of the excited structures written for furan, and that in consequence resonance with these structures should be less important than in pyrrole and thiophene, where the less electronegative atoms nitrogen and sulfur are involved. The values of the stabilizing resonance energy 21, 23, and 31 kcal./mole, respectively, for furan, pyrrole, and thiophene reported by Pauling and Sherman[16] are not in agreement with the great difference of degree of resonance in furan and pyrrole indicated by the electron diffraction investigation. We have recalculated values of the resonance energy from combustion data[17] for several furan and pyrrole derivatives; these values are listed in Table IX, together with our estimates of that part of the resonance energy which is to be attributed to the heterocyclic nuclei, obtained by subtracting the following corrections: 39 kcal./mole for benzene resonance, 6 kcal./mole for conjugation with phenyl, vinyl, or aldehyde group, 1.5 kcal./mole for conjugation with methyl or ethyl group, and 3 kcal./mole for conjugation with a hydroxyl group. These values[18] indicate that the resonance energy of the pyrrole nucleus is actually greater than that of the furan nucleus by about 8 kcal./mole, the probable values being approximately 23 and 31 kcal./mole, respectively. It accordingly seems likely that the value given in the literature for the heat of combustion of pyrrole is about 8 kcal./mole high.

TABLE IX

VALUES OF RESONANCE ENERGY OF DERIVATIVES OF FURAN AND PYRROLE

Substance	Resonance energy, kcal./mole	Resonance energy of nucleus, kcal./mole
Furan	23	23
Furfural	29.5	23.5
Furylethylene	28	22
Furfuryl alcohol	32	29
Pyrrole	23	23
Pyrrole aldehyde	40	34
N-Phenylpyrrole	76	31
2,4,5-Trimethyl-3-ethylpyrrole	33.5	27.5
2,4-Dimethyl-3-ethylpyrrole aldehyde	42.4	32

The new value for the resonance energy of pyrrole is just equal to that for thiophene. Unfortunately we have been unable to find combustion data for derivatives of thiophene to use in verifying the thiophene value. The interatomic distance data indicate greater resonance for thiophene than for pyrrole, which presumably would be accompanied by greater resonance energy; it is possible, however, that the magnitude of the resonance integrals for a molecule involving a heavier atom (sulfur) is less than for molecules containing only light atoms, and that the resonance energies of thiophene and pyrrole cannot be directly compared to obtain the relative amounts of resonance in the two molecules.

The electric dipole moments in units 1×10^{-18} e. s. u. of these molecules and their derivatives by hydrogenation measured[19] in benzene solution are the following: furan, 0.670; 2,5-dihydrofuran, 1.53; tetrahydrofuran, 1.68; pyrrole, 1.80; pyrroline, 1.42; pyrrolidine, 1.57; thiophene, 0.54; and tetrahydrothiophene, 1.87. We now give a very rough interpretation of these quantities based on the bond moments given

(16) L. Pauling and J. Sherman, *J. Chem. Phys.*, **1**, 606 (1933).

(17) M. S. Kharasch, *Bur. Standards J. Research*, **2**, 359 (1929); Landolt–Börnstein, "Tabellen."

(18) Our recalculation for furan itself led to a small change from the value given by Pauling and Sherman.

(19) H. de Vries Robles, *Rec. trav. chim.*, **58**, 111 (1939); appendix to Symposium, *Trans. Faraday Soc.*, **30**, 904 (1934).

TABLE X

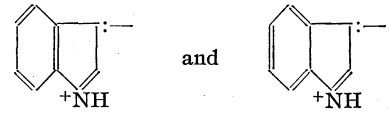
SUMMARY OF DISTANCES AND ANGLES

	C–H, Å.	C–C, Å.	C–X	C=C	Angle CXC	Angle XC=C	Angle C=C–C
Benzene	1.08±0.04	1.39±0.02	.....	.....	...	...	...
Pyridine	1.09	1.39	1.37±0.03	.....	Angles ~ 120°, "meta" distances approximately equal		
Pyrazine	1.09	1.39	1.35± .02	.....			
Butadiene[a]	1.06	1.46± .03	.....	1.35±0.02	...	...	124±2°
Cyclopentadiene	1.09	1.46± .04	1.53	1.35	101±4°	109±3°	110±2°
Furan	1.09	1.46	1.41± .02	1.35	107±4°	109±3°	107±2°
Pyrrole	1.09	1.44	1.42± .02	1.35	105±4°	110±3°	108±2°
Thiophene	1.09	1.44	1.74± .03	1.35	91±4°	112±3°	113±3°

[a] Probably coplanar *trans* configuration.

by Smyth[20] and on the usual approximate treatment[21] of the effect on electric dipole moment of resonance with polar structures. A simple calculation suggests that the difference 0.15 *D* in moment between the dihydro and tetrahydro derivatives of furan and pyrrole may be accounted for as the result of change in the direction and number of C–H bonds having moments of about 0.4 *D*. The differences of moments of tetrahydrofuran and furan, and tetrahydrothiophene and thiophene, which are 1.01 and 1.33 *D*, respectively, consist of contributions of 0.05 to 0.10 *D* due to the change of C–H moments, combined with resonance moments, in the same direction, of about 0.95 and 1.25 *D*, respectively, the effects of changing the angles in the ring being neglected. The interpretation of the moments of the pyrroles is complicated by uncertainty regarding the orientation of the N–H bond in these molecules. It seems to be impossible to make a reliable estimate of the resonance moment for pyrrole; various methods of making the calculation give values lying between 1.0 and 2.5 *D*, with 1.5 *D* the most probable value. These resonance moments, 0.95 *D* for furan, 1.5 *D* for pyrrole, and 1.25 *D* for thiophene, correspond to approximately the following total contribution of structures of Types II and III (assumed to be equally important): furan 15%, pyrrole 23%, and thiophene 16%, while the assumed C–X distances correspond to total contributions by excited structures of 10, 24, and 34%, respectively. The agreement of the estimates made in the two ways is reasonably good for furan and pyrrole. The low value found for thiophene by the dipole moment calculation indicates that structures of types IV, V, and VI are of considerable significance; the consideration of the data suggests about 10% contribution by these structures, involving more than eight electrons in the outer shell of the sulfur atom, and 20% by the structures of types II and III.

Finally, it may be said that the general chemical behavior of furan, pyrrole, and thiophene indicates this order of increasing stability and aromatic character, in agreement with this discussion. An interesting example which seems to support this conclusion is the reaction[22] with maleic anhydride of furan to give (by the Diels-Alder reaction) a product which does not contain the furan nucleus, and that of pyrrole[23] to give in part by a simple condensation a compound in which the pyrrole nucleus is retained. The α directing influence on substitution reactions of the hetero atoms in furan, pyrrole, and thiophene indicates that excited structures of type III predominate over those of type II, as would be expected from their smaller charge separation. It is interesting to note that β-substitution occurs in indole; this is the result of the fact that of the ionic excited structures, two



place a negative charge on the β-carbon atom, whereas only one such structure occurs for each of the other carbon atoms. This striking difference between pyrrole and indole thus has a simple explanation in terms of resonance.

We wish to thank Professor F. W. Bergstrom for the sample of pyrazine, Dr. W. E. Vaughan for that of tetrabromobutane, Dr. K. J. Palmer for his help with experimental work, Dr. Sidney Weinbaum for assistance in the preparation of the figures, and Dr. E. R. Buchman for discussion of the chemical properties of the substances. We are especially indebted to Professor L. O.

(20) C. P. Smyth, THIS JOURNAL, **60**, 183 (1938).

(21) See L. E. Sutton, *Trans. Faraday Soc.*, **30**, 789 (1934).

(22) O. Diels and K. Alder, *Ber.*, **62**, 554 (1929).

(23) O. Diels and K. Alder, *Ann.*, **486**, 211 (1931).

Brockway for checking our measurements of the photographs, for general assistance, and for many helpful discussions.

Summary

The results of the electron diffraction investigation reported in this paper are collected in Table X. The re-investigation of benzene confirms the value 1.39 Å. for the C–C distance and provides a rough experimental value for the C–H distance. In pyridine and pyrazine the C–N distance is greater than expected for Kekulé resonance; the effect is attributed to extra resonance with ionic structures. The electron diffraction results, electric dipole moment data, resonance energies, chemical information, and simple theoretical considerations indicate, almost uniformly, the order furan < pyrrole < thiophene for the degree of resonance stabilization of these molecules. The contributions of excited structures, other than those characteristic of the conjugated double bonds, are about 10, 24, and 34%, respectively. Part of the resonance of thiophene is with structures with ten electrons in the valence shell of the sulfur atom.

PASADENA, CALIFORNIA RECEIVED APRIL 17, 1939

[CONTRIBUTION FROM THE COLLEGE OF PHARMACY, UNIVERSITY OF MICHIGAN]

Naphthylaminoalkanes

BY F. F. BLICKE AND CHARLES E. MAXWELL[1]

A number of phenyl and hydroxyphenyl substitution products of aminoethane and aminopropane such as epinephrine, neosynephrin, ephedrine and benzedrine have found extensive use as therapeutic agents.

Since there seems to be little information in the literature relative to the pharmacological activity of naphthyl analogs of compounds such as are mentioned above, we have prepared six naphthylaminoalkanes which, with the exception of α-naphthylaminomethane, have been examined in the form of their hydrochlorides by Mr. L. W. Rowe of Parke, Davis and Company. It was found that the amines exhibited only a slight pressor activity upon initial intravenous injection in dogs with the development of tolerance to succeeding injections. An interesting property shown by the whole group is the production of a "cross tolerance," that is, little or no effect on blood pressure is produced by the administration of ephedrine if the injection of the latter is preceded by an injection of one of the naphthylaminoalkanes.

It seems that more effective compounds might be obtained by the introduction of hydroxyl groups into the naphthalene nucleus; however, Windaus and Bernthsen-Buchner[2] stated that α-[1-(4-hydroxynaphthyl)]-β-aminoethane exhibits only slight pharmacological activity.

α-Naphthylaminomethane, α-$C_{10}H_7CH_2NH_2$ (I), was obtained by interaction of α-naphthylmethyl chloride and hexamethylenetetramine in chloroform.[3]

In order to obtain 1-(α-naphthyl)-1-aminoethane, α-$C_{10}H_7CH(NH_2)CH_3$ (II), 1-(α-naphthyl)-1-aminopropane, α-$C_{10}H_7CH(NH_2)CH_2CH_3$ (IV) and 1-(α-naphthyl)-1-aminobutane, α-$C_{10}H_7CH(NH_2)CH_2CH_2CH_3$ (VI), α-naphthylmagnesium bromide was allowed to react with aceto-, propio- and butyronitrile, respectively. The ketones, prepared in this manner, were converted into the oximes and the latter reduced to the amines with sodium and alcohol.

1-(β-Naphthyl)-1-aminoethane, β-$C_{10}H_7CH(NH_2)CH_3$ (III), was synthesized by reduction of β-acetonaphthone oxime.

The naphthyl analog of benzedrine, 1-(α-naphthyl-2-aminopropane), α-$C_{10}H_7CH_2CH(NH_2)CH_3$ (V), was obtained by the following series of reactions: diethyl malonate ⟶ diethyl α-naphthylmethylmalonate ⟶ diethyl methyl-α-naphthylmethylmalonate ⟶ methyl-α-naphthylmethylmalonic acid ⟶ β-(α-naphthyl)-isobutyric acid ⟶ β-(α-naphthyl)-isobutyramide ⟶ 1-(α-naphthyl)-2-aminopropane.

β-(α-Naphthyl)-isobutyric acid (IX) was prepared by a second method according to which α-naphthaldehyde was condensed with methyl ethyl

(1) This paper represents part of a dissertation to be submitted to the Horace H. Rackham School of Graduate Studies by C. E. Maxwell in partial fulfilment of the requirements for the degree of Doctor of Philosophy in the University of Michigan.

(2) Windaus and Bernthsen-Buchner, *Ber.*, **50**, 1120 (1917).

(3) For a discussion of this interesting reaction see Heidelberger, "An Advanced Laboratory Manual of Organic Chemistry," The Chemical Catalog Company, New York, N. Y., 1923, p. 24.

ketone to yield methyl α-methyl-β-(α-naphthyl)-vinyl ketone (VII). The latter was oxidized with sodium hypobromite to α-methyl-β-(α-naphthyl)-acrylic acid (VIII). Upon reduction of the acrylic acid with sodium amalgam there was obtained β-(α-naphthyl)-isobutyric acid.

$$C_{10}H_7—CHO + CH_3—CH_2—CO—CH_3 = C_{10}H_7—CH=C(CH_3)—CO—CH_3 \quad (VII)$$

$$C_{10}H_7—CH=C(CH_3)—COOH \quad (VIII)$$

$$C_{10}H_7—CH_2—CH(CH_3)—COOH \quad (IX)$$

Incidentally, diethyl methyl-α-naphthylmethylmalonate was condensed with urea to form methyl-α-naphthylmethylbarbituric acid.

Experimental Part

α-Naphthylmethylamine (I).—A mixture of 19.4 g. (0.11 mole) of α-naphthylmethyl chloride,[4] 14 g. (0.10 mole) of finely powdered hexamethylenetetramine and 50 cc. of chloroform was heated until the compounds began to react, the heat removed for a short time and the mixture then refluxed for one-half hour. The slightly turbid solution was cooled, 150 cc. of petroleum ether (30–60°) added and the gummy precipitate, which soon became solid, filtered and dried; yield 35 g. The material was placed in a distillation flask, 82 cc. of alcohol and 30 cc. of concd. hydrochloric acid added and the mixture distilled until about one-third of the liquid had been removed. The residue was cooled, the solid product filtered, dissolved in water, the solution made alkaline with concd. alkali and the amine extracted with ether; yield 11.5 g.; b. p. 200–205° (30 mm.).[5]

An ether solution of the amine, treated with hydrogen chloride, yielded the hydrochloride; m. p. 260–262°.[6]

1-(α-Naphthyl)-1-aminoethane (II).—To α-naphthylmagnesium bromide, prepared from 103 g. of α-bromonaphthalene, 12 g. of magnesium and 300 cc. of ether, there was added, during the course of one-half hour, 21 g. of acetonitrile, dissolved in 100 cc. of ether. The mixture was refluxed for one-half hour, cooled, stirred and 150 cc. of 10% hydrochloric acid added slowly, followed by the addition of 25 cc. of concd. hydrochloric acid. The ether layer was separated, dried, the solvent removed and the α-acetonaphthone distilled; yield 62 g.; b. p. 145–147° (6 mm.).[7]

The oxime was formed in practically quantitative yield when 5 moles of sodium hydroxide was added, slowly, to one mole of the ketone, 1.5 moles of hydroxylamine hydrochloride, 360 cc. of alcohol and 75 cc. of water and the mixture refluxed for five minutes. The latter was poured into 550 cc. of concd. hydrochloric acid, diluted with 3600 cc. of water, the oxime filtered and recrystallized from dilute alcohol; m. p. 134–135°.[8]

Twenty-five grams of the oxime was reduced with sodium and alcohol,[9] the alcohol removed under reduced pressure and the amine extracted with ether. The solution was dried with stick sodium hydroxide. The amine boiled at 141–142° (5 mm.)[10]; yield 15 g.

Hydrogen chloride was passed into an ether solution of the amine and the precipitated hydrochloride recrystallized from alcohol; m. p. 236–237°.[11]

Anal. Calcd. for $C_{12}H_{14}NCl$: N, 6.75; Cl, 17.08. Found: N, 6.68; Cl, 17.02.

1-(β-Naphthyl)-1-aminoethane (III).—β-Acetonaphthone[8b] was converted into its oxime as described above; m. p. 142–143°.[12] Eight and one-half grams of the oxime, reduced with sodium and alcohol, yielded 4.4 g. of the amine; b. p. 172–174° (29 mm.).[13] The amine hydrochloride melted at 279–280°[14] after it had been precipitated from an alcoholic solution by absolute ether.

Anal. Calcd. for $C_{12}H_{14}NCl$: N, 6.75; Cl, 17.08. Found: N, 6.61; Cl, 17.02.

1-(α-Naphthyl)-1-aminopropane (IV).—α-Propionaphthone was produced in 52% yield from propionitrile and α-naphthylmagnesium bromide; b. p. 171–174° (12 mm.).[15]

The oxime was obtained in 88% yield; m. p. 55–57°.[16] Reduction of the oxime with sodium and alcohol yielded the amine in 50% yield; b. p. 148–149° (10 mm.).

The amine hydrochloride melted at 281–282° after precipitation by ether from an alcoholic solution.

Anal. Calcd. for $C_{13}H_{16}NCl$: N, 6.32; Cl, 16.00. Found: N, 6.22; Cl, 15.81.

Diethyl α-Naphthylmethylmalonate.—Two hundred and five grams of this compound was obtained from 288 g. of diethyl malonate, 360 cc. of dry, thiophene-free benzene, 20.7 g. of sodium and 158 g. of α-chloromethylnaphthalene; b. p. 199–201° (3 mm.)[17]; yield 205 g.

Diethyl Methyl-α-naphthylmethylmalonate.—This compound was obtained in 89% yield in the usual manner from 17.5 g. of sodium, 380 cc. of absolute alcohol, 227 g. of diethyl α-naphthylmethylmalonate and 170 g. of methyl iodide; b. p. 207–209° (2 mm.); m. p. 51–52° after recrystallization from alcohol. The compound is soluble in ether, benzene and alcohol.

Anal. Calcd. for $C_{19}H_{22}O_4$: C, 72.59; H, 7.06. Found: C, 72.42; H, 7.12.

Methyl-α-naphthylmethylmalonic Acid.—A mixture of 130 g. of the ester, 1000 cc. of 60% alcohol and 79 g. of potassium hydroxide was refluxed for four hours, the alcohol removed and the residue made acid to congo red; yield 97 g.; m. p. 172–173° (dec.) after recrystallization from dilute alcohol. The acid is soluble in ether and alcohol, slightly soluble in benzene.

(4) Coles and Dodds, THIS JOURNAL, **60**, 853 (1938).

(5) Von Braun, Blessing and Zobel [*Ber.*, **56**, 1996 (1923)], who reduced α-naphthonitrile, found 155° (12 mm.).

(6) The melting point[5] is reported as 262–264°.

(7) Stobbe and Lenzner [*Ann.*, **380**, 95 (1911)] found 296–298°.

(8) (a) Rousset [*Bull. soc. chim.*, [3] **15**, 60 (1896)] found 135–136°; (b) St. Pfau and Ofner [*Helv. Chim. Acta*, **9**, 671 (1926)] reported 137–138°.

(9) See "Organic Syntheses," **11**, 58 (1931), for the general procedure.

(10) (a) Samuelsson [Thesis, Univ. Lund, 1923; *C. A.*, **18**, 1833 (1924)] reported 153° (11 mm.); (b) Hayashi, *Sci. Pap. Inst. Physic. Chem. Res.*, **20**, 398; *Chem. Zentr.*, **104**, I, 1728 (1933)] found 183.5° (41 mm.).

(11) The melting point reported[8b] is 220–221° (dec.).

(12) The melting points reported are 142–143°[8a] and 145–146°.[8b]

(13) Samuelsson[10a] found 142–143° (6–7 mm.).

(14) The reported melting point is 199–200°.[10a]

(15) Rousset[8a] found 166–168° (8 mm.).

(16) The melting point reported is 57–58°[8a] (p. 63).

(17) Mayer and Sieglitz [*Ber.*, **55**, 1843 (1922)] found 221° (11 mm.); they used α-bromomethylnaphthalene.

Anal. Calcd. for $C_{15}H_{14}O_4$: C, 69.75; H, 5.47. Found: C, 69.63; H, 5.55.

β-(α-Naphthyl)-isobutyric Acid (IX).—The malonic acid was heated, in 15-g. portions, at 175–180° in an oil-bath for three to four hours. The viscous residue crystallized when rubbed and melted at 91–92° after recrystallization from petroleum ether (90–100°). The acid is soluble in ether, benzene and alcohol.

Anal. Calcd. for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59. Found: C, 78.60; H, 6.71.

According to a second procedure 11.5 g. of α-naphthaldehyde bisulfite[18] compound was treated with 10% sodium carbonate solution, the aldehyde extracted with ether, the solution dried with fused sodium sulfate and the solvent removed. The aldehyde, mixed with 7.2 g. of methyl ethyl ketone, was kept cool, 0.9 g. of hydrogen chloride passed into it, the mixture shaken for sixteen hours, washed with water and then with sodium carbonate solution. The crude, oily methyl α-methyl-β-(α-naphthyl)-vinyl ketone (VII), which possessed a camphoraceous odor, was dissolved in 100 cc. of alcohol, stirred and cooled and sodium hypobromite, prepared from 24 g. of bromine, 20 g. of sodium hydroxide and 50 cc. of water, was added. During this process the temperature was kept below 20°. The mixture was stirred for one hour at ordinary temperature, filtered and about 7 g. of sodium bisulfite added to destroy any hypobromite. The mixture was evaporated to about one-half of its original volume on a steam-bath, treated with charcoal, filtered and acidified. The precipitated α-methyl-β-(α-naphthyl)-acrylic acid (VIII) weighed 6.4 g.; m. p. 149–150°[19] after recrystallization from benzene.

To 4.2 g. of the acrylic acid, dissolved in 10% sodium carbonate solution, there was added 58 g. of 4% sodium amalgam. After forty-eight hours the alkaline solution was separated, filtered and acidified. The gummy precipitate, which solidified when cooled, weighed 3.6 g. The crude isobutyric acid melted at 91–92°.

β-(α-Naphthyl)-isobutyramide.—A mixture of 77 g. of the isobutyric acid and 50 g. of thionyl chloride was heated in an all-glass apparatus for three hours on a steam-bath, poured into 120 cc. of cold, 28% ammonia water, which was stirred vigorously, and the precipitated amide recrystallized from benzene; yield 73 g.; m. p. 134–135° after recrystallization from benzene.

The amide is soluble in alcohol and benzene and insoluble in ether.

Anal. Calcd. for $C_{14}H_{15}ON$: N, 6.57. Found: N, 6.60.

1-(α-Naphthyl)-2-aminopropane (V).—An alkaline hypobromite solution, prepared from 25.4 g. of bromine, 240 g. of sodium hydroxide and 2400 cc. of water, was cooled to 10–15° and 32 g. of the isobutyramide added. The mixture was heated at 70–80° for one and one-half hours, 24 g. of solid sodium hydroxide added and the mixture heated two hours longer; when cooled, the brown, oily precipitate became crystalline. The latter was extracted with ether; 5 g. of ether-insoluble material proved to be unchanged amide. The ether solution was extracted with 25-cc. portions of 10% hydrochloric acid and the combined extracts made alkaline. The amine was extracted with ether, the solution dried with fused sodium sulfate and treated with hydrogen chloride; 4.8 g. of the amine hydrochloride precipitated. After it had been dissolved in the smallest possible amount of hot absolute alcohol and precipitated by addition of absolute ether the hydrochloride melted at 213–214°.

Anal. Calcd. for $C_{13}H_{16}NCl$: N, 6.32; Cl, 16.00. Found: N, 6.25; Cl, 15.93.

1-(α-Naphthyl)-1-aminobutane (VI).—The required α-butyronaphthone was obtained by addition of 13.8 g. of butyronitrile, dissolved in 50 cc. of ether, to the Grignard reagent prepared from 51.8 g. of α-bromonaphthalene, 6.0 g. of magnesium and 150 cc. of ether. The mixture was refluxed for one hour, the imine decomposed with hydrochloric acid and the ketone purified by distillation; yield 13 g.; b. p. 155–157° (3 mm.).[20]

The oxime, prepared in the manner described, was extracted from the acidified reaction mixture with ether; b. p. 185–187° (8 mm.).[21]

The amine was obtained by reduction of the oxime with sodium and alcohol. The ether extract of the crude amine was shaken with 10% hydrochloric acid whereupon about one-half of the amine separated as hydrochloride after the acidic solution had remained at ordinary temperature for some time. The salt was removed, the filtrate made alkaline and the rest of the amine extracted with ether; b. p. 142–143° (4 mm.).

The amine hydrochloride melted at 281–282° after it had been precipitated from a warm alcoholic solution by the addition of ether.

Anal. Calcd. for $C_{14}H_{18}NCl$: N, 5.92; Cl, 15.05. Found: N, 5.89; Cl, 14.91.

Methyl-α-naphthylmethylbarbituric Acid.—To sodium ethylate, prepared in 30 cc. of toluene, from 0.7 g. of sodium and 1.4 g. of alcohol, there was added 7.7 g. of diethyl methyl-α-naphthylmethylmalonate. The mixture was heated for four hours at 120–125°, shaken with about 100 cc. of water, the aqueous layer separated and acidified. The oily precipitate, which soon solidified, was recrystallized from a mixture of dioxane and petroleum ether (90–100°); m. p. 127–128°.

Anal. Calcd. for $C_{16}H_{14}O_3N_2$: N, 9.92. Found: N, 9.83.

Summary

Several naphthylaminoalkanes—derivatives of methane, ethane, propane and butane—have been prepared and found to exhibit only slight pressor activity. A characteristic pharmacological feature of these compounds is the development of tolerance.

ANN ARBOR, MICHIGAN RECEIVED APRIL 18, 1939

(18) Ref. 16, p. 1846; also Ref. 4, p. 854.

(19) Rousset [*Bull. soc. chim.*, [3] **17**, 813 (1897)], who used another preparative method, reported 151°.

(20) The boiling point recorded is 316–318°,[8a] (p. 65).

(21) Rousset[8a] (p. 65) found 206–208° (13 mm.).

[CONTRIBUTION FROM THE DEPARTMENT OF RESEARCH IN PURE CHEMISTRY, MELLON INSTITUTE OF INDUSTRIAL RESEARCH]

Cinchona Alkaloids in Pneumonia. VII. Amyl and Hydroxyalkyl Apocupreine Ethers

BY MARY HOSTLER GREEN,[1] ALICE G. RENFREW AND C. L. BUTLER[2]

Recent work in the apocupreine ether series[3] has shown that on ascending in the series of alkyl ethers, a high pneumococcicidal activity is maintained through the C_4 derivatives. The situation is somewhat complicated by variations in the structure of the butyl group; however, isobutyl apocupreine dihydrochloride was shown to be as active *in vitro* as the very potent ethyl derivative. This is in marked contrast with the behavior of the corresponding hydrocupreine ethers.[4] It was also shown that hydroxyethylapocupreine,[5] which has found clinical application, has much stronger antipneumococcic activity than the corresponding hydrocupreine derivative. Further, hydroxypropyl ethers of apocupreine have very strong bacteriostatic action and much lower toxicity than the alkyl derivatives.[6] This higher activity in the apocupreine ether series is not surprising in view of the fact that apocupreine itself shows considerable activity, whereas hydrocupreine is quite low in bacteriostatic action.

The present work on β-hydroxypropyl, isomeric hydroxybutyl and isomeric amyl apocupreine ethers was undertaken in order to study further the influence of the size and structure of the ether group on antipneumococcic activity in this series. The amyl ethers were prepared readily by alkylation of apocupreine with the desired amyl *p*-toluenesulfonates. The preparation of the hydroxybutyl derivatives by alkylation with benzyloxybutyl *p*-toluenesulfonates and subsequent hydrolysis of the benzyl group offered no difficulty. Alkylations were also carried out with β-hydroxy-*n*-propyl and β-methyl-β-hydroxy-*n*-propyl *p*-toluenesulfonates. These reagents gave only very low yields of hydroxyalkyl ethers. The results are entirely in agreement with earlier data on the use of glycol monoesters in alkylations of basic phenolic substances.[5,7]

Some biological properties of the apocupreine ethers prepared in the course of the work are shown in Table I. A decided lowering in the toxicity of butyl apocupreine ethers was accomplished by introduction of the hydroxyl group into the butyl radical. This effect was accompanied by a decrease in the *in vitro* bacteriostatic activity, a decrease which was very marked in the β-methyl-β-hydroxy-*n*-propyl and the δ-hydroxy-*n*-butyl ethers. The suitability of the more active α-methylol *n*-propyl and α-methyl β-hydroxy-*n*-propyl ethers for trial in human pneumonia will

TABLE I[a]

BACTERIOSTATIC POWER AND TOXICITY OF APOCUPREINE ETHERS

Apocupreine ether dihydrochloride	*In vitro* prevents growth of pneumococcus in concn. of	Intraperitoneal Toxicity (20 g. mice) deaths at mg. dosages of 2	3	4	5	6	7	8
β-Hydroxy-*n*-propyl	1:300,000				0/30	1/30	10/30	
β-Methyl-β-hydroxy-*n*-propyl	1:50,000				1/30	19/30		
δ-Hydroxy-*n*-butyl	1:50,000				7/30	25/30		
α-Methylol *n*-propyl	1:400,000				10/30	14/30		
α-Methyl-β-hydroxy-*n*-propyl	1:400,000				6/30	20/30	30/30	
n-Amyl	1:800,000	7/30	27/30		10/10			
i-Amyl[8]	1:300,000	6/30	20/30					
s-Butylcarbinyl	1:400,000	3/30	20/30		10/10			
α-Methyl-*n*-propylcarbinyl	1:400,000	2/30	12/30	29/30				
Diethylcarbinyl	1:400,000		4/30	28/30				

[a] The experimental testing of these alkaloids was carried out by Drs. Maclachlan, Bracken and Patrick of the Mercy Hospital, Pittsburgh, Penna.

(1) Present address, American Products Company, Cincinnati, Ohio.

(2) Present address, Bennington College, Bennington, Vermont.

(3) Butler, Hostler and Cretcher, THIS JOURNAL, **59**, 2354 (1937).

(4) Morgenroth and Bumke, *Deut. Med. Wochschr.*, **40**, 539 (1914); **44**, 729 (1918); Morgenroth and Tugendreich, *Berlin. klin. Wochschr.*, **53**, 794 (1916); *Biochem. Z.*, **79**, 257 (1917).

(5) Maclachlan, Johnston, Bracken and Crum, *Am. J. Med. Sci.*, **197**, 31 (1939); Butler, Nelson, Renfrew and Cretcher, THIS JOURNAL, **57**, 575 (1935).

(6) Butler and Renfrew, THIS JOURNAL, **60**, 1473 (1938).

(7) Butler and Renfrew, *ibid.*, **60**, 1582 (1938).

(8) Miura and Okamoto, *Jap. J. Med. Sci., V*, **1**, 1 (1930).

depend on the results (not yet available) of tests for visual disturbance.

Experimental[9]

Butylene Glycol Monobenzyl Ethers.—Isomeric monobenzyl ethers were prepared by a method which has already been described.[10]

TABLE II

Substance, ether	B. p. at 6 mm. °C.	Anal. ($H_{16}O_2$: Calcd. for C_{11}- C, 73.3; H, 8.9) C	H
1,2-Butylene glycol 1-monobenzyl	128–132	73.9	9.1
2,3-Butylene glycol monobenzyl	122–125	73.0	9.0
1,4-Butylene glycol monobenzyl	146–149	73.2	9.3

Various *p*-Toluenesulfonyl Esters.—Hydroxypropyl, hydroxybutyl, benzyloxybutyl and amyl *p*-toluenesulfonates were prepared in good yields from propylene glycol, isobutylene glycol, isomeric butylene glycol, monobenzyl ethers and isomeric amyl alcohols by methods described in previous papers in this series. Suitable alkylating reagents were obtained without extensive purification. Three of the esters were crystallized from ether.

Diethylcarbinyl-*p*-toluenesulfonate, m. p. 37°.[11] β-Hydroxy-*n*-propyl-*p*-toluenesulfonate, m. p. 46°. *Anal.* Calcd. for $C_{10}H_{14}O_4S$: S, 13.9. Found: S, 13.7. α-Methyl-β-benzyloxypropyl *p*-toluenesulfonate, m. p. 47°. *Anal.* Calcd. for $C_{18}H_{22}O_4S$: S, 9.7. Found: S, 10.1.

Alkylation of Apocupreine.—Alkylations according to the previously described methods proceeded smoothly and gave good yields of final products except, as noted above, when glycol monoesters were used as reagents. In these experiments, yields of 4–8% were obtained. δ-Benzyloxybutyl apocupreine was obtained in crystalline condition from ether; m. p. 104°; specific rotation −152°.[12] *Anal.* Calcd. for $C_{30}H_{36}O_3N_2$: N, 5.9. Found: N, δ-benzyloxybutylapocupreine, 5.7; α-benzyloxymethyl *n*-propylapocupreine, 5.9; α-methyl-β-benzyloxy-*n*-propylapocupreine, 5.9.

Hydrolysis of the benzyloxybutyl ethers in 1:1 hydrochloric acid proceeded smoothly[6] and good yields of the corresponding hydroxybutyl derivatives were obtained. Some physical properties and analyses of the various ethers which were prepared are shown in Table III.

TABLE III

Apocupreine ether	Bases: M. p., °C.	Sp. rot.	Formula	Nitrogen, % Calcd.	Found	Dihydrochlorides: Sp. rot.	Formula	Chlorine, % Calcd.	Found	Moisture Calcd.	Found
β-Hydroxy-*n*-propyl	170	−180°	$C_{22}H_{28}O_3N_2$	7.6	7.7	−216°	$C_{22}H_{28}O_3N_2 \cdot 2HCl$	16.1		...	...
β-Methyl-β-hydroxy-*n*-propyl	102	−169°	$C_{23}H_{30}O_3N_2$	7.3	7.3	−218°	$C_{23}H_{30}O_3N_2 \cdot 2HCl$	15.5	14.7	...	...
δ-Hydroxy-*n*-butyl	178	−179°	$C_{23}H_{30}O_3N_2$	7.3	7.2	−213°	$C_{23}H_{30}O_3N_2 \cdot 2HCl$	15.5	15.2	...	...
α-Methylol *n*-propyl	Amor-	−165°	$C_{23}H_{30}O_3N_2$	7.3	7.4	−202°	$C_{23}H_{30}O_3N_2 \cdot 2HCl$	15.5	13.8	...	...
α-Methyl-β-hydroxy-*n*-propyl	phous	−163°	$C_{23}H_{30}O_3N_2$	7.3	7.3	−212°	$C_{23}H_{30}O_3N_2 \cdot 2HCl$	15.5	14.0	...	...
n-Amyl[13]	146	−178°	$C_{24}H_{32}O_2N_2$	7.4	7.4	−230°	$C_{24}H_{32}O_2N_2 \cdot 2HCl \cdot 1.5$ aq.	15.2	15.8	5.8	5.2
i-Amyl	175	−181°	$C_{24}H_{32}O_2N_2$	7.4	7.3	−206°	$C_{24}H_{32}O_2N_2 \cdot 2HCl \cdot 2$aq.	14.9	14.8	7.3	7.1
s-Butylcarbinyl	169	−172°	$C_{24}H_{32}O_2N_2$	7.4	7.3	−225°	$C_{24}H_{32}O_2N_2 \cdot 2HCl \cdot$aq.	15.5	14.8	3.8	3.4
Methyl-*n*-propylcarbinyl	Amor-	−163°	$C_{24}H_{32}O_2N_2$	7.4	7.1	−212°	$C_{24}H_{32}O_2N_2 \cdot 2HCl \cdot 2$aq.	14.9	15.2	7.3	7.7
Diethylcarbinyl	phous	−150°	$C_{24}H_{32}O_2N_2$	7.4	6.7	−213°	$C_{24}H_{32}O_2B_2 \cdot 2H_2O \cdot 1.5$aq.	15.2	14.6	5.8	5.5

Summary

Hydroxypropyl, isomeric hydroxybutyl and isomeric amyl apocupreine ethers have been prepared. Some biological properties of these substances, of interest in the chemotherapeutic study of pneumonia, have been presented briefly.

RECEIVED MAY 15, 1939

(9) The preparation of many of the reagents used in this work was carried out by Miss Mary Clapp.

(10) Butler, Renfrew and Clapp, THIS JOURNAL, **60**, 1472 (1938).

(11) Tabern and Volweiler, *ibid.*, **56**, 1141 (1934).

(12) Rotations of bases were measured in alcoholic solution; salts were measured in aqueous solution; $l = 1$, $c = 1$.

(13) Buttle, Henry, Solomon, Trevan and Gibbs, *Biochem. J.*, **32**, 47 (1938).

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF NEW YORK UNIVERSITY]

Steric Hindrance in Ketone–Phenol Condensations. The Synthesis of Cyclo-alkylene Phenols and Cyclo-alkyl Coumaranes[1]

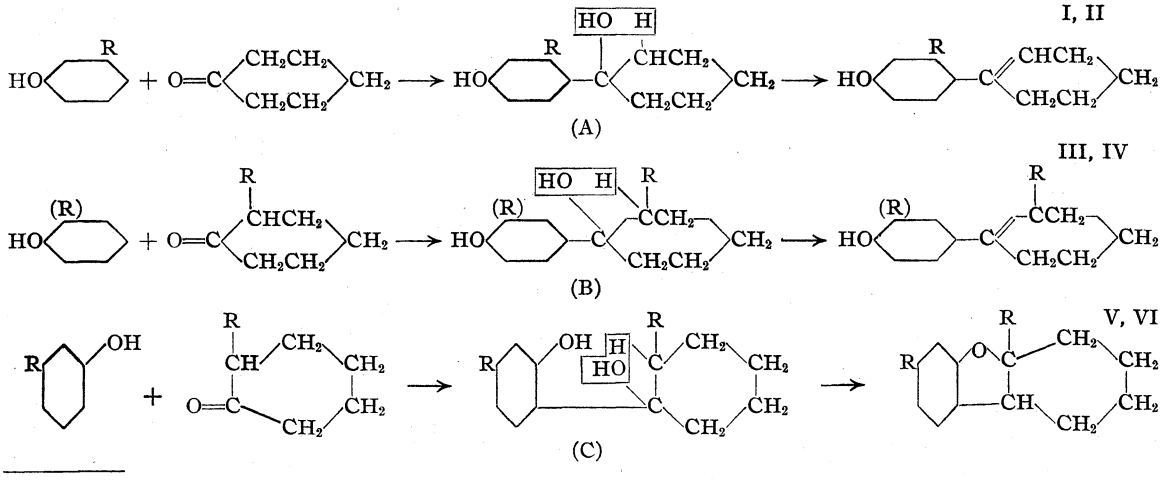
BY JOSEPH B. NIEDERL AND VICTOR NIEDERL

In a previous publication[2] it was asserted that in the condensation of ketones with phenols "the nature of the end-product is influenced not only by the type of carbonyl compound employed, but also by the type of phenol used" and that "this influence exerts itself particularly through the position of the second substituent in the benzene ring, *i. e.*, whether it is ortho, meta or para to the hydroxyl group." As shown in this communication, this hypothesis now has been substantiated fully.

In the following it has been established that meta alkylated phenols react differently than ortho alkylated phenolic compounds; the latter yield alkylidene-diphenols,[3] while the former yield unsaturated compounds in these condensations. The representative types of *m*-alkyl phenols chosen were *m*-cresol and *m*-ethylphenol. These two *m*-alkylated phenols were condensed with cyclohexanone. In each instance the respective cyclohexenyl phenol, the 1-(4′-hydroxy-2′-methyl)-phenylcyclohexene-1 (I) and the 1-(4′-hydroxy-2′-ethyl)-phenylcyclohexene-1 (II) was obtained. In both cases, the alkyl radical in the final condensation product is adjacent to the carbon carrying the cyclohexenyl radical. It appears, then, that such an arrangement in the molecule of the final condensation product inhibits the introduction of a second phenolic radical, which would be the normal course of the reaction (A).

If this hypothesis is correct, then a similar effect should be exerted when a cyclic ketone is chosen for condensation, which would give a condensation product with an alkyl radical adjacent to the carbon carrying the phenolic group. Condensation experiments with *o*-methylcyclohexanone verified this postulation. Thus when *o*-methylcyclohexanone was condensed with phenol itself and with *o*-cresol, compounds which ordinarily yield the respective cyclohexylidene-diphenol, also the unsaturated, monophenolic compound, namely, the 2-methyl-1-(4′-hydroxy)-phenylcyclohexene-1 (III) and the 2-methyl-1-(4′-hydroxy-3′-methyl)-phenylcyclohexene-1 (IV) was obtained, a fact which clearly indicates steric hindrance (B).

Since both the meta-alkylated phenols and the ortho-alkylated cyclohexanones gave rise separately to steric hindrance phenomena, it was then thought to try the extreme case, namely, the condensation of both the above mentioned reactants. The condensation was slow, but positive, but no unsaturated phenolic condensation product was obtained, instead, only coumaranes, the 2,6-dimethyl-2,3-cyclohexyl-coumarane (V), and the 2-methyl-6-ethyl-2,3-cyclohexyl-coumarane



(1) Three of the key substances (I, III, IV) presented in this paper were found by Victor Niederl in pursuance of his thesis researches. The other material presented in this paper is taken from the theses presented by J. Charney, J. Rodgeville and A. Ziering to the Graduate School of New York University in partial fulfilment of the requirements for the degree of Master of Science, June, 1939.

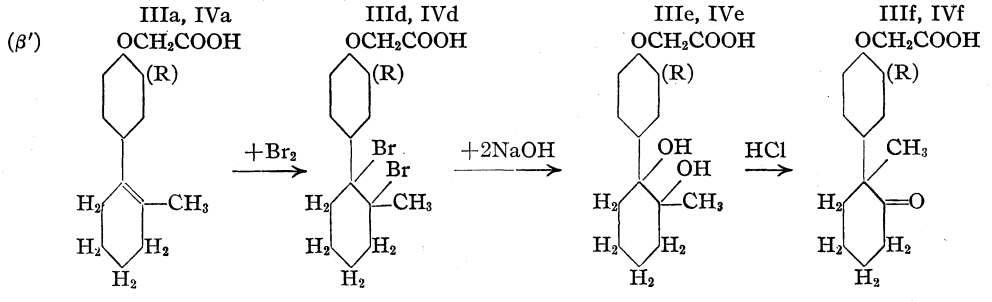
(2) J. B. Niederl and V. Niederl, THIS JOURNAL, **61**, 348 (1939).

(3) M. E. McGreal, V. Niederl and J. B. Niederl, *ibid.*, **61**, 345 (1939).

(VI) resulted. This would indicate that when steric hindrance becomes too great, ortho alkylation takes place (C).

The formation of all three types of condensation products may be formulated as shown.

Of the four crystalline phenolic key substances (I, II, III, IV), all of which exhibit feeble oestrogenic properties (0.2 mg. = 1 rat unit), the following crystalline derivatives were prepared: aryloxyacetic acids (Ia, IIa, IIIa, IVa), phenylurethans (Ib, IIb, IIIb, IVb), acetates (Ic, IIc, IIIc, IVc) and benzoates (IIIh, IVh). For the unsaturation tests the aryloxyacetic acids (Ia, IIa, IIIa, IVa) were chosen. Baeyer's permanganate test[4] was positive in all cases. In addition to this, the aryloxyacetic acids (Ia, IIa, IIIa, IVa) were brominated and the resulting crystalline bromine derivatives isolated (Id, IId, IIId, IVd). Titration of the dibromides (IIId, IVd) with either 0.1 or 0.01 *N* sodium hydroxide solution gave a neutralization equivalent of a tribasic acid, proving that in these titrations both bromine atoms were hydrolyzed, a behavior which is typical of bromine atoms attached to tertiary carbon atoms. Thus it could be shown that the ethylenic linkage is between the carbon atom carrying the phenyl radical and the carbon atom carrying the methyl group. To substantiate this further, dibromides IIId and IVd were hydrolyzed to the respective glycols (IIIe, IVe) and these in turn were subjected to pinacolone rearrangement. The resulting ketones (IIIf, IVf) were identified through their 2,4-dinitrophenylhydrazones (IIIg, IVg).



Experimental

Condensation Method

1-(4′-Hydroxy-2′-methyl)-phenylcyclohexene-1 (I).—Half molar quantities of *m*-cresol and cyclohexanone were dissolved in 100 cc. of glacial acetic acid and the mixture placed in a 1-liter, triple-necked, round-bottomed flask which was provided with a reflux condenser, a thermometer and a gas inlet tube extending to the bottom of the vessel. A vigorous stream of dry hydrogen chloride gas was passed into the system for six hours at room temperature, then the flask stoppered and left standing at room temperature for two to three weeks. After this time the reaction mixture was dissolved in 200 cc. of benzene, this solution washed several times with an equal volume of water and then extracted with 150 cc. of Claisen solution. The Claisen solution extract was acidified with dilute hydrochloric acid; the oil which precipitated out was taken up in 100 cc. of benzene, washed with water and dried with calcium chloride. The benzene was distilled off and the residue distilled under diminished pressure. The fraction boiling between 120 and 140° was collected and redistilled in vacuum; b. p. 130–133° at 4 mm.; $n^{25}D$ 1.5413. After several weeks the substance crystallized; yield 12 to 15%.

1-(4′-Hydroxy-2′-ethyl)-phenylcyclohexene-1 (II).—Half molar mixtures of *m*-ethylphenol and cyclohexanone were condensed exactly as described above and worked up in a similar manner. The pure product boiled at 145–148° and 5 mm.; $n^{25}D$ 1.5421. It also crystallized after several weeks; yield, about 15%.

2-Methyl-1-(4′-hydroxy-phenylcyclohexene-1 (III).—Half molar quantities of phenol and *o*-methylcyclohexanone were condensed as described above, except that no glacial acetic acid was used, and left standing for ten days, by which time the reaction mixture had solidified. The crystalline mass was treated with hot water, filtered off on a sintered glass filter and recrystallized from diisobutylene; yield, 55–60%.

2-Methyl-1-(4′-hydroxy-3′-methyl)-phenylcyclohexene-1 (IV).—Half molar mixtures of *o*-cresol and *o*-methylcyclohexanone were condensed in exactly the same manner as compound III. The reaction mixture, even upon prolonged standing, did not crystallize and after standing for fourteen days it was dissolved in 200 cc. of benzene and worked up as described for compound I. The product was finally distilled in vacuum and the fraction boiling between 155–160° at 12 mm. crystallized in the receiver. It was recrystallized from diisobutylene; yield, 45–50%.

Aryloxyacetic Acid Derivatives (Ia, IIa, IIIa, IVa).—These derivatives were prepared by dissolving the respective compound in 30% sodium hydroxide solution to which sufficient methyl alcohol was added to effect solution. The calculated amount of chloroacetic acid was added, the reaction mixture gently refluxed for two hours, and worked up according to the directions given in Shriner and Fuson.[5]

(4) Mulliken, "A Method for the Identification of Pure Organic Compounds," J. Wiley and Sons, Inc., New York, N. Y., 1904, p. 79.

(5) Shriner and Fuson, "The Systematic Identification of Organic Compounds," J. Wiley and Sons, Inc., New York, N. Y., 1935, pp. 148–149.

Phenylurethans (Ib, IIb, IIIb, IVb).—One gram of substance was dissolved in 1 cc. of phenyl isocyanate in a test-tube which was sealed and placed in a beaker containing boiling water. The test-tube was opened when its content had solidified and the crystalline material placed in a porous tile to dry. It was recrystallized from diisobutylene.

Acetates (Ic, IIc, IIIc, IVc).—Ten grams of the respective phenol was dissolved in 30 cc. of acetic anhydride and the mixture refluxed for four hours in a ground-glass joint apparatus. The acetic anhydride and acetic acid was distilled off and the residual oil distilled in vacuum; b. p.: (Ic) 155–157° (12 mm.), (IIc) 169–174° (12 mm.), (IIIc) 161° (10 mm.), (IVc) 172–174° (12 mm.).

Benzoates (IIIh, IVh).—These two benzoates were prepared by dissolving 0.5 g. of substance in 5 cc. of benzoyl chloride in a test-tube and refluxing the mixture for thirty minutes. Then the solution was poured into 25 cc. of 10% sodium carbonate solution and stirred thoroughly for five minutes. The oil which separated was taken up in 30 cc. of ether and the ethereal solution washed with 1% sodium hydroxide solution and then with water until neutral. The ether solution was dried with calcium chloride and then permitted to evaporate at room temperature. The crystalline residue was twice recrystallized from 80% ethyl alcohol.

Bromine Derivatives of Aryloxyacetic Acids (Id, IId, IIId, IVd).—To a suspension of the respective aryloxyacetic acid derivatives in carbon tetrachloride a solution of bromine in the same solvent (0.3 g. per cc.) was added slowly until the calculated amount of bromine had been introduced. The bromo derivative which precipitated was washed with ether to remove any unreacted acid and the ether insoluble bromine derivative was filtered off and dried on a porous tile. It was recrystallized from ethyl alcohol.

Glycols of Aryloxyacetic Acids (IIIe, IVe).—One gram of the respective aryloxyacetic acid dibromide (IIId, IVd) was dissolved in 30 cc. of 1 *N* aqueous sodium hydroxide solution and the solution was allowed to stand at room temperature for three hours. After this time, the solution was acidified with hydrochloric acid. This caused the separation of a water insoluble oil, which was taken up with ether. The ether extract was washed twice with distilled water and then allowed to evaporate at room temperature. The crystalline residue was twice recrystallized from diisobutylene. One gram of the glycol (IIIe, IVe) was added to 30 cc. of a mixture consisting of two parts of alcohol, one part of cond. hydrochloric acid and eight parts of distilled water. This mixture was refluxed for three hours. It was then diluted with an equal amount of water and twice extracted with 30 cc. of ether. The combined ether extracts were washed once with distilled water and then allowed to evaporate at room temperature. The residue (IIIf, IVf) was dissolved in 30 cc. of alcohol. To this

TABLE I

COMPOUNDS, FORMULAS AND ANALYSES

No.	Formula or derivative	M. p., °C.	Empirical formula	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found	Bromine Calcd.	Bromine Found	Mol. wt. Calcd.	Mol. wt. Fd.	Neut. equiv. Calcd.	Neut. equiv. Fd.
			1-(4′-Hydroxy-2′-methyl)-phenyl-cyclohexene-1												
I	$C_6H_3(OH)(CH_3)C_6H_9$	65	$C_{13}H_{16}O$	82.99	83.16	8.50	8.41	...	...	...	...	188	184	...	...
Ia	Aryloxyacetic ac.	160	$C_{15}H_{18}O_3$	73.18	73.06	7.31	7.25	...	...	...	...	...	...	246	251
Ib	Phenylurethan	114	$C_{20}H_{21}O_2N$	78.19	78.03	6.84	6.68	4.56	4.51	...	...	...	...	...	...
Ic	Acetate	...	$C_{15}H_{18}O_2$	78.65	78.92	7.82	7.70	...	...	...	...	...	...	...	...
Id	Bromine deriv. of Ia	150	$C_{15}H_{17}O_3Br$	55.38	55.12	5.23	5.46	...	...	24.61	23.79	...	...	...	...
			1-(4′-Hydroxy-2′-ethyl)-phenyl-cyclohexene-1												
II	$C_6H_3(OH)(C_2H_5)C_6H_9$	55	$C_{14}H_{18}O$	83.18	83.02	8.91	8.60	...	...	...	...	202	208	...	...
IIa	Aryloxyacetic ac.	117	$C_{16}H_{20}O_3$	73.86	73.51	7.69	7.86	...	...	...	...	...	...	260	264
IIb	Phenylurethan	134	$C_{21}H_{23}O_2N$	78.52	78.52	7.16	7.46	4.36	4.25	...	...	...	...	...	...
IIc	Acetate	...	$C_{16}H_{20}O_2$	78.69	78.56	8.19	7.98	...	...	...	...	...	...	...	...
IId	Bromine deriv. of IIa	146	$C_{16}H_{19}O_3Br$	56.63	56.30	5.60	6.05	...	...	23.60	23.10	...	...	...	...
			2-Methyl-1-(4′-hydroxy)-phenyl-cyclohexene-1												
III	$C_6H_4(OH)C_6H_8(CH_3)$	144	$C_{13}H_{16}O$	82.99	82.78	8.68	8.46	...	...	...	...	188	184	...	...
IIIa	Aryloxyacetic ac.	136	$C_{15}H_{18}O_3$	73.17	72.97	7.32	7.39	...	...	...	...	...	...	246	245
IIIb	Phenylurethan	160	$C_{20}H_{21}O_2N$	78.19	78.24	6.84	6.59	4.56	4.43	...	...	...	...	...	...
IIIc	Acetate	...	$C_{15}H_{18}O_2$	78.65	78.51	7.82	7.88	...	...	...	...	...	...	...	...
IIId	Bromine deriv. of IVa	104	$C_{15}H_{18}O_3Br_2$	44.12	43.89	4.66	4.63	...	...	39.41	39.34	...	...	...	...
IIIe	Glycol of IIIa	130	$C_{15}H_{20}O_5$	64.28	63.88	7.14	7.03	...	...	...	...	280	279	...	...
IIIh	Benzoate	72	$C_{19}H_{20}O_2$	82.19	82.14	6.85	6.73	...	...	...	...	...	...	...	...
			2-Methyl-1-(4′-hydroxy-3′-methyl)-phenyl-cyclohexene-1												
IV	$C_6H_3(OH)(CH_3)C_6H_8(CH_3)$	86	$C_{14}H_{18}O$	83.18	83.04	8.91	8.74	...	...	...	...	202	198	...	...
IVa	Aryloxyacetic ac.	113	$C_{16}H_{20}O_3$	73.84	73.69	7.69	7.58	...	...	...	...	...	...	260	263
IVb	Phenylurethan	134	$C_{21}H_{23}O_2N$	78.52	78.38	7.16	7.23	4.36	4.32	...	...	...	...	...	...
IVc	Acetate	...	$C_{16}H_{20}O_2$	78.69	78.51	8.18	8.17	...	...	...	...	...	...	...	...
IVd	Bromine deriv. of IVa	107	$C_{16}H_{20}O_3Br_2$	45.75	45.89	4.76	4.99	...	...	38.08	38.14	...	...	...	...
IVe	Glycol of IVa	140	$C_{16}H_{22}O_5$	65.31	65.06	7.48	7.22	...	...	...	...	294	307	...	...
IVg	Phenylhydrazone of IVf (2,4-dinitro)	87	$C_{22}H_{24}O_7N_4$	57.89	57.68	5.26	5.43	12.28	12.00	...	...	...	...	...	...
IVh	Benzoate	69	$C_{21}H_{22}O_2$	82.03	82.10	7.19	6.89	...	...	...	...	...	..	...	...
			2,6-Dimethyl-2,3-cyclohexyl-coumarane												
V	$C_6H_3O(CH_3)C_6H_9(CH_3)$	...	$C_{14}H_{18}O$	83.18	83.08	8.91	8.95	...	...	...	...	202	204	...	...
			2-Methyl-6-ethyl-2,3-cyclohexylcoumarane												
VI	$C_6H_3O(C_2H_5)(C_6H_9(CH_3)$	...	$C_{15}H_{20}O$	83.33	83.12	9.26	9.15	...	...	...	...	216	213	...	...

solution 0.75 g. of 2,4-dinitrophenylhydrazine was added and the mixture refluxed for five minutes. Upon cooling the 2,4-dinitrophenylhydrazone separated out (IIIg, IVg), which was recrystallized from alcohol.

2,6-Dimethyl-2,3-cyclohexylcoumarane (V) and 2-Methyl-6-ethyl-2,3-cyclohexylcoumarane (VI).—Half molar quantities of the respective meta-alkylated phenol and *o*-methylcyclohexanone were dissolved in 100 cc. of glacial acetic acid and condensed as described for compound I, except that the reaction was carried out while the reactants were heated on a water-bath to about 80°. The condensation mixture was left standing for fourteen days, but during this time it was resaturated with hydrogen chloride several times. The reaction product was then dissolved in 200 cc. of benzene, this solution washed several times with water and then extracted with 250 cc. of Claisen solution. Upon acidification of the Claisen solution extract only the unreacted *m*-alkylated phenol (*m*-cresol, or *m*-ethylphenol) was recovered. The benzene solution was then subjected to fractional distillation. Compound V boiled at 139–141° and 12 mm.; $n^{25}D$ 1.5338; sp. gr.^{25}, 1.0252; yield, about 40%. Compound VI boiled at 146–148° and 12 mm.; $n^{25}D$ 1.5302; sp. gr.^{25}, 1.0218; yield, about 30%.

The authors desire to express their appreciation to Reed and Carnrick, Jersey City, N. J., for the physiological tests performed.

Summary

Steric hindrance phenomena encountered in certain types of ketone–phenol condensation systems were studied.

Cycloalkylene phenols and cycloalkyl coumaranes were isolated in such condensation systems. Of the cycloalkylene phenols which represent new types of unsaturated phenols, numerous derivatives were prepared.

WASHINGTON SQUARE COLLEGE
NEW YORK, N. Y. RECEIVED APRIL 21, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

The Reaction between Hexabromobenzene and Phenylmagnesium Bromide

BY T. A. GEISSMAN AND R. C. MALLATT

The formation of hexamethyl- and hexaphenylbenzenes in the reaction between hexabromobenzene and methylmagnesium and phenylmagnesium halides was reported by Durand.[1] The identity of the hexamethylbenzene was established by comparison with an authentic sample, but the "hexaphenylbenzene" was later shown to be 1,2,4,5-tetraphenylbenzene by Dilthey,[2] who prepared this compound by an unambiguous method.

A tentative mechanism for the formation of 1,2,4,5-tetraphenylbenzene was suggested by Dilthey,[2] which involved first a replacement of four of the six bromine atoms by phenyl groups, followed by a "reduction," yielding 1,4-dimagnesiumbromide-2,3,5,6-tetraphenylbenzene which on hydrolysis would yield the tetraphenylbenzene actually obtained. No experimental evidence was offered to support this proposal other than the observation that metallic magnesium is without action on hexabromobenzene, showing that a simple removal of two bromine atoms, possibly through a free radical intermediate, did not take place.

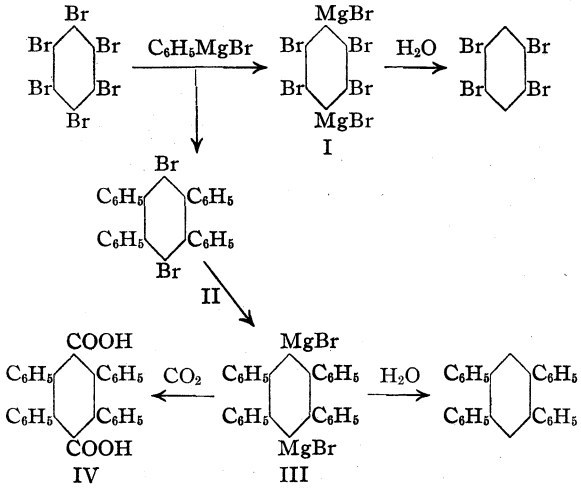
Since other mechanisms for the formation of 1,2,4,5-tetraphenylbenzene are conceivable it was considered of interest to reëxamine the reaction between hexabromobenzene and phenylmagnesium bromide and to isolate (a) intermediates and (b) other products than those mentioned, and to attempt to formulate the reaction upon a factual basis.

The reaction was carried out in ether, as described by Durand, and a few runs were made in benzene. The chief product of the reaction in either solvent was a dark resinous tar from which the products mentioned below were isolated only with difficulty and in small yields. 1,2,4,5-Tetraphenylbenzene and 1,2,4,5-tetrabromobenzene were obtained by hydrolysis of the reaction mixture, while carbonation led to the formation of 1,2,4,5-tetraphenylbenzene-3,6-dicarboxylic acid (IV). Attempts to show the derivation of the tetrabromobenzene from the postulated intermediate (I) failed to yield tetrabromoterephthalic acid. Similar results were obtained when the solutions of the Grignard reagent were filtered before addition of the hexabromobenzene. This observation, coupled with the fact that an ether–benzene solution of the magnesium–magnesium iodide complex was without effect on hexabromobenzene, leads to the conclusion that reaction be-

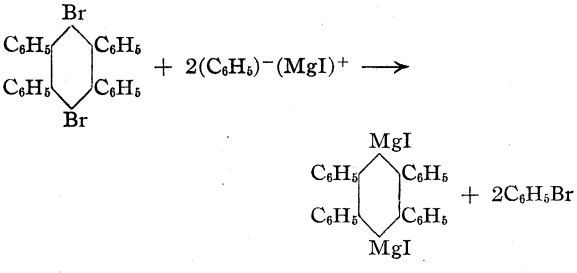
(1) Durand, *Compt. rend.*, **191**, 1460 (1930)
(2) Dilthey, *Ber.*, **67**, 2004 (1934).

tween hexabromobenzene and metallic magnesium or the magnesium–magnesium bromide complex had not occurred.

The results obtained indicate the following course for the reaction



An alternative mechanism in which I is the first intermediate from which III is derived by replacement of the four bromine atoms by phenyl groups cannot explain the formation of hexamethylbenzene when methylmagnesium iodide is used. If this were the mechanism, durene should be formed. In spite of the failure to isolate tetrabromoterephthalic acid by carbonation of the reaction mixture, the above scheme represents the most reasonable picture of the reaction. The reactions leading to I and II are considered to be concurrent and presuppose an amphoteric character in two of the six bromine atoms in hexabromobenzene. The bromine atoms in II, however, as a result of the (−T) effect of the ortho-phenyl groups (in contrast to the effect of ortho-methyl groups) are activated in the same way as the bromine atoms in such compounds as ω-bromoacetomesitylene and diaroylbromomethanes and assume a "positive" character. The reaction of hexabromobenzene with phenylmagnesium iodide then involves, as we now find, the additional step



The formation of large amounts of heavy, resinous material in the reaction can be explained by reactions occurring between the intermediates (I and II) and hexabromobenzene. That the use of a large excess of phenylmagnesium bromide nearly doubled the yield of tetraphenylbenzene substantiates this view since the reaction of II with phenylmagnesium bromide to yield III would be speeded up by a large excess of the Grignard reagent. The reaction of hexabromobenzene with phenyllithium led only to highly polymeric solid substances from which no pure substance could be isolated. This follows on the same basis, the more highly reactive lithium intermediates reacting further to form polymeric substances.

The projected study of the reaction between phenylmagnesium bromide and 1,4-dibromo-2,3,-5,6-tetraalkyl- and arylbenzenes should throw further light on the mechanism of the reaction.

Experimental

Table I presents a number of representative runs. The reactions were carried out by adding the solid hexabromobenzene to the solution of the Grignard reagent and refluxing the solution for eighteen to twenty-four hours. The hexabromobenzene is practically insoluble in ether but dissolves slowly as the reaction proceeds. Carbonation and hydrolysis of the reaction mixtures were carried out in the usual way.

The products of the reaction were worked up by steam distilling to remove diphenyl, followed by crystallization or distillation under reduced pressure.

TABLE I

C_6Br_6, g.	Moles C_6H_5MgBr per mole C_6Br_6	Solvent	$C_6H_2(C_6H_5)_4$, g.	$C_6H_2Br_4$, g.	Acid, g.
30	8.25	Ether	1.80	..	..
10	8.07	Ether	0.50	..	..
10	50.90	Ether	1.03	..	..
10	8.07	Ether	..	..	0.30
10	8.07	Ether	..	0.20	.33
10	8.07	Benzene	..	.40	..
10	8.07	Benzene	..	.50	..
10	8.07	Benzene	..	.90	.30

1,2,4,5-Tetraphenylbenzene.—Distillation of the tarry reaction product under reduced pressure followed by crystallization of the small amount of distillate from acetic acid yielded the hydrocarbon as white needles, m. p. 262–263° (Dilthey[2] reports melting point of 263°).

Anal. Calcd. for $C_{36}H_{22}$: C, 94.24; H, 5.76; mol. wt., 378. Found: C, 94.31; H, 5.62; mol. wt. (Rast), 382.

1,2,4,5-Tetrabromobenzene.—The identity of the product was established by a mixed melting point determination with an authentic sample prepared according to the method of van der Linden.[3]

(3) Van der Linden, *Rec. trav. chim.*, **57**, 781 (1938).

2,3,5,6-Tetraphenylbenzene-1,4-dicarboxylic Acid.—The reaction mixture was carbonated with gaseous carbon dioxide at 0°. After decomposition of the reaction mixture the acidic material was extracted with alkali and precipitated with dilute hydrochloric acid. The resulting solid was boiled with several portions of water to remove benzoic acid and finally crystallized from acetic acid. The acid formed tiny white needles which did not melt up to 320° (bloc Maquenne).

Anal. Calcd. for $C_{32}H_{22}O_4$: C, 81.70; H, 4.70; neut. equiv., 235. Found: C, 81.01; H, 4.71; neut. equiv., 232.

Methyl 2,3,5,6-Tetraphenylbenzene-1,4-dicarboxylate.—The acid was esterified with diazomethane in the usual way. The product crystallized from acetic acid as tiny white prisms, m. p. 280°.

Anal. Calcd. for $C_{34}H_{26}O_4$: C, 81.90; H, 5.40. Found: C, 81.50; H, 5.26.

Phenylmagnesium Iodide and Hexabromobenzene.—To the Grignard reagent prepared from 59.2 g. of iodobenzene and 7.05 g. of magnesium in ether was added 20 g. of hexabromobenzene. After refluxing for twenty-four hours the reaction mixture was hydrolyzed with ice–hydrochloric acid and steam distilled. Extraction of the distillate with ether followed by distillation yielded 3.20 g. of bromobenzene, identified by its boiling point and by the preparation of *p*-nitrobromobenzene, m. p. 127–128°; mixed with an authentic sample, m. p. 126–128°. The residue from the steam distillation yielded 0.90 g. (7.9%) of 1,2,4,5-tetraphenylbenzene, m. p. 260–262°.

Summary

1. The reaction between hexabromobenzene and phenylmagnesium bromide has been reinvestigated, and the intermediate formation of 2,3,5,6-tetraphenylbenzene-1,4-dimagnesium bromide has been established.

2. An explanation of the course of the reaction has been suggested.

URBANA, ILLINOIS RECEIVED MAY 5, 1939

[CONTRIBUTION NO. 160 FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, THE UNIVERSITY OF TEXAS]

Tertiary Alkyl Primary Amines, $RR'R''CNH_2$. I. Ethoxymethyldiallylcarbinamine and Some Analogs[1,2]

BY BRUCE B. ALLEN AND HENRY R. HENZE

There has been in progress in this Laboratory for some years an extensive study of substituted ketones of the alkoxy, aryloxy, and halogenoalkoxy alkyl (and aryl) types. Such ketones have been and are being synthesized from the appropriate substituted nitriles by means of Béhal and Sommelet's[3] modification of the Grignard reaction; with the exception of the tertiary butyl analogs, relatively little difficulty has been experienced in obtaining, for almost every series, both the straight and branched chain alkyl derivatives through the amyls. Since these numerous ketones have been synthesized with the view to their further use in the preparation of compounds having physiological activity, it became desirable to have examples in which the alkoxy alkenyl grouping was represented. Hence, an attempt was made to prepare ethoxymethyl allyl ketone from ethoxyacetonitrile and allylmagnesium bromide.

It was noted with considerable surprise, then, that when equimolecular quantities of allylmagnesium bromide, prepared independently according to Gilman,[4] and ethoxyacetonitrile were brought together, apparently only one-half of the nitrile reacted, and although a constant boiling product was obtained, no ketonic material was formed. Moreover, this product, while possessing physical constants which made impossible its being unreacted nitrile, contained nitrogen, was basic in character, formed solid derivatives with such common amine reagents as picric acid and phenyl isocyanate, but failed to undergo the typical primary amine reaction of isonitrile formation. In a subsequent preparation it was found that by increasing the ratio of Grignard reagent to nitrile from 1:1 to 2:1 no unreacted nitrile was recovered and a correspondingly greater yield of basic product was formed.

Analyses of the purified, basic substance established $C_{10}H_{19}NO$ as its empirical formula. It was possible to conceive of the addition of two molecules of allylmagnesium bromide to one of ethoxyacetonitrile and of subsequent hydrolysis of the addition product to yield a compound of molecular formula $C_{10}H_{19}NO$. Analysis of the picrate of the basic compound obtained verified this formulation.

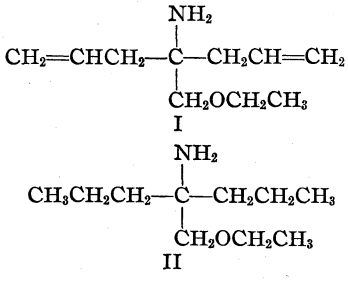
(1) Presented before the Division of Organic Chemistry at the 97th meeting of the American Chemical Society at Baltimore, Maryland, April 3–7, 1939.

(2) From the Ph.D. dissertation of B. B. Allen, June, 1938.

(3) Béhal and Sommelet, *Compt. rend.*, **138**, 89 (1904).

(4) Gilman and McGlumphy, *Bull. soc. chim.*, **43**, 1322 (1928).

Although the structure visualized for the compound (I), one which was substantiated by molecu-

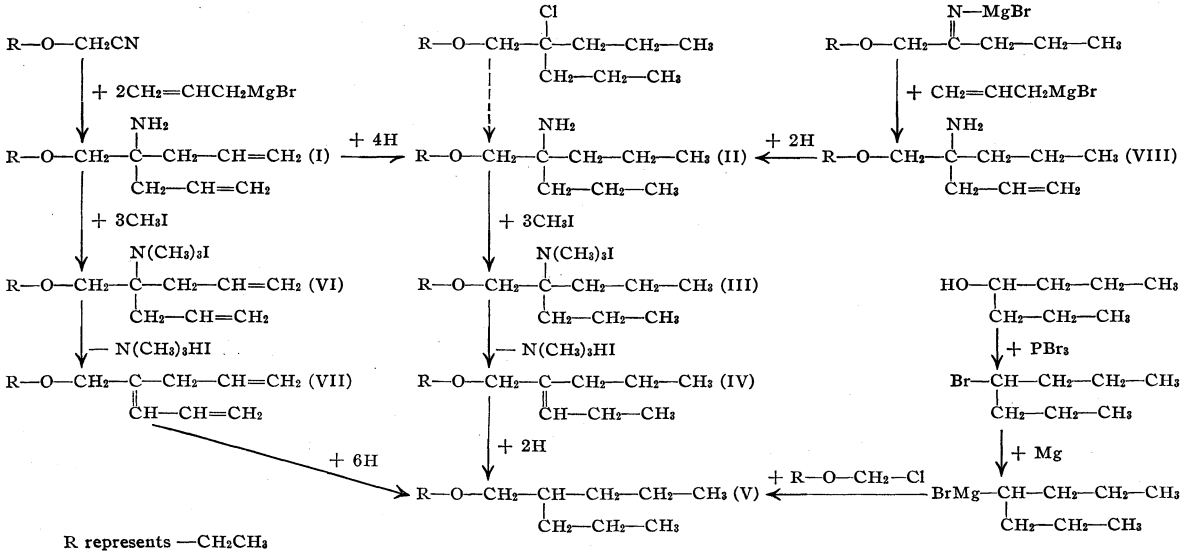


I

II

lar refraction values, required that the substance be a primary amine, actual proof that an amine of this class had been formed was not obtained until the methiodide, prepared from (I) with ease and in good yield, was analyzed. The data from these analyses indicated that one molecular weight of the amine had reacted with three of methyl iodide; only primary amines react in this proportion. Final proof of the structure of the primary amino ether (I) was obtained through degradation and through conversion into a substance of established structure. Synthesis of the amino ether by known procedures was made highly improbable, and unsuccessful attempts to do so are recorded in the experimental portion of this report, since reference to the literature indicated that simpler amines of a type in which the primary amino group is attached to a tertiary aliphatic carbon have been prepared in a very limited number of cases and usually in poor yield. Recently Adkins[5] has reported the attempt to synthesize an amine of this type and made the statement that "methods apparently are not available for the preparation in quantity of the aliphatic amines which bear the same relationship to primary amines that tertiary alcohols bear to primary alcohols."

The amino ether (I) was reduced with hydrogen catalytically to produce $C_{10}H_{23}NO$ (II); the introduction of four hydrogen atoms excluded the possibility of (I) having a ring structure. The methiodide of (II) was heated above its melting point to yield an unsaturated ether (IV) of the formula $C_{10}H_{20}O$, which was reduced to form the corresponding saturated ether (V) formulated as being 4-ethoxymethylheptane.



R represents $-CH_2CH_3$

Synthesis of (V) was visualized in the reaction of the Grignard reagent from 4-bromoheptane with chloromethyl ethyl ether. The physical properties and analytical data for the product resulting from such a reaction indicated it to be 4-ethoxymethylheptane and identical with (V). For the sake of completeness, the methiodide of (I) was decomposed in the formation of the corresponding ether containing three double linkages, and then this compound was hydrogenated to form (V). The physical constants for the three samples of 4-ethoxymethylheptane have been collected in Table I.

Additional proof of the structure of the amine (I) was obtained when equivalent amounts of allylmagnesium bromide and the addition product resulting from interaction of ethoxyacetonitrrle and propylmagnesium bromide reacted to form compound (VIII), an amine of structure intermediate between that of (I) and (II) in that of the

(5) Smith and Adkins, THIS JOURNAL, **60**, 407 (1938).

TABLE I

PHYSICAL CONSTANTS AND ANALYTICAL DATA FOR 4-ETHOXYMETHYLHEPTANE

Prepared from	B. p. °C.	B. p. Mm.	d^{20}_4	$n^{20}D$	γ^{20} dynes/cm.	MR Calcd.	MR Found	Parachor Calcd.	Parachor Found	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
Methiodide of I	170–171	740	0.7884	1.4131	22.95	50.02	50.07	444.2	439.4	75.88	76.19	14.01	14.06
Methiodide of II	170–171	740	.7881	1.4139	22.95	50.02	50.13	444.2	439.6	75.88	75.71	14.01	13.90
$(C_3H_7)_2CHMgBr$ + $C_2H_5OCH_2Cl$	169.5–171	740	.7879	1.4129	22.89	50.02	50.08	444.2	439.4	75.88	75.96	14.01	14.12

TABLE II

CERTAIN PHYSICAL CONSTANTS AND ANALYTICAL DATA FOR AMINES DERIVED FROM ALLYLMAGNESIUM BROMIDE

R	R′	R″	B. p. (corr.) °C.	Mm.	Yield, %	d^{20}_4	$n^{20}D$	γ^{20} dynes/cm.	MR Calcd.	MR Found	Parachor Calcd.	Parachor Found	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
Methyl	Allyl	Allyl	187.5–188.0	753	65.6	0.8829	1.4571	27.41	47.89	47.89	412.8	402.3	69.63	69.51	11.04	11.09	9.02	8.84
Ethyl	Allyl	Allyl	196.0–197.0	755	78.7	.8690	1.4526	28.37	52.51	52.60	451.8	449.5	70.96	70.55	11.32	11.41	8.28	8.26
Ethyl	Allyl	Propyl	197.0–198.0	753	60.7	.8580	1.4420	25.87	52.98	52.82	462.8	450.2	70.12	70.10	12.36	12.20	8.18	7.96
Ethyl	Propyl	Propyl	198	754	98.9	.8381	1.4304	24.85	53.45	53.45	473.8	461.6	69.31	69.24	13.38	13.41	8.08	7.96
i-Propyl	Allyl	Allyl	203.0–204.5	753	66.3	.8611	1.4490	26.70	57.13	57.10	490.8	483.9	72.07	72.04	11.55	11.45	7.64	7.46

groups attached to the tertiary carbon, one was propyl and another allyl. Hydrogenation of (VIII) resulted, as did reduction of (I), in the formation of (II).

Finally, the synthesis of the methoxy and isopropoxy analogs of (I) from allylmagnesium bromide and the appropriate nitriles proves definitely that this reaction is not confined to the formation of only one amine and requires qualification of the statement that there is no method for the preparation of quantities of primary amines in which the amino group is attached to a tertiary aliphatic carbon.

Experimental

Preparation of Alkoxyalkyl-diallylcarbinamines.—In each instance wherein an amine was obtained from a nitrile and allylmagnesium bromide, the Grignard reagent was prepared independently, using essentially those proportions of magnesium, ether, and allyl bromide as suggested by Gilman[4]: to three gram atoms of magnesium turnings, suspended by very rapid stirring in 200 cc. of anhydrous ether, was added the solution of one mole of allyl bromide in approximately 570 cc. of dry ether, the addition being at such a rate that from five to six hours were required. Following the introduction of the last of the bromide, the mixture was stirred for an additional hour while the flask was warmed over a hot-plate. While still slightly warm, the gray-colored ether solution of the Grignard reagent was decanted rapidly from the flask into another of the same size through a 3-inch (8-cm.) Witte plate supported in a large funnel; the funnel, Witte plate, and second flask were at 35–40° so that a fairly rapid evaporation of the solvent would occur during the transfer and thereby tend to minimize contact between moist air and the reagent.

The resulting solution of allylmagnesium bromide was then treated with such an amount of the solution of the appropriate alkoxynitrile[6] as would represent a ratio of two parts of allylmagnesium bromide to one part of nitrile in an equal volume of dry ether; a considerable heat effect was noted during the nitrile addition; hence, the rate of this introduction was moderated until the solvent just refluxed. During the latter half of the reaction period, the addition product generally began to separate as a gummy, grayish-colored solid. Reaction was completed either by allowing the mixture to stand without stirring for from eight to twelve hours or by heating gently over the hot-plate with stirring for from four to six hours.

Hydrolysis of the addition product was accomplished by adding a chilled, saturated aqueous solution of ammonium chloride until all of the solid had dissolved and two clear, liquid layers resulted. These were separated; the lower aqueous layer was extracted twice with ether, and the ether solutions of the amine were combined and

(6) The alkoxynitriles employed in this study were synthesized from the corresponding alpha chloro ethers and cuprous cyanides by following the modification of Gauthier's procedure [Gauthier, *Compt. rend.*, **143**, 831 (1906)] discussed by us previously [Allen with Henze, THIS JOURNAL, **59**, 540 (1937)].

dried over anhydrous sodium sulfate. After the ether had been removed by evaporation under reduced pressure, the amine was purified by distillation, also *in vacuo*. After two such fractionations, the amines could be distilled under atmospheric pressure with no apparent decomposition.

From a typical preparation was obtained 156.6 g. (78.7% yield) of ethoxymethyldiallylcarbinamine when 100 g. (1.18 mole) of ethoxyacetonitrile, 200 g. (8.23 g. atoms) of magnesium, 370 g. (3.06 moles) of allyl bromide, and 2400 cc. of anhydrous ether were combined in the manner described.

The amines, the physical constants, yields, and analytical data for which are summarized in Table II, are colorless oils of not unpleasant, quite characteristic odor which somewhat resembles that of molding wood.

Crystalline picrates could be prepared for all of the amines synthesized by merely dissolving the base in sulfurous acid solution and then adding a saturated aqueous solution of picric acid. The picrates were recrystallized from either water or aqueous alcohol.

Preparation of Ethoxymethylpropylallylcarbinamine.—To the ether solution of propylmagnesium bromide, prepared under the usual anhydrous conditions from 15.6 g. (0.64 atom) of magnesium, 86.3 g. (0.7 mole) of *n*-propyl bromide, and a total of 400 cc. of anhydrous ether, was added 49.5 g. (0.58 mole) of ethoxyacetonitrile dissolved in 100 cc. of ether. After approximately one-third of the nitrile solution had been introduced, separation of a white solid was noted; in order that this solid might not settle to the bottom of the flask and subsequently form the customary gummy mass, the rate of stirring was increased to the maximum possible with the mechanical device employed and kept thus throughout the remainder of the nitrile addition. This vigorous agitation resulted in maintaining the addition product in the form of a finely divided, gray-white, semi-crystalline precipitate.

Approximately thirty minutes after completion of the nitrile–propylmagnesium bromide reaction, the filtered ether solution of allylmagnesium bromide, prepared in the manner previously described from 100 g. (0.83 mole) of allyl bromide, 61 g. (2.5 atoms) of magnesium, and 500 cc. of dry ether, was run into this suspension during thirty minutes. Signs of reaction throughout this addition were feeble refluxing of the ether and, more important, a change in the color and character of the ether-insoluble addition product from the gray-white semi-solid previously described to a heavy, green-brown oil which settled to the bottom of the vessel despite the rapid stirring.

Agitation of the mixture was continued, with the latter at room temperature for one hour after the addition of the allyl compound, and then at such a temperature that the ether refluxed vigorously for two hours; during the last hour of this period the large excess of ether was reduced to a volume which permitted more ease in manipulation. Hydrolysis was accomplished by pouring the ether and viscous material into a mixture of crushed ice and saturated ammonium chloride solution which was stirred rapidly during the reaction.

After separation of the two layers resulting from hydrolysis, the ether solution of the amine was dried over sodium sulfate, the ether removed by the usual evaporation under reduced pressure, and the crude amine purified by two fractionations under the pressure of the water pump. The observed physical constants and analytical data for this compound have been included in Table II.

Preparation of Ethoxymethyldipropylcarbinamine.—This amine was prepared in two separate instances from different starting materials but by the same method, namely, by the catalytic hydrogenation of both ethoxymethyldiallylcarbinamine and ethoxymethylpropylallylcarbinamine. The reduction was accomplished in each case by shaking the solution of 0.1 mole of the unsaturated amine in 40–50 cc. of acetone in the presence of the Adams platinum catalyst and hydrogen under approximately one atmosphere pressure. After hydrogenation was complete, usually in two to six hours, the catalyst was removed by filtration, the solvent by distillation, and the saturated amine purified by fractionation under reduced pressure. The two samples of the amine thus obtained had identical physical constants. These constants, as well as certain analytical data for the amine, have been included in Table II.

Picrates were prepared from both samples of the amine, and the individual melting points and mixed melting point were determined. Both picrates melted at 123.5–124.5° (corr.) and the mixing occasioned no depression of this value.

Exhaustive Methylation of Diallyl- and Dipropylethoxymethylcarbinamines.—Into a 250-cc. Erlenmeyer flask fitted with reflux condenser was introduced in the order named, 0.14 mole of the amine, 75 cc. of 40% aqueous potassium hydroxide solution, and 0.49 mole of methyl iodide. When the flask was rotated gently, vigorous reaction commenced so that cooling with an ice-bath was required to prevent loss of material through the condenser. After reaction had subsided, a change in the density of the organic material was noted; *i. e.*, it constituted the lower layer before, and the upper after, reaction. The mixture was then refluxed gently for one hour, cooled, and transferred to a separatory funnel where it was shaken with 50 cc. of ether to remove any unreacted methyl iodide. The three layers were separated, the uppermost (ether) and the lowest (aqueous) being discarded and the middle layer shaken with an additional 100-cc. portion of ether. After several minutes the viscous quaternary ammonium iodide solidified and could then be filtered from the ether and dried. In both methylations the crude material represented about 94% of that theoretically possible.

The methiodides were recrystallized from anhydrous benzene; after three such treatments the following melting points and analytical data for the solids were obtained:

The product from ethoxymethyldiallylcarbinamine melted at 100.5–101.5° (corr.) and decomposed with effervescence above this temperature. *Anal.* Calcd. for $C_{13}H_{26}INO$: C, 46.02; H, 7.73; N, 4.14. Found: C, 46.32; H, 7.76; N, 4.27.

The product from ethoxymethyldipropylcarbinamine decomposed with effervescence at 132.5–133.5° (corr.). *Anal.* Calcd. for $C_{13}H_{30}INO$: C, 45.48; H, 8.81; N, 4.08. Found: C, 45.55; H, 8.77; N, 3.98.

Pyrolysis of the Quaternary Ammonium Iodides.—When 0.12 mole of either of the two methiodides was

packed into a 50-cc. distilling flask, which was set up as for distillation under diminished pressure, the pressure reduced to that of the water-pump (25–27 mm.), and the flask heated to 150–180° by means of an oil-bath, some effervescence occurred and a colorless liquid began to distill. Heating was continued until no more liquid was produced, at which time 16–21 cc. of crude ether (73–78%) had been collected and a white solid residue remained in the flask. The ethers were purified by distillation under reduced pressure.

In this manner, then, 4-ethoxymethyl-3-heptene was obtained from the methiodide of ethoxymethyldipropylcarbinamine, and 4-ethoxymethyl-1,3,6-heptatriene from that of ethoxymethyldiallylcarbinamine. The following physical constants were determined and analytical results obtained for these two unsaturated ethers:

For 4-ethoxymethyl-3-heptene: yield, 77.8%; b. p. 72.0–73.0° (17 mm.), 173.5–175.0° (corr.) (740 mm.); d^{20}_4 0.8059; $n^{20}D$ 1.4298; *MR* calcd., 49.56; *MR* found, 50.07; γ^{20} 25.08 dynes/cm.; *P* calcd., 433.2; *P* found, 433.9. *Anal.* Calcd. for $C_{10}H_{20}O$: C, 76.86; H, 12.90. Found: C, 77.02; H, 12.91.

For 4-ethoxymethyl-1,3,6-heptatriene: yield, 73.0%; b. p. 71–72° (16–17 mm.); d^{20}_4 0.8484; $n^{20}D$ 1.4701; *MR* calcd., 50.07; *MR* found, 48.62[7]; γ^{20} 25.79 dynes/cm.; *P* calcd., 411.2; *P* found, 404.4. *Anal.* Calcd. for $C_{10}H_{16}O$: C, 78.89; H, 10.59. Found: C, 78.89; H, 10.43.

Preparation of 4-Ethoxymethylheptane.—Three different specimens of this compound were prepared from separate and different starting materials. The physical properties, yields, and analytical data for these three specimens have been referred to previously in Table I.

Two of the three samples were obtained through catalytic hydrogenation of 4-ethoxymethyl-3-heptene and 4-ethoxymethyl-1,3,6-heptatriene using platinum black as a catalyst, acetone as a solvent, and hydrogen under one atmosphere pressure.

The third sample of this ether was obtained as the product of the interaction of chloromethyl ethyl ether and the appropriate heptylmagnesium bromide: to the ether solution of heptylmagnesium bromide, prepared from 8.1 g. (0.33 atom) of magnesium, 67.0 g. (0.38 mole) of 4-bromoheptane,[8] and 260 cc. of anhydrous ether, was added the solution of 31 g. (0.33 mole) of freshly distilled chloromethyl ethyl ether[9] in an equal volume of dry ether.

The pure product from this reaction was obtained after the reaction mixture had been treated with crushed ice and dilute acid (in this case to neutralize the basic salt from any unreacted Grignard reagent) and the ether solution of the product processed in the customary manner.

The analytical data and observed physical properties for this compound likewise appear in Table I.

Attempted Preparation of Ethoxymethyldiallylcarbinamine (4-Amino-4-ethoxymethylheptane).—The methods employed in attempts to synthesize this amine (other than the method described previously) all required the use of the appropriate alkyl halide, namely, 4-chloro-4-ethoxymethylheptane. This halide in turn required the preparation of the tertiary alcohol, 4-hydroxy-4-ethoxymethylheptane. The latter was obtained in 94.6% yield from the interaction of two moles of propylmagnesium bromide and one of *n*-propyl ethoxyacetate[10]; the following constants and analytical data were observed: b. p. 200.0–201.0° (corr.) (752 mm.); d^{20}_4 0.8706; $n^{20}D$ 1.4286; γ^{20} 26.24 dynes/cm.; *MR* calcd., 51.55; *MR* found, 51.57; *P* calcd., 464.2; *P* found, 453.1. *Anal.* Calcd. for $C_{10}H_{22}O_2$: C, 68.91; H, 12.72. Found: C, 69.01; H, 12.67.

This alcohol was converted in 40.7% yield into the desired 4-chloro-4-ethoxymethylheptane merely by shaking it with concentrated hydrochloric acid. The following data were collected concerning this halide: b. p. 94–95° (25 mm.); d^{20}_4 0.9115; $n^{20}D$ 1.4344; γ^{20} 26.33 dynes/cm.; *MR* calcd., 54.89; *MR* found, 55.11; *P* calcd., 481.4; *P* found, 479.0. *Anal.* Calcd. for $C_{10}H_{21}ClO$: Cl, 18.40. Found: Cl, 18.10.

All attempts to convert this chloride into the desired amine were unsuccessful. The methods employed were the Grignard reagent–chloroamine reaction of Coleman, Gabriel's primary amine synthesis, and both liquid ammonia and sodium amide in liquid ammonia treatment. In all instances the chloride was recovered, and no basic material was obtained. The Coleman reaction failed primarily because the halide did not react with magnesium to form the desired Grignard reagent.

Summary

1. An abnormal reaction has been noted between allylmagnesium bromide and ethoxyacetonitrile as a result of which, instead of the anticipated ketone, was produced ethoxymethyldiallylcarbinamine, an amine of unusual type, namely, one in which the primary amino group is attached to a tertiary carbon.

2. The reaction has been shown to be of application more general than to this one isolated case through its utilization in the synthesis of two analogous alkoxyalkyldiallylcarbinamines.

3. Allylmagnesium bromide has been shown to be capable of reaction with a typical Grignard reaction product, namely, that resulting from interaction of *n*-propylmagnesium bromide and ethoxyacetonitrile.

AUSTIN, TEXAS RECEIVED MARCH 30, 1939

(7) The specific exaltation, obtained from the difference between calculated and observed molecular refractivity, is, in this case, 0.96. This value compares favorably with an average value for specific exaltation determined by Auwers and Eisenlohr, *J. prakt. Chem.*, [2] **84**, 1 (1911), as equal to 1.10.

(8) Heptanol-4 was prepared in 53% yield by the action of propylmagnesium bromide upon butyraldehyde: b. p. 71.5–72.5° (25.5–26 mm.); d^{20}_4 0.8183; $n^{20}D$ 1.4205. From this alcohol, a 78.6% yield of 4-bromoheptane was obtained by treatment with phosphorus tribromide: b. p. 64–65° (21–22 mm.); d^{20}_4 1.1373; $n^{20}D$ 1.4498; *MR* calcd., 42.29; *MR* found, 42.31. *Cf.* Sherrill, THIS JOURNAL, **52**, 1982 (1930).

(9) This alpha chloro ether was synthesized after the manner of Henry, *Bull. Acad. Roy. Belg.*, [3] **25**, 439 (1893); and was collected during distillation at 79–80° (748 mm.).

(10) Obtained by passing hydrogen chloride through a solution of ethoxyacetonitrile in *n*-propyl alcohol: yield, 83.4%; b. p. 173.5° (corr.) (748 mm.); d^{20}_4 0.9594; $n^{20}D$ 1.4083; γ^{20} 28.34 dynes/cm.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE PENNSYLVANIA STATE COLLEGE]

Hydrogen Fluoride as a Condensing Agent. VII.[1] The Acylation of Aromatic Compounds

BY J. H. SIMONS, D. I. RANDALL AND S. ARCHER

The acylation of aromatic compounds is usually accomplished by the use of metallic halides such as aluminum chloride with acid anhydrides or acid halides as the reagents. The carboxylic acids themselves are not generally useful as the reagents and acidic condensing agents such as sulfuric acid can be used for these reactions only in special cases.[2] In our first experiments using hydrogen fluoride as the condensing agent for acylation reactions we attempted reactions between acetyl chloride and also benzoyl chloride and benzene at both ice temperature and the boiling point of hydrogen fluoride. In these reactions hydrogen chloride is immediately and copiously evolved and the acid fluoride formed, but no detectable amounts of ketones could be isolated.

As our previous work had shown reactions between alcohols and aromatic compounds with the elimination of water, it was believed that the carboxylic acids would react similarly to hydroxyl containing compounds. It has been shown[3] that the carboxylic acids in liquid hydrogen fluoride are analogous to the alcohols in that they both add hydrogen ions, *i. e.*, act as basic substances, to form conducting solutions. This hypothesis is substantiated as it has been found that acetic acid, benzoic acid, and valeric acid produced ketones when mixed with toluene or phenol and hydrogen fluoride, and when the reaction mixture was sealed in a copper bomb and heated at 80 to 100°.

Under similar conditions and at the same temperature it was found that acetyl chloride and benzoyl chloride would react with benzene or toluene to produce the expected ketones. In order to prevent a high pressure from developing in the bomb, at least the major portion of the hydrogen chloride, produced by the reaction between the chlorides and hydrogen fluoride, was allowed to escape before the bomb was sealed and while it was below the boiling point of hydrogen fluoride.

Acetic anhydride has been shown by Fredenhagen[4] to react with hydrogen fluoride to produce a mixture of acetic acid and acetyl fluoride. It would, therefore, be expected to react in a similar manner to acetic acid or acetyl chloride. In a reaction with toluene *p*-methylacetophenone was formed.

It is observed in the two experiments using acetic acid but with different amounts of hydrogen fluoride that larger amounts of the latter result in higher yields of the product. This is to be expected as water is a reaction product which would reduce the activity of the hydrogen fluoride. As hydrogen fluoride forms additional compounds with oxygen containing organic substances, greater amounts are required than in reactions of olefins, or alkyl halides.

The yields reported are calculated on the basis of the amount of acylating reagent added to the original mixture. No attempts were made to recover any unreacted reagents but these were washed out with the hydrogen fluoride. As relatively small amounts of residues were obtained upon distillation of the reaction products, the amounts of side reactions occurring were small. Yields calculated on the difference between the amounts of reagents added and remaining after stopping the reaction would be much higher than those reported.

Experimental

These reactions were all carried out in copper bombs which were made of three-inch (7.6-cm.) copper tubing with one-eighth-inch (3.2-mm.) copper plates silver soldered onto the ends. In one end a three-eighth-inch (9.5-mm.) copper tube was silver soldered. This was capped with a compression fitting which carried a sealed-off piece of tubing. The bombs were about twelve inches (31 cm.) long.

The hydrogen fluoride was run directly into the bomb containing the reaction mixture from the copper condenser which in turn connected to the storage cylinder. The bomb was then sealed, placed in a steam-bath, and heated. Eighteen to twenty-four hours later it was cooled, placed in ice, opened, and the contents poured into iced water. The acid was neutralized with sodium carbonate and the organic materials removed,

(1) For the previous paper of this series see Simons and Archer, THIS JOURNAL, **61**, 1521 (1939).

(2) For a recent reaction using sulfuric acid see Crawford, *ibid.*, **61**, 608 (1939).

(3) Simons, *Chem. Rev.*, **8**, 213 (1931).

(4) Fredenhagen, *Z. physik. Chem.*, **A164**, 176 (1933).

TABLE I

Acylating reagent	Amount used, g.	Aromatic compound	Amount used, g.	Hydrogen fluoride used, g.	Time, hrs.	Product formed	Yield, %
Acetic acid	40	Toluene	345	200	20	*p*-Methylacetophenone	31.7
Acetic acid	40	Toluene	345	67	17	*p*-Methylacetophenone	4
Acetic acid	40	Phenol	225	104	17	*p*-Hydroxyacetophenone	40
Valeric acid	66	Toluene	345	250	20	*p*-Tolyl *n*-butyl ketone	35.6
Benzoic acid	81.3	Toluene	345	335	20	*p*-Tolyl phenyl ketone	55
Acetic anhydride	33.6	Toluene	345	352	24	*p*-Methylacetophenone	27.3
						2,4-Diacetyltoluene	9
Acetyl chloride	19.6	Benzene	150	150	30	Acetophenone	13
Benzoyl chloride	30.3	Toluene	265	160	17	*p*-Tolyl phenyl ketone	45

TABLE II

Compound	M. p., °C.	B. p., °C.	n^{20}	Derivative
p-Methylacetophenone		104–104.5 at 15 mm.	1.5335	Semicarb., m. p. 205°
p-Tolyl *n*-butyl ketone		144.5 at 15 mm.	1.5287	Semicarb., m. p. 199–201°, mixed m. p. with known sample 199–200°
p-Hydroxyacetophenone	109–110			Semicarb., m. p. 199–200°
p-Tolyl phenyl ketone	53–55			4,4′-Dimethylbenzpinacol, m. p. 170–171.5°[5]
2,4-Diacetyltoluene		110 at 3 mm.		Benzene 1,2,4-tricarboxylic acid, m. p. 320–325°

separated, and purified. In Table I the results of the experiments are recorded and in Table II are the properties of the derivatives made for identification.

Conclusions

The results of these experiments demonstrate the effectiveness of hydrogen fluoride to promote acylation reactions. The ability to use the carboxylic acids for such reactions should be of considerable value. It has not been found necessary to subject the reagents to extensive purification. Commercial grades of all substances including hydrogen fluoride were entirely satisfactory.

(5) Bachman, THIS JOURNAL, **49**, 236 (1927).

Summary

Hydrogen fluoride has been found effective in the synthesis of ketones from aromatic compounds and carboxylic acids, acid anhydrides, and acyl halides. The reactions proceed at 80 to 100° in copper bombs, and the yields are increased with increasing amounts of hydrogen fluoride. Acetic acid, valeric acid, benzoic acid, acetic anhydride, acetyl chloride, and benzoyl chloride were caused to react with benzene, toluene and phenol to form the expected ketones.

STATE COLLEGE, PENNA. RECEIVED MAY 10, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY]

Diphenylmethane as a Thermometric Standard at 25°

BY THOMAS DE VRIES AND HENRY A. STROW[1]

Because a need exists to have a convenient thermometric standard near 25°, it was decided to investigate the melting point of diphenylmethane which has been reported at various times at temperatures ranging from 25 to 27°.[2] The best value seems to be 25.15° which was reported by Smith and Andrews[3] on a sample purified by repeated distillation at reduced pressure. In this investigation we found the value 25.09°.

Experimental.—Two seven-junction copper–constantan thermels were constructed from No. 30 B. and S. gage wire using all the precautions recommended by White.[4] In order to show that the deviations from the thermocouple reference table were nearly linear over the range from 0 to 100°, it was necessary to use a Leeds and Northrup type K potentiometer. Below 10,000 microvolts a White potentiometer was used, namely, for the calibration of the thermels at the transition point of sodium sulfate and for the determination of the melting point of diphenylmethane

(1) Present address: The Udylite Co., Detroit, Mich. This paper is an abstract of a thesis submitted by H. A. Strow in partial fulfilment of the requirements for the degree of Master of Science in Chemistry. (Original manuscript received December 12, 1938.)

(2) Huffman, Parks and Daniels, THIS JOURNAL, **52**, 1547 (1930); Krahl, *ibid.*, **54**, 1256 (1932).

(3) Smith and Andrews, *ibid.*, **53**, 3644 (1931).

(4) White, *ibid.*, **36**, 2292 (1914).

The cold junctions of the thermels were maintained at 0° by a "cold cell" of the type first described by White.[5] The thermels were calibrated at the boiling point of water in an hypsometer with copper double walls. The two thermels gave identical electromotive forces. One value of 161 and four values of 162 were obtained as the deviation in microvolts from the reference table,[6] with the boiling point of the water known to 0.01° from the corrected barometric pressure. The barometric readings are known to be accurate to 0.1 mm. by comparison with a Gaertner cathetometer. For the calibration of the thermels at the transition temperature of sodium sulfate decahydrate, the procedure of Dickinson and Mueller[7] was used. The hydrate was prepared from Mallinckrodt Analytical Reagent grade anhydrous sodium sulfate. It was further purified by six recrystallizations. Conductivity water was used throughout. A sharp transition point was obtained. Eight different measurements were made, five giving 60.5 as the deviation from the reference table, and one value each of 60.4, 60.6 and 60.7, the average being 60.5. The two thermels gave identical electromotive forces.

Purification of Diphenylmethane and Results.—The melting point of the diphenylmethane as obtained from the Eastman Kodak Co., was 24.5°. Several methods of purification were tried. Crystallization was decided upon as most likely to give a pure product. First recrystallization from absolute alcohol was attempted, but the alcohol was too difficult to separate from the diphenylmethane. After several other attempts the following method was found to be satisfactory and requiring little attention. The diphenylmethane was frozen slowly over a period of eight to twelve hours until between 5 to 10 cc. was left unfrozen. This was poured off and discarded. For the initial purification about 300 cc. (300 g.) was used. At the end of twenty such recrystallizations about 150 cc. of pure diphenylmethane was obtained. To obtain a uniform cooling rate an apparatus was constructed which gave uniform results regardless of the room temperature. Tap water in the laboratory has a temperature of about 16° and varies only slightly. A metal container was built of two cans so placed as to form a double-walled container. The inside can was of sufficient size to hold a 400-cc. beaker with a clearance of about half an inch (1.25 cm.) on each side. The bottom was covered with an asbestos pad. Tap water was circulated in the space between the two walls and a cover was placed on top. Diphenylmethane was recrystallized daily until a constant melting point was obtained. Seventeen recrystallizations were sufficient, there was less than a 0.001° change for an additional sixteen recrystallizations. Twelve recrystallizations raised the melting point to 25.082°; 5 more to 25.091°; 2 more raised it to 25.092°, and 14 additional recrystallizations produced no further change.

The melting point was determined with the thermel immersed 8 cm. into the diphenylmethane, about one-third of which was liquid. The mixture was stirred in a glass tube, 33 mm. in diameter and 150 mm. deep. Generally the room temperature was such that the diphenylmethane was melting slowly while the measurements were made. The melting point as calculated from the electromotive force was 25.092°. The values relative to each other are not in error exceeding 0.001°, but since the reference tables are consistent to only 0.01°, we report 25.09 ± 0.01° as the melting point of pure diphenylmethane.

Change of Melting Point.—Early in the work it was observed that a sample of diphenylmethane which had been kept in a clear glass bottle in the presence of diffused sunlight showed a marked lowering of the melting point. As a result of long exposure to light a brown color developed in the diphenylmethane and the melting point dropped to 24.1°. The effect of light on the change in the melting point was determined by measuring the melting point of a sample in a clear glass bottle exposed to diffused sunlight and another sample in a brown bottle kept away from light. Melting points were taken over a period of four weeks. The results are given in Table I.

TABLE I

CHANGE OF MELTING POINT UPON STANDING

Time	Melting points, °C. Brown bottle	Clear bottle
0	25.092	25.092
4 days	25.091	25.078
1 week	25.091	25.065
2 weeks	25.091	25.040
3 weeks	25.091	25.013
4 weeks	25.090	24.982

Four recrystallizations were needed to bring the sample in the brown bottle back to its correct melting point.

A more extended test was made by sealing a sample under its own vapor pressure in a tube containing a thermometer well, so that melting points could be taken without admitting air. This tube was kept in the dark over a period of five months except when melting points were determined. A similar sample was kept in an unsealed tube. The readings given in Fig. 1 were taken on these samples. Seven recrystallizations were necessary to bring each sample back to its original melting point.

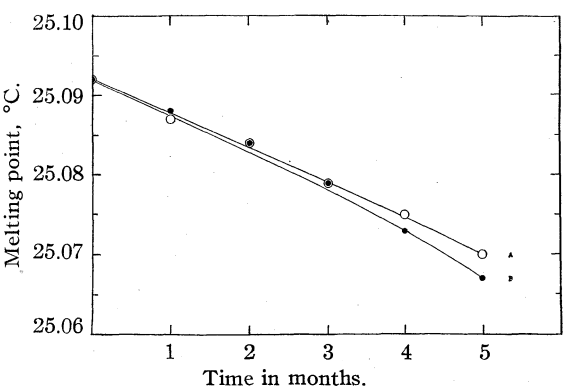


Fig. 1.—Decomposition of diphenylmethane kept in the dark: A, sealed tube, no air present; B, open tube.

Samples of pure diphenylmethane were dried over calcium chloride and over concentrated sulfuric acid in a desiccator without changing the melting point.

Summary

1. The use of diphenylmethane as a thermo-

(5) White, THIS JOURNAL, **56**, 20 (1934).

(6) "International Critical Tables," McGraw-Hill Book Co., Inc., New York, N. Y., 1926, Vol. I, p. 58.

(7) Dickinson and Mueller, *ibid.*, **29**, 1381 (1907).

metric standard in the neighborhood of 25° was investigated.

2. The melting point of purified diphenylmethane was determined to be 25.09 ± 0.01°. Seven junction thermels were used.

3. A spontaneous decomposition occurs, which is accelerated by the presence of light, and which causes lowering of the melting point over a period of time.

WEST LAFAYETTE, INDIANA RECEIVED MAY 15, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF NEW YORK UNIVERSITY]

The Reaction of Zinc with Copper Sulfate in Aqueous Solution

BY F. W. VAN STRATEN[1] AND W. F. EHRET

Although it has long been known[2] that the reaction of zinc with copper sulfate solution is not one of simple displacement, many authors in modern scientific literature still retain the idea that only metallic copper is produced along with zinc sulfate. At the outset of this investigation, sufficient work had been done by others to permit the generalization that in displacement reactions the deposit of the more noble metal is rich in base metal if these metals show a tendency to form compounds when cooled from the melt.[3] That the deposits formed by the action of zinc on copper sulfate were heterogeneous had been noted, particularly by Galecki and Tomaszewski,[4] who studied the variation in their coherence, color, and composition with change in concentration and acidity of the copper ion solution.

In the present work it was hoped that a systematic study of the variation in composition of such deposits with the conditions prevailing during their formation would permit postulating a mechanism for the reactions—particularly since this study involved, in addition to the determination of the over-all chemical composition, an X-ray investigation of the solid phases formed.

Experimental

Materials and Apparatus.—The copper sulfate used was Kahlbaum "pro analyse"; the zinc sulfate, Merck reagent.

The zinc was Baker zinc metal, for standardization. The zinc strips were first washed, rinsed, and then rubbed dry with towels. Next, they were annealed by placing in a glass tube which was evacuated and heated to 200°. The cooling was fairly rapid and vacuum was maintained until the strips reached room temperature. The thickness of each strip was approximately 0.3 mm., which was sufficient to lend rigidity to the metal without introducing end effects by reaction along the sides. In order to prevent reaction on both sides of the strip, one side was covered with spar varnish. Immediately before a run was made, the four strips of zinc necessary to make the run were immersed for thirty seconds in an etching reagent made by mixing 144 ml. of hydrogen peroxide (3%), 24 ml. of concd. ammonium hydroxide, and 144 ml. of distilled water. After rinsing a few times with water, the strips were ready for the run.

A brass stirrer was constructed as shown in Fig. 1a. It was hollow and able to pump liquid from the bottom of the vessel as well as provide efficient turbulent stirring. Cavitation was prevented by insertion of two copper baffles in the solution studied. Both the stirrer and baffles were varnished to prevent reaction with the solution. The latter always had a volume of 1 liter and was contained in a 1-liter beaker immersed in a thermostat. The temperature regulation was to ±0.01° at 25° and to ±0.02° at the higher temperatures. The stirring speed was controlled to ±3 r. p. m.

The zinc strips (four) were attached to a glass cage (Fig. 1b) by cutting them slightly longer than required and folding the extra length, top and bottom, around the horizontal supports of the cage. The effective area of the exposed surface of each zinc strip was 9.6 by 1.25 cm. The long arms of the cage could be inserted in appropriate slots along the bearing of the rotor so that the cage was coaxial with the rotor and could be raised out of the solution being stirred until the latter acquired the proper temperature and until the stirrer was rotating at the required speed. At such time as everything was ready for the run, the cage with the zinc strips could be lowered rapidly into the solution. A stop at the top of one of the long arms of the cage enabled the experimenter, in one operation, to raise, swing, and lower the shaft of the rotor supporting the cage into a beaker of water, permitting the reaction to be stopped almost instantaneously and providing also for the rinsing of the deposit. The strips were placed on the cage with the varnished sides away from the rotor and so that the reacting surfaces were equidistant from the center of the shaft. The duration of all reactions, unless otherwise noted, was one minute at 25°, one-half minute at 50°, and one-fourth minute at 75°.

(1) From a thesis submitted by F. W. van Straten in partial fulfilment of the requirements for the degree of Doctor of Philosophy at New York University.

(2) Wetzlar, *Schweigger's J.*, **60**, 98 (1827); Fischer, "Verhältnis der chemischen Verwandschaft zur galvanischen Elektrizität," Berlin, 1830; Odling, *J. Chem. Soc.*, **9**, 289 (1857); Raoult, *Compt. rend.*, **76**, 156 (1873); Mylius and Fromm, *Ber.*, **27**, 630 (1894); Kutzelnigg, *Z. Elektrochem.*, **38**, 154 (1932).

(3) Tammann, *Nachr. Ges. Wiss. Göttingen*, 332 (1918).

(4) Galecki and Tomaszewski, *Roczniki Chem.*, **10**, 601 (1930).

X-rays were generated by means of a copper target in a Seemann-type tube, using nickel filters. Three Bohlin-type focusing cameras, made according to the specifications of Phragmén and reported by Westgren,[5] were used in connection with the usual powder technique of crystal analysis. The photograms obtained from the deposits were compared with those of known brasses prepared in the manner described elsewhere.[6]

Chemical Analysis.—The chemical analyses of the deposits were made according to a method already outlined.[6] In brief, the method consisted in the removal of the deposit from the zinc strips with a rubber brush, the strips having been rinsed previously with water for one minute, alcohol for ten seconds, and dried for one-half hour. Two samples of about 20–30 mg. were removed and weighed in a goose-neck weighing flask. The deposit was dissolved by the addition of 1.5 ml. of concd. nitric acid and 2 ml. of concd. sulfuric acid. The flasks were then transferred to a crucible furnace, heated to 400°, and kept at that temperature until all traces of sulfuric acid were removed. After cooling, the flasks were again weighed, the contents dissolved in distilled water, and analyzed for copper iodimetrically.

This procedure yields the following information directly: the weight of sample, the weight of combined zinc and copper sulfates, and the weight of copper. The weight of copper sulfate present after evaporation with sulfuric acid is calculated from the weight of copper, and the difference between this value and the weight of mixed sulfates corresponds to the weight of zinc sulfate. From this figure, the weight of zinc may be found.

Every sample of deposit included, in addition to the metals copper and zinc or their alloys, compounds of these with oxygen, hydrogen, and, or, sulfate. The non-metallic portion could not be determined directly by the method of analysis since it was destroyed by the action of the acids used in the solution of the deposits. However, the quantity of these materials could be found indirectly, since the combined weight of copper and zinc was less than that of the deposit by the amount of these radicals originally present. At 25°, this amounted to about 6% of the deposit. At higher temperatures, the value increased to about 9%.

The exact constitution of the compounds of copper and zinc present defied the authors' attempts at complete analysis. This material might consist of one or more or possibly all of the following compounds: cupric and cuprous oxides, zinc oxide, cupric hydroxide, zinc hydroxide, basic salts of copper and zinc, varying degrees of water of hydration, adsorbed water, and adsorbed hydrogen. A serious attempt was made to estimate some of these materials as present in a deposit obtained from a particular run in order to be able to interpret properly subsequent analyses.

The deposit from a representative run containing 6.2% of non-metallic constituents was heated to 230° in a nitrogen atmosphere to determine the amount of adsorbed gas, water and water of hydration (item 2 in Table I). A subsequent heating to the same temperature in a hydrogen atmosphere effected a reduction of the oxides of copper without reducing zinc oxide. The loss in weight due to the removal of oxygen from the oxides of copper is given by item 3. Further, the total amount of $SO_4^=$ was determined using microanalytical technique (item 4). Items 2, 3, and 4 subtracted from item 1 gives the % oxygen combined with zinc. It was also found that the leaching of a fresh sample of deposit with ammonia water under air-free conditions in an apparatus already described[7] resulted in the solution of 3.7% copper and 15.1% zinc. The zinc was present from two sources: the solution of zinc compounds and as a result of the interaction between metallic zinc and copper compounds. In the measure in which the zinc was too high, the percentage of copper found in solution was too low.

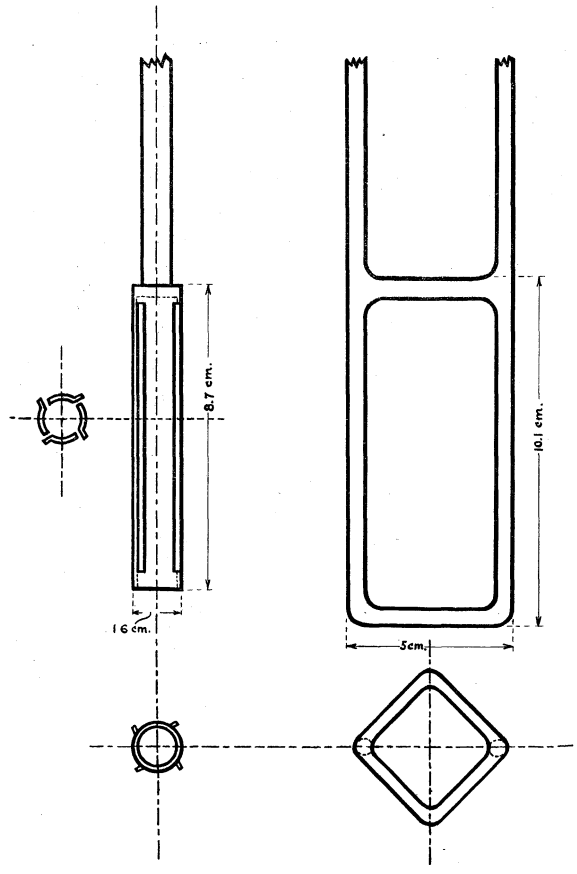


Fig. 1a.—Pump and stirrer.

Fig. 1b.—Glass cage.

These data were coördinated with the previous values in an attempt to ascertain the total composition of the deposits. First, the percentages of copper combining with 2.1% oxygen as cuprous and as cupric oxides were calculated (items 6 and 7). These values for copper lead to the amounts of this metal which were displaced by zinc during the leaching experiments (9 and 10), and also to the amount of zinc so dissolved (11 and 12).

(5) Westgren, *Trans. Inst. Min. Met. Eng.*, Inst. of Metals Div., p. 13 (1931).

(6) Van Straten, Master's Thesis, New York University, 1937.

(7) Van Straten and Ehret, *Mikrochemie*, **26**, 56 (1939).

Items 13 and 14 then show how much zinc had been present as oxide in the original deposit and 15 and 16 the percentage of oxygen combined with the zinc. In this dual set of data, one item represents the assumption that the cupric was the only oxide of copper present and the other that only cuprous oxide was present. Items 15 and 16 must be compared to item 5. Since there is a closer approximation between item 15 and item 5, it is deduced that cuprous oxide is present predominantly. The presence of cuprous oxide may be accounted for by the interaction of copper with cupric ions or by the incomplete reduction of cupric ions by zinc.

TABLE I

1	% non-metallic constituents (100 minus total % Cu minus total % Zn)	6.2
2	% adsorbed gases, water, etc.	1.6
3	% oxygen combined with Cu as cupric or cuprous oxide	2.1
4	% sulfate combined with Zn[a]	1.1
5	% oxygen combined with Zn as zinc oxide	1.4

[a] Sulfate is considered to be combined only with zinc since copper sulfate if present during washing and drying operations would have been given ample opportunity to react with metallic zinc or alloy.

CALCULATIONS

6	% Cu which was combined with oxygen (item 3) if only cuprous and no cupric oxide were present	16.8
7	% Cu which was combined with oxygen (item 3) if cupric oxide were the only oxide of Cu present	8.4
8	% Zn combined with sulfate (item 4)	0.7
9	Item 6 minus 3.7% (leaching data) equals the % Cu which was displaced by Zn	13.1
10	Item 7 minus 3.7% equals the % of Cu which was displaced by Zn	4.7
11	On basis $[Cu(NH_3)_4]^{++} + Zn \longrightarrow Cu + [Zn(NH_3)_4]^{++}$, % Zn equivalent to item 10	4.7
12	On basis $2[Cu(NH_3)_2]^{+} + Zn \longrightarrow 2Cu + [Zn(NH_3)_4]^{++}$, % Zn equivalent to item 9	6.6
13	15.1 (leaching data) minus item 12 minus item 8 equals the % Zn present which was combined with oxygen as zinc oxide	7.7
14	15.1 minus item 11 minus item 8 equals the % Zn present which was combined with oxygen as zinc oxide	9.7
15	% oxygen which was combined with Zn as per item 13	1.9
16	% oxygen which was combined with Zn as per item 14	2.4

These determinations made it possible to offer a complete analysis for a representative sample of deposit formed at 25° (Table II). The authors believe that this is as close an approximation to the true composition as can be made with present methods.

TABLE II

	%
Water and adsorbed gases	1.6
Cuprous oxide	18.9
Zinc oxide	7.0
Zinc sulfate	1.8
Zinc and copper as metal or alloy	70.7
	100.0

Experimental Results.—In Fig. 2 are given the results of the experiments designed to show the variation in the composition of the deposits with change in stirring speed. The X-ray photogram of all the deposits shown by points on the graph, except for those on curve 5, indicated the presence of copper as principal phase and α-solid solution as secondary. The deposits shown on curve 5 consisted of a mixture of α- and β-brasses.

The variations in composition of the deposits with increase in reaction time and increase in the length of time that the deposits, already formed, were in contact with copper sulfate solution are shown in Figs. 3 and 4. In the former, curve 1 represents runs made at 25° and the additional time is given in fractions of a minute beyond the first minute; curve 2 gives results obtained at 50° and the additional time represents fractions of a half-minute beyond the first half-minute. The deposits used for the runs of Fig. 4 were obtained by one-minute immersion of zinc in 0.0484 *M* copper sulfate solution at 25° and 1000 r. p. m.

X-ray analyses of the deposits from the runs shown in Fig. 5 indicated copper as the principal phase with α-brass of variable concentration secondary at 25°. At the higher temperatures and for low concentrations of copper sulfate there were increasing amounts of α as well as some β-brass.

Figure 6 and Table III show the influence of the addition of zinc sulfate to the bulk solution. The results of the X-ray examination here were particularly interesting and will be referred to later. The symbols used under the column headed *phases* have the usual significance, *i. e.*, Cu > α means there was more of the copper phase than of α; $\alpha \gg \beta$ means there was mostly α and very little β, etc.

The change in *p*H during representative runs is given in Table IV and when these figures are compared with those of Table V in which changes in

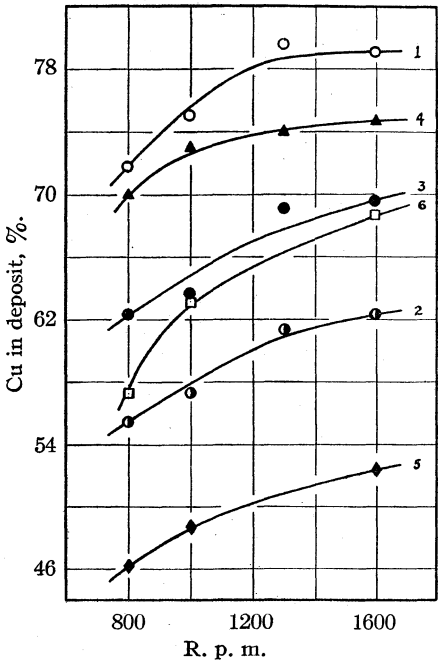


Fig. 2.—Variation in composition of deposit with change in stirring speed in $CuSO_4$: 1, 0.0847 *M*, 25°; 2, 0.0121 *M*, 50°; 3, 0.0484 *M*, 50°; 4, 0.0847 *M*, 50°; 5, 0.0121 *M*, 75°; 6, 0.0484 *M*, 75°.

TABLE III

VARIATION IN COMPOSITION OF DEPOSITS FORMED WITH ADDITION OF VARYING AMOUNTS OF ZINC SULFATE, SOLUTIONS STIRRED AT 1000 R. P. M.

M $CuSO_4$	*M* $ZnSO_4$	Temp., °C.	% Cu in deposit	Phases
0.0242	0.0000	25	65.1	Cu $\gg \alpha$
	.0254		64.1	
	.0381		60.7	
	.0508		60.3	α
.0484	.0000		68.1	Cu $> \alpha$
	.0508		63.5	α
	.0762		62.9	Cu, satd. α
	.1016		61.4	Cu $\gg \alpha$
.0242	.0000	50	61.7	$\alpha > \beta$
	.0254		55.6	$\alpha > \beta$
	.0381		55.2	$\beta > \alpha$
	.0508		52.0	α ($\gg \beta$?)
.0484	.0000		63.7	Cu $> \alpha$
	.0508		59.3	α
	.0762		58.6	$\alpha > \beta$
	.1016		58.3	$\alpha \gg \beta$

composition with deliberate changes in acidity are recorded, it is seen that hydrolytic influences play a negligible part in the displacement experiments here reported.

Discussion

Preliminary to the interpretation of the experimental results it will be well to discuss the chemistry of the reaction and the mechanism which will account for the results obtained.

A displacement of this sort is obviously an electrochemical reaction in which the anodic and

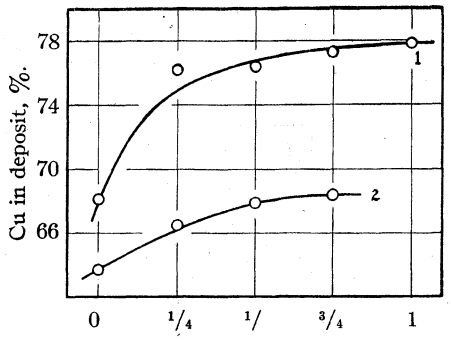


Fig. 3.—Additional time deposit on strip was in contact with $CuSO_4$ solution: 1, 0.0484 *M*, 25°; 2, 0.0242 *M*, 50°.

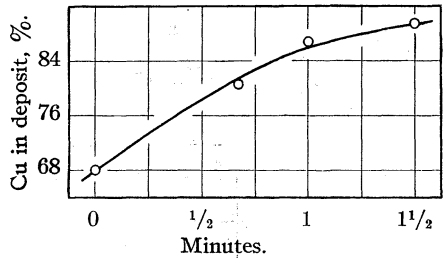


Fig. 4.—Additional time deposit removed from strip was in contact with 0.0484 *M* $CuSO_4$ soln. at room temperature.

TABLE IV

COMPARISON OF THE *p*H OF SOLUTIONS MOST FREQUENTLY USED

Values reported for solutions at 25°. *p*H of same solutions at other temperatures comparable.

M $CuSO_4$	*M* $ZnSO_4$	*p*H before run	*p*H after run
0.0242	....	4.61	4.61
.0484	....	4.42	4.39
.0847	....	4.25	4.27
.0242	0.0508	4.62	4.55
.0484	0.1016	4.40	4.36

TABLE V

VARIATION IN COMPOSITION OF DEPOSIT FORMED WITH CHANGE IN ACIDITY OF SOLUTION

Deposited in 0.0484 *M* $CuSO_4$ at 1000 r. p. m., H_2SO_4 added.

Temp., °C.	*p*H	% Cu in deposit	Phases
25	4.42	68.1	Cu $> \alpha$
	3.86	69.0	Cu $\gg \alpha$
	3.48	72.3	Cu $\gg$ satd. α
	3.35	72.3	Cu $\gg$ satd. α
50	4.00	63.7	Cu $> \alpha$
	3.80	67.6	Cu
	3.59	69.1	Cu $\gg \alpha$
	3.50	68.7	Cu $\gg \alpha$

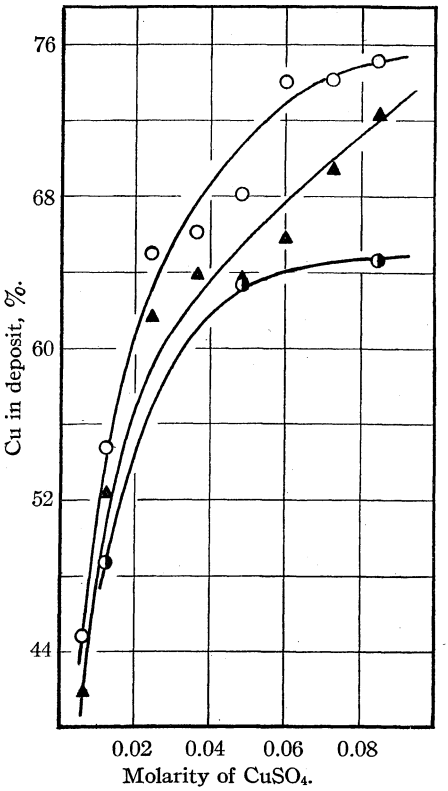


Fig. 5.—Influence of change in concentration of the solution upon the composition of the deposit, at 1000 r. p. m.: ○, 25°; ▲, 50°; ◑, 75°.

cathodic areas are in close contact with each other, forming local elements. The initial reaction is the simple one in which zinc goes into solution and copper plates out at the less active points. According to Erbacher[8] this process is initiated by surface inequalities forming "solubility" local elements whereby one portion of the more active element passes into solution more readily than another, thus resulting in an exchange of surface atoms, less noble for more noble.

This process causes a building up in zinc sulfate concentration due to the solution of metallic zinc. The local elements, Zn/Cu, are bathed, therefore, in a solution of both copper and zinc sulfates. From such a solution brass is deposited rather than pure copper. From this point on, local cells of the type $Zn/ZnSO_4$, $CuSO_4$/brass play an important part in the formation of the deposit. Variation in the composition of the brass makes it possible for one crystal, poor in copper, to act as anode while another, rich in copper, is cathodic. Also both can act as cathode with respect to the

(8) Erbacher, *Z. physik. Chem.*, **A163**, 196 (1933).

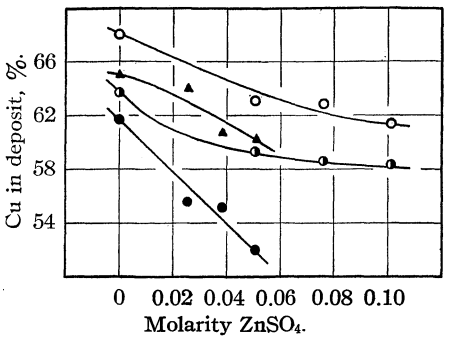


Fig. 6.—Composition of deposits as affected by zinc sulfate addition, in $CuSO_4$ at 1000 r. p. m.: ▲, 0.0242, 25°; ○, 0.0484, 25°; ●, 0.0242, 50°; ◑, 0.0484, 50°.

original zinc. However, as the deposit grows out from the zinc strip, this last reaction becomes less prominent due to the distance between the outermost deposit and the zinc. The main reaction is then the one caused by having brasses of different phase and composition act as cathode and anode. The potential developed by such cells is considerably less than that of the original cell, Zn/Cu, and the proportion of zinc which is plated out on the fringes of the deposit must be reduced greatly since a fairly high potential would be required to deposit zinc-rich alloys. This reduction in zinc is enhanced further by the fact that any zinc and all the copper that plate out, do so at the expense of zinc already laid down in the deposit.

In our work, this effect was somewhat counterbalanced by another. Turbulent stirring and the increased bulk of the loosely adherent deposit caused the ripping off of some of the outer layers. This was only prominent when the run was long or when the reaction was rapid as at the higher temperatures and concentrations of copper sulfate. Since the outer layers were richer in copper than the inner ones and since it was the outer layers which ripped off when droppage occurred, more copper than zinc was lost, and the remaining adherent deposit was thus made relatively zinc rich. Since the deposit lost from the strip was not recovered, the net result was the increase in zinc concentration in the deposit analyzed.

The mechanism postulated above will probably hold for all cases of displacement in which the more noble and the baser metal show a tendency to form compounds or solid solutions. It seems quite capable of explaining the results of Natta[9] who, using the electron diffraction method,

(9) Natta, *Gazz. chim. ital.*, **67**, 10 (1937).

identified the solid solutions formed when palladium, silver or gold was displaced by copper. A similar mechanism with but minor modification was used by Hoar and Price[10] to explain the atmospheric corrosion of base metals.

Although the mechanism given above is capable of explaining the nature of our deposits, it should be noted that the *rates* of displacement were governed by a physical process, diffusion. This was demonstrated both by experiments in which the viscosity of the reacting solution was increased by means of sugar, thus decreasing the diffusion rate and the proportion of copper in the deposit, and by the experiments (Fig. 2) involving the simultaneous increase in stirring speed, diffusion rate, and proportion of copper in the deposit.

The diminishing slope of the curves representing the experiments in Fig. 2 may be accounted for as follows. The higher the stirring speed, the greater was the droppage of deposit, and since, as mentioned earlier, increased droppage corresponds to a decrease in the amount of copper found, the rate of increase in copper due to an increase in stirring speed would be counteracted by the decrease due to droppage.

Statements concerning the effect of droppage on the composition of the deposit are justified by the data shown in Figs. 3 and 4. As the deposit grows out from the zinc strip, beyond a certain point, it becomes progressively richer in copper, due to the decrease in the amount of zinc present in the solution with increasing distance from the zinc strip and also due to the secondary reaction by which zinc is dissolved out of already deposited brass and is replaced by more copper. This process is indicated by the data in Fig. 4, which may be considered a study of secondary reactions. In getting the information for this figure, deposit from a regular run was removed from the zinc strip and then placed in contact with further amounts of solution for varying lengths of time. All the deposit was then analyzed. It was immediately apparent that the rise in copper concentration in the deposit for this material is much greater than that for the deposit formed when the zinc strip with the adherent deposit remains in contact with copper sulfate solution for longer periods of time (Fig. 3). In this latter case, the huge increase noticed in the former is counterbalanced by droppage.

(10) Hoar and Price, *Trans. Faraday Soc.*, **34**, 867 (1938).

Examination of Fig. 5 makes it immediately apparent that although increase in concentration of the copper sulfate increases the concentration of copper in the deposit, the effect is more pronounced when the solution is dilute than when it is concentrated. This phenomenon, the authors believe, can be explained by the fact that in the dilute solutions, little deposit is formed during the specified time of reaction. In this way, even the outermost part of the deposit, at the end of the reaction, is not far removed from the zinc strip, accounting both for the high percentage of zinc in the deposit and the large decrease in this percentage with slight increase in concentration of the copper sulfate. The former is explained by the fact that with such intimate contact between the bulk of the deposit and the zinc strip, this continues to furnish the bulk of the anodic areas for the electrochemical reaction so that there is little solution of the zinc which has already plated out with the copper, and the total zinc concentration in the deposit remains high. The latter effect, the rapid increase with increased concentration, is probably due to the absence of droppage. The outermost layers which are relatively rich in copper are not ripped off so that the full effect of these last layers of copper-rich brass is felt in the analyses. The change in slope as the solution becomes more concentrated, as well as the slight irregularities of the points with respect to the curve, may be explained by the appearance of droppage at these concentrations.

The data of Table III and the corresponding Fig. 6 show the effect produced on the composition of the deposit by the addition of zinc sulfate to the copper sulfate solution. Although the effect is not particularly marked in three of the four cases, it is nevertheless true that increase in the amount of zinc ions in the solution decreases the copper in the deposit. The X-ray data for the lowest of the four curves show that these deposits contain a much greater proportion of β-brass than do the others, which in turn indicates that the conditions in the solution were made progressively more favorable for the deposition of β-brass as the concentration of copper sulfate was lowered and the temperature and zinc sulfate concentration increased. The more rapid descent of the curve in this case is probably due to this preferential β-brass formation. The gradual descent of the other curves may be explained by the nature of the diffusion gradient of the zinc sulfate

solution. In the case of deposition from pure copper sulfate solution, the concentration of zinc sulfate drops from a relatively high value immediately adjacent to the zinc strip to a very low value at the edge of the deposit where this is in contact with the bulk solution. This corresponds to a progressive diminution in zinc ion concentration in contact with the deposit as the deposit is further removed from the zinc strip. When the bulk solution already contains zinc ions, the rate of diminution in zinc ion concentration with distance is not as rapid. However, even fairly large additions of zinc sulfate cause but small alteration in the composition of the deposit, since the over-all increase in zinc ion concentration throughout the deposit is small.

The X-ray part of this investigation was undertaken primarily to prove irrefutably that various kinds of brass are formed by displacement reactions and that change in concentration of the solution from which the deposit is formed may change the phases plated out. However, due to the limitations of the X-ray method of analysis, the data obtained were not very useful in the interpretation of the results. The production of satisfactory X-ray photograms depends to a large extent upon having present a sufficient number of diffracting crystals of dimensions greater than 1×10^{-6} cm. Judging from the line-breadths and general scattering produced, our deposits often contained particles of about this magnitude or smaller. It is not possible to determine the lattice parameters of such crystals and sometimes impossible to detect the phases themselves. The absence of any X-ray indication of the gamma phase (or any other zinc-rich phase) which must be present according to the corresponding chemical analysis, is probably due to this limitation of the X-ray method.

Summary

1. A study was made of the displacement reactions involving the formation of brasses by reaction of zinc with copper sulfate solution at 25, 50, and 75°.

2. The compositions of the deposits obtained by displacement were determined by chemical and X-ray diffraction methods.

3. An increase in concentration of copper sulfate was found to increase the copper content of the deposits, whereas zinc sulfate, added to the copper sulfate solutions, decreased the copper content. These results are in general agreement with work reported by Galecki and Tomaszewski although in their experiments the conditions were less carefully controlled.

4. The amount of copper in the deposit increased with increased stirring of the solution, an indication that the reaction was diffusion controlled.

5. The influence of the changing acidity of the solutions on the nature of the deposits was found to be negligible in the course of the time allotted to a run.

6. An investigation was made of the secondary reactions resulting from prolonged exposure of deposits, in and out of contact with zinc, to copper sulfate solution.

7. An electrochemical mechanism is offered to explain the formation of brasses by displacement.

WASHINGTON SQUARE COLLEGE
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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE OHIO STATE UNIVERSITY]

Photovoltaic Cells: The Spectral Sensitivities of Copper, Silver and Gold Electrodes in Solutions of Electrolytes

BY PAUL E. CLARK AND A. B. GARRETT

The spectral sensitivities of metal and coated-metal electrodes are useful data, in conjunction with other cell characteristics, for the interpretation of the mechanism involved in photovoltaic cells. Spectral sensitivities may also prove to be valuable for the determination of the potential barrier at a metal–solution interface.[1] Moreover, information concerning the effect of light of different wave lengths upon metals commonly used for various types of electromotive force measurements should be made available. This paper reports the determination of spectral sensitivity values of copper, silver, and gold electrodes from λ = 3650 to 6908 Å. These three metals were chosen for this work chiefly because (1) copper and silver are known to have definite photovoltaic action,[2,3] so much so that silver electrodes must be protected from light when used in the potentiometric titration of halides and (2) copper, silver and gold are closely related due to their similar electron configuration.

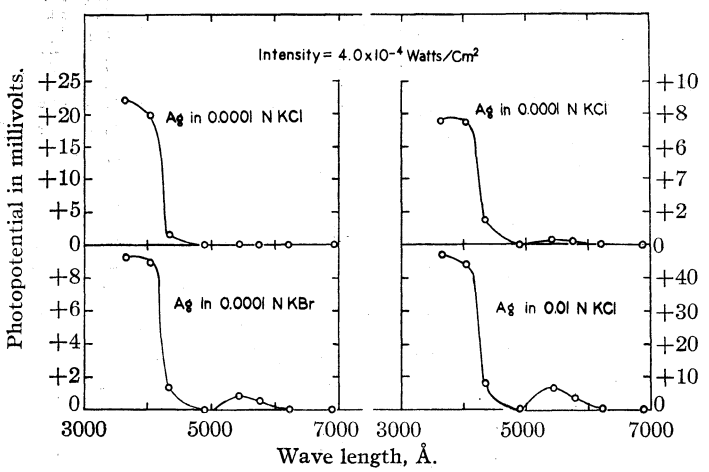


Fig. 1.

Some previous work on observations of photovoltaic cells composed of metal electrodes in solutions of electrolytes has been reported by several workers,[4–7] but no systematic study of the spectral sensitivities is reported for this type of cell. However, Athanasiu[8] has determined the spectral sensitivity of coated metal electrodes of Ag–AgI and Hg–Hg_2I_2 electrodes. Other reported work on spectral sensitivities of coated electrodes is less quantitative and not complete enough for the purpose outlined above.

Experimental

The Solutions.—All solutions used were prepared volumetrically from reagent quality chemicals. Conductivity water was used in all of these preparations.

The Cells.—The cell used was H-type with a chemical Pyrex[9] window through which one electrode could be illuminated and which transmitted radiation from λ = 3300 to 25,000 Å. The electrodes were stamped from sheet metal giving uniform disks approximately 8 mm. in diameter. These were fused to wire of the same metal, polished with 4/0 polishing cloth, annealed in an atmosphere of hydrogen and again cleaned and polished.

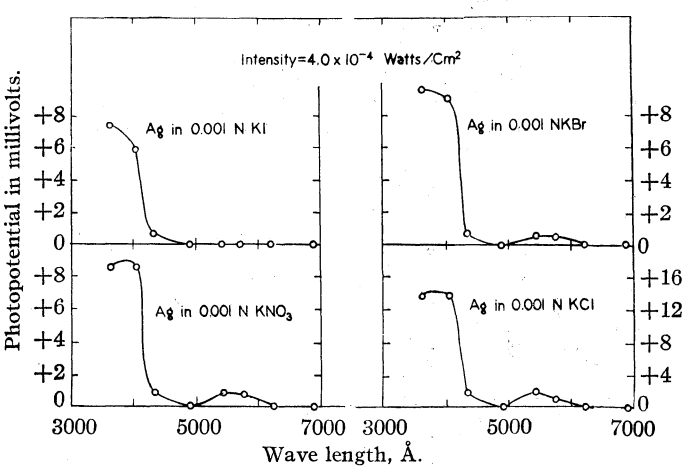


Fig. 2.

(1) Gurney, "Ions in Solution," The University Press, Cambridge, England, 1936.

(2) Copeland, "The Photovoltaic Effect," M.S. Thesis, The Ohio State University, 1936. This gives a complete bibliography of the literature concerning Photovoltaic Cells.

(3) Hughes and DuBridge, "Photoelectric Phenomena," McGraw-Hill Book Company, Inc., New York City, N. Y., 1932, Chapter IX.

(4) Athanasiu, *Compt. rend.*, **178**, 386 (1924); **178**, 561 (1924).

(5) Sihvonen, *Ann. Acad. Sci. Fennicae*, **26A**, 3 (1926).

(6) Schlivitch, *Compt. rend.*, **182**, 891 (1926).

(7) Audubert, *ibid.*, **177**, 818 (1923); *ibid.*, **177**, 1110 (1923); **194**, 82 (1932); **189**, 800 (1929); **189**, 1295 (1929); *J. chim. phys.*, **24**, 357 (1927); *J. phys.*, **6**, 313 (1925).

(8) Athanasiu, *Compt. rend.*, **181**, 101 (1925); *Ann. phys.*, [11] **4**, 377 (1935).

(9) The Corning Glass Works, Corning, New York.

Each wire lead was then drawn through a small glass cylinder filled with paraffin, one side of the disk was coated with paraffin and the other side again polished. These were

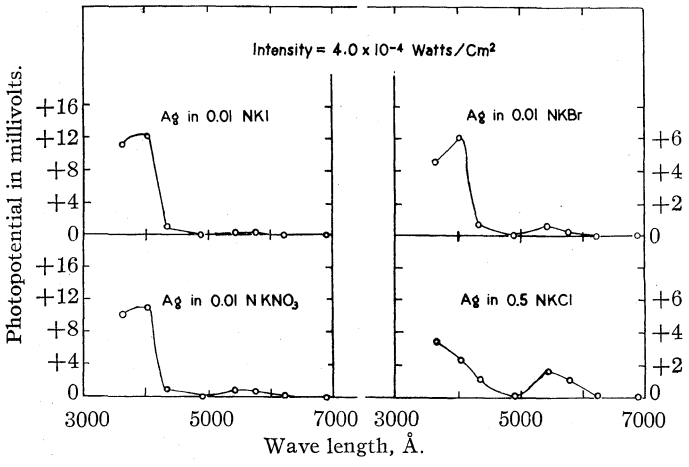


Fig. 3.

washed carefully in conductivity water and placed in the solution in which they were to be used. The silver electrodes were made of Eimer and Amend[10] 999 fine silver, the gold electrodes of Eimer and Amend 24 carat gold and the copper electrodes of pure annealed sheet copper. The copper oxide coating was obtained by heating the copper electrodes in an atmosphere of oxygen. The silver bromide electrodes were obtained by electrolyzing silver electrodes in a solution of silver bromide. The bimetallic electrodes were prepared by electroplating processes recommended by Blum and Hogaboom.[11]

The Thermostat.—The thermostat was a water-bath insulated by means of four concentric tanks of mirror tin, which were separated by wood, air and glass wool, respectively. A top for the bath was of similar construction. This insulation reduced heat transfer to a minimum and eliminated the necessity of an electrical thermostat control which might have been a source of parasitic currents to be picked up by the Pliotron circuit. This type of thermostat gave very steady temperature control; any temperature change in this thermostat was of a unidirectional nature rather than of a fluctuating nature. Such a characteristic is valuable in determining accurately the dark potential drift of the cells studied if any of the potential drift is due to a thermal effect. A chemical Pyrex glass[9] window was mounted in one side of the thermostat. A camera shutter and a glass filter holder were mounted opposite the glass window on the outside of the thermostat. The cell was placed in line with the glass window, in the thermostat, on a mounting on which could also be mounted a thermopile in the place of the cell. The wire leads to the cell were carried through the thermostat wall in glass cylinders filled with sulfur.

The Illumination Source.—A 100-watt mercury vapor lamp, type H-4, manufactured by the General Electric Company, was used as the source of illumination. The characteristics of this lamp are given in Table I.

Monochromatic radiation was obtained by means of a series of glass filters manufactured by the Corning Glass Company.

The Intensity Measurements.—A Moll Microthermopile was used for the measurement of the intensity of the radiation for each filter at various positions of the mercury lamp. This thermopile was calibrated by means of a standard carbon filament lamp which was standardized by the National Bureau of Standards. The calibration was extended to higher intensities than those obtained from the standard lamp at the distance specified by the National Bureau of Standards. This was done with the use of a second standard lamp working at a higher current and by the methods suggested by Leighton and Leighton,[12] as well as by Forbes.[13] A linear relationship of (galvanometer deflection/intensity) for the galvanometer–thermopile system was obtained up to 30 cm. deflection; this

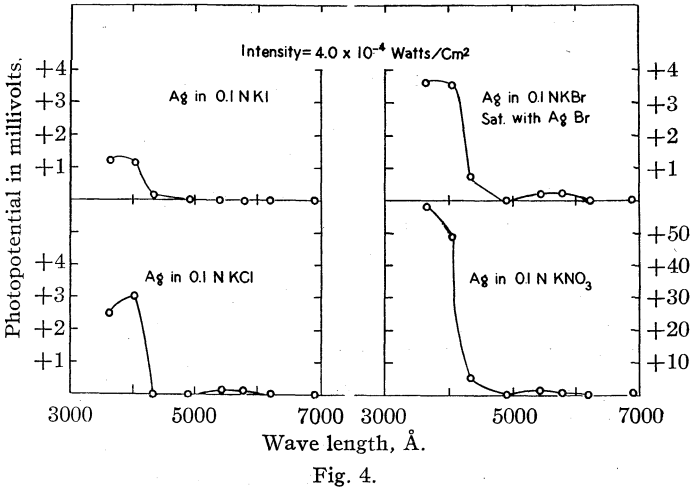


Fig. 4.

TABLE I

SPECTRAL DISTRIBUTION DATA FOR ILLUMINATION SOURCE

As given by the General Electric Vapor Lamp Co.

Wave length, Å.	Spectral intensities (microwatts per cm.² at one meter distance from lamp axis) developed by 100-watt, Type H-4 lamp
14,000–40,000	285
7,000–14,000	39
6,500– 7,000	5
5,500– 6,500	23
4,650– 5,500	37
3,900– 4,650	36
3,000– 3,900	35

(10) Eimer and Amend, Third Avenue, New York, N. Y.

(11) Blum and Hogaboom, "Principles of Electroplating and Electroforming," 2d ed., McGraw-Hill Book Co., Inc., New York, N. Y., 1930, p. 362 for gold on silver or platinum, p. 219 for copper on silver.

(12) Leighton and Leighton, *J. Phys. Chem.*, **36**, 1882 (1932).

(13) Forbes, *ibid.*, **32**, 490 (1928).

TABLE II

PHOTOPOTENTIALS IN MILLIVOLTS FOR IRRADIATION AT STANDARD INTENSITY OF 4×10^{-4} WATTS/SQ. CM.

Electrode	Solution N	Cpd.	3650 Å.	4047 Å.	4358 Å.	4916 Å.	5461 Å.	5780 Å.	6234 Å.	6908 Å.
Ag	0.0001	KCl	+22.0	+19.7	+1.5	0.0	0.0	0.0	0.0	0.0
Ag	.001	KCl	+13.5	+13.7	+1.8	.0	+1.8	+1.0	+ .1	.0
Ag	.01	KCl	+46.8	+43.6	+7.8	+ .3	+6.7	+3.4	.0	.0
Ag	.1	KCl	+ 2.5	+ 3.0	0.0	.0	+0.1	+0.1	.0	.0
Ag	.5	KCl	+ 3.4[a]	+ 2.3[a]	+1.0	.0	+1.6	+1.0	.0	.0
Ag	.0001	KBr	+ 9.2	+ 8.9	+1.3	.0	+0.8	+0.5	.0	.0
Ag	.001	KBr	+ 9.5	+ 9.0	+0.7	.0	+ .5	+ .5	.0	.0
Ag	.01	KBr	+ 4.5	+ 6.0	+ .7	.0	+ .6	+ .2	.0	+ .1
Ag	.1	KBr	+ 1.0	+ 1.5	+ .4	.0	+ .3	+ .1	.0	.0
Ag	.0001	KI	+ 7.5	+ 7.4	+1.5	.0	+ .3	+ .2	.0	.0
Ag	.001	KI	+ 7.3	+ 5.9	+0.6	.0	.0	+ .1	.0	.0
Ag	.01	KI	+11.0	+12.1	+1.0	.0	+ .2	+ .2	.0	.0
Ag	.1	KI	+ 1.2	+ 1.1	+0.1	.0	.0	.0	.0	.0
Ag	.1	KBr satd. with AgBr	+ 3.6	+ 3.5	+ .7	.0	+ .2	+ .2	.0	.0
Ag	.001	KNO_3	+ 8.5	+ 8.5	+ .8	.0	+ .8	+ .7	.0	.0
Ag	.01	KNO_3	+10.0[a]	+10.7[a]	+ .9[a]	.0	+ .9[a]	+ .6[a]	.0	.0
Ag	.1	KNO_3	+58.0	+48.3	+5.2	.0	+1.3	+ .6	.0	.0
Ag	1.0	KNO_3	− 4.3	− 1.3	−0.7	.0	−0.1	.0	.0	.0
Ag	0.001	$AgNO_3$	− 1.3	− 1.2	.0	.0	.0	.0	.0	.0
Ag	.01	$AgNO_3$	− 1.2	− 1.3	− .2	.0	− .6	.0	.0	.0
Ag	.001 .01	KBr KNO_3	+ 2.0[a]	+ 2.1[a]	+ .7[a]	+ .1	+ .6[a]	+ .5[a]	+ .2	.0
Ag	.001 .1	KBr KNO_3	+ 2.8	+ 2.0	+ .6	.0	+ .3	.0	.0	.0
Ag	.001 .5	KBr KNO_3	+ 2.3[a]	+ 2.0[a]	+ .7[a]	.0	+ .3	+ .2	.0	.0
Ag	.001 .1	KBr CCl_3COOH	+ 4.2	+ 3.9	+ .5	.0	+ .1	.0	.0	.0
Ag coated with AgBr	.001	KBr	+ 5.5	+ 5.2	+3.6	+ .3	+2.8	+1.6	+ .1	+ .4
	.001	KI	+ 1.9	+ 0.7	+0.6	.0	+0.4	+0.2	.0	.0
Au	1.0	KNO_3	− 1.4	− 1.2	− .2	.0	.0	.0	.0	.0
Au on Pt	0.001	KBr	+ 1.1	+ 1.7	.0	.0	+ .1	.0	.0	.0
Au on Ag	.001	KNO_3	+ 3.3	+ 3.8	.0	.0	.0	.0	.0	.0
Au on Ag	.001	KBr	+22.8	+22.8	+3.0	.0	+ .8	+ .4	.0	.0
Au on Ag	.001	KI	+11.4	+10.6	+1.7	.0	+ .7	+ .4	.0	.0
Cu	.001	KBr	+ 3.1	+ 4.9	+1.0	.0	+ .3	.0	.0	.0
Cu on Ag	.001	KNO_3	+ 1.8	+ 1.8	+0.3	.0	.0	.0	.0	.0
Cu on Ag	.001	KBr	+12.6	+10.6	+2.0	.0	.0	.0	.0	.0
Cu on Ag	.001	KI	+ 3.7	+ 5.4	+0.3	.0	+ .1	.0	.0	.0
Cu coated with CuO	.001	KBr	+41.2	+41.4	+24.0	+7.5	+30.0	+20.0	+2.0	+15.0

[a] These showed an initial negative surge.

was extrapolated to 50 cm. deflection. Such an extrapolation is justified for this work since the values at these high intensities were of several filters for which the photoresponses were extremely small or nil. In the main, the working intensity was within the limit of the intensity range of calibration of the thermopile.

The Measurement of the Photopotentials.—In some cases the photopotentials were measured with a Leeds and Northrup type-K potentiometer and galvanometer whose sensitivity was 1×10^{-9} amp./mm. All leads were protected with grounded shields.

In most cases, however, the photopotentials were measured with the aid of an F. P. 54 Pliotron tube in a balanced bridge type of circuit designed by Brown and DuBridge.[14] The galvanometer used in this circuit was the same as the one above. The entire circuit was shielded; in addition, the main circuit was protected from humidity effects. In comparison with the potentiometer system this circuit had the advantage of eliminating effects due to polarization since the grid current was of

(14) Brown and DuBridge, *Rev. Sci. Instruments*, **4**, 532 (1933).

the magnitude of 10^{-15} amp.[15] The Pliotron circuit was calibrated with the aid of a voltage divider and the potentiometer circuit described above.

The Data.—The data are shown in Table II and Figs. 1–9, inclusive. These data are all transposed to the same intensity of the 4047 Å. line.

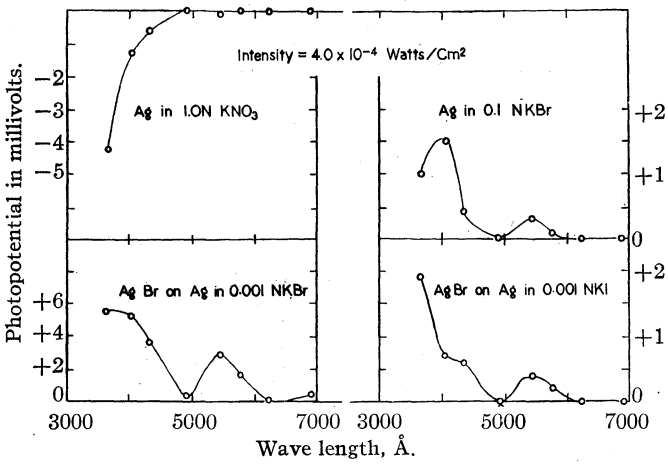


Fig. 5.

This transposition was effected by determining the change in photopotential with the change in intensity for each filter and interpolating or extrapolating the data so obtained.

The accuracy of these data can be determined from the sensitivity of the measuring instruments, the reproducibility of the measurements (relative to each other for a given cell) and the error involved in transposing the data to a standard intensity. The potentiometer circuit had a sensitivity of 1×10^{-5} volt and the vacuum tube circuit 4×10^{-5} volt; the measurements of a cell for each filter were reproducible to $\pm 5\%$ relative to those measurements with other filters of the same cell; the error involved in transposing the data to a standard intensity is not more than 5% of the value of the photopotential of the line chosen as the standard of reference.

The accuracy of the absolute values depends upon their magnitude; thus an expression of the error involved in the absolute values is difficult to formulate. However, since the major merit of the data is their comparative utility, it is safe to conclude that the maximum probable error is not more than $\pm 5\%$ of the value of the photopotential of the 4047 Å. line at the standard intensity of 4.0×10^{-4} watts/sq. cm. and that in most cases it is much lower than this.

The error involved in expressing the threshold value is controlled by the distance between the lines of monochromatic radiation used. Hence it is only possible to suggest that the threshold value lies some place between $\lambda = 4358$ and 4916 Å. and more probably very near $\lambda = 4916$ Å.

In order to detect any possible effect of "activation" by short wave length, a number of cells were studied by consecutive irradiations from the long wave lengths to the short wave lengths then back to the long wave lengths again; these studies showed no "activation."

Drift in the vacuum tube circuit and drift due to slow dark potential changes were determined by a series of potential readings before and after illumination. These drift values, together with the values of the potential on illumination, were plotted as ordinates and times were plotted as abscissas; by this method the value of the photopotential was determined graphically.

The effect of temperature reported by Athanasiu[16] was investigated for a number of the cells.

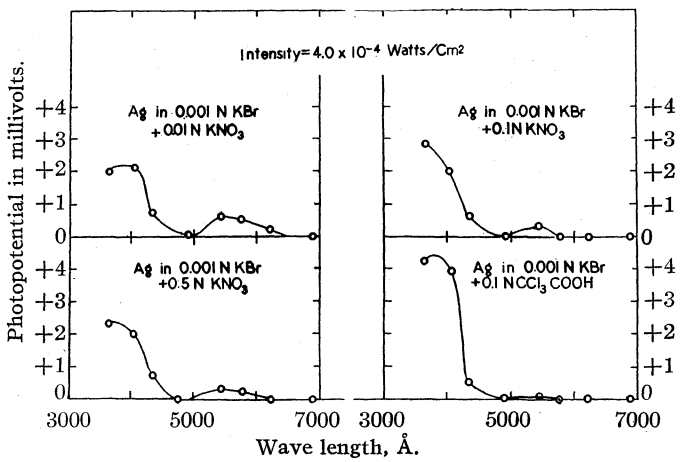


Fig. 6.

Several factors indicate that the potentials developed on illumination were not the direct result of temperature effects. Of those factors can be listed the following: (1) the long wave lengths of light are relatively ineffective in developing photo-

(15) The authors are indebted to Dr. P. M. Harris for suggestions relative to the use of this circuit.

(16) Athanasiu, *Compt. rend.*, **180**, 587 (1925); **181**, 101 (1925

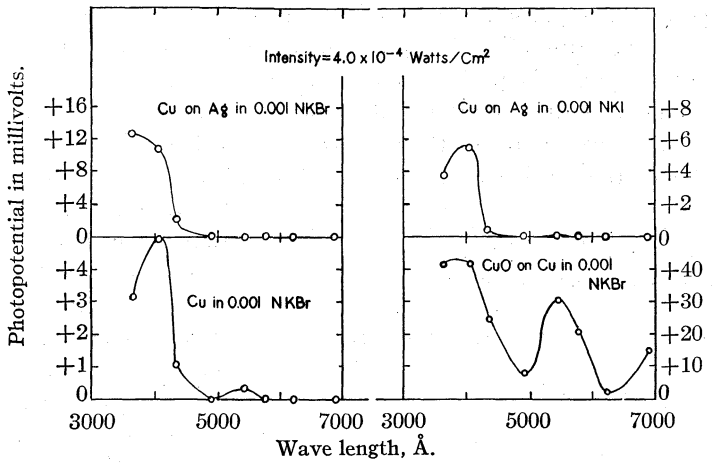


Fig. 9.

strongly to the fact that the above relationship is apparently more than a fortuitous one.

TABLE III

APPROXIMATE[a] PHOTOELECTRIC THRESHOLDS OF SILVER, GOLD AND COPPER

Metal	Metal in solution	Threshold wave length, Å. Metal in a vacuum No outgassing	Partial outgassing	Extended outgassing
Silver	4900	3200–3400	2900–3100	2600–2700
Gold	4900	2625	2600–2800	2650–2610
Copper	4900	2700–3000	2700–3000	

[a] Column 2, this research; columns 3, 4, and 5, compiled from those given by Hughes and DuBridge, ref. 3, p. 75.

Summary

The spectral sensitivities of copper, silver and gold electrodes have been determined for a number of lines of monochromatic radiation ranging from $\lambda = 3650$ to $\lambda = 6908$ Å. The photovoltaic threshold values for these metal electrodes have been determined.

The sensitivity of coated metal electrodes and some metal electrodes at $\lambda = 5461$ Å. is attributed to the coating on the electrode.

A similarity in the mechanism of the photovoltaic and photoelectric effects is suggested from a comparison of the photoelectric threshold values of metals at various stages of outgassing and the photovoltaic threshold value.

A vacuum tube circuit employing an F.P.-54 Pliotron tube is described as suitable for the measurement of photopotentials.

COLUMBUS, OHIO RECEIVED DECEMBER 30, 1938

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF OKLAHOMA AGRICULTURAL AND MECHANICAL COLLEGE]

The Preparation and Identification of Three Alkali Molybdotellurates[1]

BY S. R. WOOD AND ARTHUR CARLSON

The systematic preparation and study of salts of the complex heteropolyacids of molybdenum and tellurium are comparatively recent developments in inorganic chemistry. In 1910 Miolati[2] prepared a compound of apparent formula Te_2O_{11}-K_{10}·$12MoO_3$·$18H_2O$, or possibly TeO_6·K_5H·$6MoO_3$·$8H_2O$. In 1929 Meloche and Woodstock[3] isolated and analyzed two ammonium molybdotellurates, which proved to have the empirical formulas $3(NH_4)_2O$·$2TeO_3$·$6MoO_3$·$10H_2O$ and $3(NH_4)_2O$·TeO_3·$6MoO_3$·$7H_2O$. Since that time Hansen[4] prepared and described a potassium salt, $3K_2O$·TeO_3·$6MoO_3$·$8H_2O$; Thomsen[5] studied a sodium molybdotellurate, $3Na_2O$·TeO_3·$6MoO_3$·$22H_2O$; and Dyess[6] reported the composition of the lithium salt to be $3Li_2O$·TeO_3·$6MoO_3$·$13H_2O$. Specimens of the salts of sodium, lithium, cesium,

(1) This is an abstract of a thesis submitted by S. R. Wood in partial fulfilment of the requirements for the degree of Doctor of Philosophy at the University of Wisconsin in 1933, and of a thesis submitted by Arthur Carlson to the faculty of the Department of Chemistry of Oklahoma A. and M. College in partial fulfilment of the requirements for the degree of Master of Science in 1938.

(2) Miolati, *Z. physik. Chem.*, **70**, 330–334 (1910).

(3) Meloche and Woodstock, THIS JOURNAL, **51**, 171–174 (1929).

(4) H. F. Hansen, unpublished thesis, University of Wisconsin, 1930.

(5) Thomsen, unpublished thesis, University of Wisconsin, 1933.

(6) Dyess, unpublished thesis, Oklahoma A. and M. College, 1934.

potentials; (2) the potential response appears to be inertialess; (3) the temperature effect is negative whereas the photo-response is positive for many of the cells studied. Other unpublished work[17] shows that an important factor for the reversal of the potentials of these cells is the concentration of the electrolyte. This is rather indicative that the photopotential may be the sum of several effects, but the effect due to temperature must certainly be only a minor one.

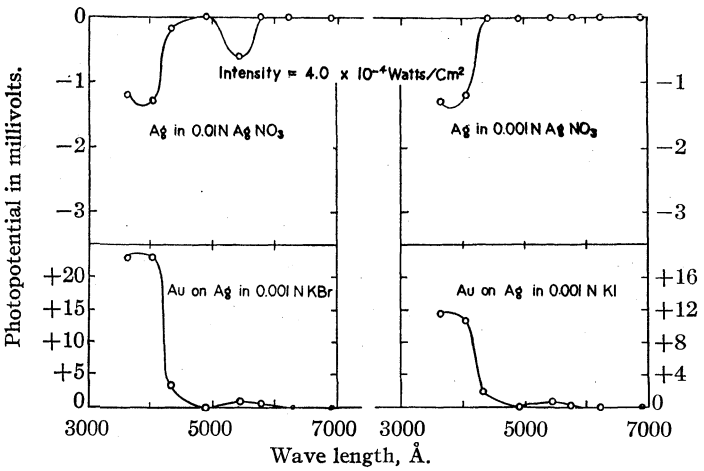


Fig. 7.

The photopotentials cannot be explained in terms of absorption by the solutions, particularly for the halides, since the longest wave lengths absorbed by the potassium halide solutions are given by A. K. Dutta[18] as follows: KCl λ = 2760 Å.; KBr λ = —— Å., and KI λ = 3600 Å. Furthermore he found no appreciable absorption for solutions more dilute than 0.1 normal in case of the chloride and iodide and no appreciable absorption above 2550 Å. for the bromide at any concentration.

The sign of the dark potential had no observable effect on the sign of the photopotential. In general the magnitude of the photopotentials for a given line at a given intensity is characteristic of each cell.

Potential reversals with time[19] were observed for cells marked (*a*). No general statement can be made concerning this phenomenon; the period of the galvanometer limited the observations of this reported negative surge. Further observations should be made concerning the characteristics of this phenomenon.

A number of cells show a hump in the wave length/photopotential graph indicating that the cells are not sensitive to light of λ = 4916 Å. but may be sensitive to λ = 5461 Å. Several cells did not show this effect. It is evident that the hump is much more pronounced in cells having a coated surface such as Cu–CuO, Ag–AgBr, etc. That observation rather suggests that those electrodes showing sensitivity at λ = 5461 probably contained a coating of oxide or halide which was responsible for such an effect.

A comparison of the photovoltaic threshold values with the photoelectric threshold values for the same metals in various stages of outgassing is interesting and is found in Table[20] III. The order of apparent decrease in the value of the work function is in the direction one might expect if the ease of removal of an electron depends upon the material at the interface. Furthermore, this suggests a similarity between the mechanisms involved in both phenomena. Other cell characteristics are necessary before conclusions can be drawn in this regard but thus far it can be said that other unpublished observations point

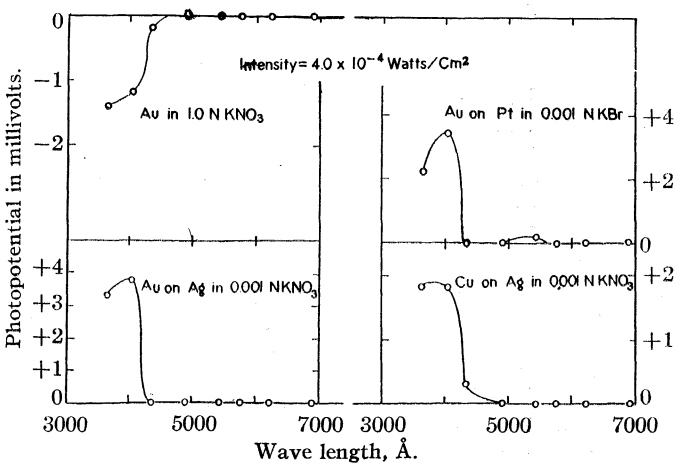


Fig. 8.

(17) This work and much of that on the effect of temperature was done by Mr. Otis Black, for whose help the authors are grateful.

(18) A. K. Dutta, *Trans. Bose Research Inst. Calcutta*, **10**, 209 (1934–35). Additional information on absorption of halide solutions is given by Getman, *J. Phys. Chem.*, **29**, 853 (1925), and by W. R. Brode, THIS JOURNAL, **48**, 1877 (1926). Unfortunately Brode's interesting work is not cited in Dutta's paper.

(19) Vanselow and Sheppard, *J. Phys. Chem.*, **33**, 331 (1929); Sheppard, Vanselow and Hall, *ibid.*, **33**, 1403 (1929).

(20) The threshold values for the metal–gas–vacuum system are taken from those compiled by Hughes and DuBridge, ref. 3, p. 75. The threshold values of the metal–solution system are those of this research.

ammonium (monotellurate) prepared by Wood and the ammonium ditellurate prepared by Meloche were subjected to crystallographic and optical examinations by Donnay and Melon.[7]

Thus most of the alkali metals form corresponding compounds of the type $3M_2O \cdot TeO_3 \cdot 6MoO_3 \cdot nH_2O$. The work here reported was undertaken to learn whether rubidium and cesium yield similar complex salts. By evaporating a solution containing alkali metal hydroxides, telluric acid, and molybdenum trioxide in the proper proportions, we have indeed obtained a rubidium salt, $3Rb_2O \cdot TeO_3 \cdot 6MoO_3 \cdot 6H_2O$ and a cesium salt, $3Cs_2O \cdot TeO_3 \cdot 6MoO_3 \cdot 7H_2O$. We also have duplicated the preparation of the sodium salt already mentioned and verified its composition. All of these salts are beautifully crystalline, but effloresce rapidly when exposed to the open air.

It is worthy of note that all the alkali metal molybdotellurates can be formulated satisfactorily according to the Miolati–Rosenheim theory[8] as $M_6[Te(MoO_4)_6] \cdot nH_2O$. The original salt of this type prepared by Miolati was apparently an acid salt, $K_5H[Te(MoO_4)_6] \cdot 8H_2O$, having the same degree of hydration as the normal salt.

Materials Used: Telluric Acid.—Pure telluric acid was prepared by a modification of the Staudenmeyer[9] method. This procedure depends on the chromic acid oxidation of pure tellurium dioxide in dilute nitric acid solution. Six recrystallizations were carried out to ensure a very pure product. Analyses of the telluric acid for tellurium showed that it was 99.86% pure.

Molybdic Oxide.—Analyzed molybdic anhydride of 99.9% purity was used.

Cesium Nitrate.—Pure cesium nitrate was used.

Rubidium Hydroxide.—The rubidium hydroxide was prepared by treating pure rubidium chloride with the stoichiometrically calculated amount of pure silver oxide. The precipitated silver chloride was filtered off, leaving rubidium hydroxide in solution. This base was recovered by evaporation.

Sodium Hydroxide.—C. P. sodium hydroxide was used.

Preparation.—In the preparation of these salts, the reagents were dissolved in water, in the ratios of 0.06 mole of the respective alkali metal compounds, sodium hydroxide, rubidium hydroxide, or cesium nitrate, to 0.01 mole of pure telluric acid to 0.06 mole of molybdenum trioxide. The clear solution was then evaporated to a small volume on a water-bath. On cooling, colorless crystals appeared. Each of the three compounds was recrystallized from water six times. In order to prepare samples for analysis, the crystals were dried by successive washings with alcohol and ether.

Methods of Analysis: Tellurium.—The tellurium content of the compounds was determined by the Lenher–Homberger[10] method in which elementary tellurium was precipitated by the combined action of water saturated with sulfur dioxide and a solution of hydrazine hydrate upon a dilute acid solution of the sample.

Molybdenum Trioxide.—The filtrate from the tellurium analysis was evaporated to dryness on a hot-plate and fumed with 10 ml. of concentrated sulfuric acid. After the resulting solution had been diluted until the acid concentration was about 6%, the molybdenum was determined by reduction in a Jones reductor and titration with potassium permanganate. The titration was corrected by a blank. Standardization of the permanganate was made upon both sodium oxalate and pure molybdenum trioxide.

Alkali Metals.—Original samples were taken for the determination of rubidium, cesium, and sodium in the respective salts. The sample was placed in a previously weighed porcelain boat, and the boat placed inside a combustion tube. It was then heated to 500° for several hours in a stream of dry hydrogen chloride gas, the temperature being observed by the use of a thermoelectric pyrometer. Tellurium and molybdenum were thus converted to volatile oxychlorides, which sublimed away to the cooler portions of the tube. This left as residue the respective alkali chlorides which were weighed.

Water.—According to the usual practice, the hydrated salt was weighed, then dried at 110° to constant weight.

Thomsen in his analysis found the sodium molybdotellurate to contain 22 moles of water to each mole of salt. His method of determining water lay in heating a 0.5-g. sample in a combustion tube for several hours at 200°, the evolved water being swept into a tared phosphorus pentoxide tube with dried air. One of us determined the water by drying to constant weight, thus verifying the formula previously found by Thomsen.

Properties.—In appearance, all of the salts are composed of crystals of very definite and characteristic qualities. The crystals in the pure state are colorless, hexagonal rhombohedra. The cesium salts tend to crystallize out as somewhat larger crystals. When the sodium salt was allowed to crystallize slowly, crystals of enormous size were obtained, some being 2–3 cm. in length. All three of the salts are of a highly efflorescent character. When newly crystallized, they are transparent to translucent and possess a decided luster. When removed from the mother liquor and left exposed to the air, the surface turns white and opaque in a few hours time, and in a few days they crumble away to an opaque white powder.

Anal. Calcd. for $3Cs_2O \cdot TeO_3 \cdot 6MoO_3 \cdot 7H_2O$: Cs_2O, 42.02; TeO_3, 8.73; MoO_3, 42.98; H_2O, 6.27. Found: Cs_2O, 42.06; TeO_3, 8.62; MoO_3, 42.92; H_2O, 6.25.

Anal. Calcd. for $3Rb_2O \cdot TeO_3 \cdot 6MoO_3 \cdot 6H_2O$: Rb_2O, 32.82; TeO_3, 10.27; MoO_3, 50.58; H_2O, 6.33. Found: Rb_2O, 32.77; TeO_3, 10.15; MoO_3, 50.53; H_2O, 6.26.

Anal. Calcd. for $3Na_2O \cdot TeO_3 \cdot 6MoO_3 \cdot 22H_2O$: Na_2O, 11.47; TeO_3, 10.82; MoO_3, 53.27; H_2O, 24.44. Found: Na_2O, 11.55; TeO_3, 10.78; MoO_3, 53.16; H_2O, 24.37.

(7) Donnay and Melon, *Am. Mineral.*, **18**, 225–247 (1933); **21**, 125–127, 250–257, 299–311 (1936); *Am. Soc. Geol. Belg. Bull.*, **57**, 39–52 (1933–1934).

(8) Ephraim, "Textbook of Inorganic Chemistry," translated by Thorne, Gurney and Jackson, London, 1934, pp. 435–437.

(9) Staudenmeyer, *Z. anorg. Chem.*, **10**, 189 (1895).

(10) Lenher and Homberger, THIS JOURNAL, **30**, 387 (1908).

Summary

A rubidium molybdotellurate, $3Rb_2O \cdot TeO_3 \cdot 6MoO_3 \cdot 6H_2O$, and a cesium molybdotellurate, $3Cs_2O \cdot TeO_3 \cdot 6MoO_3 \cdot 7H_2O$, have been isolated and analyzed for the first time. The sodium molybdotellurate described by Thomsen has again been prepared and its composition verified. The alkali metal molybdotellurates form a corresponding series with the general formula $3M_2O \cdot TeO_3 \cdot 6MoO_3 \cdot nH_2O$, perhaps to be written as $M_6[Te(MoO_4)_6] \cdot nH_2O$.

STILLWATER, OKLA. RECEIVED MAY 8, 1939

[CONTRIBUTED BY THE RESEARCH DIVISION, BAKELITE CORPORATION]

Molecular and Cybotactic Weight Measurements of Resinous and Crystalline Materials[1]

BY HOWARD L. BENDER

Introduction

In the analytical determination of molecular weight numbers for phenol-formaldehyde resins, for crystalline abietic acid, and for some crystalline materials used as standards, irregularities were noted in the boiling points of their solutions. These changes are considered as a function of the time and of the initial temperature used in making the solutions. The molecular weights calculated from the boiling points of the solutions thus showed wide fluctuations. It is not considered that actual molecular structures are varying to the extent shown by these measured changes.

Irregular variations occur in resin solutions as shown[2] by increasing and decreasing viscosity measurements on the same solution held under constant conditions. Also thixotropic and similar structural changes occur under experimental variations.

These changing viscosity data imply a very puzzling shift in the determined molecular weight where the Staudinger viscosity rule is used to calculate the magnitude of the chemical molecules.

For solutions of resins, these calculated "molecular weights" shift with change of time conditions, even though boiling point temperature measurements were made with the same solvent, same resin sample and same temperature conditions. Thus for such solutions, analytical molecular weight values are an uncertain foundation upon which to build structural molecular formulas.

Stewart[3] has coined an apt term for application to changing liquid particles to meet such a difficulty of stability phenomena in the field of pure liquids. According to this concept, the term "cybotaxis" is applied to describe the state wherein easily changed cybotactic groups of molecules are changing in particle size from dimolecules to a factor of approximately one thousand molecules. By Stewart's theory, when liquid molecules collide they temporarily adhere into groups but move from group to group so rapidly that actual particle detection is very difficult in low viscosity liquids.

It is now suggested that this term cybotaxis gives an apt and convenient term to describe the unstability state manifested by the unstability of supercooled liquid particles. Measurements are here given for this type material suspended in solvent solutions. The term cybotactic weight is thus proposed to replace the molecular weight number calculated from the effect of such resinous particles in solution. The proposed cybotactic analytical weight is thus a determined but transitory average value obtained by the use of ordinary molecular weight constants. Hence choice of terms between molecular weight and cybotactic weight depends upon a factor of constancy over an extended time period. This cybotactic weight value thus is a convenient analytical method for expressing the momentarily average particle size of an easily changed particle which will vary directly with the average disintegration of the mass in the solvent medium used. The values found for resins will vary with the conditions used for the determination so the conditions, including time, should always be carefully stated. The term cybotactic weight thus emphasizes the supercooled liquid state of resins. The high viscosity of undercooled liquids at the temperature of solidi-

(1) Delivered at the Baltimore Meeting of the A. C. S. Paint and Varnish Division, April, 1939.

(2) Alexander, "Colloid Chemistry," Vol. IV, The Chemical Catalog Company, New York, N. Y., 1926, p. 360.

(3) C. W. Stewart, *Trans. Faraday Soc.*, **33**, 238 (1937).

fication implies slow change and one expects to find such supercooled liquid groups to be slow in measured changes when compared to low viscosity liquids. Thus solid cybotactic groups of resins should be, even in solvent suspension, capable of measurement both as to average size and as to comparative change in size with time. This paper deals with measurements of change in comparative sizes rather than with their absolute size values.

A very great variety of data are available to show a type of slow change which such undercooled particles undergo. The data include variations from Staudinger's reported "Molecular Weights" of styrene polymers[4] which are reduced in value by simple passage through an orifice, from consideration of the time change of viscosity[5] in resin solution on standing, to the purposeful reduction of particle size[6] in the cellulose derivative field and in the synthetic resin masses.[7]

Speaking of ordinary pure liquids and crystalline solids, Stewart draws a clear working picture in the statement: "The melting point and likewise the boiling point depend directly and indirectly upon the forces which are responsible for the crystalline and liquid states. . . that these characteristics are carried over from the solid to the liquid up to the boiling point. This makes reasonable also characteristic structural differences in the liquid state." This theory of liquid structure gives a concept for ordinary liquids which clears up many of the past difficulties and conveniently may be carried over into the field of undercooled liquids with modification for an expected equilibrium rate change.

Puzzling data as to shifting molecular weight values have been reported previously. The clearest case so far noted has been the data by McMaster,[8] who has kindly furnished us some data in addition to those published. With a freezing point method for determination of molecular weight of a crystalline material in camphor, he obtained two values depending on rapidity of cooling. The values also varied with different solvents.

Other reports show that various rubbers differ as to the effect of heating on the viscosity. Some increase and others decrease in polymer number.[9] Also *p*H has been reported to affect the polymer number of cellulose derivatives much the same as the well-known effect of *p*H on proteins.[10] The time cycle disintegration and aggregation of cellulose derivatives as measured by solubilities and viscosities have been reported.[11]

The polymerization of acetic acid is said to be affected by heat, by some solvents and by traces of water.[12]

Additional quantitative numerical data applying directly to such a concept of cybotactic, that is, to easily changed oriented groups of molecules for supercooled liquids, are now reported.

Under some conditions, the fluctuation in boiling point of a dilute solution of resin in solvent seems to be due to fluctuations in size (and hence in numbers) of the resin masses present in the solution. Thus, under certain conditions, no means were found for obtaining continued constant boiling points even though all the known mechanical aids to reduce superheating were used. These aids included the vapor pumps, roughened glass surfaces, added particles and the very rapid vibration obtained on a 60-cycle per second shaking machine. These data seem to give emphasis to the "micro-crystalline hypothesis" (that is, the actual existence of oriented small groups of molecules) as distinguished from the "quasi-crystalline hypothesis" which is a mere statistical characterization favored by Prins.[13] These data show that the cybotactic weight of a resin changes with time at any one temperature and changes with temperature on any one time cycle. We have previously reported boiling point determinations of molecular weight on a phenol-formaldehyde Novolak resin and have obtained values of 200 to 300.[14] Other reports in the literature show generally higher values so that one wonders at the variation of data. Lignin[15] has lately been reported as having two sets of molecular weights by use of two different methods. In fact, agreement as to resin molecular weights by two different methods is the exception rather than the rule. This condition has caused us to reexamine the analytical determination of the mo-

(4) Staudinger and Heuer, *Ber.*, **67B**, 1159 (1934).
(5) Bender, Wakefield and Hoffman, *Chem. Rev.*, **15**, 123 (1934).
(6) Malm and Gardner, U. S. Patent 2,080,054; *C. A.*, **31**, 4816 (1937).
(7) Bender, U. S. Patent, 2,136,329 (1938); *C. A.*, **33**, 4812 (1939).
(8) L. McMaster, THIS JOURNAL, **56**, 204 (1934).
(9) Kirchhof, *Kautschuk*, **8**, 137 (1932).
(10) Hess and Ulmann, *Naturwissenschaften*, **20**, 296 (1932).
(11) McBain and Scott, *Ind. Eng. Chem.*, **28**, 470 (1936).
(12) P. Koteswaram, *Z. Physik*, **110**, 118 (1938).
(13) Prins, "Structure and Molecular Forces," The Faraday Society, London, 1936, p. 265.
(14) Baekeland and Bender, *Ind. Eng. Chem.*, **17**, 225 (1925).
(15) Loughborough and Stamm, *J. Phys. Chem.*, **40**, 1113 (1936).

lecular weight number for phenol-formaldehyde resins.

The data indicate that many of the past determined molecular weight numbers for resins are simply arbitrary numbers dependent upon the method of measurement and no present scheme of selection is capable of evaluating the true molecular weight, unless one relies upon the minimum weight as determined by all known methods for indicating the true molecule. The data indicate that present methods are measuring changing particles which vary in size with at least three factors and perhaps more. The factors which always vary the determined numbers are temperature, time and the previous treatment of the sample.

Bernal[16] notes the changing configuration of a liquid as a function of temperature and pressure. To this he adds that changes which require increased energy, such as high viscosity, favor the formation of glasses. "A glass being defined as a supercooled liquid in which the viscosity has become so high that the configuration remains fixed at a state not corresponding to the equilibrium configuration but one determined by the heat treatment and the time elapsed." From the present data, the conclusion is drawn that the undercooled liquid average particle is not constant in size but that such size is a function of present temperature and previous treatment. McBain[17] reports that tested high viscosity solvent solutions of cellulose derivatives are disintegrating to end at low viscosity solutions as a function of time and of solvent power. This seems to make the supposed molecular size and shape of cellulose directly dependent upon a factor of time.

In classifying the various solvents as to their various viscosity effects, those which cause swelling cause higher viscosity.[18]

This known difference of solvent effect makes necessary a choice of solvents in the Staudinger viscosity method for determining weight numbers. No good way is known to bridge the gap between solvent choice and solvent effect except the arbitrary statement that this class of solvent may be used and that one may not be used unless one uses a compensating factor. Such methods of choice simply predetermine the molecular weight numbers to agree with wished-for results. For instance, using the case of styrene polymers in solvents, the reason given by Staudinger for the preferred use of non-polar solvents is that the values obtained from the group of non-polar solvents agree well among themselves yet different values are obtained from the group of polar solvents. We now find that in use of a single solvent those conditions which favor swelling favor high number values for the so-called molecular weights.

(16) J. D. Bernal, *Trans. Faraday Soc.*, **33**, 27 (1937).
(17) McBain, Harvey and Smith, *J. Phys. Chem.*, **30**, 342 (1926).
(18) Staudinger and Huseman, *Ber.*, **68B**, 1618 (1935).

Experimental

In the following data, wherever molecular weight methods give variations of over ±5% we shall call the values obtained cybotactic weights. Yet even cybotactic weights may be closely checked at a desired number by proper control of experimental conditions. The ability to check arbitrary number values is the first requisite to their use for analytical control, but the fact that arbitrary values may be checked under arbitrary conditions does not impart an absolute significance to such obtained values. As shown by Table I, some but not all crystalline materials will give constant values.

TABLE I

STANDARDIZATION DATA. MENZIES–WRIGHT METHOD[19]
Concentration limits 0.5 to 1.0%

Substance	Theory	Found High	Found Low	Found Av.	Remarks Solvent acetone
p-Dihydroxydiphenyldimethylmethane	228	231	229	229	Vibrated 60 cycles per sec. $K = 17.2$
p-Hydroxy diphenylmethane	170	172	168	171	$K = 17.2$ Vibrated
Benzidine	184.1	187	177	184	$K = 17.2$ Vibrated
The above results indicate molecular weights.					
Abietic acid (crystalline)	302	400	359	378	$K = 17.2$ Vibrated
% variation		+32	+19	+25	Above theory
From av.		+5.8	−5.0		Range 10.8% for abietic acid indicates cybotaxis

These abietic acid values are thus uncertain and are called cybotactic weights. They may be varied at will as shown later.

A sample, No. 1, of well-washed phenol-formaldehyde fusible resin was held for one hour under 1 mm. vacuum at 240° to free from low boiling solvents, and this was tested for molecular weight effects under the same conditions. The values obtained as shown in Table II are more variable than those for the crystalline abietic acid.

The problem, then, was to find a reason for and control of these fluctuations. There was a suspicion in these data that the way in which the sample was first mixed with the solvent might in-

(19) Menzies and Wright, THIS JOURNAL, **43**, 2309 (1921).

TABLE II

CYBOTACTIC WEIGHTS. VARIATIONS WITH DIFFERENT OPERATORS

Same conditions specified. Solvent acetone, $K = 17.2$. Sample of purified phenol-formaldehyde fusible resin No. 1.

Operator	Theory 212 Monomer	High	Low	Av.
A		684	597	644
B		925	788	847
C		1195	874	965
D		822	698	732
E		705	587	661
F		718	678	705
	Deviation	+57%	−23%	762 gen. av.

fluence the determined value. This effect is shown by the data of Table III.

TABLE III

EFFECT OF MANNER OF SOLUTION IN ACETONE, DETERMINED AT B. P.

Substance	Theory	Cybotactic weights High	Low	Av.	Remarks, dissolved
Abietic acid	302	400	359	378	Hot
Abietic acid	302	530	410	458	Cold
Benzidene	184	178.1	177.9	178	Hot
Benzidene	184	187.5	184	185	Cold
Sample No. 1	..	822	698	732	Hot
Sample No. 1	..	1276	1241	1253	Cold

These variations seemed significant, so were applied to other resin determinations and results are illustrated by the data in Table IV.

TABLE IV

CYBOTACTIC WEIGHT VARIATIONS

Sample 4 phenol-formaldehyde fusible resin

	Solvent	High	Low	Av.	Remarks
A	Hot acetone	790	674	743	$K = 17.2$
B	Hot ethyl acetate	820	755	766	$K = 27.9$
C	Hot methyl alcohol	840	810	820	$K = 8.8$
D	Cold acetone, detd. b. p.	1190	1080	1135	$K = 17.2$
E	Cold ethyl ether, detn. hot	..	..	1082	$K = 21.6$
F	Hot ethyl ether	..	..	720	

On Curve 1, the effect of the original solution temperature is seen to persist in determinations of weight numbers made by the Menzies–Wright method at the boiling point of acetone. These determinations were all made after boiling for five minutes in acetone.

In attempting to use quinine sulfate as a standard to determine K for ethyl alcohol, we were able to get checking curves using $K = 11.7$, where the cybotactic values start at 470 and fall when read over five-minute time intervals until 370 is reached, when the values again rise steadily until

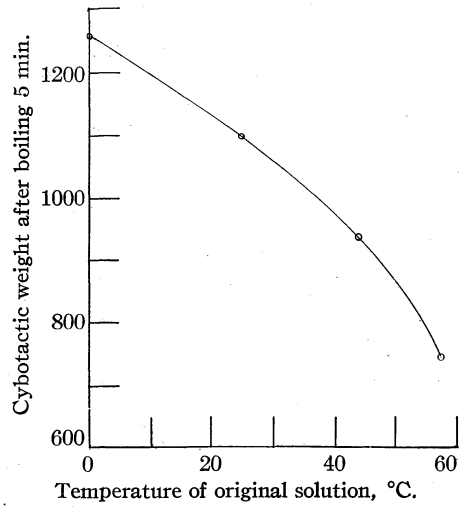


Fig. 1.—Effect of original solution temperature on cybotactic weight determinations by boiling point method. Sample, phenol–formaldehyde fusible resin and solvent acetone; $K = 17.2$.

about four constant readings may be obtained at around 600. The drop and rise cycle is completed in about one hour. Thus even crystalline standards may vary with the time factor of determination.

Curve 2 is a curve of change with time of continued reflux. At first the values drop rapidly, then after a fairly level period begin to rise. At present both the drop and rise in boiling phenomena are considered the result of change in size of the dissolved particles of a supercooled liquid. We have no present reason for attributing the changes to the acetone itself.

This Curve 2 is considered as a composite of three parts. Portion A is a curve of disintegration with time. Portion B is a curve of aggregation or growth with time. Portion C is the numerical resultant of these two factors. The intercept with the weight axis of an extension of B considered as a straight line is about 210 value. This intercept is considered as the more probable molecular weight value from these data. All values above 210 are considered as changing cybotactic weights. On this basis, solution is found as complete after two hundred and fifty minutes of reflux at 56°. In this connection, the data of McBain[17] on the viscosity drop of cellulose nitrate solutions with time of exposure at 55° are of interest.

A Cottrell[20] apparatus was assembled and mo-

(20) Cottrell, THIS JOURNAL, 41, 729 (1919).

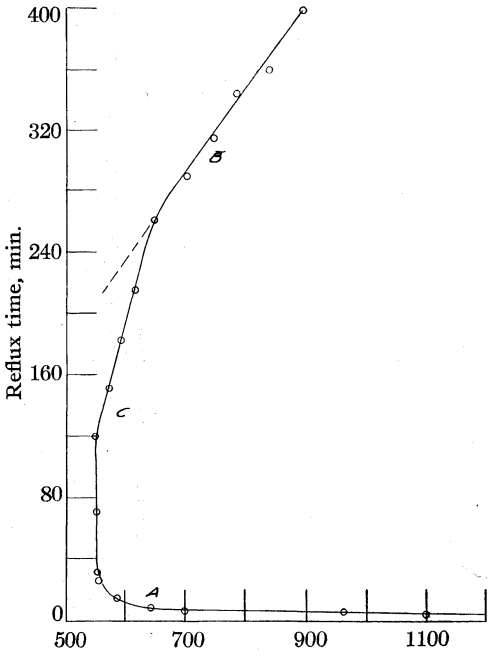


Fig. 2.—Change of weight values with continued reflux time: phenol–formaldehyde fusible resin in acetone, determination made by five-minute boiling periods.

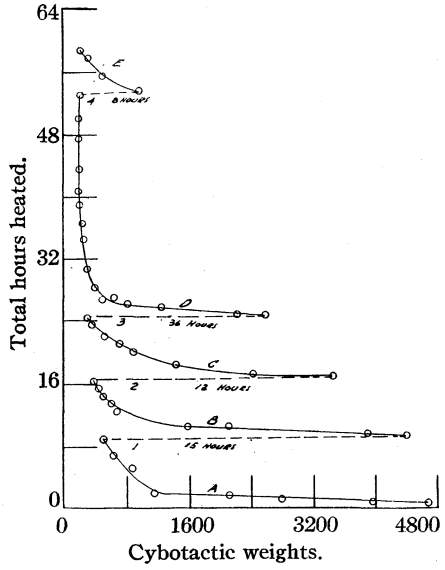


Fig. 3.—Changes in cybotactic weights on heating and on standing cold: Solvent, acetic acid; sample, phenol–formaldehyde fusible resin; K = 30.7. Sections A, B, C, D and E heated at 116° as indicated on scale. Sections 1, 2, 3 and 4 standing cold as marked.

lecular weight determinations made to establish a constant K = 30.7 for acetic acid. The apparatus was then refilled and sample of Novolak resin no. 1 placed therein. It was then closed with drying tubes and all other known precautions to avoid outside influences. Over a hundred readings of the variations of the cybotactic weights under various conditions were taken and are given on the curve. All points off the average curve are indicated.

Curve 3 shows the changes in determined values of one sample in a protected solvent system as a function of both time and temperature with actual reversal in curve direction at some undetermined temperature between the tested points of 25 and 116°. However, the decay rate at the boiling point of acetic acid was sufficiently slow to enable boiling point measurements to be made and rechecked.

Summary

The structural group in resin solutions may be varied so easily that it seems undesirable to designate such shifting particles as chemical molecules. Nor, in fact, should their weight expressions be confused with true chemical molecular weights.

The determined molecular weight numbers of a resin in solvent are shown to be changing quantities with the temporary equilibrium numerical values shifting many fold as conditions change. Any molecular weight number determined for resins is defined as an arbitrary number and considered as a cybotactic particle value, the magnitude of which value is dependent upon the conditions under which the analytical determinations are made. These measurements of what seem to be actual cybotactic particles in the resinous state change slowly in this supercooled liquid condition.

The data obtained are interpreted as in line with the expectations of the cybotactic theory as applied to glassy polymers and are contrary to the expectations of the chain molecular theory of polymeric materials.

BLOOMFIELD, N. J. RECEIVED APRIL 18, 1939

[CONTRIBUTION FROM THE FURMAN CHEMICAL LABORATORY, VANDERBILT UNIVERSITY]

Reactions of Beryllium Chloride. Normal and Basic Organic Salts of Beryllium[1]

BY GEO. B. FEILD[2]

Recent work in this Laboratory has led to an improved method for preparing anhydrous beryllium chloride and a study of the reactions of this compound has been undertaken. In the course of an investigation of the catalytic action of anhydrous beryllium chloride[3] in certain types of Friedel–Crafts reactions it was found that organic acid anhydrides react vigorously with this salt to produce beryllium salts of the acid and the corresponding acyl halide.

Anhydrous beryllium chloride also reacts smoothly with various organic acids to yield hydrogen chloride and the normal beryllium salt. Funk and Römer[4] recently have reported the reaction of formic and acetic acids with anhydrous beryllium chloride.

Although there is a fairly extensive literature on the organic salts of beryllium it cannot be reviewed in detail here, but it may be pointed out that previously the various salts have nearly always been prepared by the action of aqueous acid solutions upon beryllium carbonate or hydroxide.[5–9]

The proposed formulas for these salts usually have been calculated from the beryllium content alone. Some investigators have preferred to regard these substances as mixtures or solid solutions of the products of hydrolysis[10] rather than as definite compounds. On the other hand, there are a number of definite organo-beryllium compounds[11–13] to which rational constitutional and even configurational formulas have been assigned. In terms of the newer ideas of valence these compounds, and probably also the so-called basic beryllium salts, are covalent compounds in which beryllium is quadricovalent.[14] For example, the X-ray examination of basic beryllium acetate, presumably $Be_4O(CH_3CO_2)_6$, suggests a tetrahedral distribution of the valence bonds of beryllium.[15]

In view of the situation it was felt that the above methods for preparing the beryllium salts from beryllium chloride should be especially interesting and valuable. The point of greatest importance, aside from the convenience of the procedure, appeared to be the possibility of working in the complete absence of water. This suggested that it might be possible to obtain exclusively the normal salts, since hydrolysis could presumably be avoided. Subsequent experiments confirmed this expectation.

For the preparation of normal salts from organic acids careful preliminary drying is necessary, since only one-fourth mole equivalent of water is sufficient for the complete hydrolysis of the normal to the basic salt.

$$4Be(RCOO)_2 + H_2O = Be_4O(RCOO)_6 + 2RCOOH$$

In a special experiment 5.0 g. of normal beryllium acetate, prepared in the presence of dry benzene, remained as a stable, insoluble solid during prolonged refluxing. When the calculated amount of water (0.035 g.) was added the normal salt rapidly dissolved and the basic acetate crystallized from the mixture on cooling. For this reason it was found necessary to use an all-glass apparatus in which the initial reaction and subsequent purification of the product could be carried out without contamination from cork or rubber connections or from atmospheric moisture. It was also necessary to avoid excessive heating, inasmuch as in earlier experiments attempts to free the normal salt from excess reagents or solvent by heating *in vacuo*, either with a small flame or on an oil-bath, resulted in partial decomposition. The remainder of the product (75–80%) was always the basic salt. It is probable that the decomposition produced enough water to hydrolyze the remaining normal salt.

(1) Constructed from a thesis submitted by Geo. B. Feild in partial fulfilment of the requirements for the degree of Doctor of Philosophy, Vanderbilt University. Original manuscript received February 10, 1939.

(2) Present address: Mellon Institute, Pittsburgh, Penna.

(3) (a) Lebeau, *Ann. chim. phys.*, [7] **16**, 457 (1899); (b) Grosse and Ipatieff, *J. Org. Chem.*, **1**, 559 (1937).

(4) Funk and Römer, *Z. anorg. allgem. Chem.*, **239**, 288 (1938).

(5) (a) Tanatar and Kurowski, *J. Russ. Phys.-Chem. Soc.*, **39**, 936 (1907); (b) Tanatar, *Ber.*, **43**, 1230 (1910).

(6) Steinmetz, *Z. anorg. Chem.*, **54**, 217 (1907).

(7) Glassmann, *Chem. Ztg.*, **31**, 8 (1907).

(8) Tanatar and Kurowski, *J. Chem. Soc.*, **94**, 166 (1907).

(9) Lacomb, *Compt. rend.*, **134**, 772 (1902).

(10) (a) Parsons, *J. Phys. Chem.*, **11**, 659 (1907); (b) Parsons, "The Chemistry and Literature of Beryllium," Chem. Pub. Co., Easton, Penna., 1908, pp. 17, 40.

(11) Mills and Gotts, *J. Chem. Soc.*, 3121 (1926).

(12) Booth and Pierce, *J. Phys. Chem.*, **37**, 59 (1933).

(13) Parsons, THIS JOURNAL, **26**, 732 (1904).

(14) Sidgwick, "Electronic Theory of Valence," Oxford Press, London, 1932, p. 255.

(15) Bragg and Morgan, *Proc. Roy. Soc.* (London), **A104**, 437 (1923).

Using the indicated precautions it was possible to prepare the normal salts from formic, acetic, propionic, benzoic, and *o*-chlorobenzoic acids as well as from acetic, propionic and benzoic anhydrides. The normal salts were all microcrystalline solids, insoluble in benzene and similar solvents, but soluble with decomposition in water, dilute acids and alkalies, and in most polar solvents. The composition was determined by analysis for beryllium, or in some cases by combustion, and agreed closely with the formula $Be(RCOO)_2$.

The pure normal *n*-butyrate was not obtained from either the acid or the anhydride in spite of rigorous drying or various modifications of the procedure. With the latter reagent *n*-butyryl chloride was formed in high yields, as usual, but the crude salt was always waxy or semi-liquid. Unlike the other salts it formed an emulsion with benzene or ligroin, and could neither be crystallized nor completely freed of solvent. Distillation produced partial decomposition and the liquid distillate was identified as the basic salt by its properties and by analysis.

Most of the basic salts were first obtained as by-products during the earlier attempts to prepare the normal salts. When desired they were later prepared by carrying out the reaction with reagents of ordinary grade or by the deliberate introduction of moisture. All of the basic salts were obtained pure except the formate. Addition of the calculated amount of water to the pure normal formate did not cause the usual smooth conversion to the basic salt. However, the normal formate dissolved readily in excess water and the solution then gave a glass on evaporation. The other basic salts, except the butyrate, crystallized from benzene. They are readily soluble in most organic solvents but insoluble in water or dilute acids or alkalies. The solids melted sharply and could be sublimed without serious decomposition. The analyses agreed closely with the formula $Be_4O(RCOO)_6$.

From these results it is believed that previous attempts to prepare normal beryllium salts usually have failed because of the presence of water and that the new methods afford a convenient and reliable process for obtaining either the normal or basic salts, as desired, at least from simple monobasic acids. The results herein reported have been supplemented by small scale reactions of beryllium chloride with numerous other representative monobasic acids of various types. It was noted that all of the reactions followed the usual pattern and the products formed possessed the general properties of the basic beryllium salts. This reaction is therefore probably quite general.

In the latter connection it should be mentioned that beryllium chloride has been observed to react, usually vigorously, with practically every class of organic compounds in which active hydrogen atoms are present. Hydrogen chloride is evolved and the other product as a rule has the general properties of covalent compounds. With the exception of the reactions with acids this behavior of beryllium chloride is not reported in the literature. Although the "solubility" of beryllium chloride in ethyl alcohol and acetone has been reported, no mention is made of the fact that a chemical reaction occurs,[16,17] and no description of the products of these reactions has been given. Apparently the difficulty of obtaining anhydrous beryllium chloride has been partially responsible for the neglect of this promising field. With this reagent now more available a more detailed study of some of these reactions has been undertaken with the hope that they may yield a variety of organo-beryllium compounds not readily accessible by other methods. It is hoped that results of this work will be reported at a later date.

The author wishes to express his indebtedness to Prof. J. M. Breckenridge for direction and to Prof. A. W. Ingersoll for advice.

Experimental

Preparation of Beryllium Chloride.—Beryllium chloride is perhaps most easily prepared by heating the beryllium oxide in a stream of phosgene,[18] but the handling of this latter reagent involves numerous difficulties and hazards. An improvement of the method of Rose[19] was therefore used. This involves heating beryllium oxide with carbon in a stream of chlorine. Since adequate directions for this method of preparing beryllium chloride could not be found in the literature, the improved method may be described in some detail.

Beryllium oxide was prepared from the nitrate (Pfaltz and Bauer, Inc.) by precipitation of the hydroxide with ammonium hydroxide and ignition. This was then mixed with carbon as follows. Five hundred grams of sucrose and 50 g. of the oxide, previously ground to 200-mesh, were heated with stirring in a large evaporating dish until a viscous sirup was obtained. This was then ignited

(16) Mellor, "Inorganic and Theoretical Chemistry," Longmans, Green and Co., New York, N. Y., Vol. IV, 1930, p. 231.

(17) Parsons, "The Chemistry and Literature of Beryllium," Chemical Publishing Co., Easton, Penna., 1908, p. 20.

(18) Booth and Toorey, *J. Phys. Chem.*, **35**, 2465 (1931).

(19) Rose, *Pogg. Ann.*, **9**, 39 (1827).

and allowed to burn without further application of heat. By this means practically all volatile matter was burned off, leaving a very intimate but porous mixture of the oxide and carbon. This was crushed with care to avoid forming much fine powder.

One-third of the oxide–carbon mixture (about 16.7 g. of BeO) was then poured, without packing, into the 500-cc. Pyrex glass reaction chamber (B) of the apparatus shown in Fig. 1. The lower arm of the reaction chamber was previously closed by a loose plug of glass wool near the bulb. The train was then disconnected at the ground-glass joint (K) and the opening into the 1-liter flask (C) temporarily closed with a stopper to prevent the entrance of moisture. To facilitate connection or disconnection at K without disturbance of other connections, the entire train to the right of K was mounted on rollers. Parts of the apparatus rested upon rubber mats (G) to minimize strains. The electric furnace (J) was then slowly heated and the burners under the preheater (A) were lighted. A slow stream of nitrogen was passed through the reaction chamber and continued until the apparatus and charge were thoroughly dried. Toward the end of this process the burner at K was lighted to expel moisture at that point. The heating was so adjusted that when the apparatus was free from moisture the temperature in the preheater and furnace was about 550° or just below the softening point of Pyrex glass. This temperature was then maintained.

The movable part of the train was connected at K and the passage of chlorine, mixed with about an equal volume of nitrogen, was begun. The nitrogen was necessary to offset the decrease in volume that accompanies the reaction and to assist in removing the beryllium chloride from the reaction zone. The use of additional chlorine for this purpose is wasteful and the exit gas is objectionable from the standpoint of disposal. It also should be explained that preheating the gases permitted running the reaction at about 550°. Without preheating, a furnace temperature of about 650–700° was necessary. Use of the preheater therefore made it possible to construct the entire apparatus from Pyrex glass and thus minimize breakage due to uneven expansion of joints. The preheater was loosely filled with broken plate or Pyrex chips and was shielded by a gauze or iron pipe.

At the indicated temperature the reaction occurred readily and the beryllium chloride passed from the reactor as a smoke. The greater part settled in the exit tube and flask C. The tube was heated intermittently at K and sometimes at C and D to prevent clogging. When the stream of nitrogen was properly adjusted, about 95% of the product collected in C, about 4% in D and the greater portion of the remainder in E. Some smoke passed into the trap but the loss was found to be negligible. A charge of the size indicated could be run in about eighteen hours (two nine-hour periods) without significant loss, or in a much shorter time if some loss were permitted or more collection chambers were used. The product collecting in C could be transferred to F and removed occasionally. For this purpose C was heated gently with a large soft flame while being shielded from drafts. The product collecting in D and beyond was usually allowed to accumulate during several runs. The product was transferred and stored with minimum exposure to air.

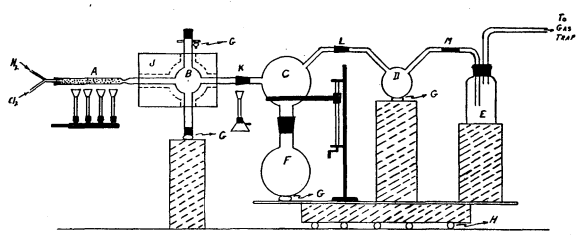


Fig. 1.

The yield of beryllium chloride was 32–37 g. in various runs. Based on the oxide taken, this is 60–70% conversion. The remaining oxide probably escaped conversion because of the removal of all carbon in direct contact with it. The spent charge was removed by withdrawing the glass wool plug from the lower limb of the reaction chamber and was then ignited to recover the oxide. This appeared to contain some non-volatile oxychlorides but was quite suitable for use in preparing another charge. In a series of runs the conversion of the oxide to the chloride was therefore practically quantitative.

In a series of preliminary experiments attempts were made to prepare beryllium chloride from the mixture of iron, aluminum and beryllium oxides obtained from beryl. Although the sublimation points of the corresponding chlorides are reported as 177.8, 315 and 475°, respectively, no appreciable separation could be effected by fractional sublimation. For this reason, commercial beryllium salts as well as the oxide, were unsuitable for the present work.

Preparation of Organic Salts. (a) **Materials.**—The anhydrides were purified by distilling C. P. reagents and collecting the appropriate fraction. Formic acid was prepared by treating the 99% material with phosphorus pentoxide and distillation, with rejection of the forerun. The liquid acids were refluxed with a small amount of the corresponding anhydrides and distilled. The solid acids were recrystallized and dried in a desiccator. Benzene, toluene and ligroin were dried with magnesium perchlorate and distilled.

(b) **Procedure.**—This already has been outlined briefly. In the preparation of normal salts by the use of organic acids, an all-glass apparatus constructed as follows was used. A 250-cc. round-bottomed flask was fitted with a separatory funnel and a side-arm distilling column. A water jacket was fitted into the distilling column, thus enabling refluxing or distillation at will without dismantling. All connections were made by means of ground glass joints. A weighed quantity of the powdered chloride was placed in the flask. The equivalent amount or a slight excess of the acid dissolved in about 5 parts of dry benzene or toluene was then admitted through the separatory funnel. When the initial reaction subsided the mixture was refluxed gently for about one hour, and was then distilled on a water-bath. A little fresh diluent was admitted and the distillation repeated. Analysis of the distillate accounted for approximately the theoretical amount of hydrogen chloride. The residual salt was washed repeatedly with dry benzene and ligroin (b. p. 30–60°), filtered by suction and dried *in vacuo* at room temperature or on a steam-bath. This procedure removed any excess acid and any

TABLE I

Beryllium salt	Class	Form	M. p., °C.	% BeO Found	% BeO Calcd.	Notes
Formate	Normal	Micro-cryst.	d. 150	25.12	25.37	*b, g*
	Basic	Glassy	.....	...	...	*b*
Acetate	Normal	Micro-cryst.	d. 294–296	19.78	19.68	*c*
	Basic	Tetrahedral	283–284	24.54	24.64	*d, g*
Propionate	Normal	Micro-cryst.	d. 75–78	16.73	16.13	*b*
	Basic	Monoclinic prismatic	133–134	20.01	20.18	*e*
Butyrate	Normal	Impure	.....	...	...	*a*
	Basic	Liquid	b. 225, 25 mm.	17.78	17.41	*e*
Benzoate	Normal	Micro-cryst.	d. 307–309	10.34	9.97	*a*
	Basic	Pinacoidal triclinic	317–318	13.04	12.85	*a, f*
o-Chlorobenzoate	Normal	Micro-cryst.	d. 245–249	7.78	7.81	*a*
	Basic	Prisms	255–256	10.05	10.15	*a*

[a] Not mentioned in the literature. [b] Tanatar and Kurowski, ref. 5. Disclaimed by Parsons, ref. 10. [c] Steinmetz, ref. 6. [d] Glassmann, ref. 7, and Steinmetz, ref. 6. [e] Impure product by Lacomb, ref. 9. Pure salt by Morgan and Bragg, ref. 15. [f] Amorphous product by Tanatar and Kurowski, ref. 8. [g] Funk and Römer, ref. 4.

basic salt. The normal salts were stable during brief exposure to moist air, but on prolonged exposure gave the odor of the corresponding acid and changed to the basic salt.

A similar procedure was used with acid anhydrides, except that the volatile acyl chlorides distilled with the benzene or toluene while benzoyl chloride was recovered from the filtered washings. In semi-quantitative experiments the acyl halides were isolated in 60–80% yields by fractional distillation and were identified by their boiling points or by conversion to anilides.

Reactions were also carried out with a large excess of the liquid acids or anhydrides in the absence of benzene but the procedure was less satisfactory because of the difficulty of removing the excess reagent.

Most of the basic salts were first prepared as by-products in preliminary experiments in which anhydrous conditions were not maintained. Alternatively, the procedure for forming the normal salts was followed and then moist benzene was added. The mixture was refluxed until the product dissolved. The hot filtered solution deposited the basic salt on cooling. Basic beryllium acetate could also be crystallized from acetic acid.

(c) **Analyses.**—The salts were dissolved in hot, concentrated nitric acid. For the basic salts it usually was necessary to reflux for a few minutes to complete the decomposition and in this case care was taken that none of the material was lost by volatilization. The solution was then diluted and the beryllium was precipitated as hydroxide with excess ammonium hydroxide and ignited to the oxide. In the case of the benzoates and *o*-chlorobenzoates the partially nitrated acid appeared on dilution but dissolved in an excess of ammonia. Although calculated values of BeO were obtained in this way, these analyses were also confirmed in some cases by combustion, using the method of Fieser.[20] The properties and analyses are recorded in the table.

Summary

1. A convenient procedure for the preparation of anhydrous beryllium chloride is described.

2. A new method is described for the preparation of beryllium salts by means of the reactions of anhydrous beryllium chloride with organic acids or acid anhydrides.

3. Normal beryllium formate, acetate, propionate, benzoate, and *o*-chlorobenzoate and also basic beryllium acetate, propionate, *n*-butyrate, benzoate and *o*-chlorobenzoate were prepared and analyzed.

NASHVILLE, TENNESSEE RECEIVED MAY 19, 1939

(20) Fieser, "Experiments in Organic Chemistry," D. C. Heath & Co., New York, N. Y., 1925, p. 350.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE PENNSYLVANIA STATE COLLEGE]

Hydrogen Fluoride as a Condensing Agent. VIII.[1] The Alkylation of Benzene by Esters

BY J. H. SIMONS, S. ARCHER AND D. I. RANDALL

The alkylation of aromatic compounds by esters recently has been reported by Kane and Lowy,[2] by Bowden,[3] who used aluminum chloride, and by McKenna and Sowa,[4] who employed boron trifluoride as the condensing agent.

In this communication it is shown that in the presence of hydrogen fluoride esters react with benzene to produce mainly alkylbenzenes. The reaction may be represented by the equation

$$RCOOR' + C_6H_6 = RCOOH + C_6H_5R''$$

where R'' may be the same as R' or a rearranged form thereof. As it has been found[1] that acids can acylate aromatic compounds in the presence of hydrogen fluoride, the presence of ketones in the reaction products would be expected from a reaction of the liberated acid with either benzene or the alkylbenzene present. This actually proved to be the case, as in a number of experiments ketones were isolated in sufficient quantities to permit characterization. Bowden[3] in his study of this type of reaction using aluminum chloride, did not isolate any carbonyl compounds although he made a special effort to do so.

McKenna and Sowa[4] postulated that this type of alkylation proceeded through two stages, first, the formation of an olefin and an acid from the ester and second, the reaction of the olefin with benzene to give the alkylated benzene. An alternative mechanism, which they rejected, involved a metathesis between the ester and the aromatic compound. Rejection was based on the fact that esters of straight chain alcohols do not give normal alkylbenzenes. There is, however, another mechanism by which this reaction can occur. Hydrogen fluoride is an extremely powerful ionizing solvent. The ester may ionize to produce a positive alkyl ion and a negative acyl ion. This reaction would be assisted by the strong acid properties of the solvent, which would neutralize the acyl ion to form the carboxylic acid which in turn would further react with the solvent.[5] As the charge on the alkyl ion probably would not be localized, reaction would occur with the carbon atom which would result in the greatest reduction of free energy. A rearranged product could be formed.

$$RCO_2R' + HF = RCO_2H_2^+ + R'^+ + 2F^-$$

The fact that benzyl acetate will react with benzene to give, in the presence of hydrogen fluoride, diphenylmethane in yields of 75% of the theoretical seems to be strong evidence supporting the ionic rather than the olefin mechanism.

In accordance with the observations of previous investigators it was found that *n*-butyl acetate and *s*-butyl isobutyrate gave *s*-butylbenzene, isopropyl acetate gave isopropylbenzene, and *t*-butyl and benzyl acetates gave the corresponding alkylbenzenes.

Experimental

TABLE I

In every case one-third mole of ester and 400 cc. benzene were used. All boiling points are at 742 mm. unless otherwise noted.

Ester	G. HF	Time, hrs.	Product[6] % yield	Name	B. p., °C.	n^{20}
t-Butyl acetate	89	16	71	*t*-Butylbenzene	170–171	1.4921
t-Butyl acetate	169	16	73	*t*-Butylbenzene	72 at 32 mm.	1.4923
Isopropyl acetate	165	17	53	Isopropylbenzene	149–150	1.4911
n-Butyl acetate	180	17	60	*s*-Butylbenzene	170.5–171	1.4902
s-Butyl isobutyrate	90	17	56	*s*-Butylbenzene	170–171	1.4901
Benzyl acetate	70	15	75	Diphenylmethane	259–261	

The reactions were carried out in a copper bomb at steam-bath temperature in a manner reported previously.[1] All the acetates except *t*-butyl were made from the alcohol, acetic anhydride, and sodium acetate. *t*-Butyl acetate

(1) For previous paper in this series see THIS JOURNAL, **61**, 1795 (1939).

(2) Kane and Lowy, *ibid.*, **58**, 2605 (1936).

(3) Bowden, *ibid.*, **60**, 645 (1938).

(4) McKenna and Sowa, *ibid.*, **59**, 1204 (1937).

(5) Simons, *Chem. Rev.*, **8**, 213 (1931).

(6) The physical constants checked closely those reported in the summary by Ward and Kurtz, *Ind. Eng. Chem., Anal. Ed.*, **10**, 559 (1938).

was prepared according to the method of Norris and Rigby.[7] *s*-Butyl isobutyrate was made from the proper alcohol and acid using sulfuric acid as catalyst. The boiling points of the esters were *t*-butyl acetate 109–110°, isopropyl acetate 86–87°, *n*-butyl acetate 123.5–124°, *s*-butyl isobutyrate 141–142°, all at 734 mm., and benzyl acetate 105–105.5° (18 mm.).

The reaction of *t*-butyl acetate in which 169 g. of HF was used gave 3 g. of acetophenone, identified by means of its semicarbazone. The melting point was 198–199°, and when mixed with a known sample gave a melting point of 197–199°. Isopropyl acetate gave 4 g. of acetophenone, m. p. and mixed m. p. of the semicarbazone was 197–199°. A higher boiling ketonic fraction weighing 5 g. was also obtained. Its oxime melted at 68–69.5°. Widman[8] reports the melting point of *p*-isopropyl acetophenone oxime as 70–71°. When treated with semicarbazide in the usual manner a crystalline solid, m. p. 197°, was obtained. When mixed with acetophenone semicarbazone the m. p. was 169–175°.

Some higher boiling fractions were obtained in other experiments, but in quantities too small to permit positive identification.

To prove that the alkylbenzene obtained from *n*-butyl acetate and *s*-butyl isobutyrate was in both cases *s*-butylbenzene a diacetamino derivative was prepared. That of the *n*-butyl acetate melted at 188–189° and when mixed with the same derivative of the latter compound did not depress in melting point.

(7) Norris and Rigby, THIS JOURNAL, **54**, 2088 (1932).
(8) Widman, *Ber.*, **21**, 2226 (1888).

Summary

Hydrogen fluoride has been found to be an effective agent to alkylate benzene by means of esters. Reactions were carried out in a copper bomb at 80 to 100°. *t*-Butylbenzene, isopropylbenzene, and diphenylmethane were made from benzene and the acetates. *n*-Butyl acetate and *s*-butyl isobutyrate both gave secondary butylbenzene. Ketones also were formed in the reactions. Acetophenone was identified from those reactions in which acetates were used.

STATE COLLEGE, PENNA. RECEIVED MAY 22, 1939

[CONTRIBUTION FROM THE BIOCHEMISTRY DEPARTMENT OF THE UNIVERSITY OF OKLAHOMA MEDICAL SCHOOL]

The Isolation of Keturonic Acids as Crystalline Alkaloidal Salts[1]

BY J. P. HART AND M. R. EVERETT

In studies of the bromine oxidation of dilute solutions of more than 50 carbohydrates, Everett and Sheppard[2] have demonstrated the accumulation of keturonic acids. They found the yields of these substances to be related to the *cis–trans* structures of the original carbohydrates. Structural studies of the keturonic acids required their isolation in pure form. We are now reporting the isolation of alkaloidal salts of several keturonic acids, and the structures indicated by the properties of these salts. In order to avoid confusion the authors have named the keturonic acids as ketose derivatives.[3] Individual acids are differentiated by numbering the carboxyl carbon, the terminal carbon nearest the potential carbonyl being called one.[4]

Calcium *l*-sorbo-6-uronate has been isolated previously from *d*-glucose and *d*-gluconic lactone solutions oxidized by bromine,[5,6] and has been shown to be identical in properties with the calcium salts of Boutroux[7] and Kiliani.[8]

(1) Aided by a grant from the Research Appropriation of the University of Oklahoma Medical School.

(2) M. R. Everett and Fay Sheppard, University of Oklahoma Medical School Monograph, "Oxidation of Carbohydrates in Acid Solution," 1936.

(3) J. P. Hart and M. R. Everett, "A Suggested Nomenclature for Keturonic Acids," Abs. of Papers, 96th meeting of Am. Chem. Soc.

(4) The principal group of keturonic acids described in this paper are named as follows:

Keturonic acid	Parent aldohexoses
d-Sorbo-6-uronic	*l*-Glucose, *d*-Idose
l-Sorbo-6-uronic	*d*-Glucose, *l*-Idose
d-Fructo-6-uronic	*l*-Gulose, *d*-Mannose
l-Fructo-6-uronic	*d*-Gulose, *l*-Mannose
d-Tagato-6-uronic	*d*-Altrose, *l*-Galactose
l-Tagato-6-uronic	*l*-Altrose, *d*-Galactose
d-Psico-6-uronic	*l*-Allose, *d*-Talose
l-Psico-6-uronic	*d*-Allose, *l*-Talose

(5) E. W. Cook and R. T. Major, THIS JOURNAL, **57**, 773 (1935).
(6) J. P. Hart, Fay Sheppard, M. R. Everett, *J. Biol. Chem.*, **123**, lii (1938).
(7) L. Boutroux, *Compt. rend.*, **127**, 1225 (1907).
(8) H. Kiliani, *Ber.*, **55**, 2817 (1923).

TABLE I

Brucine-	M. p., °C.[a]	Ultimate analysis, % Found C	Found H	Calcd. C	Calcd. H	Formula	Source
l-Sorbo-6-uronate[b,c]	174–175 (dec.)	57.45	6.31	57.42	6.33	$C_{23}H_{26}N_2O_4 \cdot C_6H_{10}O_7 \cdot H_2O$	Ca-*l*-sorbo-6-uronate
l-Sorbo-6-uronate[b]	174–175 (dec.)	57.42	6.38	57.42	6.33	$C_{23}H_{26}N_2O_4 \cdot C_6H_{10}O_7 \cdot H_2O$	Oxidized *d*-glucose
d-Fructo-6-uronate[d]	192–192.5 (dec.)	59.44	6.22	59.19	6.17	$C_{23}H_{26}N_2O_4 \cdot C_6H_{10}O_7$	Oxidized *d*-mannose
l-Fructo-6-uronate[d]	165–166	57.42	6.46	57.42	6.33	$C_{23}H_{26}N_2O_4 \cdot C_6H_{10}O_7 \cdot H_2O$	Oxidized *d*-gulonic lactone
l-Fructo-6-uronate	165–166	57.63	6.33	57.42	6.33	$C_{23}H_{26}N_2O_4 \cdot C_6H_{10}O_7 \cdot H_2O$	Oxidized *l*-rhamnose
l-Tagato-6-uronate	189–189.5 (dec.)	59.12	6.18	59.19	6.17	$C_{23}H_{26}N_2O_4 \cdot C_6H_{10}O_7$	Oxidized *d*-galactose
d-Xyloketuronate	168–169	58.39	6.36	58.32	6.30	$C_{23}H_{26}N_2O_4 \cdot C_5H_8O_6 \cdot H_2O$	Oxidized *d*-xylose
1-Desoxy-*l*-fructo-6-uronate	128–129	58.75	6.53	58.97	6.49	$C_{23}H_{26}N_2O_4 \cdot C_6H_{10}O_6 \cdot H_2O$	Oxidized *l*-rhamnose

[a] All melting points uncorrected with short stem thermometers. [b] M. p. two samples mixed 174–175° (dec.). [c] A dihydrate, m. p. 182° (dec.), obtained by recrystallization from 80% alcohol. [d] M. p. of two samples mixed 165–166°.

The authors have prepared the crystalline brucine salt of *l*-sorbo-6-uronic acid by decomposition of the pure calcium salt. They have found it to be identical in all of its properties with the brucine salt prepared from *d*-glucose solutions oxidized by bromine for forty-two days. Ultimate analyses of the reducing brucine salts isolated from similarly oxidized solutions of *d*-mannose, *d*-gulonic lactone, and *d*-galactose show that these compounds were all salts of hexuronic acids (Table I). The stability of these acids in bromine water, compared with the rapid oxidation of alduronic acids by bromine,[9] indicates that they have ketose structures. The naphthoresorcinol, orcinol, and Molisch tests for the principal reducing brucine salts isolated from oxidized solutions of the four aldohexoses (Table II) are characteristic and identical. This implies by analogy structures stereoisomeric with *l*-sorbo-6-uronic acid, but proof of structure is to be the subject of further investigations. Melting points, optical rotations, and Sumner reducing equivalents show each compound to be pure and unique (see Tables I and III). These findings verify the conclusions of Everett and Sheppard[2,10] based on quantitative studies of oxidized hexose solutions. The position of the carbonyl in the keturonic acid isolated from the oxidized solutions of *d*-xylose is undetermined. Ultimate analysis and the stability of this acid in the presence of bromine establish it as a ketopenturonic acid.

TABLE II

COLOR REACTIONS OF THE BRUCINE SALTS OF KETURONIC ACIDS[10]

Brucine-	Naphtho-resorcinol	Bials	Molisch
l-Sorbo-6-uronate	Blue	Light green	Red
d-Fructo-6-uronate	Blue	Light green	Red
l-Fructo-6-uronate	Blue	Light green	Red
l-Tagato-6-uronate	Blue	Light green	Red
d-Xyloketuronate	Pink	Negative	Brown
1-Desoxy-*l*-fructo-6-uronate	Red brown	Negative	Negative

TABLE III

ROTATIONS AND REDUCTIONS OF THE BRUCINE SALTS OF KETURONIC ACIDS

Brucine-	$[\alpha]^{25}D$[a]	*d*-Glucose equivalent by Sumner's method[b] Salt	Calcd. for free acid
l-Sorbo-6-uronate	−24°	0.25	0.80
d-Fructo-6-uronate	−15.5°	.31	.98
l-Fructo-6-uronate	−24.5°	.32	.95
l-Tagato-6-uronate	−17°	.28	.85
d-Xyloketuronate	− 9°	.22	.75
1-Desoxy-*l*-fructo-6-uronate	−32°	.37	1.21

[a] For 1% aqueous solution. [b] For 2 mg. per ml. concentrations of the salts.

Oxidation of *l*-rhamnose for twenty-one days produces two keturonic acids, 1-desoxy-*l*-fructo-6-uronic acid and *l*-fructo-6-uronic acid, which have been isolated and separated by fractional crystallization of their brucine salts. The lactone of the desoxyketuronic acid has been isolated by Votoček and Malachta.[11] An identical brucine salt of *l*-fructo-6-uronic acid has been isolated from oxidized solutions of *d*-gulonic lactone. This acid evidently arises from oxidation of the methyl group of *l*-rhamnose, *l*-rhamnonic acid or 1-desoxy-*l*-fructo-6-uronic acid to a primary alcoholic group, an unusual reaction, previously unrecognized.

Experimental

Oxidation of Carbohydrate Solutions.—One per cent. carbohydrate solutions were oxidized with bromine for forty-two days, using the procedure of Everett and Sheppard.[2,9] Four hundred ml. of a 1% aqueous solution of each carbohydrate was placed in a glass-stoppered bottle. Fifteen ml. of bromine was then added and the mixture kept in the dark at approximately 25°. The solution was shaken at two to three day intervals, and more bromine was added whenever the liquid phase disappeared during the oxidation. After forty-two days the solution was aerated with washed air.

(9) M. R. Everett, B. Edwards and Fay Sheppard, *J. Biol. Chem.*, **104**, 11 (1934).

(10) M. R. Everett and Fay Sheppard, *Proc. Soc. Expil. Biol. Med.*, **34**, 7 (1936).

(11) E. Votoček and S. Malachta, *An. soc. espan. fis. quím.*, **27**, 494 (1929).

General Method for Isolation of Mixed Barium Salts.—The aerated oxidized carbohydrate solution was shaken with an excess of lead carbonate, filtered, allowed to remain in the refrigerator at 10° for twenty-four hours, and filtered again. The remaining bromide ion was removed by shaking with moist freshly prepared silver carbonate, centrifuging, decanting and immediately saturating the solution with hydrogen sulfide. The precipitated lead and silver sulfides were filtered off, and the filtrate aerated to remove excess hydrogen sulfide. This treatment removed most of the dibasic sugar acids present in the oxidized solutions.[2,6] Analysis by the Sumner method showed little loss of reducing material. The solution was then treated with an excess of barium carbonate at 40 to 45° for two hours. The filtrate was concentrated *in vacuo* to one-twelfth volume, and the barium salts were precipitated by addition of 8 volumes of alcohol. The salts were allowed to settle, filtered with suction, and washed twice with alcohol and twice with ether. They were dried in a desiccator and the barium content determined gravimetrically. Yields of barium salts obtained from 4 g. of original carbohydrates were as follows: *d*-glucose, 3.9 g.; *d*-mannose, 3.0 g.; *d*-gulonic lactone, 3.1 g.; *d*-galactose, 2.0 g.; and *d*-xylose, 4.1 g.

General Method of Preparing Solutions of Brucine Salts.—Weighed portions of the mixed barium salts were dissolved in two to three times their weight of water, and the barium was removed quantitatively by addition of the calculated quantities of *N* sulfuric acid. Enough alcohol was then added to produce a 70% solution. The mixture was placed in the refrigerator for fifteen minutes, then centrifuged free of barium sulfate and the calculated quantity of 10% alcoholic brucine solution was added.

Brucine *l*-Sorbo-6-uronate.—A solution of brucine salts was prepared from 2.5 g. of the mixed barium salts obtained from oxidized *d*-glucose. Crystallization began in fifteen minutes and apparently was complete after eighteen hours in the refrigerator. The brucine salt was filtered off, washed three times with alcohol and once with ether, and dried in a desiccator. The 2.2 g. yield was recrystallized from a small quantity of hot water, from which it separated as the monohydrate on cooling. It also was obtained as the dihydrate by dissolving in the least amount of hot water, adding 5 volumes of alcohol and allowing to crystallize in the refrigerator.

The same salt was prepared by decomposing a suspension of calcium *l*-sorbo-6-uronate in dioxane with the calculated quantity of sulfuric acid. After removal of calcium sulfate the dioxane was removed *in vacuo*, and the sirupy acid dissolved in a little water. After addition of an equivalent quantity of alcoholic brucine solution, the salt was crystallized as above.

Brucine *d*-Fructo-6-uronate.—A solution of this salt was prepared from 1 g. of the mixed barium salts from oxidized *d*-mannose. Crystallization started during slow concentration of the solution *in vacuo*. The mixture was then placed in a desiccator in the refrigerator, and the small fraction of crystalline material that separated in two hours was discarded. The mother liquors gave a second crop (0.3 g.) of crystals of the desired salt within twenty-four hours. This material was recrystallized by dissolving in a little hot water and adding 5 volumes of methyl alcohol.

Brucine *l*-Fructo-6-uronate.—A solution of this salt was prepared from 2 g. of the mixed barium salts from oxidized *d*-gulonic lactone. The solution was concentrated *in vacuo* until crystals began to form, and was then placed in a desiccator in the refrigerator. After twelve hours 0.58 g. of the salt was obtained. It was recrystallized by dissolving in hot water and adding 4 volumes of alcohol.

Brucine *l*-Tagato-6-uronate.—A solution of the salt was prepared from 4 g. of the mixed barium salts from oxidized *d*-galactose. In this preparation methyl alcohol was substituted for ethyl alcohol. The solution was concentrated to 30 ml. *in vacuo* and placed in a desiccator in the refrigerator. After twelve hours a small fraction of non-reducing salt was filtered off. A large fraction of a second non-reducing salt was separated in three days. After one week a third fraction of crystals appeared. It contained the reducing salt, which was purified by dissolving in a small quantity of hot water, adding 8 volumes of alcohol and allowing to crystallize in the refrigerator. The yield of recrystallized salt was 0.52 g.

Brucine *d*-Xyloketuronate.—A solution of brucine salts was prepared from 1 g. of the mixed barium salts from oxidized *d*-xylose. The solution was concentrated to one-half volume *in vacuo* and then placed in a desiccator in the refrigerator. With occasional scratching, 0.2 g. of crystalline material separated in twelve hours. The salt was recrystallized by dissolving in a small quantity of hot water and adding 5 volumes of alcohol.

Brucine 1-Desoxy-*l*-fructo-6-uronate.—The mixed barium salts from *l*-rhamnose solution, that had been oxidized twenty-one days, were obtained as a viscous gum. The product from 4 g. of *l*-rhamnose was dissolved in 50 ml. of water, and an aliquot was analyzed for barium. The barium was removed with an equivalent amount of sulfuric acid, and the solution was concentrated to 20 ml. The calculated quantity of brucine was dissolved in 30 ml. of alcohol and added to the solution. The latter slowly was concentrated *in vacuo* until crystals appeared. The solution was then placed in a desiccator in the refrigerator for twenty-four hours. The yield was 1.1 g. of the brucine salt of *l*-fructo-6-uronic acid. After another twenty-four hours the mother liquor deposited 4.1 g. of brucine 1-desoxy-*l*-fructo-6-uronate. This salt was recrystallized by dissolving in a small volume of hot water, adding 6 volumes of alcohol, and placing in the refrigerator for three days.

Summary

1. Six keturonic acids have been isolated as crystalline brucine salts.

2. Brucine *d*-fructo-6-uronate, *l*-fructo-6-uronate, *l*-tagato-6-uronate, and *d*-xyloketuronate are the first pure preparations of these acids described.

3. Isolation of *l*-fructo-6-uronic acid from oxidized *l*-rhamnose solution demonstrates that the methyl group is susceptible to controlled oxidation.

OKLAHOMA CITY, OKLA. RECEIVED APRIL 25, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE UNIVERSAL OIL PRODUCTS COMPANY]

Reaction of Propene with Isoolefins in the Presence of Sulfuric Acid

BY V. N. IPATIEFF, HERMAN PINES AND B. S. FRIEDMAN

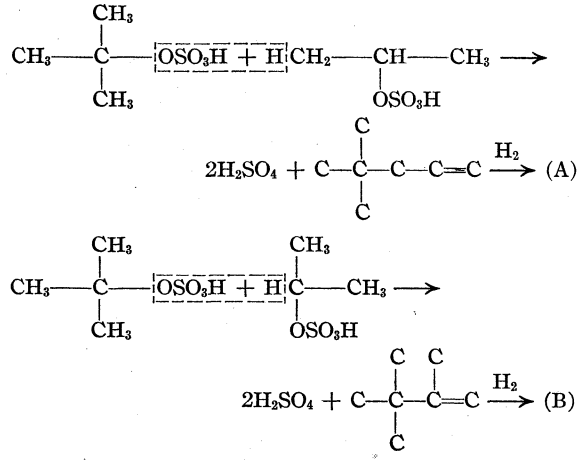
It was previously[1] shown that under the influence of sulfuric acid aliphatic olefins containing four or more carbon atoms undergo conjunct polymerization yielding, in addition to polymeric olefins, paraffinic and cyclic hydrocarbons. The predominance of the one or other type of hydrocarbon depends greatly upon the concentration and amount of sulfuric acid used.

Propene was found to be more resistant to polymerization for when contacted under atmospheric pressure with 96% sulfuric acid at 0 and 25°, it yielded chiefly isopropyl sulfates and only negligible amounts of hydrocarbons. The addition of cupric sulfate or mercuric sulfate to the sulfuric acid did not promote the polymerization of propene.[2]

However, when mixed with more reactive olefins such as isobutene or isopentenes and then contacted with sulfuric acid, the propene reacted with the other olefins to yield among other products heptenes and octenes, respectively. No hydrocarbons corresponding to the dimer or trimer of propene were found in the reaction product. With straight chain olefins such as *n*-butene scarcely any of the propene reacted to form liquid hydrocarbons when contacted with concentrated sulfuric acid.

The amount of heptenes formed from the reaction of isobutene with propene varied from 8 to 35% (based on the liquid hydrocarbons produced) and was dependent on the concentration of the acid, temperature, and mode of addition of the olefins. The reaction of isopentenes with propene yielded hydrocarbons of which 16% were octenes and 17% tridecenes.

The combined lower boiling fractions of a number of isobutene–propene experiments were hydrogenated and then distilled through a 100-plate bubble cap still.[3] Fractions amounting to 45% of the heptanes present were identified by physical properties and Raman spectra analysis as 2,2-dimethylpentane (A) and 5% as 2,2,3-trimethylbutane (B); another fraction (15% of the heptanes) consisted of 2,3-dimethylpentane (C). (A) and (B) possess the carbon skeletons expected of primary polymers



but (C) probably results from a rearrangement of the 2,2-dimethylpentenes and/or 2,2,3-trimethylbutene under the influence of the sulfuric acid. Similar carbon skeleton isomerizations in the presence of acid catalysts have been observed by others.[4]

Several experiments were made in which the propene–isoolefin mixture was treated with isopropyl esters prepared by combining one mole of propene with one mole of 96% sulfuric acid. The proportion of propene which reacted with isoolefins was greater than in the case when sulfuric acid alone was used as a catalyst.

Experimental

Apparatus and Procedure.—The apparatus used for reactions at ordinary pressure was essentially the same as that described for previous experiments.[1] When higher temperatures and pressures were employed, a stainless steel stirring autoclave equipped with a copper liner was used. The sulfuric acid or its esters was placed in the reaction flask or in the autoclave and the olefin mixture passed into the rapidly stirred catalysts through an inlet tube. During the addition of the olefins the temperature was controlled by surrounding the reaction flask or chamber by an ice-bath or water-bath. The time required for the addition of the hydrocarbons varied from two to seven hours.

After being allowed to stand overnight at room temperature the two layers of the reaction product were separated.

(1) Ipatieff and Pines, *J. Org. Chem.*, **1**, 464 (1936).

(2) Ormandy and Craven, *J. Inst. Petr. Tech.*, **13**, 844 (1927), and *J. Soc. Chem. Ind.*, **47**, 317T (1928), found that propene underwent polymerization when passed slowly into 98% sulfuric acid.

(3) Bruun and Faulconer, *Ind. Eng. Chem., Anal. Ed.*, **9**, 192 (1937).

(4) (a) Laughlin, Nash and Whitmore, THIS JOURNAL, **56**, 1395 (1934); (b) Cramer and Glasebrook, *ibid.*, **61**, 230 (1939); (c) Drake, Kline and Rose, *ibid.*, **56**, 2076 (1934); (d) *cf.* review by Wachter, *Ind. Eng. Chem.*, **30**, 826 (1938).

TABLE I

Expt.	Temp., °C.	Reactants, g. Catalyst	C_3H_6	i-C_4H_8	Reaction products, g. Acid layer	Hydrocarbon layer	Unreacted C_3H_6	Propene reacting to form HC, g.	Wt. % of liquid hydrocarbon product
1[a]	0–20	273[b]	369	442	384	624	36	122	8.2% C_7 range
2[c]	−18	388[d]	295	310	383	509	70	132	14.2% C_7 range
3	65–70[f]	150[e]	99	126	234	97	66		29.5% C_7 range
4	100–110[g]	150[e]	99	126			14		35% C_7 range
5[a]	0–17	273[b]	375	573[h]	396	711	64	53	16% C_8 range
									17% C_{13} range

[a] Total of three experiments. [b] 96% sulfuric acid. [c] Total of two experiments. [d] Monoisopropyl sulfate used; it was prepared by the addition of 2.74 moles of propene to 2.67 moles of 96% sulfuric acid. [e] 64% sulfuric acid. [f] Maximum pressure 191 lb./sq. in. [g] Maximum pressure 180 lb./sq. in. [h] Isopentenes used.

The hydrocarbon layer was steam-distilled from over alkali, dried, and distilled from over sodium. The sulfuric acid layer was decomposed with water, rendered alkaline with sodium hydroxide, and subjected to steam distillation. The distillate so obtained was saturated with potassium carbonate to complete the separation of the alcohols. The latter were dried and distilled.

Material non-volatile with steam was not analyzed; the nature and constitution of these high boiling fractions have been discussed in an earlier work.[1] The experimental conditions are given in Table I.

Isobutene–Propene Mixed Polymerization

Hydrocarbon Layer.—From the hydrocarbon product of the mixed polymerization of isobutene and propene there was obtained material boiling 75.2 to 78.6°; d^{20}_4 0.689. *Anal.* Calcd. for C_7H_{14}: C, 85.62; H, 14.38; mol. wt., 98. Found: C, 85.60; H, 14.45; mol. wt., 97.

The presence of a *t*-butyl group in the heptene was shown by the method of depolyalkylation.[5a] Fifteen cc. of the heptenes was dissolved in 19 g. of *t*-butylbenzene and the mixture was shaken with 10 cc. of 96% sulfuric acid at 0°. The hydrocarbon was then separated from the sulfuric acid, washed with alkali and water, and distilled. The fraction boiling 238–250° contained crystals of *p*-di-*t*-butylbenzene.

The combined lower boiling fractions of runs 1 and 2 were hydrogenated at 60° in the presence of nickel catalyst[5b] and hydrogen, 100 kg./cm.² initial pressure. From the resulting paraffins the following fractions were separated by distillation through a 100-plate[3] column.

Fraction	Cc.	B. p., °C. 750 mm.	$n^{20}D$	d^{20}_4
1–3	29	69–77		
4	63	77–78	1.3838	0.6764
5	61	78–78.8	1.3830	.6738
6–10	59	78.8–88		
11	41	88–90.4	1.3928	.6960
		Literature Data		
2,2-Dimethylpentane[6]		78.9 (760)	1.38233	0.6737
2,2,3-Trimethylbutane[6]		80.9 (760)	1.38940	.6900[7]
2,3-Dimethylpentane[6]		89.7 (760)	1.39201	.6952

(5) (a) Ipatieff and Pines, THIS JOURNAL, **58**, 1056 (1936); (b) Ipatieff and Corson, *Ind. Eng. Chem.*, **30**, 1039 (1938).

(6) Edgar and Calingaert, THIS JOURNAL, **51**, 1540 (1929); Edgar, Calingaert and Marker, *ibid.*, **51**, 1483 (1929).

(7) Levene and Marker, *J. Biol. Chem.*, **91**, 77 (1931).

Raman Spectrum Analysis.[8]—Fractions 4 and 5 consisted of 90–95% 2,2-dimethylpentane, and 5–10% of 2,2,3-trimethylbutane. Fraction 11 consisted solely of 2,3-dimethylpentane.

Sulfuric Acid Layer.—The alcohols obtained from the sulfuric acid layer by the method described above were fractionated in a precision still. The following fractions were separated: (1) 79.4–80.0°, 78%, $n^{20}D$ 1.3782; (2) 80–84°, 17.5%, $n^{20}D$ 1.3785.

In order to determine whether *t*-butyl or isopropyl alcohol was produced, the entire product was dehydrated over alumina at 300°.[9] By distillation on a low temperature Podbielniak distilling apparatus and by sulfuric acid absorption it was determined that the olefins formed consisted of pure propene.

Isopentene–Propene Mixed Polymerization

Hydrocarbon Layer.—Sixteen per cent. of the hydrocarbons consisted of octenes, b. p. 96–125°. The fraction boiling 100–116°, $n^{20}D$ 1.4174–1.4203, was hydrogenated at 100° (initial hydrogen pressure of 100 kg./sq. cm.) in the presence of a nickel catalyst. The hydrogenated product distilled between 112 and 116°; $n^{20}D$ 1.4033–1.4042; d^{20}_4 0.7168. *Anal.* Calcd. for C_8H_{18}: C, 84.10; H, 15.90; mol. wt., 114. Found: C, 83.95; H, 16.00; mol. wt., 113.

Sulfuric Acid Layer.—From the acid layer there was isolated an alcohol identified as isopropyl alcohol, b. p. 79–82°, $n^{20}D$ 1.3779–1.3782; 3,5-dinitrobenzoate, m. p. 121.5–122.[10]

Summary

Sulfuric acid catalyzed the reaction between propene–isobutene and propene–isopentenes to yield among other products heptenes and octenes, respectively. The hydrogenated heptenes contained 2,2-dimethylpentane, 2,3-dimethylpentane and some 2,2,3-trimethylbutane. These heptanes were identified by physical constants and Raman spectra analysis.

Propene alone under similar conditions does not undergo polymerization.

RIVERSIDE, ILLINOIS RECEIVED MAY 8, 1939

(8) Raman spectra analyses by Dr. E. J. Rosenbaum, University of Chicago.

(9) Ipatieff, *Ber.*, **36**, 2011 (1903); Pines, THIS JOURNAL, **55**, 3892 (1933).

(10) Malone and Reid, *ibid.*, **51**, 3424 (1929).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

Tritylation Experiments in the Sugar Alcohol Series

BY M. L. WOLFROM, W. J. BURKE AND S. W. WAISBROT

For the purposes of another problem under investigation in this Laboratory, we were interested in the tritylation,[1] by the Helferich procedure,[2] of sugar alcohols of the five and six carbon atom series. By this general reaction of tritylation, followed by acetylation and detritylation, the 2,3,4,-5-tetraacetate[3] and 2,3,4,5-tetrabenzoate[4] of *d*-mannitol have been prepared previously. We were able to obtain a monotrityl ether of mannitol as its crystalline pentaacetate by treating an excess of mannitol with trityl chloride. This derivative is of interest because the two terminal positions of mannitol are chemically equivalent.

The methylpentitols offer the interesting case of presenting only one primary hydroxyl group to react with the tritylation reagent and accordingly the 2,3,4,5-tetraacetate of *l*-fucitol was synthesized. The detritylation of trityl-*l*-fucitol tetraacetate presented some difficulty as the Helferich detritylation procedure using hydrogen bromide in glacial acetic acid resulted in the formation of the bromide rather than the free hydroxyl group. This type of behavior was reported previously from this Laboratory[5] with acyclic derivatives of glucose and galactose. To avoid this bromine replacement, detritylation of this substance was effected with hot dilute acetic acid according to the procedure of Kuhn and co-workers.[6] Retritylation of the fucitol tetraacetate produced the original trityl-*l*-fucitol tetraacetate and treatment of the tetraacetate with hydrogen bromide yielded the same bromide tetraacetate that was obtained on detritylation by the Helferich procedure. The pentaacetate of *l*-fucitol was also synthesized in crystalline form. In the pentitol series, we have also obtained ditrityl-xylitol triacetate.

The tritylation of dulcitol presents an interesting case. Valentin[7] reports that dulcitol does not form a trityl compound when treated with a pyridine solution of trityl chloride. We found that a ditrityl compound was formed but that it separated from the reaction mixture as a dipyridinium hydrochloride addition compound. The acidity of this addition compound was sufficient to detritylate the dulcitol when the compound was recrystallized from hot ethanol. The dipyridinium compound was decomposed readily by bases without detritylation and in this manner ditrityl dulcitol was obtained. Ditrityl dulcitol crystallizes from ethanol with one mole of alcohol of crystallization. This behavior of ditrityl dulcitol with pyridine hydrochloride is reminiscent of the behavior of *d*-sorbitol with pyridine, wherein a readily crystallizable pyridine compound is formed.[8]

Acetylation of ditrityl dulcitol yielded the ditrityl dulcitol tetraacetate, from which 1,6-dibromodulcitol tetraacetate was obtained on detritylation with hydrogen bromide in glacial acetic acid. Ditrityl dulcitol formed a dibenzylidene compound without detritylation. In preparing this substance we removed the excess of benzaldehyde by allowing it to oxidize in the air to benzoic acid and removing the latter with a mild alkali.

Experimental

1-Trityl *l*-Fucitol Tetraacetate.—*l*-Fucitol (1.5 g., 1 mol) and 2.6 g. (1 mol) of trityl chloride were dissolved in 20 cc. of warm, dry pyridine and kept at 60° for two days. To the cooled solution was added 18 cc. of acetic anhydride and the solution kept at 45° for twenty-four hours. The product crystallized from the reaction mixture and was recrystallized from ethanol: yield 2.4 g., m. p. 152°, spec. rot. −18° (30°, *c* 1.9, $CHCl_3$).[9] A further quantity of the substance (0.6 g.) was obtained by pouring the pyridine mother liquor into ice and water.

Anal. Calcd. for $C_6H_9O_5(COCH_3)_4C(C_6H_5)_3$: $C(C_6H_5)_3$, 42.2; CH_3CO, 6.94 cc. 0.1 *N* NaOH per 100 mg. Found: $C(C_6H_5)_3$ (7), 41.9; CH_3CO, 6.89 cc.

The same product was obtained on acetylation of the trityl-*l*-fucitol of Valentin.[7]

1-Bromo-*l*-fucitol Tetraacetate.—To a solution of 2.5 g. (1 mol) of 1-trityl-*l*-fucitol tetraacetate in 10 cc. of glacial acetic acid was added 2 cc. of a glacial acetic acid solution of hydrogen bromide (4 mols). The precipitated

(1) Trityl = triphenylmethyl.

(2) B. Helferich, P. E. Speidel and W. Toeldte, *Ber.*, **56**, 766 (1923); B. Helferich and J. Becker, *Ann.*, **440**, 1 (1924); B. Helferich, *Z. angew. Chem.*, **41**, 871 (1928), review paper.

(3) F. Micheel, *Ber.*, **65**, 262 (1932).

(4) F. Micheel, *Ann.*, **496**, 77 (1932); A. Müller, *Ber.*, **65**, 1051 (1932).

(5) M. L. Wolfrom, J. L. Quinn and C. C. Christman, THIS JOURNAL, **57**, 713 (1935); M. L. Wolfrom and C. C. Christman, *ibid.*, **58**, 39 (1936).

(6) R. Kuhn, H. Rudy and F. Weygand, *Ber.*, **69**, 1546 (1936).

(7) F. Valentin, *Coll. Czechoslov. Chem. Commun.*, **3**, 499 (1931).

(8) H. H. Strain, THIS JOURNAL, **56**, 1756 (1934).

(9) All specific rotations are recorded to the D-line of sodium light; 30° is the temperature; *c* is the concentration in g. per 100 cc. of soln., the chloroform used was U. S. P. (United States Pharmacopoeia). All substances were recrystallized to constant rotation and melting point.

trityl bromide was removed by filtration and the filtrate was poured into ice and water. The crystalline precipitate was removed by filtration and recrystallized from ethanol; yield 0.9 g., m. p. 142–143°; spec. rot. −9.8° (22°, *c* 1.76, $CHCl_3$).

The compound was readily soluble in glacial acetic acid, chloroform, acetone and hot ethanol. It was practically insoluble in water and petroleum ether.

Anal. Calcd. for $C_6H_9O_4(COCH_3)_4Br$: CH_3CO, 10.1 cc. 0.1 *N* NaOH per 100 mg.; Br, 20.1. Found: CH_3CO (Freudenberg method[10]), 10.1 cc.; Br, 20.4.

l-Fucitol 2,3,4,5-Tetraacetate.—1-Trityl *l*-fucitol tetraacetate (10 g.) was dissolved in 40 cc. of warm glacial acetic acid and the mixture heated under a reflux condenser. Water (10 cc.) was added in 2-cc. portions and the mixture was refluxed for one hour. Water (50 cc.) was then added, the mixture cooled to room temperature and the separated trityl carbinol (4.3 g., 95%) separated by filtration. The sirup obtained on solvent removal under reduced pressure was taken up in ether and the ether solution was shaken first with a suspension of calcium carbonate in water and finally with water. The dried ether extract (carboraffin) was treated with petroleum ether to incipient opalescence and allowed to stand overnight at icebox temperature; yield 1.2 g., m. p. 92–94°. A second crop (0.7 g., m. p. 92–94°) was obtained from the mother liquor on the addition of more petroleum ether. The substance is readily recrystallized from xylene; m. p. 92–94°, spec. rot. −15° (25°, *c* 3.0, $CHCl_3$). The above procedure is essentially the detritylation procedure of Kuhn, Rudy and Weygand.[6]

The compound crystallizes in elongated prisms from water. It is readily soluble in chloroform, acetone, ethanol, acetic acid, warm ether and warm xylene and is practically insoluble in petroleum ether. It is slightly soluble in cold and fairly soluble in hot water.

Anal. Calcd. for $C_6H_{10}O_5(COCH_3)_4$: C, 50.3; H, 6.64; CH_3CO, 12.0 cc. 0.1 *N* NaOH per 100 mg. Found: C, 50.5; H, 6.59; CH_3CO, 11.9 cc.

The original 1-bromo-*l*-fucitol tetraacetate was regenerated on treatment of *l*-fucitol tetraacetate (0.25 g.) in glacial acetic acid (8 cc.) with 4 cc. of acetic acid saturated with hydrogen bromide and allowing the mixture to stand for three hours. The crystalline product obtained on pouring the reaction mixture into ice and water was removed by filtration, washed with water and recrystallized from 60% ethanol; yield 0.13 g., m. p. 143° (mixed m. p. unchanged).

l-Fucitol Pentaacetate.—*l*-Fucitol (0.95 g.) was acetylated with pyridine (5 cc.) and acetic anhydride (10 cc.) for sixteen hours at room temperature and the reaction product obtained crystalline on pouring the acetylation mixture into ice and water; yield 2.0 g. (93%), m. p. 126°. The product was recrystallized from ethanol; m. p. 127°, spec. rot. +20.5° (25°, *c* 3.0, $CHCl_3$).

The substance crystallizes from ethanol in prisms and is insoluble in petroleum ether, soluble in hot ethanol and is readily soluble in chloroform, acetone and acetic acid.

Anal. Calcd. for $C_6H_9O_5(COCH_3)_5$: C, 51.0; H, 6.43; CH_3CO, 13.3 cc. 0.1 *N* NaOH per 100 mg. Found: C, 51.1; H, 6.33; CH_3CO, 13.3 cc.

(10) K. Freudenberg and M. Harder, *Ann.*, **433**, 230 (1923).

1,6-Ditrityl Dulcitol Dipyridinium Hydrochloride.—Five grams (1 mol) of dulcitol and 16 g. (2 mols) of trityl chloride were added to 30 cc. of dry pyridine. The mixture was shaken intermittently for five days. The dulcitol gradually went into solution and a product precipitated. The product was removed by filtration and washed with pyridine and then with water; m. p. 182–184°, mixed m. p. 172–178° with ditrityl dulcitol (see below) of m. p. 184°. Upon acetylation with pyridine and acetic anhydride the product was converted into ditrityl dulcitol tetraacetate (see below); m. p. 233°, mixed m. p. unchanged. When the product was dissolved in hot ethanol, dulcitol, identified by melting point and mixed melting point, separated on cooling. From the mother liquor trityl ethyl ether (m. p. 83°, mixed m. p. unchanged) was recovered. When the product (odorless) was heated a distinct odor of pyridine was observed.

Anal. Calcd. for $C_6H_{12}O_6[C(C_6H_5)_3]_2 \cdot [C_5H_5N \cdot HCl]_2$: Cl, 7.90; HCl, 2.23 cc. 0.1 *N* NaOH per 100 mg. Found: Cl, 8.2; HCl, 2.16 cc.

1,6-Ditrityl Dulcitol Ethyl Alcoholate.—The 1,6-ditrityl dulcitol dipyridinium hydrochloride obtained from 5 g. of dulcitol was suspended in 250 cc. of water, 0.1 *N* sodium hydroxide was added until the solution was basic, mechanical stirring was then maintained for two hours and the product removed by filtration and washed with water, yield 18 g.; after two recrystallizations from ethanol, yield 14 g., m. p. 183–184° (slight sintering at 80°).

The compound crystallizes in rectangular prisms from ethanol. It is readily soluble in benzene, moderately so in pyridine, chloroform and hot ethanol and insoluble in water and petroleum ether.

Anal. Calcd. for $C_6H_{12}O_6[C(C_6H_5)_3]_2C_2H_5OH$: $C(C_6H_5)_3$, 68.3; C_2H_5OH, 6.46. Found: $C(C_6H_5)_3$, 68.4; C_2H_5OH (loss in weight at 110° under reduced pressure), 6.38; OC_2H_5, present.

1,6-Ditrityl Dulcitol.—This substance was obtained as a crystalline residue on heating its ethyl alcoholate for sixteen hours at 110° under reduced pressure and over phosphorus pentoxide; yield quantitative, m. p. 183–184°.

Anal. Calcd. for $C_6H_{12}O_6[C(C_6H_5)_3]_2$: $C(C_6H_5)_3$, 73.0; C, 79.2; H, 6.33. Found: $C(C_6H_5)_3$, 72.7; C, 78.9; H, 6.31.

1,6-Ditrityl Dulcitol Tetraacetate.—1,6-Ditrityl dulcitol ethyl alcoholate (2.5 g.) was dissolved in 23 cc. of pyridine, cooled to 0°, 15 cc. of acetic anhydride added slowly and the mixture kept at icebox temperature. In about three hours crystals began to form and crystallization was completed on standing overnight; yield 2.5 g., m. p. 232–234°. Pure material was obtained on recrystallization from trichloroethylene; m. p. 237–238°.

Anal. Calcd. for $C_{14}H_{20}O_{10}[C(C_6H_5)_3]_2$: C, 74.8; H, 6.04; $C(C_6H_5)_3$, 58.3; mol. wt., 838.4. Found: C, 74.3; H, 6.03; $C(C_6H_5)_3$, 58.7; mol. wt. (Rast), 870, 824.

1,6-Dibromodulcitol Tetraacetate.—1,6-Ditrityl dulcitol tetraacetate (4.5 g.) was detritylated with hydrogen bromide in glacial acetic acid as described previously for the synthesis of 1-bromo-*l*-fucitol tetraacetate, except that the filtrate from the trityl bromide was poured into chloroform (100 cc.) and the chloroform was washed with cold water until free of halogen. The residue obtained on solvent

removal was triturated with ether and recrystallized several times from ethyl acetate; yield 1.1 g., m. p. 197–198°. The substance was practically insoluble in ether and alcohol but was soluble in chloroform, hot ethyl acetate and hot benzene.

Anal. Calcd. for $C_6H_8O_4(COCH_3)_4Br_2$: CH_3CO, 8.40 cc. 0.1 *N* NaOH per 100 mg.; Br, 33.57. Found: CH_3CO, 8.38 cc. (Freudenberg method[10]); Br, 33.45.

1,6-Dityityl Dibenzylidene Dulcitol.—1,6-Dityityl dulcitol (3 g.) was dissolved in 10 cc. of benzaldehyde and 3 to 4 g. of freshly fused zinc chloride was added. The mixture was shaken until the zinc chloride dissolved and kept overnight at room temperature. Chloroform (50 cc.) was then added and the solution washed with water to remove the zinc chloride, dried and placed in a 12-inch (30-cm.) evaporating dish. The solution was heated over a light bulb and dry, warm air was blown over its surface. After about a day there was only a very faint odor of benzaldehyde. The resulting crystalline mass was dissolved in chloroform, washed repeatedly with an aqueous solution of sodium bicarbonate to remove the benzoic acid and finally with water. The crystalline residue obtained on solvent removal from the dried (carboraffin) chloroform solution was recrystallized from trichloroethylene; yield 2.9 g., m. p. 233–234°, optically inactive in chloroform solution for the D-line of sodium light. When the substance was dissolved in concentrated sulfuric acid and diluted with water, a distinct odor of benzaldehyde could be noted.

Anal. Calcd. for $C_{20}H_{20}O_6[C(C_6H_5)_3]_2$: C, 82.6; H, 5.98; $C(C_6H_5)_3$, 57.7. Found: C, 82.4; H, 5.78; $C(C_6H_5)_3$, 57.3.

1,5-Dityityl Xylitol Triacetate.—Nineteen grams (2 mols) of trityl chloride was added to 5 g. (1 mol) of xylitol sirup in 25 cc. of dry pyridine and the solution was kept at room temperature for four days, whereupon 15 cc. of acetic anhydride was added. In a few hours a crystalline product separated from the reaction mixture. Recrystallization was effected by solution in hot xylene (carboraffin) followed by the addition of ethanol; yield 17 g., m. p. 206°.

Anal. Calcd. for $C_5H_7O_5(COCH_3)_3[C(C_6H_5)_3]_2$: $C(C_6H_5)_3$, 63.8; CH_3CO, 3.94 cc. 0.1 *N* NaOH per 100 mg. Found: $C(C_6H_5)_3$, 63.7; CH_3CO, 3.81 cc.

1-Trityl[11]-*d*-mannitol Pentaacetate.—Ten grams (2 mols) of dry mannitol, 7.8 g. (1 mol) of trityl chloride and 60 cc. of dry pyridine were heated at 90° for twelve hours, whereupon the solution was cooled and poured in a thin stream into ice and water (2 liters). The precipitated mass hardened on standing at ice box temperature for several hours and was identified as ditrityl mannitol tetraacetate[3] on acetylation; yield of ditrityl mannitol tetraacetate 10 g., m. p. 183–184° (mixed m. p. with an authentic specimen unchanged).

(11) Positions 1 and 6 are equivalent.

The aqueous filtrate above was concentrated until a sticky mass separated. This was removed by chloroform extraction and the sirup obtained on solvent removal from the dried extract was acetylated overnight with pyridine (20 cc.) and acetic anhydride (15 cc.). The crystalline product obtained on pouring the acetylation mixture into ice and water was removed by filtration, washed with water, dried and recrystallized from xylene (carboraffin); yield 4 g., m. p. 163–164°, spec. rot. +35.5° (25°, *c* 4, $CHCl_3$).

Anal. Calcd. for $C_6H_8O_6(COCH_3)_5C(C_6H_5)_3$: $C(C_6H_5)_3$, 38.3; CH_3CO, 7.88 cc. 0.1 *N* NaOH per 100 mg. Found: $C(C_6H_5)_3$, 37.9; CH_3CO, 7.92 cc.

We wish to express our indebtedness to the Atlas Powder Co. for furnishing the mannitol used in this investigation and also for preparing the other sugar alcohols from the corresponding aldoses by high pressure, catalytic reduction. We also wish to express our indebtedness to Mr. H. S. Clark for the microcombustion analyses.

Summary

1. The acetates of monotrityl-*d*-mannitol, dityityl-xylitol, trityl-*l*-fucitol and dityityl-dulcitol have been synthesized.

2. *l*-Fucitol 2,3,4,5-tetraacetate has been synthesized.

3. Detritylation of trityl-*l*-fucitol tetraacetate and of dityityl dulcitol tetraacetate with hydrogen bromide in acetic acid resulted in bromine replacement of the trityl groups.

4. *l*-Fucitol 2,3,4,5-tetraacetate on retritylation produces the original trityl-*l*-fucitol tetraacetate and on treatment with hydrogen bromide the same acetylated bromide is obtained as on detritylation with hydrogen bromide in acetic acid.

5. *l*-Fucitol pentaacetate has been synthesized.

6. On tritylation of dulcitol with pyridine and trityl chloride, a dipyridinium hydrochloride compound of the reaction product is formed, from which the dityityl dulcitol may be obtained, as a monoethyl alcoholate or in the non-solvated form.

7. Dibenzylidene dityityl dulcitol has been synthesized.

8. All compounds reported were obtained in crystalline form and were purified to constant rotation and melting point.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF KANSAS]

The Syntheses of 2-Thio-4-arylthiazolines

BY F. B. DAINS AND ORLAND A. KROBER

Previous investigations[1] have shown that the alkyl and aryl thiocyanates in general add thio acids yielding esters of an acyldithiocarbamic acid. Thus benzyl thiocyanate and thiobenzoic acid gave the benzyl ester of benzoyl-dithiocarbamic acid, $C_6H_5CONHCSSCH_2C_6H_5$, and ethyl thiocyanate and thioacetic acid, the corresponding acetyl-ethyldithiocarbamate. In some cases the reaction is not so smooth and decomposition products are formed.

In view of this interesting addition to the SCN grouping, a study has been made of the action of the thio acids on the phenacyl thiocyanates which contained a labile keto grouping, and hence are capable of secondary reactions. Our results show that phenacyl thiocyanate readily adds thiobenzoic acid, yielding the phenacyl ester of benzoyl-dithiocarbamic acid, $C_6H_5CONHCSSCHCOC_6H_5$, which on heating with dilute hydrochloric acid reacts in the enol form, losing benzoic acid and closing the ring with the formation of 2-thio-4-phenylthiazoline.

$$\underset{\text{S—CS—NHC}(C_6H_5)=\text{CH}}{\text{S—CS—NHC}(C_6H_5)=\text{CH}}$$

In the case of thioacetic acid, only the end-product, the thiazoline, could be isolated.

Experimental

The phenacyl thiocyanates are prepared readily by this general procedure.

A mixture of *p*-bromophenacyl chloride (50 g.), potassium thiocyanate (20 g.) and ethanol (100 cc.) was refluxed for two hours or until the sharp odor of the chloride had disappeared completely. Water was then added and the solid product washed free from mineral salts; the *p*-bromophenacyl thiocyanate (I) (m. p. 147°) was purified by crystallization from alcohol.

The following thiocyanates were synthesized for later use: (II) *p*-chloro, (III) *p*-iodo, (IV) *p*-methoxy and (V) *m*-nitrophenacyl thiocyanate.

TABLE I

			M. p., °C.	N, % Calcd.	N, % Found	S, % Calcd.	S, % Found
I	*p*-Bromophenacyl thiocyanate	C_9H_6BrNOS	147			12.50	12.12
II	*p*-Chlorophenacyl thiocyanate	C_9H_6ClNOS	135	6.64	6.74		
III	*p*-Iodophenacyl thiocyanate	C_9H_6INOS	152	4.63	4.48		
IV	*p*-Methoxyphenacyl thiocyanate	$C_{10}H_9NO_2S$	121			1 .46	15.56
V	*m*-Nitrophenacyl thiocyanate	$C_9H_6N_2O_3S$	119			14.41	14.27
VI	2-Thio-4-phenylthiazoline	$C_9H_7NS_2$	168	7.25	7.19	33.16	33.34
VII	Benzoyl-phenacyl-dithiocarbamate	$C_{16}H_{13}NO_2S_2$	95	4.44	4.51		
VIII	2-Thio-*p*-chlorophenylthiazoline	$C_9H_6ClNS_2$	199			28.13	28.12
IX	Benzoyl-*p*-chlorophenyldithiocarbamate	$C_{16}H_{12}ClNO_2S_2$	148	4.00	4.53		
X	2-Thio-4-bromophenylthiazoline	$C_9H_6BrNS_2$	214	5.19	5.02		
XI	Benzoyl-*p*-bromophenacyl dithiocarbamate	$C_{16}H_{11}BrNO_2S_2$	158	3.55	3.88		
XII	2-Thio-4-iodophenylthiazoline	$C_9H_6INS_2$	220	4.39	4.44	20.06	20.20
XIII	2-Thio-4-*p*-methoxyphenylthiazoline	$C_{10}H_9ONS_2$	194	6.30	6.28	28.73	28.83
XIV	2-Thio-4-*m*-nitrophenylthiazoline	$C_9H_6N_2O_2S_2$	209	11.77	11.59	26.92	26.86
XV	Benzoyl-*m*-nitrophenacyl dithiocarbamate	$C_{16}H_{12}N_2O_4S_2$	157	7.74	7.87	17.80	18.26
XVI	2-Thio-4,5-diphenylthiazoline	$C_{15}H_{11}NS_2$	214	5.20	5.10	23.84	23.78
XVII	2-Benzylthio-4,5-diphenylthiazoline	$C_{22}H_{17}NS_2$	106	3.90	3.40		
XVIII	2-Thio-4-thiazolidone	$C_3H_3NOS_2$	168	10.53	10.37		

Synthesis of the Thiazolines

2-Thio-4-phenylthiazoline (VI).[2]—Phenacyl thiocyanate (14 g.), thioacetic acid (12 g.) and benzene (60 cc.) were heated for three hours on a steam-bath. After concentrating the solution and cooling, the thiazoline was filtered off and purified from alcohol. The light yellow crystals which were soluble in alkali melted at 168°.

The intermediate acetyl-phenacyldithiocarbamate was not isolated in this or any other case where thioacetic acid was used, but with thiobenzoic acid such intermediate

(1) Chanlaroff, *Ber.*, **15**, 1887 (1882); Wheeler and Merriam, THIS JOURNAL, **23**, 283 (1901); Wheeler, *Am. Chem. J.*, **26**, 345 (1901); Wheeler and Johnson, *ibid.*, **26**, 185 (1901).

(2) The compound had been made previously by Miolati by the action of phenacyl bromide on ammonium dithiocarbamate [*Gazz. chim. ital.*, **23**, I, 580 (1893)].

dithiocarbamates were more stable and were obtained in a pure condition.

Action of Thiobenzoic Acid.—Molar quantities of phenacyl thiocyanate and thiobenzoic acid were heated in benzene solution for four hours. The product isolated melted at 95° and corresponded to benzoyl-phenacyl-dithiocarbamate (VII), $C_6H_5CONHCSSCH_2COC_6H_5$, since on heating with dilute hydrochloric acid it gave benzoic acid and the thiazoline (VI), m. p. 168°.

As shown in the table, thiazolines were obtained from thiocyanates I–V, using thioacetic and thiobenzoic acids, but the intermediate dithiocarbamates were isolated only in some cases with thiobenzoic acid.

2-Thio-4,5-diphenylthiazoline (XVI).—Desyl thiocyanate and thioacetic acid gave in good yield this thiazoline (m. p. 214°).

Wheeler and Johnson[3] on treating the desyl thiocyanate with thiobenzoic acid, had isolated an unidentified compound melting at 137°, which was doubtless the benzoyl addition product. Using the same reagents, evidence was obtained of an immediate product melting about 132–133° which went over readily into the diphenylthiazoline (m. p. 214°).

The enol nature of the thiazoline was shown by the formation of a 2-benzyl ether (XVII) when the diphenylthiazoline was treated with benzyl chloride.

Rhodanine. 2-Thio-4-thiazolidone, XVIII.—Diethyl thiocyanomalonate was heated in benzene solution with thiobenzoic acid.[4] On distilling off the benzene, an oil was left which failed to crystallize and had the odor of ethyl benzoate. When this oil was evaporated to dryness with dilute hydrochloric acid, rhodanine was obtained (m. p. 166°). Its identity was proved by analysis and comparison with a synthetic specimen.

(3) Wheeler and Johnson, *Am. Chem. J.*, **26**, 202 (1901).

Summary

This paper describes the syntheses of several substituted aryl thiocyanates and their behavior with thioacetic and thiobenzoic acids. The final products in all cases were 2-thio-4-arylthiazolines, but with thiobenzoic acid the more stable intermediates, benzoyl-phenacyl-dithiocarbamates, were isolated.

(4) Wheeler, *Am. Chem. J.*, **26**, 351 (1911), described the intermediate, the benzoyl-dithiourethan; but did not hydrolyze it. Rhodanine was also obtained by Miolati [*Ann.*, **262**, 62–85 (1891)] from chloroethyl acetate and ammonium dithiocarbamate.

LAWRENCE, KANSAS RECEIVED MAY 15, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF BRYN MAWR COLLEGE, AND FROM THE NATIONAL INSTITUTE OF HEALTH, U. S. PUBLIC HEALTH SERVICE]

2,4,6-Trimethyl-β-phenyl- and Benzyl-D-glucosides[1]

BY NELSON K. RICHTMYER

In a previous study on the cleavage of glycosides by catalytic hydrogenation,[2] mention was made of a trimethyl-β-phenylglucoside and a trimethyl-β-benzylglucoside in which the methyl groups were located presumably in the 2,4,6-positions of the glucose chain. The appearance of four recent papers dealing with 2,4,6-trimethylglucose and its derivatives makes a description of the two named glucosides seem desirable at this time.

2,4,6-Trimethyl-D-glucose was obtained first by Haworth and Sedgwick[3] through the hydrolysis of partially methylated glucose and sucrose. The allocation of methoxyl groups was confirmed later by Oldham[4] through a synthesis, the details of which have just been published. Recently, Lake and Peat[5] isolated 2,4,6-trimethylglucose by acid hydrolysis of the corresponding β-methylglucoside which is one of the products resulting from the action of boiling sodium methylate on 4,6-dimethyl-2,3-anhydro-β-methyl-D-mannoside. Barker, Hirst and Jones[6] have separated it from the products arising from incomplete methylation of α-methylglucoside with methyl iodide and thallous hydroxide. Freudenberg and Plankenhorn[7] synthesized it by methylation of 3-benzylglucose, followed by reductive cleavage of the benzyl group and acid hydrolysis of the glycosidic methoxyl group. It is of interest to note also that, from the cell wall of yeast, Zechmeister and Tóth[8] have isolated a glucose polysaccharide, which, after methylation and hydrolysis, furnished this same 2,4,6-trimethylglucose.

Tetraacetyl-β-phenylglucoside is readily accessible through the condensation of phenol with glucose pentaacetate, in the presence of *p*-toluenesulfonic acid as catalyst according to Helferich and Schmitz-Hillebrecht.[9] The incomplete

(1) Publication authorized by the Surgeon General, U. S. Public Health Service.

(2) Richtmyer, THIS JOURNAL, **56**, 1637 (1934).

(3) Haworth and Sedgwick, *J. Chem. Soc.*, 2573 (1926).

(4) Oldham, THIS JOURNAL, **56**, 1360 (1934); Oldham and Oldham, *ibid.*, **61**, 1112 (1939).

(5) Lake and Peat, *J. Chem. Soc.*, 1417 (1938).

(6) Barker, Hirst and Jones, *ibid.*, 1695 (1938).

(7) Freudenberg and Plankenhorn, *Ann.*, **536**, 256 (1938).

(8) Zechmeister and Tóth, *Biochem. Z.*, **270**, 309 (1934).

(9) Helferich and Schmitz-Hillebrecht, *Ber.*, **66**, 380 (1933).

methylation of β-phenylglucoside or its tetraacetate with methyl sulfate and alkali, as described below, yields crystalline 2,4,6-trimethyl-β-phenyl-D-glucoside as the product most readily separated from the mixture[10]; this series of reactions, followed by acid hydrolysis of the glucoside, offers a suitable method for the preparation of crystalline 2,4,6-trimethyl-D-glucose.

Crystalline 2,4,6-trimethyl-β-benzyl-D-glucoside has been obtained similarly from the incomplete methylation of β-benzylglucoside.

Experimental

2,4,6-Trimethyl-β-phenyl-D-glucoside.—To a solution of 100 g. of β-phenyl-D-glucoside dihydrate in 200 cc. of water (or an equivalent amount of tetraacetyl-β-phenyl-D-glucoside suspended in sufficient 50% aqueous sodium hydroxide to deacetylate it) was added 180 cc. of 50% aqueous sodium hydroxide and 100 cc. of methyl sulfate. The mixture was stirred mechanically, heated to 95° in a water-bath, cooled, and the process repeated until a total of 2160 cc. of alkali and 1200 cc. of methyl sulfate had been added. The methylated phenylglucoside, which crystallized in needles or small pellets when the reaction mixture was cooled, was extracted completely with ether, and the ethereal solution washed with water, dried with granular calcium chloride and concentrated. From the sirup, by fractional crystallization with ether and petroleum ether (b. p. 26–30°), was isolated 14.5 g. of 2,4,6-trimethyl-β-phenyl-D-glucoside in glistening, prismatic needles, melting at 108–109°, and with $[\alpha]_D$ −57.5° in chloroform (*c*, 2).

Anal. Calcd. for $C_{15}H_{22}O_6$: C, 60.37; H, 7.44; OCH_3, 31.21. Found: C, 60.38; H, 7.58; OCH_3, 30.95.

A second product having the composition also of a trimethyl-β-phenyl-D-glucoside was isolated in small amounts. It melted at 105–106°; a mixture with the 2,4,6-isomer melted at 80–95°.

Anal. Calcd. for $C_{15}H_{22}O_6$: C, 60.37; H, 7.44; OCH_3, 31.21. Found: C, 60.31; H, 7.33; OCH_3, 31.21.

Hydrolysis to 2,4,6-Trimethyl-D-glucose.—A solution of 3 g. of the 108–109° trimethylphenylglucoside in 200 cc. of 5% aqueous hydrochloric acid was boiled four hours under a reflux condenser. The solution was neutralized with solid barium carbonate, concentrated *in vacuo* to a small volume, and extracted with ether in a Soxhlet apparatus arranged for the continuous extraction of liquids. The ethereal solution deposited prismatic needles of 2,4,6-trimethyl-D-glucose which was identified by direct comparison with a specimen supplied through the courtesy of Dr. J. W. H. Oldham.[4] The two specimens, alone or mixed, melted at 122–123° when heated rapidly, and at 113–122° when heated slowly in soft glass melting point tubes. A mixture of the new 2,4,6-isomer with an authentic sample of 2,3,6-trimethylglucose melted at 87–105°. The rotation, $[\alpha]_D^{20}$ +111° in methyl alcohol (*c*, 1), changed in six days at 20° to $[\alpha]_D^{20}$ +71° (constant) upon the addition of a drop of concentrated hydrochloric acid; these values are in agreement with the earlier data, and distinguish clearly between the 2,4,6- and the 2,3,6-trimethylglucoses.[7]

Anal. Calcd. for $C_9H_{18}O_6$: C, 48.62; H, 8.17; OCH_3, 41.90. Found: C, 48.58; H, 7.96; OCH_3, 41.93.

2,4,6-Trimethyl-β-benzyl-D-glucoside.—To a solution of 32 g. of β-benzyl-D-glucoside in 100 cc. of water was added 44 cc. of methyl sulfate and 80 cc. of 50% aqueous sodium hydroxide; the mixture was stirred mechanically, heated to 70° with a water-bath, cooled, and the process repeated with nine more portions of methyl sulfate and alkali. After the final addition, the water was kept at 100° for one hour to decompose any excess methyl sulfate. The product was extracted with chloroform, concentrated, and methylated again with the same quantities of reagents. The methylated benzylglucoside was extracted with chloroform, and the chloroform solution washed with water, dried over calcium chloride, and concentrated *in vacuo*. With the aid of ether and petroleum ether (b. p. 26–30°) there was obtained 4.6 g. of 2,4,6-trimethyl-β-benzyl-D-glucoside; a thrice recrystallized sample melted at 94–95°, and showed $[\alpha]_D^{20}$ −49.1° in chloroform (*c*, 2).

Anal. Calcd. for $C_{16}H_{24}O_6$: C, 61.50; H, 7.75; OCH_3, 29.81. Found: C, 61.54; H, 8.15; OCH_3, 29.50.

Hydrolysis to 2,4,6-Trimethyl-D-glucose.—A 1.5-g. sample of the trimethylbenzylglucoside was heated with 5% aqueous hydrochloric acid, and the product isolated and identified as described above.

This work has been aided by a grant from the Cyrus M. Warren Fund of the American Academy of Arts and Sciences. The author desires to thank the Chemical Foundation of New York for a Research Associateship which he held while completing a portion of the research.

Summary

2,4,6-Trimethyl-β-phenyl-D-glucoside has been obtained through incomplete methylation of β-phenyl-D-glucoside. The method is recommended for the preparation of 2,4,6-trimethyl-D-glucose.

2,4,6-Trimethyl-β-benzyl-D-glucoside has been described.

WASHINGTON, D. C. RECEIVED MAY 8, 1939

(10) Work on the separation of the other components has been discontinued; tetramethyl-β-phenyl-D-glucoside is described by Voss and Wachs, *Ann.*, **522**, 252 (1936).

[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF HEALTH, U. S. PUBLIC HEALTH SERVICE]

The Behavior of Glucose Dimethylacetal toward Carbohydrases[1]

BY NELSON K. RICHTMYER, MILDRED ADAMS AND C. S. HUDSON

Under the title "The Enzymotic Cleavage of Acetals," Neuberg and Ziffer[2] have reported that acetal itself (acetaldehyde diethylacetal) is subject to enzymotic hydrolysis by top yeast, by taka-diastase, and by commercial emulsin, in aqueous solution at 37° in the presence of calcium carbonate and toluene. Upon the appearance of that paper, our own experiments, which were then in progress, on the behavior of glucose dimethylacetal[3] toward various carbohydrases were extended to include the conditions used by Neuberg and Ziffer. In no case, however, have we been able to detect any cleavage of glucose dimethylacetal by top yeast, taka-diastase, emulsin, maltase, invertase, pancreatic amylase, or malt amylase. The conditions of temperature, time, *p*H, and the final rotation of the solutions are recorded in Table I; the details of the enzyme preparations, amounts, and activities are reported in the Experimental section.

TABLE I

GLUCOSE DIMETHYLACETAL AND CARBOHYDRASES

Enzyme	*p*H	Buffer	Time, hrs.	Temp., °C.	$[\alpha]^{20}D$[a]
Invertase	7.1	Phosphate[b]	20	20	+14.2°
Invertase	5.1	Phosphate	20	20	15.3
Maltase	6.9	Phosphate	21	20	14.0
Emulsin	5.4	Acetate[c]	68	20	14.7
Malt amylase	4.6	Acetate	65	20	14.3
Pancreatic amylase	7.1	Phosphate[d]	22	20	14.2
Taka-diastase	5.2	Phosphate	20	20	14.4
Taka-diastase	7.1	Phosphate	20	20	14.1
"Clarase"	5.3	Phosphate	23	20	14.0
Taka-diastase (concd.)	5.5	Acetate	24	20	13.7
Taka-diastase (concd.)	[e]	[e]	24	38	14.6
Emulsin	[e]	[e]	24	38	15.6
Top yeast	[e]	[e]	45	38	14.2

[a] The specific rotation of the glucose dimethylacetal was +14.3 ± 0.3° in water (*c*, 5); if completely hydrolyzed to glucose its apparent specific rotation would be +41.8°. All other specific rotations are correct to ±0.9°. [b] The phosphate buffers are about 1% in sodium phosphates. [c] The acetate buffers are about 0.1 or 0.2 *N* in acetic acid–sodium acetate mixtures. [d] The solution was also 0.04 *M* in sodium chloride. [e] The aqueous solution contained no buffer except solid calcium carbonate; two drops of toluene were added.

Our results are in accord with the statement by Pacsu[4] that fructose dimethylacetal is not affected by yeast at *p*H 7, or by invertase at *p*H 4 or 7. The failure of these glucose and fructose acetals to be cleaved by enzymes, however, must not be construed as evidence that other acetals may not be susceptible to enzymotic hydrolysis.

Experimental

Cleavage Experiments.—A weighed amount of glucose dimethylacetal[3] in a volumetric flask, such that the final concentration would be 2 g. per 100 cc., was dissolved in the desired buffer solution, a definite weight or volume of the enzyme added, and the flask filled to the mark with additional buffer solution. After standing for the length of time and at the temperature noted in Table I, the solution was adjusted to volume and filtered if necessary, and the rotation observed in a 1-dm. tube at 20°.

Invertase.—An autolysate of bakers' yeast was dialyzed, and treated with bentonite as described previously.[5] The eluate was concentrated and purified further by precipitation with ammonium sulfate; the aqueous extract, after dialysis, contained 32.6 invertase units[6] in 100 cc., with a time value[6] of 0.20 minute. For the cleavage experiments, 0.5 g. of the acetal, in the desired buffer solution, was treated with 1 cc. of the invertase solution in a total volume of 25 cc.

Maltase.—The fractional autolysis of brewers' yeast according to Weidenhagen[7] produced a maltase solution of concentration such that 1.25 g. of maltose in a total volume of 25 cc., containing 1% phosphate buffer of *p*H 6.9, was 50% hydrolyzed by 5 cc. of the enzyme solution in one hundred and eighty-seven minutes at 20°. The enzyme solution was capable also of hydrolyzing α-methylglucoside. For the cleavage experiment, 5 cc. of the maltase solution was used with 0.5 g. of the acetal.

Emulsin.—Sweet almond emulsin was obtained by the zinc sulfate and tannic acid procedure of Helferich and his collaborators.[8] The activity of the enzyme was such that 25 cc. of a 2% solution of salicin in about 0.2 *N* sodium acetate buffer of *p*H 5.0 was 50% hydrolyzed by 1 cc. of emulsin solution in ten and two-tenths minutes at 20°. For the cleavage experiments 1 cc. of emulsin was added to 0.5 g. of the acetal.

Malt Amylase.—The aqueous extract from distillers' barley malt was purified by the method of Sherman, Caldwell and Doebbeling.[9] The enzyme preparation had an activity of 1240 on the scale of Sherman, Kendall and Clark[10]; this is a measure of the saccharogenic rather than

(1) Publication authorized by the Surgeon General, U. S. Public Health Service.

(2) Neuberg and Ziffer, *Enzymologia*, **5**, 389 (1939).

(3) Wolfrom and Waisbrot, THIS JOURNAL, **60**, 855 (1938).

(4) Pacsu, THIS JOURNAL, **60**, 2278 (1938).

(5) Adams and Hudson, *ibid.*, **60**, 982 (1938).

(6) C. Oppenheimer, "Die Fermente und ihre Wirkungen," fifth edition, 1928, Vol. III, pp. 770–774.

(7) Weidenhagen, *Z. Ver. deut. Zuckerind.*, **80**, Tech. Tl. 157 (1930).

(8) Helferich, Winkler, Gootz, Peters and Günther, *Z. physiol. Chem.*, **208**, 95 (1932).

(9) Sherman, Caldwell and Doebbeling, *J. Biol. Chem.*, **104**, 501 (1934).

(10) Sherman, Kendall and Clark, *J. Biol. Chem.*, **32**, 1073 (1910).

of the amyloclastic power. No cleavage was observed when 10 mg. of enzyme was added to 0.2 g. of the acetal.

Pancreatic Amylase.—The method of purification of Sherman and Schlesinger[11] yielded a product with a saccharogenic activity[10] of 3300. Of this amylase, 6 mg. was without effect on 0.5 g. of the acetal.

Taka-diastase.—This was a commercial preparation with a saccharogenic activity of 10.

"Clarase."—This was a more concentrated commercial preparation of the amylase from *Aspergillus oryzae*, and had a saccharogenic activity of 28. With each of these last two preparations 15 mg. was added to 0.5 g. of the acetal.

Taka-diastase, Concentrated.—Commercial taka-diastase was purified to a saccharogenic activity of 390 by the method of Sherman and Tanberg[12]; it had no action when 10 mg. was added to 0.2 g. of the acetal.

Top Yeast.—To 0.5 g. of the acetal was added 100 mg. of washed top yeast, from the Gunther Brewing Co. of Baltimore, Maryland.

(11) Sherman and Schlesinger, THIS JOURNAL, **34**, 1104 (1912).

One of the authors (N. K. R.) desires to thank the Chemical Foundation of New York for a Research Associateship.

Summary

Glucose dimethylacetal was not hydrolyzed, under a variety of conditions, by invertase, maltase, emulsin, malt amylase, pancreatic amylase, taka-diastase, or top yeast.

(12) Sherman and Tanberg, *ibid.*, **38**, 1638 (1916).

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[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF HEALTH, U. S. PUBLIC HEALTH SERVICE]

The Cleavage of Cellobiose and Celtrobiose by Emulsin[1]

BY NELSON K. RICHTMYER AND C. S. HUDSON

In a recent paper by Helferich and Pigman[2] it was reported that the β-galactosido linkage of neolactose (4-β-D-galactosido-D-altrose)[3] was cleaved by sweet almond emulsin only one-seventh as rapidly as the similar linkage of lactose (4-β-D-galactosido-D-glucose). The difference in the ease of hydrolysis of the two β-galactosides was attributed to the change in configuration of the third carbon atom of the glucose molecule which occurs (together with an inversion about the second carbon atom) during the transformation of lactose into neolactose; the effect was likened to that of ortho-substitution, contrasted to that of meta- or para-substitution, in the hydrolysis of phenylglucosides by sweet almond emulsin.[4]

With the corresponding β-glucosides, cellobiose (4-β-D-glucosido-D-glucose) and celtrobiose (4-β-D-glucosido-D-altrose),[5] available in this Laboratory, we decided to make a similar comparison of their behavior toward sweet almond emulsin. The cleavage of cellobiose by emulsin was observed first by Fischer and Zemplén,[6] and has been studied more recently by Weidenhagen[7] and by Helferich, Gootz and Sparmberg.[8]

In Tables I and II are recorded the data obtained in our comparisons of the action of emulsin upon the two disaccharides. The hydrolysis constants are based on the assumption that the reactions are unimolecular. The ratio of the average value of the constants, 10.8:1.59, indicates that cellobiose is hydrolyzed 6.8 times more rapidly than celtrobiose under the same conditions. The lengths of time required for 50% hydrolysis of the disaccharides, as obtained by interpolation, are 281 and 2105 minutes for cellobiose and celtrobiose, respectively; their ratio indicates that cellobiose is hydrolyzed 7.5 times more rapidly than celtrobiose. For 25% hydrolysis, a quotient of 6.7 is obtained. Thus it appears that the inversion of H and OH which is brought about on the second and especially on the third carbon atoms of the reducing glucose molecule in the transformation of cellobiose to celtrobiose has the same effect upon the rates of hydrolysis of these disaccharides as does the similar change of configuration in the corresponding β-galactosides lactose and neolactose. The

(1) Publication authorized by the Surgeon General, U. S. Public Health Service.

(2) Helferich and Pigman, *Ber.*, **72**, 212 (1939).

(3) Richtmyer and Hudson, THIS JOURNAL, **57**, 1716 (1935).

(4) Helferich and Scheiber, *Z. physiol. Chem.*, **226**, 272 (1934).

(5) Richtmyer and Hudson, THIS JOURNAL, **58**, 2534 (1936).

(6) Fischer and Zemplén, *Ann.*, **365**, 1 (1909).

(7) Weidenhagen, *Z. Ver. deut. Zuckerind.*, **80**, Tech. Tl. 11 (1930).

(8) Helferich, Gootz and Sparmberg, *Z. physiol. Chem.*, **205**, 201 (1932).

change from D-glucose to D-altrose in the "aglycone" portion of the glycosides, which has resulted in the hydroxyl on carbon atom 3 being nearer spatially to the glycosidic union at carbon atom 4, as interpreted by the customary models, has produced such a steric hindrance to cleavage of the disaccharide linkage at carbon atom 4 that the velocity of hydrolysis has been reduced to one-seventh of its original rate.

The fact that celtrobiose is hydrolyzed by the β-glucosidase of sweet almond emulsin, and is not cleaved by maltase (an α-glucosidase), confirms the assignment of the β-glucosidic linkage in celtrobiose; this linkage had been assumed previously because the sugar was prepared from cellobiose.

TABLE I

THE CLEAVAGE OF CELLOBIOSE BY EMULSIN AT 20° AND *p*H 5.0

Time, min.	$\alpha^{20}D$	% cleavage	$K \times 10^4$
0	(+1.68°)	0	..
60	1.80	12.8	9.9
65	1.82	14.9	10.8
120	1.94	26.3	11.1
180	2.04	37.4	11.3
210	2.09	42.7	11.5
255	2.14	47.0	10.8
300	2.18	52.0	10.6
420	2.29	63.0	10.3
(∞)	(2.65)	(100.0)	..
		Average	10.8

TABLE II

THE CLEAVAGE OF CELTROBIOSE BY EMULSIN AT 20° AND *p*H 5.0

Time, min.	$\alpha^{20}D$	% cleavage	$K \times 10^4$
0	(+0.69°)	0	..
75	.74	3.6	2.09
420	.91	15.2	1.70
1440	1.27	40.3	1.55
1860	1.37	47.2	1.49
2850	1.55	59.0	1.36
3300	1.62	63.8	1.35
(∞)	(2.15)	(100.0)	..
		Average	1.59

Experimental

Emulsin (β-D-Glucosidase) was prepared[9] by extraction of defatted sweet almond meal with zinc sulfate solution, fractional precipitation of the enzyme with tannic acid, removal of the tannic acid with acetone and extraction of the emulsin from the residue with water. The product had a small negative rotation, necessitating a slight correction in later observations. Although the actual β-glucosidase value was not determined, the activity of the enzyme was such that 25 cc. of a 2% solution of salicin in about 0.2 *N* acetic acid–sodium acetate buffer of *p*H 5.0 was 50% hydrolyzed by 1 cc. of emulsin solution in 10.2 minutes at 20°.

The enzymotic hydrolyses were carried out by dissolving 4.000 g. of cellobiose or 4.211 g. of celtrobiose monohydrate, respectively, in about 0.2 *N* acetic acid–sodium acetate buffer of *p*H 5.0, adding 4 cc. of the emulsin solution at zero time, and diluting with a small additional amount of buffer exactly to 100 cc. at 20°. The cellobiose solution was kept in a water-bath at 20 ± 0.1°, and the celtrobiose solution in a room at 20 ± 1°. At appropriate times, a 15-cc. portion of the desired solution was removed, and 10 cc. of *N* aqueous sodium carbonate added to stop the enzyme action and to complete the mutarotation of the sugars. The optical rotation was observed after five minutes, in a 2-dm. tube at 20°. The data are recorded in Tables I and II, with the percentage cleavage, and the hydrolysis constants calculated in minutes and decimal logarithms.

Maltase (α-D-Glucosidase) was prepared by the fractional autolysis of brewers' yeast with ethyl acetate according to Weidenhagen[10]; although the solution was decidedly active toward maltose and α-methyl-D-glucoside, no evidence of cleavage of celtrobiose could be detected at *p*H 7.0 in forty-eight hours at 20°.

One of the authors (N. K. R.) desires to thank the Chemical Foundation of New York for a Research Associateship.

Summary

Celtrobiose is hydrolyzed by sweet almond emulsin only one-seventh as rapidly as cellobiose. This relationship is in agreement with the experience of Helferich and Pigman with the corresponding galactosides, neolactose and lactose.

The cleavage of celtrobiose by emulsin, but not by maltase, is presented as confirmatory evidence for a β-glucosidic linkage in celtrobiose (4-β-D-glucosido-D-altrose).

WASHINGTON, D. C. RECEIVED MAY 24, 1939

(9) Helferich, Winkler, Gootz, Peters and Günther, *Z. physiol. Chem.*, **208**, 95 (1932).

(10) Weidenhagen, *Z. Ver. deut. Zuckerind.*, **80**, Tech. Tl. 157 (1930).

[CONTRIBUTION FROM THE BUREAU OF ENTOMOLOGY AND PLANT QUARANTINE, UNITED STATES DEPARTMENT OF AGRICULTURE]

The Constituents of Certain Species of Helenium. II. Tenulin

BY E. P. CLARK

In the first paper of this series[1] attention was directed to a statement by Reeb[2] that helenalin from *Helenium autumnale* is a vermifuge. The writer has found it to be a fairly effective fish poison, and in unpublished experiments entomologists of this Bureau have shown that it has possibilities as an insecticide. These facts stimulated investigation of other species of the genus for possible sources of helenalin or other materials likely to be related to it. The results of this work have shown that *Helenium macrocephalum* also contains helenalin, while three other species—*H. tenuifolium*, *H. elegans*, and *H. badium*—contain a crystalline substance hitherto unreported. This material has been named "tenulin" from *H. tenuifolium*, the plant from which it was first obtained.

Tenulin was prepared from the species of *Helenium* mentioned above by extraction and crystallization from organic solvents. Because of the retention of solvent of crystallization, it separates from a number of such solvents with different melting points, but after undergoing some purification it may be recrystallized from water or aqueous organic solvents and then has a constant composition represented by $C_{17}H_{22}O_5$ and a melting point of 193–195°.

It is bitter and mildly sternutative and has a pronounced toxic effect upon fish in a concentration of 1–5000.

Tenulin is optically active; $[\alpha]^{20}D$ is $-21.7°$ in ethanol. Reactions for hydroxyl, carboxyl, and carbonyl groups have so far given negative results. Alkoxyl groups are absent, but it does give a small quantity of alkyl iodide, which when calculated to methoxyl corresponds to approximately 0.5%. Hydrogenation of tenulin yields a dihydro compound which readily gives a phenylhydrazone, whereas the unreduced material does not. Upon bromination, two atoms of bromine are added, indicating a double bond or its equivalent. One of the bromine atoms, however, is readily lost, and a monobromo compound is formed. When a small tube containing tenulin is plunged into a bath at 300°, the material melts with the rapid evolution of gas. As the bath cools to 275°, the reaction is complete and a golden-colored melt results, which yields a crystalline substance, m. p. 172°. This has been shown by analysis to be anhydrotenulin, $C_{17}H_{20}O_4$. The action of acetic anhydride and sodium acetate upon tenulin is anomalous. A product is obtained which analyzes for $C_{22}H_{26}O_5$ but does not contain acetyl.

Mild treatment of tenulin with alkali converts it to an isomer which melts, according to the method of making it, at 158–162°. The following procedures were used to obtain this isomer, which has been designated isotenulin: (1) triturating finely powdered tenulin with 0.1 *N* sodium hydroxide for three minutes; (2) triturating finely powdered tenulin with 5% sodium carbonate solution and allowing the mixture to stand for periods of fifteen minutes to twenty-four hours; (3) boiling an aqueous solution of tenulin with norit, which because of the alkaline reaction imparted to the solution by the carbon caused isomerization; and finally (4) treating an aqueous methanolic solution with a small quantity of 1% sodium hydroxide.

According to the procedure used, practically pure isotenulin or a mixture of isotenulin and a new substance, $C_{15}H_{20}O_4$, m. p. 255°, may be obtained.

Isotenulin is of interest because it is the compound described in 1937 by Buehler, Whitehead, and Goodge,[3] which they obtained from *Helenium tenuifolium*. These investigators reported upon an indefinite material which melted over a range of 152–170°. It was not purified or analyzed, but upon treatment with dilute sodium carbonate solution gave a well-defined compound, $C_{17}H_{22}O_5$, which melted at 158°. This is the material designated above as isotenulin. They record three derivatives of it: a monobromo compound, m. p. 200°; a dihydro compound, m. p. 150.8°; and a phenylhydrazone of the latter, m. p. 209–210°.

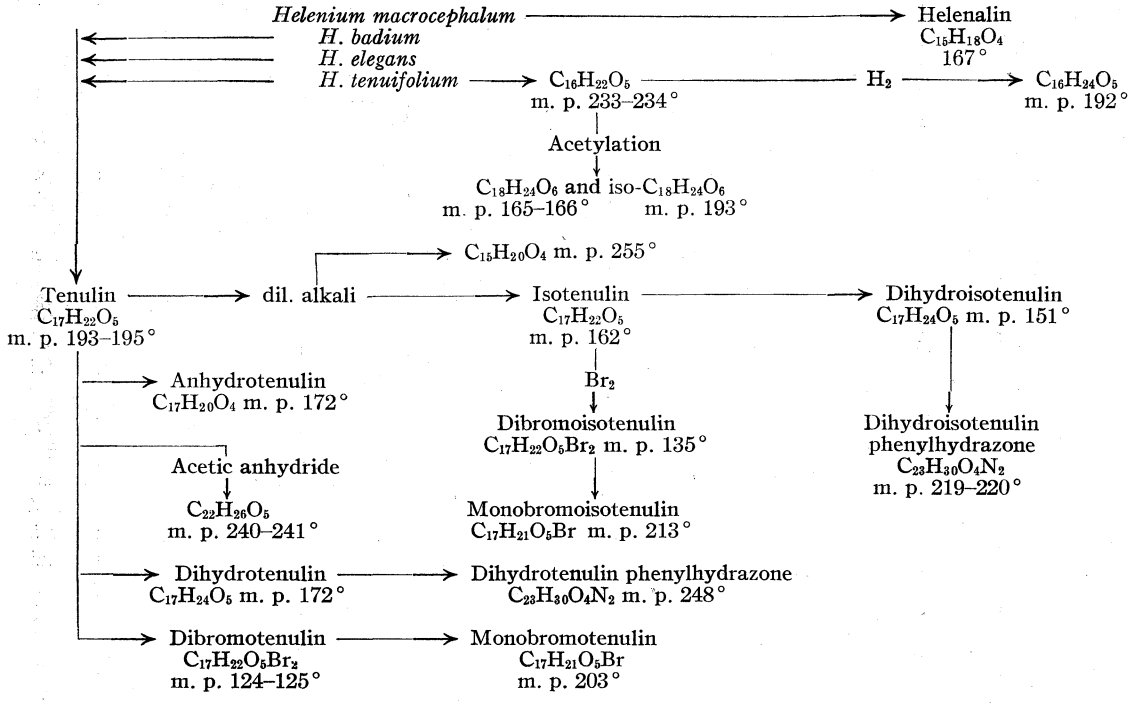
A comparison of the melting points recorded by Buehler and co-workers for these substances with isotenulin and the corresponding derivatives which were made for the purpose agree only in two

(1) Clark, THIS JOURNAL, **58**, 1982 (1936).

(2) Reeb, *J. Pharm. Elsas Lothringen*, **37**, 149 (1910).

(3) Buehler, Whitehead and Goodge, THIS JOURNAL, **59**, 2299 (1937).

DIAGRAM SHOWING THE INTERRELATIONS OF THE VARIOUS SUBSTANCES UNDER CONSIDERATION



instances, namely, isotenulin and its dihydro derivative. The phenylhydrazone of dihydroisotenulin melts at 219–220°, and bromination of isotenulin according to Buehler's method yields a dibromo compound, m. p. 135°. This, however, can be converted readily to a monobromo derivative, m. p. 213°. In spite of these differences, it is quite safe to say that the material obtained by Buehler and co-workers is isotenulin, for in working up plant extracts according to their directions the writer obtained isotenulin.

The preparation of tenulin from different lots of *Helenium tenuifolium* was accompanied by considerable variation in yields and in the ease with which the material was obtained. Some samples contained relatively large quantities of non-crystallizable material, which greatly inhibited the crystallization of tenulin. One shipment of *H. tenuifolium*, obtained in 1936, gave with difficulty poor yields of crystalline material, while the same drug, obtained in 1934 from essentially the same location, gave a clean extractive from which tenulin was obtained with ease.

Upon treatment for purification the material used in 1936 was found to consist of about 60% of tenulin and 40% of another compound, $C_{16}H_{22}O_5$. This C_{16} material gave a dihydro derivative, $C_{16}H_{24}O_5$, and two isomeric monoacetyl derivatives. One of these, obtained by the action of boiling acetic anhydride and sodium acetate, melted at 165–166°; the other, made by allowing the material to react with acetic anhydride and cold pyridine, melted at 193°. The new compound contains no alkoxyl groups, but under the conditions employed to determine these groups an alkyl iodide was obtained, which when calculated to methoxyl corresponded to 3.8%. This reaction strongly indicates a diortho-substituted isopropyl group.[4]

No attempt is made here to interpret the reactions under consideration, but they serve to characterize tenulin, show its relation to Buehler, Whitehead, and Goodge's compound, and indicate the occurrence of several apparently closely related compounds in certain species of *Helenium*. A summary of the sources of the various products under consideration and their relation to each other is given in the accompanying diagram.

Experimental

Helenalin from Helenium macrocephalum.—This plant, which yields helenalin, was treated in the manner described for obtaining helenalin from *H. autumnale*.[1]

Preparation of Tenulin from Different Plant Sources.—The following procedure for preparing tenulin is the most satisfactory of several employed. This method was used in processing all three species of *Helenium* containing tenulin mentioned before.

(4) Clark, THIS JOURNAL, **51**, 1479 (1929); Adams and Butterbaugh, *ibid.*, **60**, 2174 (1938).

Twenty-five hundred grams of ground whole plant was moistened with 2 liters of chloroform and allowed to stand in a tight container overnight. The drug was then packed in a percolator and extracted with 10 liters of chloroform. The extract was concentrated under diminished pressure to a thick sirup and then dissolved in 1.5 liters of hot ethanol. The alcoholic liquid was diluted with 6 liters of boiling water and acidified (litmus) with acetic acid, and a solution of 20 g. of normal lead acetate was added. After standing overnight the solution cleared and was filtered through a folded filter paper. The filtrate was evaporated under reduced pressure to 1 liter and then extracted with chloroform. The chloroform extract was dried with sodium sulfate and evaporated under reduced pressure to a thick sirup, which was dissolved in boiling benzene and allowed to crystallize.

This procedure gave satisfactory results with all species of *Helenium* except occasionally *tenuifolium*. In these cases the thick chloroform extract was dissolved in 250 cc. of methanol, 75 cc. of ethylene glycol was added, and most of the methanol removed by distillation under reduced pressure. The resulting glycol solution was removed from the flask with the aid of 20 cc. of hot methanol and treated with water until turbidity occurred. It was then placed in a cool box and allowed to crystallize. The yield was usually 1.5% of the weight of the drug.

The purification of the material obtained by either of the foregoing procedures was accomplished in several ways:

(1) Five grams of crude tenulin was dissolved in 20 cc. of hot ethylene glycol. To this solution was added 60 cc. of water. Crystallization soon began and yielded 3.6 g., m. p. 183°.

(2) Tenulin was dissolved in the necessary quantity of *n*-butanol, and 4 volumes of *n*-butyl ether was added. The material melted at 191° and cleared at 196°. The melting point frequently varied, however, as illustrated in the following experiment. Tenulin with a melting point of 191° was recrystallized several times from butanol and butyl ether as above. The first recrystallization gave a product which melted at 178°, the second at 183°, the third at 186°, and the fourth at 175°. In all cases the product separated as dense prisms. Apparently all the different specimens were pure but contained solvent.

(3) The best method thus far found was to dissolve the crude substance in acetone and add to this a relatively large quantity of hot water (250 cc. of water to 5 g. of tenulin), then evaporate the resulting liquid under reduced pressure, and remove the crystals from time to time. When pure material thus prepared was allowed to dry in the air, it melted at 193–195° and analyzed for a compound with the composition $C_{17}H_{22}O_5$.

(4) Highly colored material was purified as follows. A solution of 10 g. of substance in 10 cc. of boiling *n*-butanol was diluted with 80 cc. of benzene and allowed to crystallize. This removed much of the color, and it could then be recrystallized from water.

When pure and recrystallized from water, tenulin consists of six-sided plates, frequently forming clusters which break into angular fragments. It melts at 193–195°. Its indices of refraction, determined by the immersion method, are: η_α, 1.525; η_β, 1.565; η_γ, 1.585; all ± 0.003. All the indices are readily found. The birefringence is extremely strong, and the polarization colors are brilliant. In convergent polarized light (crossed nicols) partial biaxial figures are seen on many of the plates. The optic axis is perpendicular to many of them. The acute bisectrix was difficult to obtain; therefore, a determination of the axial angle could not be made.[5]

Tenulin is optically active; 115.46 mg. dissolved in 2.28 cc. of ethanol ($C = 5.2$) at 20° rotated the plane of polarized light in a 96-mm. tube 1.1° to the left; $[\alpha]^{20}D$ is −21.6°. 4.74 mg. of tenulin dissolved in 49.95 mg. of camphor; Δ, 11.75°. This corresponds to a molecular weight of 323.

Anal. Calcd. for $C_{17}H_{22}O_5$: C, 66.65; H, 7.27; mol. wt., 306.4. Found: C, 66.52; H, 7.51; mol. wt., 323. Recrystallized from *n*-butanol and *n*-butyl ether, m. p. 191. Found: C, 66.61; H, 7.47.

Dihydrotenulin.—One gram of tenulin dissolved in 50 cc. of ethyl acetate was reduced at atmospheric pressure with hydrogen and the platinum catalyst of Voorhees and Adams.[6] One mole of hydrogen was absorbed. The catalyst was removed and the solution evaporated to 5 cc. To this 10 cc. of benzene was added. There was obtained 0.9 g. of colorless crystals, which sintered at about 160°, with the evolution of benzene (benzene of crystallization). The material finally melted at 180°.

This was recrystallized from its solution in 10 cc. of methanol upon the addition of three volumes of hot water. Thus obtained, it consisted of short, thick rods, which melted at 182°. The rods appeared to contain solvent of crystallization, for upon exposure to the air for some time the crystals became broken and had an effloresced appearance. It then melted at 172°. The material in this condition was analyzed.

Anal. Calcd. for $C_{17}H_{24}O_5$: C, 66.21; H, 7.84. Found: C, 66.05; H, 7.83.

Dihydrotenulin Phenylhydrazone.—An ethanolic solution of 0.1 g. of dihydrotenulin, 0.1 g. of phenylhydrazine, and 2 drops of acetic acid was diluted with sufficient water to produce cloudiness. A drop of ethanol was then added to clarify the liquid. Upon standing for a few minutes colorless rods, m. p. 238–240°, separated. These were recrystallized from their methanolic solution upon the addition of water. The purified material consisted of long, thin, square-ended rods, which melted and flowed with decomposition at 248°.

Anal. Calcd. for $C_{23}H_{30}O_4N_2$: N, 7.03. Found: N, 6.96.

Dibromotenulin.—An ethyl acetate solution of 0.5 g. of tenulin was treated portionwise with 0.26 g. of bromine (2 atoms) dissolved in ethyl acetate. The reaction was rapid, and when it was complete the ethyl acetate was removed by distillation under reduced pressure. The residue was dissolved from the flask with 10 cc. of methanol and poured into 200 cc. of water. The white amorphous precipitate was removed and air-dried. The yield was 0.75 g. The reaction was entirely addition, as no hydrobromic acid was formed.

(5) The optical data recorded in this communication were determined by George L. Keenan, of the Food and Drug Administration of the U. S. Department of Agriculture.

(6) Voorhees and Adams, THIS JOURNAL, **44**, 1397 (1922).

The material was crystallized from its solution in the necessary quantity of boiling methanol by adding 0.5 volume of hot water. It separated as rosets of fine colorless needles and melted with decomposition at 124–125°. Further recrystallization did not change its melting point.

Anal. Calcd. for $C_{17}H_{22}O_5Br_2$: Br, 34.3. Found: Br, 34.1.

Monobromotenulin.—After standing for two to three days, the mother liquors from recrystallizing dibromotenulin became acid to congo red and deposited a white material. This was separated and dissolved in hot methanol. The solution was filtered and then crystallized by adding an equal volume of hot water. Thin, colorless, rectangular plates, melting at 198–199°, were obtained. When recrystallized from dilute methanol, it melted with decomposition at 202–203°.

Anal. Calcd. for $C_{17}H_{21}O_5Br$: Br, 20.7. Found: Br, 20.3.

Anhydrotenulin.—A test-tube containing 0.5 g. of tenulin was placed in a small bath of fused sodium and potassium nitrates at 300°. The tenulin melted with the evolution of gas. By the time the bath had cooled to 275° the reaction was complete, and a golden-colored melt resulted. This was dissolved in 2 cc. of boiling methanol, and an equal volume of water was added. Crystallization began at once and yielded 0.35 g. of crystals which melted at 163°. These were dissolved in methanol, and the filtered solution was crystallized by adding an equal volume of water. The product consisted of colorless crystals which melted at 172°.

Anal. Calcd. for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99; mol. wt., 288.3. Found: C, 71.03; H, 7.09; mol. wt., 294.

Action of Acetic Anhydride and Sodium Acetate upon Tenulin.—A mixture of 2 g. of tenulin, 15 cc. of acetic anhydride, and 0.5 g. of dry sodium acetate was boiled for one hour. Most of the excess anhydride was removed by distillation, and the residue was treated with water. After standing for some time, with occasional stirring, the resulting oil was dissolved in methanol. Crystallization began at once. There was obtained 0.6 g. of material which melted at 230°. It was recrystallized from boiling butanol and when pure melted at 240°.

Anal. Calcd. for $C_{22}H_{26}O_5$: C, 71.33; H, 7.08; mol. wt. 370.4; $C_{22}H_{28}O_5$: C, 70.94; H, 7.58; mol. wt. 372.4. Found: C, 71.21, 71.18; H, 7.27, 7.18; mol. wt. (Rast), 355; acetyl was negative.

Isotenulin.—One gram of finely powdered tenulin in a mortar was triturated for three minutes with 50 cc. of 0.1 *N* sodium hydroxide. The mixture was then acidified with sulfuric acid, and a crystalline material with a melting point of 158° was obtained. The yield was 0.75 g.

It was recrystallized from its solution in the necessary quantity of *n*-butanol by adding four volumes of *n*-butyl ether. The product consisted of long colorless rods, which melted at 162°. Its indices of refraction are: η_α 1.519; η_β not determined, only faint interference figures were observed: η_γ 1.555, both ± 0.003. η_α is shown lengthwise, and η_γ is shown crosswise on the rods. In parallel polarized light (crossed nicols) the polarization colors are brilliant, the extinction is parallel, and the elongation is negative. In convergent polarized light (crossed nicols) only faint biaxial figures showing the acute bisectrix are observed. Apparently 2E is large.

Anal. Calcd. for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24. Found: C, 66.81; H, 7.37.

When finely powdered tenulin was triturated for fifteen minutes with 5% sodium carbonate solution and then filtered, almost pure isotenulin, m. p. 162°, was obtained.

A solution of 0.5 g. of tenulin dissolved in 80 cc. of water was boiled for two minutes with 0.5 g. of norit. Upon cooling, isotenulin separated as colorless needles, m. p. 160–161°. The identity of the material was established by comparing it with an authentic sample made by the action of sodium carbonate upon tenulin. There was no depression of the melting point. Since norit suspended in water imparts to the latter an alkaline reaction, *p*H 7.5, it was assumed that the alkali was the cause of the transformation. This was proved to be the case, since an aqueous solution of tenulin acidified with acetic acid and then treated with norit failed to isomerize.

Still another procedure which yielded isotenulin is the following. To a solution of 0.5 g. of tenulin dissolved in 2 cc. of boiling methanol was added 10 cc. of hot water. Immediately 1 cc. of 1% sodium hydroxide solution was added. The turbid liquid was stirred for three minutes, during which time crystallization occurred. It was then acidified and allowed to stand for a few minutes, and the crystals, m. p. 157°, were removed. The yield was 0.37 g.

The Substance, m. p. 255°, Obtained by the Action of Alkali upon Tenulin.—When finely powdered tenulin is triturated occasionally during twenty-four hours with a 5% sodium carbonate solution, isotenulin is the main product of the reaction, but another substance also is formed. One gram of tenulin thus treated yielded 0.7 g. of yellow crystals, which melted unsharply at 155°. These were suspended in 5 cc. of hot methanol, and the mixture was then cooled and filtered. There was obtained 0.1 g. of a substance which melted at 241° and cleared at 246°. This was recrystallized to constant melting point from *n*-butanol. It consisted of short, thick, colorless rhombs, which melted at 255°. Analysis showed that the material had the composition $C_{15}H_{20}O_4$.

Anal. Calcd. for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.08; H, 7.69.

Upon dilution with three volumes of water, the methanolic mother liquors from which the foregoing substance was obtained gave light yellow isotenulin, m. p. 160°.

The material that melted at 255° is also formed when finely powdered tenulin is triturated occasionally with 0.1 *N* sodium hydroxide for one and one-half hours. The yield is essentially the same as that obtained with sodium carbonate, but no isotenulin could be obtained by this procedure.

Dihydroisotenulin.—This compound was prepared in the same manner as dihydrotenulin. The ethyl acetate solution was evaporated to dryness, dissolved in methanol, and crystallized by adding water. The crude material had a melting point of 150°. It was recrystallized from its methanolic solution by adding two volumes of boiling water. It separated as thick, colorless prisms, many of which were rhombs. Its melting point was 151°.

Anal. Calcd. for $C_{17}H_{24}O_5$: C, 66.21; H, 7.84. Found: C, 66.30; H, 8.07.

Dihydroisotenulin Phenylhydrazone.—This material was prepared by the same procedure as dihydrotenulin phenylhydrazone. When recrystallized by adding water to its methanolic solution, it melted at 219–220°.

Anal. Calcd. for $C_{23}H_{30}O_4N_2$: N, 7.03. Found: N, 7.00.

Dibromoisotenulin.—This compound was made in the same manner as dibromotenulin, and also by the procedure given by Buehler and co-workers.[3] In each case the material was purified by dissolving it in the necessary quantity of boiling methanol and adding 0.5 volume of hot water. It separated as dense, irregular-shaped prisms tending to be octahedra. It melted at 135° with decomposition.

Anal. Calcd. for $C_{17}H_{22}O_5Br_2$: Br, 34.3. Found: Br, 34.2.

Monobromoisotenulin.—Dibromoisotenulin was boiled for three minutes in a 5% methanolic solution of potassium acetate. The liquid was then diluted with three volumes of water and allowed to crystallize. The yield was quantitative, and the product was quite pure. By dissolving it in the necessary quantity of boiling methanol and adding three volumes of hot water, it was brought to a constant melting point of 213° with decomposition.

Anal. Calcd. for $C_{17}H_{21}O_5Br$: Br, 20.7. Found: Br, 21.3.

The Substance $C_{16}H_{22}O_5$ Found in One Shipment of Helenium tenuifolium.—In one shipment of *H. tenuifolium* obtained in 1936 it was difficult to obtain tenulin. The material obtained after the extract had stood for a long time gave roughly 60% of tenulin and 40% of another compound relatively insoluble in ethanol. Because of this property the unknown compound was readily separated from tenulin and purified by recrystallization from boiling ethanol. It consisted of long, thin, fluffy colorless rods, which melted at 233–234°. An alkoxyl determination gave a value corresponding to 3.85% of methoxyl.

Anal. Calcd. for $C_{16}H_{22}O_5$: C, 65.29; H, 7.55. Found: C, 65.22, 65.36; H, 7.58, 7.55.

Dihydro Derivative of $C_{16}H_{22}O_5$.—One gram of the C_{16} compound was suspended in ethyl acetate and hydrogenated as was tenulin. The suspension gradually disappeared, and when the reaction was completed one mole of hydrogen was consumed. The filtered solution was concentrated and crystallized. The material separated as colorless rods with a melting point of 192°. Recrystallization from boiling ethyl acetate did not change the melting point.

Anal. Calcd. for $C_{16}H_{24}O_5$: C, 64.84; H, 8.16. Found: C, 64.78; H, 8.11.

Acetyl Derivatives of the Substance $C_{16}H_{22}O_5$.—(1) A mixture of 1 g. of the C_{16} compound, 0.25 g. of dry sodium acetate, and 4 cc. of acetic anhydride was boiled for one hour. Most of the excess anhydride was then removed by distillation, and the residue was treated with water. After being stirred for some time, a semicrystalline material separated. This was dissolved in methanol and crystallized by adding water. The yield was 0.7 g. of a substance which melted at about 150°. Upon repeated recrystallization from 50% methanol the substance melted at 163°.

Anal. Calcd. for $C_{18}H_{24}O_6$: C, 64.27; H, 7.19; acetyl, 12.8. Found: C, 64.17; H, 7.30; acetyl, 10.9.

(2) When a solution of 0.5 g. of the new material in 3 cc. of pyridine and 2 cc. of acetic anhydride was allowed to stand overnight and then treated with water, crystallization occurred at once. Six-tenths gram of thick prisms, m. p. 193°, was obtained. Recrystallization of this material from its methanolic solution by adding 4 volumes of water did not change the melting point. The product consisted of thick colorless prisms many of which were hexagonal.

Anal. Found: C, 64.28; H, 7.32; acetyl, 10.8.

Summary

Helenium macrocephalum has been found to contain helenalin. *Helenium tenuifolium*, *H. elegans* and *H. badium* contain a hitherto unrecorded compound, $C_{17}H_{22}O_5$, which has been designated tenulin. Some derivatives of tenulin have been prepared which suffice to establish definitely the molecular formula given for tenulin and at the same time show that the compound obtained from *H. tenuifolium* and reported by Buehler, Whitehead, and Goodge is isotenulin. In one lot of *H. tenuifolium*, another new substance, $C_{16}H_{22}O_5$, was isolated. Several derivatives of this material have been prepared.

A diagram showing the relation between the various compounds and their origin is presented.

WASHINGTON, D. C. RECEIVED MAY 18, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY, SCHOOL OF MEDICINE, DUKE UNIVERSITY]

The Apparent Shape of Protein Molecules[1]

BY HANS NEURATH

It has been recognized for some time that the term *globular proteins* does not necessarily imply spherical shape. Measurements of the double refraction of flow,[2-5] dielectric dispersion,[6,7] and viscosity[8-11] of protein solutions have in many instances proved that protein molecules may be unsymmetric. Whether a protein molecule is spherical may also be determined from combined sedimentation and diffusion measurements, as Svedberg[12] showed many years ago. The application of Svedberg's theory to the calculation of the relative dimensions of a number of representative protein molecules was described by us on a previous occasion, incidental to a discussion of the diffusion of proteins.[10]

In the present paper, further studies are reported on the *relative* and *absolute* dimensions of protein molecules and their respective dissociation and aggregation products. After a brief outline of the theory and its implications and limitations, the results are presented, and discussed from the general viewpoint of protein structure.

Theoretical

Svedberg[12,13] has introduced the term *dissymmetry constant* as an indirect measure for the deviations of molecules from spherical shape. The ratio f/f_0, where f is the measured molar frictional coefficient, and f_0 the theoretical molar frictional coefficient for a spherical molecule of the same molecular weight, ought to be unity for spherical molecules, and greater than unity for elongated molecules. The dissymmetry constant is related to the sedimentation constant, s, the molecular weight, M, the diffusion constant, D, the partial specific volume of the solute, V, and the density of the solution, ρ, according to equation (1).

$$f/f_0 = \frac{M(1 - V\rho)/s}{6\pi\eta N(3MV/4\pi N)^{1/3}} \qquad (1)$$

From the way in which this equation was derived it follows that, in the ideal case, f/f_0 must be identical with the ratio D_0/D, where D is the observed diffusion constant, and D_0 the diffusion constant of a spherical molecule of the same molecular weight. Hence, f/f_0 may be calculated merely from the molecular weight, the partial specific volume, and the observed diffusion constant, according to equation (2)

$$f/f_0 = \frac{kT}{6\pi\eta N(3MV/4\pi N)^{1/3}}\frac{1}{D} \qquad (2)$$

where k is the Boltzmann constant, η, the viscosity of the solvent, and N, the Avogadro number.

The strict validity of equations (1) and (2) requires the use of such dilute solutions that interactions between solute molecules become negligible. While this requirement may be fulfilled by sedimentation measurements, diffusion measurements necessarily have to be confined to more concentrated solutions. It is only when the experimentally determined value for f, calculated from either sedimentation equilibrium or diffusion measurements, is found to be independent of the protein concentration, that an unambiguous value may be ascribed to f/f_0.[14]

Difficulties also arise in assigning a true value to f_0. It is known that molecular weight data may be in error by as much as 10%. Although the molecular weight enters into the calculation of f_0 only as the cube root, yet small variations in f/f_0 may result in significant variations in shape factors calculated therefrom.

Another source of uncertainty in the calculation of shape factors relates to the influence of hydration.[16,17] While the theoretical molar frictional coefficient, f_0, is calculated from the molecular weight and partial specific volume of the unhy-

(1) Acknowledgment is made to the Lederle Laboratories, Pearl River, New York, for a grant-in-aid.

(2) Muralt and Edsall, *J. Biol. Chem.*, **89**, 351 (1930).

(3) Böhm and Signer, *Helv. Chim. Acta*, **14**, 1370 (1931).

(4) Lauffer and Stanley, *J. Biol. Chem.*, **123**, 507 (1938).

(5) Mehl, *Symposia Quant. Biol.*, **6**, 218 (1938).

(6) Oncley, THIS JOURNAL, **60**, 1115 (1938); Ferry and Oncley, *ibid.*, **60**, 1123 (1938).

(7) Elliott and Williams, *ibid.*, **61**, 718 (1939).

(8) Daniel and Cohn, *ibid.*, **58**, 415 (1936).

(9) Polson, *Nature*, **137**, 740 (1936).

(10) Neurath, *Symposia Quant. Biol.*, **6**, 196 (1938).

(11) Fahey and Green, THIS JOURNAL, **60**, 3039 (1938).

(12) Svedberg, *Z. physik. Chem.*, **127**, 51 (1925).

(13) Svedberg and Sjögren, THIS JOURNAL, **51**, 3594 (1929).

(14) Lamm and Polson,[15] for instance, reported an increase of the diffusion constants of egg albumin, hemoglobin and serum albumin in dilute protein solutions. In the case of egg albumin, serum albumin, insulin and pepsin, for instance, the molar frictional coefficient calculated from diffusion, f_d, differs from that calculated from sedimentation, f_s, by about 10 p. c., whereas equation (1) assumes equality of f_d and f_s.

(15) Lamm and Polson, *Biochem. J.*, **30**, 528 (1936).

(16) Adair and Adair, *Proc. Roy. Soc.* (London), **B120**, 422 (1936).

(17) Mehl and Williams, *Symposia Quant. Biol.*, **6**, 216 (1938).

drated molecule, the measured molar frictional coefficient, f, is determined by the hydrated molecule of higher partial specific volume, and molecular weight. If deviations of the dissymmetry constant from unity were to be ascribed exclusively to effects of hydration, a value of $f/f_0 = 1.1$ would correspond to $V = 0.82$ (assuming 20% hydration), whereas higher values of f/f_0 would result in V greater than unity. While it cannot be denied that the influence of hydration would tend to decrease the apparent dissymmetry constant to some extent, it is evident that hydration cannot account for values of f/f_0 greater than 1.1, even if the high values for the partial specific volume and hydration, suggested by Adair and Adair,[16] are used. As an approximation, we have assumed in this paper that the influence of hydration on dissymmetry constants is of second order. Specifically, the dissymmetry constants have been related to the apparent shape of the *unhydrated* protein molecules.

A quantitative relation between the relative dimensions of proteins and the dissymmetry constant may be obtained by combination of equation (2) with Perrin's[18] equation for the linear diffusion of ellipsoidal molecules. This equation, derived from hydrodynamic considerations, relates the ratio of the short to long axis of a prolate ellipsoid of revolution, a/b, to the ratio of the diffusion constants, D/D_0.[19]

$$\frac{D}{D_0} = \frac{(a/b)^{2/3}}{\sqrt{1-(a/b)^2}} \ln \frac{1+\sqrt{1-(a/b)^2}}{a/b} \quad (3)$$

The absolute values of the length of the short and long axis, a and b, may be estimated by combining equation (3) with the equation for the volume of a prolate ellipsoid of revolution. If M is the molecular weight, V the partial specific volume of the protein, and N the Avogadro number, then

$$MV = a^2 b \pi N/6 \quad (4)$$

It has to be emphasized that the results of such calculations may be subject to considerable error. The true values of b/a depend on the effective shape of the molecules, on the nature of their surface, and on the extent of interaction between solute and solvent. If the surface of the solute molecules is irregular and if there is marked interaction between solute and solvent (hydration), there will be, in addition to the frictional resistance due to the molecular shape, a frictional resistance produced by the surface of the molecules. Perrin's equation is for the specific case of a molecule having the shape of a prolate ellipsoid of revolution and devoid of any interaction with the solvent.

Further uncertainties are due to the fact that the dissymmetry constants recorded in the literature are exact only to one significant place, whereas variations in the second significant place may produce marked changes in the absolute dimensions, b and a. The true values of these constants are, in addition, largely dependent on the exact molecular shape. Thus, if one assumes as effective shape a cylinder, for instance, the short axis of the molecule would be one-third shorter than that of an ellipsoid of revolution of equal length. As, however, the shape of an ellipsoid of revolution is used for the calculation of the *relative* dimensions, the use of the same model for calculating the *absolute* dimensions will most likely give the best results.

Calculations

In spite of these theoretical uncertainties, we have calculated the relative and absolute dimensions of a large number of proteins, with equations (2), (3), and (4). It was felt that sufficient evidence has accumulated by other experimental methods for the belief that a physical meaning may be ascribed to the great variations in the observed dissymmetry constants. The limits of the error involved in these calculations may be appreciated by considering the assumptions discussed in the preceding paragraphs. Most of the calculations have been based on the values for the dissymmetry constants tabulated by Svedberg.[20] In some instances these have been recalculated from values for the molecular weight and diffusion constant. Where marked discrepancies between our and Svedberg's values have been found, both values have been listed (see Table II). For convenience, $V = 0.75$ has been assumed throughout the calculations.

In Table I, values for f/f_0, b/a, b, and a, are given. Unless stated otherwise, they have been calculated from f_d, and from the molecular weight as determined by diffusion and sedimentation velocity measurements. For reasons to be mentioned in the discussion, the proteins have been arranged according to increasing values of the short diameter of the molecule, a. In Table II the corre-

(18) Perrin, *J. phys. Radium*, **7**, 1 (1936).

(19) A similar relation exists for flat ellipsoids of revolution, but in all probability such a model has no significance for considerations of protein molecules.

(20) Svedberg, *Ind. Eng. Chem.*, **30**, 113 (1938); *Kolloid .Z.*, **85**, 119 (1938).

sponding values for proteins and their respective dissociation and aggregation compounds are listed. The values for the hemocyanins have been taken from the work by Eriksson-Quensel and Svedberg.[21]

TABLE I

APPROXIMATE RELATIVE AND ABSOLUTE DIMENSIONS OF PROTEIN MOLECULES[a]

M = molecular weight. f/f_0 = dissymmetry constant. a = short diameter. b = long diameter.

	Protein	M	f/f_0	b/a	a, Å.	b, Å.
1	Zein	35,000	2.0	20.1	16	322
2	Cytochrome C	15,600	1.3	5.8	18	98
3	Gliadin	26,000	1.6	11.1	18	196
4	Hordein	27,500	1.6	11.1	18	196
5	Erythrocruorin (*Chironimus*)[b]	31,400	1.6	11.1	19	208
6	Serum albumin, urea denatured[22]	67,100	1.98	19.4	20	359
7	Lactalbumin α	17,500	1.2	4.3	21	91
8	Erythrocruorin (*Lampetra*)	17,100	1.2	4.3	22	94
9	Bence–Jones β	37,700	1.3	5.8	25	144
10	Myoglobin	17,200	1.1	2.9	24	70
11	Crotoxin	30,000	1.2	4.3	25	109
12	Concanavalin B	42,000	1.3	5.8	26	149
13	Tuberculin protein	32,000	1.2	4.3	26	112
14	Lactoglobulin	41,800	1.2	4.3	28	122
15	Pepsin	35,500	1.08	2.7	31	84
16	Insulin	40,900	1.13	3.3	31	102
17	Egg albumin[b]	40,500	1.1	2.9	32	91
18	Hemoglobin (horse)	69,000	1.24	4.8	32	155
19	Serum albumin (horse)[b]	67,100	1.2	4.3	34	145
20	Yellow ferment	82,800	1.2	4.3	36	152
21	Canavalin	113,000	1.3	5.8	36	207
22	Serum globulin	167,000	1.4	7.5	37	280
23	Diphtheria toxin[23]	72,000	1.2	4.3	34	145
24	Antipneumococcus serum globulin (rabbit)	157,000	1.4	7.5	37	274
25	Antipneumococcus serum globulin (man)	195,000	1.5	9.2	37	338
26	Concanavalin A	96,000	1.1	2.9	43	124
27	Erythrocruorin (*Arc a*)[b]	33,600	1.0	1	43	43
28	Bence-Jones α[b]	35,000	1.0	1	43	43
29	Catalase	248,000	1.3	5.8	46	297
30	Antipneumococcus serum globulin (horse)	920,000	2.0	20.1	47	950
31	Phycoerythrin (*Ceramium*)	290,000	1.2	4.3	54	232
32	Amandin	329,000	1.3	5.8	51	291
33	Thyroglobulin	628,000	1.5	9.2	54	498
34	Edestin	309,000	1.2	4.3	55	237
35	Excelsin	294,000	1.1	2.9	62	179
36	Urease	483,000	1.2	4.3	64	274
37	Hemocyanin (*Palinurus*)	446,000	1.2	4.3	62	268

[a] Unless otherwise stated, the values on which these calculations are based have been taken from Svedberg's tables.[17]

[b] Calculated from sedimentation equilibrium values.

Discussion

It is striking that, with a few exceptions, protein molecules are not spherical, and most exhibit high molecular dissymmetry.

Also it is well known that the apparent shape of macromolecules frequently reflects in some manner their stereo-chemical structure. If proteins are considered to consist of polypeptide chains, folded or fully extended, the long diameter of the molecule may be thought of as being determined by the length of the chains, whereas the short diameter would reflect the number of chains within the molecule. Led by such considerations, we have arranged, in Table I, the proteins according to their absolute dimensions. The length of the short diameter has been chosen as the criterion for our classification. It is interesting to note that proteins which belong to different groups as regards their molecular weight become members of the same group if arranged in this manner. Thus, cytochrome C, gliadin, and erythrocruorin (*Chironimus*), with the molecular weights of 15,600, 26,000 and 31,400, respectively, are found to have a common short diameter of about 18 Å. Likewise proteins of molecular weight 35,000, 96,000, 248,000 and 920,000, respectively, fall into one group. Although the calculated absolute dimensions may be subject to considerable error, we feel that their value for comparative purposes is unquestionable.

TABLE II

APPROXIMATE RELATIVE AND ABSOLUTE DIMENSIONS OF PROTEINS AND THEIR RESPECTIVE DISSOCIATION AND AGGREGATION COMPONENTS

M = molecular weight. f/f_0 = dissymmetry constant. a = short diameter of molecule. b = long diameter of molecule. The arrows indicate the direction of cleavage: → parallel to long axis; ↓ parallel to short axis.

Protein	M	f/f_0	b/a	a, Å.	b, Å.	Cleavage
Hemoglobin						
Main component	69,000	1.24[a]	4.8	32	155	
Dissociation component[24]	39,000	1.20[a]	4.3	28	118	Probably ↓
Phycocyan (*Ceramium*)[25]						
Main component	272,000	1.26[a]	5.3	49	261	
		1.2	4.3	53	228	
Dissociation component	131,000	1.4	7.5	34	258	→
Hemocyanin (*Eledone*)[21]						
Main component	2,791,000	1.4	7.4	95	715	
Dissociation component	457,000	1.92	18.2	39	707	→
Hemocyanin (*Helix pomatia*)[21]						
Main component	6,630,000	1.2	4.3	153	660	
Dissociation component	814,000	1.66[a]	12.4	54	663	→
		1.9	17.8	48	845	
Dissociation component	502,000	1.81[a]	15.7	42	661	→
		1.5	9.2	50	463	↓
Hemocyanin (*Busycon*)[21]						
Aggregation component	9,980,000	1.27[a]	5.4	159	922	
		1.3	..	...	...	
Main component	6,814,000	1.2	4.3	155	665	↓
Dissociation component	379,000	1.4	7.5	57	430	↓→

[a] f/f_0 recalculated from the values for D and M given by the authors.

(21) Eriksson-Quensel and Svedberg, *Biol. Bull.*, **71**, 488 (1936).

(22) Neurath and Saum, *J. Biol. Chem.*, **128**, 347 (1939).

(23) Lundgren, Pappenheimer and Williams, THIS JOURNAL, **61**, 533 (1939).

(24) Steinhardt, *J. Biol. Chem.*, **123**, 543 (1938).

(25) Eriksson-Quensel, *Biochem. J.*, **32**, 585 (1938).

The importance of such considerations becomes even more apparent if the dimensions of protein are compared with those of their respective dissociation and aggregation components.[26] From Table II it may be seen that dissociation of phycocyan (*Ceramium*) for instance, affects only the length of the short axis, when the molecular weight is halved. Similarly, dissociation of hemocyanin (*Eledone*) only decreases the short axis when the molecular weight drops from 2,790,000 to 457,000. Such data immediately suggest that these molecules split in the direction parallel to the major molecular axis. In other cases, only the major axis is shortened during dissociation indicating that splitting takes place at right angles to the major axis. In Table II, the apparent direction of splitting is indicated by arrows, a horizontal arrow indicating cleavage along the major axis, and a vertical arrow cleavage along the minor axis.[27]

Comparison of the absolute dimensions of the anti-pneumococcus serum globulins indicates a similar relationship. These proteins seem to differ chiefly in respect to the length of the molecule, if the species from rabbit, man, and horse are compared with each other (Table I). An exact interpretation of the molecular dimensions in terms of chemical configuration would be premature at present. Only in a few isolated cases, such as zein,[7] or hemoglobin,[29] has yet a satisfactory agreement between the shape factors determined by different independent methods been established. Further experimental work is needed before the values recorded in Tables I and II can be accepted as exact values.

The work of Astbury[30] and of Bergmann and Niemann[31] has furnished much evidence for the hypothesis that the difference between fibrous and globular proteins is merely a quantitative one. The data presented in this paper likewise illustrate the fibrous character of the globular proteins, thus lending support to the theory that both types of proteins are structurally closely related.

(26) Here the influence of hydration is most likely the same for the undissociated protein and its respective dissociation products.

(27) In the case of the dissociation of hemoglobin by urea, this regularity does not seem to hold exactly. It appears from such considerations, as well as from others,[28] that the value for the dissymmetry constant of this protein is somewhat too low.

(28) Neurath, *Symposia Quant. Biol.*, **6**, 23 (1938).

Summary

A method for the estimation of the relative and absolute dimensions of protein molecules from the dissymmetry constant and Perrin's diffusion equation is outlined and its limitations discussed. The data indicate that most proteins are unsymmetric in shape. A certain regularity exists, independent of the molecular weight, when proteins are grouped on the basis of their molecular dimensions. Comparison of the dimensions of proteins with those of their respective dissociation and aggregation products indicates that cleavage occurs only in directions parallel to either the major or minor molecular axis.

(29) Arrhenius, *Physik. Z.*, **39**, 559 (1938).

(30) Astbury, *Nature*, **140**, 968 (1937).

(31) Bergmann and Niemann, *J. Biol. Chem.*, **115**, 77 (1936); **118**, 301 (1937).

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The Hydroxylation of Unsaturated Substances. V. The Catalytic Hydroxylation of Certain Unsaturated Substances with Functional Groups

BY NICHOLAS A. MILAS, SIDNEY SUSSMAN AND HOWARD S. MASON

Further application of the recent hydroxylation method developed in this Laboratory[1] has led to the production of a number of useful products which hitherto have been rather difficult to procure in satisfactory yields. Of particular interest along this line is the production of glycolaldehyde from divinyl ether in yields as high as 96%. Furthermore, it has been found possible to add hydroxyl groups to substances containing double bonds adjacent to carbonyl groups. Böeseken,[2] for example, has found that ethyl fumarate and ethyl maleate were not appreciably oxidized with perbenzoic acid, and in the case of unsaturated ketones having the same arrangement of groups he reports[3] oxidation of the ketones without the formation of epoxy derivatives but with cleavage

(1) Milas and Sussman, THIS JOURNAL, **58**, 1302 (1936); **59**, 2345 (1937).

(2) Böeseken, *Rec. trav. chim.*, **45**, 838 (1926).

(3) Böeseken and co-workers, *ibid.*, **50**, 827 (1931); **52**, 874 (1933); **55**, 786 (1936).

of the carbon–carbon bond next to the double bond or the carbonyl group. Table I summarizes some of the results obtained in the present investigation.

TABLE I

SUMMARY OF HYDROXYLATION EXPERIMENTS

Olefinic substance	Main product	% yield
Ethyl crotonate	Ethyl dihydroxybutyrate	56
Diethyl maleate	Diethyl mesotartrate	41
Diethyl fumarate	Diethyl racemate	58
Mesityl oxide	2-Methylpentanediol-2,3-one-4	23
Vinyl acetate	Glycolaldehyde	60
Divinyl ether	Glycolaldehyde	96.0
Vinyl bromide	Glycolaldehyde	12.5(?)
Oleic acid	9,10-Dihydroxystearic acid	60
Cinnamyl alcohol	β-Phenylglycerol	12.2
	Di-[β-phenylglycerol] ether	4.5

In the case of the vinyl compounds it was not found possible to isolate the corresponding glycols since these rearranged spontaneously to yield glycolaldehyde. With cinnamyl alcohol the greater portion of the β-phenylglycerol formed was further oxidized to benzaldehyde and glycolaldehyde, both of which were isolated.

Experimental

Ethyl Dihydroxybutyrate from Ethyl Crotonate.—Ethyl crotonate was prepared in accordance with the method of Michael[4] and was purified by fractionation under reduced pressure; b. p. 43–45° (17 mm.). To 8.55 g. (0.075 mole) of this ester was added 42.9 cc. (0.075 mole) of 5.95% hydrogen peroxide reagent[1] in *t*-butyl alcohol, the solution cooled to 0° and to it added 1 cc. of osmium tetroxide solution likewise in *t*-butyl alcohol. The reaction was complete in three days at 0° when the solvent was removed by distillation at the temperature of the water-bath and the residue fractionated under reduced pressure. The fraction boiling at 123–125° (18 mm.) was collected and found to have the following properties. Unlike the ethyl crotonate, it was completely soluble in water and had a neutralization equivalent of 146 as compared with 148 for ethyl dihydroxybutyrate. A yield of 56% was obtained based on the amount of ethyl crotonate used.

Diethyl Mesotartrate from Diethyl Maleate.—Eight and six-tenths grams (0.05 mole) of diethyl maleate (Eastman Kodak Company) was dissolved in 28.6 cc. (0.05 mole) of a 5.95% solution of the hydrogen peroxide reagent, the solution cooled to 0° and to it added 1.5 cc. of the osmium tetroxide catalyst, but since no noticeable reaction occurred after four days at this temperature, the mixture was allowed to come to room temperature, at which the reaction was completed at the end of two days. The solvent was then removed by distillation and the residue fractionated under reduced pressure and the fraction boiling at 162–166° (18 mm.) collected. Kuhn and Wagner-Jauregg[5] reported a b. p. for diethyl mesotartrate of 157.5° (14 mm.) and a m. p. of 55°. Our compound was a highly viscous liquid which when crystallized from ether had a m. p. of 53.5–55°. A neutralization equivalent gave a value of 107 as against 103 calculated for diethyl mesotartrate. A yield of 41% was obtained based on the amount of diethyl maleate consumed.

Diethyl Racemate from Diethyl Fumarate.—Eight and six-tenths grams of diethyl fumarate (Eastman Kodak Company) was dissolved in 28.6 cc. of a 5.95% solution of hydrogen peroxide reagent, the solution cooled to 0° and to it added 1.5 cc. of the osmium tetroxide reagent. As in the case of diethyl maleate the reaction mixture was brought, after four days at 0°, to room temperature, at which it was found to be complete at the end of one day. The solvent was then removed by distillation, the residue fractionated under reduced pressure and the fraction boiling at 163–167° (21 mm.) was collected. Anschuetz and Pictet[6] reported a b. p. of 162° (19 mm.) for diethyl *d*-tartrate and Perkin[7] has shown that the b. p. of this ester is identical with that of diethyl racemate. Attempts to crystallize this ester were unsuccessful. The saponification equivalent was found to be 106 as against 103 calculated for diethyl racemate. The yield of diethyl racemate was 58% based on the amount of diethyl fumarate used.

2-Methylpentanediol-2,3-one-4 from Mesityl Oxide.—To 9.8 g. (0.1 mole) of mesityl oxide (Eastman Kodak Company) was added 57.2 cc. (0.1 mole) of a 5.95% solution of hydrogen peroxide reagent, the solution cooled to 0° and to it added 0.5 cc. of the osmium tetroxide catalyst. After two days at 0° the reaction was complete, the solvent distilled, the residue fractionated under reduced pressure and the fraction boiling at 104–110° (16 mm.) collected. Harries and Pappos[8] reported a b. p. of 109° (19 mm.) for 2-methylpentanediol-2,3-one-4. Our product was found to reduce Fehling's solution instantly in the cold.

This glycol has not been characterized fully and in order to characterize it, the *p*-nitrophenylosazone was prepared by allowing it to react, at the temperature of the water-bath, with *p*-nitrophenylhydrazine in dilute acetic acid. The dark red precipitate obtained from this reaction was recrystallized several times from pyridine; m. p. 251–253°, with decomposition. This substance was analyzed for nitrogen.

Anal. Calcd. for $C_{18}H_{20}O_5N_6$: N, 21.00. Found: N, 20.87.

A yield of 23% was obtained based on the amount of mesityl oxide consumed.

Glycolaldehyde from Vinyl Acetate.—The vinyl acetate (Eastman Kodak Company) used was fractionated just before the experiments through a Vigreux column and the fraction boiling at 72.5–73° collected. To 17.7 g. of this substance was added 110 cc. of 6.23% hydrogen peroxide reagent, the mixture cooled to 0° and to it added 1 cc. of the osmium tetroxide catalyst. After five days at 0° the reaction mixture turned brown and the peroxide had disappeared completely. The mixture was then distilled to remove the solvent and the unconverted vinyl acetate and the residue fractionated under reduced pressure and the fraction boiling at 90–98° (4.5 mm.) collected and examined for glycolaldehyde. Fischer and Feldmann[9]

(4) Michael, *Ber.*, **33**, 3766 (1900).
(5) Kuhn and Wagner-Jauregg, *ibid.*, **61**, 485 (1928).
(6) Anschuetz and Pictet, *ibid.*, **13**, 1177 (1880).
(7) Perkin, *J. Chem. Soc.*, **51**, 364 (1887).
(8) Harries and Pappos, *Ber.*, **34**, 2979 (1901).
(9) Fischer and Feldmann, *Ber.*, **62**, 854 (1929).

reported a b. p. of 110–120° (12 mm.) for glycolaldehyde. Our product reduced Fehling's solution in the cold and with *p*-nitrophenylhydrazine formed an osazone which on recrystallization from pyridine had a m. p. of 306–307°. A m. p. of 308.5° is recorded in the literature[10] for this substance. Mixed m. p. with an authentic sample gave a m. p. of 306.5°. A yield of 60% of glycolaldehyde was obtained based on the amount of vinyl acetate consumed. Identical yields were obtained when the reaction was run with larger quantities: 86 g. of vinyl acetate and 630 cc. of the peroxide reagent.

In this reaction, the glycolaldehyde is formed as the result of a rearrangement of the initial glycol in accordance with the equation

$$CH_2{=}CHOAc + HOOH \xrightarrow{OsO_4} CH_2(OH){-}CH(OH){-}OAc \longrightarrow CH_2(OH){-}C(=O){-}H + AcOH$$

and may serve as a general reaction for the preparation of α-hydroxy aldehydes

$$RCH{=}CHOAc \xrightarrow{HOOH} RCH(OH){-}C(=O){-}H + AcOH$$

Glycolaldehyde from Divinyl Ether.—The divinyl ether used in this work was kindly supplied by Merck and Co. through the courtesy of Dr. R. T. Major. It was fractionated through a Davis column and the fraction boiling at 28.3° collected and used in our experiments.

To 3.5 g. of divinyl ether was added 60 cc. of 6.23% hydrogen peroxide reagent, the mixture cooled to 0° and to it added 0.5 cc. of the osmium tetroxide catalyst. The mixture warmed up considerably so that the flask had to be connected to a reflux condenser and thence to a trap immersed in solid carbon dioxide so that any volatile products could be condensed and isolated. At the end of three days the reaction was over and the mixture fractionated to remove the unconverted ether as well as the acetaldehyde which was formed almost in equal quantities with glycolaldehyde showing that only one of the double bonds hydroxylated and the product thus formed rearranged spontaneously. In the low boiling fractions the acetaldehyde was estimated by preparing its *p*-nitrophenylhydrazone, whereas in the residue the glycolaldehyde was estimated by precipitating its *p*-nitrophenylosazone. On recrystallization from pyridine, the latter had a m. p. of 306.5–307°. A yield of 96% of glycolaldehyde was obtained based on the amount of divinyl ether reacted.

Glycolaldehyde from Vinyl Bromide.—Vinyl bromide was prepared from ethylene dibromide and alcoholic potash,[11] b. p. 16°.

To 10.7 g. of freshly prepared vinyl bromide was added 64 cc. of 5.27% hydrogen peroxide reagent, the mixture cooled to 0° and to it added 2 cc. of the osmium tetroxide catalyst and 10 g. of finely powdered calcium carbonate to take up the hydrogen bromide evolved during the reaction. The mixture was allowed to stand in an ice-box at 5–10° for twenty-four days, then worked up for the presence of glycolaldehyde; a yield of 12.5% of this aldehyde was obtained.

9,10-Dihydroxystearic Acid from Oleic Acid.—Seven grams of oleic acid, b. p. 230–235 (21 mm.), was mixed with 14.3 cc. of 5.95% solution of the hydrogen peroxide reagent, the mixture cooled to 0° and to it added 0.5 cc. of the osmium tetroxide catalyst; the solution became orange and after standing overnight at this temperature turned colorless and the reaction was complete. A considerable amount of the 9,10-dihydroxystearic acid had precipitated out. The solvent was removed under reduced pressure and the residue washed thoroughly with ether to remove the unconverted oleic acid and the crude solid recrystallized from absolute alcohol; m. p. 129–131° (corr.). Le Sueur[12] has reported a m. p. of 131–132° (corr.) for the high melting 9,10-dihydroxystearic acid. A neutralization equivalent was taken and found to be 319 as against 316 calculated for 9,10-dihydroxystearic acid. The yield obtained amounted to 60%.

Phenylglycerol from Cinnamyl Alcohol.—To 24.5 g. of cinnamyl alcohol (Eastman Kodak Company) was added 171 cc. of 5.43% hydrogen peroxide, the mixture stirred at 0° and to it added 2 cc. of the osmium tetroxide catalyst. If stirring were omitted in this experiment, it was not found possible to isolate phenylglycerol which, due to local heating, was rapidly oxidized to benzaldehyde and glycolaldehyde. The reaction was complete in four days, the solvent removed under reduced pressure, the highly viscous residue (26 g.) fractionated and the fraction coming over at 171° (1 mm.) failed to crystallize, but when treated with benzoyl chloride in pyridine it yielded chiefly a tribenzoate, m. p. 115.5–116°. The tribenzoate of β-phenylglycerol has been found by Prévost and Losson[13] to melt at 116.5°.

In the purification of the crude tribenzoate, a small amount of a product was found to be sparingly soluble in methanol. This was successively recrystallized from benzene, a 50–50 mixture of ethanol and methanol, and a 50–50 mixture of petroleum ether and benzene into fine white needles; m. p. 217°.

Anal. Calcd. for $C_{46}H_{38}O_9$: C, 75.20; H, 5.18. Found: C, 75.11; H, 5.24.

This analysis seems to agree very well with that calculated for the tetrabenzoate of a mono-ether of β-phenylglycerol. In view of the small quantities available no further work was done on this product.

The viscous residue from the original fractionation, after the volatile products and the β-phenylglycerol had been removed, was extracted several times with hot water and the hot aqueous extract decolorized with charcoal whereby a white crystalline product soluble in hot but sparingly soluble in cold water separated out. It was recrystallized several times from water; m. p. 155.5–156°. It is soluble in ethanol and glacial acetic acid but sparingly soluble in ether and chloroform.

Anal. Calcd. for $C_{18}H_{22}O_5$: C, 67.92; H, 6.91. Found: C, 67.36, 67.68; H, 6.86, 6.92.

A micromolecular weight determination in camphor gave a value of 345 as against 318 calculated for $C_{18}H_{22}O_5$, another mono-ether of β-phenylglycerol.

This product was then benzoylated in pyridine and the

(10) Milas, THIS JOURNAL, **53**, 231 (1931).
(11) Marderosian, B.S. Thesis, M. I. T., 1935.
(12) Le Sueur, *J. Chem. Soc.*, **79**, 1315 (1901).
(13) Prévost and Losson, *Compt. rend.*, **198**, 659 (1934).

benzoate recrystallized from a 50–50 mixture of petroleum ether and benzene; m. p. 118–119°. A mixed m. p. with the tribenzoate of β-phenylglycerol gave a m. p. of 104–106°, showing that the two are different.

Anal. Calcd. for $C_{46}H_{38}O_9$: C, 75.20; H, 5.18. Found: C, 75.52, 75.12; H, 4.99, 5.19.

Hydrolysis of this product gave back the mono-ether of β-phenylglycerol, m. p. 155.5–156°. It is therefore the tetrabenzoate of another mono-ether of β-phenylglycerol and is certainly different from the one obtained in small quantities from the distillate of the main reaction product.

The yield of the β-phenylglycerol amounted to about 12.2% while that of its mono-ethers amounted to about 4.5%. A considerable amount of the cinnamyl alcohol went over to a resin as well as benzaldehyde and glyceraldehyde, both of which were isolated.

Summary

1. The hydroxylation of certain unsaturated substances with functional groups using hydrogen peroxide in *t*-butyl alcohol and osmium tetroxide as the catalyst has led to the production of a number of useful glycols.

2. From ethyl crotonate, diethyl maleate, and diethyl fumarate, the corresponding hydroxylated esters were obtained in fairly good yields.

3. From mesityl oxide, 2-methylpentanediol-2,3-one-4 was obtained in about 23% yield.

4. From vinyl acetate, divinyl ether, and vinyl bromide, glycolaldehyde was obtained in yields of 60, 96, and 12.5%, respectively.

5. From oleic acid a yield of 60% of the high melting dihydroxy stearic acid was obtained.

6. From cinnamyl alcohol was obtained β-phenylglycerol and two different new mono ethers of this glycerol. The tetrabenzoates of the ethers were prepared and analyzed.

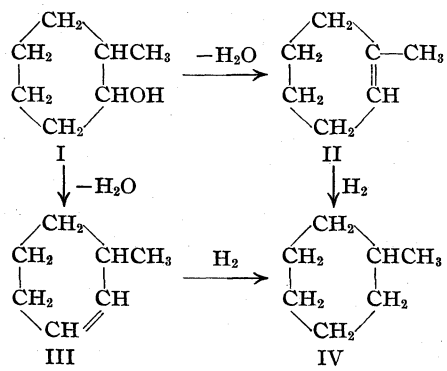
CAMBRIDGE, MASS. RECEIVED MAY 12, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

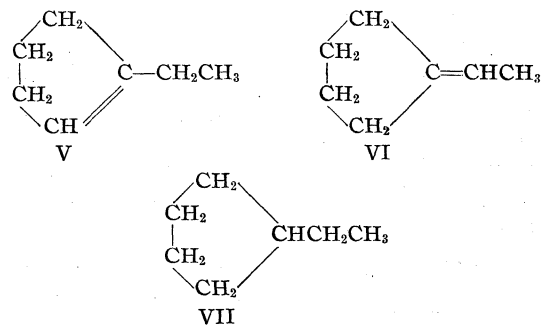
The Dehydration of *trans*-2-Methylcyclohexanol

BY CHARLES C. PRICE

It recently has been reported[1] that the dehydration of 2-methylcyclohexanol with phosphoric anhydride, followed by hydrogenation of the olefin thus obtained, yielded a methylcyclohexane differing in its physical properties from any previously reported. It was suggested that this material was a new isomer, arising from the non-planar nature of the cyclohexane ring. Since the properties reported for the cyclo-olefin and cycloparaffin closely resembled those of 1-ethyl-1-cyclopentene and ethylcyclopentane, respectively, and since ring contraction could conceivably occur during the dehydration, the olefin intermediate in the transformation of the alcohol to the cycloparaffin has been examined carefully.



(1) Vogel, *J. Chem. Soc.*, 1323 (1938).



An examination of Table I reveals the similarity in physical properties of the cycloölefin obtained by Vogel with the cycloölefins III and V, as well as the similarity between his cycloparaffin and VII.

The dehydrations of *trans*-2-methylcyclohexanol carried out in this Laboratory, however, using phosphoric anhydride at temperatures varying from 140 to 230°, always resulted in the formation of a mixture containing only compounds II and III. The mixtures contained 35 to 50% of II; the components could be separated by fractional distillation.

The structures of the cycloölefins were determined by oxidation of the crude mixture with aqueous potassium permanganate. The products isolated were ε-ketoheptanoic acid (as its semi-

TABLE I

PHYSICAL PROPERTIES OF THE VARIOUS HYDROCARBONS

	B. p., °C.	$n^{20}D$	d^{20}_4	$M^{20}D$ (found)	$M^{20}D$ (calcd.)
1-Methyl-1-cyclohexene (II)[a]	111 –112	1.4496	0.8110	31.85	
3-Methyl-1-cyclohexene (III)[b]	106 –107	1.4423	.799	31.90	
1-Ethyl-1-cyclopentene (V)[c]	106.5–107	1.4426	.8000	31.85	31.87
Cycloölefin (Vogel)	106 –106.5	1.4462	.7938	32.32	
Ethylidenecyclopentane (VI)[d]	114	1.4481	.8020	32.12	
Methylcyclohexane (IV)[e]	100.8	1.4231 (d_{He})	.7694	32.40	
Cycloparaffin (Vogel)	102 –103	1.4231	.7679	32.56	32.34
Ethylcyclopentane (VII)[c]	103 –103.2	1.4201	.7669 (15°)		
Ethylcyclopentane (VII)[f]	100.5–101	1.4184 (d_{He})	.7610	32.55	

[a] Wallach, *Ann.*, **359**, 297 (1908). [b] Wallach, *ibid.*, **329**, 371 (1903). [c] Chavanne and Becker, *Bull. soc. chim. Belg.*, **36**, 591 (1927). [d] Wallach, *Ann.*, **365**, 274 (1909). [e] Wibaut, *Chem. and Ind.*, 753 (1938). [f] Eisenlohr, *Fortschritte der Chemie, Physik, physikal. Chem.*, **18**, 521 (1925).

carbazone) from II and succinic acid[2] from III. In spite of careful examination, no oxidation products corresponding to V or VI could be detected. Ring contraction on dehydration must therefore be negligible, if it occurs at all.

It was found that 1-methyl-1-cyclohexene (II) was quite sensitive to exposure to air and moisture, its physical properties changing appreciably in a day or so even when the material was loosely stoppered. Over 10% of high boiling material was isolated from a sample of the pure olefin which had been standing in a glass-stoppered bottle for several months. The boiling point and index of refraction indicated that this material consisted chiefly of methylcyclohexanol and cyclohexylcyclohexene.

Considerable difficulty was encountered in attempting to hydrogenate the olefin mixture using Raney nickel or Adams platinum catalyst, even after repeated distillation.[3] Conversion to the saturated compound was readily accomplished, however, after the crude olefin had been distilled with alcohol, with which it forms an azeotropic mixture boiling at 70–72°. Removal of the catalyst poison in this manner yielded material which absorbed hydrogen readily to form methylcyclohexane identical in every respect with an authentic sample prepared from cyclohexanone by treatment with methylmagnesium chloride followed by dehydration and hydrogenation. The pure methylcyclohexane, moreover, showed no change in physical properties, even after standing a month.

Experimental

***trans*-2-Methylcyclohexanol (I).**—The material employed was a commercial grade. It was redistilled and the portion boiling from 164–166°, $n^{20}D$ 1.5625, was used. The unrecrystallized phenylurethan, prepared by treating the alcohol with phenyl isocyanate, had a melting point of 102–103°, indicating that the starting material must have consisted of more than 95% of the *trans*-isomer.[4]

Dehydration of I.—To 115 g. of the alcohol in a 500-cc. modified Claisen flask was added 60–80 g. of phosphoric anhydride rapidly and the flask immediately stoppered. The mixture boiled vigorously and considerable olefin distilled. After the initial vigorous reaction the mixture was heated gradually to 210–220°; 65–75 g. (68–78%) of olefin was obtained. In other experiments, the reaction mixture was kept cool during the addition of the phosphoric anhydride and then gradually heated. Olefin was evolved continuously at reaction mixture temperatures from 130–250°. The composition of olefin from different experiments and at different temperatures did not vary greatly, consisting of 35 to 50% II, the remainder being III. The percentage of the two constituents was determined by refractive index and density measurements as well as separation of the components by repeated fractional distillation. The purest sample of 3-methyl-1-cyclohexene (III) separated from this mixture by repeated fractional distillation had the following properties: b. p. 106–106.5°; $n^{20}D$ 1.4426; d^{20}_4 0.7986; $M^{20}D$ (found) 31.85; $M^{20}D$ (calcd.) 31.87.

A typical distillation of the crude olefin mixture gave fractions as follows.

B. p., °C.	Cc.	$n^{20}D$	d^{20}_4	$M^{20}D$
105–108	3.5	1.4448	0.8009	31.87
108–109	2.0	1.4458	.8033	31.85
109–110	3.5	1.4469	.8058	31.84
110–111	2.5	1.4480	.8063	31.86

Oxidation.—Ten grams of olefin mixture (40% II as determined by the index of refraction) was oxidized with 40 g. of potassium permanganate in 250 cc. of water at 0° for twenty-four hours with vigorous mechanical stirring. After filtration and ether extraction, 50 cc. of concentrated hydrochloric acid and 200–300 g. of ammonium sulfate were added. Ten extractions with 10–15 cc. portions of ether followed by evaporation of the ether left 8 g. of water-soluble acids as a yellow oil. On treatment with saturated semicarbazide solution this formed a precipitate of 2.5 g. (60%) of ε-ketoheptanoic acid semicarbazone, m.

(2) The primary oxidation product, α-methyladipic acid, has a tertiary hydrogen atom α to a carboxyl group. Such a structure is not stable toward alkaline potassium permanganate.

(3) Vogel also noted this difficulty in attempting to hydrogenate his cycloölefin.

(4) Vavon, Perlin and Horeau, *Bull. soc. chim.*, [4] **51**, 648 (1932).

p. 142–143°.[5] Extraction of this mother liquor with ether recovered 6 g. of the straw-yellow oil, the major portion of which crystallized. Dried on a clay plate, the crystalline material had the correct melting point (m. p. 183–185°) and neutral equivalent (neut. equiv. 62) for succinic acid.

Hydrogenation.—Five grams of olefin mixture (distilled with alcohol, washed with water to remove the alcohol and then fractionated, 30% II) was dissolved in 25 cc. of alcohol and 2–3 g. of Raney nickel added. Hydrogenation at three atmospheres pressure was complete in three or four hours. The product had the following properties: b. p. 101–101.5°; $n^{20}D$ 1.4230; d^{20}_4 0.7712; $M^{20}D$ (found) 32.36; $M^{20}D$ (calcd.) 32.34.

1-Methyl-1-cyclohexene (II).—This compound was obtained by dehydration of 1-methyl-1-cyclohexanol prepared from cyclohexanone and methylmagnesium chloride. Its properties agreed with those reported in the literature: b. p. 110–110.5°; $n^{20}D$ 1.4500; d^{20}_4 0.8103; $M^{20}D$ (found) 31.84; $M^{20}D$ (calcd.) 31.87.

(5) Wallach, *Ann.*, **329**, 371 (1903).

Oxidation.—Oxidation of 0.7 g. of this olefin (II) with permanganate as above yielded 0.6–0.7 g. (50%) of the semicarbazone of ε-ketoheptanoic acid, m. p. 142–143°.

Hydrogenation.—Hydrogen added readily to this olefin (II) using Adams catalyst in alcohol at three atmospheres pressure. The product had the same properties as the methylcyclohexane prepared from III: b. p. 101.5–102°; $n^{20}D$ 1.4234; d^{20}_4 0.7711; $M^{20}D$ (found) 32.35; $M^{20}D$ (calcd.) 32.34.

Summary

The dehydration of *trans*-2-methylcyclohexanol with phosphoric anhydride yielded a mixture of 1-methyl-1-cyclohexene and 3-methyl-1-cyclohexene. The methylcyclohexane obtained by hydrogenation of this olefin mixture was found to be identical in every respect with other authentic samples of this hydrocarbon.

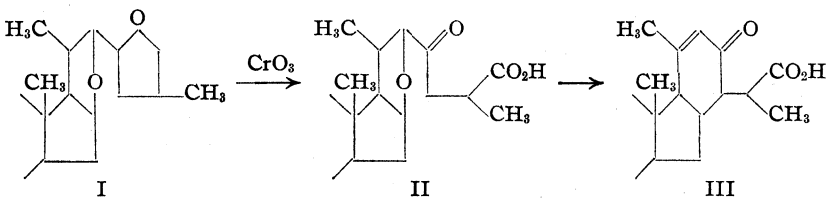
URBANA, ILLINOIS RECEIVED MAY 26, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Sarsasapogenin. IV. Further Observations Concerning Sarsasapogenoic Acid and Related Compounds

BY LOUIS F. FIESER, EDWARD M. FRY[1] AND R. NORMAN JONES[2]

From the work of Jacobsen in this Laboratory[3] it was concluded that anhydrosarsasapogenoic acid has the partial structure III and that its formation from sarsasapogenin by oxidation to sarsasapogenoic acid and treatment of the latter with alcoholic alkali is most plausibly interpreted by regarding these substances as having the structures I and II, first tentatively suggested by Tschesche and Hagedorn.[4] The structure III for the anhydro compound was based upon the results of oxidation and reduction experiments and upon spectrographic evidence[5] of the presence of an α,β-unsaturated carbonyl system. The spectrographic evidence has now been extended by a determination of the ultraviolet absorption spectrum of the methyl ester acetate of anhydrosarsasapogenoic acid in absolute alcohol[5] (curve 1, Fig. 1). This and the other determinations reported were made by one of us (R. N. J.) by a technique which will be described in a future paper (measurements at room temperature, slit width 0.12 mm.). Both the principal and the secondary absorption bands at 243 mμ (log ε = 4.13) and 303 mμ (log ε = 1.86) correspond in position and intensity with those characteristic of α,β-unsaturated ketones,[6] in conformity with formula III. The dibasic acid $C_{27}H_{40}O_7$[3b] resulting from the permanganate oxidation of anhydrosarsasapogenoic acid was regarded as having two carbonyl groups. The absorption spectrum of the dimethyl ester of this acid (curve 2, Fig. 1) definitely has carbonyl characteristics and lacks the original feature of conjugation, but it is hardly possible from the spectrographic evidence to distinguish between a monoketo and diketo carboxylic acid.



I II III

The spectrum of the acetate of sarsasapogenoic acid (curve 2, Fig. 2) is characterized by the ap-

(1) Du Pont Research Fellow.
(2) Commonwealth Fund Fellow.
(3) Fieser and Jacobsen, THIS JOURNAL, **60**, (a) 28, (b) 2753, (c) 2761 (1938).
(4) Tschesche and Hagedorn, *Ber.*, **68**, 1412, 2247 (1935).
(5) Fieser and Jones, THIS JOURNAL, **61**, 532 (1939).
(6) For example, see Mohler, *Helv. Chim. Acta*, **20**, 289 (1937).

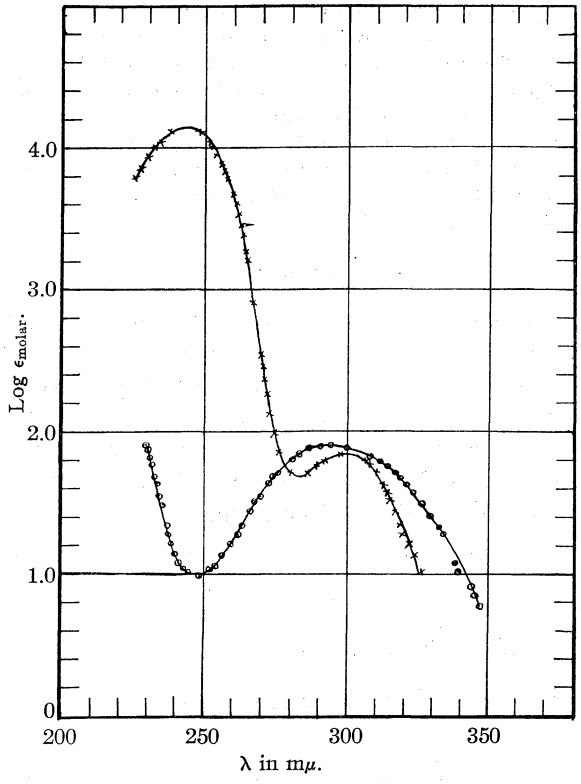


Fig. 1.—Curve 1 (crosses), anhydrosarsasapogenoic acid methyl ester acetate in absolute alcohol; curve 2 (circles), dimethyl ester of dibasic acid $C_{27}H_{40}O_7$ in absolute alcohol.

pearance of a low intensity band at 281 mμ (log ε = 1.92), which is indicative of the presence of a non-conjugated carbonyl group, as in formula II. A determination made with a sample of chlorogenoic acid diacetate monohydrate[7] kindly supplied by Professor C. R. Noller gave a practically identical result (maximum at 286 mμ, log ε = 1.91; solvent, 95% alcohol). A similar absorption curve (curve 1, Fig. 2) was found for the acidic oxidation product obtained[3c] from desoxysarsasapogenin and previously regarded as an unsaturated, conjugated diketo acid in the form of a hydrate, $C_{27}H_{40}O_4 \cdot H_2O$. Reëxamination of the acid has provided indications that it is indeed a hydrate, but the spectrum shows that it lacks conjugation. The similarity to the above sapogenoic acid suggests that the substance in question may be a mono-carbonyl compound of the same type, namely, desoxysarsasapogenoic acid. The analyses reported[3c] for the acid agree satisfactorily with the revised formula $C_{27}H_{42}O_4 \cdot H_2O$, and the results for the unhydrated methyl ester and monoxime accord better with the new formulation than with that originally proposed. The apparent presence of an active hydrogen atom in the ester[3c] may be due to enolization or other change. Another acid which appears to be of the same type has been obtained by the oxidation of sarsasapogenone with chromic acid. Analyses of the acid and its methyl ester point to the formula $C_{27}H_{40}O_5$ of dehydrosarsasapogenoic acid, and this designation is supported by the sensitivity of the compound to alkali.

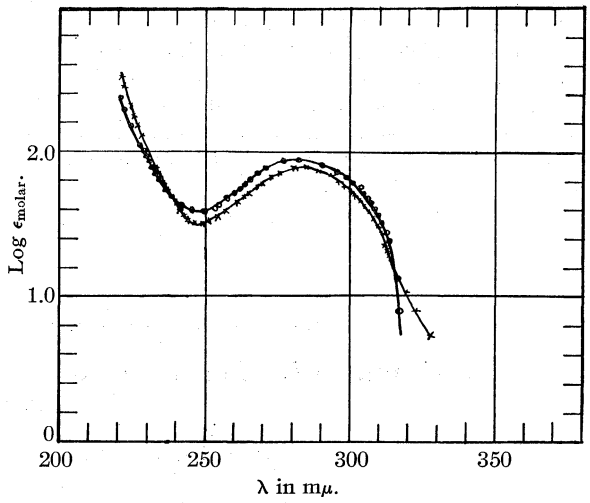
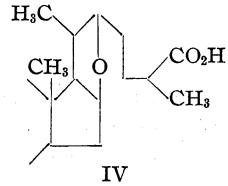


Fig. 2.—Curve 1 (crosses), desoxysarsasapogenoic acid ($C_{27}H_{42}O_4 \cdot H_2O$) in absolute alcohol; curve 2 (circles), sarsasapogenoic acid acetate in absolute alcohol.

Spectrographic examination was also made of the "anhydrotetrahydrosarsasapogenoic acid"[3b] resulting from the slow and irregular catalytic hydrogenation of the sapogenoic acid. The formula of a γ-keto acid, previously considered as a possibility, is definitely eliminated by the present observation that the substance shows no selective absorption in the ultraviolet region. Since this is true also of sarsasapogenin, the reduction product probably contains one of the original oxidic linkages and has the structure IV. On this interpretation the reaction consists in the reduction of the carbonyl group of II to a methylene group, which would account for the slow and irregular absorption of hydrogen. The same formula has been ascribed by Marker and Rohrmann[8] to an



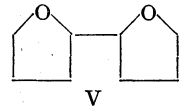
IV

(7) McMillan and Noller, THIS JOURNAL, **60**, 1630 (1938).

(8) Marker and Rohrmann, *ibid.*, **61**, 846 (1939).

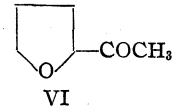
acid (sarsasapogentic acid) obtained by hydrogenating sarsasapogenin in an acidic medium and oxidizing the resulting crude 3-acetate dihydride. Their acid is stated to melt at "187°" ("189°" is given in the theoretical discussion) and to form a crystalline methyl ester. Our acid, like certain other compounds of the series, melts over a characteristically long range (174–184°, corr.) and gives a liquid methyl ester, isolated as the crystalline acetate and benzoate.

Marker and Rohrmann[8] found that sarsasapogenin not only can be hydrogenated in acid solution, but also can be reduced by the Clemmensen method, and brominated in the presence of hydrogen bromide. These workers also noted that the sapogenin acetate is attacked by selenium dioxide in acetic acid–benzene, but no reaction product was isolated.[9] They considered these observations to indicate the presence of a spiro ketone acetal grouping in the side chain and suggested that formula I should be modified by transposing the terminal oxidic linkage from C_{23} to C_{22}. This formulation seems contrary to the evidence from our oxidation experiments, particularly since it provides no rational interpretation of the formation and properties of anhydrosarsasapogenoic acid (III). On the other hand, the newly observed transformations at least can be formulated on the basis of the side chain structure I postulated by Tschesche and Hagedorn. It is a more subtle problem to decide whether such a formulation is justifiable. The most distinctive feature of the hydrogenation, reduction, and halogenation reactions is that they proceed only in acidic media, and their occurrence, therefore, may well be dependent upon the same structural features which are responsible for the well-known sensitivity of the sapogenin side chain to cleavage[10,3a] and isomerization[3a,8] by mineral acids. The susceptibility to attack by acids is, to be sure, a matter of degree, for while the side chain is subject both to fission by hydrochloric–acetic acid[10,3a] and to reductive cleavage in the Clemmensen reaction,[8] conditions have been found under which the carbonyl group of sarsasapogenone can be reduced by the Clemmensen method without disturbance of the oxidic side chain.[3c,11] Furthermore, no alteration of the genin occurs during its liberation from the glycoside by acid hydrolysis.[10] There is little basis for deciding from known analogy if a substance having the oxidic structure I should show acid sensitivity of just the degree found in the natural product; on the keto acetal formulation the persistence of the oxide ring structure in the Clemmensen reduction of sarsasapogenone would seem to require explanation. Marker and Rohrmann[8] observed that under the conditions employed for the acid-specific reactions of the sapogenin, tetrahydrofurfuryl acetate is resistant to hydrogenation, bromination, and oxidation with selenium dioxide, and they considered this an argument against formula I. The monocyclic acetate did not seem to us an adequate model, and we consequently investigated octahydro-α,α'-difuryl (V). This compound is attacked readily by acids.



V

Acetolysis of sarsasapogenin can be accomplished by short heating at 90° with equal volumes of acetic acid and concentrated hydrochloric acid, and under the same conditions V is converted largely into a higher boiling liquid which appears to be a chlorohydrin formed by cleavage of one of the oxide rings. Octahydro-α,α'-difuryl also slowly absorbs a full mole of bromine in acetic–hydrobromic acid solution and is attacked by chromic acid at 60°. The freshly purified material did not undergo hydrogenation under conditions similar to those employed by Marker and Rohrmann[8] and was inert to selenium dioxide, although on standing in the air the material rapidly became contaminated with an impurity which is oxidized by this reagent. Since the nature of the selenium dioxide reaction on the sapogenin is unknown and occurrence or absence of hydrogenation dependent upon the nature of the catalyst as well as the presence of acids, the similarities between octahydro-α,α'-difuryl and sarsasapogenin seem more striking than the differences. We also examined α-acetotetrahydrofuran (VI) as a possible model



VI

for sarsasapogenoic acid, formulated as in II, and found that, like this acid, the simpler compound

(9) We have observed that sarsasapogenin, or its acetate, is oxidized rapidly by lead tetraacetate in acetic acid or acetic anhydride solution at temperatures from 60 to 100°. With either one or two moles of oxidizing agent considerable starting material was recovered and the remainder was non-crystalline.

(10) Jacobs and Simpson, *J. Biol. Chem.*, **105**, 501 (1934).

(11) Marker and Rohrmann, THIS JOURNAL, **61**, 1284 (1939).

is sensitive to alcoholic alkali and rapidly undergoes alteration.

From these observations we conclude that on present evidence the Tschesche–Hagedorn formulation provides the most satisfactory expression of the known properties of the sapogenins.

Experimental Part[12]

Preparation of Desoxysarsasapogenin.—Results obtained by the procedure[3c] previously given for the Clemmensen reduction of sarsasapogenone were somewhat irregular. After several trials it was found that the reduction proceeds better when the proportion of benzene (to methanol) is decreased, and that with very brisk refluxing the time can be greatly decreased. The identification of the product is somewhat uncertain because the melting point is close to that of the starting material and because mixtures of the two substances show no depression. There is little difference in the optical rotations of the compounds, the value found for desoxysarsasapogenin being $\alpha^{24}D$ −59.6° (1.5% in benzene), while that for sarsasapogenone was $\alpha^{27}D$ −45° (1.2% in benzene). A convenient method of separation and identification was found in the removal of the ketone as the oxime. The following procedure is believed to provide a reliable method of obtaining the pure desoxy compound, and the yield is considerably better than by the previously reported process[3c] or by reduction with unamalgamated zinc in alcohol according to Marker and Rohrmann.[11]

A mixture of 2 g. of sarsasapogenone, 20 g. of zinc (treated with 2 g. of mercuric chloride), 75 cc. of methanol, 75 cc. of benzene, and 20 cc. of 6 *N* hydrochloric acid was refluxed very vigorously on the steam-bath for six and one-half hours, adding 5-cc. portions of concentrated hydrochloric acid after the second and fourth hours. After dilution with water and separation, the aqueous layer was extracted with ether and the extracts combined with the benzene layer and concentrated to the point of crystallization. The crystalline material obtained in successive crops was freed of adhering oil by washing with cold alcohol, giving 1.51 g. of crude desoxysarsasapogenin. This was suspended with 1.5 g. of hydroxylamine hydrochloride in 5 cc. of pyridine and 10 cc. of alcohol and the mixture was refluxed for two hours. The desoxy compound did not dissolve to any noticeable extent, and after cooling the suspension the solid was collected and washed with water and alcohol, giving 1.3 g. (68%) of satisfactory desoxysarsasapogenin, m. p. 213–217°. The mother liquor afforded 0.13 g. of crude material, m. p. about 130°, which probably is sarsasapogenone oxime.

Desoxysarsasapogenoic Acid.—The oxidation of desoxysarsasapogenin (5 g.) was conducted essentially as before[3c] (in 450 cc. of solvent, adding 4.6 g. of chromic anhydride in 15 cc. of water) but at a lower temperature (45–50°) and for a longer time (eight hours). After filtering from 0.15 g. of starting material the acidic fraction was worked up as described, giving after crystallization from dilute acetone 1.41 g. (26%) of product. This melted at 109–114° to a jelly-like mass which became clear at 121°; $\alpha^{24}D$ −112° (0.65% in alcohol). None of the high melting acid[3c] was observed.

The reported analyses[3c] are to be compared with the percentages calculated for the revised formula $C_{27}H_{42}O_4 \cdot H_2O$: C, 72.28; H, 9.89; ester ($C_{28}H_{44}O_4$): C, 75.63; H, 9.97; oxime ($C_{27}H_{43}O_4N$): C, 72.77; H, 9.73; N, 3.14.

When the acid was heated in a bath at 200° a gas was evolved and a condensate formed on the cool portion of the tube and then evaporated. After adding ether (moist) to the oil remaining on cooling, the material crystallized and was identified as the starting material (hydrate). Contrary to the previous observations,[3c] the acid slowly decolorizes permanganate even in the cold, giving largely non-crystalline material. The compound undergoes alteration in alkaline solution even in the cold and the change could be followed by observing the optical rotation, but no crystalline product was isolated. The alkali-modified material absorbed hydrogen in an acidic medium in the presence of Adams catalyst. No hydrogenation was observed with desoxysarsasapogenoic acid itself, although the methyl ester absorbed somewhat less than one mole of gas, giving unchanged ester and an oil.

Dehydrosarsasapogenoic Acid.—A solution of 5 g. of sarsasapogenone in 390 cc. of glacial acetic acid was stirred at room temperature (30°) and treated with a solution of 4.2 g. of chromic anhydride in 75 cc. of 80% acetic acid. At the beginning this was added at the slow rate at which the reagent was consumed, but after half of the oxidant had been added (eight hours) the remainder was introduced rapidly and stirring was continued for fourteen hours longer at 33°. After dilution with water the cloudy reaction mixture was extracted with ether and the washed solution was extracted with 1 *N* alkali. Fine needles of a sodium salt separated at this point, but as the material was not easily filtered the alkaline suspension was acidified and the product taken into ether. After evaporation of the solvent the oily residue gave a crystalline salt when treated with 1 *N* sodium hydroxide solution. This was collected and washed with 1 *N* alkali, and when a solution of the salt in water was acidified there was obtained 1.28 g. of fairly pure, crystalline dehydrosarsasapogenoic acid. The alkaline mother liquor remaining after removal of the crystalline sodium salt gave on acidification 2 g. of a crusty, non-crystalline acid mixture. No satisfactory acid, ester, or semicarbazone was isolated. The neutral fraction (1 g.) from the oxidation yielded unidentified material crystallizing in plates, m. p. 202–209°. Oxidations at temperatures up to 75° gave lower yields of the crystalline sodium salt.

Dehydrosarsasapogenoic acid crystallized from dilute alcohol in needle clusters. Water of crystallization was held tenaciously but was removed on drying for three hours at 130° and 10 mm. The substance melts at 164–165°; $\alpha^{25}D$ (air dried) −105° (1.1% in alcohol).

Anal. Calcd. for $C_{27}H_{40}O_5$: C, 72.94; H, 9.07; neut. equiv., 445. Found: C, 72.82; H, 9.12; neut. equiv., 445, 442.

The acid absorbed about 2 moles of hydrogen in acetic acid solution using Adams catalyst, giving a small amount of product, m. p. about 200°. The sapogenoic acid is attacked rapidly by alkaline permanganate and is converted into an oily reaction product on refluxing for ten

(12) Experiments by E. M. Fry. All melting points are corrected. Microanalyses by Lyon Southworth.

minutes with 1 *N* alkali. After being heated at 85° with a 1:1 mixture of acetic acid and concentrated hydrochloric acid for two hours, only about one-third of the acid could be recovered as the sodium salt, and the remainder was an oil. Sarsasapogenoic acid is also altered on similar treatment.

The **methyl ester** was obtained by esterification both with diazomethane and with methanol and hydrogen chloride. The substance crystallizes from dilute acetone in the form of rectangular plates, m. p. 125–126°; $\alpha^{27}D$ −101° (1.5% in alcohol). The analytical sample was dried at 66° and 10 mm.

Anal. Calcd. for $C_{28}H_{42}O_5$: C, 73.32; H, 9.23. Found: C, 73.16, 73.35; H, 9.61, 9.30.

Octahydro-α,α′-difuryl (V).—α,α′-Difuryl was obtained by the method of Reichstein and co-workers[13] as a colorless oil, b. p. 67° at 12 mm. Hydrogenation was tried without success in alcoholic solution in the presence of Adams catalyst or palladium charcoal, but in the same solvent with Raney nickel the reaction proceeded satisfactorily at 150° in the pressure apparatus. The octahydride distilled as a colorless liquid, b. p. 73–76° at 12.5 mm., completely soluble in water and giving a negative test for the furan nucleus. Kondo and co-workers[14] effected the hydrogenation with palladium charcoal in acetone and found the b. p. 77–80° at 13 mm.

Anal. Calcd. for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.37; H, 9.66.

Bromination of V.—A solution of 1.03 g. of octahydro-α,α′-difuryl in 35 cc. of glacial acetic acid was treated with 2 drops of 48% hydrobromic acid and a solution of 1.15 g. of bromine in 3 cc. of glacial acetic acid was run in slowly to the solution held at 55°. The reagent was absorbed slowly and the molecular amount was consumed in the course of a day.

Oxidation and Hydrogenation Tests.—A solution of 0.05 g. of V in 90% acetic acid consumed 0.035 g. of chromic anhydride in about two hours at 60°.

On heating 2.05 g. of octahydro-α,α′-difuryl on the steam-bath with a solution of 2.7 g. of selenium dioxide in 11 cc. of acetic acid and 1 cc. of water, a red precipitate of selenium formed almost at once and did not increase in amount in the course of one hour. The excess dioxide was then neutralized with potassium acetate and the solvent removed by distillation at reduced pressure. The recovered oil distilling at 50–70° at 13 mm. was redistilled twice over sodium carbonate, giving 1.3 g. of purified octahydro-α,α′-difuryl, b. p. 75.5–76.5° at 12.5 mm.

Anal. Calcd. for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.34; H, 10.28.

This purified and freshly distilled material was not attacked by selenium dioxide under the above conditions, but after standing for two days the same sample again gave a positive test for oxidation by this reagent. The freshly purified substance (0.6 g.) likewise absorbed no hydrogen in a mixture of alcohol (9 cc.) and concentrated hydrochloric acid (1 cc.) in the presence of Adams catalyst (50 mg.). A sample (1 g.) which had not been purified with selenium dioxide under similar conditions absorbed about 17% of the theoretical amount of hydrogen; the reaction then stopped and did not proceed further on adding fresh catalyst. The recovered material boiled at 78° (13 mm.).

Acid Cleavage of V.—A mixture of 2.21 g. of octahydro-α,α′-difuryl, 2 cc. of glacial acetic acid, and 2 cc. of concentrated hydrochloric acid was heated on the steam-bath (88°) for two hours, the solution acquiring a brown color. After evaporation at reduced pressure the remaining oil was neutralized with solid sodium carbonate and distilled, giving a fore-run of 0.98 g. of starting material, b. p. 75° (12 mm.), and a fraction (0.93 g.) boiling at 140–143° (12 mm.). This material, only grossly purified, was found to have approximately the composition of a chlorohydrin $C_8H_{15}O_2Cl$ (Calcd.: C, 53.9; H, 8.5; Cl, 19.8. Found: C, 54.9; H, 8.3; Cl, 18.6). A diester was obtained by heating 0.08 g. of the substance with 0.2 g. of 3,5-dinitrobenzoyl chloride on the steam-bath for six hours. The mixture was treated with 1 *N* sodium hydroxide at room temperature, and after the excess reagent had been destroyed the extracted oil was caused to crystallize from alcohol–ether (0.1 g.). The substance has no m. p. but decrepitates with explosive violence. It is sparingly soluble in the usual solvents and decomposes easily. For purification it was dissolved in alcohol (15 cc.) and the solution allowed to evaporate, giving hexagonal crystals. The analysis corresponds approximately to the formula of a dinitrobenzoate of the glycol corresponding to the chlorohydrin.

Anal. Calcd. for $C_{22}H_{20}O_{13}N_4$: N, 10.22. Found: N, 10.71.

The crystalline derivative (32 mg.) on hydrolysis with 0.5 *N* alkali gave 20 mg. of 3,5-dinitrobenzoic acid.

α-Acetotetrahydrofuran (VI).—The starting material, **tetrahydrofuroamide** was prepared by the hydrogenation of recrystallized commercial furoamide in alcohol at atmospheric pressure and room temperature using 10% palladium charcoal catalyst. Purified by crystallization from benzene and distillation, the substance boiled at 135–138° (10 mm.) and showed a wide range of m. p. (65–76°). The composition (C, 52.3; H, 7.2) is close to that calculated for $C_5H_9O_2N$ (C, 52.1; H, 7.8). Wienhaus and Sorge[15] give about the same b. p. but state that this was at 20 mm.; they make no mention of the range in m. p.

This amide (9.8 g.) was suspended in a Soxhlet thimble in the drip from a condenser in a flask containing the Grignard reagent prepared from 8.5 g. of magnesium, 250 cc. of ether, and excess methyl chloride. As the amide was carried into the solution on refluxing a vigorous reaction ensued with separation of a white complex. After refluxing and stirring for forty-five hours, the mixture was treated with water and 20 cc. of glacial acetic acid and extracted thoroughly with ether. The oil from the ether on first distillation afforded 5.9 g. of colorless ketone, b. p. 53–58° (10 mm.). After three further distillations the substance boiled at 52.3–54.8° (10 mm.); the analysis indicates that it probably contained some water (Calcd.: C, 63.1; H, 8.8. Found: C, 62.4; H, 8.9).

(13) Reichstein, Grüssner and Zschokke, *Helv. Chim. Acta*, **15**, 1068 (1932).

(14) Kondo, Suzuki and Takeda, *J. Pharm. Soc. Japan*, **55**, 142 (1935).

(15) Wienhaus and Sorge, *Ber.*, **46**, 1930 (1913).

For characterization the aceto compound (0.15 g.) was refluxed in alcohol (10 cc.) and acetic acid (5 drops) with 2,4-dinitrophenylhydrazine (0.2 g.). The product separating in bright yellow crystals (0.24 g.) proved to be a mixture of stereoisomers present in about equal amounts. Fractional crystallization from alcohol gave orange plates, m. p. 122–124°, and yellow needles, m. p. 135–136°, of the isomeric **2,4-dinitrophenylhydrazones.**

Anal. Calcd. for $C_{12}H_{14}O_5N_4$: C, 48.98; H, 4.79; N, 19.04. Found, plates: C, 48.92; H, 4.73; N, 18.89. Found, needles: C, 48.92; H, 4.59; N, 18.75.

Action of Alkali on α-Acetotetrahydrofuran.—The ketone (2 g.) was refluxed for two hours with 16 cc. of alcohol and 4 cc. of 10 *N* sodium hydroxide, 10 cc. of alcohol was added to the two-phase, dark red mixture and refluxing was continued for two hours. After removing the alcohol at reduced pressure the alkaline liquor was extracted with ether. Distillation gave a small fraction (0.35 g.) of colorless liquid of b. p. close to that of the starting material (61–63° at 10 mm.). The remainder was a dark red oil which did not distil to an appreciable extent up to 190° (8 mm.). In another experiment the proportion of red oil was about the same after refluxing for only one hour. This oil seemed to contain an alcoholic reaction product for there were indications of interaction with dinitrobenzoyl chloride in pyridine and with both phenyl isocyanate and α-naphthyl isocyanate; the products were obtained only as oils. There was no reaction with dinitrophenylhydrazine and the reagent was recovered unchanged.

Summary

Spectrographic evidence confirms the previous indications that anhydrosarsasapogenoic acid contains an α,β-unsaturated carbonyl group and that sarsasapogenoic is a non-conjugated carbonyl compound. Another compound of the sapogenoic acid type has been obtained by the oxidation of sarsasapogenone, and a previously described oxidation product has been recognized as desoxysarsasapogenoic acid. Anhydrotetrahydrosarsasapogenoic acid shows no selective absorption in the ultraviolet and hence does not contain a carbonyl group as previously supposed; a new formula is suggested.

Octahydro-α,α′-difuryl, examined as a possible model for the Tschesche-Hagedorn formulation of the side chain, exhibits sensitivity to acids comparable with that characteristic of the sapogenins. It is considered that this formulation accounts satisfactorily for the acid-specific reactions as well as for the oxidation results.

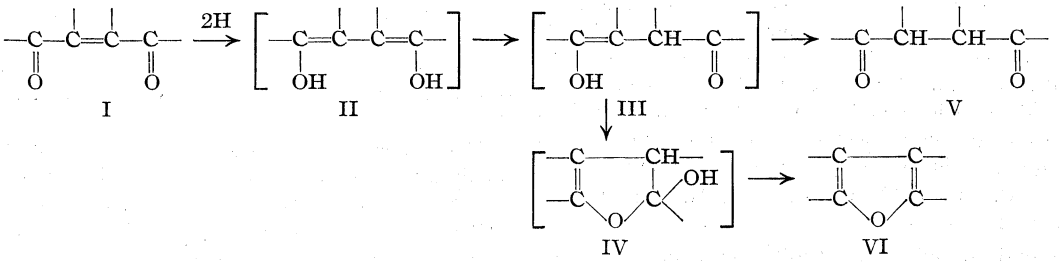
CONVERSE MEMORIAL LABORATORY
CAMBRIDGE, MASSACHUSETTS RECEIVED MAY 17, 1939

[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY, UNIVERSITY OF VIRGINIA]

The Mechanism of Reduction of Conjugated Systems with Terminal Carbonyl Groups. Dienols Obtained from Unsaturated 1,4-Diketones[1]

BY ROBERT E. LUTZ AND WILLIAM G. REVELEY

There is definite evidence that reductions of unsaturated 1,4-diketones by means of soluble reducing agents, by metal combinations, and even by catalytic hydrogen under certain conditions, proceed largely if not exclusively through 1,6-addition of hydrogen or its equivalent at the oxygen atoms with the formation of intermediate dienols (II) which correspond to hydroquinones formed in the reduction of quinones, but which are unstable and ketonize quickly to the saturated 1,4-diketones (V) or undergo dehydration to the corresponding furans (VI).[2]



The furans probably are not formed directly from the dienol but rather through rearrangement to the monoenol III, cyclization to IV, and finally loss of water. In support of this sequence of changes mention should be made of the formation of the furan from the monoenol produced by 1,4-

(1) This paper was presented at the Baltimore meeting of the American Chemical Society, April 4, 1939.

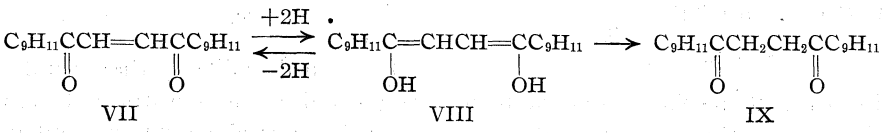
(2) *Cf.* (a) Conant and Lutz, THIS JOURNAL, **45**, 1047 (1923) (b) Lutz, *ibid.*, **51**, 3008 (1929); (c) Lutz and Palmer, *ibid.*, **57**, 1947 1953, 1957 (1935).

addition of hydrogen chloride to the α,β-unsaturated ketone system of $C_6H_5COCH{=}C(Cl)CO-C_6H_5$,[3] and the close analogy for cyclization of the type suggested in the ready formation of hydroxyfuranones from 1,2,4-triketone enols.

It has been shown that reduction of the analogous conjugated system of the α-diketones with zinc or catalytic hydrogen proceeds 1,4 to give mobile intermediate ene-diols of the type RC(OH)=C(OH)R which could be fixed and isolated as diacetates.[4] Recently the important discovery that enols of mesityl ketones are extraordinarily persistent and slow to ketonize[5a] has been utilized to demonstrate this mechanism: catalytic reduction of three monomesityl α-diketones[5b,c] of the type $C_9H_{11}COCOR$ produces fairly persistent ene-diols which undergo rearrangement to the α-hydroxy ketones or ready oxidation back to the α-diketones; and dimesityl diketone is reducible to stereoisomeric metastable crystalline ene-diols.[4b,6] The extraordinary persistence of these ene-diols appears to be at a maximum in compounds such as the dimesityl derivative where the migrating hydrogen must go to a carbon directly linked to a mesityl nucleus.

Further experiments on 1,4-dimesityl unsaturated 1,4-diketones were suggested by the above facts and have been carried out in order to obtain more information concerning reduction of conjugated systems of the type involved and the chemistry of the dienols which are produced.

Hydrogenation of di-(trimethylbenzoyl)-ethylene (VII) in ethanol at 0° with platinum as catalyst takes place rapidly with absorption of one molecule of hydrogen. Di-(trimethylbenzoyl)-ethane (IX) is obtained practically quantitatively when the reaction mixture is allowed to stand for a period of time under hydrogen, preferably with a small amount of added piperidine to catalyze ketonization.



The dienol VIII was shown to be the chief primary product under these conditions by filtering the solution rapidly under an atmosphere of nitrogen and running it directly into a solution of a known amount of iodine, the unused excess then being determined by titration with standard sodium thiosulfate. Assuming the amount of iodine used up to be a measure of the amount of the dienol present, yields of over 90% were demonstrated in several experiments. The oxidation of the dienol is presumably a 1,6-process and analogous to the oxidation of *p*-hydroquinones.

Reduction of di-(trimethylbenzoyl)-ethylene (VII) by means of zinc and acetic acid, a representative metal combination, ordinarily produces di-(trimethylbenzoyl)-ethane (IX) in good yield. It has been possible to show that here also the chief primary product is the dienol VIII. The reaction was carried out under modified conditions at 0°, and the resulting solution filtered from the zinc directly into iodine solution under an atmosphere of nitrogen; 61% of one mole of iodine was reduced. The dienol is decidedly mobile in the type of solvent used, however, as was shown in catalytic hydrogenations carried out in a somewhat similar solvent combination. Assuming a comparable rate of ketonization during manipulation in the zinc–acetic acid reduction and making due allowance, the result indicates that addition was practically exclusively 1,6, as would be expected.[2a]

In many of the experiments using the iodine oxidation method of analysis of the products of reduction, the results were checked by actual isolation and separation of the mixture of saturated and unsaturated 1,4-diketones. Fractional crystallization, while effective and successful in several instances, was laborious and inaccurate. A rapid and convenient method of separating was developed utilizing the conversion of the unsaturated diketone into the water soluble addition product X by the action of a boiling solution of sodium bisulfite in 60% ethanol; the water soluble sulfonate could be separated easily from the saturated diketone which was recovered and

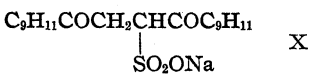
(3) Lutz and Wilder, THIS JOURNAL, **56**, 1193 (1934).

(4) (a) Thiele, *Ann.*, **306**, 142 (1899); (b) Thompson, THIS JOURNAL, **61**, 1281 (1939).

(5) (a) Kohler, Tishler and Potter, *ibid.*, **57**, 2517 (1935); (b) Kohler and Thompson, *ibid.*, **59**, 887 (1937); (c) Lutz and Wood, *ibid.*, **60**, 705 (1938).

(6) Fuson and Corse, *ibid.*, **61**, 975 (1939). Incidentally, in connection with the above facts, attention may be called to the significant parallelisms between 1,4-reductions of α-diketones, pinacol reduction and dimolecular reduction of acid chlorides [*cf.* Werner, *Chem. Ztg.*, **1**, 4; Erlenmeyer, *J. prakt. Chem.*, **65**, 351 (1902); Klinger, *Ber.*, **24**, 1268, 1271 (1891); **31**, 1217 (1898)], and between the 1,4-oxidation of ene-diols and 1,2-glycols.

weighed, the amount of the unsaturated diketone being determined by difference.



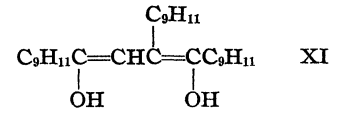
X

In connection with the mechanism of the main course of reduction in these experiments, 1,2-addition directly at the ethylene linkage, or 1,4-reduction of the α,β-unsaturated ketone grouping with the formation of an intermediate monoenol of the type III, giving intermediate products oxidizable directly or through subsequent enolizations to the unsaturated 1,4-diketone, could not account for the formation of the easily oxidizable dienol and are therefore excluded. Enols and dienols in this series would be unstable and enolization of a carbonyl group during or after reduction would be most unlikely under the conditions of these experiments. Furthermore, there is now evidence in another series for the existence of four substituted monoenols of the type III, one of which has been isolated crystalline; and none of these are oxidizable by air or iodine nor enolized further under ordinary conditions.[7]

Experiments were made to determine the persistence of the dienol (VIII). The best yields were obtained by reduction in ethanol at 0°. Ketonization under these conditions is evidently very slow in spite of the manipulations covering nearly three hours between initiation of hydrogenation and the reaction with iodine. Solutions of the dienol, filtered from catalyst under an atmosphere of nitrogen and allowed to stand quietly at 26–29°, were found to possess a half life period of about twelve hours; however, when shaken at room temperature either in the hydrogenation flask and in the presence of the catalyst, or in another vessel, filtered from catalyst and under an atmosphere of nitrogen, the half life period was considerably less (approximately two hours). The dienol, then, is moderately persistent even though there is no hindering group directly attached to either of the carbons to which the enol hydrogens migrate.

Preliminary attempts to isolate the dienol have not been successful. Attempted reaction with diazomethane brought about ketonization instead. However, a crystalline dienol of this type, namely, XI, melting at 70–71°, has been obtained in the 1,2,4-trimesityl series and will be described in a later report.[7]

(7) Lutz and Kibler, results to be published shortly.



XI

It seemed unlikely that catalytic hydrogen would add 1,6 to unsaturated 1,4-diketones exclusively under all conditions, and an attempt was made to find conditions favoring normal hydrogenation at the ethylene linkage. Of course the conditions tested were necessarily limited to those under which the dienol would likely be persistent. In ethanol solution, temperature has a very marked effect as shown by a typical experiment carried out at room temperature instead of 0°, the time elapsing between initiation of reduction and analysis of the resulting mixture being held to a minimum (seven minutes). The amount of dienol formed, allowing for the small amount of ketonization which would occur during the manipulation, was approximately 30%, in contrast with 90–94% obtained in the experiments carried out at 0°. It is therefore evident that the reduction is more ordered and consistently 1,6 at lowered temperatures.

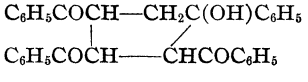
A series of reductions using platinum as catalyst was carried out at 0° in different solvents, the products being analyzed by the iodine oxidation method. The following percentages of dienol were found: in 95% ethanol, 91–94%; in a 4–1 dioxane–ethanol mixture, 90%; in ethyl acetate, 78%; in isopropyl ether, 60%; in benzene (at 5°), 54%; in *n*-hexane, 60%; and in decalin, 17%. These reductions must have proceeded 1,6 at least to the extent of the figures given, and possibly a little more since a small amount of ketonization may have occurred before completion of hydrogenation and analysis of the solution. The amount of ketonization in these solvents at 0° is probably very small and there is no reason to suspect that there would be an abnormally high rate in decalin, the one solvent in which the yield of dienol is very low.

The catalytic reduction of VII in an acetic–propionic acid mixture at 0° gave a yield of dienol on the order of 40–50%. This value is a rough approximation only, because of the mobility of the dienol under these conditions, and was estimated by extrapolation from values determined in several runs in which the time of shaking the reaction mixture was varied.

From the foregoing results it is obvious that conditions have a marked and varied influence on

the mode of catalytic hydrogenation of di-(trimethylbenzoyl)-ethylene, and that there is no consistent solvent effect. The contrasting yields of dienol obtained in *n*-hexane and in decalin are surprising. In the latter solvent when 1,6-addition is at a minimum, 1,2-addition directly at the ethylene linkage is probably the dominant reaction, although of course 1,4-addition is also possible.

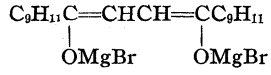
In this connection attention should be called to the effect of solvent and conditions on the yield of cyclic dimolecular products in the catalytic reduction of dibenzoylethylene.[2c] In alcohol as one extreme a mechanism involving at least one carbonyl must be involved in view of the large yield of cyclic dimolecular product (XII). On the other hand, when hydrogenation is carried out in decalin as the solvent, complications involving enolic intermediates are at a minimum with normal net hydrogenation at the ethylene linkage predominant. In the case of reduction of the allyl ether system of pseudocodeine types, conditions also have a marked effect on the course of addition, some consistently favoring one mode over another.[8]



XII

This work is being extended to other and longer conjugated systems, including types in which an aromatic nucleus furnishes one or more of the double bonds involved in the system connecting the two carbonyl groups.

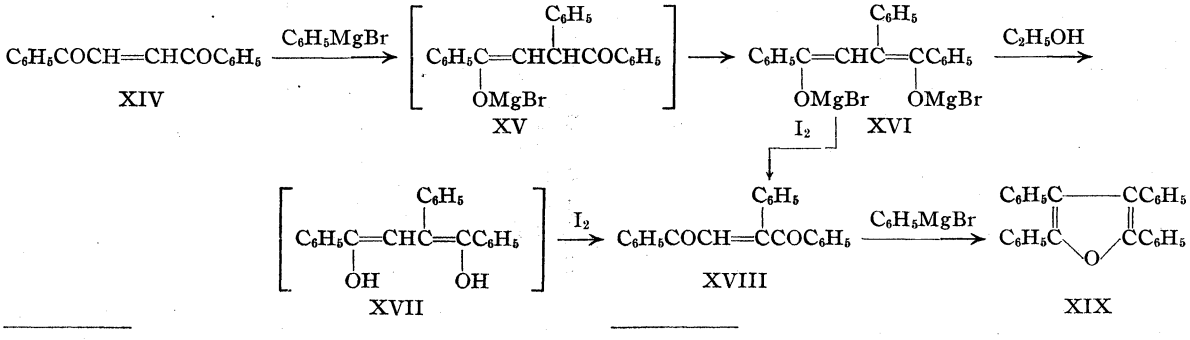
The fact that the dienol produced in reduction of di-(trimethylbenzoyl)-ethylene is sufficiently persistent to permit oxidation back suggested a simple method of converting the 1,4-dimesityl saturated 1,4-diketones into the corresponding unsaturated diketones through hydrolysis of the dimagnesium dienolate under oxidizing conditions. This method is of value because it makes possible the synthesis of a type of unsaturated diketone which cannot be prepared by the usually convenient nitric acid oxidation of the corresponding furan. In the case of di-(trimethylbenzoyl)-ethane, the dimagnesium dienolate (XIII) is easily made by heating the saturated diketone (IX) with an excess of phenylmagnesium bromide at 110° in isoamyl ether. The mixture, when poured into a precooled solution of iodine in 95% ethanol, gave *trans*-di-(trimethylbenzoyl)-ethylene (VII).



XIII

The above procedure has proved useful in the preparation of dimesityl unsaturated diketones with substituents on the ethylene linkage, utilizing the dimagnesium dienolates produced by the action of the Grignard reagent on di-(trimethylbenzoyl)-ethylene.[7,9]

It would be expected that the dienols of ordinary saturated 1,4-diketones such as dibenzoylethane would be extremely unstable and would undergo rapid ketonization if formed in any reaction. Nevertheless, it seemed possible that some dienols of this type might exist long enough to be caught by the oxidation reaction. No simple method is available to study the dienol of dibenzoylethane and the dimagnesium dienolate has not been made. However, ether solutions of a phenylated analog, namely, the dimagnesium dienolate XVI formed by the addition of phenylmagnesium bromide to dibenzoylethylene (XIV), is readily available;[9] when decomposed in cold alcoholic iodine solution *cis*-dibenzoylphenylethylene (XVIII) is obtained and none of the saturated diketone. This result is of particular significance in that it demonstrates in another way the correctness of the mechanism proposed for the action of the aryl Grignard reagents on unsaturated 1,4-diketones.[9]



(8) Lutz and Small, THIS JOURNAL, **54**, 4715 (1932).

(9) Lutz and Tyson, *ibid.*, **56**, 1341 (1934).

An interesting result was observed when the ether solution of the dimagnesium dienolate XVI, containing a large excess of phenylmagnesium bromide, was poured into a cooled ether solution of an excess of iodine. Tetraphenylfuran (XIX) was produced. Evidently the dienolate XVI was first oxidized directly to dibenzoylphenylethylene (XVIII), and was then converted into tetraphenylfuran by 1,4-addition of phenylmagnesium bromide followed by the equivalent of dehydration, the latter reactions (known[10]) competing favorably with cleavage of phenylmagnesium bromide by iodine.

Experimental Part

The Catalytic Reduction of Di-(trimethylbenzoyl)-ethylene.—In a number of preliminary experiments an apparatus was devised to carry out hydrogenations at −5 to 0° with an arrangement for manipulating the solution afterward under an inert atmosphere. The hydrogenation flask was immersed in a cooling bath. The main side neck of the flask was fitted with a glass tube slip joint holding a siphon tube with a stopcock; this siphon tube could be pushed down into a small depression blown in the bottom of the flask whereby the solution could be drawn out by suction. A separatory funnel was sealed to the neck of the flask for introduction of solvent. The siphon was connected to a sintered glass funnel and this in turn to a receiving flask arranged for sweeping with nitrogen and for application of suction. The material being reduced was first dissolved in the hot solvent and the solution quickly chilled to produce fine crystals (since the reactions were run at 0° the solid unsaturated diketone was usually present but passed into solution as the hydrogenation proceeded). Completion of the reduction was indicated by the marked slowing down or stopping of hydrogen absorption after approximately one molecule had been used up, and by solution of the unsaturated diketone and discharge of its yellow color. Upon completion of reduction, the siphon was lowered and the solution drawn over by suction, through the sintered glass funnel to remove the catalyst, protected by an atmosphere of hydrogen or nitrogen, into the receiving flask. The hydrogenation flask was then rinsed with several portions of pure solvent. In most of the experiments the receiving flask contained an excess of aqueous or alcoholic iodine (a known amount); the dienol present was oxidized immediately by the iodine, and the unreacted iodine was then determined at leisure by titration with standardized sodium thiosulfate. In some experiments the receiving flask was used as a means of storage for testing the stability of the dienol under certain conditions, and for experiments on the dienol itself, suitable arrangements being made for the introduction of reagents or for the removal of aliquot parts, all under a protective atmosphere of purified nitrogen.

In a number of experiments carried out at room temperature an attempt was made to minimize the time elapsing between initiation of reduction and analysis of the product. A device was used to introduce the catalyst after arranging and sweeping the apparatus because it was found that hydrogenation started to some extent before shaking was begun. The catalyst was placed in a thin glass bulb blown on the end of a glass tube passing through a rubber stopper into the main side neck of the flask; this was filled with alcohol; the siphon tube, also filled with alcohol, was inserted into the glass bulb through a rubber tube slip joint and served as a plunger; when ready the siphon tube was pressed down breaking the glass bulb and allowing the catalyst to drop into the mixture, shaking being started immediately thereafter.

In several runs with certain batches of catalyst, only small amounts of dienol were obtained and in these instances it was demonstrated that there was present in the catalyst a trace of alkali sufficient to be detectable by indicators in the washings. This trace of alkali was not easily removed. In a typical case a sample of catalyst containing alkali was treated as follows: it was washed, repeatedly with water, then with dilute nitric acid, and again with water; it was dried *in vacuo* at 200°; it was then washed with dilute ammonium hydroxide and successive portions of water and dried at 200° *in vacuo*, the process being repeated a second time. Only at the end of this treatment was the sample of catalyst free from alkali or acid, giving, when reduced with hydrogen in pure water, an aqueous suspension which was neutral to indicators. This batch of catalyst, though less active than other preparations, brought about reduction of di-(trimethylbenzoyl)-ethylene to the dienol in 90% yield through the usual manipulation. The production of traces of alkali in the catalyst apparently was minimized by lowering the sodium nitrate fusion temperature during the preparation.

The results of a series of experiments under different conditions of temperature, solvent and time, are listed in the table.

SOME TYPICAL CATALYTIC HYDROGENATIONS OF DI-(TRIMETHYLBENZOYL)-ETHYLENE

Solvent	Vol. of solvent per g.,[a] cc.	Time, min.	at °C. (Temp.)	Dienol,[b] % obtained
95% Ethanol	120	7	−5 to 0	31.5
95% Ethanol	120	180	−5 to 0	90.5
95% Ethanol	121	172	−5 to 0	93.7[c]
95% Ethanol	117	125[d]	−5 to 0	
		and 2.0 hrs.	26	83.2
		6.3 hrs.	26	65.3
		11.5 hrs.	26	48.4
		20.5 hrs.	26–29	19.0
		35.2 hrs.	26	1.4
95% Ethanol	116	60	−5 to 0	
		and 90[e]	24	56.2
Acetic Acid	113	12.5	−5 to 0	30.7
(37% propionic	158	42	−5 to 0	12.9
acid)[f]	123	60	−5 to 0	3.3
Dioxane (20%				
ethanol)[g]	143	65	−5 to 0	90.3[c]
Ethyl acetate[h]	116	60	−5 to 0	76.2
Isopropyl ether[i]	128	65	−5 to 0	59.5[c]
Benzene[i]	135	85	+5	53.5[c]
n-Hexane[ij]	148	120	−5 to 0	59.5
Decalin[i]	167	135	−5 to 0	16.7[c]

[a] The amount of VII used in each run was 0.5 to 0.6 g. The amount of catalyst (PtO_2) per gram was 0.15 to 0.30

(10) Hahn and Murray, THIS JOURNAL, **36**, 1484 (1914).

g. [b] Determined by iodine oxidation and titration for unused iodine. [c] These results were checked by separation of the products after iodine oxidation, using the sodium bisulfite method, and isolating and weighing the saturated 1,4-diketone (IX). [d] The solution containing the reduction products (largely dienol) was filtered from the catalyst and allowed to stand quietly under an atmosphere of purified nitrogen for the lengths of time and at the temperatures given, aliquot parts then being drawn off and analyzed by the iodine oxidation method. A larger amount of VII was used in this experiment (1.2 g). [e] The solution of reduction products was allowed to come to room temperature; then, without removing the catalyst, the shaking was continued 90 min. [f] 63% by volume of acetic acid. The purpose of adding propionic acid was to lower the freezing point so that the reaction could be run at 0°. [g] 80% by volume dioxane; the ethanol was added to lower the freezing point. [h] Dried over anhydrous sodium sulfate and distilled once. [i] Dried over sodium and distilled twice. [j] A larger amount of catalyst was used here in order to speed up the reaction.

Semi-quantitative checks on many of the determinations of the dienol yields were made as follows: the product, consisting of a mixture of the saturated and the unsaturated diketones (VII and IX), was isolated, dried and weighed. This mixture was then subjected to the action of a boiling 60% ethanol solution containing a large excess of sodium bisulfite until the yellow color of the unsaturated diketone was thoroughly bleached. The mixture was then diluted with water and the precipitate of unreacted di-(trimethylbenzoyl)-ethane was filtered off and weighed. The amount of unsaturated 1,4-diketone was determined by difference and corresponded to the amount of dienol which had been oxidized. In every case indicated in the table the results of the iodine oxidation and titration for unused iodine were checked by this method within a few per cent.

In some cases the absorption of hydrogen was apparently low due to temperature fluctuation in the cooling system or to reduction getting under way before shaking was begun. In several such instances the check analysis by the bisulfite method showed that reduction had actually been complete; if reduction had not been complete the yield of the saturated diketone would have been lower and the yield of unsaturated diketone higher than the values indicated by the iodine oxidation analysis.

1,4-Dimesitylbutane-1,4-dione-2-sulfonic Acid (see X).—Two grams of di-(trimethylbenzoyl)-ethylene (VII) and 2 g. of sodium bisulfite were added to 25 cc. of 60% ethyl alcohol and the mixture refluxed on a steam-bath for fifteen minutes. The free sulfonic acid, liberated by pouring the reaction mixture into dilute hydrochloric acid, crystallized out as white plates; it was moderately soluble in water and in ether; the yield was 2.2 g. (88%). It was purified by conversion into the *lead salt* in aqueous medium, using lead acetate, and by repeated crystallization of this from methanol–water mixtures.

Anal. Calcd. for $C_{16}H_{18}O_5SPb$: Pb, 20.5. Found: Pb, 20.1.

Zinc and Acetic Acid Reduction.—A hot solution of 3 g. of VII in 40 cc. of concd. acetic acid, 40 cc. of diethyl ether and 1 cc. of water was cooled to −5 to 0°, fine crystals being produced, and 1.5 g. of zinc dust was then added over a period of three minutes. The mixture was shaken for twenty minutes and was filtered and washed directly into cooled alcoholic iodine. The whole operation was carried out under a protective atmosphere of purified nitrogen. Previous experiments had shown that reduction was complete within this time. Analysis for the unused iodine showed 60.9% dienol to have been present at the moment of filtration.

Preparation of *trans*-Di-(trimethylbenzoyl)-ethylene (VII) from Di-(trimethylbenzoyl)-ethane (IX).—A sample of IX (0.79 g.) was treated with an excess of methylmagnesium iodide in isoamyl ether and the mixture heated for seventy-five minutes at 110°; at the end of this time the evolution of methane had ceased, approximately two moles being liberated (collected). The mixture was then poured into a cooled solution (0°) of 1.6 g. of iodine in 60 cc. of 95% ethanol. The solvent was removed by distillation and 0.33 g. of VII was recovered (42%).

Preparation of *cis*-1,2,4-Triphenylbutenedione-1,4 (Dibenzoylphenylethylene) (XVIII) and Tetraphenylfuran (XIX) from Dibenzoylethylene (XIV).—Four grams of dibenzoylethylene was added to a solution of phenylmagnesium bromide made from 2.5 g. of magnesium and 10 cc. of bromobenzene in 100 cc. of absolute ether. The mixture was refluxed for twenty minutes, cooled to 0°, and poured into 200 cc. of 95% ethanol containing 9 g. of iodine (cooled to the same temperature). After removal of the solvents, a brown oil was obtained from which 0.65 g. of *cis*-dibenzoylphenylethylene was isolated (12.3%) and identified by mixture melting point with an authentic sample.

A solution of phenylmagnesium bromide, made from 3 g. of magnesium, was treated with 4.75 g. of dibenzoylethylene (added slowly), and the mixture poured into a cooled absolute ether solution of iodine; as the iodine color faded, more was added so that an excess was maintained (except momentarily during the addition). On hydrolysis, washing out the iodine, and working up the product, 2.1 g. (38%) of nearly pure tetraphenylfuran was isolated and identified (m. p. 174°).

Summary

Reduction of di-(trimethylbenzoyl)-ethylene by zinc and acetic acid or by catalytic hydrogen in certain solvents at 0° has been shown to be largely 1,6 by the formation of the moderately persistent dienol which is readily oxidizable back to the unsaturated 1,4-diketone.

Unsaturated dimesityl 1,4-diketones are prepared in a new way by hydrolysis under oxidizing conditions of the dimagnesium dienolates made from the saturated 1,4-diketone directly or from the unsaturated 1,4-diketone by reaction with an arylmagnesium halide.

CHARLOTTESVILLE, VIRGINIA RECEIVED MAY 12, 1939

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, No. 708]

The Structure of Proteins

BY LINUS PAULING AND CARL NIEMANN

1. Introduction

It is our opinion that the polypeptide chain structure of proteins,[1] with hydrogen bonds and other interatomic forces (weaker than those corresponding to covalent bond formation) acting between polypeptide chains, parts of chains, and side-chains, is compatible not only with the chemical and physical properties of proteins but also with the detailed information about molecular structure in general which has been provided by the experimental and theoretical researches of the last decade. Some of the evidence substantiating this opinion is mentioned in Section 6 of this paper.

Some time ago the alternative suggestion was made by Frank[2] that hexagonal rings occur in proteins, resulting from the transfer of hydrogen atoms from secondary amino to carbonyl groups with the formation of carbon–nitrogen single bonds. This *cyclol hypothesis* has been developed extensively by Wrinch,[3] who has considered the geometry of cyclol molecules and has given discussions of the qualitative correlations of the hypothesis and the known properties of proteins.

It has been recognized by workers in the field of modern structural chemistry that the lack of conformity of the cyclol structures with the rules found to hold for simple molecules makes it very improbable that any protein molecules contain structural elements of the cyclol type. Until recently no evidence worthy of consideration had been adduced in favor of the cyclol hypothesis. Now, however, there has been published[4] an interpretation of Crowfoot's valuable X-ray data on crystalline insulin[5] which is considered by the authors to provide proof[6] that the insulin molecule actually has the structure of the space-enclosing cyclol C_2. Because of the great and widespread interest in the question of the structure of proteins, it is important that this claim that insulin has been proved to have the cyclol structure be investigated thoroughly. We have carefully examined the X-ray arguments and other arguments which have been advanced in support of the cyclol hypothesis, and have reached the conclusions that there exists no evidence whatever in support of this hypothesis and that instead strong evidence can be advanced in support of the contention that bonds of the cyclol type do not occur at all in any protein. A detailed discussion of the more important pro-cyclol and anti-cyclol arguments is given in the following paragraphs.

2. X-Ray Evidence Regarding Protein Structure

It has not yet been possible to make a complete determination with X-rays of the positions of the atoms in any protein crystal; and the great complexity of proteins makes it unlikely that a complete structure determination for a protein will ever be made by X-ray methods alone.[7] Nevertheless the X-ray studies of silk fibroin by Herzog and Jancke,[8] Brill,[9] and Meyer and Mark[10] and of β-keratin and certain other proteins by Astbury and his collaborators[11] have provided strong (but

(1) E. Fischer, "Untersuchungen über Aminosäuren, Polypeptide und Protein," J. Springer, Berlin, 1906 and 1923.

(2) F. C. Frank, *Nature*, **138**, 242 (1936); this idea was first proposed by Frank in 1933: see W. T. Astbury, *J. Textile Inst.*, **27**, 282 (1936).

(3) D. M. Wrinch, (a) *Nature*, **137**, 411 (1936); (b) **138**, 241 (1936); (c) **139**, 651, 972 (1937); (d) *Proc. Roy. Soc.* (London), **A160**, 59 (1937); (e) **A161**, 505 (1937); (f) *Trans. Faraday Soc.*, **33**, 1368 (1937); (g) *Phil. Mag.*, **26**, 313 (1938); (h) *Nature*, **143**, 482 (1939); etc.

(4) (a) D. M. Wrinch, *Science*, **88**, 148 (1938); (b) THIS JOURNAL, **60**, 2005 (1938); (c) D. M. Wrinch and I. Langmuir, *ibid.*, **60**, 2247 (1938); (d) I. Langmuir and D. M. Wrinch, *Nature*, **142**, 581 (1938).

(5) D. Crowfoot, *Proc. Roy. Soc.* (London), **A164**, 580 (1938).

(6) In ref. 4d, for example, the authors write "The superposability of these two sets of points represented the first stage in the proof of the correctness of the C_2 structure proposed for insulin. ... These investigations, showing that it is possible to deduce that the insulin molecule is a polyhedral cage structure of the shape and size predicted, give some indication of the powerful weapon which the geometrical method puts at our disposal."

(7) A protein molecule, containing hundreds of amino acid residues, is immensely more complicated than a molecule of an amino acid or of diketopiperazine. Yet despite attacks by numerous investigators no complete structure determination for any amino acid had been made until within the last year, when Albrecht and Corey succeeded, by use of the Patterson method, in accurately locating the atoms in crystalline glycine [G. A. Albrecht and R. B. Corey, THIS JOURNAL, **61**, 1087 (1939)]. The only other crystal with a close structural relation to proteins for which a complete structure determination has been made is diketopiperazine [R. B. Corey, *ibid.*, **60**, 1598 (1938)]. The investigation of the structure of crystals of relatively simple substances related to proteins is being continued in these Laboratories.

(8) R. O. Herzog and W. Jancke, *Ber.*, **53**, 2162 (1920).

(9) R. Brill, *Ann.*, **434**, 204 (1923).

(10) K. H. Meyer and H. Mark, *Ber.*, **61**, 1932 (1928).

(11) W. T. Astbury, *J Soc. Chem. Ind.*, **49**, 441 (1930); W. T. Astbury and A. Street, *Phil. Trans. Roy. Soc.*, **A230**, 75 (1931); W. T. Astbury and H. J. Woods, *ibid.*, **A232**, 333 (1933); etc.

not rigorous) evidence that these fibrous proteins contain polypeptide chains in the extended configuration. This evidence has been strengthened by the fact that the observed identity distances correspond closely to those calculated with the covalent bond lengths, bond angles, and N-H $\cdots$ O hydrogen bond lengths found by Corey in diketopiperazine.

The X-ray work of Astbury also provides evidence that α-keratin and certain other fibrous proteins contain polypeptide chains with a folded rather than an extended configuration. The X-ray data have not led to the determination of the atomic arrangement, however, and there exists no reliable evidence regarding the detailed nature of the folding.

X-Ray studies of crystalline globular proteins have provided values of the dimensions of the units of structure, from which some qualitative conclusions might be drawn regarding the shapes of the protein molecules. An interesting attempt to go farther was made by Crowfoot,[5] who used her X-ray data for crystalline insulin to calculate Patterson and Patterson–Harker diagrams.[12] Crowfoot discussed these diagrams in a sensible way, and pointed out that since the X-ray data correspond to effective interplanar distances not less than 7 Å. they do not permit the determination of the positions of individual atoms;[13] the diagrams instead give some information about large-scale fluctuations in scattering power within the crystal. Crowfoot also stated that the diagrams provide no reliable evidence regarding either a polypeptide chain or a cyclol structure for insulin.

Wrinch and Langmuir[4] have, however, contended that Crowfoot's X-ray data correspond in great detail to the structure predicted for the insulin molecule on the basis of the cyclol theory, and thus provide the experimental proof of the theory. We wish to point out that the evidence adduced by Wrinch and Langmuir has very little value, because their comparison of the X-ray data and the cyclol structure involves so many arbitrary assumptions as to remove all significance from the agreement obtained. In order to attempt to account for the maxima and minima appearing on Crowfoot's diagrams, Wrinch and Langmuir made the assumption that certain regions of the crystal (center of molecule, center of lacunae) have an electron density less than the average, and others (slits, zinc atoms) have an electron density greater than the average. The positions of these regions are predicted by the cyclol theory, but the magnitudes of the electron density are not predicted quantitatively by the theory. Accordingly the authors had at their disposal seven parameters, to which arbitrary values could be assigned in order to give agreement with the data. Despite the numbers of these parameters, however, it was necessary to introduce additional arbitrary parameters, bearing no predicted relation whatever to the cyclol structure, before rough agreement with the Crowfoot diagrams could be obtained. Thus the peak B″, which is the most pronounced peak in the $P(xy0)$ section (Fig. 2 of Wrinch and Langmuir's paper) and is one of the four well-defined isolated maxima reported, is accounted for by use of a region (V) of very large negative deviation located at a completely arbitrary position in the crystal; and this region is not used by the authors in interpreting any other features of the diagrams. This introduction of four arbitrary parameters (the three coördinates and the intensity of the region V) to account for one feature of the experimental diagrams would in itself make the argument advanced by Wrinch and Langmuir unconvincing; the fact that many other parameters were also assigned arbitrary values removes all significance from their argument.

It has been pointed out by Bernal,[14] moreover, that the authors did not make the comparison of their suggested structure and the experimental diagrams correctly. They compared only a fraction of the vectors defined by their regions with the Crowfoot diagrams, and neglected the rest of the vectors. Bernal reports that he has made the complete calculation on the basis of their structure, and has found that the resultant diagrams show no relation whatever to the experimental diagrams. He states also that with seven density values at closest-packed positions as arbitrary parameters he has found that a large number of structures which give rough agreement with the experimental diagrams can be formulated.

We accordingly conclude that there exists no satisfactory X-ray evidence for the cyclol structure for insulin.

(12) A. L. Patterson, *Z. Krist.*, **90**, 517 (1935); D. Harker, *J. Chem. Phys.*, **4**, 825 (1936).

(13) It has also been pointed out by J. M. Robertson, *Nature*, **143**, 75 (1939), that the intensities of 60 planes could not provide sufficient information to locate the several thousand atoms in the insulin molecule.

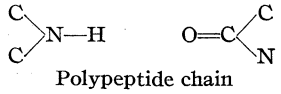
(14) J. D. Bernal, *Nature*, **143**, 74 (1939); see also D. P. Riley and I. Fankuchen, *ibid.*, **143**, 648 (1939).

3. Thermochemical Evidence Regarding Protein Structure

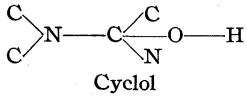
It is, moreover, possible to advance a strong argument in support of the contention that the cyclol structure does not occur to any extent in any protein.

X-Ray photographs of denatured globular proteins are similar to those of β-keratin, and thus indicate strongly that these denatured proteins contain extended polypeptide chains.[15] Astbury[16] has also obtained evidence that in protein films on surfaces the protein molecules have the extended-chain configuration, and this view is shared by Langmuir, who has obtained independent evidence in support of it.[17] Now the heat of denaturation of a protein is small—less than one hundred kilogram calories per mole of protein molecules for denaturation in solution,[18] that is, only a fraction of a kilogram calorie per mole of amino acid residues. Consequently the structure of native proteins must be such that only a very small energy change is involved in conversion to the polypeptide chain configuration.

It is unfortunate that there exist no substances known to have the cyclol structure; otherwise their heats of formation could be found experimentally for comparison with those of substances such as diketopiperazine which are known to contain polypeptide chains or rings. It is possible, however, to make this comparison indirectly in various ways. A system of values of bond energies and resonance energies has been formulated[19] which permits the total energy of a molecule of known structure to be predicted with an average uncertainty of only about 1 kcal./mole for a molecule the size of the average amino acid residue. The polypeptide chain (amide form) and cyclol can be represented by the following diagrams

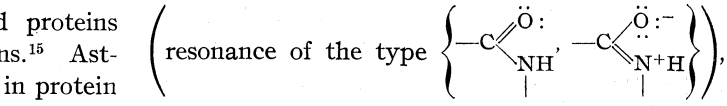


Polypeptide chain



Cyclol

The change in bonds from polypeptide chain to cyclol is N–H + C=O ⟶ N–C + C–O + O–H. With N–H = 83.3, C=O = 152.0, N–C = 48.6, C–O = 70.0, and O–H = 110.2 kcal./mole, the bonds of an amino acid residue are found to be 6.5 kcal./mole less stable for the cyclol configuration than for the chain configuration. This must further be corrected for resonance of the double bond



which amounts for an amide to about 21 kcal./mole[19]; there is no corresponding resonance for the cyclol, which involves only single bonds. We conclude that the cyclol structure is less stable than the polypeptide chain structure by 27.5 kcal./mole per amino acid residue.

This value relates to gaseous molecules, containing no hydrogen bonds, and with the ordinary van der Waals forces also neglected. It is probable that the ordinary van der Waals forces would have nearly the same value for a cyclol as for a polypeptide chain; and the available evidence[19,20] indicates that the polypeptide hydrogen bonds would be slightly stronger than the hydrogen bonds for the cyclol structure. Moreover, the observed small values (about 2 kcal./mole) for the heat of solution of amides and alcohols show that the stability relations in solution are little different from those of the crystalline substances. We accordingly conclude that the polypeptide chain structure for a protein is more stable than the cyclol structure by about 28 kcal./mole per amino acid residue, either for a solid protein or a protein in solution (with the active groups hydrated[21]).

The comparison of the polypeptide chain and cyclol can also be made without the use of bond energy values. The heat of combustion of crystalline diketopiperazine, which contains two glycine residues forming a polypeptide chain,[22] is known;[23] from its value, 474.6 kcal./mole, the heat of formation of crystalline diketopiperazine (from elements in their standard states) is calculated to be 128.4 kcal./mole, or 64.2 kcal./mole per glycine residue. A similar calculation cannot be made directly for the cyclol structure, because no sub-

(15) W. T. Astbury, S. Dickinson and K. Bailey, *Biochem. J.*, **29**, 2351 (1935).

(16) W. T. Astbury, *Nature*, **143**, 280 (1939).

(17) I. Langmuir, *ibid.*, **143**, 280 (1939).

(18) M. L. Anson and A. E. Mirsky, *J. Gen. Physiol.*, **17**, 393, 399 (1934).

(19) (a) L. Pauling and J. Sherman, *J. Chem. Phys.*, **1**, 606 (1933); (b) L. Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 1939. The values quoted above are from the latter source; they involve no significant change from the earlier set.

(20) M. L. Huggins, *J. Org. Chem.*, **1**, 407 (1936).

(21) The suggestion has been made [F. C. Frank, *Nature*, **138**, 242 (1936)] that the energy of hydration of hydroxyl groups might be very much greater than that of the carbonyl and secondary amino groups of a polypeptide chain; there exists, however, no evidence indicating that this is so.

(22) R. B. Corey, ref. 7.

(23) M. S. Kharasch, *Bur. Standards J. Research*, **2**, 359 (1929).

stance is known to have the cyclol structure; but an indirect calculation can be made in many ways, such as the following. One hexamethylenetetramine molecule and one pentaerythritol molecule contain the same bonds as four cyclized glycine residues and three methane molecules; hence the heat of formation of a glycine cyclol per residue is predicted to have the value 32.2 kcal./mole found experimentally[24] for $\frac{1}{4}C_6H_{12}N_4(c) + \frac{1}{4}C(CH_2OH)_4(c) - \frac{3}{4}CH_4(c)$. Similarly the value for $N(C_2H_5)_3(c) + C_2H_5OH(c) - 3C_2H_6(c)$ is 40.2 kcal./mole. The average of several calculations of this type, 36 kcal./mole, differs from the experimental value of the heat of formation of diketopiperazine per residue, 64 kcal./mole, by 28 kcal./mole. This agrees closely with the value 27.5 kcal./mole found by the use of bond energies, and we can be sure that the suggested cyclol structure for proteins is less stable than the polypeptide chain structure by about this amount per amino acid residue. Since denatured proteins are known to consist of polypeptide chains, and native proteins differ in energy from denatured proteins by only a very small amount (less than 1 kcal./mole per residue), we draw the rigorous conclusion that *the cyclol structure cannot be of primary importance for proteins; if it occurs at all (which is unlikely because of its great energetic disadvantage relative to polypeptide chains) not more than about three per cent. of the amino acid residues could possess this configuration.*

The above conclusion is not changed if the assumption be made that polypeptide chains are in the imide rather than the amide form,[3b] since this would occur only if the imide form were the more stable. In this case the experimental values of heats of formation (such as that of diketopiperazine) would still be used as the basis for comparison with the predicted value for the cyclol structure, and the same energy difference would result from the calculation.

It has been recognized[25-27] that energy relations present some difficulty for the cyclol theory (although the seriousness of the difficulty seems not to have been appreciated), and various suggestions have been made in the attempt to avoid the difficulty. In her latest communication[3h] Wrinch writes, "The stability of the globular proteins, under special conditions, in solution and in the crystal, we attribute to definite stabilizing factors;[26,27] namely, (1) hydrogen bonds between the oxygens of certain of the triazine rings, (2) the multiple paths of linkage between atoms in the fabric, (3) the closing of the fabric into a polyhedral surface which eliminates boundaries of the fabric and greatly increases the symmetry, and (4) the coalescence of the hydrophobic groups in the interior of the cage." These factors are, however, far from sufficient to stabilize the cyclol structure relative to the polypeptide chain structure. (1) The hydrogen bonds between hydroxyl groups in the cyclol structure would have nearly the same energy (about 5 kcal./mole) as those involving the secondary amino and carbonyl groups of the polypeptide chain. The suggestion[26] that resonance of the protons between oxygen atoms would provide further stabilization is not acceptable, since the frequencies of nuclear motion are so small compared with electronic frequencies that no appreciable resonance energy can be obtained by resonance involving the motion of nuclei. (2) We are unable to find any aspects of the bond distribution in cyclols which are not taken into consideration in our energy calculation given above. (3) There is no type of interatomic interaction known to us which would lead to additional stability of a cage cyclol as the result of eliminating boundaries and increasing the symmetry. (4) The stabilizing effect of the coalescence of the hydrophobic groups has been estimated[26] to be about 2 kcal./mole per CH_2 group, and to amount to a total for the insulin molecule of about 600 kcal./mole. It seems improbable to us that the van der Waals interactions of these groups are much less than this for polypeptides. The maximum of 600 kcal./mole from this source is still negligibly small compared with the total energy difference to be overcome, amounting to about 8000 kcal./mole for a protein containing about 288 residues.[28]

We accordingly conclude that the cyclol structure is so unstable relative to the polypeptide structure that it cannot be of significance for proteins.

It may be pointed out that a number of experiments[29-31] have added the weight of their evi-

(24) The values of heats of combustion used are $C_6H_{12}N_4(c)$, 1006.7; $C(CH_2OH)_4(c)$, 661.2; $CH_4(c)$, 210.6; $N(C_2H_5)_3(c)$, 1035.5; $C_2H_5OH(c)$, 325.7; $C_2H_6(c)$, 370.0 kcal./mole.

(25) F. C. Frank, *Nature*, **138**, 242 (1936).

(26) I. Langmuir and D. Wrinch, *ibid.*, **143**, 49 (1939).

(27) D. Wrinch, *Symposia on Quant. Biol.*, **6**, 122 (1938).

(28) Other suggestions regarding the source of stabilizing energy which have been made hardly merit discussion. "Foreign molecules" (Wrinch, ref. 27), for example, cannot be discussed until we have some information as to their nature.

(29) G. I. Jenkins and T. W. J. Taylor, *J. Chem. Soc.*, 495 (1937).

(30) L. Kellner, *Nature*, **140**, 193 (1937).

(31) H. Meyer and W. Hohenemser, *ibid.*, **141**, 1138 (1938).

dence to the general conclusion reached in this communication that the cyclol bond and the cyclol fabric are energetically impossible.

4. Further Arguments Indicating the Non-existence of the Cyclol Structure

There are many additional arguments which indicate more or less strongly that the cyclol structure does not exist. Of these we shall mention only a few.

It has been found experimentally that two atoms in adjacent molecules or in the same molecule but not bonded directly to one another reach equilibrium at a distance which can be represented approximately as the sum of certain van der Waals radii for the atoms.[19,32] Two carbon atoms of methyl or methylene groups not bonded to the same atom never approach one another more closely than about 4.0 Å., and two hydrogen atoms not bonded to the same atom are always at least 2.0 Å. apart. It has been pointed out by Huggins[33] that the cyclol structure places the carbon atoms of side chains only 2.45 Å. apart, and that in the C_2 structure for insulin there are hydrogen atoms only 0.67 Å. apart. We agree with Huggins that this difficulty alone makes the cyclol hypothesis unacceptable.

A closely related argument, dealing with the small area available for the side chains of a cyclol fabric, has been advanced by Neurath and Bull.[34] The area provided per side chain by the cyclol fabric, about 10 sq. Å., is far smaller than that required; and, as Neurath and Bull point out, the suggestion[3e,26] that some of the side chains pass through the lacunae of the fabric to the other side cannot be accepted, because this would require non-bonded interatomic distances much less than the minimum values found in crystals.

One of the most striking features of the cyclol fabric is the presence of great numbers of hydroxyl groups: in the case of cyclol C_2 there are 288 hydroxyl groups exclusive of those present in the side chains. Recently Haurowitz[35,36] has subjected the cyclol hypothesis to experimental tests on the basis of the existence or non-existence of cage hydroxyl groups. In the first communication[35] Haurowitz concludes on the basis of his and previous experiments[37-39] on the acylation and alkylation of proteins that the experimental evidence is in decided opposition to the conception that proteins possess great numbers of hydroxyl groups and therefore to the cyclol hypothesis. It seems to us that the objection raised by Haurowitz[36] is worthy of consideration and it certainly cannot be disposed of on the grounds that the original structure has been destroyed unless some concrete evidence can be submitted to indicate that this is the case. In a second communication Haurowitz and Astrup[36] write that "According to the classical theory of protein structure the carboxyl and amino groups found after hydrolytic splitting of a protein come from —CO—NH— bonds. According to the cyclol hypothesis, however, the free carboxyl and amino groups must be formed, during the splitting, from bonds of the structure =C(OH)—N=. The classical theory would predict on hydrolysis no great change in the absorption spectrum below 2400 Å. because the CO groups of the amino acids and of the peptide bonds both are strongly absorbing in this region.[40] On the other hand, the cyclol hypothesis would predict a greatly increased absorption because of the formation of new CO groups. . . . The absorption for genuine and for hydrolyzed protein is about equal. This seems to be in greater accordance with the classical theory of the structure of proteins than with the cyclol theory."

Mention may also be made of the facts that no simple substances with the cyclol structure have ever been synthesized[29] and that in general chemical reactions involving the breaking of covalent bonds are slow, whereas rapid interconversion of polypeptide and cyclol structure must be assumed to occur in, for example, surface denaturation. These chemical arguments indicate strongly that the cyclol theory is not acceptable.[41]

5. A Discussion of Arguments Advanced in Support of the Cyclol Theory

Although a great number of papers dealing with the cyclol theory have been published, we have

(32) N. V. Sidgwick, "The Covalent Link in Chemistry," Cornell University Press, Ithaca, N. Y., 1933; E. Mack, Jr., THIS JOURNAL, **54**, 2141 (1932); S. B. Hendricks, *Chem. Rev.*, **7**, 431 (1930); M. L. Huggins, *ibid.*, **10**, 427 (1932).

(33) M. L. Huggins, THIS JOURNAL, **61**, 755 (1939).

(34) H. Neurath and H. D. Bull, *Chem. Rev.*, **23**, 427 (1938).

(35) T. Haurowitz, *Z. physiol. Chem.*, **256**, 28 (1938).

(36) T. Haurowitz and T. Astrup, *Nature*, **143**, 118 (1939).

(37) J. Herzig and K. Landsteiner, *Biochem. Z.*, **61**, 458 (1914).

(38) B. M. Hendrix and F. Paquin, Jr., *J. Biol. Chem.*, **124**, 135 (1938).

(39) K. G. Stern and A. White, *ibid.*, **122**, 371 (1938).

(40) M. A. Magill, R. E. Steiger and A. J. Allen, *Biochem. J.*, **31**, 188 (1937).

(41) Another argument against cyclols of the C_2 type can be based on the results reported by J. L. Oncley, J. D. Ferry and J. Shack, *Symposia on Quant. Biol.*, **6**, 21 (1938), H. Neurath, *ibid.*, **6**, 196 (1938), and J. W. Williams and C. C. Watson, *ibid.*, **6**, 208 (1938), who have shown that dielectric constant measurements and diffusion measurements indicate that the molecules of many proteins are far from spherical in shape.

had difficulty in finding in them many points of comparison with experiment (aside from the X-ray work mentioned above) which were put forth as definite arguments in support of the structure.

One argument which has been advanced is that the cyclol theory "readily interprets the total number of amino acid residues per molecule, without the introduction of any *ad hoc* hypothesis"[3e] and that "The group of proteins with molecular weights ranging rom 33,600 to 40,500 are closed cyclols of the type C_2 containing 288 amino acid residues."[3e] Now the presence of imino acids (proline, oxyproline) in a protein prevents its formation of a complete cyclol such as C_2, and many proteins in this molecular weight range are known to contain significant amounts of proline: for insulin 10% is reported,[3f] for egg albumin 4%,[42] for zein 9%,[43] for Bence–Jones protein 3%,[44] and for pepsin 5%.[45] Wrinch has stated that "a future modification" (in regard to the number of residues) "is also introduced if imino acids are present"[3c]; "these numbers perhaps being modified if imino acids are present",[3e] and "if certain numbers of imino acid residues are present, these numbers" (of residues) "may be correspondingly modified."[3g] This uncertainty regarding the effect of the presence of imino acids in cyclols on the expected number of residues leaves the argument little force. In fact, even the qualitative claim that the cyclol hypothesis implies the existence of polyhedral structures containing certain numbers of amino acid residues and so predicts that globular proteins have molecular weights which fall into a sequence of separated classes can be doubted for the same reason.

It has been claimed[36] that the cyclol hypothesis explains the facts that proteins contain certain numbers of various particular amino acid residues and that these numbers are frequently powers of 2 and 3,[46] and it is proper that we inquire into the nature of the argument. Wrinch states[27] "An individual R group" (side chain) "is presumably attached, not to just any α-carbon atom, but only to those whose environment makes them appropriate in view of its specific nature. As an example of different environments, we may refer to the cyclol cages; here the pairs of residues at a slit have 'different environments' and the residues not at a slit fall into sets which again have 'different environments.' We therefore expect characteristic proportions to be associated with aromatic, basic, acidic, and hydrocarbon R groups, respectively, even perhaps with individual R groups. In any case a non-random distribution of the proportions of each residue in proteins in general is to be expected on any fabric hypothesis. On the cyclol hypothesis, for example, α-carbons having equivalent environments occur in powers of 2 and 3. . . . It is difficult to avoid interpreting the many cases which have recently been summarized in which the proportions of many types of residue are powers of 2 and 3 as further direct evidence in favor of the cyclol fabric. This fabric consists of an alternation of diazine and triazine hexagons, with symmetries respectively 2 and 3." Also it has been said by Langmuir[47] that "The occurrence of these factors, 2 and 3, furnishes a powerful argument for a geometrical interpretation such as that given by the cyclol theory. In fact, the hexagonal arrangement of atoms in the cyclol fabric gives directly and automatically a reason for the existence of the factors 2 and 3 and the non-occurrence of such factors as 5 and 7."

On examining the cyclol C_2, however, we find that these statements are not justified. The only factors of 288 are of the form $2^n\ 3^m$; moreover, the framework of the cyclol C_2 has the tetrahedral symmetry T, so that if the distribution of side chains conforms to the symmetry of the framework the amino acid residues would occur in equivalent groups of twelve. But in view of the rapid decrease in magnitude of interatomic forces with distance there would seem to be little reason for the distribution of side chains over a large protein molecule to conform to the symmetry T; it is accordingly evident that any residue numbers might occur for the cyclol C_2. We conclude that the cyclol hypothesis does not provide an explanation of the occurrence of amino acid residues in numbers equal to products of powers of 2 and 3.

Although there is little reason to expect that the distribution of side chains would correspond to the symmetry of the framework, it is interesting to note that the logical application of the methods of argument used by Wrinch suggests strongly that sixty residues of each of two amino acids should be present in a C_2 cyclol. This cyclol contains twenty lacunae of a particular type—each surrounded by a nearly coplanar border of twelve diazine and triazine

(42) H. O. Calvery, *J. Biol. Chem.*, **94**, 613 (1931).

(43) T. B. Osborne and L. M. Liddle, *Am. J. Physiol.*, **26**, 304 (1910).

(44) C. L. A. Schmidt, "Chemistry of Amino Acids and Proteins," C. C. Thomas, Springfield, Ill., 1938.

(45) Unpublished determination by one of the authors.

(46) M. Bergmann and C. Niemann, *J. Biol. Chem.*, **115**, 77 (1936); **118** 307 (1937).

(47) I. Langmuir, *Symposia on Quant. Biol.*, **6**, 135 (1938).

rings. Each of these has trigonal symmetry so far as this near environment is concerned. Hence it might well be expected that a particular amino acid would be represented by three residues about each of these twenty lacunae, giving a total of sixty residues. But the number 60 cannot be expressed in the form $2^n 3^m$, it is not a factor of 288, and the integer nearest the quotient 288/60, 5, also cannot be expressed in the form $2^n 3^m$.

One of the most straightforward arguments advanced by Wrinch[3c,d] is that a protein surface film must have all its side chains on the same side, which would be the case for a cyclol fabric but not for an extended polypeptide chain. This argument now has lost its significance through the recently obtained strong evidence that proteins in films have the polypeptide structure,[16,17] and not the cyclol structure.

There can be found in the papers by Wrinch many additional statements which might be construed as arguments in support of the cyclol structure. None of these seems to us to have enough significance to justify discussion.

6. The Present State of the Protein Problem

The amount of experimental information about proteins is very great, but in general the processes of deducing conclusions regarding the structure of proteins from the experimental results are so involved, the arguments are so lacking in rigor, and the conclusions are so indefinite that it would not be possible to present the experimental evidence at the basis of our ideas of protein structure[48] in a brief discussion. In the following paragraphs we outline our present opinions regarding the structure of protein molecules, without attempting to do more than indicate the general nature of the evidence supporting them. These opinions were formed by the consideration not only of the experimental evidence obtained from proteins themselves but also of the information regarding interatomic interactions and molecular structure in general which has been gathered by the study of simpler molecules.

We are interested here only in the role of amino acids in proteins—that is, in the simple proteins (consisting only of α-amino and α-imino acids) and the corresponding parts of conjugated proteins; the structure and linkages of prosthetic groups will be ignored.

The great body of evidence indicating strongly that the amino acids in proteins are linked together by peptide bonds need not be reviewed here.

The question now arises as to whether the polypeptide chains or rings contain many or few amino acid residues. We believe that the chains or rings contain many residues—usually several hundred. The fact that in general proteins in solution retain molecular weights of the order of 17,000 or more until they are subjected to conditions under which peptide hydrolysis occurs gives strong support to this view. It seems to us highly unlikely that any protein consist of peptide rings containing a small number of residues (two to six) held together by hydrogen bonds or similar relatively weak forces, since, contrary to fact, in acid or basic solution a protein molecule of this type would be decomposed at once into its constituent small molecules.

There exists little evidence as to whether a long peptide chain in a protein has free ends or forms one more peptide bond to become a ring. This is, in fact, a relatively unimportant question with respect to the structure, as it involves only one peptide bond in hundreds, but it may be of considerable importance with respect to enzymatic attack and biological behavior in general.

A native protein molecule with specific properties must possess a definite configuration, involving the coiling of the polypeptide chain or chains in a rather well-defined way.[49] The forces holding the molecule in this configuration may arise in part from peptide bonds between side-chain amino and carboxyl groups or from side-chain ester bonds or S–S bonds; in the main, however, they are probably due to hydrogen bonds and similar interatomic interactions. Interactions of this type, while individually weak, can by combining their forces stabilize a particular structure for a molecule as large as that of a protein. In some cases (trypsin, hemoglobin) the structure of the native protein is the most stable of those accessible to the polypeptide chain; the structure can then be reassumed by the molecule after denaturation. In other cases (antibodies) the native configuration is not the most stable of those accessible, but is an unstable configuration impressed on the molecule by its environment (the influence of the antigen) during its synthesis; denaturation is not reversible for such a protein.

Crystal structure investigations have shown

(48) We believe that our views regarding the structure of protein molecules are essentially the same as those of many other investigators interested in this problem.

(49) H. Wu, *Chinese J. Physiol.*, **5**, 321 (1931); A. E. Mirsky and L. Pauling, *Proc. Nat. Acad. Sci.*, **22**, 439 (1936).

that in general the distribution of matter in a molecule is rather uniform. A protein layer in which the peptide backbones are essentially coplanar (as in the β-keratin structure) has a thickness of about 10 Å. If these layers were arranged as surfaces of a polyhedron, forming a cage molecule, there would occur great steric interactions of the side chains at the edges and corners. (This has been used above as one of the arguments against the C_2 cyclol structure.) We accordingly believe that *proteins do not have such cage structures*.[50] A compact structure for a globular protein might involve the superposition of several parallel layers, as suggested by Astbury, or the folding of the polypeptide chain in a more complex way.

One feature of the cyclol hypothesis—the restriction of the molecule to one of a few configurations, such as C_2—seems to us unsatisfactory rather than desirable. The great versatility of antibodies in complementing antigens of the most varied nature must be the reflection of a correspondingly wide choice of configuration by the antibody precursor. We feel that the biological significance of proteins is the result in large part of their versatility, of the ability of the polypeptide chain to accept and retain that configuration which is suited to a special purpose from among the very great number of possible configurations accessible to it.

Proteins are known to contain the residues of some twenty-five amino acids and it is not unlikely that this number will be increased in the future. A great problem in protein chemistry is that of the order of the constituent amino acid residues in the peptide chains. Considerable evidence has been accumulated[46] suggesting strongly that the stoichiometry of the polypeptide framework of protein molecules can be interpreted in terms of a simple basic principle. This principle states that the number of each individual amino acid residue and the total number of all amino acid residues contained in a protein molecule can be expressed as the product of powers of the integers two and three. Although there is no direct and unambiguous experimental evidence confirming the idea that the constituent amino acid residues are arranged in a periodic manner along the peptide chain, there is also no experimental evidence which would deny such a possibility, and it seems probable that steric factors might well cause every second or third residue in a chain to be a glycine residue, for example.

The evidence regarding frequencies of residues involving powers of two and three leads to the conclusion that there are 288 residues in the molecules of some simple proteins. It is not to be expected that this number will be adhered to rigorously. Some variation in structure at the ends of a peptide chain might be anticipated; moreover, amino acids might enter into the structure of proteins in some other way than the cyclic sequence along the main chain.[51] The structural significance of the number 288 is not clear at present. It seems to us, however, very unlikely that the existence of favored molecular weights (or residue numbers) of proteins is the result of greater thermodynamic stability of these molecules than of similar molecules which are somewhat smaller or larger, since there are no interatomic forces known which could effect this additional stabilization of molecules of certain sizes. It seems probable that the phenomenon is to be given a biological rather than a chemical explanation—we believe that the existence of molecular-weight classes of proteins is due to the retention of this protein property through the long process of the evolution of species.

We wish to express our thanks to Dr. R. B. Corey for his continued assistance and advice in the preparation of this paper, and also to other colleagues who have discussed these questions with us.

Summary

It is concluded from a critical examination of the X-ray evidence and other arguments which have been proposed in support of the cyclol hypothesis of the structure of proteins that these arguments have little force. Bond energy values and heats of combustion of substances are shown to lead to the prediction that a protein with the cyclol structure would be less stable than with the polypeptide chain structure by a very large amount, about 28 kcal./mole of amino acid residues; and the conclusion is drawn that proteins do not have the cyclol structure. Other arguments leading to the same conclusion are also presented. A brief discussion is given summarizing the present state of the protein problem, with especial reference to polypeptide chain structures.

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(50) Wrinch recently has suggested[9h] that even if proteins are not cyclols the cage structure might be significant.

(51) H. Jensen and E. A. Evans, Jr., *J. Biol. Chem.*, **108**, 1 (1935), have shown that insulin probably contains several phenylalanine groups attached only by side-chain bonds to the main peptide chain.

[CONTRIBUTION FROM THE MALLINCKRODT CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Heats of Organic Reactions. VIII. Some Further Hydrogenations, Including Those of Some Acetylenes

BY JOHN B. CONN, G. B. KISTIAKOWSKY AND ELGENE A. SMITH

In the previous publications of this series[1] have been reported the heats of addition of hydrogen to a wide variety of unsaturated organic molecules as well as the heats of addition of chlorine and bromine to some of the simpler ethylenic hydrocarbons. The data previously presented have shown correlation between molecular constitution and the thermal effects accompanying these addition reactions. The generalizations drawn and semi-empirical rules formulated have been amplified and modified as the progress of the investigation justified. In the present paper we shall present some additional data, and, it being essentially the final report on this work, we shall give a discussion of the entire set of data from a concordant point of view. The information of general significance which emerges from it concerns the rather strong interactions between non-bonded atoms or atomic groups within a molecule.

Preparation of Materials

We are indebted to the late Professor E. P. Kohler and his co-workers for the cyclic compounds used in this work; their preparation is reported elsewhere.[2]

Acetylene.—Tank acetylene (Prest-O-Lite) was purified by passage through a series of 10 spiral wash bottles, which contained in order: (1) saturated sodium bisulfite solution, (2) water, (3) and (4) 0.2 *N* iodine in aqueous potassium iodide solution, (5) and (6) sodium thiosulfate solution, (7) and (8) alkaline sodium hydrosulfite with sodium anthraquinone β-sulfonate as indicator and oxygen carrier, (9) and (10) 10% aqueous potassium hydroxide solution. The gas then traversed a trap in Dry-Ice and two large drying tubes, the first of which contained calcium chloride and the second, Dehydrite. A 38-cm. mercury escape valve served to ensure a constant back pressure. The solutions described above were renewed just prior to each run and never became exhausted during their period of use.[3]

Methylacetylene.—Sodium acetylide was prepared by passing acetylene, purified as above, into a Dry-Ice cooled solution of 72 g. of sodium in 1 l. of liquid ammonia until the blue color disappeared.

Methyl sulfate (400 g.) which had been washed previously with sodium bicarbonate solution and dried with anhydrous magnesium sulfate was next introduced by means of a special dropping funnel, so designed as to deliver small droplets, and containing a side-arm on both the stem and the pressure equalizer tube through which a slow stream of nitrogen passed. This device protected the tip and the liquid in the funnel from contact with ammonia. It had been found previously that an ordinary funnel not only delivered drops of such size as to cause an almost explosive reaction, but also soon became plugged with a white solid (presumably $CH_3NH_3SO_4CH_3$).

When introduction of methyl sulfate was started the bath was allowed to warm up to the boiling point of the ammonia. The exit gases were freed from ammonia by passage through 2.5 liters of water and 1.5 liters of 12 *N* sulfuric acid. The latter solution never became alkaline. The hydrocarbon was dried with a large calcium chloride tower and then condensed in a trap immersed in Dry-Ice–methanol mixture. The yield of crude methylacetylene was 83%, in agreement with the observation of Vaughn, Hennion, Vogt and Nieuwland.[4]

The product was given a double bulb-to-bulb distillation to free it as well as possible from acetylene, and then fractionated in a six-foot (1.8-meter) vacuum-jacketed Podbielniak type column. The middle fraction, which boiled at $-23.23 \pm 0.05°$[5] (760 mm.) was transferred *in vacuo* to a small monel metal tank just before use. The freezing point was $-102.74°$.[6]

Dimethylacetylene.—Initial attempts to prepare this hydrocarbon from sodium methylacetylide and methyl sulfate gave unsatisfactory yields: however, the dialkyl acetylene synthesis described by Bried and Hennion[7] was found to work very well. Sodium acetylide was prepared in the usual manner from 25 g. of sodium in 500 cc. of liquid ammonia, and to this a suspension of sodamide from 30 g. of sodium in 500 cc. of liquid ammonia[8] was added, followed by 266 g. of methyl sulfate with stirring. After standing overnight at −80°, the contents of the flask were boiled off; the ammonia was removed as before, and the hydrocarbon was condensed in a series of two traps, the first of which was kept at −20°, and the second at −80°. Nearly all of the dimethylacetylene was caught in the first trap. The yield of crude product was 80%. The hydrocarbon was fractionated in the six-foot Podbielniak column; the portion reserved for calorimetric study boiled at $26.69 \pm 0.03°$ (760 mm.).[9]

Dimethyldiacetylene.—Methylacetylene was generated from purified propylene bromide and potassium hydroxide in boiling butyl alcohol according to Heisig and Davis.[9] The yield was 81%.

(1) THIS JOURNAL, **57**, 65 (1935); **57**, 876 (1935); **58**, 137 (1936); **58**, 146 (1936); **59**, 831 (1937); **60**, 440 (1938); **60**, 2764 (1938). These are referred to hereinafter as I to VII.

(2) Kohler, Tishler, Thompson and Potter, *ibid.*, **61**, 1057 (1939).

(3) We are indebted to Dr. F. B. Downing of E. I. du Pont de Nemours and Co. for suggesting this system to us.

(4) Vaughn, Hennion, Vogt and Nieuwland, *J. Org. Chem.*, **2**, 1 (1937).

(5) Heisig and Hurd, THIS JOURNAL, **55**, 3845 (1933), give the boiling point of methylacetylene as −23° from vapor pressure data.

(6) Maass and Wright, *ibid.*, **43**, 1098 (1921), give f. p. −104.7°.

(7) Bried and Hennion, *ibid.*, **59**, 1310 (1937).

(8) Vaughn, Vogt and Nieuwland, *ibid.*, **56**, 2120 (1934).

(9) Heisig and Davis, *ibid.*, **57**, 339 (1935), give 27.2° as the boiling point.

TABLE I

HYDROGENATION OF CYCLIC HYDROCARBONS

Compound	Reactant B. p. (760 mm.), °C.	Reactant $n^{20}D$	Product, $n^{20}D$	Expts. made	Reaction, $-\Delta H_{355}$, cal./mole	Estimated over-all accuracy
C_7H_{12}	114.35 ± 0.03[a]	1.4580[b]	1.4449 ± 0.0001[d]	2	26,515 ± 20	150
C_7H_{10}	121.52 ± .01[a]	1.4991	1.4449 ± .0001[d]	3	51,260 ± 49	150
C_7H_8	115.55 ± .05[a]	1.5213	1.4449 ± .0001[d]	2	72,846 ± 10	300
C_8H_{14}	144.52 ± .01[c]	1.4702[c]	1.4583 ± .0001[c]	3	23,525 ± 35	150

[a] Willstätter, *Ann.*, **317**, 219 (1901), reports b. p. (724 mm.) 115° for cycloheptene, b. p. (724 mm.) 120–121° for cycloheptadiene, and b. p. (724 mm.) 116° for cycloheptatriene. [b] Rosanov, *J. Russ. Phys.-Chem. Soc.*, **48**, 317 (1916), reports $n^{20}D$ 1.4552. [c] Willstätter and Waser, *Ber.*, **43**, 1180 (1910), report b. p. (730 mm.) 145° and $n^{20}D$ 1.474 for cyclooctene and $n^{20}D$ 1.4586 for cycloöctane. [d] Reference *b* reports $n^{20}D$ 1.4440 for cycloheptane.

The methylacetylene was now converted to the cuprous salt by passing it slowly into a vigorously stirred solution of 1.5 times the theoretical amount of ammoniacal cuprous chloride. Absorption was complete. The cuprous methylacetylide was filtered off and preserved in a desiccator containing concentrated ammonia water.

When an attempt was made to oxidize all of the cuprous salt at once with potassium ferricyanide as described by Griner,[10] much methylacetylene was regenerated and very little of the desired product was obtained. However, when the salt was added in small portions to the hot, rapidly stirred ferricyanide solution, the yield was 42%. The hydrocarbon sublimed cleanly with steam from the reaction flask and was washed with distilled water and dried over Dehydrite. It developed a slight yellow tinge on long standing, but could be freed from this impurity by subliming with steam.

Results

Cyclic Hydrocarbons.—Incompleteness of reaction was tested for by the usual bromine (II) titration. In no case was unsaturation found in the product. There was no irreversible adsorption on the cobalt–nickel catalyst and a large variation of relative rates of flow of hydrogen and hydrocarbon had no effect on the heat evolved. As Kohler, Tishler, Thompson and Potter[2] have indicated, it is very difficult to obtain these hydrocarbons in a pure state as judged by the freezing point method. The difficulty of their preparation in general precludes the use of Column A for their distillation, and repeated fractionations through Column B failed to give a product with a flat freezing curve. Two reasons lead us to believe that this failure is not serious. The first is the extremely large freezing point depression constants which uniformly characterize these hydrocarbons. Thus even a minute amount of impurity would give the material a poor freezing point. The second is a result of repeated hydrogenations of cycloheptene using samples of different purities as judged by the freezing points. Three different samples were used which gave samples of cycloheptane freezing at −12.2°, −8.4° and −8.4°.[11] However, the heat of hydrogenation of the entire set can be expressed as 26,419 ± 56 cal. per mole. The average of the two runs with cycloheptene which had been distilled through column A is about 100 cal. higher than this average and represents what we consider the correct value. The earlier results are quoted only to show how much more sensitive the freezing point test is than the heat of the reaction. The cycloheptene itself tended to form a glass and it was difficult to get good freezing curves. The best sample froze at about −56°.

The cycloheptadiene gave a good freezing flat at −110.4°. The product of hydrogenation gave an excellent flat at −7.98°. This we take to be the true freezing point of cycloheptane.

Cycloheptatriene gave only a fair "flat" at −79.5°, and its hydrogenation product froze at −8.3°.

The cycloöctene froze at −22.1° and the hydrogenation product froze at 7.95°. Both of these determinations left much to be desired as freezing points but do not indicate any large amounts of impurities. Table I shows the pertinent data on these compounds.

Cyclic Ketones.—The hydrogenation of the cyclic ketones proceeded smoothly on the cobalt–nickel catalyst. There was no irreversible adsorption, and variations in the rates of flow produced no effect. As was the case with acetone and methyl ethyl ketone, the hydrogenation was not complete. This incompleteness was measured in the following manner: 0.5 cc. of the product was mixed with an equal volume of sodium methoxide and 1 cc. of a standard solution of *p*-nitrobenzaldehyde in methyl alcohol. After heating gently for two minutes the color was matched with that produced by a 0.5% solution of the ke-

(10) Griner, *Ann. chim.*, [6] **26**, 354 (1892).

(11) Willstätter and Kametaka, *Ber.*, **41**, 1481 (1908), report −12 to −13°.

TABLE II

HYDROGENATION OF CYCLIC KETONES

Compound	B. p., °C.	Mm.	Reactant F. p., °C.	$n^{20}D$	Product F. p., °C.	$n^{20}D$
C_5H_8O	131.15	774[a]	−51.64[b]	1.4370[a]	....	1.4535 ± 0.0005[e]
$C_6H_{10}O$	155.47	767[a]	−29.05	1.4512[c]	20.99[d]	1.4667 ± .0001

Compound	Expts. made	Reaction, $-\Delta H_{355}$ meas.	% incomplete	$-\Delta H_{355}$ corr.	Estimated over-all accuracy
C_5H_8O	3	12,374 ± 61	0.9	12,498 ± 61	150
$C_6H_{10}O$	3	15,317 ± 81	.7	15,424 ± 81	150

[a] Beilstein gives b. p. 155.4° for cyclohexanone; for cyclopentanone, b. p. 130.0–130.5°. [b] Timmermans, *Bull. soc. chim. Belg.*, **36**, 502 (1922), gives f. p. −52.8°. [c] Landolt–Börnstein gives $n^{20}D$ 1.4507. [d] Lange, *Z. physik. Chem.*, **A161**, 77 (1933), gives f. p. 25.47°. [e] Noller and Adams, THIS JOURNAL, **48**, 1084 (1926), give $n^{20}D$ 1.4530.

tone in methyl alcohol, by diluting the unknown with methyl alcohol until a match was obtained. This test consistently showed a concentration of 0.9% of ketone in the case of the cyclopentanone and 0.7% in the case of the cyclohexanone. No trace of dimolecular reduction could be detected by carefully fractionating samples of the product in a small Podbielniak still.

A calculation of the incompleteness of the hydrogenation from the freezing point of the product in the case of the cyclohexanone yields a figure in substantial agreement with that found by means of the above test. The true freezing point of cyclohexanol was used as 25.47° and the freezing point depression constant was taken from "I. C. T." Table II lists the pertinent data on these compounds.

Acetylenic Compounds.—Acetylene and methylacetylene were hydrogenated over a 10% platinum on asbestos catalyst. In neither case could any irreversible adsorption be detected. Wide variations in the rate of gas flows failed to show any effect on the heat produced. Ammoniacal silver nitrate solution was used to test for 1-acetylenes in the product; the exit gases were passed through the reagent for five minutes. In every case this test was negative. Samples of the ethane and propane from the hydrogenations were collected and subjected to vapor pressure measurements in a differential manometer. No significant differences in vapor pressure between the first and last fractions to vaporize could be detected. Thus polymers were shown to be absent. Dimethylacetylene would not hydrogenate completely over the 10% platinum catalyst, and therefore the reaction was carried out on cobalt–nickel, at 82°. A bromine titration test showed only 0.01% unsaturation in the hydrogenation product, but the irreversible adsorption test was somewhat inconclusive. There may have been a small amount of condensation on the catalyst, which also was manifested by a slight progressive change in the heat liberated with the repetition of the measurements. We believe that the true heat of reaction is slightly higher than reported and are increasing the estimate of the over-all error to care for this possibility. An attempt was made to hydrogenate dimethyldiacetylene but due to an incomplete reaction on the platinum catalyst and considerable irreversible adsorption on cobalt–nickel the effort was unsuccessful. Table III gives the data on these compounds.

TABLE III

HYDROGENATION OF ACETYLENES

Compound	Expts. made	$-\Delta H_{355}$	Estimated over-all accuracy
C_2H_2	3	75,062 ± 66	150
$CH_3C{\equiv}CH$	3	69,703 ± 14	150
$CH_3C{\equiv}CCH_3$	3	65,581 ± 130	300

Discussion

1. The New Experimental Data.—Rather large variations of the heats of hydrogenation in the cycloölefin series are reported here and in the preceding papers (III and V). The numerical values, which range from 28.59 kcal. for cyclohexene to 23.52 kcal. for cycloöctene, are spread over almost as wide a range as those observed in the ethylene (32.82 kcal.) to tetramethylethylene (26.63 kcal.) series, although in the present case a constant number of alkyl groups *are* adjacent to the double bond. The following discussion will make plausible the contention that the same fundamental cause is responsible for the variations of the reaction heats in both series of compounds, namely, the interactions of the newly formed bonds with near-by, non-bonded atoms and atomic groups.

Hydrogenation of rings with increased unsaturation has provided information on the resonance energy in these conjugated systems. If, in ac-

TABLE IV

EFFECT OF SUBSTITUENTS ON THE HEATS OF HYDROGENATION

Reaction	ΔH_{355}, kcal.	Diff.	Reaction	ΔH_{355}, kcal.	Diff.
$C_2H_2 + H_2$	−42.24	2.65	$C_2H_4 + H_2$	−32.82	2.71
$CH_3C{\equiv}CH + H_2$	−39.59	1.96	$CH_3CH{=}CH_2 + H_2$	−30.11	2.16
$CH_3C{\equiv}CCH_3 + H_2$	−37.63[a]		$CH_3CH{=}CHCH_3 + H_2$	−27.95[a]	

[a] To and from an equilibrium mixture of *cis*- and *trans*-butenes-2.

cordance with the procedure used in earlier papers of this series, the resonance energy in a diene is taken as the difference in the heats of hydrogenation of the diene to an olefin and of this olefin to the paraffin, then cycloheptadiene has 2.77 kcal. resonance energy. Comparison with cyclohexadiene (1.81 kcal.) and cyclopentadiene (2.96 kcal.) shows that it is substantially the same in all ring compounds, but is somewhat smaller than in the open chain dienes (3 to 4 kcal., *cf.* V). It should be noted, however, that the steric effects discussed later make the calculation of the resonance energy in all these instances somewhat doubtful.

A subtraction of the heat of hydrogenation of cycloheptatriene from that of cycloheptene, taken three times, leaves 6.7 kcal. as the resonance energy in the former. Steric effects again make the absolute magnitude of this value somewhat uncertain, but they should be substantially eliminated by taking the ratio of the resonance energies of cycloheptatriene and diene. This is found equal to 2.4, while Pauling and Sherman and later Lennard-Jones[12] calculated for open chain trienes and dienes the ratio 2.1.

The heats of hydrogenation of cyclic ketones are of some interest because they reproduce the trend established for cycloölefins, the six-membered ring compound having again the higher heat of reaction. In the present case, however, it is cyclopentanone which has a reaction heat (12.50 kcal.) close to that of its open chain homologs (13.34 and 13.17 kcal. for acetone and methyl ethyl ketone, respectively, *cf.* VI), while the heat evolution with cyclohexanone is almost as large as with acetaldehyde (15.42 and 16.75 kcal., respectively).

The heats of hydrogenation of acetylene and its homologs vary with substitution of alkyl groups in much the same manner as do those of ethylene and its homologs. The analogy between the two series of compounds is even quantitative, as the following Table IV shows. This constitutes additional evidence for the conclusion reached (VII) on the basis of the heats of bromination of olefins, that the variations in the heats of addition reactions are caused mainly by the steric effect of substituents on the addenda used in the reactions. Were the effects of substituents on the several carbon–carbon bonds involved in hydrogenations considerable, the result of Table IV would be a rather improbable accident.

The following discussion is an effort to evaluate the character and magnitude of these effects.

2. The General Nature of Steric Effects.—Of all the available data the heats of hydrogenation of unsaturated ring compounds supply perhaps the most direct, although qualitative, information on the character of interactions of nonbonded atoms within a molecule. In a paper of this series (V) comments were made on the heats of hydrogenation of five-membered rings which, being some 2 kcal. lower than those of corresponding six-membered systems and of open chain disubstituted ethylenes, seemed to disprove the existence of strain energy in cyclopentene and cyclopentadiene although the bond angles in these compounds deviate from tetrahedral values. In the meantime Professor Pauling has told one of the present authors that in the opinion of Dr. V. Schomaker this conclusion is subject to revision because five-carbon systems are planar, while six-carbon rings are puckered. In the planar rings the C–H bonds must be in the eclipsed configuration, while in puckered rings they may take up staggered positions; hence the relative heats of hydrogenation may be employed to evaluate the strain energy in cyclopentene only after correction has been made for these steric effects. Studies of the internal rotation of methyl groups in ethane[13] have indeed shown that approximately 2.75 kcal. energy difference exists between the staggered and the eclipsed (in-line) configuration of the C–H bonds in the two methyl groups.

Two alternatives must now be considered, both of which are consistent with the observations on ethane: the configuration of lowest energy may be that in which C–H bonds are farthest apart

(12) Pauling and Sherman, *J. Chem. Phys.*, **1**, 679 (1933); Lennard-Jones, *Proc. Roy. Soc.* (London), **A158**, 280 (1937).

(13) See Kistiakowsky, Lacher and Stitt, *J. Chem. Phys.*, **7**, 289 (1939), for other references.

(staggered) or that in which they are closest together. If the former is true, then the low heats of hydrogenation of cyclopentene and pentadiene are due to the placement of hydrogen atoms into positions of higher energy as compared with the reaction of cyclohexene and a correction for this effect will result in values at least qualitatively consistent with the expected strain energies of the unsaturated C_5 rings. But if this explanation is the correct one, then the heat of combustion of cyclopentane, per CH_2 group, should be larger than that in open chain paraffins by about 3 kcal. because in the former the carbon bonds are not free to take up the (staggered) positions of lowest energy. Experimental data[14] give 157.9 kcal. (Swietoslawski) heat of combustion per CH_2 group in cyclopentane and 157.5 kcal. (Swietoslawski) in methylcyclopentane as against 157.9 kcal. (Richards) or 157.2 kcal. (Swietoslawski) in cyclohexane and 157.1 (Rossini) in normal open chain hydrocarbons, all referred to the vapor phase. These data suggest about 0.5 kcal. excess energy content per CH_2 group in cyclopentane and are in poor agreement with the discussed interpretation (the uncertainties are, however, large). Nevertheless, the other alternative leads to much greater inconsistencies. Cyclohexane, in which, due to puckering, the C–H bonds cannot all have in-line configuration, has nearly the same heat of combustion per CH_2 group as the open chain hydrocarbons, instead of being considerably higher. Furthermore, the lower heats of hydrogenation of the C_5 rings now must mean that the strain energy decreases with increasing unsaturation (*i. e.*, with increasing deviation from tetrahedral angles!), becoming negative unless the experimental heat of combustion of cyclopentane is in error by being too low. In this case, however, large strain energy would have to be assigned to cyclopentane, even though the C–C–C angles in this compound (108°) barely deviate from tetrahedral values. All this is so improbable that we select the first alternative unreservedly and assume that the positions of minimum energy are those in which the C–H bonds are farthest apart, *i. e.*, the staggered configuration of ethane.

The greater stability of the staggered configuration of C–H bonds may be formally ascribed to the existence of repulsive interactions ("steric hindrance") between non-bonded atoms in polyatomic molecules. The observed lower heats of hydrogenation of rings larger than cyclohexene are consistent with this idea since hydrogen atoms on non-adjacent carbons are forced close together in such rings because of their extensive puckering. Further supporting evidence is offered by the observations that the energy content difference of *cis*- and *trans*-butenes-2 is 0.95 kcal.[15] at 355°K. The planar zig-zag hydrocarbon chains in crystals also speak for the staggered configuration being the stable one. It appears[16] that the heats of fusion of the normal hydrocarbons are substantially higher than those of corresponding cyclo-paraffins. Supposing that the staggered configuration of the crystalline straight chain compounds were the strained one, the opposite relation could be expected. Still other favorable facts will be cited in the following.

3. The Relative Energies of Steric Hindrance.—The repulsive interactions in polyatomic molecules result in inconstancy of bond energies. However, whichever one speaks of, one is beset by a rather fundamental difficulty in stating a precise experimental definition of the magnitude of the interaction energy or of the variable bond strength. Consider, for instance, the two hypothetical reactions: $CH_4 \rightarrow CH_3 + H + E_1$ and $C_2H_6 \rightarrow C_2H_5 + H + E_2$. The difference $E_2 - E_1$ may be taken as the direct measure of the difference in bond energies, that is, of the difference in steric hindrances on a hydrogen atom in ethane and methane. Strictly speaking, however, this is incorrect as the removal of a hydrogen atom from the two molecules has probably altered to a different extent the bonding energies of the remaining atoms. Nevertheless only the first procedure can be followed through consistently with the available data and it will be used therefore in the following.

From Rossini's[17] combustion data the following thermochemical equations can be set up

$$2CH_4 \longrightarrow C_2H_6 + H_2 + 15.54 \text{ kcal.} \quad (1)$$

$$CH_4 + C_2H_6 \longrightarrow C_3H_8 + H_2 + 13.28 \quad (2)$$

(14) Kharasch, *Bur. Standards J. Research*, **2**, 359 (1929); Rossini, see references below.

(15) The as yet unpublished measurements on the gaseous heat capacities of these compounds indicate that at absolute zero their energy difference is even larger.

(16) Parks, Huffman and Thomas, THIS JOURNAL, **52**, 1032, 4381 (1930).

(17) Rossini, *Bur. Standards J. Research*, **6**, 37 (1931); **12**, 735 (1934); **13**, 201 (1934); *J. Chem. Phys.*, **6**, 168 (1938). Room temperature data referring to the gaseous state have been used here and in the following. A conversion to absolute zero is so uncertain for most of the compounds considered that the accruing theoretical improvement would be wholly fictitious. We do not believe that such a conversion will change the results significantly.

$$2C_2H_6 \longrightarrow n\text{-}C_4H_{10} + H_2 + 10.63 \quad (3)$$
$$2C_3H_8 \longrightarrow n\text{-}C_6H_{14} + H_2 + 9.57 \quad (4)$$
$$CH_4 + C_3H_8 \longrightarrow (CH_3)_3CH + H_2 + 11.26 \quad (5)$$
$$CH_4 + (CH_3)_3CH \longrightarrow C(CH_3)_4 + H_2 + 9.80 \quad (6)$$

The reactions involved all consist in the severance of two C–H bonds and a formation of an H–H and a C–C bond, the changes in the heats therefore being due exclusively to the variable steric hindrance. To what extent this latter may rise under exceptional circumstances is brought out by the calorimetric measurement of Bent and Cuthbertson:[18] $2(C_6H_5)_3CH \rightarrow (C_6H_5)_3C\text{–}C(C_6H_5)_3 + H_2 + 40$ kcal.

The heats of reactions (3) and (4) are sufficiently near together to justify an assumption that only substitutions on the same atoms to which the bonds considered belong have substantial effects on the *relative* magnitude of steric hindrance. This assumption is in accord with conclusions drawn by Rossini.[17]

Using the following notation

A : energy of severance of a C–H bond in methane
A-X: energy of severance of a C–H bond in ethane (or primary C–H bonds in higher homologs)
A-Y: energy of severance of a secondary C–H bond in propane
A-Z: energy of severance of a tertiary C–H bond in isobutane
B : energy of severance of a C–C bond in ethane
B-x: energy of severance of a C–C bond in propane
B-y: energy of severance of an internal C–C bond in butane
B-y': energy of severance of a C–C bond in isobutane
B-z : energy of severance of a C–C bond in neopentane

one obtains from equations (1) to (6)

$$\text{from (1) – (2)} : X - x = 2.26 \text{ kcal.} \quad (7)$$
$$\text{from (1) – (3)} : 2X - y = 4.91 \quad (8)$$
$$\text{from (1) – (5)} : Y - y' = 4.28 \quad (9)$$
$$\text{from (1) – (6)} : Z - z = 5.74 \quad (10)$$

The simplest assumption concerning steric hindrance is to treat the effects of substituent alkyl groups as additive, so that $Y = 2X$; $Z = 3X$; $y = 2x$; $y' = 2x$; $z = 3x$. The following are the results

$$\text{from (1) – (2)} : X - x = 2.26 \quad (11)$$
$$\text{from (1) – (3)} : X - x = 2.45 \quad (12)$$
$$\text{from (1) – (5)} : X - x = 2.14 \quad (13)$$
$$\text{from (1) – (6)} : X - x = 1.91 \quad (14)$$

The assumption of additivity of the steric effects evidently is fairly but not completely successful. Better agreement can be obtained, of course, by using more parameters but their introduction would be difficult to justify.

(18) Bent and Cuthbertson, THIS JOURNAL, **58**, 170 (1936).

As seen above, thermal data on saturated hydrocarbons alone cannot disentangle the steric effects upon the C–H and the C–C bonds, only a difference appearing in the final equations. This is true of all thermochemical data, barring direct measurements of the heats of formation of free radicals; therefore an assumption is required to obtain individual values. One which we shall make is that the entire observed effect of alkyl substituents upon the heats of addition reactions to unsaturated hydrocarbons is due to their steric hindrance on the newly formed bonds (*cf.* p. 9). This means that their effect upon a $=CR_1R_2$ group is equal to their effect upon the group $-CHR_1R_2$ resulting from hydrogenation.

From the heats of hydrogenation of various olefins the mean effect of substitution of one alkyl group into ethylene is found equal to 2.6 kcal. (± 0.1). Substitution of the second alkyl group in symmetric position lowers the heat of hydrogenation by another 2.3 kcal. (± 0.1) if the heat of hydrogenation of the equilibrium mixture of the isomeric pentenes-2 or butenes-2 is taken for this calculation. This choice is justified by the consideration that the resultant normal pentane or *n*-butane has presumably approximately the same proportions of the *cis*- and the *trans*-configurations as the olefins.

The introduction of the third methyl group lowers the heat evolution by 1.0 kcal. and the fourth decreases it another 0.3 kcal. The trend of these figures is qualitatively the same as that observed in equations (11) to (14) but the quantitative agreement is imperfect, showing the crudeness of the underlying assumptions. Taking for the differential effect of a methyl group upon a C–H bond (X) the mean of 2.6 and 2.3 kcal., 2.45 kcal., and substituting into equation (11) or (12) one finds that x is very nearly zero, hence that the energy of the C–C bonds is constant in saturated hydrocarbons. The energy of the multiple carbon–carbon bonds is similarly independent of substitution since an identical differential effect of methyl groups has been assumed for all carbon–carbon bonds and has now been found equal to zero.

Heats of bromination (VII) reveal with the aid of the same assumption as above that for the C–Br bond the order of the hydrogen and the methyl group hindrances is reversed, the former hindering more, the quantity corresponding to X in equation (11) being *ca.* – 0.5 kcal. In the same

manner Rossini's combustion data on primary alcohols[19] show that the methyl groups have lesser steric hindrance on the C–O bond. It seems that the relative steric effectiveness of hydrogen atoms and of methyl groups is correlated with the polarity of the bond on which the hindrance is exercised.

Some years ago Eyring[20] made an approximate wave-mechanical calculation of the interactions between non-bonded atoms in methane and in ethane, concluding that in the latter, because of greater steric hindrance of a CH_3 group, the C–H bond is effectively weaker by 3 kcal. On the preceding pages 2.5 kcal. was estimated for the same effect in excellent agreement with Eyring's calculation. To reduce the mathematical complexity of the problem, Eyring had to make several drastic simplifications, in view of which and of the frequent failure of approximate quantum mechanical calculations to obtain accurate interaction energies at close distances of approach, the agreement of his and of the present values is surprising; we are inclined to regard it as somewhat accidental because in other details Eyring's calculation does not agree so well with experimental data.

4. Hindrance of Internal Rotation.—According to Eyring the energy difference between the staggered and the eclipsed configurations of ethane is only 0.35 kcal., while observations give 2.75 kcal.[13] This large discrepancy has now led him to suggest[21] that some other effects are responsible for the hindrance of internal rotation. However, the general steric hindrance and the hindrance of internal rotation change in such analogous manner from case to case that the introduction of new effects seems rather unnecessary. Methyl groups were shown above to exert greater steric hindrance upon C–H bonds and parallel to this it is found that the hindrance of internal rotation changes from 2.75 kcal. in ethane to approximately 3.2 kcal. in propane,[22,23] 3.8 in isobutane[22] and 4.2 in neopentane.[22] In propylene[22,23] the hindrance of internal rotation was found equal to only 0.8 kcal., indications being that only three angular positions of minimum potential energy exist for the methyl group. This suggests, in accord with the facts to be considered later, that the steric effect of a $=CH_2$ group is not much larger than that of a hydrogen atom or a methyl group, although the existence of only three equilibrium positions, if confirmed, must be in addition explained by some special properties of a double bond (*cf.* ref. 23). The consideration of the case of cyclopentane has shown that the staggered position of C–H bonds is that of lower energy, which again agrees with steric hindrance as the cause of the hindrance of internal rotation.

Between the two alternatives: postulating different mechanisms for the steric hindrances and for the hindrances of internal rotation or considering Eyring's calculations as only qualitatively correct, we prefer the second. To reconcile various facts cited above with calculations of the type made by Eyring, the energy of repulsive interactions should be made a steeper function of distance and be made larger at short distances.

5. Energies of Steric Hindrance.—Some facts which we shall consider now suggest indeed that steric hindrance by atoms bonded to the same carbon upon another of its bonds is considerably larger than the 2.5 kcal. calculated by Eyring for a hydrogen–hydrogen interaction in methane.

The hydrogenation of the first double bond in allene evolves 11 kcal. more heat than the hydrogenation of propylene. To correlate this observation with other discussed facts we suppose again that the steric hindrance of a methylene group is not much larger than that of a methyl group or even of a hydrogen atom. Then the large heat evolution in the reaction of allene is obtained because the secondary hydrogen in the resultant propylene has no other hydrogen neighbors on the same carbon, while the primary hydrogen of the methyl group has steric hindrance from only one hydrogen atom on the adjacent carbon. It is, of course, impossible to separate all these effects, but an estimate of something of the order of 9 kcal. for the hydrogen–hydrogen interaction on the same carbon seems not unlikely, considering that this interaction occurs over the shortest distance.

The preservation of tetrahedral angles in halogenated methanes occasionally has been cited as evidence of rather weak interactions between non-bonded atoms, but actually this evidence merely shows that the difference between interactions of a halogen with another halogen and with hydrogen is rather small. This conclusion is confirmed by many other facts, only the obser-

(19) Rossini, *J. Research Natl. Bur. Standards*, **13**, 189 (1934).
(20) Eyring, THIS JOURNAL, **54**, 3191 (1932).
(21) Abstracts of papers presented at the Baltimore meeting of A. C. S., April, 1939.
(22) Pitzer, *J. Chem. Phys.*, **5**, 473 (1937).
(23) Kistiakowsky, Lacher and Ransom, *ibid.*, **6**, 900 (1938).

vations of Beach and Palmer[24] on the strong hindrance of internal rotation in *sym.* dihalogenethanes being possibly in disagreement with it.

The manner in which the absolute magnitude of the steric hindrances could be found would be by removing some of the atoms present. Fortunately this is at least approximately realized in molecules in which the carbon atom forms a double bond and indeed spectroscopic evidence[25] points strongly to the H–C–H angle being greater than the tetrahedral value in formaldehyde and in ethylene. It may be argued, of course, that this is the "natural" configuration of carbon bonds, when one of them is double, but until this is conclusively proved we choose to think that the increase of the angle is due to repulsions between hydrogen atoms.

Considerable interest has been aroused by the finding of Herzberg that in methylacetylene the single carbon–carbon bond is appreciably shortened in comparison with those in saturated compounds.[26] Similar observations have been since made on the C–Cl and C–Br bonds in halogenated acetylenes[27] and the effect has been ascribed to resonance. Pauling[28] has pointed out that resonance cannot account for a decrease of the C–H distance in acetylene as compared with that in methane and yet, as Table V shows, the fractional change of the bond distances is nearly the same in all observed cases. The slight increase of the effect from the C–H to the C–Br bond is quite likely due to additional contribution of resonance, manifested by the changed dipole moments of the carbon–halogen bonds in acetylenes. For the C–H bond, however, wholly and for the C–C bond predominantly, we consider the reduced steric hindrance by adjacent atoms to be the cause of bond shortening in acetylenic compounds.

TABLE V

EFFECT OF ADJACENT CARBON–CARBON BONDS UPON INTERATOMIC DISTANCES

	Single, Å.	Triple, Å.	S:T ratio
C–H	1.093[a]	1.058[b]	1.034 (±0.005)
C–C	1.54 ±0.03[c]	1.463[d]	1.051 (± .025)
C–Cl	1.77 ± .02[c]	1.68 ±0.04[e]	1.052 (± .035)
C–Br	1.91 ± .02[c]	1.80 ± .03[e]	1.060 (± .028)

[a] Ginsburg and Barker, *J. Chem. Phys.*, **3**, 668 (1935). [b] Herzberg and Spinks, *Z. Physik*, **91**, 386 (1934). [c] Brockway, *Rev. Mod. Phys.*, **8**, 231 (1936). [d] Herzberg, Patat and Verleger, *J. Phys. Chem.*, **41**, 123 (1937). [e] Brockway and Coop, *Trans. Faraday Soc.*, **34**, 1429 (1938).

This requires that a ≡CH group exercise much smaller steric hindrance than do three hydrogen atoms in methane, a conclusion which is a natural extension of the earlier remarks on the effect of a methylene group. If the steric effects of a —CH_3, =CH_2 and a ≡CH group upon a C–H or a C–C bond do not differ greatly, then one may perhaps conclude also that the difference in the steric effects of a hydrogen atom and a methyl group upon all these groups is approximately the same. Such a conclusion is supported by data of Table IV and already has been made use of in section 3.

A numerical relation between bond length and bond energy, similar to those between bond length and the force constant, is not known, but one can surmise that a reduction of the bond length by some 3 to 4% causes much more than a proportionate increase in the bond energy. Hence repulsive interactions between atoms in methane must reduce the energy of the "isolated" C–H bond by a considerable amount.

In ethylenic compounds the C–H and the C–C bond length should be the mean of those in acetylene and in ethane, that is, 1.075 and 1.50 to 1.51 Å., respectively. The former would require the H–C–H angle in formaldehyde and in ethylene to be about 120°. It is claimed that in ethylenic compounds the C–C distance is the same as in paraffins but a difference of 0.04 Å. is so close to the admitted experimental error (0.03) that the evidence of electron diffraction is not yet conclusive.

In the partial hydrogenation of butadiene and other dienes, the added secondary hydrogen atom is subjected to steric hindrance by the group —CH=CH_2 rather than by —CH_2—CH_3 as in the hydrogenation of olefins. According to what has been said before, this means lower steric hindrance and hence higher heat of hydrogenation. Therefore resonance energies calculated in the beginning of this discussion by a simple procedure should be increased by 1 or even as much as 2 kcal. (*cf.* discussion of allene) which would bring their absolute magnitude into better agreement with theoretical values calculated by Lennard-Jones[12] and Coulson.[29]

(24) Beach and Palmer, *J. Chem. Phys.*, **6**, 639 (1938).

(25) Dieke and Kistiakowsky, *Phys. Rev.*, **45**, 4 (1934); Badger, *ibid.*, **45**, 648 (1934); Penney, *Proc. Roy. Soc.* (London), **A144**, 166 (1934).

(26) Herzberg and Spinks, *Z. Physik*, **91**, 386 (1936); Herzberg, Patat and Verleger, *J. Phys. Chem.*, **41**, 123 (1937).

(27) Brockway and Coop, *Trans. Faraday Soc.*, **34**, 1429 (1938).

(28) Pauling, Springall and Palmer, THIS JOURNAL, **61**, 927 (1939).

(29) Coulson, *Proc. Roy. Soc.* (London), **A164**, 383 (1938).

We have restricted our discussion to the simplest organic compounds because only for them reliable thermochemical and structural data exist, but one could readily extend it *ad infinitum* by borrowing from the more qualitative organic evidence. Concluding, we wish to stress that steric hindrance in the sense discussed above is generally responsible for the effects of substituents upon the "standard" properties of functional groups in polyatomic molecules and that therefore it is rightly placed next to resonance in importance as the source of variety among organic compounds.

Acknowledgment.—We are indebted to the late Professor E. P. Kohler and Dr. J. B. Conant for much helpful advice. Professor E. B. Wilson has been kind enough to criticize the general part of this paper. Some of the ideas contained in it found their inception while one of the present authors (G. B. K.) was a Baker Non-Resident Lecturer at Cornell University and he wishes to express his gratitude to the staff of the Cornell Department of Chemistry for many valuable discussions. Drs. Ralph B. Thompson and W. E. Vaughan and Mr. M. A. Dolliver have taken part in the earlier experiments here described. A grant from the Rockefeller Foundation made this work possible.

Summary

The following heats of hydrogenation have been determined. All data refer to 355°K. in the gaseous phase.

$C_7H_{12} + H_2 \longrightarrow C_7H_{14} - 26{,}515 \pm 20\ (150)$ cal./mole
$C_7H_{10} + 2H_2 \longrightarrow C_7H_{14} - 51{,}260 \pm 49\ (150)$
$C_7H_8 + 3H_2 \longrightarrow C_7H_{14} - 72{,}846 \pm 10\ (300)$
$C_8H_{14} + H_2 \longrightarrow C_8H_{16} - 23{,}525 \pm 35\ (150)$
$C_6H_8O + H_2 \longrightarrow C_6H_9OH - 12{,}498 \pm 61\ (150)$
$C_6H_{10}O + H_2 \longrightarrow C_6H_{11}OH - 15{,}424 \pm 81\ (150)$
$C_2H_2 + 2H_2 \longrightarrow C_2H_6 - 75{,}062 \pm 66\ (150)$
$C_3H_4 + 2H_2 \longrightarrow C_3H_8 - 69{,}703 \pm 14\ (150)$
$C_4H_6 + 2H_2 \longrightarrow C_4H_{10} - 65{,}581 \pm 130\ (300)$

A consideration of the entire work on the heats of addition reactions and of other experimental data found in the literature reveals the large magnitude of steric hindrances exercised by nonbonded atoms in simple organic molecules. These repulsive interactions are stronger than supposed hitherto and contribute largely to the variation in the properties of the functional groups.

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Internal Rotation and Resonance in Hydrocarbons

BY EVERETT GORIN, JOHN WALTER AND HENRY EYRING

Introduction

Recent experimental evidence indicates the existence of a potential barrier of the order of 3000 cal. restricting the rotation of the methyl groups about the C–C bond in ethane. The data on the specific heat of ethane gas at low temperatures[1] and the entropy of ethane as determined both from the third law and from the hydrogenation of ethylene are in accord with this assumption.[2] The structure of the rotation bands in the ethane spectrum has also been interpreted as indicating a barrier of at least 2000 cal.[3]

On the other hand the repulsion due to the hydrogen atoms calculated according to standard quantum mechanical procedure for the usual valence bond structure yields a potential barrier of 300 cal. with a minimum corresponding to the staggered position of symmetry D_{3d}. In this calculation the van der Waals attractive potential between hydrogens was taken as $101/R^6$.[4]

It was pointed out by Penney[5] that with the Slater–Pauling model for the carbon bond in ethane the repulsions taken account of in the above calculation are the only ones present if we use the single valence structure.

Barrier Height if Protons Replace Hydrogen Atoms.—If we suppose the hydrogen atoms be replaced by protons, the structure otherwise remaining unchanged, the potential barrier from the coulomb repulsions is 5200 cal. with a minimum in the staggered position. This is of course an upper limit and a more exact calculation than

(1) Kistiakowsky and Nazmi, *J. Chem. Phys.*, **6**, 18 (1938); Hunsman, *Z. physik. Chem.*, **B39**, 23 (1938); Wilson, *J. Chem. Phys.*, **6**, 740 (1938); see, however, Eucken and Weigert, *Z. physik. Chem.*, **B23**, 265 (1933).

(2) Smith and Vaughan, *J. Chem. Phys.*, **3**, 341 (1935); Teller and Topley, *J. Chem. Soc.*, 876 (1935); Kemp and Pitzer, THIS JOURNAL, **59**, 276 (1937).

(3) Howard, *J. Chem. Phys.*, **5**, 451 (1937).

(4) H. Eyring, THIS JOURNAL, **54**, 319 (1932).

(5) W. G. Penney, *Proc. Roy. Soc.* (London), **A144**, 166 (1934).

the one which yielded 300 cal. could not give a much larger value since it can only be a small fraction of the 5200 cal.

Lack of Cylindricity of the C–C Bond.—The carbon–carbon bonding orbitals are distorted by the presence of the three hydrogen atoms on each methyl radical so that they are no longer cylindrically symmetric about the C–C bond. If this distortion were large, conceivably a large barrier might arise simply from the lack of cylindrical symmetry of the interaction between the carbon–carbon bonding orbitals. The orbital of lowest energy which can be added is limited by symmetry considerations to the $4f$ orbital, $\psi_{4f} = f(r) \sin^3\theta \cos 3\varphi$, that is, the C–C bonding eigenfunction can be written as

$$\psi = c_1\psi_{2t\sigma} + c_2\psi_{4f}$$

where $\psi_{2t\sigma}$ is the tetrahedral function whose axis lies along the bond direction.

This $4f$ orbital overlaps the hydrogen nuclei only very slightly so that the perturbations of the hydrogen atoms can at most give rise to a very small value for c_2. If we consider that the interaction of the hydrogen atoms can be represented by their coulombic attraction for the C–C bonding orbitals, we can estimate roughly an upper limit for the barrier resulting from this cause. That this neglect of the exchange integrals will not change the order of magnitude of the coefficient c_2^2 is indicated by the calculations of Wood on methane,[6] where he finds the exchange and coulombic interactions are approximately equal in magnitude. The position of maximum binding is given by the position of maximum overlap of the two bond distributions if the exchange term in the (ff) interaction predominates, or by the position of minimum overlap if the coulombic term predominates. The potential barrier is of the form $V_0/2 \cos 3\chi$ where χ is the angle of rotation with respect to the opposed position as zero. V_0 is given by $c_2^2\,(ff)$, where (ff) is the interaction between the f orbitals on the two carbon atoms. A variational calculation indicates that c_2 is of the order of magnitude of 0.015. Since the energy of an f orbital is near the ionization limit, we expect the (ff) binding to be considerably less than the binding due to the tetrahedral carbon orbitals. As the barrier is proportional to c_2^2, which as we see is small, we conclude that the contribution to the barrier from the distortion in the cylindrical symmetry of the carbon–carbon bonding orbitals is negligibly small.

Barrier Due to Hybridization between Tetrahedral and 3d Orbitals.—It is also possible to modify the C–H bonding functions in such a way that the sum of their charge distributions is not cylindrically symmetric about the C–C bond. To do this it is necessary to take such a linear combination of the $2s$, $2p$, and $3d$ orbitals as to give three equivalent bonds. For simplicity, we have taken the combination which gives four equivalent tetrahedral bonds.[7]

$$\begin{aligned}
\psi_{111} &= c_1 s + \frac{c_2}{(3)^{1/2}}(p_x + p_y + p_z) + \\
&\qquad \frac{c_3}{(3)^{1/2}}(d_{x+y} + d_{x+z} + d_{y+z}) \\
\psi_{1\bar{1}\bar{1}} &= c_1 s + \frac{c_2}{(3)^{1/2}}(p_x - p_y - p_z) + \\
&\qquad \frac{c_3}{(3)^{1/2}}(-d_{x+y} - d_{x-z} + d_{y+z}) \\
\psi_{\bar{1}1\bar{1}} &= c_1 s + \frac{c_2}{(3)^{1/2}}(-p_x + p_y - p_z) + \\
&\qquad \frac{c_3}{(3)^{1/2}}(-d_{x+y} + d_{x+z} - d_{y+z}) \\
\psi_{\bar{1}\bar{1}1} &= c_1 s + \frac{c_2}{(3)^{1/2}}(-p_x - p_y + p_z) + \\
&\qquad \frac{c_3}{(3)^{1/2}}(+d_{x+y} - d_{x+z} - d_{y+z})
\end{aligned} \qquad (2)$$

The coördinate system used here is so defined that the carbon atom is located at the origin. The x, y and z axes are perpendicular to the faces of the cube about the carbon atom as center. The four orbitals point out toward the 111, $1\bar{1}\bar{1}$, $\bar{1}1\bar{1}$ and $\bar{1}\bar{1}1$ corners of the cube.

Slater's wave functions were used for the s and p orbitals with effective nuclear charge equal to 3.25. This same effective nuclear charge was also used in the d orbitals. No doubt a better value for the energy could have been obtained by introducing the effective nuclear charge as a variable parameter in the d functions. This, however, has not been done as we were only interested in a rough estimate of the energy. The coefficients are chosen so that the functions are normalized and orthogonal. We have considered that as a good approximation the amount of d-ness in the C–H bonds of ethane is the same as in methane. The third relationship necessary to fix the values of the coefficients is given by the condition that the total energy of methane must be a minimum. The energy of the methane molecule upon the assumption of electron pairing can be expressed approximately as

$$E = Q_1 + 4\alpha - 3(\beta + \gamma + 2\delta). \qquad (3)$$

(6) Wood, *Trans. Faraday Soc.*, **28**, 877 (1932).

(7) L. Pauling, THIS JOURNAL, **53**, 1367 (1931).

Q_1 = orbital energy + coulombic interaction between all orbitals.
α = exchange energy of C–H bond.
δ = exchange energy of C with H orbitals not bound together.
β = exchange energy between two H atoms.
γ = exchange energy of carbon orbitals.

The coefficient c_3 in equation (2) can be determined by minimizing the energy as expressed in (3). The exchange integral α gives a contribution of the same sign and the same order of magnitude as the coulombic integrals, while the integrals β and δ are small. Neglecting the integrals α, β, δ, since the effect of including α, β, δ would be to increase c_3, we calculate a minimum value for $c_3 = 0.086$. If we assume, as is reasonable from Wood's calculation on methane, that the exchange and coulombic integrals are equal, we get a value twice as large. The sums of the squares of the eigenfunctions give for the non-cylindrically symmetric part of the charge distribution the expression

$$\frac{2}{3\pi}\left(\frac{15}{2}\right)^{1/2} c_2 c_3 \, f(r) \sin^3\theta \cos 3\varphi \qquad (4)$$

where $f(r)$ is the product of the normalized radial part of the $2p$ and $3d$ eigenfunctions. The electrostatic interaction of the two charge distributions also gives a barrier of the form

$$(V_0/2) \cos 3\chi$$

Rigorously, we would have to subtract from V_0 an amount corresponding to one-half the exchange interactions between those parts of the orbitals not bound together which depend upon the angle χ. This can at most be equal to $^1/_2 V_0$, and probably would be considerably less. Since for the electrostatic repulsion between the electrons the coulombic integral is always greater than the neglected exchange integral, V_0 is equal to the coulombic interaction between the two charge distributions, one on each carbon atom, given by (4).

In kcal., the calculated value of V_0 is $23.2c_3^2$. Including the exchange integrals would approximately double the calculated value $c_3 = 0.086$ so that we take as a reasonable value $c_3 = 0.15$; we have a maximum for the barrier due to this interaction between the hybridized C orbitals of 500 cal. favoring the staggered configuration.

There is still one other contribution to the barrier arising from this hybridization, *i. e.*, that due to interaction between the H atoms on one carbon with the carbon orbital on the other. Again we will consider only the coulombic interaction since including the exchange integrals would at most reduce the barrier arising in this way by a factor of two. The coulombic potential of an electron in the field of a hydrogen atom is given by $-\frac{e^2}{a_0}\left(1 - \frac{a_0}{r}\right)e^{-2r/a_0}$. The coulombic integral between the non-symmetrical part of the charge distribution about the carbon atom is therefore given by

$$-\frac{e^2}{a_0}\left(\frac{3.25}{a_0}\right)^6 \frac{6^{1/2} c_2 c_3}{729\pi} \int r_a^3 \exp.(-5/6 \cdot 3.25 r_a/a_0)(x_a^3 - 3x_a y_a^2)\left(1 + \frac{a_0}{r_b}\right)\exp.(-2r_b/a_0)\,d\tau \qquad (5)$$

Here r_a, x_a, y_a, z_a refer to a coördinate system about the carbon atom as center and the z-axis lies along the C–C bond direction. r_b refers to the hydrogen atom as center of coördinates. Upon evaluating this integral and introducing the value 0.15 for c_3 we obtain for a hydrogen atom in the opposed position 120 cal. Due to the three-fold symmetry of the charge distribution all hydrogen atoms are equivalent. In the staggered position the integral is just the negative of this, *i. e.*, −120 cal. The barrier is thus equal to 12 × 120 cal. or 1440 cal. This is larger than the effect calculated previously and of opposite direction. If we included exchange interactions this would be reduced at most to 700 cal. Summarizing the results, then, we get the following contributions to the barrier, 300 cal. staggered from the hydrogen repulsions, 250 minimum to 500 cal. maximum from the interaction between the hybridized carbon orbitals with the staggered configuration favored and 700 minimum to 1400 maximum cal. from the interactions between the hydrogen atoms and the hybridized carbon orbitals with the opposed configuration stable. We thus see that the sum of these effects gives a small barrier of up to 600 cal. with the opposed configuration the stable one. It is a rather surprising result that there should be enough resonance between the tetrahedral sp^3 configuration of carbon and the higher configurations containing $3d$ orbitals to actually change the stable form from the staggered to the opposed configuration. However, there are still other resonance effects to consider which we will now discuss.

Resonance Involving Double Bond Structures.—In discussing the resonance between the single and double bond structures it is convenient to adopt the nomenclature for the electronic orbitals indicated by the letters in Fig. 1. Reso-

nance between the following bond structures was considered in the usual quantum mechanical scheme to find the lowest energy. The eigenfunctions are indicated by writing together the

$$\begin{vmatrix} 3\alpha - \frac{W}{3} & \frac{3}{4}(\xi + \mu - 2\zeta) \\ \frac{3}{4}(\xi + \mu - 2\zeta) & \frac{15}{4}\alpha + \frac{3}{4}(\xi + \mu + 2\zeta) - \frac{3}{4}W \\ \frac{3}{2}(\epsilon + \varphi - 2\eta) & -\frac{3}{2}(\gamma + \beta) \end{vmatrix}$$

two letters which form a bond.

$$\begin{aligned} \psi_1 &= ae\ cg\ bf\ dh\ kn\ il\ jm \\ \psi_2 &= ae\ fl\ bi\ dh\ cg\ kn\ jm \\ \psi_3 &= em\ aj\ dh\ bf\ cg\ il\ kn \\ \psi_4 &= gn\ ck\ dh\ ae\ bf\ il\ jm \\ \psi_5 &= bk\ fn\ dh\ ae\ cg\ jm\ il \\ \psi_6 &= fm\ bj\ ae\ cg\ dh\ kn\ il \\ \psi_7 &= el\ ai\ dh\ bf\ cg\ kn\ jm \\ \psi_8 &= en\ ak\ dh\ cg\ bf\ jm\ il \\ \psi_9 &= ci\ gl\ ae\ bf\ jm\ kn\ dh \\ \psi_{10} &= cj\ gm\ ae\ bf\ dh\ kn\ il \end{aligned} \quad (6)$$

From symmetry considerations we know that the proper linear combination of eigenfunctions must have the form

$$\varphi = a\psi_1 + b\sum_{i=2}^{4}\psi_i + c\sum_{j=5}^{10}\psi_j \quad (7)$$

This leads to the following secular equation

$$\begin{aligned} &a(H_{11} - S_{11}E) + 3b(H_{12} - S_{12}E) + 6c(H_{1,10} - S_{1,10}E) = 0 \\ &3a(H_{12} - S_{12}E) + b[3H_{22} + 6H_{23} - (3S_{22} + 6S_{23})E] \\ &+ 6c[H_{10,2} + H_{10,3} + H_{10,4} - (S_{10,2} + S_{10,3} + S_{10,4})E] = 0 \\ &(6a[H_{1,10} - S_{1,10}E) + 6b[H_{10,2} + H_{10,3} + H_{10,4} \\ &- (S_{10,2} + S_{10,3} + S_{10,4})E] + 6c[H_{55} + 2H_{56} + 3H_{57} \\ &-(S_{55} + 2S_{56} + 3S_{57})E] = 0 \end{aligned} \quad (8)$$

The exchange integrals between the following pairs of orbitals are indicated by the Greek letters.

$$\begin{aligned} \alpha &= ae = bf = cg = kn = jm = il \\ \theta &= dh \\ \xi &= bi = aj = ck \\ \mu &= fl = em = gn \\ \zeta &= am = cn = bl = if = je = kg \\ \epsilon &= cj = ci = ak = ai = bk = bj \\ \varphi &= gm = gl = em = el = fn = fm \\ \eta &= cm = cl = al = an = bn = bm = ie \\ &= ig = jf = jg = kf = ke \\ \delta &= ec = eb = fa = fc = ga = gb = il \\ &= in = jl = jn = km = kl = df = de \\ &= dg = lh = hm = hn \\ \beta &= eg = ef = fg = lm = mn = nl \\ \gamma &= ac = ab = bc = ij = jk = ik = db \\ &= ad = cd = jh = ih = kh \\ \sigma &= dm = dl = dn = hf = he = hg \\ \lambda &= di = dj = dk = ah = eh = ch \end{aligned} \quad (9)$$

The matrix components were calculated in the way described by Eyring and Kimball.[8] Determinant (8) after the slight rearrangement corresponding to orthogonalizing the three eigenfunctions which are the coefficients of a, b and c in equation (7) takes the simplified form

$$\begin{vmatrix} \frac{3}{2}(\epsilon + \varphi - 2\eta) & & \\ -\frac{3}{2}(\gamma + \beta) & & = 0 \\ \frac{15}{2}\alpha + \frac{3}{2}(\epsilon + \varphi + 2\eta) + 3\delta - \frac{3}{2}(\gamma + \beta) - \frac{3}{2}W & & \end{vmatrix} \quad (10)$$

W of equation 10 is related to E by

$$W = E - Q + 1/2\Sigma - 3/2\,\theta,$$

where E is the actual total bonding energy for ethane formed from two quadrivalent carbon atoms. Q is the coulombic energy and Σ is the sum of the 91 exchange integrals listed in (9).

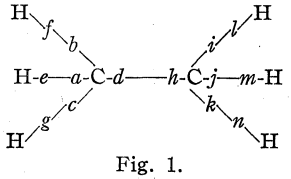


Fig. 1.

In the following numerical calculations for the difference in energy between staggered and opposed forms due to the double bonds we assume the usual tetrahedral carbon bonds. In Table I we list the values for the exchange integrals occurring in (10) for the various calculations of interest. All values in Table I are in kcal.

In all the calculations of Table I where the value of an integral for a staggered configuration is not explicitly given it was taken equal to the corresponding value in calculation 1. The same is true for opposed configurations. In calculating the integrals α and δ the values given by Van Vleck[9] for the elementary $N_{\sigma\sigma} = 2.3$, $N_{ss} = +2.0$, $N_{\pi\pi} = -0.6$ and $N_{\sigma s} = +1.0$ in volts were used in his formulas

$$\begin{aligned} -4\alpha &= N_{ss} + 3N_{\sigma\sigma} + 2(3)^{1/2}N_{\sigma s} \\ -12\delta &= 3N_{ss} + N_{\sigma\sigma} + 8N_{\pi\pi} - 2(3)^{1/2}N_{\sigma s} \end{aligned}$$

to give his values $\alpha = 72$ cal., $\delta \approx 0$. Van Vleck's formula

$$16\gamma = F_0(2s;\ 2s) - 2F_0(2s;\ 2p) + F_0(2p;\ 2p) + 28\,F_2 + 4\,G_1$$

with the value given by Voge[10] for the F's and G's was used to calculate γ. β was taken from the H–H Morse curve with the constants $D = 102.4$, $r_0 = 0.74$, $\omega_0 = 4375$ which gives a value for Morse's a of 1.94. The exchange binding was

(8) H. Eyring and G. E. Kimball, *J. Chem. Phys.*, **1**, 239 (1933); see, also, Pauling, *ibid.*, **1**, 280 (1933).

(9) J. H. Van Vleck, *J. Chem. Phys.*, **2**, 20 (1933).

(10) H. H. Voge, *ibid.*, **4**, 581 (1936).

TABLE I

	α	β	γ	δ	ϵ	φ	η	μ	ξ	ζ	W	ΔW	ΔE
Calcd. 1 staggered	72	19.4	−20.7	0	17.2	1.9	0	0.4	28.7	3.7	658.0	1.4	0.7
opposed	72	19.4	−20.7	0	17.2	0.5	1.1	3.8	28.7	1.5	659.4		
Calcd. 2 staggered						5.4		1.6			660.9	2.2	1.3
opposed						2.4		8.6			663.1		
Calcd. 3 staggered					18.2				26.7		658.0	2.0	1.3
opposed					16.2				30.7		660.0		
Calcd. 4 staggered					18.2	5.4		1.6	26.7		660.9	2.8	1.9
opposed					16.2	2.4		8.6	30.7		663.7		
Calcd. 5 staggered					12.3	5.4		1.6	38.7		662.6	−1.3	−2.2
opposed					22.3	2.4		8.6	18.7		661.3		

taken as 0.8 of the total. ζ and η are special cases of the more general integral

$$I = 3/4 \left\{ C_1^2 N_{\sigma\sigma} + \frac{2}{\sqrt{3}} C_1 N_{\sigma s} + 1/3 N_{ss} + (C_2^2 + C_3^2) N_{\pi\pi} \right\}$$

where

$$C_1 = 2/3 \sqrt{2}\, a \cos\varphi + b/3$$
$$C_2 = (1 - a^2 \sin^2\varphi)^{-1/2}(-2/3\, 2^{1/2}\, b - 1/3\, a \cos\varphi)$$
$$C_3 = (1 - a^2 \sin^2\varphi)^{-1/2}(2/3\, 2^{1/2}\, a^2 \sin\varphi \cos\varphi - 1/3\, ab \sin\varphi).$$

in which $a = 0.486$, $b = -0.874$. φ is the angle of rotation of the hydrogen atom about the C–C axis. $\varphi = 0$ where the hydrogen atom and the interacting carbon orbital lie in a plane which includes the C–C bond direction. ζ is obtained from these formulas by inserting $\varphi = 0$ for the opposed form and $\varphi = 180°$ for the staggered configuration. For η, one should use $\varphi = 120°$ for the opposed form and $\varphi = 60°$ for the staggered. The integrals $N_{\sigma\sigma}$, $N_{\sigma s}$, etc., were assumed to vary with the distance in the way given by a C–H Morse curve.

The exchange interaction between carbon orbitals other than those forming the carbon–carbon bond and on opposite carbons can be expressed in terms of the more fundamental integrals by the formula

$$I_{\text{carbon–carbon}} = C_2^4 (N_{yy,yy} - N_{xy,xy}) \cos^2\omega + \{C_1^2 C_2^2 (2N_{ssyy} + 2N_{syys}) + C_1 C_2^2 C_3 (4N_{syyz} + 2N_{yysz}) + C_2^2 C_3^2 (2N_{yyzz} + 2N_{yzzy})\} \cos\omega + C_1^4 N_{ssss} + C_2^4 N_{xyxy} + C_3^4 N_{zzzz} + 2C_1^2 C_2^2 N_{ysys} + C_1^2 C_3^2 \{2N_{sszz} + 4N_{szsz}\} + 2C_2^2 C_3^2 N_{yzyz} + 4C_1 C_3^3 N_{zzzs} + 4C_1^3 C_3 + C_1 C_2^2 C_3 \{4N_{ysyz} + 2N_{yysz}\}$$ where $c_1 = 1/2$ $c_2 = (2/3)^{1/2}$ $c_3 = (2(3)^{1/2})^{-1}$

where the integrals $N_{mn,op}$ are defined by the expression

$$N_{mn,op} = \int\int \psi_{am}(1)\, \psi_{bn}(1)\, H'\, \psi_{ao}(2)\, \psi_{bp}(2)\, d\nu_1\, d\nu_2$$

where a refers to the function ψ_a about carbon atom a as center and b to function ψ_b about the carbon atom b.

$$H' = e^2 \left(1/r_{12} + \frac{z^2}{R} - \frac{z}{r_{a1}} - \frac{z}{r_{b2}} \right)$$

z is the effective nuclear charge of the carbon atom. The coefficient $(N_{yy,yy} - N_{xy,xy})$ of $\cos^2\omega$ is $(C_{\pi\pi\pi\pi} - C_{\pi\pi'\pi'\pi})$ in Penney's notation.[11] We have used the value of 1.5 e. v. given for this quantity by Pauling and Wheland.[12] The estimates given by Penney[13] were used as a basis for evaluating the part of the integral that is independent of ω. The estimates are listed below:

$N_{ssss} = C_{ssss}$	$= 1.0$	$N_{szsz} = C_{s\sigma\sigma s}$	$\cong 1.75$
$N_{xyxy} = C_{\pi\pi'\pi'\pi}$	$\cong 0$	$N_{zzss} = C_{\sigma s\sigma\sigma}$	$\cong 2.29$
$N_{zzzz} = C_{\sigma\sigma\sigma\sigma}$	$= 3.0$	$N_{sssz} =$	$\cong 1.32$
$N_{szsz} = C_{s\sigma\sigma s}$	$\cong 1.75$	$N_{yzyz} =$	-0.5
		$N_{ysys} =$	-0.4

No integrals similar to $N_{yz,yz}$ were estimated by Penney. They must be negative, however, since due to orthogonality only the electrostatic repulsion term e^2/r_{12} need be considered. From similar integrals evaluated by Bartlett[14] we can expect them to be relatively small. We arbitrarily take for the integrals $N_{yz,yz}$ and $N_{ys,ys}$ the values -0.5 and -0.4 volt, respectively. None of the integrals involved in the coefficient of $\cos\omega$ have been evaluated. However, we would expect this coefficient to be small since the integrals involved are alternately + and −, *i. e.*, the integrals $N_{ss,yy}$, $N_{yy,sz}$ and $N_{yy,zz}$ are positive in the sense here used, *i. e.*, positive energy corresponds to attraction, while $N_{sy,ys}$, $N_{sy,yz}$ and $N_{yz,zy}$ are negative. The coefficient should be positive since the maximum binding should be obtained when the orbitals are *cis* where their overlap is greatest. Also similar integrals evaluated by Bartlett indicate that the positive integrals are considerably greater in

(11) W. G. Penney and G. B. B. M. Sutherland, *J. Chem. Phys.*, **2**, 492 (1934).

(12) L. Pauling and G. W. Wheland, *ibid.*, **1**, 362 (1933).

(13) W. G. Penney, *Proc. Roy. Soc.* (London), **A146**, 223 (1934).

(14) J. H. Bartlett, *Phys. Rev.*, **37**, 507 (1931); Furry and Bartlett, *ibid.*, **38**, 1615 (1931); **39**, 210 (1932).

magnitude than the negative ones. In calculations 1 and 2 the coefficient of cos ω was chosen to be zero while in 3 and 4 it was taken to be 2 kcal. The value of I_{C-C} in kcal. is then

$$I_{C-C} = 15.3 \cos^2 \omega + 13.4 \text{ in calculations 1 and 2} \quad (11)$$

$$I_{C-C} = 15.3 \cos^2 \omega + 2.0 \cos \omega + 13.4 \text{ in calculations 3 and 4}$$

ξ in the opposed form is obtained by inserting $\omega = 0$ in (11), while in the staggered configuration $\omega = 180°$. η is obtained from (11) by using the values $\omega = 60$ and 180° for the staggered and opposed configurations, respectively. In calculations 1 and 3 the Heitler–London values were used for the hydrogen–hydrogen interactions, μ and φ, while in calculations 2 and 4 80% of the Morse curve values were taken.

Calculation 5 was undertaken to show that by a proper choice of the unknown coefficient of cos ω in the exchange integral I_{C-C} the staggered form could be made stable with respect to the opposed. The coefficient was taken to be −10 kcal. This seems to us to be unreasonable since it makes this interaction stronger in the *trans* position than in the *cis* position while one would expect that since the overlap is strongest in the *cis* position that it would be more stable. The last column gives the difference ΔE in the energies of the staggered and opposed configuration when the van der Waals forces are neglected. If the van der Waals forces are included about 400 cal. should be added to this figure. The effect of the *d*-ness would also be approximately additive since the presence of a small amount of *d*-ness in our wave functions should not appreciably affect the resonance energy. If this effect is included, then an additional 300 to 900 cal. should be added to ΔE.

Possible Effect of Resonance on Melting Points.—There is a well-known rule that the more symmetrical a molecule, other things being equal, the higher its melting point. In certain cases at least this is associated with the fact that the more symmetrical compounds are able to make their rotational transitions at low temperatures, *i. e.*, in the solid state and therefore there is not the incentive to melt that there otherwise would be. We see this most readily from the equation connecting the heat and entropy of melting $\Delta F = 0 = \Delta H - T\Delta S$ or $T = \Delta H/\Delta S$. Thus effects which increase ΔS or decrease ΔH lower the melting point. In Fig. 2 are plotted the heats, temperatures and entropies of melting for the paraffins. The values for methane are taken from Bichowsky and Rossini.[15] Those for ethane are from Witt and Kemp,[16] while those for propane are from Kemp and Egan.[17] Parks, Shomate, Kennedy and Crawford[18] provide the values for butane while the other values are from the treatise, "The Science of Petroleum."[19]

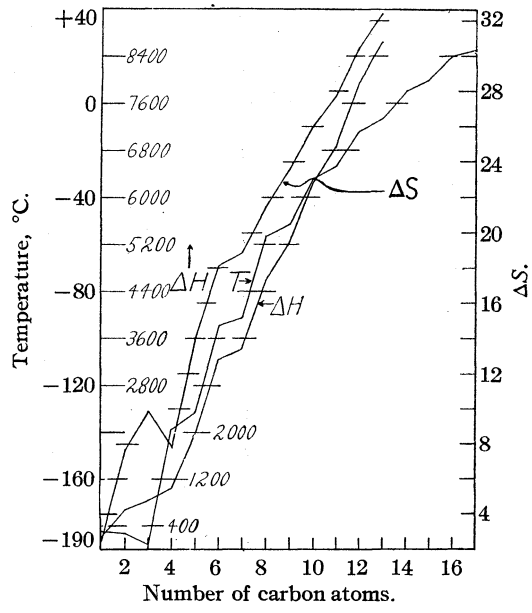


Fig. 2.—Heat, entropy and temperature of melting of paraffins.

The initial drop in the melting points from methane to propane is associated with an increase in the entropy of fusion which more than offsets the increase in the heat of fusion. This may be understood in the following way. In the liquid state these molecules presumably rotate very nearly freely about all axes as is shown by their normal entropy of vaporization at their boiling points. The entropies of vaporization from methane to butane are 19.37, 19.09, 19.42, 19.50. The value for methane is from the "International Critical Tables." The other values come from the sources quoted above. The almost spherical structure of methane permits it to rotate in the solid so that we expect a value only slightly larger than the two units of communal entropy.[20] The

(15) Bichowsky and Rossini, "Thermochemistry," Reinhold Publ. Corp., New York, N. Y., 1936.

(16) Witt and Kemp, THIS JOURNAL, **59**, 273 (1937).

(17) Kemp and Egan, *ibid.*, **60**, 1521 (1938).

(18) Parks, Shomate, Kennedy and Crawford, *J. Chem. Phys.*, **5**, 359 (1937)

(19) "The Science of Petroleum," Oxford University Press, New York, N. Y., 1938.

(20) J. Hirschfelder, D. Stevenson and H. Eyring, *J. Chem. Phys.*, **5**, 896 (1936).

observed value is 2.48 e. u. On the other hand ethane being able to rotate only about the C–C axis in the solid would be expected to get an increase in entropy due to changing from oscillation to free rotation about the other two axes. The observed value is 7.60 e. u. If the end of the vector which coincides with the C–C axis is free to describe ten times as large a solid angle in the liquid as in the solid it would explain the increase of entropy from 2.48 to 7.60. The greater value of 9.86 e. u. for propane arises in all probability from restricted rotation about all three axes in the solid state. Butane has a lower entropy change of 7.79 e. u. For longer hydrocarbons than butane there is little even–odd alternation except near hexane. The older entropy quoted by Landolt–Börnstein for hexane would fall more nearly on the straight line through the higher values. We must conclude that the considerable alternation above butane in the melting points arises principally from ΔH rather than ΔS. Going with large ΔH values of fusion we will necessarily have large changes in the density. The problem is thus reduced to a determination of the cause of the relatively better packing in the solid for the even members of the series. Müller,[21] for example, concludes, from his X-ray studies, that the relatively higher melting points of the even dicarboxylic acids is associated with closer packing and with different symmetry properties associated with a modified crystal form. Malkin[22] has criticized the theories advanced by Nekrassow,[23] Müller,[21] and Pauly[24] to explain alternating properties which are based on the fact that in the even series the terminal groups are *trans* while in the odd compounds they are *cis* with respect to one another. He shows that in the case of vertical chains there is no difference in the spacing of the planes containing the terminal groups and therefore there should be no difference in melting point for even and odd compounds. Malkin then divides long chain compounds into two series: those that show alternation and those that do not. The monobasic acids, dibasic acids, and their methyl esters, for example, belong to the alternating series. In all these substances there is a transition in the solid just below the melting point from the vertical chain structure to one where they are tilted with respect to the long axis of the crystal. Malkin finds that for the tilted chains there is a large difference in the spacing of the terminal planes for the even and odd compounds, *i. e.*, the density is greater for the even compounds than for the odd ones. He gives a geometrical explanation for the observed difference in spacing. By this he explains the fact that the even compounds melt higher and also why the transition to the tilted structure takes place with greater ease in the even series.

Those compounds which, according to Malkin, do not show alternation such as the paraffins, ethyl esters, and alcohols possess vertical chains and do not show a transition to the tilted form.

Beach[25] has explained alternating properties on the basis of alternating strong and weak bonds while Cuy[26] and Pauly[24] attribute the phenomena to alternately positive and negative carbon atoms. Malkin criticizes these theories since one would expect alternation in other physical properties as well as melting points which are not in general observed.[27]

The paraffins and ethyl esters which are cited by Malkin as examples of non-alternating series of compounds really do show alternation as is illustrated for the paraffins in the figure. Since these cases are not explained on a purely geometrical basis, some other explanation must be sought. We propose a theory which has some points of similarity to Beach's theory of alternating strong and weak bonds. Our calculations on ethane have shown that resonance with double bond structures lowered the total energy by about 12 kcal. in the opposed form and 10 kcal. in the staggered form. Now if we consider propane we see that it is possible to have a double bond between any two of the neighboring carbon atoms but not between both simultaneously as the structure corresponding to drawing two double bonds on the same carbon lies so high in energy above the normal state as not to contribute appreciably to the stability of the molecule. In the case of butane, however, it is possible to have structures containing two double bonds simultaneously which contribute to the total energy in the same way as in ethane. Thus we see in general that in the odd series both end carbons cannot be simultaneously double bonded while in the even compounds the end carbons can both be double bonded simul-

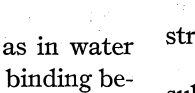
(21) Müller, *Proc. Roy. Soc.* (London), **A124**, 317 (1929).
(22) Malkin, *J. Chem. Soc.*, 2796 (1931).
(23) Nekrassow, *Z. physik. Chem.*, **128**, 208 (1927).
(24) Pauly, *Z. anorg. Chem.*, **119**, 271 (1922).
(25) Beach, *Z. physik. Chem.*, **50**, 43 (1905).
(26) Cuy, *Z. anorg. Chem.*, **115**, 273 (1921).
(27) Verkade, Coops and Hartman, *Rec. trav. chim.*, **45**, 373, 503 (1926).

taneously. The hydrogen atoms attached to the end carbons in the even series will thus be more free on the average to form bonds of a coördination type with other molecules than in the odd series. This is because there is a somewhat unoccupied 1s level on a hydrogen attached to a carbon that has become double bonded, which is available for coördination bonding with similar atoms on neighboring molecules. We call such binding intermolecular coördination to distinguish it from the intramolecular coördination binding between the hydrogen atoms in a single ethane molecule. Thus the intermolecular forces will be stronger in the even than in the odd compounds and they will consequently melt higher. Most of these coördination bonds would be broken in the liquid state due to the expansion which usually takes place upon melting. One would expect as is observed, therefore, that alternation in physical properties should be much less marked in the liquid state. This relative lack of alternating properties in the liquids is due to the lack of alternation in the molar refraction of even and odd compounds, and indicates that the binding forces in the liquid are largely of the polarization type. The importance of coördination type of binding in determining the stability of crystals and its relative unimportance for the stability of normal liquids is illustrated in the case of ethylene. Thus ethylene melts 13° higher than ethane but boils 17° lower. This can be explained by the tendency of the electrons forming the double bond to couple on to the double bond of another ethylene molecule. The coördination binding between the double bonds would not be nearly as strong in the liquid because of rotation and therefore liquid ethylene would be expected to boil lower than ethane due to its fewer number of hydrogen atoms. Because ethylene rotates in the liquid it is less dense than liquid ethane.

In the ordinary hydrogen bonding as in water there is in addition to the electrostatic binding between the hydrogen and oxygen atoms of neighboring molecules a large amount of this coördination type of binding. Due to the large electrostatic contribution we would expect the hydrogen bonding in water to be much stronger than the intermolecular binding discussed above. This coordination binding may also explain why one gets tilting of the chains in the cases discussed by Malkin and thus enhancement of the alternating phenomena. For example, according to Malkin, the methyl esters form double molecules in the crystal and tilted chains while the ethyl esters form only single molecules in the crystals and vertical chains. This property of forming tilted chains is evidently connected with how well the ends of the molecules form bonds with their neighbors. Thus, in the methyl esters, part of the double bond in the carbonyl group will tend to go over toward the methyl group, thus releasing the methyl hydrogens to form coördination bonds with the atoms at the end of the chain of the neighboring molecules. When the methyl group is replaced by an ethyl group, the same tendency to loosen the hydrogen atoms at the end of the molecule will no longer be present since the end methyl group is now farther removed from the carbonyl group and also because of the alternation in double bond effect. The methyl esters would thus be expected to form double molecules and tilted chains much more readily than the ethyl esters.

This phenomenon of the tendency of a double bond to be partially shared by its neighboring single bonds is illustrated by the general reactivity of the α-carbon atom in the carboxylic acids and especially by the marked reactivity of the hydrogens attached to the α-carbon in malonic acid. This type of effect is also illustrated by the definite shortening of the C–C single bond in methylacetylene as compared with its value in saturated hydrocarbons.[28a] The shortening of a single bond which is next to a double or triple bond has been discussed by Pauling, Brockway and Beach.[28b]

An interesting example of what we have called intermolecular coördination is exhibited by the solid hydroboranes. Bauer and Pauling[29] have pointed out that the twenty-one structures for diborane each having two one-electron bonds resonate to form the stable molecule. One of the structures is the following



As a result all the hydrogens will on the average be sharing less than the usual two electrons and so will tend to form coördination compounds with neighboring molecules. Since such bonds are short range they will decrease rapidly with the expansion accompanying either a rise of temperature or the melting process. This will give

(28) (a) G. Herzberg, F. Patat and H. Verleger, *J. Phys. Chem.*, **41**, 121 (1937); (b) Pauling, Brockway and Beach, THIS JOURNAL, **57**, 2705 (1935).

(29) Bauer and Pauling, *ibid.*, **58**, 2403 (1936); Bauer, *ibid.*, **59**, 1096 (1937).

a relatively higher ΔH for melting without a corresponding increase in ΔS so that from the formula $\Delta H/\Delta S = T$ we expect higher melting points for the boranes than for the corresponding hydrocarbons in spite of the fact that the former contain two less electrons. That this is true is shown by the following comparisons

	B_2H_6	C_2H_6	B_4H_{10}	C_4H_{10}	BCl_3	$CHCl_3$
M. p., °C.	−165.5	−183.2	−120	−139	−107	−70
B. p., °C.	− 92.5	− 89	18	−0.6	18.2	61.2

When this coördination cannot take place as in BCl_3, we have a melting point considerably lower, rather than higher, than $CHCl_3$ the most nearly analogous carbon compound containing two more electrons.

X-Ray and Other Evidence Concerning Relative Stabilities of Staggered and Opposed Configurations.—The X-ray evidence on solid hydrocarbons[30] indicates that they are in the form of a zigzag chain with all the carbon atoms in a plane. This structure corresponds to the staggered configuration about all of the carbon–carbon linkages. This seems to us to be a serious objection against any theory which postulates the opposed as the stable structure as does the theory of intramolecular coördination proposed above. This objection possibly can be met in the following way. The same carbon atom cannot support two double bonds simultaneously, so that we would expect that the carbon–carbon bonds would be alternately double and single. Thus in butane we would have two double bonds at the end carbons with a single bond in the middle. If we assume that the single bond can assume the staggered configuration this would lead to a plane structure for butane. However, when a fifth carbon atom is added it would no longer tend to be in the plane of the other four. Thus, in order to get a plane zigzag structure it is necessary to assume that every fifth carlon atom is forced into the plane by the crystal forces, which expenditure of energy is compensated for by the resultant better packing. Since the crystal energy that is available is of the order 4000 kcal. per C–C bond, as is shown by the heat of sublimation of the hydrocarbons, this is by no means impossible. Electron diffraction and Raman investigations on dichloroethane[31] indicate that the chlorine atoms are in the *trans* position, *i. e.*, that the configuration is the staggered one about the C–C axis. The electronegativity of the chlorines, however, withdraws electrons away from the carbons so that a double bond cannot be formed easily between the carbon atoms. We would thus expect that the C–C bond would remain single and that the repulsions of the chlorines would determine the stability of the *trans* position. The importance of the electron affinity of the halogen in chemical reactions is shown by the results of Conn, Kistiakowsky and Smith[32] on the heats of halogenation of substituted ethylenes. The greater the number of substituted alkyl radicals the higher is the heat of halogenation. This is explained easily by the fact that in the substituted compounds there is a greater reservoir of electrons for the chlorines to draw upon. This effect more than compensates for the increased steric repulsions in the substituted compounds.

Attempts have been made to interpret the infrared and Raman spectra of liquid ethane as indicating the stability of either the opposed or the staggered structure. Thus Bartholemé, Karweil and Schafer[33,34] conclude on the basis of Raman spectra that the molecular symmetry is D_{3h}, *i. e.*, opposed since the observed frequency at 2260 cm.$^{-1}$ cannot be fitted to D_{3d}, the staggered form. Crawford, Avery and Linnett[35] have attempted to effect a complete analysis of the vibrational spectrum of ethane and conclude that at the present time the evidence is insufficient to exclude the D_{3d} configuration. Prof. E. B. Wilson[36] informs us that the most recent considerations do not allow them to reach any conclusion concerning the relative stabilities of the staggered and opposed forms.

It is interesting to compare the relative stabilities of cyclopentane and cyclohexane. In cyclopentane the configuration about all the carbon–carbon bonds is the opposed form. In cyclohexane, however, in the chair form all the bonds are staggered, we might expect, therefore, that if the staggered structure is the stable one, then cyclohexane would be more stable by 3 kcal. per methylene group. Heat of combustion data[37] show, however, that cyclohexane is only slightly more stable than cyclopentane, the heat of com-

(30) See "Structurbericht," 1913–1928.

(31) J. Y. Beach and K. J. Palmer, *J. Chem. Phys.*, **6**, 639 (1938); B. Trumpy, *Z. Physik*, **90**, 133 (1934); **93**, 624 (1935).

(32) J. B. Conn, G. B. Kistiakowsky and E. A. Smith, THIS JOURNAL, **60**, 2764 (1938).

(33) E. Bartholemé and J. Karweil, *Z. physik. Chem.*, **39B**, 1 (1938).

(34) J. Karweil and K. Schafer, *ibid.*, **B40**, 382 (1938).

(35) B. L. Crawford, Jr., W. H. Avery and J. W. Linnett, *J. Chem. Phys.*, **6**, 682 (1938).

(36) E. B. Wilson, private communication.

(37) Kharasch, *J. Research Bur. Standards*, **2**, 359 (1929).

bustion per methylene group being 157.5 kcal. as compared with 157.9 kcal. for cyclopentane. In the boat form of cyclohexane, however, two of the bonds can be opposed, while the greater possibility of resonance with double bonded structures in cyclohexane would tend to stabilize it with respect to cyclopentane. Cyclopentane would also be expected to have some strain, so that the above evidence can be reconciled with the opposed structure. If cyclohexane were flat, for example, all the bonds would be opposed. The fact that among the cyclic hydrocarbons the even members melt higher is exactly as would be expected on the coördination theory but cannot be understood on the theory of Malkin for straight chain compounds. This alternation is illustrated in Fig. 3. With the information available we are unable to rule out the possibility that alternations in entropy are more important in the cyclic than in the straight chain paraffins. We see no reason for expecting this, however.

Eyring[38] has derived a formula for the mean length of a hydrocarbon chain which as was stated is valid under conditions of free rotation. This formula in simplified form is

$$C_a = C_1\left\{\frac{n - x(2 + nx - 2x^n)}{(1 - x)^2}\right\}^{1/2}$$

where C_a is the length of the molecule, C_1 is the distance between neighboring carbon atoms, x is the cosine of the valence angle. Several investigators have concluded that the agreement between experimentally determined lengths and the result given by this formula is evidence of free rotation in these long chain compounds. We would like to point out, however, that even with high barriers one obtains the same result if the molecule vibrates about two equivalent minima 180° apart, three equivalent minima 120° apart, or any higher number of symmetrically placed equivalent minima.

The fact that agreement of observed lengths with this formula implies a random distribution of the orientations about the single bonds would seem at first sight inconsistent with the long zigzag chain observed in the solid compounds. However, the measurements of lengths which fit this formula were made in solvents consisting of small molecules. When the long chain compounds are dissolved in a solvent of this kind there is no longer the advantages in lying flat that they would have if they were present in an environment of their own molecules and consequently they can curl up with little or no extra energy.

(38) H. Eyring, *Phys. Rev.*, **38**, 746 (1932).

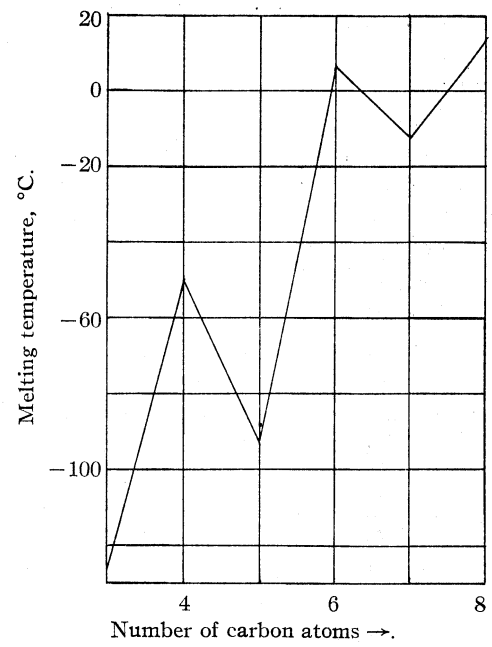


Fig. 3.—Melting temperatures of cycloparaffins.

Addendum.—Since this paper was completed, an article by Eucken and Schäffer[39] has appeared in which the view is put forward that the potential barrier in ethane arises from the induction by the C–H dipoles on each methyl group of a lack of cylindrical symmetry in the carbon–carbon bonding orbitals. They write the perturbed orbital in the form $\psi_{2t\sigma}(1 + 0.1 \cos 3\varphi)$ where $\psi_{2t\sigma}$ is the unperturbed bonding orbital and the factor $(0.1 \cos 3\varphi)$ arises from perturbation of the carbon–hydrogen orbitals. Since the orbitals in this form show 4% greater overlap in the opposed as compared with the staggered configuration, the opposed configuration should be more stable by about 4% of the binding energy, giving a potential barrier of the order of 3000 kcal.

We have discussed this effect in the first section of this paper using a somewhat different potential and have concluded that this effect gives a negligibly small contribution to the barrier. In view of the results of Eucken and Schäffer we have repeated this calculation using as they did a potential due to a charge of one-tenth the electronic charge at each of the hydrogen nuclei. The perturbed eigenfunction can be written as

$$\psi'_{2t} = \psi_{2t\sigma} + \frac{0.3\int \psi_{2t\sigma}\frac{e^2}{r_b}\psi_{4f}\,d\tau}{E_0 - E_{4f}}\psi_{4f}$$

(39) Eucken and Schäffer, *Naturwissenschaften*, **8**, 122 (1939).

where the factor 0.3 arises from the fact that there are three equivalent charges of 0.1 each on each methyl group. $E_0 - E_{4f}$ is the difference in energy of the $4f$ and normal states and is about equal to the ionization potential or 10–12 electron volts. The functions $\psi_{2l\sigma}$ and ψ_{4f} were chosen to be hydrogen-like and are given below. The effective nuclear charge equal to three

$$\psi_{2l\sigma} = Are^{-3/2\,r/a_0}\,(1 + \sqrt{3}\cos\Theta)$$
$$\psi_{4f} = Br^3e^{-3/4\,r/a_0}\,\Theta_{33}\,\Phi_{3\cos\varphi}$$

is approximately that obtained by application of Slater's[40] rules for the screening constants of atomic orbitals. A and B are normalizing factors, and $AB = (2.45 \times 10^{-2})/\sqrt{\pi}$. The phase of $\Phi_{3\cos\varphi} = (1/\sqrt{\pi})\cos 3\varphi$ was so chosen that the hydrogen atoms lie in the planes $\varphi = 0$, $\pi/3$ and $2\pi/3$ corresponding to the maximum values of $\Phi_{3\cos\varphi}$. The term $1/r_b$ was expanded in terms of spherical harmonics about the center of the carbon atom. Due to orthogonality, all terms integrate out except those involving the harmonics $\Theta_{33}\phi_3\cos\varphi$ and $\Theta_{43}\phi_3\cos\varphi$. The result is that $0.3\int\psi_{2l\sigma}e^2/r_b\psi_{4f}d\tau = 1.56 \times 10^{-2}$ e. v. and the coefficient of the $4f$ function is correspondingly about 1.5×10^{-3}. This coefficient is, as we see, so small that no appreciable contribution to the barrier can come from this cause, in agreement with our earlier result and in disagreement with Eucken and Schäffer. The barrier therefore arises from other causes such as are considered in this paper.

(40) Slater, *Phys. Rev.*, **36**, 57 (1930).

We wish to express our appreciation to Drs. William Baker and John Beach for helpful discussions.

Summary

1. The problem of restricted rotation about the C–C bond in ethane is discussed. It is shown that the repulsions between the hydrogen atoms cannot account for a barrier of 3000 cal. The effect of the distortion of the spherical symmetry around the carbon atoms by the perturbations of the hydrogen atoms is considered. It is shown that this effect tends to make the opposed form more stable but also cannot account for a barrier of the required height. The effect of resonance with double bonded structures is then considered and it is shown that with reasonable assumptions concerning the angular dependence of the exchange integrals between carbon orbitals, the opposed structure is the stable one with a barrier height of 0.7 to 1.9 kcal. If we add to this the effect of the dissymmetry of the carbons a barrier of the right order of magnitude is obtained.

2. It is shown that this effect of resonance with double bonded structures can be used to explain the alternation in physical properties such as melting points of long chain compounds.

3. The experimental evidence in favor of the staggered or opposed structures for long chain and cyclic compounds is discussed.

PRINCETON, NEW JERSEY RECEIVED APRIL 28, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

Primary and Secondary Acids and Bases

BY GILBERT N. LEWIS AND GLENN T. SEABORG

The most general classification[1] of bases and acids does not extend the class of bases much beyond the group of substances now recognized under that name. On the other hand, if we define an acid as any substance one of whose atoms is capable of receiving into its valence or coördination or resonance shell the basic electron-pair of another atom, then we have a great group of generalized acids in which the hydrogen acids are not the strongest and not always the most typical members.

The self-consistency of this group of generalized acids has been brought out in a recent paper[2] which emphasizes the extraordinary similarity in every type of behavior, extending even to the colors of their compounds with indicators, between hydrogen acids and all the other acids of the class. All the acids can be ranked roughly by their strengths. Thus, for example, sulfur dioxide is ordinarily weaker than hydrochloric acid, which in turn is much weaker than boron trifluoride or stannic chloride. Aside, however, from these considerations of relative strength, there was proposed in that paper an entirely independent classification into *primary* and *secondary*

(1) Lewis, "Valence and the Structure of Atoms and Molecules," Chemical Catalog Co., New York, 1923, p. 142.

(2) Lewis, "Acids and Bases," *J. Franklin Inst.*, **226**, 293 (1938).

acids and bases which, as far as we can now see, probably represents a difference, not of degree, but of kind. It was assumed that there is a large group of acids and bases, called primary, which require no energy of activation in their mutual neutralization, but that apparently there is another group, called secondary, such that a secondary acid does not combine, even with a primary base, nor a secondary base with a primary acid, except when energy, and frequently a large energy of activation, is provided.

It is to be presumed that an acid which conforms to the defintion of our first paragraph is primary and that when a heat of activation is found to be necessary, it means that some change in the condition or structure of the molecule is needed to make it conform to that definition. Frequently we can see in advance that such a change is necessary. For example, an isolated molecule of an acid might be primary, but when dissolved in a basic solvent may be completely neutralized by forming a complex with the solvent, which would have to be dissociated before the acid could combine with some stronger base. We should then expect a heat of activation which may be smaller, but cannot be larger, than the heat of dissociation of the complex. In other cases a known structural change must occur, as, for example, in the change from a keto to an enol form, before a substance shows marked acid properties. Such a substance has been called by Hantzsch[3] a pseudo acid.

The Possibility of Electromerism

Such cases of secondary acids and bases as we have just mentioned, in which the acid or basic properties appear only after the breaking of some bond or the rearrangement of the atoms within a molecule, are familiar. We are going to see, however, that there are numerous secondary acids and bases which do not appear to conform to these specifications of what we may call the classical type. The explanation of the behavior of these substances is a perplexing and at present an unsolved problem. There is one possible explanation which must be considered.

A quarter of a century ago many chemists hoped to find isomers of the type called *electromers*, that is, two forms of a molecule with the atoms in the same, or nearly the same, relative position, but with a difference in electronic distribution. The advent of the electron-pair bond and the associated idea of the mobility of this bond under inductive influence seemed to make assumption of such electromers superfluous in the case of simple molecules.[4] Moreover, the development of the concept of resonance has appeared to exclude electromerism in all cases except the trivial one in which two parts of a molecule are so far insulated from one another that they behave like separate molecules.

When in a given substance there is said to be resonance between two or more limiting structures, the phenomenon is most marked when there is little difference of energy or of spacial position in the resonating structures, but we assume that even when these conditions are not fulfilled there will be some resonance effect, although perhaps minute. On the other hand, there are structures which we must believe are prohibited from any mutual resonance whatsoever. Such a prohibition occurs when one of the structures is paramagnetic and the other diamagnetic. In other cases, even when spins are not considered, the quantum mechanical equation sometimes has two sets of solutions which are not mutually "combining." A structure representing one set and a structure representing the other should be incapable of mutual resonance, and therefore should behave as true electromers. We are going to consider the electromeric hypothesis as a possible method of accounting for the sharp distinction between primary and secondary acids and bases, although we are by no means convinced that this is the only possible way of accounting for the phenomena that we shall describe.

Some Secondary Acids and Bases

In our still mysterious group of secondary acids the most familiar one is carbon dioxide. It has long been known that a cold aqueous solution of carbon dioxide cannot be titrated instantly with alkali. By using another solvent and lower temperature this phenomenon can be rendered more striking, as shown in the experimental section. Among organic substances with the carbon–oxygen double bond it seems likely that the acid chlorides and the acid anhydrides will in general prove to be secondary acids. By analogy it was thought that compounds containing the carbon–carbon double bond might show secondary characteristics, and several compounds of this type

(3) Hantzsch, *Ber.*, **32**, 575 (1899).

(4) Lewis, "The Atom and the Molecule," THIS JOURNAL, **38**, 762 (1916).

will be discussed in the experimental section. None of the latter proved to be secondary acids or bases.

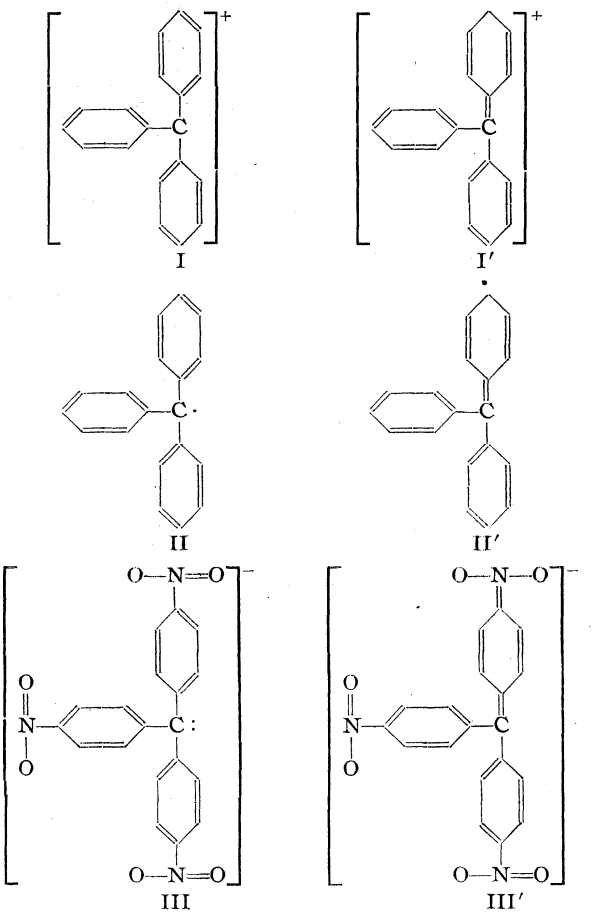
Another large group of secondary acids is found in the triphenylmethyl cation and its many derivatives. Such ions as those of crystal violet and malachite green combine slowly with hydroxide ion to form the carbinol, and the heat of activation is large. Even triphenylmethyl chloride in chlorobenzene is partly ionized and when circumstances produce a recombination of the ions this process is a slow one, especially at 0°, as shown in the preceding paper.[2]

Before considering the problem of secondary bases let us consider for a moment the class of substances which in a sense is intermediate between acids and bases, namely, the odd molecules. It has been supposed that the union of two odd molecules should not require activation energy. This supposition, moreover, was supported by experimental observations. Thus nitric oxide and oxygen, in both of which there are odd electrons, combine instantly at the temperature of liquid air. However, it has been discovered by Ziegler[5] that two molecules of triphenylmethyl require an activation energy of 6–8 kcal. when combining to form one molecule of hexaphenylethane. We shall try to explain this interesting fact by assumptions entirely similar to those which we are going to make in interpreting the behavior of the triphenylmethyl cation.

The question now arises as to whether we can find any secondary bases. By analogy to the compounds we have just been discussing it seemed likely that the negative triphenylmethide ion might prove to be such a substance. This ion itself is not very convenient to study, but it has long been known that 4,4′,4″-trinitrotriphenylmethane behaves as a weak acid. It dissolves in alkaline alcohol to give an intense blue color which is due to the substituted triphenylmethide ion, the investigation of which we describe in the paper immediately following. There we show that this ion is truly a secondary base since at low temperatures it is neutralized slowly by a wide variety of acids, the heat of activation in each case being approximately 9 kcal.

The only other group of secondary bases which is now known to us was called to our attention by Professor Branch. Nitromethane and many of its derivatives form salts in alkaline solution and the anions thus produced are only slowly neutralized by weak acids to give back the nitromethane. The general course of this process of neutralization, even to the inhibiting effect of strong acids, is so similar to the behavior of the trinitrotriphenylmethide ion that a common explanation is strongly suggested.

Let us now consider how we should regard triphenylmethyl and its ions if we are to adopt the electromeric hypothesis. In the accompanying graphical scheme formulas I, II and III show what may be called the old-fashioned representations of the triphenylmethyl cation, the triphenylmethyl free radical and the trinitrotriphenylmethide anion. In each of these the central carbon has only three bonds and the formulation indicates that the central carbon is the seat of the respective behaviors as acid, odd molecule and base.



The formulas I′, II′ and III′ represent, somewhat inadequately, the resonance structures which we now believe to characterize these molecules in their normal state. Formula I′, for example, exhibits but one of the nine structures which almost

(5) Ziegler, Orth and Weber, *Ann.*, **504**, 131 (1933).

equally contribute to the resultant resonance state. Thus the central carbon may be doubly bonded to any one of the three phenyl groups and any one of the ortho or para carbons may be regarded as possessing the acid character and the positive charge. Similarly in II′ the odd electron may be placed upon any one of nine carbon atoms. In formula III′ the basic property is to be equally distributed among the three nitro groups.

The structures on the left in our scheme have heretofore been assumed to contribute to a greater or less degree to the general resonating molecule. We are now suggesting the possibility that they do not contribute to any degree whatsoever to the molecule in its normal state. According to this hypothesis we may have in solution two distinct substances, each with its own properties, and, if the two are in equilibrium with each other, their relative concentrations will depend chiefly upon the temperature and upon the difference in their energies. Each member of an electromeric pair must be assumed to have not only its own physical properties, such as color, but also its specific chemical properties. It is by the latter that we may ordinarily expect to detect the existence of the two forms. Thus, for example, each of the two forms II and II′ is an odd molecule, but the first will combine instantly with another odd molecule at the central carbon atom. So two molecules of II will combine instantly to form hexaphenylethane, while two molecules of II′ can combine without activation only to form another dimer in which two phenyl groups are directly attached. It seems probable that such a dimer exists in small amount, in rapid equilibrium with the monomers, in any system containing such free radicals.

Similar conditions are to be assumed in the case of the trinitrotriphenylmethide ion. In form III the central carbon should behave as a typical primary base. When we go over to the more stable ion III′ the basic character has not been lost, but the pair of electrons, which was on the central carbon, is now resonating chiefly between the three nitro groups. If, therefore, a strong enough acid is added to the blue ion, we should expect hydrogen ion to add, and add instantly, at one of these positions. This is one of the phenomena which will be described in the paper immediately following. The fact that a substance may act as a secondary acid or base with respect to neutralization at one point in the molecule and at the same time behave as a primary acid or base with respect to some other point of neutralization must be constantly borne in mind.

Unless the distinction between primary and secondary acids and bases is a fundamental one, it would be expected that the number of slow neutralizations, which have been observed in the neighborhood of room temperature, would rapidly increase as we study reactions at successively lower temperatures. We shall see, however, in our experiments which were carried out progressively at lower and lower temperatures, until finally numerous experiments were made at $-160°$, that not a single case was found of a secondary acid or base, except those already listed.

Other Possible Explanations

At present we have no definite clue as to the origin of the distinction between secondary and primary acids and bases. Neither are we able to predict, except by analogy to other substances of a similar sort, when we may expect to find substances of the secondary type. One suggestion is worth serious consideration. In the case of each secondary acid or base that we have found, the process of neutralization causes a notable change in the geometry of the molecule. Thus CO_2, which is linear, becomes a planar structure when it adds to OH^-. In triphenylmethyl ion, the central carbon, and the three phenyl carbons to which it is attached, are presumably coplanar, but when the ion adds OH^- or Cl^- a tetrahedral molecule results. If our trinitrotriphenylmethide ion is completely representable by formula III′, once more the central atom and the three attached carbons should be coplanar. On the other hand, if it were all in the form III, it should be tetrahedral like ammonia. If both forms were in resonance together, then we should expect a slightly pyramidal form, the departure from coplanarity being dependent upon the contribution that formula III makes to the resonance state.

Is the activation energy which is required in the neutralization of secondary acids and bases to be regarded as a consequence of these important changes in the geometry of the system? Our present answer is in the negative, chiefly because of two experiements which will be described and which were designed expressly to test this point. The strong acids boron trichloride and trifluoride are in all probability completely planar, like triphenylmethyl ion, and go over into tetrahedra

when a base is added. It therefore seemed important to ascertain whether these acids show any signs of secondary behavior. We shall see that they both behave as primary acids and are neutralized instantly (within a fraction of a second) even at the extremely low temperature $-160°$. As an even closer analog to triphenylmethyl ion it would be interesting to study the rate of neutralization of the acid triphenylboron.

The only remaining alternative to the electromeric hypothesis that has occurred to us is that when a substance acts as a secondary acid or base with respect to neutralization at a certain point in the molecule, this point is covered and protected, either by some chelation in the molecule itself, or by some hitherto unsuspected type of combination with the solvent or other solute molecules. We have pointed out the great similarity between our new secondary base and the anion of the derivatives of nitromethane. In the new edition of Sidgwick's "*Organic Chemistry of Nitrogen*"[6] there is a very full discussion of the various structures of such an ion which have been suggested to account for the observed properties, especially the retention of optical activity. It is there pointed out that no one of these structures appears to be satisfactory. It is our opinion that the observed properties of nitromethide ions are not those of any substance which can be expressed by a formula which ignores a complex with the solvent, and indeed if a solvent could be found which does not form such complexes, the properties of the ion would be entirely different. Assuming now one or more molecules of the solvent, usually alcohol, attached to the simple ion, such molecules might conceivably form such a chelated system as to protect the methide carbon from immediate attack. The process of activation would then consist in breaking the attachment. Moreover, as our studies have progressed, we have found numerous examples of the formation of peculiar complexes with solvent molecules of the type which might conceivably lead to such protection of an atom as to prevent its action as a primary acid or base. Nevertheless, after considering all the cases now available, and especially the simplest and most typical case of carbon dioxide in water or alcohol, we regard the electromeric hypothesis as the most probable explanation of our phenomena.

Whatever the explanation may be, our immediate purpose must be to substantiate the idea that a secondary acid or base exists in two different forms, in only one of which neutralization at a given point proceeds rapidly and without activation.

(6) Sidgwick, Clarendon Press, Oxford, England, 1937.

Kinetics

Recognition of the distinction between primary and secondary acids and bases leads to certain kinetic considerations which were implied in the preceding paper[2] and which we must now subject to careful analysis. We are going to discuss two theses, neither of which can be regarded as proved, but both of which have become increasingly plausible as our experiments have proceeded.

Thesis I.—The first thesis, which is a direct consequence of our assumptions, is that in the neutralization of a secondary acid or base the rate of the reaction will frequently be determined, either by the rate of formation of the primary form from the secondary form, or by the concentration of the primary which is in equilibrium with the secondary form.

Let A be any primary acid and let B_S be the ordinary state of a secondary base, whose primary form, of higher energy, may be called B_P, and let us consider the following sequence of reactions

$$B_S \longrightarrow B_P \qquad B_P + A \longrightarrow BA \qquad (1)$$

We may first consider the case in which the first step is slow compared with the second; in other words, the first is the rate determining process. This rate of forming B_P from B_S will be given by an expression of the Arrhenius form in which the coefficient involves probabilities, and the exponent contains the heat of activation q, which is the difference in energy between B_P and B_S. As long, therefore, as the first step is rate determining, the rate of the reaction, at each temperature, will be independent of the concentration and of the nature of A. If this case can be realized experimentally, under conditions which permit no misinterpretation of the experiments, we shall have the most direct proof of our assumptions. We have not yet found a case of this sort.

Let us next consider the case in which the second step of reaction (1) is much slower than the first. Then B_S and B_P are in equilibrium, so that (ignoring differences in entropy) c_P/c_S, the ratio of the two concentrations, is proportional to exp. $(-q/RT)$. If then the reaction is bimolecular with respect to acid and B_P, it is also bimolecular with respect to acid and B_S. Once more q will be

the heat of activation. Therefore according to our assumptions we may expect to find in reactions of this type a heat of activation which is often independent of the nature of the acid.

Ordinarily it would be assumed that the process that we are considering would occur, not as represented in mechanism 1, but by the mechanism of the activated complex. According to the latter view a molecule of B_S and a molecule of A occasionally would collide with sufficient energy so that in a single step the combined system could pass over some potential barrier to produce the stable molecule BA. With a given base the height of the barrier and therefore the heat of activation would vary with the nature of the acid. According to our view also this would be the mechanism if an acid were found for which the barrier that we have just mentioned is lower than the difference in energy between B_S and B_P. Supposing, for example, that this barrier were proportional to some inverse function of the strength of the acid, then according to the theory of the activated complex, the heat of activation found for different acids would be expected to fall upon line I of the schematic diagram, Fig. 1. On the other hand, according to our view, the experimentally found heat of activation might follow the same line up to a point, but from that point on the values would be constant (line II). This would be approximately the point at which the height of the barrier of the activated complex would begin to exceed the heat of activation of mechanism 1, namely, $E_P - E_S$.

In the following paper we show that in the neutralization of trinitrotriphenylmethide ion the heat of activation is essentially constant with acids covering the great range from chloroacetic acid to ethyl alcohol. In other words all these cases seem to fall on the horizontal line (line II) of Fig. 1. It would seem almost impossible to interpret these results by the theory of the activated complex.

Thesis II.—The second of our main theses is much wider in its scope, since it concerns, not the rarer cases of the secondary kind, but rather all molecules of the resonance type. When a substance is said to resonate between several structures, then, if the energy calculated for one of the structures is very much larger than that for the actual substance, that structure is said to contribute very little to the actual state of the substance. The question however is one of degree

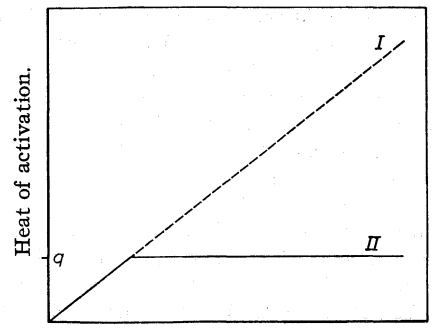


Fig. 1.

and we may assume, except when there is an absolute prohibition of resonance such as we have been discussing, that all possible electronic structures, no matter how small their contribution, must be regarded as members of the resonance family.

It has been assumed that if a resonating molecule reacts in a way which could only be interpreted as a behavior peculiar to one of the contributing structures, and if this structure is one of high energy, then such a reaction must require a heat of activation corresponding roughly to the difference between the normal energy of the molecule and the energy calculated for that particular structure.[7] Just the *opposite* of this assumption is the one we are now going to propose as our second thesis.

Let S be any resonating molecule in its state of lowest energy, and let S_1, S_2, . . . be individual structures which may be said to contribute to the actual molecule S. Let E be the actual energy and E_1, E_2, . . . the higher energies calculated for the hypothetical individual structures. Now we are going to assume that, to permit a reaction characteristic of the form S_1, we do not require an activation energy of the order of $E_1 - E$ but that the process *may* occur without any activation no matter how large this energy difference is. With respect to heat of activation, the difference between a set of tautomers and a set of resonating forms may be expressed as follows. A tautomer can be converted into another tautomer of higher energy only when the requisite energy is obtained from an external source; on the other hand, a resonating molecule, even when isolated, may be said to pass through its various phases, some of low energy and some of high, by processes which were forbidden in the old mechanics but permitted in the new.

(7) See for example Anderson, *J. Chem. Soc.*, 1042 (1936).

What we have said pertains to the exponential part of the Arrhenius expression for reaction velocity. Does the coefficient of this expression, which depends, in the case of a bimolecular reaction, upon the probability that each collision is effective, vary greatly with the extent to which the structure S_1 contributes to the general resonance state S? We have at present no answer to give to this question except for the following remark.

It is occasionally convenient to consider that in a resonating molecule there is a rapid oscillation in the electron cloud so that the system approaches now one, now another, of the particular structures such as S_1, S_2, ... If we take this view we have to consider, not only what fraction of the time the molecule can react as though it were in the form S_1, but also how frequently this state or phase recurs, or, in other words, the resonance frequency. In the case of a gaseous collision the duration of the collision is presumably of the same order of magnitude as the resonance time. In such a case the chance of an effective collision might depend very greatly upon whether the reacting form is a major or minor constituent of the resonating molecule. On the other hand, in a liquid, if two molecules come together, they probably remain together for a considerable time, during which a resonating molecule may pass many times through its various phases. In such case it would appear that the probability of effective collision would not depend very greatly upon the extent to which the reacting form contributes to the resonance state. As a matter of fact the experiments we are to describe are consistent with the latter supposition.

When we apply our second thesis specifically to acids and bases we find the following consequences. When one of the contributing structures of a resonating substance, no matter how small the contribution may be, has the form of an acid or a base, the substance will behave as a primary acid or base, and when it combines with any primary base or acid it will do so without activation. There is no connection whatsoever between the ability to act as a primary acid or base and the acid or basic strength. All of the substances of secondary type that we have found have been moderately strong acids and bases. On the other hand, we are going to describe experiments with extraordinarily weak bases which do not combine to any appreciable extent except with the very strongest acids; but insofar as the process of neutralization occurs, it occurs instantly, even at very low temperatures.

Some of the bases that we have used in our experiments have ionization constants which we estimate to be as low as 10^{-22} and a very rough calculation of $E_1 - E$ in such a case would give something like 20–30 kcal. Nevertheless our experiments show that such bases are neutralized within a fraction of a second at $-160°$. Considering the dilution of our solutions, we may state that the heat of activation, if it exists at all, cannot be greater than 4 kcal.

Experiments

Carbon Dioxide as a Secondary Acid.—If at $-60°$ we dissolve carbon dioxide in alcohol and divide the solution equally between two tubes, A and A′, and if at the same temperature we have an alcohol solution containing dilute sodium ethylate and a little indicator, such as brom cresol purple, divided equally between the two tubes, B and B′, then if A is added to B at once there is no immediate change of color. However, on standing for some fifteen minutes the carbon dioxide neutralizes the ethylate ion and the indicator passes slowly through its color changes. If now, having stood for half an hour or so, the contents of A′ are added to B′, the indicator goes at once to the acid color. We have not yet ascertained whether the time required to produce the acid color is the same in the two cases.

The latter of these experiments, which shows that the solution of carbon dioxide in alcohol only slowly becomes an acid, might conceivably, although improbably, be explained on the assumption that the oxygen of C_2H_5OH adds immediately to the carbon of CO_2 but that it takes time for the hydrogen to pass over to one of the oxygens of the CO_2, producing the ordinary ethyl ester of carbonic acid. However, the former experiment shows the falsity of this explanation. In that case the basic ion $C_2H_5O^-$ can add directly to the carbon of CO_2 to give the final stable product. The fact that it does not do so immediately at low temperatures shows that a heat of activation is necessary, or in other words, that carbon dioxide is a secondary acid.

Methods of Studying Reactions with Indicators at Very Low Temperatures.—Numerous experiments were made with reactions at a variety of low temperatures, but since these were all repeated at our lowest temperature, with identical results, we shall proceed immediately to describe a series of experiments made at $-160°$ (113°K.). As far as we are aware, this is the lowest temperature at which chemical reactions have been observed except in the case already cited of the instantaneous union of the two odd molecules NO and O_2 at 90°K. At the temperature of $-160°$ we may be sure that if any instantaneous reaction has any heat of activation at all it cannot be greater than about 4 kcal. To obtain any evidence for a smaller heat of activation than this it will be necessary to use indirect methods, of which several are available, but which we have not yet tried.

The experimental method first used was extremely simple. The acid or base to be tested was dissolved in petroleum ether of freezing point $-160°$. This was placed in a flask which could be attached to the vacuum line by a ground-glass joint. The solution was then frozen and the flask exhausted. The contents were then melted and in order to get rid of the small amount of air remaining, the process of freezing and exhausting was repeated. The connection between the flask and line now being closed by a stopcock, the line, comprising about 50 cc., was filled with the vapor of the base or acid to be used for the neutralization, at a pressure of about 10 cm. The liquid air, which had been used for freezing, was now

removed and the solution in the flask was agitated by a small piece of iron enclosed in glass which had been placed at the bottom of the flask and was now moved by means of a small permanent magnet held outside the flask. When the contents of the flask were about half melted the experiment was performed by opening the stopcock. When the vapor is such as produces a color change, then at the instant at which the vapor impinges upon the surface of the solution the color appears. This color then spreads through the solution, soon after which sometimes a colored precipitate forms. The time from opening the stopcock to appearance of bright color is not more than a few tenths of a second.

Although the amount of vapor entering the flask is very small, it seemed possible that the surface temperature might be raised appreciably by it. Therefore the more crucial experiments were repeated in a new apparatus in which constancy of temperature was assured. This apparatus was attached to the vacuum line by a horizontal ground glass joint. In a plane perpendicular to the axis of the joint an inverted Y-tube could be rotated so as to mix and stir the contents of the tube. With acid in one limb and base in the other, each dissolved in petroleum ether, the whole was immersed in a large bath of half-frozen petroleum ether. When completely cooled the apparatus was then rocked and as the liquids mixed an instantaneous color change was observed. Observations with the two types of apparatus were in every case identical. All the following experiments were made at −160° and in petroleum ether as solvent.

Boron Trichloride as an Extremely Strong Primary Acid.—When boron trichloride was added to a solution of butter-yellow there formed instantly the pure red which is characteristic of the compounds of this indicator with all acids, whether of the hydrogenic or the non-hydrogenic type. Within a few seconds a red precipitate was formed. This experiment proves that boron trichloride, in spite of its geometrical resemblance to triphenylmethyl ion, is a primary acid, at least if we decide for the present to call all acids and bases primary which are neutralized instantly at −160°. Incidentally this experiment shows also that butter-yellow is a primary base.

Boron Trifluoride as an Extremely Strong Primary Acid.—The previous experiment was repeated with boron trifluoride instead of boron trichloride. The result was the same, showing that boron trifluoride is a primary acid. It is generally assumed that boron trifluoride is on the average a stronger acid than boron trichloride, but as far as our experiments have gone this idea is not confirmed. Since, moreover, boron trifluoride is in general more destructive to organic substances than boron trichloride, the latter has been used in the majority of our further experiments.

Trinitrobenzene and Trinitrotoluene as Weak Primary Acids.—These two substances stand alone among common indicators in that their acid behavior is not due to giving up hydrogen ion, or forming a hydrogen bond, but is due to the direct addition of a base. When solutions of these two substances are treated with ammonia gas at our lowest temperature they at once change from colorless to bright red. The reason that ammonia was used in this experiment, rather than a stronger base such as diethylamine, we shall discuss in another paper. Incidentally this experiment shows that ammonia is a primary base.

Dibenzalacetone and its Analogs as Very Weak Primary Bases.—Dibenzalacetone, dipiperonalacetone and dianisalacetone give in concentrated sulfuric acid strongly colored solutions, orange, purple and red, respectively. Their relative basic strengths in this solvent were estimated through the method of Baeyer and Villiger by Stobbe and Haertel,[8] who found that the basicity increased in the order listed. We find that they are all stronger bases than acetone, although the difference is not great in the case of the first substance; for in this case the gradual addition of acetone to the colored solution in 95% sulfuric acid destroys the greater part of the color. When these three substances are dissolved in concentrated aqueous hydrochloric acid the first shows only the yellow color characteristic of the uncombined substance, the second gives a pale purple and the last a stronger red. If these substances are dissolved in petroleum ether and gaseous boron trichloride added, the initial colors produced are, as far as can be noted visually, identical with those in sulfuric acid. When boron trichloride was introduced at −160° all three color changes were instantaneous, showing that all three substances are primary bases.

Unsymmetrical Diphenylethylene as a Very Weak Primary Base.—This substance treated with boron trichloride in the usual way at the lowest temperature gave an instantaneous red color. It is therefore, by our present criterion, a primary base. It is a stronger base than the symmetrical compound, stilbene, which is not appreciably neutralized by boron trichloride in petroleum ether. Another base which also proved too weak is diphenyloctatetraene. This last substance, and the other polyene which we are about to discuss, were kindly furnished to us by Dr. M. Calvin. Also the tetracyclic hydrocarbon, perylene which was kindly furnished to us by Professor L. F. Fieser, proved to be too weak a base for our purpose, although in 95% sulfuric acid it is colored.

Symmetrical Diphenyldodecahexaene and β-Carotene as Extremely Weak Primary Bases.—These substances represent the very weakest bases that are appreciably neutralized by boron trichloride in petroleum ether. They both give a blue color in 95% sulfuric acid and an intense blue in fuming acid. They both prove to be primary bases. Carotene at our low temperature gave with boron trichloride an instantaneous blue color, followed in a few seconds by a green precipitate. The diphenyldodecahexaene also gave an instantaneous brilliant color, but instead of the expected blue a brilliant orange appeared. However, upon warming to about −80°, the color changed to blue, while the orange color reappeared when the solution was once more cooled. Apparently the compound adds more than one molecule of boron trichloride at very low temperatures.

Summary

Most acids and bases neutralize one another rapidly at all temperatures. These are called primary. Some other acids and bases, called secondary, require heat of activation for the neu-

(8) Stobbe and Haertel, *Ann.*, **370**, 99 (1909).

tralization process. Sometimes this secondary behavior is predictable from familiar considerations based on solvation or tautomerism. However, there are other cases where such considerations do not at present suffice for an adequate explanation.

In an attempt to find new secondary acids and bases, involving in their neutralization small heats of activation, the neutralization process has been studied in numerous cases at temperatures as low as −160°C. (113°K.). No new cases of secondary behavior were found. These results indicate a striking distinction between primary and secondary. It is suggested that every secondary acid or base also exists in an independent primary form and that the relative amounts and the difference in energy of the two forms can be ascertained by kinetic studies.

In order to interpret the distinction between the two forms various hypotheses are considered. The hypothesis that at present seems most probable is that two electromeric forms may exist, incapable of resonance with one another, and differing in the laws which govern electronic distribution. Such a hypothetical electromerism is illustrated not only for acids and bases but also for a certain class of odd molecules.

Our second kinetic thesis concerns systems in which there is resonance between a number of contributing structures. It asserts that a resonating molecule may without activation take part in a reaction characteristic of one of its contributing structures, even though the contribution of that structure may be extremely small and the calculated energy of that structure extremely high. This thesis is demonstrated by experiments upon numerous acids and bases at a very low temperature.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

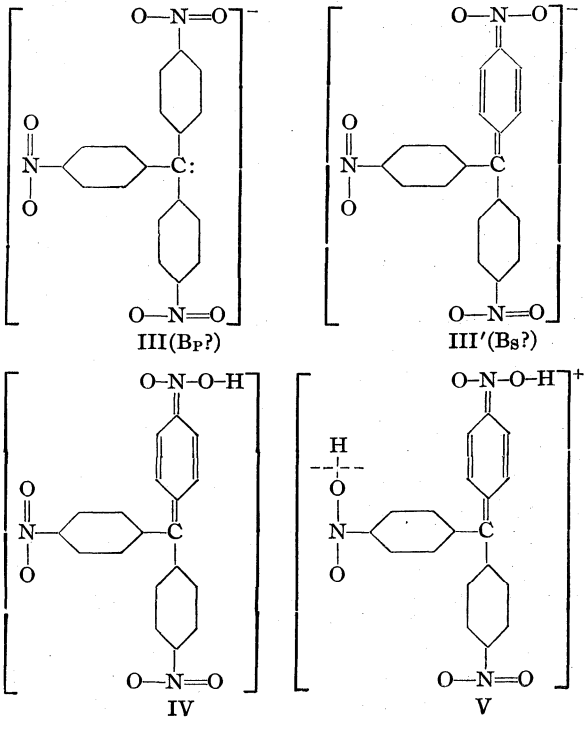
Trinitrotriphenylmethide Ion as a Secondary and Primary Base

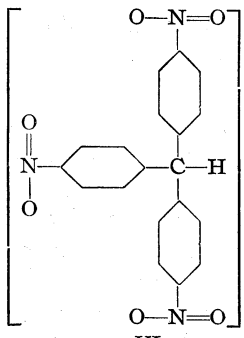
BY GILBERT N. LEWIS AND GLENN T. SEABORG

When we started this investigation we were unacquainted with any typical secondary base. It seemed not unlikely, however, by analogy to the variously substituted positive triphenylmethyl ions, all of which behave as secondary acids, that the negative triphenylmethide ions would prove to be secondary bases.

The substance chosen for investigation was 4,4′,4″-trinitrotriphenylmethane, which is represented by formula VI in the accompanying graphical scheme. This substance in alkaline alcoholic solution loses hydrogen ion, giving the intensely blue trinitrotriphenylmethide ion which may be represented by formula III′. According to our expectation this solution, when acidified with acetic acid at temperatures ranging from −30 to −80°, fades slowly, and fades more slowly the lower the temperature, thus showing that the blue ion is not behaving as a primary base with respect to the addition of an acid at the central carbon atom.

According to the views expressed in the paper just preceding, a secondary base of this sort should exist in two forms. One form is to be identified with the substance as it ordinarily is, in the state of a secondary base. The other form, of higher energy, is one in which the substance be-





VI

haves as a primary base. If there are these two forms we must see whether the difference in energy between them can be ascertained from a study of the kinetics of the neutralization process.

We have also discussed certain hypotheses to account for the behavior of secondary acids and bases. It is unnecessary in the present paper to commit ourselves to any hypothesis, but for the sake of clarity we show in formulas III and III′ the two states of the trinitrotriphenylmethide ion in terms of the electromeric hypothesis. The former is capable of adding acid directly to the central carbon atom, the latter is not. Since, however, we are now concerned only with our more fundamental assumptions, we shall represent the primary substance as B_P^- and the secondary as B_S^-.

At first we had intended to study the trinitrotriphenylmethide ion only far enough to demonstrate its behavior as a secondary base, but some intricacies of behavior, which were puzzling at first, led us to make an extensive, although not very exact, experimental survey of the kinetics of this system.

When the blue ion has been formed and the central carbon has lost its power of acting immediately as a base, the basic character has, in a certain sense, been transferred to the three nitro groups. Therefore a sufficiently strong acid should attach itself at one of the nitro groups and in this process the blue ion should act as a primary base. This expectation was verified. If to the blue alcoholic solution at low temperature we add hydrochloric acid instead of acetic, a brilliant orange appears. An excess of sodium ethylate restores the blue color and we may titrate back and forth between blue and orange with sodium ethylate and hydrochloric acid. These changes even at $-85°$ are instantaneous. At first it was thought that the orange compound might correspond to formula IV, although it is hard to see why a compound of that formula should show any color, except perhaps a pale yellow. In fact we shall see that more than one equivalent of H^+ is used in the formation of the orange compound from the blue ion.

The Kinetics of the Neutralization of the Blue Ion.—Trinitrotriphenylmethane, which was kindly prepared for us by Mr. R. L. Caswell, under the direction of Professor T. D. Stewart, may be purified rapidly by successive recrystallizations from toluene and may be kept for weeks unchanged, either as solid or in the toluene solution. In alcohol, especially in the presence of alkali, the substance is sensitive to oxygen and to small amounts of substances of the type of the organic peroxides. A stock solution in toluene was kept and added to alcohol just before each experiment. Our solvent, therefore, in all the experiments to be described, contained by volume 85% absolute ethyl alcohol and 15% toluene, except when otherwise stated. That very nearly the same results would have been obtained in pure alcohol was shown by experiments in which the percentage of toluene was varied.

The reaction vessel in the form of an inverted Y was exhausted to the point where the small amount of residual oxygen no longer had any deleterious effects. This vessel, with the alkaline solution in one limb and the acid in the other, was placed in the low temperature bath (of acetone and carbon dioxide). When the temperature equilibrium was attained the vessel was tipped rapidly back and forth until the contents were thoroughly mixed. The reaction was then followed by comparing the color with a set of standard color tubes. After the experiments had indicated that the reaction was always of first order with respect to the colored ion, the procedure was simplified further. The time was taken merely between the mixing and the matching of a single color standard.

In each experiment one limb of the reaction vessel contained 5.5 cc. of the blue alkaline solution and the other limb contained 1.0 cc. of the acid solution. The concentrations given refer to the total volume of 6.5 cc. after mixing. The initial alkaline solution was always the same and contained 0.0015 *M* sodium ethylate and 0.001 *M* trinitrotriphenylmethane. Later experiments showed that in this solution only one-eighth of the methane is in the form of the blue methide ion. After mixing the reaction was allowed to continue until this ion fell to one-sixteenth of its initial concentration, or a little less than 0.00001 *M*, when the elapsed time was read. The acids varied in concentration from 0.003 to 1.0 *M*, from which we obtain the actual concentration by subtracting the concentration of the ethylate, ignoring the very small concentration of the blue ion.

An accuracy of 10% in the measurement of the time was all that was sought. In a work of this sort, which is prospecting in a large field, it seems undesirable to spend much time upon the refinement of the technique of measurement, or even upon the purification of the reagents. Of the sixteen acids used in the following experiments several were far from pure, and our conclusions

must be drawn from the results as a whole, and not from those obtained with a single acid. There is, moreover, a more fundamental reason for distrusting the generality of results obtained from a given acid. When we are comparing reactions of a given substance with various other substances and under various conditions, it is important that that given substance should be the same in the several experiments. In our case, however, we are going to conclude that this is not in general true. There is every reason to believe that the blue ion in alcohol is a complex between trinitrotriphenylmethide ion and the solvent. Now when a new solute is added, such as one of the acids used for the titration, it may replace some of the solvent molecules in the complex, thus changing the nature of the reacting substance and its heat of activation. We are going to show that at least three substances, phenol, boric acid, and water appear to form such new complexes.

The first experiments were carried out with acetic acid. Here, as with many other acids, the rate of the reaction was found, within our limits of accuracy, to be proportional to the concentration, when the acid concentration is small. At higher concentrations the rate increased less rapidly than the concentration, the discrepancy amounting to 20% at 0.015 *M*. It seems probable that this effect is due to departures from the ideal solution. In the more dilute solutions the reaction may be regarded as strictly bimolecular.

Added salts were found to have no appreciable influence upon the rate, except in the case of silver salts, which produce insoluble compounds with the blue substance. The rate with acetic acid was also found to be unaffected by sodium acetate, showing that the rate is determined solely by the undissociated acid and not by the small concentration of hydrogen ion which is present. It was fortunate that while doubtless many of our solutions were supersaturated at the temperature of the measurements, there was no precipitation during the course of the measurements except in one or two cases, notably in the case where sodium chloroacetate was formed.

Since the reaction was found to be bimolecular and free from catalysis or neutral salt effect, we may calculate the heat of activation without ambiguity. If $-dc_B/dt$ represents the diminution per second of the concentration of the ion B_S^-, the rate constant k is determined by the equation $-dc_B/dt = kc_Ac_B$ where c_A is the molal concentration of the acid. Values of k for acetic acid (0.0046 *M*) were obtained at the four temperatures −53, −63, −76 and −82°. Plotting log k against $1/T$ gave a good straight line, the individual departures corresponding to differences in k of only a few per cent. Here, however, we are only testing the experimental method. No such accuracy is claimed for the results as a whole, nor was it desired, as we have already explained.

We shall attempt to interpret our results in terms of the following mechanism.

$$B_S^- \xrightarrow{(a)} B_P^-$$

$$B_P^- + HY \xrightarrow{(b)} BHY^- \xrightarrow{(c)} HB + Y^- \qquad (1)$$

We assume that (b) is the rate-determining step. Then the concentration of B_P^- depends upon the concentration of B_S^-, the temperature, and the difference in energy between B_P^- and B_S^-. If the reaction proceeds through this mechanism and not through that of the activated complex, the measured heat of activation should be the same for the several acids and equal to the difference in energy between the primary and secondary forms of the base.

We have collected in Table I the results obtained with various acids. The question marks indicate that only one or two observations were made. The acids are arranged according to the ionization constant, K_{H_2O}, in water at room temperature. The ionization constants in alcohol at low temperature are certainly of a quite different order of magnitude but probably are roughly in the same order. The rate constant k at −60° is given in the third column, concentrations being in moles per liter and time in seconds. With the six strongest acids in this list the reaction proved to be bimolecular and from the temperature co-

TABLE I

Acid	$-\log K_{H_2O}$	k	Heat of activation, kcal.
Chloroacetic (+ $CH_2ClCOOLi$)	2.80	30	10.2
Furoic	3.15	10	8.8
α-Naphthoic	3.70	5.3	8.5
Lactic	3.85	3.2	8.9
Benzoic	4.15	5.1	10.0
Acetic	4.75	3.0	8.6
p-Nitrophenol	7.10	1.0 (?)	
2,4-Dichlorophenol	7.55	0.87 (?)	
Hydrocyanic	9.15	.13	
Boric	9.20	.090	
Catechol	9.50	.27 (?) (0.15 *M*)	
β-Naphthol	9.60	.12	
Phenol	9.85	.090	

efficient of k we have calculated the heats of activation given in column 4.

We regard the several values of the heat of activation as equal within the limits of experimental error and of uncertainties concerning the constancy of composition of the blue ion, of which more will be said later. The average value is 9.1 kcal. which we may take as the difference in energy between the primary and secondary forms of the base. A still more striking verification of the constancy of the heat of activation will be furnished presently. The study of stronger acids than chloroacetic would have been extremely interesting but was prevented by the formation of the orange compound.

It will be noticed that k increases regularly with acid strength. It appears as though increasing electrical polarization of the acid, by its orienting effect, increases the probability that a given collision between the acid and the primary base will be effective. Taking the highest rate constant, $k = 30$, obtained for chloroacetic acid, we may obtain an idea of the rate constant for the primary base itself. It has become common in a case of this kind to calculate the ratio of the concentrations of two forms from the difference in their energies by means of the Boltzmann equation. Such a calculation shows B_S^- to be 2×10^9 times as concentrated as B_P^-, whence the rate constant for B_P^- would be $30 \times 2 \times 10^9 = 6 \times 10^{10}$. Comparing this with other bimolecular rate constants we would conclude that B_P^- and $CH_2ClCOOH$ have a very large chance of reacting at each collision. We believe, however, that this calculation is erroneous. The ratio of the concentrations depends not only upon the change of energy but also upon the change of entropy. There are no data from which the latter can be calculated but we may make a guess. In going from B_S^- to B_P^- there is likely to be a loss of attached alcohol molecules, together with a loosening of constraints such as those operating upon the nitro groups. Both of these changes would produce an increase in entropy. It is therefore probable that the concentration of B_P^- is considerably larger than that which we have just calculated, and the rate constant correspondingly smaller.

When we come to the weaker acids of Table I the values of k are those calculated formally from the velocity at 0.015 M, but k is no longer a true constant, for the rate is no longer proportional to the acid concentration. The most extreme cases are that of phenol, in which changing from 0.015 to 0.15 M only doubles the rate, and that of boric acid in which, through the same range of concentration, the rate increases by only 10%. This result was at first perplexing. The evidence is entirely against the supposition that either of these two acids is much polymerized in alcohol. Another possible explanation was suggested by the fact that there are slight but perceptible differences in color when different acids are used. We already have alluded to the possibility that the blue ion in alcohol, which presumably holds alcohol molecules through hydrogen bonds at the three nitro groups, may have some of these alcohol molecules replaced by solute molecules when certain substances are dissolved. The fact that phenol and boric acid give lower rates than hydrocyanic acid and β-naphthol, and also show the least effect of concentration upon reaction rate, suggested that phenol and boric acid displace the alcohol from the nitro groups to an extent depending upon their concentration, and that the ion with phenol attached is less reactive than the corresponding alcohol compound. These assumptions would explain qualitatively both the reduced reaction rate and the small effect of concentration.

In order to test these assumptions quantitatively the rate of fading of the blue color was studied with a mixture containing large amounts of phenol or boric acid and small amounts of acetic or benzoic acid. Although the effects were small, of the order of 10–30%, they were always in the same direction, namely, the rate in the mixture was smaller than that calculated from the behavior of the pure acids. We have, therefore, evidence that boric acid and phenol do form complexes with the reacting substance, which diminish its reactivity, and we shall later obtain more conclusive evidence on this point. On the other hand, the magnitude of the effect is by no means sufficient to account for the fact that the rate with boric acid and phenol is nearly independent of the concentration.

The true explanation of this effect proved to be a very simple one. Alcohol is itself an acid, and although its acid strength is not high enough to cause the fading of the blue color to occur to any great extent before equilibrium is established, it does, in the presence of a stronger acid, play an important and sometimes preponderating part in the mechanism of the fading process. This is due to the relatively large number of alcohol molecules present. Side by side, therefore, with the reaction we have considered so far, is this reaction with the solvent, which may be written as

$$B_P^- \xrightarrow{(a)} B_P^-$$

$$B_P + HOR \xrightarrow{(b)} (BHOR)^- \xrightarrow{(c)} HB + OR^- \quad (2)$$

to which must be added $OR^- + HY \longrightarrow HOR + Y^-$ in the presence of another acid such as phenol.

In order to determine the rate of the pure reaction (2) in the absence of any other acid than alcohol we have proceeded indirectly. In some experiments with *m*-cresol, and also in experiments with phenol to which sodium phenolate was added, the fading of the blue color did not run to an end but came to an equilibrium color. Evidently as concerns its dissociation to form the blue ion, the trinitrotriphenylmethane is an acid of about the same strength as phenol. So also in alcohol containing varying amounts of sodium ethylate we were able to measure the equilibrium ratio of B_S^- to HB. This ratio at a given temperature is proportional to the concentration of ethylate ion and at a given concentration of the latter increases with increasing temperature. From measurements at a series of temperatures, which we shall not give in detail, we were able to obtain the increase in energy in going from HB + OR^- to HOR + B_S^-. This amounts to 2.2 kcal. The equilibrium constant $(B_S^-)/(HB)(OR^-)$ at $-60°$ is 15.8.

In certain experiments the color of the equilibrium solution was studied when small amounts of water were added successively to the alcohol. If the ethylate ion is largely hydrolyzed in the presence of small quantities of water, we should expect the essential equilibrium now to be that between HB + OH^- and H_2O + B_S^- and therefore we should expect the amount of color to diminish rapidly as the water is added. In fact no change in color was found until the water had reached nearly 10 mole per cent. At first sight this seemed to indicate that the ethylate ion is not largely hydrolyzed. This, however, is not the probable explanation. We are presently going to produce evidence that water replaces alcohol in the blue ion forming a more stable substance. Apparently this effect is just counteracting the expected effect, when water is added to the solution.

Starting with a solution of trinitrotriphenylmethane in alcohol and adding a solution of sodium ethylate, we were able to study the rate of formation of the blue ion in a range sufficiently remote from equilibrium. The rate of this reaction, which is the reverse of reaction (2), is strictly proportional to the concentration of ethylate ion and of HB. From such measurements at different temperatures we obtained the value of the rate constant at $-60°$, and the heat of activation, which amounts to 11.1 kcal.

Subtracting from this heat of activation the heat of reaction obtained from the equilibrium measurements, we obtain 8.9 kcal. as the heat of activation of reaction (2). No great accuracy can be claimed for this determination, but the agreement of this value with the value 9.1 kcal. obtained as a mean for the much stronger acids, ranging from chloroacetic to acetic, very strongly substantiates our assumption that the heat of activation in all these cases is the heat required to form B_P^- from B_S . If the activation occurred only at the moment of collision between the reacting molecules, it would be hard to explain why the heat of activation or, in other words, the potential barrier in the activated complex should be the same for such very different substances as alcohol and our other acids.

When we came to determine the rate constant of reaction (2) by finding the ratio between the equilibrium constant and the rate constant in the reverse direction, we expected to find the rate due to the alcohol alone a little smaller than the rate which had been observed with dilute solutions of phenol and boric acid. In fact, however, the rate which we calculated was nearly twice the one observed in the presence of those two substances. This result was at the time so surprising that the whole determination was repeated with greater care, but the result was the same. We see no explanation except in the assumption for which we have already shown other evidence, namely, that the blue ion is a different substance when small amounts of phenol or boric acid are present.

If the blue ion in alcohol itself is not as simple as indicated in structure III′, but rather has alcohol molecules attached by hydrogen bonds to the several nitro groups, and if when certain substances such as phenol are added (and this may be true to some extent for any of the other acids we have employed), the solute molecules replace the alcohol molecules in the complex, then these new and more stable molecules may be expected to react more slowly either by reaction (1) or (2). In the course of another investigation we have found that crystal violet in toluene forms complexes with alcohols and acids, and the stability of these compounds reaches a maximum in the case of phenol.

In this connection we may mention the effect of water upon the reaction rates that we have been discussing. If, for example, to a 0.01 molal solution of acetic acid in alcohol we add water to the extent of 2 *M*, the rate of the reaction is reduced by one-half. This effect we attribute mainly to the formation of a stabler complex in which water replaces alcohol in the blue ion.

Colors and Reactions with the Chloroacetic Acids

When to the alkaline solution containing the blue ion B_S^- at low temperatures we add trichloroacetic acid, the same orange color is obtained as with hydrogen chloride and, as in that case, this color fades very slowly compared with the rate of fading of the blue color in the presence of acids like acetic. In other words, trichloroacetic acid, although even at room temperature in alcohol[1] its ionization constant is smaller than that in water by a factor lying between 10^4 and 10^5, still behaves as a strong acid toward our indicator.

If now we use dichloroacetic acid we obtain the same pure orange color but the fading of this color is much faster. This was interpreted to mean that the solution contains an amount of the blue ion too small to be observed visually, but large enough, because of its much higher specific reaction rate, to permit the rapid disappearance of the orange color. In other words, on account of the rapid equilibrium between orange and blue, the color disappears chiefly through the reaction of the latter. This view was supported by further experiments and it was found possible to make a rough estimate of the fraction of the substance in the blue form.

We wished to ascertain whether the orange substance is produced from the blue by the addition of undissociated acid or by the addition of free hydrogen ion, and by "free" we do not mean uncombined with the solvent but only uncombined with the dichloroacetate ion. Therefore we added various amounts of sodium dichloroacetate in addition to that which was regularly produced in the reaction vessel. The effect was large. With increasing concentration of salt the color changed regularly from orange to blue and the rate of reaction increased correspondingly. Now this addition of dichloroacetate does not appreciably affect the activity of the undissociated acid, but it diminishes greatly the activity of hydrogen ion, and it is therefore evident that the orange compound is formed from the blue by the addition of free hydrogen ions.

The question as to whether the orange is produced from the blue substance by the addition of one hydrogen ion or more seems to be decided by our experiments on the rate of fading at different concentrations of dichloroacetic acid. If we assume here, as in our other cases, that the rate of fading is proportional to the product of the concentrations of blue ion and of the acid, then it is evident that if only one H^+ is required to change the blue substance to the orange, the rate of the reaction could not be diminished by increasing the acid concentration. In fact, however, the rate is diminished. In going from 0.003 *M* $CHCl_2COOH$ (where the color is not quite pure orange) to 0.03 *M*, the rate decreases about threefold. We conclude therefore that our orange substance does not correspond to formula IV, but rather to a formula such as V with either two or three hydrogen ions attached to the nitro groups. Attempts to find direct proof of the existence of the intermediate pale or colorless substance failed, and this may indicate that it exists over a very narrow range of H^+ concentration. This would not be surprising, for IV is a less resonating form lying between the strongly resonating forms III′ and V, as in the numerous similar cases discovered by Schwarzenbach.[2]

Turning now to monochloroacetic acid we find at corresponding concentrations very much less of the orange compound and much faster fading. When the acid is at 0.0015 *M* the solution appears to be pure blue. Making allowance for the smaller specific absorption of the orange substance, it would be hard to believe that this solution contains more than 10–20% of the orange. Therefore its rate of fading should be nearly as high as if the substance were all blue. This proves to be very far from the case. If to this solution, which already contains a small amount of chloroacetate ion, we add lithium chloroacetate (the sodium salt being peculiarly insoluble) we find a great increase in the reaction rate. When the salt is at 0.015 *M* the rate has increased threefold and is then unaffected by further addition of the salt. The values so obtained are used in Table I. Although these measurements should be extended and quantitative studies of the absorption spectrum made, at present the simplest explanation of these facts is that in addition to the blue and orange the colorless form is present which, compared to the blue, is relatively unreactive.

The Fading of the Orange Compound

The behavior of the orange compound, which we have identified tentatively with formula V, is not our immediate concern. However, some

(1) Kraus, "The Properties of Electrically Conducting Systems," The Chemical Catalog Co., New York, 1922, p. 185.

(2) Schwarzenbach, Ott and Hagger, *Helv. Chim. Acta*, **20**, 498 (1937).

study was made of the rate of its conversion into trinitrotriphenylmethane. This rate proves to be strictly unimolecular with respect to the orange substance and entirely independent of the acid concentration. It is, moreover, the same for hydrochloric and trichloroacetic acids.

The rate is, however, extremely sensitive to water content and this effect is in the opposite direction to the one found with the blue ion. The rate increases with water concentration more rapidly than that concentration itself. Thus at $-34°$ with 2, 3 and 6% water (by volume) the times required to reach the same color standard were, respectively, 360, 135, and 41 seconds.

Since this phenomenon was not investigated further, any explanation must be provisional, but we suggest the following. Since the transfer of an electron pair to the central carbon, forming a primary base at that point (as in formula III), becomes less and less probable as hydrogen atoms are added at the nitro groups, such a configuration occurs too rarely to permit the direct addition of hydrogen ion at that point to contribute appreciably to the reaction rate. On the other hand, the hydrogens on the nitro groups are too far removed from the central carbon to permit a direct rearrangement. If, however, we imagine a chain of water molecules attached at one end to one of the hydrogens of formula V while the other end may come in contact with the central carbon, such a chain might act as a resonating system which could remove hydrogen from the nitro group and add it to the central carbon *as a single act.* This is entirely analogous to the explanation of the very high mobility of hydrogen ion in water, namely, that hydrogen ion is added at one end of a water chain while another hydrogen ion can be removed at the other end. This peculiar mobility of hydrogen ion, although very much smaller, is still present in alcohol solutions, and we may therefore, by analogy, suppose that our rearrangement, although slow, would still exist, even in completely dry alcohol.

Summary

Trinitrotriphenylmethide ion was expected and has proved to be a secondary base. In alcohol when this blue ion is added to any weak acid at temperatures between -30 and $-80°$ the formation of the corresponding methane is slow and can be followed colorimetrically. The rate of neutralization was studied with numerous acids and under like conditions the rates diminish with diminishing acid strength. With the weakest acids the rates are not proportional to the concentration of acid, and this fact is explained. With the six acids of intermediate strength the rates were found proportional to the concentrations of blue ion and of un-ionized acid, and unaffected by neutral salts. In these cases the heat of activation was calculated from the temperature coefficient of the rates and was found approximately constant with a mean value of 9.1 kcal. By indirect methods the rate of neutralization by alcohol itself was determined. Here the heat of activation is found to be 8.9 kcal. The constancy of the heat of activation over the great range from chloroacetic acid to alcohol can hardly be explained by the theory of an activated complex. The value obtained is taken as a measure of the difference in energy between the primary and secondary forms of the base. The small departures from this constant value are attributed in part to experimental error, but especially to differences in the actual composition of the reacting ion. Several kinds of evidence are adduced to show that the actual composition of the blue ion depends not only upon the solvent but in several cases upon the presence of other solutes.

While the trinitrotriphenylmethide ion is a secondary base with respect to addition of acid to the central carbon, it is a primary base with respect to addition of acid to the nitro groups. In the presence of strong acids an orange substance is thus formed which contains more than one free hydrogen ion per molecule. The very slow rate of fading of the orange compound is studied, and an explanation is suggested for the large catalytic effect of water. Mono- and dichloroacetic acids give mixtures of the orange and blue substances and the rate of fading in these solutions leads to some of the conclusions already mentioned.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF WISCONSIN]

The Sterols of Rye Germ Oil

BY STEWART W. GLOYER[1] AND H. A. SCHUETTE

Early investigators found indications of a marked similarity in the sterols which they isolated from wheat and rye germ oils. Interest in the unsaponifiable matter of the latter, however, has not kept pace with that aroused by the former for the sterols of wheat germ oil have been extensively investigated since the turn of the century. For this reason it was deemed desirable to re-investigate the nature of the sterols of rye germ oil; particularly in the light of the newer knowledge[2] that the principal phytosterol, sitosterol, is indeed a mixture of several sterols. These are now designated, in the order of the insolubility in the common non-aqueous solvents, as γ-, β-, and α-sitosterol.

γ-Sitosterol, which is the least soluble of this group, was isolated by Anderson and co-workers[2] from corn and wheat germ oils. Wallis and Chakravorty[3] found that the β-form is the major component of the sterol fraction of cottonseed oil and Ichiba[4] isolated it from wheat germ oil. Wallis and Fernholz[5] succeeded in separating from the most soluble sterol fraction of wheat germ oil two components which they designated as α_1- and α_2-sitosterol, respectively. We have succeeded in isolating from rye germ oil not only those sterols which are known to be characteristic of wheat germ oil, or α_1-, β-, and γ-sitosterol, but also a hitherto unreported compound which we tentatively designated as α_3-sitosterol.

α_1-Sitosterol was isolated from the most soluble sterol fraction by taking advantage of the fact, as did Wallis and Fernholz,[5] that the corresponding *m*-dinitrobenzoates differ greatly in solubility, the α_1-sitosterol derivative having the lesser solubility. They isolated α_2-sitosteryl *m*-dinitrobenzoate from the mother liquor. We found no evidence for the presence of this sterol in rye germ oil. In its place there was isolated a sterol-like compound which we have named α_3-sitosterol. Combustion data on the dinitrobenzoate indicate the empirical formula $C_{36}H_{50}N_2O_6$ which corresponds to $C_{29}H_{48}O$ for the free sterol. Perbenzoic acid titrations indicate the presence of two double bonds, thereby making α_3-sitosterol an isomer of stigmasterol and also of α_1-sitosterol.

α_1- and α_3-sitosterol give the Liebermann–Burchard color reaction, the final color being a dark purple. The Salkowski reaction for both is similar to that of ergosterol in that the sulfuric acid layer becomes colored while the chloroform layer remains colorless. The Rosenheim color reaction with chloroacetic acid is negative for both. α_1- and α_3-sitosterol are precipitated by digitonin.

Dihydrositosterol, which has been reported in as much as from 1–1.5% yields in wheat germ oil, has not been isolated from rye germ oil in this study. Although the specific rotation could be reduced from −31.53 to −8.41 by recrystallization, nevertheless the amounts present were too small to isolate by either the Schöenheimer[6] or the Anderson–Nabenhauer[7] methods.

Experimental

Approximately 12 kg. of rye oil was obtained by extracting thoroughly sifted, cleaned rye germ stock[8] with ethyl ether, first in the cold and then in a continuous extractor. An ether extraction of the saponified oil yielded some 800 g. of orange-colored unsaponifiable matter.

The sterol fraction was separated from the non-crystalline fraction with ice-cold petroleum ether yielding 474 g. of crude sterol, which is equivalent to 58% of the unsaponifiable matter. The crude sterol was submitted to a systematic triangle scheme of crystallization from alcohol and benzene in which, during the course of 115 recrystallizations, 12 fractions were obtained.

Isolation of γ-Sitosteryl Acetate.—The third and fourth top fractions (m. p. 141–142°, $[\alpha]^{27}D$ −31.26; m. p. 140–141°, $[\alpha]^{27}D$ −30.68) were acetylated and then brominated.[9] A small amount of material precipitated. It was debrominated by refluxing its alcohol solution with zinc and acetic acid, after which it was recrystallized from alcohol. The melting point, 138–139°, $[\alpha]^{24}D$ −41.51, showed that it was not stigmasteryl acetate.

The dibromide from the filtrate of the original brominated solution was precipitated, by the addition of water,

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(2) R. J. Anderson, R. L. Shriner and G. O. Burr, THIS JOURNAL, **48**, 2897 (1926); see also Anderson and Shriner, *ibid.*, **48**, 2976.

(3) E. S. Wallis and P. N. Chakravorty, *J. Org. Chem.*, **2**, 335 (1937).

(4) A. Ichiba, *Sci. Papers Inst. Phys. Chem. Research* (Tokyo), **28**, 112 (1935).

(5) E. S. Wallis and E. Fernholz, THIS JOURNAL, **58**, 2446 (1936).

(6) R. Schöenheimer, *Z. physiol. Chem.*, **192**, 81 (1930).

(7) R. J. Anderson and F. P. Nabenhauer, THIS JOURNAL, **46**, 1957 (1924).

(8) Acknowledgment is made to the Messrs. Frank H. Blodgett, Inc., of Janesville, Wisconsin, who contributed some 700 pounds of rye germ stock for this investigation.

(9) A. Windaus and A. Hauth, *Ber.*, **39**, 4378 (1906).

debrominated, and recrystallized sixteen times from alcohol. The remaining material, which melted at 143–143.5°, $[\alpha]^{23}D$ −45.02, corresponded to pure γ-sitosteryl acetate (26.24 mg. in 2 cc. of chloroform in a 2-dm. tube gave $\alpha^{23}D$ −1.094).

Anal. Calcd. for $C_{31}H_{52}O_2$: C, 81.51; H, 11.48. Found: C, 81.62; H, 11.45.

γ-Sitosterol.—The acetate was hydrolyzed with a 2% alcoholic solution of potassium hydroxide, precipitated with water and recrystallized twice from alcohol, yielding the free sterol. It melted at 146°, $[\alpha]^{24}D$ −42.02 (21.29 mg. in 2 cc. of chloroform).

Anal. Calcd. for $C_{29}H_{50}O$: C, 83.98; H, 12.16. Found: C, 83.96, 84.03; H, 12.33, 12.47.

Isolation of β-Sitosteryl Benzoate.—The three bottom or most soluble fractions, weighing 63 g. (m. p. 139.5–140°, $[\alpha]^{27}D$ −17.90; m. p. 139.5–140°, $[\alpha]^{27}D$ −17.00; m. p. 139.5–140°, $[\alpha]^{24}D$ −17.66), were dissolved in 260 cc. of pyridine. To this solution there was added benzoyl chloride (55 cc.), after which the mixture was heated on a boiling water-bath for one hour. After working up the product in the usual manner, the benzoate was four times recrystallized. It melted at 146–147°; $[\alpha]^{24}D$ −13.75 (30.54 mg. in 2 cc. chloroform in a 2-dm. tube gave $\alpha^{24}D$ −0.389).

Anal. Calcd. for $C_{36}H_{56}O_2$: C, 83.33; H, 10.50. Found: C, 83.28; H, 10.61.

β-Sitosterol.—The benzoate was hydrolyzed and the liberated sterol precipitated as before. On recrystallization from alcohol it melted at 137–137.5°; $[\alpha]^{24}D$ −36.66 (23.82 mg. in 2 cc. of chloroform).

Anal. Calcd. for $C_{29}H_{50}O$: C, 83.98; H, 12.16. Found: C, 84.03; H, 12.26.

Isolation of α_1-Sitosteryl *m*-Dinitrobenzoate.—In the mother liquor from the first crystalliation of β-sitosteryl benzoate there remained the most soluble corresponding α-derivative. These benzoates were saponified with alcoholic potassium hydroxide solution. Conversion to the *m*-dinitrobenzoates was effected by dissolving the free sterol in 110 cc. of pyridine and adding 15 g. of *m*-dinitrobenzoyl chloride. This mixture was kept on a boiling water-bath for two hours, after which it was worked up in the usual manner. The crude dinitrobenzoate was recrystallized four times from ethyl acetate, yielding 0.8 g. of very insoluble, tiny needles of m. p. 225°; $[\alpha]^{25}D$ +37.05 (19.16 mg. in 2 cc. of chloroform).

Anal. Calcd. for $C_{36}H_{50}N_2O_6$: C, 71.24; H, 8.31; N, 4.62. Found: C, 71.12; H, 8.32; N, 4.67.

α_1-Sitosterol.—The dinitrobenzoate was hydrolyzed and the liberated sterol precipitated as before. On recrystallization from alcohol it melted at 163°; $[\alpha]^{25}D$ −1.84 (26.42 mg. in 2 cc. of chloroform).

Anal. Calcd. for $C_{29}H_{48}O$: C, 84.38; H, 11.73. Found: C, 83.93[10]; H, 11.68.

α_1-Sitosteryl Benzoate.—The free sterol was converted to the benzoate in pyridine solution in the usual manner. On recrystallization from alcohol it had a melting point of 167–168°; $[\alpha]^{26}D$ +40.77 (22.69 mg. in 2 cc. of chloroform).

Anal. Calcd. for $C_{36}H_{52}O_2$: C, 83.68; H, 10.15. Found: C, 83.62; H, 10.42.

Titration with Perbenzoic Acid.—To 19.56 and 26.14 mg. of α_1-sitosteryl *m*-dinitrobenzoate there was added an excess of a chloroform solution of perbenzoic acid. After standing in the refrigerator at −7° for fifty-six hours there was added 5 cc. of a 10% potassium iodide solution, and the liberated iodine titrated with 0.02007 *N* sodium thiosulfate solution. The compound consumed 0.98 and 1.32 mg. of oxygen, respectively. The theoretical amount for 2 atoms of oxygen is 1.03 and 1.37 mg., respectively. These results correspond to 1.91 atoms of oxygen consumed, thus indicating the presence of two double bonds.

Isolation of α_3-Sitosteryl *m*-Dinitrobenzoate.—To the concentrated mother liquor from the first crystallization of α_1-sitosteryl *m*-dinitrobenzoate alcohol was added, while the solution was being boiled, until needles began to crystallize out. The material thus obtained (m. p. 183–184°) was recrystallized five times from ethyl acetate and alcohol, and twice from acetone, after which the melting point and the specific rotation remained unchanged. The yield of pure α_3-sitosteryl *m*-dinitrobenzoate was increased by concentrating and recrystallizing the material in the mother liquors from α_1-sitosteryl *m*-dinitrobenzoate, and by giving similar treatment to the material from the mother liquors obtained in recrystallizing the crude α_3-dinitrobenzoate. The total yield was 3 g. The product had a melting point of 202.5–203°; $[\alpha]^{27}D$ +15.35 (31.69 mg. in 2 cc. of chloroform).

Anal. Calcd. for $C_{36}H_{50}N_2O_6$: C, 71.24; H, 8.31; N, 4.62. Found: C, 71.23, 71.04; H, 8.32, 8.55; N, 4.72.

α_3-Sitosterol.—The dinitrobenzoate was hydrolyzed and the liberated sterol precipitated as before. On recrystallization from alcohol it melted at 142°, $[\alpha]^{25}D$ +1.65 (25.72 mg. in 2 cc. of chloroform).

Anal. Calcd. for $C_{29}H_{48}O$: C, 84.38; H, 11.73. Found: C, 83.65, 83.81[10]; H, 11.55, 11.64.

α_3-Sitosteryl Benzoate.—The free sterol was converted to the benzoate in pyridine solution in the usual manner. On recrystallization from alcohol it melted at 167.5–168°; $[\alpha]^{28}D$ +14.85 (22.20 mg. in 2 cc. of chloroform).

Anal. Calcd. for $C_{36}H_{52}O_2$: C, 83.68; H, 10.15. Found: C, 83.65; H, 9.89.

Titration with Perbenzoic Acid.—To 17.42 and 28.16 mg. of α_3-sitosteryl *m*-dinitrobenzoate was added an excess of a chloroform solution of perbenzoic acid. After standing in the refrigerator at −7° for a week there was added 5 cc. of a 10% potassium iodide solution, and the liberated iodine titrated with 0.02007 *N* sodium thiosulfate solution. The compound consumed 0.96 and 1.24 mg. of oxygen, respectively. The theoretical amount for two atoms of oxygen is 0.92 and 1.47 mg., respectively. These results correspond to 2.10 and 1.70 atoms of oxygen consumed, giving an average of 1.90 atoms of oxygen. These results, although not as good as those obtained with α_1-sitosteryl *m*-dinitrobenzoate, indicate the presence of two double bonds in this sterol.

Attempted Isolation of Dihydrositosterol.—The two top fractions were investigated for the presence of dihydrositosterol and stigmasterol. These fractions, $[\alpha]^{27}D$

(10) These sterols apparently retain a small amount of solvent of crystallization, thereby lowering the value for the percentage of carbon.

-28.62, and $[\alpha]^{27}D$ -28.06, respectively, were brominated by the Schöenheimer[6] method. To the reaction mixture was added a one per cent. solution of digitonin. A small amount of digitonide precipitated, which upon decomposition with pyridine[11] yielded a sterol of somewhat lower rotation, $[\alpha]^{24}D$ -21.30. This value seemed to indicate that dihydrositosterol, if present, would be found only in very small amount.

The dibromide still in solution was precipitated with water, debrominated, and then acetylated. The acetyl derivative was recrystallized ten times in the hope of concentrating the dihydrositosterol, if present, in the top fraction. It was then brominated,[9] but since no precipitate of insoluble stigmasterol tetrabromide was formed, the presence of this sterol was eliminated. The dibromide was precipitated with water and debrominated according to the method of Anderson and Nabenhauer.[7] The regenerated acetyl derivative was dissolved in carbon tetrachloride and treated twenty times with portions of acetic anhydride and sulfuric acid. There was only a slight color reaction after these treatments. The carbon tetrachloride was evaporated but only a small amount of brown resinous mass remained from which no crystals of dihydrositosterol could be obtained.

A separate sample of 33 g. of crude sterol (m. p. 138–139°; $[\alpha]^{25}D$ -31.53) was recrystallized twenty-three times, after which it had a melting point of 137°; $[\alpha]^{24}D$ -8.41. This sample was now dissolved in alcohol, brominated by the Schöenheimer method[6] and an excess of digitonin solution added. However, no insoluble digitonide was formed.

The fact that the specific rotation could be lowered to -8.41 and that the rotation of the two top fractions was lowered by treatment with digitonin would indicate the possibility that small amounts of dihydrositosterol were present. However, these amounts were too small for isolation.

(11) R. Schöenheimer and H. Dam, *Z. physiol. Chem.*, **215**, 59 (1933).

Summary

A new doubly unsaturated sterol which is an isomer of stigmasterol has been isolated in a pure state from the most soluble sterol fraction of rye germ oil.

The presence of α_1-, β-, and γ-sitosterol has been demonstrated.

The absence of α_2-sitosterol and stigmasterol has been shown.

An analysis for dihydrositosterol failed to yield the pure compound by either the Schöenheimer[6] or Anderson–Nabenhauer[7] method.

MADISON, WISCONSIN RECEIVED JUNE 12, 1939

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

Studies in the Sitosterol Complex. The Isolation of α_3-Sitosterol

BY SEYMOUR BERNSTEIN[1] AND EVERETT S. WALLIS

That sitosterol is in reality a mixture of several sterols was first shown by Anderson and his co-workers.[2] These investigators showed that sitosterol obtained from various sources contains dihydrositosterol and at least three other sterols which they named α-, β- and γ-sitosterol.

In 1936 Wallis and Fernholz[3] showed that the most soluble fraction of the sitosterol complex from wheat germ oil named by Anderson and his co-workers α-sitosterol was in reality a mixture of at least two new sterols α_1- and α_2-sitosterol. A detailed method of their separation and isolation was given, and certain properties of these sterols and their derivatives were listed.

In this paper we wish to report the results of certain experiments which show that a third sterol, α_3-sitosterol, is also present in the sterol complex from wheat germ oil. Our work in this connection was prompted by the fact that for continuance of our studies on the structure of α_1-sitosterol, the results of which will be reported shortly in another paper, it was necessary to obtain further quantities of this interesting material. Following the procedure described by Wallis and Fernholz,[3] we obtained from recrystallization of 1627 g. of a sitosterol from wheat germ oil, 6.5 g. of α_1-sitosteryl *m*-dinitrobenzoate and 6.0 g. of the more soluble fraction which in melting point corresponded to α_2-sitosteryl *m*-dinitrobenzoate. Hydrolysis of this latter fraction and conversion into its acetate gave a product from which not only α_2-sitosteryl acetate (m. p. 126°, $[\alpha]D$ $+17$) was isolated but also there was obtained in a pure condition 1.0 g. of a new acetate, α_3-sitosteryl acetate (m. p. 152–153° $[\alpha]^{20}D$ $+6.1$).

Several derivatives of this new sterol were prepared and their properties together with those of α_1- and α_2-sitosterol are given in Table I.

(1) Research Assistant on Special Funds from the Rockefeller Foundation.

(2) Anderson, Shriner and Burr, THIS JOURNAL, **48**, 2987 (1926). See also Anderson, *ibid.*, **46**, 1450 (1924).

(3) Wallis and Fernholz, *ibid.*, **58**, 2446 (1936).

TABLE I

Derivative	α_1-Sitosterol M. p., °C.	α_1-Sitosterol $[\alpha]_D$	α_2-Sitosterol M. p., °C.	α_2-Sitosterol $[\alpha]_D$	α_3-Sitosterol M. p., °C.	α_3-Sitosterol $[\alpha]_D$
Sterol	164–166	− 1.7	156	+ 3.5	142–143	+ 5.2
Acetate	137	+29	124–126	+17	152–153	+ 6.1
Benzoate	168–172	+42	164–166	+27	173–175	+12.0
m-Dinitrobenzoate	222	+37	206	+26	210–211.5	+12.2

We also wish to report certain other important observations. α_3-Sitosterol in all probability is an isomer of stigmasterol, $C_{29}H_{48}O$, and α_1-sitosterol, $C_{29}H_{48}O$. Titration with perbenzoic acid shows that two double bonds are present. That the two double bonds are not conjugated is indicated by an absorption spectrum study. No maxima were found in the ultraviolet region of the spectrum. α_3-Sitosterol gives a positive Liebermann color reaction. The final color is a dark blue with a reddish tint. The Salkowski reaction for α_3-sitosterol is similar to that of ergosterol, α_1- and α_2-sitosterol; the sulfuric acid layer becomes colored, while the chloroform stays colorless. The opposite is true for cholesterol, γ-sitosterol, and stigmasterol. α_3-Sitosterol is precipitated by digitonin.

Experimental Part

Sixteen hundred and twenty-seven grams of a crude sitosterol (source, wheat germ oil) was worked up according to the method of Wallis and Fernholz,[3] and yielded 6.5 g. of α_1-sitosteryl *m*-dinitrobenzoate and 6.0 g. of a material which in melting point (206°) corresponded with that of α_2-sitosteryl *m*-dinitrobenzoate previously described by Wallis and Fernholz.[3]

Isolation of α_3-Sitosteryl Acetate.—The above described material (m. p. 206°) was hydrolyzed by refluxing it with a 5% alcoholic potash solution. The free sterol, so obtained, was then converted into the acetate by refluxing with acetic anhydride. Crystallization of the crude acetate from ethyl alcohol, gave two distinct fractions. The more insoluble fraction, α_3-sitosteryl acetate (plates, wt. 1.0 g.), melted at 152–153°, $[\alpha]^{20}D$ +6.1 (0.0264 g. in 2 cc. of chloroform solution gave $\alpha^{20}D$ +0.08). The more soluble portion was found to be the α_2-sitosteryl acetate (m. p. 124–126°, $[\alpha]^{25}D$ +17) already described by Wallis and Fernholz. The melting point of the sterol acetate (152–153°) is depressed by α_2-sitosteryl acetate.

Anal. Calcd. for $C_{31}H_{50}O_2$: C, 81.88; H, 11.08. Found: C, 81.8; H, 11.3.

α_3-Sitosterol.—A portion of the above described α_3-sitosteryl acetate was hydrolyzed with a 5% alcoholic potash solution by heating on the water-bath for one hour. The free sterol was worked up in ether. Crystallization from alcohol gave platelets which melted at 142–143°, $[\alpha]^{20}D$ +5.2° (0.0482 g. in 5 cc. of chloroform solution). α_3-Sitosterol is precipitated by digitonin.

Anal. Calcd. for $C_{29}H_{48}O$: C, 84.40; H, 11.73. Found: C, 84.44; H, 11.83.

An absorption spectrum study of α_2-sitosterol was carried out by Dr. T. J. Webb of the Research Laboratories of Merck and Company, Inc. No maxima were found in the ultraviolet region of the spectrum.

α_3-Sitosteryl Benzoate.—One-tenth of a gram of α_3-sitosterol dissolved in pyridine was heated for one hour on the water-bath with benzoyl chloride. The benzoate was worked up in ether. Crystallization from benzene and alcohol gave plates of m. p. 173–175°, $[\alpha]^{20}D$ +12.0° (0.0266 g. in 2 cc. of chloroform).

Anal. Calcd. for $C_{36}H_{52}O_2$: C, 83.66; H, 10.14. Found: C, 83.4, 83.5; H, 10.18, 10.00.

α_3-Sitosteryl *m*-Dinitrobenzoate.—A sample of α_3-sitosterol, dissolved in pyridine, was heated for one hour on the water-bath with *m*-dinitrobenzoyl chloride. The product was extracted with ether and the ether solution was decolorized with animal charcoal and worked up in the usual manner. Recrystallization from ethyl acetate and alcohol gave needles which were white with a very slight yellow luster; m. p. 210–211.5°; $[\alpha]^{20}D$ +12.2° (0.0312 g. in 2 cc. of chloroform solution).

Anal. Calcd. for $C_{36}H_{50}N_2O_6$: C, 71.25; H, 8.31; N, 4.62. Found: C, 71.40, 71.13; H, 8.36, 8.37; N, 4.80.

Titration with Perbenzoic Acid.—Thirty-three and three-tenths milligrams of α_3-sitosteryl acetate took up 2.12 mg. of oxygen on standing for three days at −2°, with an excess of a chloroform solution of perbenzoic acid. The theoretical amount for two atoms of oxygen is 2.34 mg.

We wish to take this opportunity to express our thanks to the Rockefeller Foundation for a grant-in-aid for this work, to Merck and Company, Inc., of Rahway, New Jersey, for the analyses and absorption data published in this paper, and to Dr. O. H. Emerson of the University of California for kindly furnishing part of the crude sterol from wheat germ oil used in this work.

Summary

1. A new doubly unsaturated sterol, α_3-sitosterol, has been isolated from the most soluble fraction of the sitosterol complex obtained from wheat germ oil.

2. The acetate, benzoate and *m*-dinitrobenzoate of the new sterol have been prepared and characterized.

3. An absorption spectrum study indicates that the two double bonds in the new sterol are not conjugated.

4. The new sterol is precipitated by digitonin.

5. α_3-Sitosterol is probably an isomer of stigmasterol, and α_1-sitosterol.

PRINCETON, N. J. RECEIVED JUNE 15, 1939

[CONTRIBUTION FROM THE DIVISION OF INDUSTRIAL AND CELLULOSE CHEMISTRY, MCGILL UNIVERSITY]

Studies on Reactions Relating to Carbohydrates and Polysaccharides. LVI. The Synthesis of the Higher Polyoxyethylene Glycols[1]

BY REID FORDYCE,[2] EDWIN L. LOVELL[3] AND HAROLD HIBBERT

During the past ten years interest in the preparation and properties of long-chain polymers, of their derivatives and of co-polymers has been intensified because of their importance in the manufacture of plastics and synthetic fibers. One of the most important considerations has been the question of whether very high polymeric substances of the polyethylene oxide and cellulose types exist in solution as long macro-molecules, completely dispersed, or as aggregations of much shorter molecules associated in the micellar state.

One of the chief proponents of the former view, Staudinger[4] has carried out an immense amount of invaluable work on the viscosity of solutions of such linear polymers. His conclusions regarding chain length have been based almost entirely on such measurements interpreted on the basis of the Staudinger viscosity relation, $\eta_{sp}/c = K_m M$.

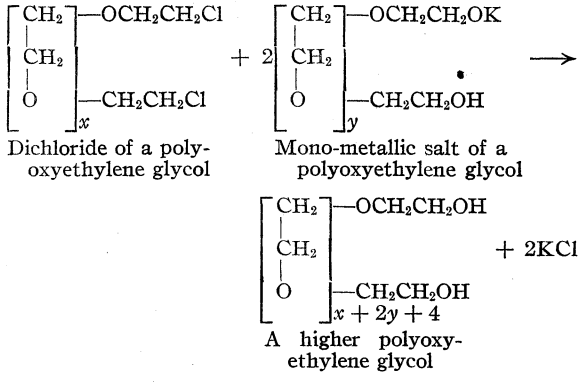
Staudinger's researches in the high molecular weight range were admittedly carried out on polymeric mixtures obtained by fractional precipitation, because apart from the synthetic long chain polypeptides of Emil Fischer[5] and Abderhalden and Fodor,[6] no other chemically pure, homogeneous long-chain polymers were available.

In view of this, an investigation was commenced ten years ago in this Division on the synthesis of pure homogeneous long-chain polyoxyethylene glycols, since it has been definitely established that these are identical in structure with Staudinger's polyethylene oxides.[7]

Considerable experimental difficulties have been encountered with increase in chain length and the present communication deals with the synthesis, purification and characterization of the lower polymers, *viz.*, hexaoxyethylene glycol $HO(CH_2CH_2O)_6H$, octadekaoxyethylene glycol $HO(CH_2CH_2O)_{18}H$ and dotetracontaoxyethylene glycol $HO(CH_2CH_2O)_{42}H$.

Polyethylene glycols were first prepared by Lourenco[8] and later by Wurtz[9] who heated ethylene glycol with water.

However, the first direct method of synthesizing a given polyoxyethylene glycol was that of Perry and Hibbert.[7] Their reaction may be written generally as



Dichloride of a polyoxyethylene glycol

Mono-metallic salt of a polyoxyethylene glycol

A higher polyoxyethylene glycol

This method, with certain modifications, was used in the present work to synthesize the 6-, 18- and 42-membered polyoxyethylene glycols.

From the nature of the reaction it is essential that the mono rather than the dimetallic salt of the glycol be used since, if the latter were present in appreciable quantities, a chain condensation reaction could take place yielding polyoxyethylene glycols of indefinite length. For this reason, the sodium salt of diethylene glycol formed during the synthesis of hexaoxyethylene glycol was isolated in the crystalline state and, by conversion to its trityl derivative, was shown to be the monosodium salt.

The potassium salts of the 6- and the 18-membered polyoxyethylene glycols were not isolated. No formation of hydrogen chloride was detectable during the condensation reaction and in each case the potassium chloride formed was isolated in the theoretical amounts.

For the synthesis of the hexaoxyethylene glycol

(1) Paper presented at the Baltimore meeting of the American Chemical Society, April, 1939.

(2) Holder of a Bursary and Studentship under the National Research Council of Canada, 1937–1939.

(3) Holder of a Scholarship donated by Spruce Falls Power and Paper Company, Ltd., 1937–1938.

(4) (a) Staudinger, "Der Aufbau der hochmolekülaren organischen Verbindungen—Kautschuk und Cellulose," Verlag von Julius Springer, Berlin, 1932; (b) recent review by Staudinger, *Papier Fabr.*, **36**, 373, 381, 473 (1938).

(5) Fischer, *Ber.*, **40**, 1754–1767 (1907).

(6) Abderhalden and Fodor, *ibid.*, **49**, 561–578 (1916).

(7) (a) Perry and Hibbert, *Can. J. Research*, **B14**, 77–83 (1936); (b) Barnes and Ross, THIS JOURNAL, **58**, 1129 (1936); (c) Perry, Ph.D. Thesis, McGill University, 1938.

(8) Lourenco, *Compt. rend.*, **49**, 619 (1859).

(9) Wurtz, *ibid.*, **49**, 813 (1859); *Ann. chim.*, [3] **69**, 331 (1863).

2 moles of the monosodium salt of diethylene glycol was condensed with 1 mole of β,β'-dichloroethyl ether. In the preparation of the 18- and 42-membered glycols, 2 moles of the monopotassium salt of hexaoxyethylene glycol and 2 moles of the potassium salt of 18-membered oxyethylene glycol, respectively, was condensed with one mole of hexaoxyethylene glycol dichloride.

In addition to the evidence for structure provided in the actual synthesis various other supporting data were obtained. Hydrogen was evolved in every case by interaction with metallic potassium and the presence of hydroxyl confirmed by the Grignard reagent. The molecular weights of the individual glycols were proved by chlorine analysis of their dichlorides and by cryoscopic molecular weights. The polyoxyethylene glycols synthesized were found free from halogen.

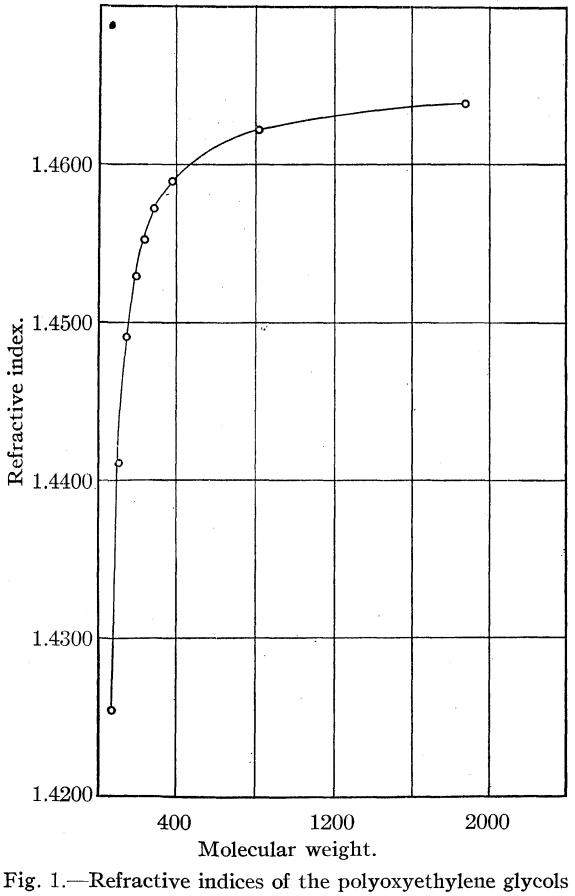


Fig. 1.—Refractive indices of the polyoxyethylene glycols at 40°.

As Fig. 1 shows, refractive index measurements of the synthetic polyoxyethylene glycols were found in agreement with their respective positions in the polyoxyethylene glycol series, although it is evident that this property does not differentiate sharply between the higher glycols.

The agreement of the calculated molecular refractive indices with the observed values is interesting but it is not significant in establishing the identity of each glycol since the controlling factor in determining both values is the molecular weight itself.

The polyoxyethylene glycols show a uniform solubility behavior. They are readily soluble in water and the usual organic solvents, with the exception of ether and petroleum ether. Hexaoxyethylene glycol dichloride is soluble in ether and insoluble in water; while the 18-membered and the 42-membered polyoxyethylene glycol dichlorides are completely soluble in water and rather less soluble in ether, although to a greater extent than the corresponding glycol. Otherwise the solubilities of the dichlorides are quite similar to those of the glycols.

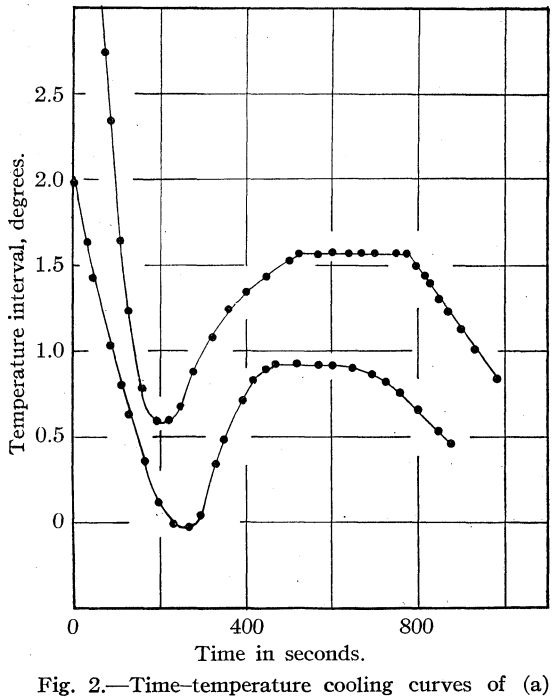


Fig. 2.—Time–temperature cooling curves of (a) hexaoxyethylene glycol (upper); and (b) hexaoxyethylene glycol containing 2.5 mole per cent. 42-membered oxyethylene glycol (lower).

The glycols crystallize in the form of characteristic, radiating clusters of thread-like crystals, which, under the polarizing microscope, show complete extinction of plane-polarized light.

It is obviously of great importance to establish, with certainty, the purity of these polyoxyethylene glycols. The shape of the time–temperature cool-

ing curve is perhaps the most significant, non-comparative, criterion of purity of a chemical compound[10] and was therefore applied in the present research. A sharp break in the cooling curve when freezing is complete is perhaps one of the most sensitive effects observable with a very pure substance, as well as the actual length of the flat portion. From Figs. 2, 3, 4 and 5 it is evident that the polyoxyethylene glycols show both these effects and also that the addition of a small amount of a second component gives rise to a definite "rounding-out" of the break at the end of the flat portion. The cooling curve obtained from a polymeric mixture of glycols prepared and fractionated according to Staudinger[4] shows no flat portion (compare Fig. 3), as is to be expected from such polymeric mixtures in contrast to chemically pure, homogeneous substances.

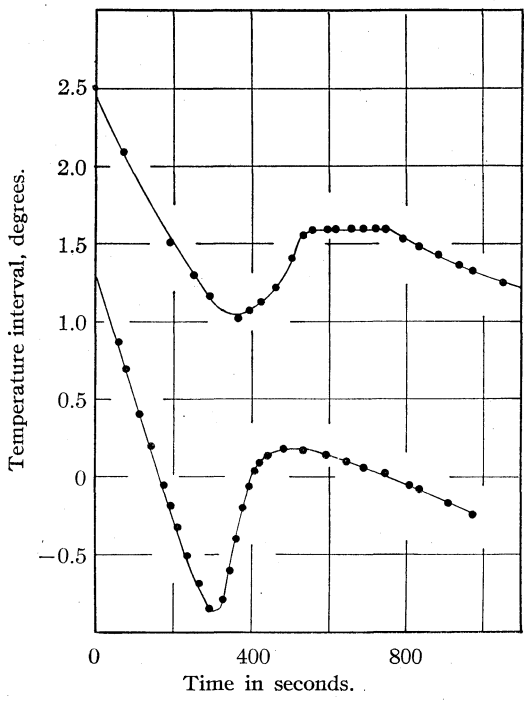


Fig. 3.—Time–temperature cooling curves of (a) 18-membered oxyethylene glycol (upper); and (b) the polymeric mixture of glycols (lower).

Experimental Part

Materials.—Commercial diethylene glycol and β,β'-dichloroethyl ether were prepared by careful fractionation. Since the glycols are hygroscopic, all reagents, solvents and apparatus were thoroughly dried prior to use and an atmosphere of dry, oxygen-free nitrogen maintained in the reaction flask during the formation of the monometallic salts of the glycols and their condensation with the dihalides.

(10) Skau, *Proc. Am. Acad. Arts Sci.*, **67**, 551 (1932).

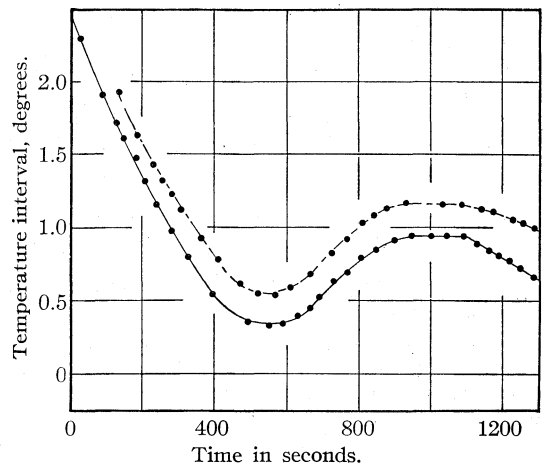


Fig. 4.—Time–temperature cooling curves of (a) 42-membered oxyethylene glycol (lower); and (b) 42-membered oxyethylene glycol containing 6.12 mole per cent. 18-membered oxyethylene glycol (upper).

Synthesis of Hexaoxyethylene Glycol, $HO(CH_2CH_2O)_6H$.—Ninety-two grams (4.0 moles) of sodium was dissolved in 700 cc. of methanol in a 2-liter Claisen flask, 900 g. (8.5 moles) of diethylene glycol added and the solution stirred at 40° for fifteen minutes. The methanol was then removed from the reaction mixture at 100° (20 mm.). Pure β,β'-dichloroethyl ether (314.6 g., 2.2 moles, 10% excess) was then added slowly and continuously through a dropping funnel during a three-hour period, the mixture being maintained at 95° and stirred vigorously throughout the addition, and then for a further three days at the same temperature. The neutral reaction mixture (phenolphthalein) was filtered from sodium

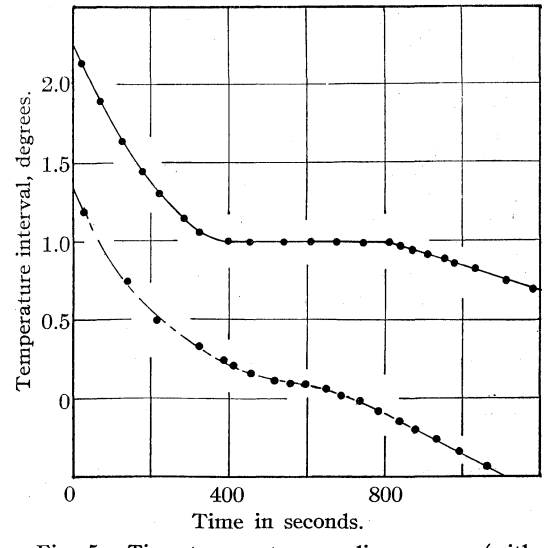


Fig. 5.—Time–temperature cooling curves (without supercooling) of (a) 42-membered oxyethylene glycol (upper); and (b) 42-membered oxyethylene glycol containing 24 mole per cent. 18-membered oxyethylene glycol (lower).

chloride and the filtrate distilled at 2 mm. pressure until everything boiling up to 200° had been removed. Repeated high vacuum distillation of the residual liquid yielded 260 g. (48% of theoretical) of hexaoxyethylene glycol as a colorless oil; b. p. 185–185.7° (0.015 mm.). The refractive index remained constant throughout the distillation.

Isolation of the Sodium Salt of Diethylene Glycol and Conversion into Trityl Derivative

If, during the previous synthesis of hexaoxyethylene glycol, the solution containing the sodium salt of diethylene glycol left after removal of the methanol is allowed to cool, large, hygroscopic, transparent crystals of the monosodium salt containing 1 mole of diethylene glycol of crystallization separate out. These crystals were separated by filtration, washed repeatedly with dioxane, then ether and dried.

Anal. Calcd. for $C_8H_{19}O_6Na$: Na, 9.83. Found: Na, 9.65, 9.44.

Trityl Derivative.—To a solution of 8.0 g. (0.0287 mole) of trityl chloride in 80 cc. of dioxane heated to 70° was added with stirring 6.7 g. (0.0287 mole) of the sodium salt and the reaction product kept at this temperature for two hours. It was then poured into twenty volumes of ice water. The resulting trityl derivative was recrystallized from a mixture of benzene–petroleum ether (30–50°): yield 9.0 g. (90%); m. p. 116–116.5°.

Anal. Calcd. for $C_{23}H_{24}O_3$ (monotrityl derivative): C, 79.3; H, 6.9. Found: C, 79.1, 79.2; H, 6.87, 6.97.

Preparation of Hexaoxyethylene Glycol Dichloride.—To 350 g. (1.24 moles) of hexaoxyethylene glycol dissolved in 205.8 g. of anhydrous pyridine was added slowly and with vigorous stirring at 45°, over a period of twenty minutes, 310.8 g. (2.67 moles, 10% excess) of thionyl chloride. The temperature of the reaction mixture rose to 80° during the addition and stirring was continued at this temperature for a further ten minutes. After cooling to room temperature the reaction mixture was extracted three times using 500, 400 and 300 cc. of ether, respectively. The extract was neutralized with sodium carbonate, and filtered, and the pyridine, ether and excess thionyl chloride removed at 100° (10 mm.). The residual oil on vacuum distillation yielded 245 g. (77%) of hexaoxyethylene glycol dichloride as a colorless liquid: b. p. 168–169° (0.100 mm.); f. p. −12.4°.

Anal. Calcd. for $Cl(CH_2CH_2O)_5CH_2CH_2Cl$: Cl, 22.26; mol. wt., 319. Found: Cl, 22.20, 22.34; mol. wt. (cryoscopic), 310.

Synthesis of Octadecaoxyethylene Glycol, $HO(CH_2CH_2O)_{18}H$.—Hexaoxyethylene glycol (230 g., 0.817 mole) was placed in a flask and covered with a layer of petroleum ether (b. p. 100–110°) and then, at room temperature, potassium metal (21.8 g., 0.56 mole) added in the form of small pieces. After stirring for fifteen hours at room temperature, this gradually was raised to 65° to complete the potassium salt formation. Hexaoxyethylene glycol dichloride (97.6 g., 0.306 mole, 10% excess) was then added, with stirring, at 135° over a two-hour period. After stirring at 175° for a further five hours, the reaction mixture was neutral to phenolphthalein. The precipitated potassium chloride was removed by filtration and the filtrate distilled at a bath temperature of 265° (0.010 mm.) using a Claisen flask immersed to the side-arm.

The residual oil was then continuously extracted with ether (500 cc.) for three to four days. Methanol was added at room temperature to the ether extract until the glycol which had separated during extraction just dissolved. This solution was now decolorized by stirring for two hours with charcoal, filtered, the clear solution cooled to −11° and allowed to stand overnight at this temperature. The crude crystalline product was filtered, washed with anhydrous ether, then transferred to a flask and warmed gently with about 750 cc. of anhydrous ether. Most of the glycol remained undissolved and just sufficient anhydrous methanol was added (approx. 165 cc.) to effect its complete solution. Crystallization again was brought about by cooling at −11°. This recrystallization process was repeated six or seven times under the same conditions and with the same volumes of solvents until the freezing point of the final product remained constant: yield 113 g. (50.3%); f. p. 23.8°.

Preparation of Octadecaoxyethylene Glycol Dichloride.—Octadecaoxyethylene glycol (5.04 g., 0.00623 mole) was dissolved in pyridine (3.96 g.); to this was added, dropwise, thionyl chloride (1.92 g., 0.0161 mole, 30% excess) and the mixture stirred at 65° for three hours. The reaction mixture was then extracted with four 25-cc. portions of ether, solid sodium bicarbonate added to the combined extracts and the mixture allowed to stand until neutral. After filtration, the filtrate was distilled at 0.0025 mm. to a temperature of 175° to remove lower boiling constituents. The residual oil was dissolved in ether, decolorized with charcoal and then recrystallized three times at −80° from pure ether: yield 2.02 g. (38.5%), white crystalline solid; f. p. 22.9°.

Anal. Calcd. for $Cl(CH_2CH_2O)_{17}CH_2CH_2Cl$: Cl, 8.38. Found: Cl, 8.51, 8.50.

Synthesis of the Dotetracontaoxyethylene Glycol, $HO(CH_2CH_2)_{42}H$.—Octadecaoxyethylene glycol (141.2 g., 0.1745 mole) was placed in a three-necked flask, fitted with mercury seal stirrer and nitrogen inlet tube and covered with a layer of petroleum ether (b. p. 100–110°). Potassium metal (6.83 g., 0.1745 mole) previously weighed and cut into small pieces under anhydrous petroleum ether (b. p. 50°) was introduced in one addition to the stirred mixture at room temperature and the stirring maintained for about seventeen hours. The temperature was now gradually raised, over the following three-hour period to 135°, and the mixture stirred at this temperature for a further two hours to complete the potassium salt formation. Hexaoxyethylene glycol dichloride (30.6 g., 0.0958 mole, 10% excess) was now added at 135° with stirring during some fifteen minutes and after a further period of stirring for seventeen hours at the same temperature the reaction mixture reacted neutral to phenolphthalein. Filtration while still warm removed the precipitated potassium chloride and the filtrate was then continuously extracted with ether (250 cc.) for three days. Anhydrous methanol, about 40 cc., was then added at room temperature to the ether extract until the oily glycol, which had separated out during the extraction process, just dissolved. The mixture was cooled in a

TABLE I

PHYSICAL CONSTANTS OF POLYOXYETHYLENE GLYCOLS AND THEIR DICHLORIDES

Substance	Appearance	Refr. index, $n^{60°}D$	Density, $d_4^{60°}$	F. p., °C.	Mol. wt. Calcd.	Mol. wt. Obsd.	Mol. refr. index Calcd.[a]	Mol. refr. index Obsd.
Hexaoxyethylene glycol	Colorless liquid	1.4500	1.0948	2.1	282	289	68.881	69.22
Hexaoxyethylene glycol dichloride	Colorless liquid	1.4510	1.1307	−12.4	319	311	75.565	75.97
18-Membered oxyethylene glycol	White crystalline solid	1.4550	1.0949	23.8	810	803	199.431	200.7
18-Membered oxyethylene glycol dichloride	White crystalline solid	1.4560	1.1060	22.9			206.115	208.2
42-Membered oxyethylene glycol	White crystalline solid	1.4563	1.0951	33.8	1866	1748	460.526	463.7
42-Membered oxyethylene glycol dichloride	White crystalline solid	1.4564	1.1001	33.4			467.209	461.4

[a] Calculations are based on the atomic values suggested by Auwers and Eisenlohr, *Ber.*, **43**, 806 (1910).

brine-bath (−11°) and the crude glycol crystallized out. It was filtered, washed with anhydrous ether, then recrystallized from a mixture of 600 cc. of ether and just enough anhydrous methanol (*ca.* 155 cc.) to effect a solution of the glycol, and again recrystallized by cooling. After six or seven such crystallizations to constant freezing point, the pure 42-membered oxyethylene glycol was obtained: yield 113 g. (47% of theoretical); mol. wt. calcd. 1866, found (cryoscopic) 1748; f. p. 33.8°.

Preparation of the Dotetracontaoxyethylene Glycol Dichloride, $Cl(CH_2CH_2O)_{41}CH_2CH_2Cl$.—The 42-membered oxyethylene glycol (4.35 g., 0.00233 mole) was dissolved in 5 cc. of pyridine and to this was added, dropwise, thionyl chloride (0.722 g., 0.00607 mole, 30% excess). The mixture was stirred for two and one-half hours at 65° and the reaction mixture then extracted with six 400-cc. portions of ether. Any acid present was removed by adding solid sodium bicarbonate to the combined ether extracts and allowing to stand for one and one-half hours. After filtration, the ether, thionyl chloride and pyridine were removed at 100° (10 mm.). The residual oil was recrystallized three times from about 50 cc. of ether and gave 1.25 g. (28.1% of theoretical) of a white crystalline solid; f. p. 33.4°.

Anal. Calcd. for $Cl(CH_2CH_2)_{41}CH_2CH_2Cl$: Cl, 3.72. Found: Cl, 3.69, 3.71.

Physical Properties and Constants of the Polyoxyethylene Glycols and their Dihalides.—Refractive indices were measured by means of an Abbe refractometer fitted with compensating prisms. Birefringence was observed with this instrument with the 18- and 42-membered oxyethylene glycols at a temperature 1° below their freezing points.

The freezing points ("setting" points) have been reported for these compounds rather than melting points because the former are known in general to be much more reproducible than the latter.[11] With the glycols investigated they were found to be reproducible to ±0.1°.

The molecular weight values were determined cryoscopically in a standard Beckmann freezing-point apparatus, access of moisture to the solutions being prevented by a slow stream of dry air directed into the side-arm of the cryoscopic tube. For the 6-membered glycol and its dichloride, as well as for the 18-membered glycol, carbon tetrachloride (cryoscopic constant, 29) was used as solvent; for the 42-membered glycol, pure, dry dioxane[12] (K = 4.8) in which the polyglycols are not associated,[4] was employed. The results given are the average in each case of several determinations at concentrations in the range 0.07 to 1 mole per cent.

Density measurements were carried out by using a small specific gravity bottle (volume 1.8 cc.), having a removable ground-in capillary and cap. The temperature of the bath used in these measurements was maintained constant to within ±0.02°.

The reproducible time–temperature cooling curves were obtained by using an alcohol thermometer of low heat capacity and reading to ±0.01°. This was immersed in 5 cc. of the sample contained in a suitably lagged test-tube surrounded by a cooling bath maintained about 8° below the freezing point of the sample. In Fig. 2 cooling curves for both pure hexaoxyethylene glycol and for a mixture of this with 2.5 moles of diethylene glycol are shown. Figure 3 shows the cooling curve for the 18-membered oxyethylene glycol and also that of a polymeric mixture of glycols, freezing point 26.0°, which had been obtained by the fractionation procedure outlined by Staudinger. The effect of a 6.12 mole per cent. addition of the 18-membered ethylene glycol to the 42-membered glycol upon the cooling curve is shown in Fig. 4, while Fig. 5 shows the complete distortion produced when 24 mole per cent. impurity is added.

In conclusion, the authors wish to express their indebtedness to Dr. J. C. Pullman for preliminary experimental work in connection with this method of synthesis.

Summary

1. The syntheses and properties of pure straight chain polyoxyethylene glycols of the general formula $HO(CH_2CH_2O)_nH$, where n = 6, 18 and 42, are described.

2. The purity of these compounds was established by the time–temperature cooling

(11) Frances and Collins, *J. Chem. Soc.*, 137 (1936).

(12) Eigenberger, *J. prakt. Chem.*, [2] **130**, 75 (1931).

curve method and supported by cryoscopic molecular weight determinations and analysis of the dichlorides.

MONTREAL, CANADA RECEIVED MAY 1, 1939

[CONTRIBUTION FROM THE DIVISION OF INDUSTRIAL AND CELLULOSE CHEMISTRY, MCGILL UNIVERSITY]

Studies on Reactions Relating to Carbohydrates and Polysaccharides. LVII. The Synthesis of 90-Membered Oxyethylene and 186-Membered Oxyethylene Glycols[1]

BY REID FORDYCE[2] AND HAROLD HIBBERT

The Williamson ether synthesis described previously[3] has been used to synthesize further higher members of the polyoxyethylene glycol series, namely, the 90-membered and the 186-membered polyoxyethylene glycols $HO(CH_2CH_2O)_{90}H$ and $HO(CH_2CH_2O)_{186}H$, respectively.

These were synthesized by reaction of 2 moles of the respective monosodium salts of 42- and 90-membered oxyethylene glycols with one mole each of the 6-membered oxyethylene glycol dichloride.

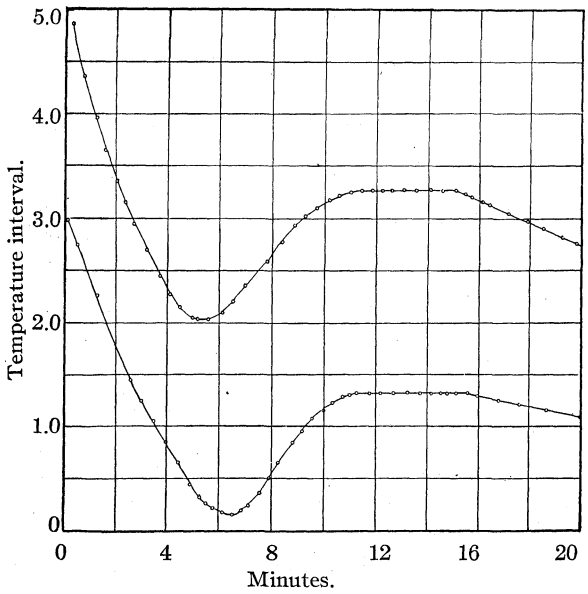


Fig. 1.—Time–temperature cooling curves of (a) 186-membered oxyethylene glycol (upper); (b) 90-membered oxyethylene glycol (lower).

Chlorine could not be detected in either of the isolated reaction products and their refractive indices gave the values to be expected for such higher members of this series.

Their purity was shown by the constancy of the freezing point following several recrystallizations. A further series of recrystallizations was carried out on the pure glycols and, while the final product represented only about 60% of the starting material, it was found that the freezing point of initial and final products was the same. Additional evidence of the purity of the 90- and 186-membered oxyethylene glycols was found in their time–temperature cooling curves (Fig. 1).

The preparation of derivatives of the two glycols suitable for end-group molecular weight determinations proved impracticable because the solubility and other physical characteristics of such derivatives were found to parallel those of the corresponding glycols so closely, even when large groups were attached, that their isolation in the pure state was rendered almost impossible.

Cryoscopic molecular weights, also, could not be employed as they had no significance due to the difficulty in measuring accurately the small freezing-point depression in question.[4]

The method of synthesis of the glycols together with the evidence of their purity, as shown by their physical properties, is strong evidence for the establishment of their molecular weights. Furthermore, the freezing points are shown to vary in a regular manner with the molecular weight and in ascendancy with a relationship developed by Lovell and Hibbert.[5]

The solubility characteristics of 90- and 186-membered glycols are the same as those of the lower members of the series. One of the most outstanding properties of these long chain compounds is their ready solubility in common solvents.

The birefringence observed[3] with the lower members of this series is shown in the photomicrograph

(1) Paper presented at the Baltimore meeting of the American Chemical Society, April, 1939.

(2) Holder of a Bursary and Studentship from the National Research Council of Canada, 1937–1939.

(3) Fordyce, Lovell and Hibbert, THIS JOURNAL, **61**, 1905 (1939).

(4) An investigation of the determination of the molecular weights of the polyoxyethylene glycols by the "spinning top" method is being carried out by Professor McBain, Stanford University, and it is our intention to obtain supporting evidence from osmotic pressure measurements.

(5) Lovell and Hibbert, THIS JOURNAL, **61**, 1916 (1939).

of the extinction cross produced through crossed nicols by a thin film of 90-membered oxyethylene glycol when allowed to cool slowly. A similar effect has also been observed by Staudinger, Staudinger and Sauter[6] for higher molecular weight polyethylene oxides.

Experimental Part

The operations were carried out by the method described previously[3] and the same precautions taken to ensure purity and freedom from moisture of the necessary reagents. Because of the very small amounts of sodium required to form the sodium salts of the 42- and 90-membered polyoxyethylene glycols, respectively, it was necessary to carefully free these glycols from all trace of water prior to use. This was accomplished by passing a very fine stream of dry air through the glycol at 100° at a pressure of 0.010 mm. After four hours of this treatment the glycol was moisture free. The vacuum was then broken by admitting, very carefully, dried oxygen-free nitrogen and an atmosphere of the gas maintained in the flask throughout the sodium salt formation and the ensuing reaction with the dichloride.

Synthesis of the 90-Membered Oxyethylene Glycol, $HO(CH_2CH_2O)_{90}H$.—42-Membered oxyethylene glycol (20.0 g., 0.0108 mole) was placed in a 50-cc. side-arm distilling flask and dried as described above. Metallic sodium (0.25 g., 0.0108 mole), which had been cut and weighed under petroleum ether (b. p. 30–50°), was added in one addition at 80° to the glycol, kept under a nitrogen atmosphere. The reaction mixture was stirred by a mercury seal type of stirrer and a slow stream of nitrogen was kept flowing constantly through the side arm. After stirring for eleven hours at 80° the temperature was raised during two hours to 135° and then stirred at this temperature for a further three hours to complete the sodium salt formation. Hexaoxyethylene glycol dichloride (1.91 g., 0.006 mole, 10% excess) was then added at 135°, dropwise, to the glycol solution of the sodium during a twenty-five minute period and stirring continued for a further nineteen hours until the solution reacted neutral to phenolphthalein.

The reaction mixture was cooled, mixed with four volumes of dioxane, centrifuged and, after decanting from the precipitated potassium chloride, the dioxane removed at 100° (0.15 mm.).

The residual oil was dissolved in 100 cc. of methanol, 350 cc. of ether added and then decolorized by stirring for four hours with charcoal (3 g.). After filtration, the crude crystalline glycol was obtained by cooling to −11° in a brine-bath. The product was filtered, washed with anhydrous ether, redissolved in a mixture of methanol (100 cc.) and ether (350 cc.) and recrystallized at −11°.

Repeated recrystallizations under the same conditions to constant freezing point gave the pure 90-membered oxyethylene glycol (8.0 g., 36.7%); f. p., 40.6°; $n^{60°}D$ 1.4570.

(6) Staudinger, Staudinger and Sauter, *Z. physik. Chem.*, **B37**, 403 (1937).

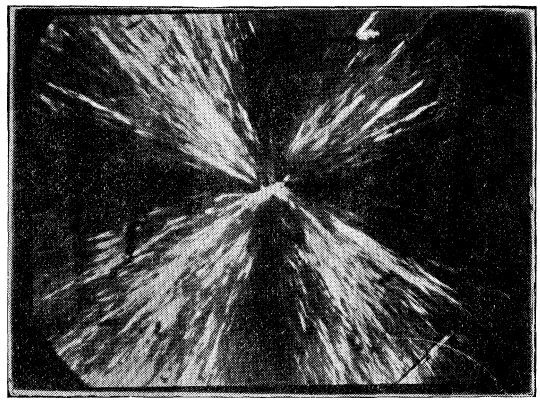


Fig. 2.

Synthesis of 186-Membered Oxyethylene Glycol, $HO(CH_2CH_2O)_{186}H$.—The 90-membered oxyethylene glycol (14.3 g., 0.0036 mole), contained in a 50-cc. side-arm distilling flask, was dried as above under vacuum in a nitrogen atmosphere. Metallic sodium (0.08 g., 0.0035 mole) which had been cut and weighed under petroleum ether (30–50°) was added in one addition at 80°. The reaction mixture was stirred with a mercury seal type of stirrer and a dry nitrogen atmosphere maintained throughout the reaction. After stirring for seventeen and one-half hours at 80° the temperature was raised during one hour to 135° and stirring continued at that temperature for an additional five and one-half hours to complete the sodium salt formation. Hexaoxyethylene glycol dichloride (0.60 g., 0.00188 mole, 4% excess) was then added dropwise during a period of five minutes and stirring continued at the same temperature for six and one-half hours until neutral (phenolphthalein). The reaction mixture was cooled, dissolved in four volumes of anhydrous dioxane, centrifuged and after decanting from the precipitated potassium chloride the dioxane then removed at 100° (15 mm.).

The residual oil was dissolved in 135 cc. of methanol and 35 cc. of ether added, the solution decolorized by stirring for three hours with charcoal and the crystalline glycol isolated by cooling to −11°. It was filtered, washed with anhydrous ether, then dissolved in methanol (135 cc.), ether (35 cc.) added, and recrystallized again by cooling. After ten or eleven such crystallizations to constant freezing point, pure 186-membered oxyethylene glycol was obtained: yield, 4.72 g. (47% of theoretical); f. p., 44.1°; $n^{60°}D$ 1.4572.

Summary

1. The syntheses of 90-membered oxyethylene glycol, $HO(CH_2CH_2O)_{90}H$, and 186-membered oxyethylene glycol, $HO(CH_2CH_2O)_{186}H$, are described.

2. The time–temperature cooling curves of the recrystallized products serve to indicate their purity.

MONTREAL, CANADA RECEIVED MAY 1, 1939

[CONTRIBUTION FROM THE DIVISION OF INDUSTRIAL AND CELLULOSE CHEMISTRY, MCGILL UNIVERSITY]

Studies on Reactions Relating to Carbohydrates and Polysaccharides. LVIII. The Relation between Chain Length and Viscosity of the Polyoxyethylene Glycols[1]

BY REID FORDYCE[2] AND HAROLD HIBBERT

Introduction

In applying the Staudinger equation, $\eta_{sp.}/c = K_m M$, to the determination of the chain length of polymeric substances or, conversely, as a method of determining its validity, Staudinger[3] has found it necessary to restrict the experimental conditions surrounding its application within certain definite limits based both on theoretical and practical considerations, a fact which many investigators have unfortunately ignored.

In the first instance, the products under investigation must be the members of a polymer homologous series having a straight chain structure and a relatively high molecular weight. That both these requirements are satisfied in the case of the synthetic polyoxyethylene glycol polymers has been shown in previous communications.[4]

In addition, Staudinger considers it advisable, if not actually necessary, to carry out the viscosity measurements in homopolar solvents since only under these conditions are the long chain molecules surrounded by a monomolecular layer of solvent molecules.[5] The applicability of the equation has been further extended recently by Staudinger and Daumiller[6] to include certain heteropolar solvents, as, for example, cellulose in phosphoric acid. In the present investigation only solvents of homopolar character, namely, 1,4-dioxane and carbon tetrachloride, have been employed.

A further and very important factor emphasized by Staudinger is that all viscosity measurements must be made in very dilute solutions. This restriction is based upon his concept of the "sol" and "gel" states of macromolecules in solution and is a point of view emphasized by him repeatedly in numerous publications.[7] The viscosities reported in the present communication are those for "ground molar" solutions (4.4% by weight) of the polyoxyethylene glycols. The viscosities have been determined at three different temperatures, 20, 40 and 60°, in order to show the effect of temperature variation on the validity of the Staudinger relationship connecting specific viscosity and chain length.

Materials and Methods

The synthesis and purification of the polyoxyethylene glycols already have been reported.[4] The triethylene glycol was a commercial product purified by careful fractionation. 1,4-Dioxane was purified according to the method of Eigenberger[8] (f. p. 11.7°). The carbon tetrachloride was allowed to stand over solid potassium hydroxide for three days and then distilled from it, a middle fraction being employed (b. p. 76.5° at 750 mm.).

The viscometer was an Ostwald type instrument constructed according to the specifications given in British Engineering Standards[9] with dimensions corresponding to those for a uniform capillary of diameter 0.493 mm. and having a range of 0.9 to 7.2 cp.

Kinetic energy corrections were not necessary with this instrument since, using water as standard, a value was found for the absolute viscosity of aniline at 20°, agreeing within 0.35% with that obtained by Appleby.[10] Density corrections were not applied to the viscosity measurements of the polyoxyethylene glycol solutions since Staudinger[3] has shown, and confirmation is provided by the authors, that the change in density of such dilute solutions can be neglected. Since the volume of fluid is adjusted within the viscometer itself, no error is introduced by thermal expansion of the fluid or the viscometer.

The temperature of the bath used was kept constant within ±0.02°. Loss of solvent due to volatilization at high temperatures, as well as contamination of the solutions in the viscometer with moisture, was prevented by means of the customary connection joining the upper parts of the two limbs of the instrument.

Discussion of Results

The tabulated specific viscosities of the polyoxyethylene glycols in carbon tetrachloride and dioxane at 20, 40 and 60° are shown in Tables I and II. It can be seen that the curves (Fig. 1) obtained by plotting specific viscosity against molecular weight (or chain length), both in dioxane and carbon tetrachloride and at different tempera-

(1) Paper presented at the Baltimore meeting of the American Chemical Society, April, 1939.

(2) Holder of a Bursary and Studentship under the National Research Council of Canada, 1937–1939.

(3) Staudinger, "Der Aufbau der hochmolekülaren organischen Verbindungen," Verlag von Julius Springer, Berlin, 1932.

(4) (a) Fordyce, Lovell and Hibbert, THIS JOURNAL, **61**, 1905 (1939); (b) Fordyce and Hibbert, *ibid.*, **61**, 1910 (1939).

(5) Staudinger, *Trans. Faraday Soc.*, **29**, 30 (1933).

(6) Staudinger and Daumiller, *Ber.*, **70B**, 2508 (1937).

(7) (a) Staudinger, *Trans. Faraday Soc.*, **30**, 110 (1935); (b) *Ber.*, **68B**, 1682 (1935).

(8) Eigenberger, *J. prakt. Chem.*, **130**, 75 (1935).

(9) British Standard Specification No. 188–1929, British Engineering Standards Association, London, May, 1929.

(10) Appleby, *J. Chem. Soc.*, **127**, 1836 (1925).

TABLE I

VISCOSITIES IN CARBON TETRACHLORIDE

Members in oxyethylene glycol	20° $\eta_{sp.}/c$	20° $K_m \times 10^4$ Staudinger	20° $K_m \times 10^4$ Eq. 1 ($\beta = 0.187$)	40° $\eta_{sp.}/c$	40° $K_m \times 10^4$ Staudinger	40° $K'_m \times 10^4$ Eq. 1 ($\beta = 0.159$)	60° $\eta_{sp.}/c$	60° $K_m \times 10^4$ Staudinger	60° $K'_m \times 10^4$ Eq. 1 ($\beta = 0.121$)
6	0.156	5.52		0.127	4.50		0.097	3.43	
18	.240	2.96	0.64	.199	2.46	0.49	.148	1.83	0.33
42	.275	1.47	.47	.242	1.30	.45	.184	0.98	.34
90	.414	1.04	.57	.343	0.86	.47	.261	.66	.34
186	.678	0.83	.60	.560	.68	.49	.393	.48	.33
		Average	0.57			0.48			0.34

TABLE II

VISCOSITIES IN DIOXANE

Members in oxyethylene glycol	20° $\eta_{sp.}/c$	20° $K_m \times 10^4$ Staudinger	20° $K'_m \times 10^4$ Eq. 1 ($\beta = 0.128$)	40° $\eta_{sp.}/c$	40° $K_m \times 10^4$ Staudinger	40° $K'_m \times 10^4$ Eq. 1 ($\beta = 0.119$)	60° $\eta_{sp.}/c$	60° $K_m \times 10^4$ Staudinger	60° $K'_m \times 10^4$ Eq. 1 ($\beta = 0.095$)
2	0.076	7.16		0.064	6.04		0.047	4.46	
3	.082	5.48		.073	4.86		.056	3.71	
6	.135	4.73		.102	3.63		.083	2.95	
18	.195	2.40	0.67	.179	2.21	0.59	.159	1.96	0.59
42	.239	1.28	.54	.214	1.15	.50	.189	1.01	.43
90	.383	0.96	.61	.351	0.88	.55	.320	0.81	.53
186	.686	0.83	.67	.623	0.76	.60	.597	0.73	.59
		Average	0.62			0.56			0.53

tures, all have the same general shape, namely, a linear form within the molecular weight range 810–8200, and characterized in the lower members of the series by a sharp departure from the linear form.

A curve of the same general type is obtained by plotting the values found by Staudinger for the viscosities of his fractionated polyethylene oxide polymers in dioxane at 20°. The deviations found in the case of the lower members, namely, diethylene-, triethylene- and hexaoxyethylene glycols, from the linear relationship is to be expected, since Staudinger[3] has emphasized repeatedly that the lower members of any polymer homologous series do not obey his viscosity law, which is strictly applicable only to the longer chain molecules of a series. In other words, it is confined to the class of long, linear, thread-like molecules and does not include polymers of low molecular weight whose configuration is not far removed from a spherical shape.

The effect of increase in temperature upon the shape of the $\eta_{sp.}/c$–mol. wt. curve was found to vary in the two solvents. From Table II it can be seen that in dioxane there is only a slight lowering of the specific viscosity value, in other words, K_m changes only slightly with increasing temperature in this solvent. Similar results were also found by Staudinger[3] for dioxane solutions of his polyethylene oxide polymers. In carbon tetrachloride (Table I), on the other hand, there is a considerable decrease in specific viscosity as the temperature is increased. The general shape of

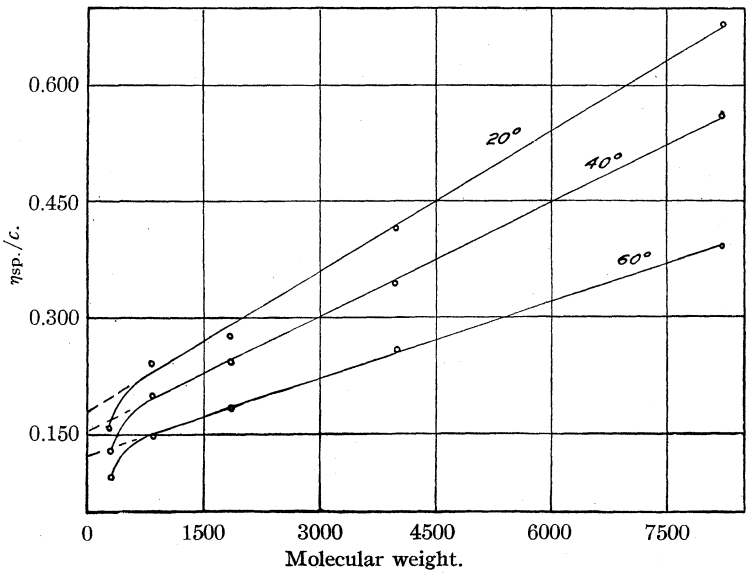


Fig. 1.—The mol. wt.–$\eta_{sp.}/c$ curves for carbon tetrachloride solutions of polyoxyethylene glycols at 20, 40 and 60°.

the specific viscosity–molecular weight curve for polyoxyethylene glycols in carbon tetrachloride is indicated in Fig. 1, as well as the influence of an increase in temperature. This latter effect can be regarded as a desolvation of the solute molecules brought about by an increase in temperature.

Of far greater significance than temperature variation of specific viscosity is the fact that a *linear relationship between specific viscosity and chain length is clearly shown to exist, both in different solvents and at different temperatures.* The validity of the Staudinger viscosity equation has been disputed by Hess and Rabinovitch,[11] Sakurada,[12] Karrer and Ferri,[13] Meyer and Van der Wijk,[14] and many others, but there are presented here, for the first time, viscosity data based on pure, long chain, chemical individuals, and which definitely point to a straight line relationship between specific viscosity and molecular weight in the case of solutions having the same "ground molar" concentration.

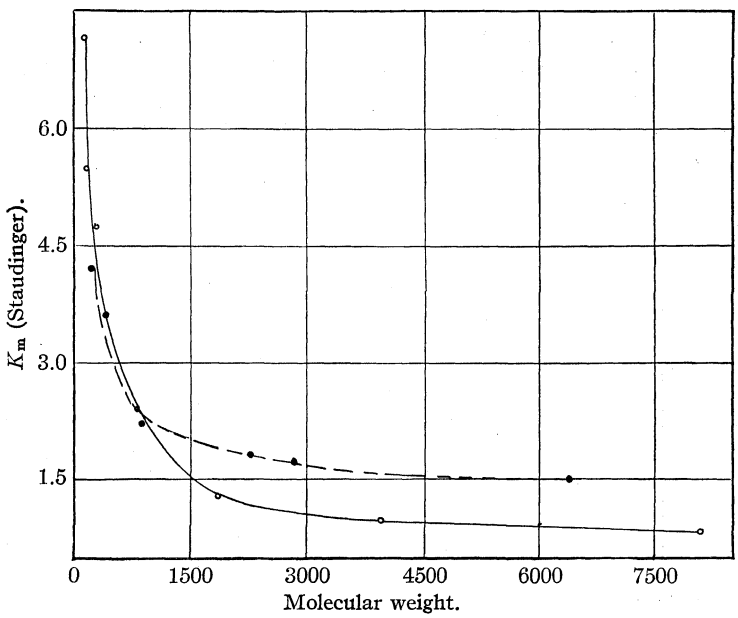


Fig. 2.—Variation of K_m with mol. wt.: (a) pure polyoxyethylene glycols, solid curve ○; (b) Staudinger's polyethylene oxides, broken curve ●.

The Staudinger equation, $\eta_{sp.}/c = K_m M$, which expresses a linear relationship between $\eta_{sp.}/c$ and M, implies a straight line passing through the origin. However, extrapolation of the linear section of the specific viscosity–molecular weight curves obtained from the data presented here, as well as those based on Staudinger's own data for other polymer homologous series, in general, shows an intercept on the specific viscosity axis. In other words, neglecting the lower members of a given series, the new data submitted indicate that the Staudinger equation should be modified as follows

$$\eta_{sp.}/c = K'_m M + \beta \qquad (1)$$

where β is the $\eta_{sp.}/c$ intercept.

The values of K'_m and β, as well as the values of K_m calculated according to the Staudinger equation, are tabulated in Tables I and II. It can be seen that K'_m has a constant value, especially for carbon tetrachloride solutions at 40 and at 60° whereas the Staudinger constant K_m is still only *approaching* a constant value. For higher molecular weights the effect of the $\eta_{sp.}/c$ intercept upon the value of K_m in Staudinger's equation becomes negligible and K_m then has a constant value.

More recently Staudinger and Daumiller[15] have published data concerning the variation of K_m of cellulose triacetates with degrees of polymerization varying from those of the oligosaccharide acetates to the very high molecular weight cellulose acetates. The general trend of the K_m variation in that series is quite similar to that observed in the present investigation of the polyoxyethylene glycols (Fig. 2). It would seem from this that more accurate values for the molecular weight of the lower members of a series, and still within the range of validity of the Staudinger viscosity law, can be obtained by the application of the authors' modified viscosity equation, (1). While it is true that Staudinger[3] also has postulated a similar equation $\eta_{sp.}/c = ny + x$, this is derived from an entirely different concept than the one on which that of the authors is based. Moreover, the application of the above modified Staudinger equation has been confined almost entirely to polymeric homologous forms of hydrocarbon series.

In any interpretation and comparison of the viscosity results obtained with pure polyoxyethylene glycols, it must be remembered that the present results are based on an examination, for

(11) Hess and Rabinovitch, *Ber.*, **65B**, 1407 (1932).
(12) Sakurada, *ibid.*, **67B**, 1045 (1934).
(13) Karrer and Ferri, *Helv. Chim. Acta*, **17**, 358 (1934).
(14) Meyer and Van der Wijk, *ibid.*, **18**, 1067 (1935).
(15) Staudinger and Daumiller, *Ann.*, **529**, 219 (1937).

the first time, of the behavior of pure, homogeneous, individual, long chain polymers, whereas all similar investigations in this field have been carried out on polymers obtained by fractionation of synthetic and natural polymers, and therefore necessarily mixtures. From the form of the Staudinger viscosity equation as well as from consideration of the assumptions involved in its evolution, it readily can be shown that the viscosity-producing influence of extremely long molecules is very great as compared with that exerted by those of shorter chain length. In brief, the solution viscosity of a polymeric mixture is influenced profoundly by the distribution of molecular weights about the mean value. Schulz[16] has derived an equation connecting the value of K_m for a polymer of uniform chain length with that of a polymeric mixture of the same substance, in terms of a defined distribution function. He shows, experimentally, as well as theoretically, that in the case of the polyisobutylene polymers it is possible for the value of K_m of such a polymeric mixture to be double that of a pure polymer of the same series.

In Fig. 2 the variation of K_m with increasing degree of polymerization in the case of the pure polyoxyethylene glycols is compared with that found by Staudinger and Lohmann[3] (p. 287) for polymeric ethylene oxide mixtures. It is readily seen from this that the K_m value for the pure glycol is lower than that of the polymeric mixture of the same average molecular weight. The observed lower K_m values for the uniform polymers are in agreement with the views of Schulz.

Work is in progress in these Laboratories with the object of obtaining a quantitative relationship between these two constants in terms of the distribution function.

Regarding the question of Staudinger's much-discussed "Fadenmolekül" very little can be said concerning the configuration of the polyoxyethylene glycols. Sakurada,[17] Mark[18] and Huggins[19] have demonstrated quite conclusively that there is no *a priori* reason for assuming a rigid stretched-out form of the molecule in order to explain a linear relationship between molecular weight and specific viscosity. The presence of numerous ether linkages in the polyoxyethylene glycols, considering the well-known difference in, and variability of, the oxygen valence angle as compared with carbon,[20] indicates that these compounds probably exist in solution in a convoluted form rather than as rigid rod-like structures.

Summary

1. The solution viscosities of long chain polyoxyethylene glycols have been measured in carbon tetrachloride and dioxane at 20, 40 and 60° and agreement with the Staudinger linear relationship between chain length and $\eta_{sp.}/c$ has been obtained in each case.

2. A slightly modified form of the Staudinger equation, *viz.*, $\eta_{sp.}/c = K'_m M + \beta$, is suggested as a more accurate mathematical expression, especially in the case of the lower members of a given homologous series.

MONTREAL, CANADA RECEIVED MAY 1, 1939

(16) Schulz, *Z. physik. Chem.*, **B32**, 27 (1936).

(17) Sakurada, *Naturwissenschaften*, **25**, 523 (1937).

(18) Mark, "Der feste Körper. Vorträge an der Tagung der Physikalischen Gesellschaft Zürich anlässlich der Feier ihres 50 jährigen Bestehens," S. Hirzel, Leipzig, 1938, p. 65.

(19) Huggins, *J. Phys. Chem.*, **43**, 439 (1939).

(20) Allen and Hibbert, *Ber.*, **65**, 1362 (1932).

[CONTRIBUTION FROM THE DIVISION OF INDUSTRIAL AND CELLULOSE CHEMISTRY, MCGILL UNIVERSITY]

Studies on Reactions Relating to Carbohydrates and Polysaccharides. LIX. The Precipitability of Pure Hemicolloidal Polyoxyethylene Glycols

BY EDWIN L. LOVELL[1] AND HAROLD HIBBERT

Introduction

In a recent communication describing the quantitative precipitation behavior of a polymer homologous series of polystyrenes, G. V. Schulz[2] has investigated a new property of these high molecular products which it is suggested may lead to a new method for the determination of molecular weights of moderately high polymeric substances. This property is the "precipitability (γ)," or relative proportion of a non-solvent which must be added to the solution of a polymer in order to initiate precipitation. Schulz has endeavored to correlate the precipitability of such high polymers with their solubility and degree of polymerization, respectively, and, proceeding on the basis of certain assumptions, has arrived at two equations expressing these relationships

$$\ln c = a - b\gamma \quad (1)$$

$$\gamma^* = \alpha + (\beta/P) \quad (2)$$

where c is the solubility of the polymer in grams per liter, in a mixture of solvents having the composition represented by γ, γ^* is the precipitability expressed as percentage of non-solvent added to bring about precipitation at any particular solubility value, and P the degree of polymerization. The other symbols refer to constants. In the first equation P is regarded as constant, while in the second the solubility c is constant.

Such a mathematical derivation is of great interest to all workers in the field of macro-molecular chemistry, not only from the purely practical point of view, since it would seem to offer a simple and accurate means of molecular weight determination, but also from the theoretical standpoint in that it concerns the solution states of long molecules. However, the only experimental data so far available have been those obtained by Staudinger and Heuer[3] on a single type of polymer, namely, the polystyrenes. Nevertheless Schulz's conclusions, as he has shown, appear to find support in the molecular weight data of these authors, as obtained from viscosity measurements on these same products. In the present case, the solubility and precipitability of four pure, long chain polyoxyethylene glycols, with molecular weights ranging from 1000 to 9000, have been studied in methanol–ether and dioxane–ether mixtures at 0° with a view to determining the general validity of the relations between the variables, postulated by Schulz.

It appears from this work that the relationship between the precipitability and degree of polymerization is not in conformity with the Schulz generalization, but instead follows a simple empirical law which also seems to fit the polystyrene data of Staudinger and Heuer. The relation between precipitability and solubility for these crystalline polyoxyethylene glycol polymers follows the law to be expected in the case of *pure crystalline* substances.

Experimental

The measurements were carried out in a very simple apparatus (Fig. 5), consisting of a removable glass cylinder open at one end and attached, by means of a large ground-glass joint, to a second glass cylinder provided with a pair of side arms into which the delivery ends of two microburets were closely fitted. The first cylinder had a capacity of about 20 ml. of solution. Precautions were taken to avoid entrance of moisture into either the solution undergoing precipitation or the anhydrous solvents contained in the burets. The latter were used without lubricating grease. The apparatus was provided with a suitable stirring arrangement.

The preparation, purification and identification of the pure polyoxyethylene glycols used in this work have been described in previous papers.[4] The solvents used were carefully purified, anhydrous products.

In determining the precipitation point at various concentrations, usually about 0.1–0.4 g. of glycol was weighed into the precipitation cylinder, together with 1–8 g. of solvent. The resulting solution was cooled to 0°, by surrounding it with a large beaker of ice, and then titrated slowly with the non-solvent—observing the solution meanwhile under strong illumination, and with the use of a black background, until minute crystals first became visible. The amount of precipitate at the end-point was always negligible as compared with the amount remaining in solution. This precipitation point could be reproduced to within $\pm 1\%$ or better, the quantity of ether added being obtained by direct weighing, rather than by volume measurement.

(1) Holder of a Bursary under the National Research Council of Canada, 1938–1939.

(2) Schulz, *Z. physik. Chem.*, **A179**, 321 (1937).

(3) Staudinger and Heuer, *Z. physik. Chem.*, **A171**, 129 (1934).

(4) (a) Fordyce, Lovell and Hibbert, THIS JOURNAL, **61**, 1905 (1939); (b) Fordyce and Hibbert, *ibid.*, **61**, 1910 (1939).

The method of determining solubility in mixed solvents by measuring the precipitation concentration has been used both by Brönsted[5] and by Staudinger and Heuer,[3] for high molecular polystyrenes.

The measurements in dioxane solution were carried out in a slightly different manner. Ground-molar solutions (44 mg./cc.) of the glycols in dioxane were made up and in each case a volume of just 2 cc. was placed in a 15-cc. precipitation tube by means of a pipet. Titration with ether was then carried out as described above, but the volume of non-solvent required was read directly from the microburet. Suitable precautions were taken to avoid evaporation of the ether during an experiment.

Treatment and Discussion of Results

In Table I are given the solubility (mg. of glycol per gram of mixed solvent added) and precipitability values for each of the five polyoxyethylene glycols $HO(CH_2CH_2O)_PH$ investigated, using methanol as the solvent and ether as the precipitant. The data are expressed graphically in Figs. 1 and 2. It is seen that in all cases the solubility varies in logarithmic fashion with the precipitability, in agreement with the behavior of the polystyrene polymers.

TABLE I

SOLUBILITY IN METHANOL–ETHER AT 0°

Glycol (P)	γ* %	c (mg./g.)	Log$_{10}$ c
6	90.2	360.0	
	90.9	322.2	
18	86.4	68.0	1.8325
	87.0	52.3	1.7185
	87.8	31.9	1.5038
42	68.4	38.9	1.5894
	68.7	35.6	1.5519
	70.2	24.4	1.3878
	70.8	28.8	1.4597
	71.5	20.4	1.3096
90	42.9	37.3	1.5715
	43.4	34.0	1.5311
	45.1	29.8	1.4744
	45.1	25.3	1.4031
	47.2	19.9	1.2995
186	29.6	32.25	1.5085
	28.3	29.49	1.4697
	26.0	44.19	1.3836
	25.4	17.39	1.2403
	28.4	24.25	1.3847
	22.3	11.27	1.0519
	20.8	8.77	0.9430
	23.8	14.63	1.1652
	23.1	11.20	1.0492

It may be remarked that Brönsted[5] found that the solubility of a very high-molecular polystyrene (mol. wt. 600,000) had no effect on the precipitability at very high dilutions.

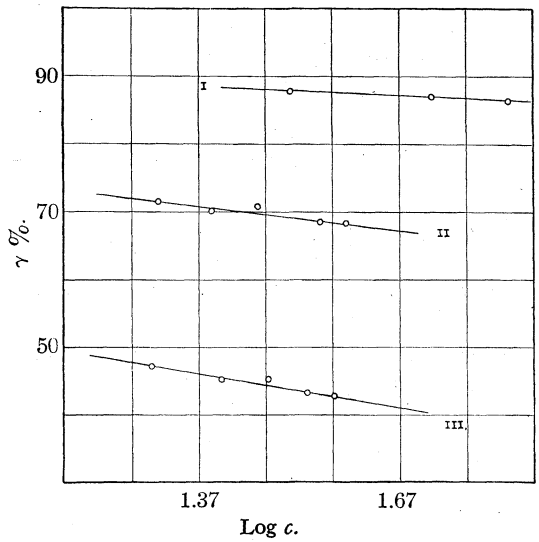


Fig. 1.—The relation between solubility c (mg./gr.) and precipitability in methanol–ether: I, 18-membered; II, 42-membered; III, 90-membered.

Methanol Solutions.—Before considering the effect of degree of polymerization on the precipitability of these glycols at constant solubility, it is necessary to examine the underlying basis of the Schulz equations, (1) and (2). The assumptions made by him in deriving these equations are really adapted to a specific case, namely, that of the high-polymeric polystyrenes or related polymers; they are based on the theory that these products are not precipitable in a purely crystalline form, and on the fact that their melting points are in general high or indeterminable. Neither of these conditions apply to the polyoxyethylene glycols used in the present experiments. There is no doubt as to the crystallinity of the latter when precipitated in the manner described, as has been shown in a previous communication.[4] Furthermore the relatively low setting points (25–45°) of each of these pure glycols have been determined very accurately. It is found that they are in very close agreement with the values derived from the equation

$$t_s = P/(a + bP) \qquad (3)$$

(Fig. 4) where t_s is the setting point in degrees centigrade, P the degree of polymerization and a and b constants having the values of 0.391 and 0.02036, respectively. The equation of Austin[6] connecting the melting points and molecular

(5) Brönsted, *Compt. rend. trav. lab. Carlsberg, sér. chim.*, **22**, 99 (1938).

(6) Austin, THIS JOURNAL, **52**, 1049 (1930).

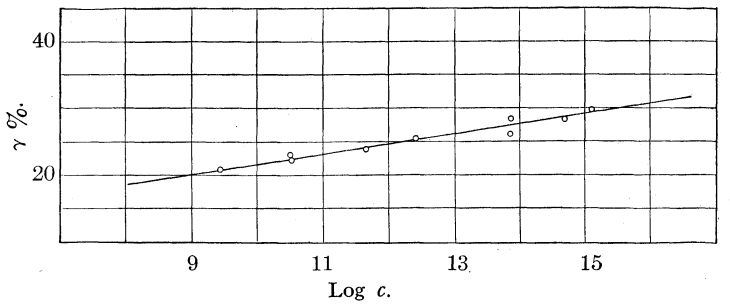


Fig. 2.—Effect of increasing concentration of ether upon the solubility of 186-membered glycol in methanol.

weights of the series of paraffin hydrocarbons, alcohols, etc., is quite inapplicable in the case of these polymer homologous glycols.

It follows that with the pure crystalline products used by the authors it is not necessary to resort to the assumptions and approximations applied by Schulz; instead it is possible to find very simply a theoretical equation connecting the variables—degree of polymerization, precipitability and solubility, of this type of polymer—by applying the thermodynamic solubility equation[7]

$$\ln N_2 = \frac{Q}{RT}\frac{T_s - T}{T_s} \qquad (4)$$

where N_2 is the mole fraction of solute, T_s the absolute melting point and Q the molecular heat of solution. According to Schulz, on the basis of experiments with the polystyrenes

$$Q = P(A' + B'\gamma) \qquad (5)$$

where A' and B' are constants. This may be expected to be a general relation for the heats of solution of polymer homologous substances. For high-molecular substances dissolved in common solvents, it may further be written approximately that

$$N_2 \doteq c/M \qquad (6)$$

where M is the molecular weight of the polymer, nearly a simple multiple of P. Combining equations (3), (4), (5) and (6) gives

$$RT \ln c = RT \ln P + \frac{A'P^2}{a' + b'P} + \frac{B'P^2}{a' + b'P}\gamma \qquad (7)$$

where $a' = 273a$, $b' = 1 + 273b$ and the other symbols and constants have the same values as previously mentioned. For a given polymer (P constant) this last equation becomes identical in form with (1) which is in good agreement with the present experimental data. If c is regarded as constant, the result obviously is not in accord with Schulz's generalization (equation 2), and indeed Table II shows that γ is not a linear function of $1/P$.

The validity of this treatment may be confirmed semiquantitatively by measuring the ratio of the log c–γ slopes for two glycols. The calculated ratio from the coefficient of γ in equation (7) for the 18- and 42-membered glycols is 2.26 (using the empirical constants of equation (3)); the observed ratio is 2.3, in excellent agreement. The slope of this curve for the 90-membered glycol, however, is somewhat less (ratio 1.4) than that calculated in this manner (ratio 1.55), while that of the 186-member is actually negative, over the concentration range 0.9–3.2% (Fig. 2).

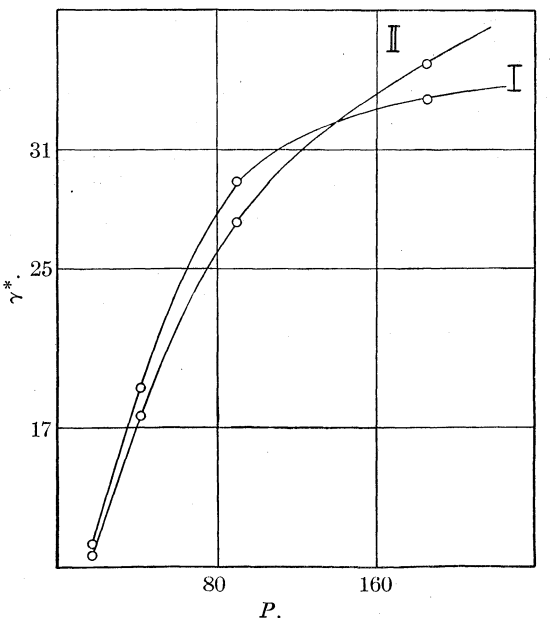


Fig. 3.—Precipitation of the polyoxyethylene glycols at two concentrations: curve II ground-molar (4.4%); I 0.5 ground-molar (2.2%).

TABLE II

PRECIPITATION FROM METHANOL SOLUTIONS

P	γ^* % c = 2.2% (0.5 grd.-molar)	γ^* % c = 2.6% (0.6 grd.-molar)	γ^* % c = 4.4% (1.0 grd.-molar)	$\frac{1000}{P}$
18	88.6	88.2	87.3	55.56
42	71.0	70.2	67.5	23.81
90	46.5	45.2	41.5	11.11
186	26.7	27.9	31.3	5.38

A very careful study of the system methanol–ether which has been made by Sapgir[8] shows that

(7) Hildebrand, "Solubility of Non-electrolytes," Reinhold Pub. Co., New York, N. Y., 1936.

(8) Sapgir, *Bull. soc. chim. Belg.*, **38**, 392 (1929).

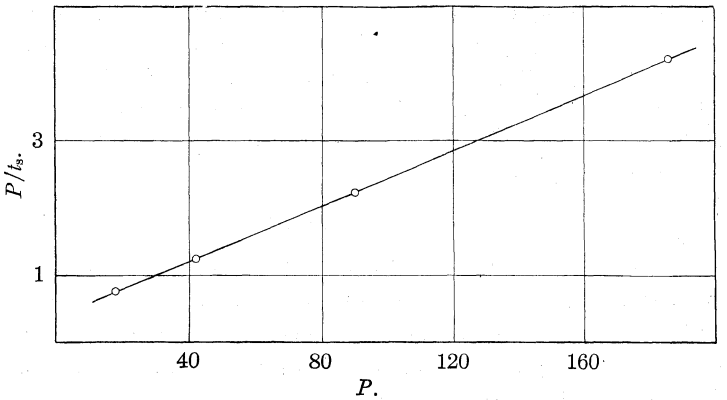


Fig. 4.—Setting points of the polyoxyethylene glycols.

these two solvents do not form mutual complexes, such as might have a complicating effect on the solubility relations of any substance in the mixture. The effect, however, appears to be peculiar to the methanol solutions, for in dioxane solution the 186-membered glycol shows the normal decrease in solubility with increasing proportion of precipitant (Table III). It is not entirely clear, however, why the 186-membered glycol, alone of all the glycols studied, should show this abnormal behavior in methanol.

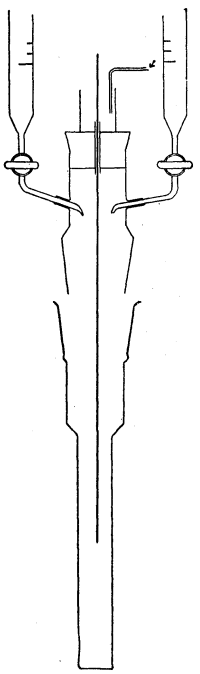


Fig. 5.—Apparatus.

Dioxane Experiments.—These results are given in Table III; here γ_0 is the volume percentage of non-solvent at the end-point when a 4.4% solution of the glycol is titrated. This quantity is shown in Curve I of Fig. 6 to be a direct linear function of the degree of polymerization.

TABLE III

PRECIPITATION OF 4.4% DIOXANE SOLUTIONS

P	10 × vol. Et_2O per cc. initial volume	γ_0, vol. %	c (end-point), mg./cc.
18	2.5	71.4	12.58
42	16	61.5	16.92
90	10.4	51.0	21.58
90	17.1	(63.1)	16.23[a]
186	2.95	22.7	33.99
186	...	(39.2)	20.12[b]

[a] Experiment at 8.6°.
[b] c init. = 33.02 mg./cc.

The characteristic precipitability γ_0 for any polymer differs from the γ^* used above in that the latter quantity is expressed always at the same solubility for the polymeric series, while the solubility value corresponding to γ_0 is necessarily different for each polymer, as of course the volume of the solution being titrated changes with the amount of precipitant which it is necessary to add. To bring the results of the methanol experiments into line with those in dioxane, the data of Table II are recalculated in Table IV in terms of volume percentages; these in turn are readily converted into γ_0 values, also given in the Table. Figure 6 demonstrates that these values also show

TABLE IV

PRECIPITATION OF 4.4% METHANOL SOLUTIONS

P	γ, vol. %	c mg./cc.	γ_0 calcd.
18	88.4	31.80	92.2
	89.7	15.89	
42	69.8	32.46	76.3
	73.3	16.21	
90	44.2	33.44	46.9
	49.2	16.61	
186	33.68	33.80	33.0
	28.86	17.00	

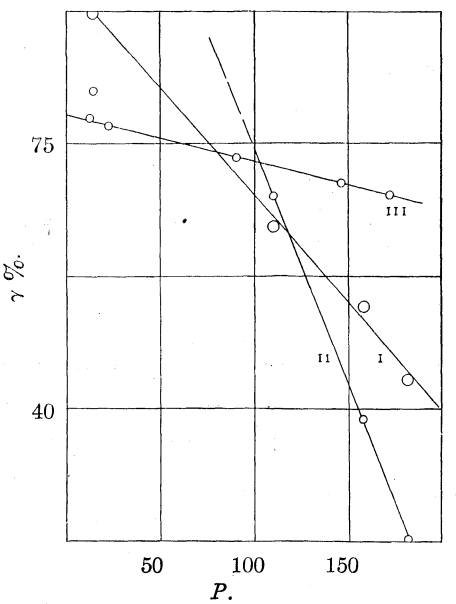


Fig. 6.—Relation between degree of polymerization (P) and precipitability of ground-molar solutions (γ_0): polyoxyethylene glycols, (I) in dioxane–ether; (II) in methanol–ether; polystyrenes[3] (III) in benzene–ethanol (scale m. wt./50).

a linear variation of γ_0 with P although, as might be expected from the result discussed previously, the 186-membered glycol does not fit the curve.

To further establish the validity of this wider generalization, the precipitability results of Staudinger and Heuer[3] for the hemicolloidal polystyrenes are included in Fig. 6. It is obvious from these curves that both types of polymers conform to this simple relationship.

Conclusion.—A point of interest in connection with the above experiments is the significance of the log c–γ slope changes as the higher degrees of polymerization are reached. It is customary to fractionate mixtures of polymer homologous compounds by successive additions of some precipitant to a solution of the mixture, the higher members being first precipitated and followed in order by the lower members as the precipitant concentration is increased.[9]

However, if the concentrations and nature of solvents used are such that the situation expressed in Fig. 3 exists, the results of such a fractionation would be unlikely to lead to the simple separation of high and low members expected. Indeed, the literature contains not a few examples of fractional precipitations which have apparently resulted in the low molecular weight members being precipitated first,[10] but little attention seems to have been paid to this fact. The importance of obtaining as nearly uniform polymers (in chain length) as possible in studies of the macromolecular state points to the advantage and desirability of *quantitative* studies of precipitation and fractionation phenomena.

(9) Schulz, *Z. physik. Chem.*, **B32**, 27 (1936).

(10) See, for example, Okamura, *Cellulosechemie*, **14**, 135 (1933); Glückmann, *Kolloid-Z.*, **76**, 84 (1936).

Summary

1. The relationships between the precipitability, solubility and degree of polymerization of a number of pure long-chain polyoxyethylene glycols have been determined in methanol–ether and dioxane–ether mixtures.

2. For each glycol, the logarithm of the solubility (in per cent.) was found to be a linear function of the percentage of precipitant (ether) in the mixed solvent methanol–ether.

3. An anomalous behavior of the 186-membered glycol, in this respect, is recorded, and its possible significance for the customary methods of fractionation of higher polymers, especially those of a micro-crystalline character, is pointed out.

4. The experimental results have been compared with those of other authors on polystyrene polymers, and certain theoretical and actual differences indicated. A new generalization relating the precipitability factor to the degree of polymerization is suggested, which brings both these sets of results into general agreement.

MONTREAL, CANADA RECEIVED MAY 3, 1939

NOTES

The Crystal Structure of Synthetic Antimony Trisulfide

BY HAROLD P. KLUG AND G. B. HEISIG

Red (orange) and black varieties of antimony trisulfide have been prepared in various ways from very early times, and likewise occur in nature.[1] The red variety has been regarded as amorphous, while the black variety is crystalline and reported to be identical with the mineral stibnite, Sb_2S_3, except in sp. gr.[1] Stibnite has been investigated by several workers,[2] but no one seems to have reported X-ray observations on the artificial sulfides. Recently we have been interested in the two varieties of antimony trisulfide as prepared in the laboratory, and have examined them with X-rays. The results are in accord with earlier observations by other methods, and we report them primarily as a matter of record.

Red antimony trisulfide was prepared by passing a current of hydrogen sulfide through a hydrochloric acid solution of antimony trichloride

(1) Mellor, "Comprehensive Treatise on Inorganic and Physical Chemistry," Vol. IX, Longmans, Green and Co., New York, 1929, p. 512.

(2) See for example: Gottfried, *Z. Krist.*, **65**, 428 (1927); Gottfried and Lubberger, *ibid.*, **71**, 257 (1929); Hoffmann, *ibid.*, **86**, 225 (1933).

containing tartaric acid. The red variety was converted into the black variety by heating at 115°.

X-Ray powder photographs were taken at room temperature using CuK and FeK radiation. The above red product, and a sample of the red sulfide from Kahlbaum, both gave photographs showing absolutely no evidence of a crystalline nature. The black variety prepared above gave a pattern identical with that of stibnite, both as to position and intensity of the lines, indicating that there could be little if any amorphous material in the product.

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RECEIVED MAY 26, 1939

Sulfonic Acid Esters of 4,4′-Dihydroxydiphenyl

BY STEWART E. HAZLET

In connection with some other work in progress in this Laboratory a number of aryl sulfonic acid esters of 4,4′-dihydroxydiphenyl have been prepared. The method of preparation used was the same as that previously reported[1] except that the phenol (5 g.) was treated with 2.1 molecular proportions of the necessary acid chloride. The crystalline products were colorless except in the case of the *m*-nitrobenzenesulfonate, which was obtained as tan flakes. Of the esters, the benzene- and the *o*-nitrobenzenesulfonyl derivatives are best suited for use as derivatives for the identification of the phenol, for they are the ones most readily purified. The experimental results are summarized in Table I.

TABLE I

SULFONIC ACID ESTERS OF 4,4′-DIHYDROXYDIPHENYL

Sulfonyl chloride used	Solvent	Yield,[a] %	M. p., °C.	Formula	Analyses, % Calcd.	Found
Benzene	*n*-PrOH	89	148	$C_{24}H_{18}O_6S_2$	S, 13.73	13.97
p-Toluene	*n*-PrOH	Quant.	187–188[b]	$C_{26}H_{22}O_6S_2$		
o-Nitrobenzene	Gl. AcOH	Quant.	191–192	$C_{24}H_{16}O_{10}N_2S_2$	S, 11.51	11.93
m-Nitrobenzene	Cyclohexanol	Quant.	216–217	$C_{24}H_{16}O_{10}N_2S_2$	S, 11.51	11.51
p-Nitrobenzene	1,4-Dioxane	87	231	$C_{24}H_{16}O_{10}N_2S_2$	S, 11.51	11.44
p-Bromobenzene	[c]	Quant.	201–202	$C_{24}H_{16}O_6Br_2S_2$	Br, 25.64	25.98

[a] Crude product. [b] This compound was prepared by Gilman, Beaber and Myers [THIS JOURNAL, **47**, 2047 (1925)] by treating the phenol with the acid chloride in the presence of potassium hydroxide. Benzene was used for crystallization and a product melting at 189–190° was obtained in 21.2% yield. [c] The compound was first dissolved in acetone and then precipitated by the addition of water; it was purified by crystallization from cyclohexanol and finally by washing with ethanol.

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STATE COLLEGE OF WASHINGTON
PULLMAN, WASHINGTON

RECEIVED MAY 8, 1939

(1) Hazlet, THIS JOURNAL, **59**, 287 (1937).

Sterols. LXVII. Sarsasapogenin Derivatives. Bromo Compounds

BY RUSSELL E. MARKER AND EWALD ROHRMANN

In a preceding paper[1] of this series the reaction of sarsasapogenin acetate with bromine to yield a monobromo derivative of the composition $C_{29}H_{45}O_4Br$ was described. We have made several additional observations which are of interest concerning the nature of the bromo compounds.

The great ease of bromination of sarsasapogenin and its derivatives is exemplified by the fact that sarsasapogenone reacts with one mole of bromine to give a compound which is identical with the compound formed when bromosarsasapogenin is oxidized at 25° with chromic anhydride.

The bromo compounds are peculiar in that they appear to be unaffected by boiling with pyridine or by treatment with pyridine and silver nitrate in the cold. The bromine is, however, easily eliminated by other reactions. Catalytic hydrogenation of bromosarsasapogenin acetate in hot acetic acid followed by hydrolysis gave a rather poor yield of dihydrosarsasapogenin.[1] Treatment of bromosarsasapogenin acetate with sodium and amyl alcohol gave a good yield of sarsasapogenin. Similar results were obtained with sodium and ethanol. Treatment of bromosarsasapogenin acetate with zinc dust and acetic acid gave sarsasapogenin acetate. Attempts to hydrolyze the bromo compounds with potassium acetate were unsuccessful, non-crystalline mixtures being obtained. Bromosarsasapogenin, upon Clemmensen reduction in alcohol solution with amalgamated zinc, gave a good yield of tetrahydrosarsasapogenin.

We wish to thank Parke, Davis and Company for their generous support and assistance in the various phases of this work.

(1) Marker and Rohrmann, *ibid.*, **61**, 846 (1939).

Experimental Part

Bromosarsasapogenin.—A solution of 820 mg. of sarsasapogenin in 50 cc. of glacial acetic acid was cooled to 20°. Two drops of 48% hydrobromic acid was added and 2.1 cc. of 1.05 *M* bromine in acetic acid solution run in dropwise. The bromine was taken up readily with the liberation of hydrogen bromide. The mixture was poured into water and the precipitated solid collected and washed with water. The residue was crystallized from aqueous acetone to give white needles which began to decompose at about 125°.

Anal. Calcd. for $C_{27}H_{43}O_3Br$: C, 65.4; H, 8.8. Found: C, 65.1; H, 8.8.

In carrying out the bromination of sarsasapogenin derivative on a somewhat larger scale (5–10 g.) the reaction mixture often became deep blue in color.

Bromosarsasapogenone from Bromosarsasapogenin.—To a solution of 100 mg. of bromosarsasapogenin in 50 cc. of glacial acetic acid was added 300 mg. of chromic anhydride in 10 cc. of 80% acetic acid. After standing at room temperature for forty minutes the mixture was poured into water, the precipitated material was extracted with ether and the ethereal extract washed with sodium carbonate solution and water. The ether was evaporated on the steam-bath and the residue crystallized from acetone to give pale tan crystals, m. p. 191° dec. This gave no depression with a sample of bromosarsasapogenone prepared by the direct bromination of sarsasapogenone.

Anal. Calcd. for $C_{27}H_{41}O_3Br$: C, 65.7; H, 8.4. Found: C, 65.3; H, 8.3.

Bromination of Sarsasapogenone.—Sarsasapogenone was treated with bromine as described in the preceding experiments. The material was crystallized from acetone to give white crystals, m. p. 190° dec. The material evidently was contaminated with some of the dibromo compound as is shown by the analysis. The material gave no depression with the product obtained in the preceding experiment.

Anal. Calcd. for $C_{27}H_{41}O_3Br$: C, 65.7; H, 8.4. Found: C, 65.1; H, 8.0.

Reduction of Bromosarsasapogenin Acetate. (a) **With Zinc and Acetic Acid.**—To a solution of 500 mg. of bromosarsasapogenin acetate in 50 cc. of glacial acetic acid heated on the steam-bath was added with shaking 3 g. of zinc dust in small portions over a period of twenty minutes. White crystals had separated out at the end of this time. The mixture was poured into water and extracted with ether. The ethereal extract was washed first with sodium carbonate solution and then with water. Evaporation of the ethereal solution gave a crystalline residue which was crystallized from acetone to give white needles, m. p. 142°; yield 250 mg. This gave no depression with an authentic sample of sarsasapogenin acetate. The mother liquors yielded some unchanged bromosarsasapogenin acetate.

(b) **With Sodium and Amyl Alcohol.**—To a boiling solution of 700 mg. of bromosarsasapogenin acetate in 50 cc. of *n*-amyl alcohol was added 2.5 g. of sodium in small pieces over a period of two hours. The mixture was cooled and shaken first with an excess of dilute hydrochloric acid and then with water. The amyl alcohol was evaporated on the steam-bath and the residue, after treatment with Norite, was crystallized from acetone to give white needles of sarsasapogenin, m. p. 197°, which gave no depression with an authentic sample.

Similar results were obtained with sodium and absolute ethanol.

(c) **By Catalytic Hydrogenation.**—A mixture of 1 g. of bromosarsasapogenin acetate, 0.5 g. of Adams catalyst, and 80 cc. of glacial acetic acid was shaken with hydrogen at 3 atmospheres and 70° for eight hours. The mixture was filtered and the filtrate evaporated *in vacuo*. The oily residue was diluted with water and the mixture extracted with ether. The ethereal solution was washed with water and the ether evaporated. The residue would not crystallize; it was refluxed for fifteen minutes with an excess of alcoholic potassium hydroxide, poured into water and extracted with ether. The ethereal extract was washed with water and the ether evaporated on the steam-bath. The residue was crystallized from ether–pentane to give white needles, m. p. 163°. This gave no depression with a sample of dihydrosarsasapogenin. The yield was rather poor and the mother liquors contained brominated products.

Anal. Calcd. for $C_{27}H_{46}O_3$: C, 77.4; H, 11.1. Found: C, 77.3; H, 11.2.

(d) **By Clemmensen Reduction.**—Reduction of 500 mg. of the bromoacetate by the Clemmensen method, as described in a previous paper for sarsasapogenin acetate gave a product which crystallized from acetone as compact white crystals, m. p. 191°; yield 375 mg. This gave no depression with an authentic sample of tetrahydrosarsasapogenin, m. p. 193°.

(e) **Treatment with Pyridine.**—Treatment of bromosarsasapogenin acetate with boiling pyridine for twelve hours did not remove the bromine. Treatment with pyridine and silver nitrate at 25° for twenty-four hours was likewise without effect on the substance.

Dibromosarsasapogenone.—To a solution of 7 g. of sarsasapogenone in 350 cc. of glacial acetic acid was added 5 drops of 48% hydrobromic acid and 33.8 cc. of 1.05 *M* bromine in glacial acetic acid was slowly run in over a period of forty minutes at room temperature. The solution became intensely blue and much hydrogen bromide was liberated. The solution was poured into 2 liters of water and the precipitate collected and washed with water. The dried material was crystallized from acetone–ethyl acetate to give small compact white crystals, m. p. 190° dec.

Anal. Calcd. for $C_{27}H_{40}O_3Br_2$: C, 56.7; H, 7.1. Found: C, 57.2; H, 7.3.

SCHOOL OF CHEMISTRY AND PHYSICS
THE PENNSYLVANIA STATE COLLEGE
STATE COLLEGE, PENNA. RECEIVED APRIL 1, 1939

Sterols. LXVIII. Highly Branched Aliphatic Esters of Estrone and α-Estrodiol

BY RUSSELL E. MARKER AND EWALD ROHRMANN

The trimethylacetates and the *t*-butylacetates of estrone and α-estrodiol were prepared by the

reaction of these compounds with the corresponding acid chlorides in pyridine. Catalytic hydrogenation of the estrone derivatives in neutral medium yielded the mono esters of α-estrodiol. Estrone *t*-butylacetate was also prepared by the Schotten–Baumann procedure. The esters prepared appear to be somewhat more soluble than are many of the other well known esters of these substances.

We wish to thank Parke, Davis and Company for their generous help and assistance in the various phases of this work.

Experimental Part

Estrone Trimethylacetate.—To a solution of 300 mg. of estrone in 12 cc. of dry pyridine was added 1 cc. of trimethylacetyl chloride. The resulting mixture, after standing at room temperature for thirty-six hours, was diluted with water and the precipitated solid taken up in ether. The ethereal extract was washed with dilute hydrochloric acid and dilute sodium carbonate solution. Evaporation of the ether gave white needles which was recrystallized from acetone–methanol as thick white needles, m. p. 164–166°.

Anal. Calcd. for $C_{23}H_{30}O_3$: C, 77.9; H, 8.5. Found: C, 77.6; H, 8.3.

α-Estrodiol-3-trimethylacetate.—A mixture of 200 mg. of estrone trimethylacetate, 300 mg. of Adams catalyst, 50 cc. of ether and 50 cc. of ethanol was shaken with hydrogen at 1 atmosphere pressure at room temperature for eighteen hours. The mixture was filtered and the filtrate evaporated *in vacuo*. The residual sirup was treated with Norite and crystallized from aqueous methanol as white needles, m. p. 178–180°.

Anal. Calcd. for $C_{23}H_{32}O_3$: C, 77.5; H, 9.0. Found: C, 77.7; H, 9.0.

α-Estrodiol-3,17-*bis*-trimethylacetate.—A mixture of 100 mg. of α-estrodiol, 10 cc. of pyridine and 0.5 cc. of trimethylacetyl chloride was treated as described for the preparation of estrone trimethylacetate. The product was crystallized from acetone–methanol as white needles, m. p. 174–176°.

Anal. Calcd. for $C_{28}H_{40}O_4$: C, 76.3; H, 9.15. Found: C, 76.0; H, 9.2.

Estrone *t*-Butylacetate.—Estrone *t*-butylacetate was prepared by the pyridine method as described for estrone trimethylacetate. The product was crystallized from methanol as white plates, m. p. 148–150°.

Anal. Calcd. for $C_{24}H_{32}O_3$: C, 78.2; H, 8.7. Found: C, 78.1; H, 8.6.

To a solution of 50 mg. of estrone in 150 cc. of 10% aqueous potassium hydroxide was added 1 cc. of *t*-butylacetyl chloride. The mixture was shaken vigorously for five minutes, and the solid collected, washed and dried. The product crystallized from methanol as white plates, m. p. 147.5–149.5°. This gave no depression with that prepared above.

α-Estrodiol-3-*t*-butylacetate.—This was prepared as described for α-estrodiol-3-trimethylacetate. The product was crystallized from aqueous methanol as white needles, m. p. 127–129°.

Anal. Calcd. for $C_{24}H_{34}O_3$: C, 77.8; H, 9.2. Found: C, 78.1; H, 9.4.

α-Estrodiol-3,17-di-*t*-butylacetate.—This was prepared from α-estrodiol as described for α-estrodiol-3,17-*bis*-trimethylacetate. The product was crystallized from methanol as white plates, m. p. 98–100°.

Anal. Calcd. for $C_{30}H_{44}O_4$: C, 76.9; H, 9.5. Found: C, 76.9; H, 9.5.

SCHOOL OF CHEMISTRY AND PHYSICS
THE PENNSYLVANIA STATE COLLEGE
STATE COLLEGE, PENNA. RECEIVED APRIL 28, 1939

COMMUNICATIONS TO THE EDITOR

THE ANTIHEMORRHAGIC ACTIVITY OF CERTAIN NAPHTHOQUINONES

Sir:

We have briefly reported on the antihemorrhagic activity of phthiocol, 2-methyl-3-hydroxy-1,4-naphthoquinone, the first completely identified form of vitamin K [THIS JOURNAL, **61** 1611 (1939)]. Phthiocol has been isolated as the pigment of *Mycobacterium tuberculosis* (human) and synthesized by Anderson and co-workers [*J. Biol. Chem.*, **101,** 773 (1933); **103,** 197 (1933); **105,** 279 (1934)]. This organism is known to contain vitamin K [*Proc. Soc. Exp. Biol. Med.*, **38,** 336 (1938)].

Treatment of vitamin K concentrates with sodium methylate produces a reddish pigment the quantity of which is proportional to the activity of the concentrate [THIS JOURNAL, **61,** 1610 (1939)]. The pigment has a strong red color in alkaline media, from which it can be extracted by adding hexane or ethyl ether and acidifying. It then assumes a yellow color. These color changes of the derived pigment are very similar to those exhibited by phthiocol and similarly

substituted naphthoquinones. A positive color reaction for 2-hydroxy-1,4-naphthoquinones [*ibid.*, **58,** 1174 (1936)] was obtained with highly purified concentrates of vitamin K from alfalfa.

The positions of ultraviolet absorption maxima reported in vitamin K concentrates, especially at 328 and 248 mμ [*Helv. Chim. Acta*, **22,** 310 (1939)], are close to the 334 and 250 maxima of phthiocol [*J. Biol. Chem.*, **115,** 479 (1936)], and the general shapes of the absorption curves are similar.

We have made quantitative assays by our improved method [*Biochem. J.*, in press] of phthiocol and several related compounds. In addition to the substances listed in Table I, we have tested lapachol and lomatiol. Both of these proved inactive, first at a 20-mg. level and later at a 100-mg. level. A preliminary test of a preparation of phthiocol monoacetate indicated a greater degree of activity than that of phthiocol.

An aqueous solution of phthiocol was made by dissolving 2 mg. in each cc. of a 0.05 molal phosphate buffer, *p*H 7.4. The *p*H of the final solution was 7.0. Sufficient of this solution was injected daily into the breast muscle of chicks to equal the amount consumed by chicks on the 20-mg. level. A control group received the same amount of solution orally. The average prothrombin time for 6 injected chicks was 31.9 seconds, while that for 6 orally fed chicks was 32.4 seconds. An 0.05 molal phosphate buffer, *p*H 7.8, dissolved 4 mg. of phthiocol per cc. to a final *p*H of 7.1. Chicks receiving no vitamin K in the diet were given intravenously 2 mg. each of phthiocol in aqueous solution. A comparable group of chicks was given the same dosage orally. After an interval of two days, the prothrombin time of 5 injected chicks was 29.6 seconds, and that of 5 orally fed chicks 30.3 seconds. Phthiocol appeared to exhibit approximately the same activity whether given in the diet or as a solution orally, intramuscularly or intravenously.

The antihemorrhagic activity of phthiocol lies between that of the methyl naphthoquinone and the hydroxy naphthoquinone (Table I). Consideration of the activities of various compounds indicates that the methyl group is functionally important, while the hydroxyl group seems to reduce activity. The latter effect may be largely physical. Phthiocol is obviously lower in activity than the more complex form of vitamin K existing in alfalfa. This lower activity is more than compensated for by the low cost of preparation and great convenience of administration of the compound.

TABLE I[a]

ANTIHEMORRHAGIC ACTIVITY OF SEVERAL NAPHTHOQUINONES

Substance	Level fed per kg. of diet	Av. prothrombin time, seconds	Act. in terms of cc. of ref. std. per g.
Ref. std.[b]	2 cc.	54.5	
Ref. std.	4 cc.	37.4	
Ref. std.	8 cc.	26.7	
Phthiocol	5 mg.	80.6	268
Phthiocol	20 mg.	32.0	263
Phthiocol	20 mg.	31.6	270
2-Methyl-1,4-naphthoquinone	20 mg.	26.1	435
	50 mg.	23.2	
2-Hydroxy-1,4-naphthoquinone	100 mg.	26.4	84
Alfalfa concentrate	2 mg.	26.1	4350

[a] Received June 22, 1939.

[b] Standard hexane extract of dried alfalfa representing 1 g. per cc.

We are indebted to Professor R. J. Anderson for the phthiocol and a sample of lapachol, and to Professor L. F. Fieser for samples of lapachol and lomatiol. Our work has been aided by a grant from Merck and Co., Inc.

DIVISION OF POULTRY HUSBANDRY
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H. J. ALMQUIST
A. A. KLOSE

RECEIVED JUNE 21, 1939

SIMPLE COMPOUNDS WITH VITAMIN K ACTIVITY

Sir:

The announcement of Almquist and Klose [THIS JOURNAL, **61,** 1611 (1939)] that pure synthetic phthiocol has anti-hemorrhagic activity prompts us to publish certain observations on related compounds. We have found that 2-methyl-1,4-naphthoquinone is practically as active as vitamin K, and that the diacetate of the corresponding hydroquinone appears to be somewhat inferior in potency. The chicks survived doses of several thousand units of these compounds, the cure was as dramatically rapid as with natural vitamin K and the animals developed normally thereafter. The activity of phthiocol reported by Almquist and Klose was confirmed with a preparation made from the above compounds, but the potency of the phthiocol thus prepared was several hundred times less than that of vitamin K. Duroquinone was found to be inactive in doses of as high as 1 mg.

TABLE I

BIOLOGICAL DATA OF TEST SUBSTANCES

Amount administered γ	No. of chicks	B. C. T.,[a] min. before treatment	after
2-Methyl-1,4-naphthoquinone			
2500	10	>90	<1[b]
1000	20	>90	<1
500	10	>90	<1
333	10	>90	<1
100	10	>90	<1
10	10	>90	<2
5	10	>90	<3
1/2	10	>90	<6
2-Methyl-1,4-acetoxynaphthalene			
1000	10	>90	<1[b]
100	10	>90	<1
10	10	>90	<4
5	10	>90	<8
2-Methyl-3-hydroxy-1,4-naphthoquinone			
1000	10	>90	<2[c]
100	20	>90	>30[d]
10	5	>90	>30
Duroquinone			
1000	10	>90	>30

[a]B. C. T. = blood clotting time.

[b]All vitamin K-deficiency symptoms disappeared within twenty-four hours and the chicks doubled their weight within ten days.

[c]Three chicks died during the six-hour test period.

[d]Four chicks died during the six-hour test period.

We are preparing and investigating a large number of quinones and hydroquinones, particularly those with a long aliphatic side chain to which class vitamins K_1 and K_2 [Binkley, *et al.*, THIS JOURNAL, **61**, 1612 (1939)] appear to belong.

THE SQUIBB INSTITUTE FOR MEDICAL RESEARCH
DIVISION OF ORGANIC CHEMISTRY
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S. ANSBACHER
ERHARD FERNHOLZ

RECEIVED JUNE 20, 1939

QUINONES HAVING VITAMIN K ACTIVITY

Sir:

Certain indications from recent publications of others and from preliminary oxido-reduction potential measurements conducted at Northwestern University have led us to postulate that the antihemorrhagic vitamin K_1 of alfalfa is a 2,3-dialkyl-1,4-naphthoquinone. From the similarity of vitamin K_2 [Doisy, *et al.*, THIS JOURNAL, **61**, 1295, 1612 (1939)] in absorption spectrum, ease of oxidation of the hydroquinone and other properties, it is probable that this substance is of the same type. As a specific hypothesis it is suggested (L. F. F.) that vitamin K_1 may be 2,6(?)-dimethyl-3-phytyl-1,4-naphthoquinone (or the 2-monomethyl compound) and vitamin K_2 2,3-difarnesyl-1,4-naphthoquinone. These structures seem consistent with the spectra [Doisy, *et al.*; Dam, Karrer, *et al.*, *Helv. Chim. Acta.* **22**, 310 (1939)], the analyses and hydrogen absorption [Doisy, *et al.* (assuming the saturation of one ring of the naphthalene nucleus)], the sensitivity to heat and light, and the hindered character of the functional groups of the quinone (K_1) [Almquist, *et al.*, *J. Biol. Chem.*, **125**, 681 (1938); Riegel, Schweitzer and Smith, in press] and hydroquinone diacetates (K_1 and K_2) [Doisy, *et al.*]. They also accord with recognized processes of biogenesis: K_1 (alfalfa) from dimethylnaphthoquinone (or toluquinone plus isoprene) and phytol [occurrence in green leaves: Dam, *Z. Vitaminforsch.*, **8**, 248 (1938–39); relationship between vitamins E and K_1]; K_2 (putrefied sardine meal) from naphthoquinone and farnesol (relationship of the alcohol to squalene).

These considerations suggested (B. R. and L. F. F.) the testing of various quinones available from previous researches or from the collection of the late Samuel C. Hooker. The synthesis of compounds of the type indicated has been undertaken at Harvard. Exploratory assays of ten compounds were kindly carried out by Dr. W. L. Sampson of the Merck Institute by a procedure based on that of Ansbacher [*J. Nutrition*, **17**, 303 (1939)]. Day old chicks were placed on the Almquist vitamin K deficient diet for twelve days and given a dose of 250 γ of substance in 1 cc. of peanut oil, administered by a tube into the crop, and the blood clotting time determined (Almquist method) the following morning.

The preliminary results suggest that some of the 2-hydroxy-3-alkyl-1,4-naphthoquinones possess positive vitamin K activity at the dose level fed [compare phthiocol, Almquist and Klose, THIS JOURNAL, **61**, 1611 (1939)] and that the 2,3-dimethyl derivative is at least 1/250 as active as Doisy's vitamin K_1.

2-Allyl-1,4-naphthoquinone (m. p. 36–36.5°, found: C, 78.82; H, 5.14) was prepared from 2-allyl-1-naphthol through the azo compound and amine (W. P. C.). 2,3-Diallyl-1,4-naphthohydroquinone diacetate (m. p. 92.5–93°, found: C, 74.18; H, 6.33) was obtained by heating 1,4-naphthohydroquinone diallyl ether (m. p. 49.5–50°, found: C, 80.09; H, 6.74) with diethylaniline and acetic anhydride (M. F.). The diacetate is

TABLE I

Compound	No. of birds	Clotting times, min. 5	5–10	10–20	20–30	>30	Per cent. 10-min. birds	Remarks
Controls	20	1	3	2	..	14	20	
2,3 - Dimethyl - 1,4 - naphthoquinone	10	10	..	..	..	..	100	Very effective
Lomatiol	9	5	2	1	..	1	77	Effective
Hydroxyhydrolapachol	9	5	1	1	..	2	67	Effective
Lapachol	9	1	3	4	1	..	45	Borderline
Diallyl-1,4-hydroquinone[1]	10	3	2	2	..	3	50	Borderline
Lomatiol methyl ether[2]	9	1	3	..	..	5	45	Doubtful
Hydrolapachol	9	2	2	2	..	3	45	Borderline
Diallyl-1,4-hydroquinone diacetate[3]	8	..	3	3	2	..	37	Probably not effective
Lapachol methyl ether[4]	9	..	3	..	1	6	35	Not effective
Diallyl-1,4-benzoquinone[5]	10	3	..	..	..	7	30	Not effective

[1] M. p. 130–131°, found: C, 75.80; H, 7.40. By rearrangement of hydroquinone diallyl ether (H. B. Dunkle, Dissertation, Harvard University) along with an isomer, m. p. 87–90°, found: C, 76.17; H, 7.60 (E. M. F.).

[2] M. p. 61.5–62°, found: C, 70.96; H, 6.05; prepared with diazomethane (W. P. C.).

[3] M. p. 111–112°, found: C, 70.25; H, 6.70; from the higher melting isomer (E. M. F.).

[4] M. p. 51.5–52°, found: C, 74.76; H, 6.34 (W. P. C.).

[5] M. p. 16°, found: C, 76.71; H, 6.75; by oxidation of the 130–131° isomer with silver oxide (E. M. F.).

resistant to alkaline hydrolysis (compare Doisy's dihydro vitamin diacetates); on cleavage with a Grignard reagent and air oxidation in ether it gave a quinone, m. p. 129–130° (absorption maxima at 245, 267, and 330 mμ in ethanol). 2,3-Dimethyl-1,4-naphthoquinone shows maxima at 246 and 265 mμ (log ε between 4.2 and 4.3) and 330 mμ (log ε = 3.4). The spectra (R. N. J. and D. M. B.) resemble those reported for vitamins K_1 and K_2 (Doisy, *et al.*, Dam, Karrer, *et al.*) except for the absence of fine structure in the two intense bands.

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RECEIVED JUNE 12, 1939

SYNTHESIS OF ANTIHEMORRHAGIC COMPOUNDS

Sir:

The further bio-assays by Dr. W. L. Sampson given in Table I lend added support to our conception of the nature of vitamin K_1 and K_2. Of special significance is the contrast between the highly active 2,3-dimethyl-1,4-naphthoquinone and the much less potent 2,6- and 2,7-isomers, the contrast between quinones of the benzene and naphthalene series, and the high potency encountered in a 1,4-naphthoquinone having a β-unsaturated side-chain (allyl) in the quinonoid ring, as postulated for both vitamins. The spectrographic data of Table II also indicate a close correspondence between the natural vitamins and model substances of the postulated structure of 2,3-dialkyl-1,4-naphthoquinones. Dr. T. J. Webb of the Merck Research Laboratories independently examined 2,3-dimethyl-1,4-naphthoquinone and pointed out to us definite indications of fine structure in the two intense bands; this was subsequently discerned in a new reading of our plates. The resolution of the most intense band of the 6,7-dimethyl-2,3-diallyl compound is still more distinct, particularly in hexane. We are indebted to Dr. Webb for the other determinations indicated.

The following examples illustrate methods developed for the synthesis of quinones of the type considered favorable for vitamin K activity. (1) 2,6-Dimethyl-8-naphthol was allylated, the ether rearranged, and the once distilled allyldimethylnaphthol (b. p. 152–157° at 2 mm. Found: C, 84.20; H, 7.74) converted to the 5-amine and this oxidized in acetone suspension with ferric chloride to give 2,6-dimethyl-3-allyl-1,4-naphthoquinone, m. p. 42–42.5° (Found: C, 79.82; H, 6.36). (2) The lower melting diallylhydroquinone (87–90°) was oxidized with silver oxide to the quinone (oil); 2,3-dimethylbutadiene was added to this, the product was isomerized to a hydroquinone, and on oxidation with chromic acid this afforded 6,7-dimethyl-2,3-diallyl-1,4-naphthoquinone, m. p. 69.5–70.7° (Found: C, 81.46; H, 6.96). 6,7-Dimethyl-1,4-naphthoqui-

TABLE I

BIO-ASSAYS BY THE ANSBACHER PROCEDURE

Substance (In 1 cc. peanut oil)	No. of birds	Clotting times, min. 5	5–10	10–20	20–30	> 30	% 10-min. birds	Remarks
Controls (1st series)	20	2	4	6	..	8	30	
Peanut oil (1 cc.)	10	..	3	..	..	7	30	
Alfalfa (100 mg.)	10	5	3	1	1	..	80	
Alfalfa (50 mg.)	9	2	5	1	1	..	77	
Alfalfa (25 mg.)	10	1	4	2	1	2	50	
Alfalfa (10 mg.)	10	1	3	2	2	2	40	
2-α-Heptenyl-3-hydroxy-1,4-naphthoquinone (0.2 mg.)	10	3	4	2	..	1	70	Some activity
2-*n*-Heptyl-3-hydroxy-1,4-naphthoquinone (0.2 mg.)	10	2	6	2	..	..	80	Some activity
2-Allyl-1,4-naphthoquinone (0.2 mg.)	10	10	..	..	..	..	100	Very active
Controls (2nd series)	11	..	..	..	..	11	0	All over 60 min.
Alfalfa (150 mg.)	10	7	3	..	..	..	100	
2,3-Diallyl-1,4-naphthohydroquinone diacetate (0.2 mg.)	10	..	1	1	5	3	10	Inactive
2,6-Dimethyl-1,4-naphthoquinone (0.2 mg.)	10	..	4	..	..	6	40	Very sl. act.
2,7-Dimethyl-1,4-naphthoquinone (0.2 mg.)	10	3	3	2	..	2	60	Active

TABLE II

ABSORPTION MAXIMA

In ethanol, except as noted; log ϵ values given in parentheses

	Maxima (in mμ)		
Vitamin K_1 (Doisy, *et al.*)	243, 248	261, 270	323
(Dam, Karrer, *et al.*)	248	261, 270	328
Vitamin K_2 (Doisy, *et al.*)	249	261, 269	320
2,3-Dimethyl-1,4-naphthoquinone (T. J. Webb)	244, 249 (4.29)	264, 270 (4.27)	332 (3.39)
(D. M. B., new reading)	243, 249 (4.26)	262, 267 (4.24)	330 (3.38)
6,7-Dimethyl-2,3-diallyl-1,4-naphthoquinone	253, 260 (4.40)	273, 278 (4.12)	343 (3.45
(In hexane)	253, 260 (4.41)	271, 276 (4.14)	338 (3.46)
2-Allyl-1,4-naphthoquinone	246, 251 (4.31)	Shoulder	332 (3.43)
(In hexane)	243, 251 (4.1)	260 (3.9)	Not measured
2-Methyl-1,4-naphthoquinone (T. J. Webb)	250 (4.29)	263 (4.24)	334 (3.38)
2,6-Dimethyl-1,4-naphthoquinone (T. J. Webb)	256 (4.33)		340 (3.47)
2,6-Dimethyl-3-allyl-1,4-naphthoquinone[a]	249 (4.30) 256 (4.35)	266, 272 (4.17)	335 (3.39)

none, m. p. 118–119° (Found: C, 77.43; H, 5.61), was similarly prepared from the known diene addition product. (3) Monobutadiene-1,4-benzoquinone with allyl bromide and potassium carbonate in acetone gave 5,8-dihydro-1,4-naphthohydroquinone diallyl ether, m. p. 64–65° (Found: C, 79.51; H, 7.55), and when heated in kerosene this rearranged smoothly to 5,8-dihydro-2,3-diallyl-1,4-naphthohydroquinone, m. p. 108–109° (Found: C, 79.36; H, 7.78). Chromic acid oxidation in acetic acid gave 2,3-diallyl-1,4-naphthoquinone, m. p. 29–30° (Found: C, 80.53; H, 6.02). The substance (m. p. 130°) obtained previously by the action of ethyl or *n*-butylmagnesium bromide on 2,3-diallyl-1,4-naphthohydroquinone diacetate is a naphthoquinone (spectrum) having two hydrogen atoms more than the expected diallyl compound (Calcd. for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 80.06, 79.93; H, 6.78, 6.76). More gentle cleavage with methylmagnesium bromide and silver oxide oxidation gave 2,3-diallyl-1,4-naphthoquinone, m. p. 28.5–29.5°, identical with the above sample.

In the Dam–Karrer color test with sodium ethylate in ethanol, regarded by some as characteristic of vitamin K_1 (Almquist and Klose, THIS JOURNAL, **61**, 1610 (1939); see, however, Fernholz, *et al.*, *ibid.*, **61**, 1613 (1939)), our synthetic naphthoquinones having at least one allyl group in the quinonoid ring all give intense and transient blue or purple colors and contrast sharply with the 2,3-dimethyl compound (weak, purplish color).[a]

[a] Received June 26, 1939.

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RECEIVED JUNE 23, 1939

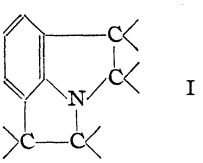
THE STEREOCHEMISTRY OF TERVALENT NITROGEN

Sir:

Jackson and Kenner [*J. Chem. Soc.*, 573 (1928)] briefly reviewed the existing evidence bearing

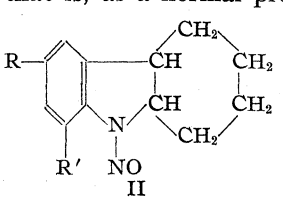
on the spatial configuration of tervalent nitrogen compounds in which three separate groups are attached to the nitrogen atom. They pointed out that "the search for isomerides demanded by a non-planar configuration has been (almost completely) unsuccessful, and it would therefore appear that, in general, the non-planar readily passes into a planar form, from which the original or its enantiomorph may be regenerated; or else the normal configuration is plane [compare Meisenheimer, *Ber.*, **57**, 1747 (1924)].

"Before, however, such conclusions can be accepted, it is desirable that the negative results on which they rest should be supplemented by positive evidence. This would be supplied by the preparation of a compound in the molecule of which a nitrogen atom is common to two ring structures which are at the same time plane and co-planar. Since . . . there is no evidence available which renders doubtful the plane configuration of five-membered ring structures, it would appear that these conditions would be fulfilled by a structure of type I, if Kekulé's formula for benzene and its derivatives be accepted."

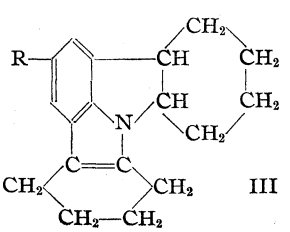


I

Jackson and Kenner were unable to report the preparation of a compound of this type. However, there had been recorded just previously some experiments by Manjunath [*J. Indian Chem. Soc.*, **4**, 271 (1927)] in which it was shown that treatment of a glacial acetic acid solution of 9-nitroso-hexahydro-carbazole (II, R,R = H) containing cyclohexanone with zinc dust, and then warming, led to formation of a crystalline substance $C_{18}H_{21}N$, which he described as "8,9-(1,2-cyclohexyl)-tetrahydro-carbazole." His structural formula for this substance is obviously incorrect as it represents a substance of formula $C_{19}H_{23}N$. Every analogy suggests that Manjunath's compound should be formulated as III (R = H), that is, as a normal product of a Fischer indole ring closure, and as a substance fulfilling the requirements of Jackson and Kenner's test.



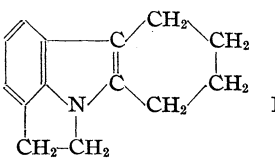
II



III

We have now confirmed Manjunath's result, and his further observation that a similar substance (III, R = CH_3) can be obtained in a similar manner from 9-nitroso-6-methyl-hexahydro-carbazole (II, R = CH_3, R′ = H). On the other hand, we have been unable to prepare a substance of similar structure from 9-nitroso-8-methyl-hexahydro-carbazole (II, R = H, R′ = CH_3) because the ortho position essential for indole ring closure has been "blocked" by the methyl group.

That the substances III have the structures assigned to them is strongly supported by the fact that addition of zinc dust to an acetic acid solution of 1-nitroso-indoline containing cyclohexanone, followed by warming, leads to formation of a colorless crystalline neutral substance, $C_{14}H_{15}N$, melting at 154°. There can be no doubt that this must be formulated as IV, so that it, also, must be regarded as fulfilling the requirements of Jackson and Kenner's test.



IV

There is thus no doubt that substances can be prepared containing a tervalent nitrogen atom with three separate atoms attached to the nitrogen, in which the three nitrogen valences must be regarded as definitely co-planar.

DEPARTMENT OF ORGANIC CHEMISTRY FRANCIS LIONS
THE UNIVERSITY OF SYDNEY ERNEST RITCHIE
SYDNEY, AUSTRALIA

RECEIVED MAY 22, 1939

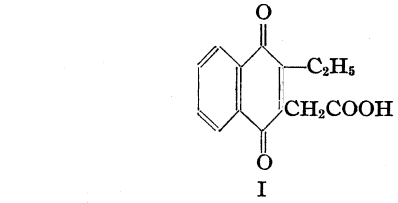
ON THE CONSTITUTION OF VITAMIN K_1

Sir:

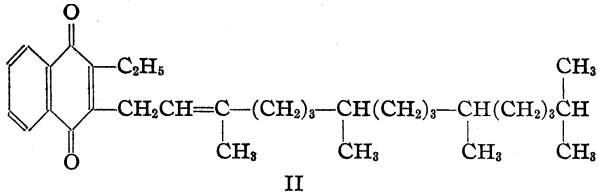
In a previous communication [THIS JOURNAL, **61**, 1295 (1939)] we suggested that vitamins K_1 and K_2 contain the quinone structure, and subsequently [*ibid.*, **61**, 1612 (1939)] we confirmed this by preparation of the diacetates by reductive acetylation. The pure yellow color of the vitamins suggests that they belong to the 1,4 series of quinones and this conclusion is supported by the discovery that 1,4-naphthoquinone has vitamin K activity whereas 1,2-naphthoquinone does not. Investigation of a considerable number of quinones has revealed only the derivatives of 1,4-naphthoquinone as having vitamin K activity.

On catalytic hydrogenation vitamin K_1 absorbs four moles of hydrogen with the formation of a hydroquinone. A naphthoquinone nucleus would account for three moles of hydrogen, the fourth mole being used in the saturation of an ethylenic linkage.

Ozonolysis of the diacetate of vitamin K_1 hydroquinone resulted in the formation of a ketone which gave a semicarbazone melting at 66–67°. *Anal.* Found: C, 70.04; H, 12.13; N, 12.83, 12.88. Calcd. for $C_{19}H_{39}ON_3$: C, 70.10, H, 12.08; N, 12.91. The semicarbazone of 2,6,10-trimethylpentadecanone-14 melts at 66–67° [G. F. Fischer and K. Lowenberg, *Ann.*, **464**, 69 (1928)]. The identity of our semicarbazone with that of Fischer and Lowenberg will be tested as soon as a specimen becomes available for determination of the mixed melting point. The formation of this ketone probably indicates the presence of a phytyl side chain in the vitamin molecule.



I



II

Vitamin K_1 was oxidized with chromic acid and the oxidation products separated into neutral and acidic fractions. Two crystalline acids were obtained from the latter fractions. One of these acids crystallized from water and had a melting point of 191° in a sealed tube. It was identified as phthalic acid by conversion to the anhydride. This melted at 127–128°. When mixed with authentic phthalic anhydride (m. p. 128–129°) the melting point was 128–129°. *Anal.* Calcd. for $C_8H_4O_3$: C, 64.87; H, 2.72. Found: C, 64.78; H, 3.05.

The second solid acid which was obtained in small amounts crystallized in well-formed yellow needles and melted with decomposition at 210°. If the phytyl radical is directly united to a 1,4-quinone ring, this would presumably be a substituted naphthoquinone acetic acid. This acid, like vitamin K_1, gives no color reaction with ethyl cyanoacetate [R. Craven, *J. Chem. Soc.*, 1605 (1931)] and so is presumably substituted in both the 3 and 4 positions. *Anal.* Calcd. for $C_{14}H_{12}O_4$: C, 68.84; H, 4.95. Found: C, 68.69; H, 4.85. The acid is probably 2-ethyl-1,4-naphthoquinone-3-acetic acid (I). The synthesis of this acid is at present in progress for purposes of comparison. On the basis of these degradation products we believe that the structure of the vitamin K_1 molecule is 2-ethyl-3-phytyl-1,4-naphthoquinone (II).

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RECEIVED JUNE 19, 1939

EVIDENCE FOR THE PRESENCE OF VITAMIN A AND CAROTENOIDS IN THE OLFACTORY AREA OF THE STEER

Sir:

In connection with our general project on the chemistry and sources of the fat-soluble vitamins, we became interested in examining the olfactory area of various animals for the presence of these vitamins, especially so for the presence of vitamin A's and their precursors. Since the absence of vitamin A from the diet causes the drying up of the mucous membranes of the body, it was suspected that the epithelia of the olfactory area together with the mucous membranes of the nasal passages in animals having normal diets might be rich in this vitamin. No work has been reported along these lines, and we decided to make a preliminary study of the olfactory area of the steer, but especially that area located at the upper end of the nasal cavity and known as the "yellow patch." This is composed of nerve filaments passing from the brain through the sieve-like cribriform plate into the nasal cavity and terminating at the upper third of this cavity. In the steer the epithelium of the olfactory area is dirty yellowish-brown in color while in the human being it is said to be yellow.

Forty heads of freshly killed steers were split open along the length of the nasal passages and by means of bone-cutters the olfactory area together with the bone and cartilage to which the epithelia were attached were removed. Most of the bone and cartilage were then removed from the yellowish-brown tissue, leaving a sample of about 470 g. This tissue was well ground and autolyzed with ethyl alcohol. Both the alcohol

extract and the autolyzed tissue were subjected to several extractions with pure ether in an atmosphere of nitrogen. The ether extracts were combined, washed with water and dried over anhydrous sodium sulfate.

An absorption spectrum of the deep yellow ethereal solution in the visible spectrum showed bands at 420, 442, 478 and 655 mμ, respectively. In petroleum ether the same extract showed bands at 420, 444, 472 and 656 mμ, respectively, while the antimony trichloride color in chloroform showed prominent bands with maxima at 420, 495 and 610 mμ, respectively.

The sample was then saponified in an atmosphere of nitrogen, the non-saponifiable fraction taken up in ether, the ethereal solution filtered at 0° and an absorption spectrum taken of the filtrate in the visible region of the spectrum. It showed bands at 446 and 474 mμ, respectively. The spectrum of the antimony trichloride color showed bands at 410, 440, 495, 620 and in one case at 690 mμ, respectively. An ultraviolet absorption spectrum of this sample in ethyl alcohol is shown plotted in Fig. 1. A maximum is readily

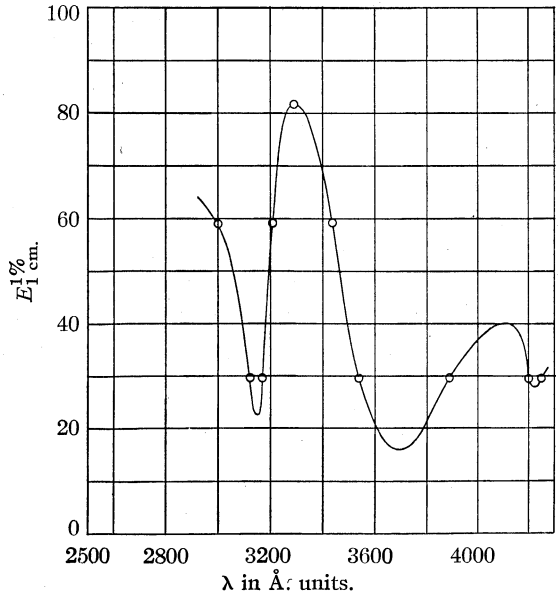

Fig. 1.

seen at 328 mμ which together with that of the antimony trichloride at 620 mμ is characteristic of vitamin A_1. The band of the antimony trichloride color at 690 mμ may be due to the presence of vitamin A_2, although the appearance of this band was not consistent. From the intensity of the maximum at 328 mμ and the concentration of the solution, we calculated $E_{1\text{ cm.}}^{1\%}$ to be 82 for our sample which, on the basis of the purest vitamin A having a potency of 3,250,000 U. S. P. vitamin A units per gram [Milas and Heggie, unpublished results] would have a potency of 116,000 U. S. P. vitamin A units per gram. In another sample taken from a single steer head we found a potency of about 76,000 U. S. P. vitamin A units per gram.

The bands of the visible spectrum at 420, 442–446, 472–478 mμ, respectively, are due to carotenoids. We have not as yet identified the other bands reported in this paper and inasmuch as we are continuing with our work, we are hoping to report a more complete account of it later.

CONTRIBUTION NO. 193 FROM THE
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CAMBRIDGE, MASSACHUSETTS

NICHOLAS A. MILAS
WILLIAM M. POSTMAN
ROBERT HEGGIE

RECEIVED JUNE 19, 1939

THE FORMATION OF α-ETHYLTHIOGLUCOPYRANOSIDE FROM GLUCOSE ETHYLMERCAPTAL

Sir:

It has been found two years ago [Green and Pacsu, THIS JOURNAL, **59,** 1205 (1937)] that α-ethyl- and α-benzylthioglucosides [Schneider, *et al.*, *Ber.*, **49,** 2054 (1916); **51,** 220 (1918); **61,** 1244 (1928)] are furanosides and not of "normal" (pyranoid) structure as their discoverers believed. This was shown by acid hydrolysis constants, conversion into ethylglucofuranoside, and calculations from Hudson's rules of isorotation. On account of certain irregularities observed by Green and Pacsu during the process of hydrolysis, the behavior of α-ethylthioglucofuranoside in 0.01 *N* hydrochloric acid at 100° was subsequently studied [Pacsu and Wilson, THIS JOURNAL, **61,** 1450 (1939)]. It was found that in this unprecedented hydrolysis about one-half of the α-ethylthioglucofuranoside changed into glucose and mercaptan whereas the other half escaped the hydrolyzing effect of the acid by shifting the furanoid ring into the acid resistant pyranoid ring. The ring shift resulted in the formation of α-ethylthioglucopyranoside, a new thioglucoside, which was isolated and characterized by its tetraacetate. In a recent paper [Brigl, Gronemeier and Schulz, *Ber.*, **72,** 1052 (1939)] which was submitted for publication one month later but appeared one month earlier than the article of Pacsu and Wilson, Brigl and co-workers re-

ported the preparation of the same α-ethylthioglucopyranoside and its tetraacetate. These authors proposed to use glucose ethylmercaptal for disaccharide synthesis and mixed the mercaptal in 22% hydrochloric acid with glucose. Instead of the desired disaccharide Brigl and co-workers obtained this α-ethylthioglucopyranoside in an apparently undetermined yield. As to the mechanism of the reaction the authors stated that the mercaptal lost one mercaptan residue which was partly transferred to the admixed glucose, the whole process being represented by the following two-stage reaction:

(a) $C_6H_{12}O_5(SC_2H_5)_2 = C_6H_{11}O_5(SC_2H_5) + C_2H_5SH$
(b) $C_2H_5SH + C_6H_{12}O_6 = C_6H_{11}O_5(SC_2H_5) + H_2O$

Since we had reasons to believe that this mechanism might not be the correct one, we repeated Brigl's experiment with the modification that we *omitted* glucose. From the reaction mixture we obtained α-ethylthioglucopyranoside in about 20% minimum yield. Also, we obtained the same compound but in somewhat smaller yield (15%) from the reaction of equimolecular quantities of glucose and ethylmercaptan in 22% hydrochloric acid. In our first experiment there was but a mere trace of glucose present in the acetone insoluble residue consisting mainly of barium chloride, whereas in the second experiment, when glucose was used as starting material, the acetone insoluble salt contained a fairly large quantity of unchanged glucose. In both instances the lower rotating component of the reaction mixture represented probably the acid resistant β-ethylthioglucopyranoside, since in neither case could we find glucose ethylmercaptal. These results seem to indicate that the formation in 22% hydrochloric acid of α-ethylthioglucopyranoside from the mercaptal on one hand, and from glucose and mercaptan on the other, are two distinct and independent reactions.

FRICK CHEMICAL LABORATORY EUGENE PACSU
PRINCETON UNIVERSITY E. JUSTIN WILSON, JR.
PRINCETON, NEW JERSEY

RECEIVED JUNE 20, 1939

VITAMIN B_6, A GROWTH PROMOTING FACTOR FOR YEAST

Sir:

The rate of proliferation of *S. cerevisiae* in purified solutions is known to be profoundly affected by a group of substances known as bioses. The multiple nature of bios is firmly established and further evidence of the multiplicity of bios was found in the discovery of the bios action of thiamine [Schultz, Atkin and Frey, THIS JOURNAL, **60,** 490 (1938)].

We have now found that crystalline vitamin B_6 has the properties of a bios factor. This substance acts on the yeast types A and B in an advantageous manner. The work with crystalline B_6 was made possible by the gift of a few milligrams by Merck and Company.

TABLE I

TWENTY-FOUR HOUR GROWTH OF YEASTS A AND B AS INFLUENCED BY VITAMIN B_6, ETC.

Total volume in each case: 30 ml. (seeded with 1 mg. of moist yeast and rocked at 30° for 24 hours). Crop × 4.54 gives mg. of moist yeast. Supplements: inositol (1) 1 mg.; β-alanine (IIA) 0.005 mg.; bios IIB 0.13 mg.; thiamine 0.01 mg.; vitamin B_6 (VI) 0.05 mg.

Ingredients of bios tests: all C. P. sugar, salts, buffer, I and IIA, plus	24-Hour crop Type A	Type B
Nil	Trace	40
II B	15	210
II B plus thiamine	100	120
Vitamin B_6 (VI)	Trace	40
II B plus Vitamin B_6	150	200
II B plus B_6, plus thiamine	170	200

The properties of crystalline B_6 are: (1) stimulation of Type A yeast to produce a 24-hour crop of 100–120; (2) removal of the inhibition imposed on Type B yeast by thiamine; (3) stimulation of Type A yeast to give a high 24-hour crop in the absence of thiamine.

Crystalline vitamin B_6 was found to have a certain activity as a fermentation accelerator under the conditions of our fermentation test [Schultz, Atkin and Frey, THIS JOURNAL, **59,** 2457 (1937)]. The stimulation is of about the same type as the nicotinic acid effect [Schultz, Atkin and Frey, *ibid.*, **60,** 1514 (1938)] and may be overcome in the same way, *i. e.*, by adding about 0.05 mg. of B_6 to each test.

There are indications that the growth method may be useful as a method for the determination of vitamin B_6. A growth test in which all factors except B_6 are present in excess will respond to solutions or concentrates in proportion to their B_6 content as indicated by rat curative tests which were made by R. F. Light and L. J. Cracas of our Laboratory.

THE FLEISCHMANN LABORATORIES ALFRED S. SCHULTZ
STANDARD BRANDS INCORPORATED LAWRENCE ATKIN
NEW YORK, N. Y. CHARLES N. FREY

RECEIVED JUNE 10, 1939

VITAMIN B_6 AS A YEAST NUTRILITE

Sir:

In corroboration of the findings of Schultz, Atkin and Frey [THIS JOURNAL **61**, 1931 (1939)], we wish to indicate that we have independently found that vitamin B_6 is effective in yeast growth stimulation. A typical experiment is outlined below.

The basal medium was similar to that used in previous work [Williams and Saunders, *Biochem. J.*, **28**, 1887 (1934)], but contained 0.1 g. of aspartic acid per liter instead of asparagin. It also contained 0.03 mg. of thiamine, 0.3 mg. of β-alanine, and 30 mg. of autolyzed liver extract per liter. The liver extract had been treated with charcoal and with fuller's earth. The yeast seeding was 0.03 mg. of a pure culture isolated from a Fleischmann cake per 12 ml. culture and the growth period was fourteen hours at 30°. The vitamin B_6 used had been generously furnished by Dr. Samuel Lepkovsky.

TABLE I

EFFECT OF VITAMIN B_6 ON YEAST GROWTH

Vitamin B_6 added (γ per culture)	Yeast crop (mg. per 12 ml. culture)
0	4.47
0	4.53
0.0005	4.44
.001	4.95
.005	6.29
.01	6.82
.05	8.01
.1	8.58
.5	7.94
1	8.27

This finding makes more emphatic the close relationship between "B" vitamins and substances effective for the stimulation of the growth of yeasts (as well as other microörganisms).

DEPT. OF CHEMISTRY
OREGON STATE COLLEGE
CORVALLIS, OREGON

ROBERT E. EAKIN
ROGER J. WILLIAMS

RECEIVED JUNE 10, 1939

VITAMIN K ACTIVITY OF SOME QUINONES

Sir:

In view of the recent note of Almquist and Klose [THIS JOURNAL, **61**, 1611 (1939)] and their conclusion "that phthiocol is the simplest member of an homologous series of anti-hemorrhagic substances," we are submitting a report on the potencies of a rather extensive series of quinones.

As soon as our investigations on vitamin K indicated a quinone structure [THIS JOURNAL, **61**, 1295 (1939)], we began a survey of the potencies of quinones.

Using the assay procedure previously described [*J. Soc. Exp. Biol. Med.*, **40**, 478 (1939); **41**, 199 (1939)] the following quinones were found to be inactive at a level of 5 mg.: anthraquinone β-sulfonic acid, thymoquinone, tolu-*p*-quinone, dihydro-anthraquinone diacetate, 1,2-naphthoquinone, phenanthraquinone, diamylhydroquinone, *p*-xyloquinone, 2-allyl-1,4-naphthoquinone (tested only at 2.0 mg.) and 1,4-benzoquinone.

With the exception of 2-allyl-1,4-naphthoquinone all of the derivatives of 1,4-naphthoquinone show vitamin K activity. Moreover, the diacetates of two of the dihydro-1,4-naphthoquinones show activity, perhaps due to hydrolysis in the gastro-intestinal tract. 2-Allyl-4-amino-1-naphthol hydrochloride in aqueous solution gives a positive reaction.

Our data are summarized in Table I. They show that the 2-methyl-1,4-naphthoquinone is the most active compound in this group; however, when compared with the natural vitamin K_1 (1000 units per mg.) or K_2 (660 units per mg.), the activity is relatively insignificant. Other more complex derivatives of 1,4-naphthoquinone are being prepared for a study of their physiological activity.

TABLE I

Active compounds	Our standard units per milligram
1,4-Naphthoquinone	1.0
2-Methyl-1,4-naphthoquinone	10.0
2-Ethyl-1,4-naphthoquinone	8.0
Phthiocol, 2-methyl-3-hydroxynaphthoquinone	2.0
2-Bromo-3-methyl-1,4-naphthoquinone	> 0.10
2,3 - Dibromo - 2 - methyl - 1,4 - dioxotetrahydronaphthalene	> 0.10
1,4-Naphthalenediol diacetate	0.50
2-Methyl-1,4-naphthalenediol diacetate	5.00

Our discovery of the activity of 1,4-naphthoquinones and the inactivity of other quinones has been of considerable assistance in developing the structure of vitamin K_1 [THIS JOURNAL, **61**, 1928 (1939)].

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S. A. THAYER
L. C. CHENEY
S. B. BINKLEY
D. W. MACCORQUODALE
E. A. DOISY

RECEIVED JUNE 19, 1939

NEW BOOKS

Volumetric Analysis Including the Analysis of Gases, with a Chapter on Simple Gravimetric Determinations. By Dr. A. J. Berry, M.A., Fellow of Downing College and University Lecturer in Chemistry, Cambridge. Fifth edition. The University Press, Cambridge: The Macmillan Company, 60 Fifth Avenue, New York, N. Y., 1939. 196 pp. 9 figs. 14 × 22 cm. Price, $2.50.

The author states in the preface that this book was written in the interests of his own pupils and that his object was to provide a practical book for students having a sufficient background of theoretical principles. He adds that it "would occupy a position intermediate between that of the elementary works of necessarily limited scope and that of standard treatises on volumetric analysis."

A chapter is included on the theory of indicators and a separate chapter has also been added to the present edition devoted to modern developments. Such items as oxidation–reduction indicators, adsorption indicators, the use of ceric sulfate, constant boiling hydrochloric acid, and the use of ammonium persulfate are included in this chapter. It appears unfortunate, however, that these newer developments have not been incorporated at their appropriate point in the body of the book.

Little use is, however, made of the modern theories of ionic reactions, and the inquiring student would find difficulty with the treatment of *p*H, since the author merely states that a convenient way of expressing hydrogen-ion concentration is to take the logarithm of the concentration, omitting the negative sign, and write this as *p*H.

The printing and binding of the book are good.

CHESTER M. ALTER

Physik für Studierende an Technischen Hochschulen und Universitäten. (Physics for Students in Technical Institutes and Universities.) By Ing. Dr. PAUL WESSEL, Lecturer, Wigan and District Mining and Technical College, Wigan. Edited by Dr. V. RIEDERER VON PAAR. Verlag von Ernst Reinhardt, Munich, Germany, 1938. xii + 548 pp. 227 figs. 13 × 21 cm. Price, Mk. 4.90.

This book is intended for university students in their first year and is supposed to be accompanied by a course of lectures and demonstrations in general physics. These students have usually had in school a fairly comprehensive course in physics. The aim of the book is to assist them to a rapid review of all the phenomena in the general field of physics, even including some of the latest discoveries and theories, with applications to modern engineering, chemistry, and medicine.

The arrangement of material follows the conventional order: mechanics, acoustics, heat, optics, magnetism, electricity, electronics, and atomic physics. It is intended to relieve the student of the necessity of taking notes on the lectures so that he can give his undivided attention to the experimental demonstrations. Following the 354 pages of very condensed text, there are 60 pages entitled "A Short Repetitorium" and including a collection of formulas. Then follow 63 pages of questions based on the text, each with a reference to a particular page where the answer may be found. Finally, there are 38 pages of tables and physical constants. The text has many diagrams which are small but very clearly drawn. The style is straightforward.

The American teacher feels the lack of experimental detail in the book and also the absence of historical and biographical references. For example, nowhere does one find a description of Michelson's classical experiment in measuring the speed of light. Anyone who is familiar with American textbooks in college physics will be astonished at the vast amount of material which can be obtained in such an inexpensive volume.

N. HENRY BLACK

Dictionary of Scientific Terms as Used in the Various Sciences. By C. M. BEADNELL, C.B., F.Z.S. Chemical Publishing Company of New York, Inc., 148 Lafayette Street, New York, N. Y., 1939. x + 235 pp. 12.5 × 19 cm. Price, $3.00.

The author in his introduction calls this a book of reference rather than a dictionary. It does indeed give a considerable amount of exact and pertinent information in its definitions and is therefore of corresponding value to the reader who is in doubt as to the meaning of an unfamiliar scientific word. Only some three thousand terms are listed, which seems to be a narrow choice from among the hundreds of thousands in use in the sciences represented. The selection, however, is good, although undoubtedly favoring the biological sciences. Newer words are not neglected.

The volume is all it claims to be, namely, a good book for the desk of the general reader, especially one with scientific training whose reading ventures into other fields than his own.

WILLIS A. BOUGHTON

Proceedings of the Sixth Summer Conference on Spectroscopy and its Application. Held at the Massachusetts Institute of Technology, Cambridge, Massachusetts, July 18–20, 1938. Edited by George R. Harrison. The Technology Press: John Wiley and Sons, Inc., 440 Fourth Avenue, New York, N. Y., 1939. vii + 172 pp. Illustrated. 19 × 25.5 cm. Price, $3.00.

Again, a list of topics of current interest, and of contributors outstanding in their respective fields. Spectroscopic equipment and method, to be sure, are not discussed at such great length as in 1937. Impressive, in this section, is the high-speed absorption spectrophotometer at Massachusetts Institute of Technology which measures and plots within a hundred seconds one thousand transmissions covering the range 10,000 to 2000 Å. Also the

account of the apparatus and methods for obtaining the new tables of 100,000 principal spectrum lines, measured in the same laboratories with accuracy of 0.01 Å. or better. Intensities are given on a scale of one hundred.

Applied photochemistry is well covered, as follows from a partial list of topics: criminal investigation, rare earths in plants, identification of minerals, vitamin determination, enzymes, medical problems, dispersion filters, dyestuffs, analysis of gas mixtures, photochemistry of vision, chemical energy from light, and the problem of the photographic latent image.

These annual demonstrations of the versatility, speed and dependability of optical and photochemical methods cannot fail to exert a beneficial influence upon scientific practice in American and foreign laboratories.

GEORGE S. FORBES

Les origines françaises de la chimie analytique. (The French Origins of Analytical Chemistry.) By A. JOUNIAUX. Hermann et Cie., Éditeurs, 6 Rue de la Sorbonne, Paris, France, 1938. 59 pp. 16.5 × 25 cm. Price, fr. 11.

It is always of academic interest to determine the actual sources of our present information. Jouniaux, in this little book, has shown the important part that French chemists have played in the development of analytical chemistry, largely by direct quotations from the original papers. Such information cannot be obtained from the textbooks of analytical chemistry. Even though an analytical procedure may be correctly credited to Gay-Lussac, for example, the original reference will not usually be given if the work dates back about one hundred years. This is partly because it is better to give an approved procedure which takes into consideration all improvements that have been made and partly because most library files are more or less deficient in journals printed at about the beginning of the nineteenth century.

The author's contention is that the French created chemical analysis and originated most of its methods. Since, however, no reference whatever is made to work done outside of France, except for publishing an illustration of an old English buret, the reviewer is left quite unconvinced.

The author's claim that gravimetric analysis began with Lavoisier is surely not correct. This claim is here based upon Lavoisier's inaccurate analyses of carbon dioxide and of water and the fact that he appears to have been the first to determine carbon and hydrogen in organic compounds by combustion in oxygen with measurement of the water and carbon dioxide formed. The Swedish chemist, Torbern Olaf Bergman (1735–1784), made many quantitative analyses of minerals before the work of Lavoisier was published. He used our present methods of fusion with sodium carbonate for decomposing silicates, and he separated calcium and magnesium ions by precipitation with ammonium oxalate. The use of the balance in the assay of ores was common several centuries previous to the work of Lavoisier, who did, to be sure, emphasize the importance of the balance in chemistry and with it he helped overthrow the phlogiston theory.

WILLIAM T. HALL

Die chromatographische Adsorptionsmethoden. Grundlagen, Methodik, Anwendungen. (Chromatographic Adsorption Methods: Principles, Methods, Applications.) By DR. L. ZECHMEISTER, Professor, and DR. L. v. CHOLNOKY, Lecturer, Chemical Institute of the University of Pécs (Ungarn). Second, revised edition. Verlag von Julius Springer, Linkstrasse 22–24, Berlin W 9, Germany, 1938. xiii + 354 pp. 74 figs. 14.5 × 21.5 cm. Price, RM. 19.80.

The second edition of this excellent book, somewhat larger than the first, is an invaluable survey of the literature of chromatographic adsorption methods. The authors have themselves contributed a great deal of research work in this field, so that their advice as to the technique and their predictions as to the possibilities in detection and purification of substances by the Tswett column analysis must be given great weight.

Their historical review of the development of the subject since Tswett's original contribution in 1906 is presented in good teaching style. The discussion of the various powders used in columns and the variations in activity due to different methods of preparing the dry powders is most helpful. The solvents and mixtures of solvents, both for adsorption media and for washing purposes, are given full attention. The various aluminas seem to be highly favored by these authors, with reason, but there are two minor points about these aluminas which might be clarified. The authors refer to "Alumina III of Brockmann." As a matter of fact the reviewer first used this phrase to describe a product sold by the Aluminum Company of America and the phrase was copied by other authors. In the same connection it might be noted that the word "Hydralo," once used by this industrial organization to describe its commercial alumina, has been discarded in favor of the phrase "activated alumina."

Biochemists, organic chemists, and analysts may well be interested in this book for it presents to them very useful tools in identification and in separation of substances. Micro chromatographic separations are included, as is a system of qualitative analysis for cations and anions. Although originally Tswett, Willstätter, and others were primarily interested in separating plant pigments by column analysis, Zechmeister and Cholnoky now present extended discussions of separation, even of purification, of dyes, hormones, enzymes, and seven vitamins. Obviously there are many of us who must own this book.

HARRY N. HOLMES

Systematic Qualitative Organic Analysis. By H. MIDDLETON, M.Sc. (Manchester), A.I.C. Lecturer in Organic Chemistry, Bradford Technical College. Longmans, Green and Company, 114 Fifth Avenue, New York, N. Y., 1939. 279 pp. Illustrated. 14.5 × 22.5 cm. Price, $2.50.

This book on qualitative organic analysis appears to have been designed for pharmaceutical students with a quite elementary knowledge of organic chemistry. The general scheme follows Mulliken closely, the first classification being made on the basis of elementary analysis and physical state. But little emphasis is placed on solubility for further subdivision. About 600 pure organic compounds,

including most of those given in the British Pharmacopoeia, are considered. These have been carefully examined by the author, and a systematic procedure which gives decisive results is described. While this should assist the beginning student to gain confidence in his work, the loss in flexibility is serious, and the book fails to provide to the full extent for that exercise in logical deduction from experiment which is the particular beauty of the best courses in qualitative organic analysis. Directions are concise and abbreviated; no descriptive or explanatory matter is included and a rather extended series of lectures on the laboratory work would be necessary to make the book effective. The procedures while generally standard depart in several instances from common practice and the extensive use of color reactions is more in keeping with pharmaceutical work. The newer derivatives for many classes of compounds have been omitted. The manual therefore does not seem well suited for the general course in qualitative organic analysis, but it may well be recommended for those students for whom it primarily was written.

THOMAS L. JACOBS

Colloidal Phenomena. An Introduction to the Science of Colloids. By ERNST A. HAUSER, Ph.D., Associate Professor of Chemical Engineering, Massachusetts Institute of Technology. McGraw-Hill Book Co., Inc., 330 West 42d St., New York, N. Y., 1939. xx + 294 pp. 123 figs. 16 × 23.5 cm. Price, $3.00.

This work by a recognized authority and successful practitioner of the art should find a place in almost every chemical and industrial library. It is a guide to the chief textbooks and monographs and to the more important recent papers and concepts in this field. It is intentionally and unfortunately not "another textbook on colloidal chemistry." It reveals the theoretical apparatus with which an important group of colloid workers operate, largely under the influence of Wo. Ostwald, there being forty-six page citations to him, thirty-nine to von Buzagh, thirty-eight to Freundlich and twenty-eight to the author. The text itself is completely non-mathematical.

The book begins with a preface emphasizing the breaking of some of the barriers of "physicochemistry," and an interesting historical introduction, followed by chapters commenting on the dispersed state, terminology, difform systems, form and shape, production, kinetics, electrical properties, surface phenomena, protection and sensitization, dispersion, coagulation, mechanical and optical properties as influenced by particle shape, aggregates bonded by primary and by secondary forces, and colloidal aggregates. Then comes one of the most valuable features, an Appendix of forty-six pages giving the formulas and equations commonly referred to, with notes on some of the experimental methods.

As presented in this monograph, the subject is clearly not an exact science, but it is one of compelling practical importance where any hint is valuable as a guide to comprehension or to remarkable industrial applications. The text is facile and readable, but if one stops to analyze the meaning, it is not clear. Much that is usually discriminated is taken as synonymous as, for example, charge and potential, dispersion and peptization; and much of the description is as vague as the undefined expression (page 171) "liquid gel," or (page 169) the statement that "a colloidal sol can be considered a statistical mixed crystal." Many statements are not intended to be taken literally. The expressions evidently serve to recall examples of materials or behavior showing parallelisms which are useful in investigating further systems because they may recur, perhaps in modified or even contrasting form.

The numerous diagrams are beautifully clear, but they are largely schematic and are not referred to actual examples or measurements.

J. W. MCBAIN

The Plant Alkaloids. By THOMAS ANDERSON HENRY, D.Sc., Director, Wellcome Chemical Research Laboratories. Third edition. P. Blakiston's Son and Company, Inc., 1012 Walnut Street, Philadelphia, Pa., 1939. viii + 689 pp. 15 × 23 cm. Price, $12.00.

The reviewer has little but praise for this excellent and scholarly treatise on the alkaloids, which represents an expansion of the second edition by 233 pages. Together with Winterstein–Trier (1931) it is indispensable in any well-equipped scientific library, or to anyone interested in natural products. The literature references are abundant, comprising approximately 6060, and extending through most of 1938. The author and publishers are to be congratulated on this feat, as well as on the comparative freedom from errors. The references have been collected at the end of each section in such compact form as to make it a little difficult to find a desired citation. The frequent designation of bibliographies is a welcome feature.

Criticisms that can be offered are very minor in nature. The structural formulas are reproduced from drawings, but are clear and accurate. An error in the sinomenine formula on page 7 has been carried over from the original publication. The term "deracemization" is somewhat unusual, and "habitués" in the sense used on p. 623 is inacceptable. It is a question, to what extent the physical properties of somewhat remote derivatives should be described in a text of this sort, since it may generally be assumed that one interested in such derivatives will have access to the literature. The occasional citation of specific rotations to the second decimal place without specification of temperature, solvent, or concentration, certainly seems inconsistent.

As in the previous edition, the listing of plant sources is unusually complete, but the illustrations of important alkaloid-bearing plants have been sacrificed. Discussion of physiological action is necessarily limited, but numerous pertinent references are supplied. Much space has been saved by omission of the details of methods of estimation of the alkaloids, which may be found easily in pharmacopoeias and special reports.

Classification of the alkaloids according to nuclear type has been followed much as in the older edition. As would be expected, the sections on the isoquinoline and indole groups have been greatly enlarged. The up-to-date discussion of the Strychnos alkaloids is most welcome

even though it is necessarily condensed. The lupinanes, phenanthridine, pyrrolidine, and quinazoline are new groups; the section on the purine bases has been omitted, as the material is easily accessible elsewhere. The book is durably and attractively bound, and well printed.

LYNDON SMALL

The Electrochemistry of Gases and Other Dielectrics. By G. GLOCKLER, Professor of Physical Chemistry, and S. C. LIND, Professor of Physical Chemistry and Dean of the Institute of Technology, University of Minnesota. John Wiley and Sons, Inc., 440 Fourth Avenue, New York, N. Y., 1939. xiii + 469 pp. 82 figs. 15.5 × 23.5 cm. Price, $6.00.

In contrast to the texts on photochemistry, which continue to multiply, there has hitherto been no monograph on research in the field of chemical reactions produced by the various types of ionizing agencies. In this present volume the need for such has been handsomely met and the authors are to be thanked sincerely for an onerous task well accomplished.

The book is divided into three sections. The first deals with typical reactions in various forms of electrical discharge, the glow discharge, silent electrical, corona, electrodeless and arc discharge, cathode rays and electrons of controlled speeds. The second part attempts to summarize the studies of reactions in the various forms of discharge the data for all forms of activation being collected together for a given substance and its reactions. The final section of the book treats of the theoretical and physical aspects of discharge reactions. As an illustration of the depth of the treatment we may cite the 47 pages on hydrogen and the hydrocarbons or the 40 pages on active nitrogen. The former summarizes the influence of spark, silent discharge and luminous discharge on the properties of hydrogen and gives *inter alia* an extended discussion of the reactions of various hydrocarbons under ozoning conditions. There is a bibliography of 123 titles to this chapter while that on active nitrogen cites 152 titles. This latter chapter illustrates, too, the breadth of the problems covered; spectroscopy, luminescence and phosphorescence, molecular structure and chemical kinetics are all involved.

The final section of the book dealing with the theoretical aspects of the subject is exceedingly interesting. After sections on electron affinities and ion mobilities a chapter is devoted to the results of mass spectroscopy with a convenient summary of the experimental results. The two following chapters on ionization produced by chemical reaction and on cathodic sputtering of metals seem to the reviewer less pertinent to the theme of this section. The final chapter of 13 pages on mechanism is all too brief for the physical chemist since here, if anywhere, is the heart of the subject from his point of view. That the chapter could not have included a discussion of the several interesting papers which have only appeared quite recently notably by Gunther, Mund, Essex and their co-workers, all dealing with reaction mechanism in this field, is to be regretted, but the student can start his inquiries in this field with the Glockler–Lind chapter and turn then to the literature of 1938–1939 for a very interesting field of fundamental research.

HUGH S. TAYLOR

BOOKS RECEIVED

May 15, 1939 to June 15, 1939

LOUIS BACHELIER. "Les nouvelles méthodes du calcul des probabilités." Gauthier-Villars, 55 Quai des Grands-Augustins, Paris 6, France. 69 pp. 25 fr.

GEORGE A. BAITSELL, Editor. "Science in Progress." Yale University Press, New Haven, Conn. 322 pp. $4.00.

WILHELM BILTZ. "Ausführung qualitativen Analysen." Fifth edition. Akademische Verlagsgesellschaft m. b. H., Sternwartenstrasse 8, Leipzig C 1, Germany. 180 pp. RM. 8.50; bound, RM. 9.60.

ALBERT CHARLES CHIBNALL. "Protein Metabolism in the Plant." Yale University Press, New Haven, Conn. 306 pp. $4.00.

HAROLD A. FALES AND FREDERIC KENNY. "Inorganic Quantitative Analysis." New edition. D. Appleton-Century Co., Inc., 35 West 32d St., New York, N. Y. 713 pp. $4.00.

A. FARKAS AND H. W. MELVILLE. "Experimental Methods in Gas Reactions." The Macmillan Co., 60 Fifth Ave., New York, N. Y. 389 pp. $7.50.

HARRY N. HOLMES. "Introductory College Chemistry." Third edition. The Macmillan Co., 60 Fifth Ave., New York, N. Y. 619 pp.

JOHN R. JOHNSON, Editor-in-Chief. "Organic Syntheses." Vol. XIX. John Wiley and Sons, Inc., 440 Fourth Ave., New York, N. Y. 105 pp. $1.75.

O. MAASS AND E. W. R. STEACIE. "An Introduction to the Principles of Physical Chemistry." Second edition. John Wiley and Sons, Inc., 440 Fourth Ave., New York, N. Y. 395 pp. $3.00.

HENRY SEMAT. "Introduction to Modern Physics." Farrar and Rinehart, Inc., 601 West 29th St., New York, N. Y. 360 pp. $3.50.

F. SHERWOOD TAYLOR. "The March of Mind. A Short History of Science." The Macmillan Co., 60 Fifth Ave., New York, N. Y. 320 pp. $3.00.

MAURICE DE KAY THOMPSON. "Theoretical and Applied Electrochemistry." Third edition. The Macmillan Co., 60 Fifth Ave., New York, N. Y. 535 pp. $5.00.

MAX VOLMER. "Kinetik des Phasenbildung." Verlag von Theodor Steinkopff, Residenzstrasse 32, Dresden-Blasewitz, Germany. 220 pp. RM. 14.25; bound, RM. 15.

ROGER J. WILLIAMS AND RAY Q. BREWSTER. "A Laboratory Manual of Organic Chemistry." Third edition. D. Van Nostrand Co., Inc., 250 Fourth Ave., New York, N. Y. 217 pp. $2.00.

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[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, THE UNIVERSITY OF ILLINOIS]

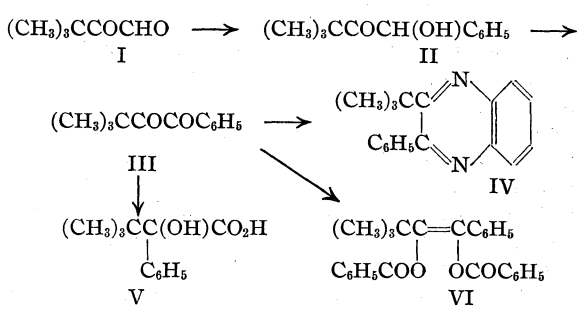
Acyloins from *t*-Butylglyoxal[1]

BY REYNOLD C. FUSON, HUGH GRAY[2] AND J. J. GOUZA

The condensation of arylglyoxals with aromatic compounds[1] provides a convenient method for making mixed benzoins. It seemed probable that the method could be used also for acyloins of the type RCOCH(OH)Ar. To test this suggestion we have prepared *t*-butylglyoxal[3] and treated it with aromatic compounds in the presence of aluminum chloride. The expected acyloins were formed in good yields.

t-Butylglyoxal (I) was synthesized from pinacolone by oxidation with selenium dioxide according to the general procedure of Riley, Morley and Friend.[4] The glyoxal was a yellow liquid boiling at 114–115°. It formed a hemihydrate, a phenylhydrazone, a 2,4-dinitrophenylhydrazone, an osazone, a semicarbazone, a dioxime and a quinoxaline derivative. Treatment with aqueous alkali transformed the glyoxal into β,β,β-trimethyllactic acid. When allowed to stand the glyoxal polymerized to a viscous liquid from which it could be regained by heating.

Condensation with benzene in the presence of aluminum chloride gave a solid product, melting at 46–47°, which proved to be the expected phenylpivalylcarbinol (II).



The latter was identified by formation of the 2,4-dinitrophenylhydrazone, the benzoate and *t*-butyl phenyl diketone (III), which was treated with *o*-phenylenediamine to give 2-*t*-butyl-3-phenylquinoxaline (IV).

Condensation of *t*-butylglyoxal with toluene, *m*-xylene and mesitylene in the presence of aluminum chloride gave the corresponding acyloins, from which the diketones were prepared by oxidation with concentrated nitric acid. The mesityl diketone was isolated as the solid mononitro derivative.

The *p*-tolyl diketone gave a quinoxaline derivative, but the *m*-xylyl and 3-nitromesityl analogs did not react with *o*-phenylenediamine under these conditions.

A rearrangement of the benzilic acid type was effected by treatment of *t*-butyl phenyl diketone with alkali, giving β,β,β-trimethylatrolactic acid (V). This is the first recorded example of such a reaction with a mixed aromatic–aliphatic 1,2-diketone.

(1) This is the fourth paper in this series. For the preceding communication see Fuson, Emerson and Weinstock, THIS JOURNAL, **61**, 412 (1939).

(2) Röhm and Haas Research Assistant, 1938–1939.

(3) Since this work was completed the synthesis of the glyoxal and its hemihydrate was reported by Taylor, Callow and Francis [*J. Chem. Soc.*, 257 (1939)].

(4) Riley, Morley and Friend, *ibid.*, 1875 (1932).

t-Butyl phenyl diketone resembled benzil[5] in its behavior with metallic sodium; benzoyl chloride converted the sodium derivative to the dibenzoate of *t*-butylphenylacetylene glycol (VI).

Experimental

***t*-Butylglyoxal.**—A mixture of 100 cc. of methyl alcohol,[6] 5 cc. of water and 111.2 g. of selenium dioxide was refluxed, with stirring, until the selenium dioxide dissolved, and then 122 cc. of pinacolone was added rapidly. The clear solution became red and then black after a few minutes. Refluxing and vigorous stirring were continued for six hours,[7] after which the reaction mixture was cooled and the precipitated selenium was removed by filtration. The yellow filtrate was distilled at atmospheric pressure from a modified Claisen flask having a 7-in. (18-cm.) column. After rejection of a fraction distilling from 65 to 110°, a yellow distillate was collected from 110 to 120°. A high-boiling residue which contained selenium was always present. Fractionation of the yellow oil gave 60 cc. of the yellow *t*-butylglyoxal, boiling at 114–115°.[8] The yield was 52% of the theoretical amount. Analyses for carbon and hydrogen showed that the product was not entirely pure. It became viscous on standing, even in a sealed container. The refractive index of the freshly distilled glyoxal increased rapidly, a typical determination showing a rise from 1.4287 to 1.4454 during the first hour. The resulting polymer was unreactive, hence it was necessary to distill the material before use. It was also found convenient to keep the glyoxal as the hydrate. The anhydrous monomer was prepared from its hydrate by dissolving the latter in methyl alcohol and subjecting the solution to fractional distillation.

Hemihydrate.—To 5 cc. of the glyoxal was added 1 cc. of water; appreciable evolution of heat was observed. The solution was allowed to stand overnight to allow the product to crystallize. It was recrystallized from 10 cc. of benzene, m. p. 91–92°,[9] with softening at 85°.

Anal. Calcd. for $C_{12}H_{22}O_5$: C, 58.51; H, 9.01. Found: C, 58.55; H, 9.10.

The 2,4-dinitrophenylhydrazone separated from alcohol as yellow crystals, m. p. 171–172°.

Anal. Calcd. for $C_{12}H_{14}O_5N_4$: C, 48.98; H, 4.80; N, 19.04. Found: C, 49.01; H, 4.87; N, 19.19.

Treatment with phenylhydrazine gave a **phenylhydrazone** or an **osazone,** depending upon the conditions employed. An excellent yield of the phenylhydrazone was obtained by allowing an alcohol solution of equimolecular amounts of the reactants to stand at room temperature for one hour. The pale yellow phenylhydrazone was precipitated by the addition of water and crystallized from ethyl acohol, m. p. 119–120°.

Anal. Calcd. for $C_{12}H_{16}ON_2$; C, 70.55; H, 7.90; N, 13.72. Found: C, 70.11; H, 7.83; N, 13.72.

The **osazone** was prepared by dissolving the theoretical amounts of the reactants in alcohol, adding a few drops of concentrated hydrochloric acid and heating the resulting solution for six hours under reflux. The warm (50°) solution was diluted with water until turbid and allowed to cool. The bright yellow osazone was recrystallized from ethyl alcohol, m. p. 119.5–120°.[10] A mixture of the osazone and the phenylhydrazone melted at about 100°.

Anal. Calcd. for $C_{18}H_{22}N_4$: C, 73.43; H, 7.54; N, 19.03. Found: C, 73.69; H, 7.60; N, 18.97.

Treatment with semicarbazide gave a **monosemicarbazone** which, after recrystallization from aqueous ethyl alcohol, melted at 134–135°.

Anal. Calcd. for $C_7H_{13}O_2N_3$: C, 49.11; H, 7.65; N, 24.55. Found: C, 49.23; H, 7.51; N, 24.35.

The dioxime was crystallized from aqueous ethyl alcohol, m. p. 100.5–101.5°.

Anal. Calcd. for $C_6H_{12}O_2N_2$: C, 49.98; H, 8.39; N, 19.43. Found: C, 50.10; H, 8.50; N, 19.11.

Wittorf,[11] who obtained this compound by the action of hydroxylamine on dibromopinacolone, reported a melting point of 101–102°.

Nitroquinoxaline.—To a refluxing solution of 1.5 g. of *p*-nitro-*o*-phenylenediamine in 25 cc. of glacial acetic acid was added 1.25 g. of *t*-butylglyoxal hydrate. The solution was refluxed for one hour, diluted with water until the appearance of turbidity, and cooled to room temperature. The nitroquinoxaline was treated with Norite and recrystallized from ethyl alcohol, m. p. 134.5–135°.

Anal. Calcd. for $C_{12}H_{13}O_2N_3$: C, 62.32; H, 5.67; N, 18.18. Found: C, 62.27; H, 5.53; N, 18.14.

β,β,β-Trimethyllactic Acid.—One gram of *t*-butylglyoxal hydrate was added to a solution of 8 g. of sodium hydroxide in 24 cc. of water. The mixture was shaken for a few minutes, and the resulting clear solution was allowed to stand at room temperature. After about one hour the sodium salt of β,β,β-trimethyllactic acid precipitated. This material was separated by filtration, dissolved in water, and the solution acidified with hydrochloric acid. The solution was extracted with three 25-cc. portions of ether, and the ether solution was dried over anhydrous magnesium sulfate. The white crystalline β,β,β-trimethyllactic acid, obtained by evaporation of the solvent, was purified by recrystallization from high-boiling petroleum ether. The yield was 93% of the theoretical amount, m. p. 86.5–87.5°. This melting point is in agreement with the findings of Favorskiĭ,[10] Wittorf[11] and Glücksmann.[12]

Phenylpivalylcarbinol.—A mixture of 54 g. (0.4 mole) of aluminum chloride and 80 cc. of dry benzene was cooled in an ice-bath and a solution of 23 g. (0.2 mole) of freshly distilled *t*-butylglyoxal in 20 cc. of dry benzene was added, with stirring, over a period of one-half hour. The reaction

(5) Nef, *Ann.*, **308**, 264 (1899).

(6) Various other solvents (dioxane, acetic anhydride and benzene) proved to be unsatisfactory due to difficulties in fractionation of the product.

(7) In several cases formation of a solid cake of precipitated selenium during the first hour made further stirring impracticable.

(8) This boiling point is in agreement with that reported by Taylor, Callow and Francis.[3]

(9) Taylor, Callow and Francis[3] give a melting point of 85°.

(10) This compound was obtained by Favorskiĭ [*J. Russ. Phys.-Chem. Soc.*, **44**, 1339 (1912); *J. prakt. Chem.*, [2] **88**, 641 (1913)] by the action of phenylhydrazine on pivalylcarbinol.

(11) Wittorf, *ibid.*, **32**, 88 (1900); *Chem. Zentr.*, **71**, II, 29 (1900).

(12) Glücksmann, *Monatsh.*, **10**, 770 (1889).

mixture became black during the addition. Stirring was continued for six hours (one hour in ice-bath, five hours at room temperature) and the mixture was allowed to stand overnight at room temperature. It was added, with vigorous stirring, to a mixture of 100 cc. of concentrated hydrochloric acid and 300 g. of ice. The yellow benzene layer was washed with dilute sodium bicarbonate solution and with water, and dried over anhydrous sodium sulfate. The residue, after evaporation of the solvent, distilled at 90–102° (2 mm.). The acyloin so obtained soon solidified, and was recrystallized from aqueous alcohol, m. p. 46–47°. The yield was 49% of the theoretical amount.

Anal. Calcd. for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 75.19; H, 8.49.

The 2,4-dinitrophenylhydrazone was recrystallized from ethyl alcohol, m. p. 174–175°.

Anal. Calcd. for $C_{18}H_{20}O_5N_4$: C, 58.05; H, 5.41; N, 15.04. Found: C, 58.12; H, 5.48; N, 14.74.

Benzoate.—One-half gram of phenylpivalylcarbinol was dissolved in 1 cc. of benzoyl chloride and warmed for a few minutes. The solution was cooled and poured into 20 cc. of water, with vigorous stirring. The water was removed by decantation and the oily residue was warmed with 5 cc. of 10% sodium hydroxide solution. The mixture was cooled overnight, and the solid material was removed by filtration and washed with water. Recrystallization from ethyl alcohol gave lustrous white crystals, m. p. 96–97°.

Anal. Calcd. for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80. Found: C, 76.94; H, 6.81.

***t*-Butyl Phenyl Diketone.**—This diketone and the others described below were made by the following method. The acyloin (0.05 mole) was added to 15 cc. of concentrated nitric acid and the mixture was warmed on the steam-cone for two hours. When cool the reaction mixture was poured into 50 cc. of water and the yellow oily layer separated. It was dissolved in ether, and the ether solution washed with aqueous sodium bicarbonate solution and with water. After the ether solution was dried over sodium sulfate, the solvent was evaporated and the residue distilled under diminished pressure, b. p. 75–76° (1 mm.); d^{20}_{20} 1.016; $n^{20}D$ 1.5086.

Anal. Calcd. for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42; M_D, 55.1.[13] Found: C, 75.71; H, 7.47; M_D, 55.8.

2-*t*-Butyl-3-phenylquinoxaline.—*t*-Butyl phenyl diketone was converted to the corresponding quinoxaline by the following procedure. The yield was nearly quantitative. To a refluxing solution of 0.6 g. of *o*-phenylenediamine and 25 cc. of glacial acetic acid was added 1 cc. of the diketone. After the refluxing had continued for two hours the solution was diluted with water to the appearance of turbidity and allowed to cool. The 2-*t*-butyl-3-phenylquinoxaline was recrystallized from aqueous ethyl alcohol, m. p. 108–109°.

Anal. Calcd. for $C_{18}H_{18}N_2$: C, 82.41; H, 6.91; N, 10.68. Found: C, 82.19; H, 6.97; N, 10.59.

(13) In this calculation as well as in those made for the molecular refractivity of other 1,2-diketones mentioned in this paper, an exaltation of 1.05 is ascribed to the conjugation of the two carbonyl groups and three olefinic linkages are assigned to the aromatic nucleus. See Auwers, *Ber.*, **51**, 1116 (1918).

***p*-Tolylpivalylcarbinol.**—The use of toluene in the Friedel–Crafts reaction gave 21.5 g., a yield of 52% of the theoretical amount, of the acyloin, m. p. 48–49°. (The crude material boiled at 115–125° at 2 mm.)

Anal. Calcd. for $C_{13}H_{18}O_2$: C, 75.69; H, 8.79. Found: C, 75.69; H, 8.67.

The diketone boiled at 97–97.5° (1 mm.); d^{20}_{20} 1.016; $n^{20}D$ 1.5125.

Anal. Calcd. for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90; M_D, 59.7. Found: C, 76.37; H, 8.01; M_D, 60.4.

2-*t*-Butyl-3-*p*-tolylquinoxaline.—By use of the procedure outlined for the phenyl analog this quinoxaline was obtained in almost the theoretical yields, m. p. 109–110°.

Anal. Calcd. for $C_{19}H_{20}N_2$: C, 82.57; H, 7.30; N, 10.14. Found: C, 82.41; H, 7.51; N, 10.18.

***m*-Xylylpivalylcarbinol.**—When *m*-xylene was used there was obtained 18.5 g. of the liquid acyloin, b. p. 133–135° (4 mm.). The yield was 42% of the theoretical amount; d^{20}_{20} 1.100; $n^{20}D$ 1.5134.

Anal. Calcd. for $C_{14}H_{20}O_2$: C, 76.32; H, 9.15; M_D, 59.6. Found: C, 76.44; H, 9.03; M_D, 60.1.

A solid material which precipitated from the crude acyloin before distillation was recrystallized from alcohol, giving 6 g. of **di-(*m*-xylyl)-pivalylmethane,** m. p. 111.5–112°.

Anal. Calcd. for $C_{22}H_{28}O$: C, 85.66; H, 9.15. Found: C, 85.84; H, 9.03.

The diketone boiled at 103–104° (1 mm.); d^{20}_{20} 1.017; $n^{20}D$ 1.5177.

Anal. Calcd. for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31; M_D, 64.3. Found: C, 76.72; H, 8.34; M_D, 65.0.

Treatment for eleven hours with a boiling solution of *o*-phenylenediamine in acetic acid failed to yield any quinoxaline. The original diketone was recovered. It was identified by conversion to 2,4-dimethyl-3,5-dinitrobenzoic acid described below.

2,4-Dimethyl-3,5-dinitrobenzoic Acid.—A mixture of 5 cc. of concentrated nitric acid and 5 cc. of concentrated sulfuric acid was cooled in an ice-bath and 0.25 cc. of *t*-butyl *m*-xylyl diketone was added dropwise, with stirring. The solution was poured on ice, with stirring, and the precipitated acid separated by filtration. It was recrystallized from glacial acetic acid, m. p. 202–203°.

Anal. Calcd. for $C_9H_8O_6N_2$: C, 45.00; H, 3.38; N, 11.66. Found: C, 45.54; H, 3.41; N, 11.35.

Claus[14] reported a melting point of 199–200° (uncorr.) for this compound.

Mesitylpivalylcarbinol.—Distillation of the excess mesitylene from the reaction product left a solid residue which was recrystallized from alcohol. There was obtained 14 g., a yield of 30% of the theoretical amount, of the acyloin, m. p. 118–118.5°.

Anal. Calcd. for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 76.91; H, 9.45.

***t*-Butyl 3-Nitromesityl Diketone.**—The mesitylpivalylcarbinol was heated for three hours with 15 cc. of concentrated nitric acid. The oil which was isolated by dilution of the mixture with water was dissolved in ether.

(14) Claus, *J. prakt. Chem.*, [2] **41**, 483 (1890).

washed and dried; it distilled at 110 to 170° (*ca.* 0.5 mm.). The distillate was heated for three hours with a fresh 15-cc. portion of nitric acid. The product was isolated, dissolved in ether, washed and dried. Evaporation of the ether gave the bright yellow diketone, which was recrystallized from aqueous methyl alcohol, m. p. 58–59°.

Anal. Calcd. for $C_{15}H_{19}O_4N$: C, 64.96; H, 6.91; N, 5.05. Found: C, 64.87; H, 7.03; N, 5.15.

Like the xylyl analog this diketone failed to give a quinoxaline. Even after fifteen hours' treatment the diketone was almost entirely recovered.

β,β,β-Trimethylatrolactic Acid.—One cubic centimeter of *t*-butyl phenyl diketone was added to a solution of 2 g. of potassium hydroxide and 1 cc. of ethyl alcohol in 10 cc. of water. This mixture was refluxed until a clear solution was obtained (about six hours). Acidification with hydrochloric acid precipitated an oily material which was separated and treated with low-boiling petroleum ether. The white solid acid which separated was removed by filtration and recrystallized from high-boiling petroleum ether, m. p. 105–106°.

Anal. Calcd. for $C_{12}H_{16}O_3$: C, 69.21; H, 7.75; neut. equiv., 208. Found: C, 69.33; H, 7.95; neut. equiv., 208.

Dibenzoate of *t*-Butylphenylacetylene Glycol.—A mixture of 0.26 g. of sodium, 20 cc. of dry toluene and 1 cc. of *t*-butyl phenyl diketone was refluxed in an atmosphere of nitrogen for two hours, with vigorous stirring. After addition of 1.25 cc. of benzoyl chloride, the dark brown reaction mixture was heated and stirred for a few minutes and then cooled to room temperature. The excess sodium and the precipitated sodium chloride were removed by filtration and the filtrate was concentrated to a viscous brown oil. The dibenzoate was recrystallized from high-boiling petroleum ether, m. p. 138–139°.

Anal. Calcd. for $C_{26}H_{25}O_4$: C, 77.98; H, 6.04. Found: C, 77.96; H, 6.12.

Summary

t-Butylglyoxal condenses with benzene, toluene, *m*-xylene and mesitylene to give acyloins of the type $(CH_3)_3CCOCH(OH)Ar$. Oxidation with nitric acid converts the acyloins to the corresponding diketones. In the case of the mesityl compound the diketone is isolated in the form of its mononitro derivative.

The diketones derived from benzene and toluene react normally with *o*-phenylenediamine to give quinoxalines. This reaction could not be effected with the *m*-xylyl or mesityl diketones.

t-Butyl phenyl diketone undergoes the benzilic acid rearrangement to give β,β,β-trimethylatrolactic acid. The sodium derivative of this diketone reacts with benzoyl chloride to give the dibenzoate of *t*-butylphenylacetylene glycol. The two foregoing types of reaction hitherto had been restricted to benzils and aliphatic 1,2-diketones.

URBANA, ILLINOIS RECEIVED APRIL 17, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

The Methylation of β-Ketonitriles

BY REYNOLD C. FUSON AND DONALD E. WOLF

The discovery that α-cyanoacetomesitylene (IV) and α-cyanopropiomesitylene gave only O-methylation products[1] suggested that the steric hindrance present in these β-ketonitriles favored O-methylation.[2] As a test of this suggestion an unhindered β-ketonitrile, *p*-bromophenacyl cyanide (I), has been methylated under similar conditions. It reacted with methyl sulfate in the presence of aqueous potassium hydroxide to give the O-methyl ether (II). When the alkylating agent was methyl iodide in the presence of sodium ethoxide, a different compound, the C-methylated product (III), was formed.

The structure of the enol methyl ether (II) was established by analysis for methoxyl and by its insolubility in alkali. Both the parent compound (I) and the C-methylated derivative (III) are soluble in 10% sodium hydroxide solution and in 10% sodium carbonate solution. Compound III was hydrolyzed easily to give *p*-bromobenzoic acid. When allowed to stand for some time it decomposed spontaneously, probably by autoxidation of its enol—a phenomenon previously noted for compounds of this type.[3]

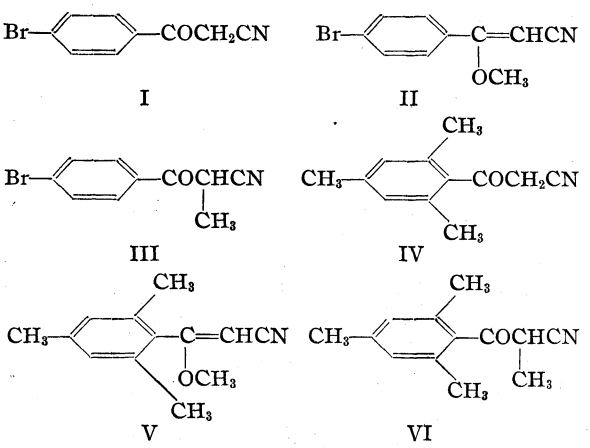
The structure of the C-methylated product, α-(*p*-bromobenzoyl)-propionitrile (III), was established by synthesis, employing the method used by Dorsch and McElvain[4] for similar compounds. Ethyl *p*-bromobenzoate was condensed with propionitrile in the presence of sodium ethoxide. The product proved to be α-(*p*-bromobenzoyl)-propionitrile (III).

(1) Fuson, Ullyot and Gehrt, THIS JOURNAL, **60**, 1199 (1938).

(2) This idea was developed by Kohler and his co-workers in connection with mesityl ketones. For a leading reference see Kohler and Thompson, *ibid.*, **59**, 887 (1937).

(3) Jenkins, *ibid.*, **57**, 2733 (1935).

(4) Dorsch and McElvain, *ibid.*, **54**, 2960 (1932).



The formation of the O-methylated derivative (II) of an unhindered phenacyl cyanide is not without precedent since Arndt and his co-workers[5] have reported recently that phenacyl cyanide reacts with diazomethane to give *trans*-β-methoxycinnamonitrile. The formation of the C-methylated derivative (III) by the method employed here seems to be a new reaction.

Inasmuch as the experimental conditions used in methylating *p*-bromophenacyl cyanide were not entirely parallel with those used by Fuson, Ullyot and Gehrt[1] in working with α-cyanoacetomesitylene, a further study was made of the latter (IV). It was found that when the methylating agent was methyl iodide in the presence of sodium ethoxide both O-methylated (V) and C-methylated (VI) derivatives were obtained in nearly equivalent amounts.

Two crystalline forms of the β-methoxy-β-mesitylacrylonitrile (V) were isolated. The identity of each was established by mixed melting points with authentic samples prepared by Fuson, Ullyot and Gehrt.[1] The structure of α-cyanopropiomesitylene (VI) was established by the synthesis of this compound, using the method described by Fuson, Ullyot and Gehrt.[1]

It therefore appears that the steric hindrance present in α-cyanoacetomesitylene favors O-methylation but not to the complete exclusion of C-methylation.

Experimental

p-Bromophenacyl Cyanide (I).—The method used by Grothaus and Dains[6] for the preparation of this compound from *p*-bromophenacyl chloride and sodium cyanide was not found satisfactory when *p*-bromophenacyl bromide was the starting material. The method accordingly was modified as follows. Ten grams of *p*-bromophenacyl bromide was dissolved in about 400 cc. of 95% ethanol. To this solution was added, dropwise and with stirring, a solution of 4.7 g. of potassium cyanide in the minimum amount of water. The reaction mixture was stirred for five hours at room temperature during which time a white crystalline precipitate formed, and then for one hour in an ice–salt bath. The precipitate was collected on a filter and dissolved in water. The cloudy aqueous solution was clarified with Darco. Treatment with hydrochloric acid gave 6 g. of a fine white precipitate of *p*-bromophenacyl cyanide (m. p. 162–163°) sufficiently pure for use.

Methylation of *p*-Bromophenacyl Cyanide with Methyl Sulfate.—A mixture of 2 g. of dry *p*-bromophenacyl cyanide and 4.6 g. of methyl sulfate was heated under reflux to 70° and 3 g. of potassium hydroxide in 40 cc. of water was added slowly, with stirring, over a fifteen-minute period while the bath temperature was raised from 70 to 130°. A yellow oil separated during the addition of potassium hydroxide solution. One and thirty-five hundredths grams of methyl sulfate was added and the heating continued for five minutes. The container was surrounded by an ice-bath and 1 g. of potassium hydroxide in 150 cc. of water was added. The yellow oil solidified leaving a clear solution. The oily solid was dried and treated with petroleum ether. The insoluble portion was starting material melting at 162–163°. The petroleum ether solution was washed with potassium carbonate solution and the solvent evaporated. The crude methoxy nitrile (II) weighed about 0.7 g. and melted at 56–58°. It was recrystallized twice from high boiling petroleum ether and melted at 58.5–59.5°.[7]

Anal. Calcd. for $C_{10}H_8BrNO$: C, 50.46; H, 3.39; OCH_3, 13.03. Found: C, 50.49; H, 3.33; OCH_3, 12.94, 12.92.

No other product could be detected.

Methylation of *p*-Bromophenacyl Cyanide with Methyl Iodide and Sodium Ethoxide.—To a solution of 0.35 g. of clean sodium in 100 cc. of absolute ethanol was added 3.45 g. of dry *p*-bromophenacyl cyanide. The reaction mixture was heated, with stirring, until it refluxed gently. Not all the solid was in solution. A solution of 3.5 cc. of methyl iodide in 40 cc. of absolute ethanol was added slowly, with stirring. The remaining solid dissolved. Refluxing was continued until samples of the reaction mixture gave a neutral test with moist litmus paper (one to one and a half hours).

The solution was concentrated to 25 cc. and the concentrate cooled to 0°. Forty cubic centimeters of ice water was added followed by 40 cc. of ether, and the solution was shaken to dissolve the solid. A few drops of 10% sodium hydroxide solution were necessary to bring about complete solution. The aqueous layer was separated and acidified with dilute sulfuric acid, giving a solid and an oil. Treatment with ether dissolved the precipitate. The ether extract was washed with saturated sodium bicarbonate solution to remove any *p*-bromobenzoic acid, then with water and finally was dried over anhydrous sodium sulfate. The solvent was evaporated yielding an oil which crystallized

(5) Arndt, Loewe, Günter and Sepahi, *Ber.*, **71B**, 1627 (1938); Arndt, Loewe, Özsöy, Ogüt, Arslan and Bagevi, *ibid.*, **71B**, 1631 (1938).

(6) Grothaus and Dains, THIS JOURNAL, **58**, 1334 (1936).

(7) The melting points reported in this paper have all been corrected.

when cooled. The product was difficult to purify because when it was heated with methyl alcohol or aqueous sodium carbonate it decomposed to give *p*-bromobenzoic acid. Purification was accomplished by dissolving the solid in cold sodium carbonate solution (10%), decolorizing with Darco and very carefully precipitating the product by addition of dilute sulfuric acid to the solution at 0° until the first appearance of turbidity. A pure product was also obtained from aqueous methanol when heating was avoided. The pure ketonitrile (III) melted at 74.5–75.5°.

Anal. Calcd. for $C_{10}H_8BrNO$: C, 50.46; H, 3.39. Found: C, 51.06; H, 3.49.

A Zeisel determination showed the absence of a methoxyl group.

The identity of the *p*-bromobenzoic acid resulting from the decomposition of the C-methyl derivative (III) was verified by a neutral equivalent determination and a mixed melting point with an authentic sample.

Synthesis of α-(*p*-Bromobenzoyl)-propionitrile (III).—A mixture of 23 g. of ethyl *p*-bromobenzoate and 6.8 g. of sodium ethoxide was warmed under reflux to 80° and stirred until it became homogeneous. Seven grams of propionitrile was added slowly, with stirring, to this mixture over a period of half an hour. Following the addition of propionitrile the temperature of the mixture was raised to 110–120° and maintained at this point for ten hours, with continuous stirring.

The reaction mixture was cooled to 0°, treated with 40 cc. of ice water and 100 cc. of ether, and shaken until the solid was dissolved. The aqueous layer was separated and acidified with dilute sulfuric acid, giving an oil and a white solid. The insoluble material was extracted with ether and washed three times with saturated sodium bicarbonate solution, then once with water, and the ether solution dried over anhydrous sodium sulfate.

When the ether was evaporated a tan oil was left which yielded crystals when cooled. The crude product was dissolved in 10% sodium carbonate solution, decolorized with Darco and precipitated by careful addition of dilute sulfuric acid to the ice cold solution until the appearance of turbidity. The melting point of the pure α-(*p*-bromobenzoyl)-propionitrile was 74.5–75.5°.

A mixed melting point with the ketonitrile (III) prepared by methylation of *p*-bromophenacyl cyanide was 74.5–75.5°.

Anal. Calcd. for $C_{10}H_8BrNO$: N, 5.89. Found: N, 5.83.

Methylation of α-Cyanoacetomesitylene with Methyl Iodide.—To a solution of 0.615 g. of clean sodium in 200 cc. of absolute ethanol was added 5 g. of α-cyanoacetomesitylene. The reaction mixture was stirred and heated until it refluxed gently, precautions being taken to preserve anhydrous conditions. To the refluxing solution was added slowly 6.7 cc. of methyl iodide dissolved in 25 cc. of absolute ethanol. Refluxing was continued for two hours following addition of the methyl iodide; at the end of this time the reaction mixture gave no basic test with moist red litmus paper.

The solution was concentrated to 50 cc., cooled in an ice-bath and poured into 100 cc. of ice water to which 5 cc. of a 10% sodium hydroxide solution had been added. The mixture was shaken with 100 cc. of ether.

The ether layer was separated and shaken with a 10% sodium carbonate solution to take out any alkali-soluble material which might be present. The ether was then dried over sodium sulfate and evaporated, giving an oil. Crystallization was brought about when methanol was added and the solution was immersed in a dry-ice–acetone bath. The crude O-methylated product (V) thus obtained melted at 64–65.5° and weighed about 0.85 g. A small amount of oil remained from which no solid product could be obtained even on long standing dissolved in ligroin. Compound V was dissolved in ligroin and allowed to crystallize slowly. The first crop consisted of small rhombic crystals which melted at 65.5–66°. This was evidently the *cis* form identical with the low melting form obtained by Fuson, Ullyot and Gehrt.[1] A mixed melting point with a sample of their compound confirmed the identity. On longer standing a second crop of crystals appeared, this time in rosets of needles melting at 68–69°. These were the mixed-crystal form consisting of both *cis* and *trans* isomers. A mixture with an authentic sample of the same form showed no lowering of the melting point.

The aqueous layer and the sodium carbonate solution employed to wash the ether layer above were treated as follows. The solution was acidified with dilute sulfuric acid and the precipitate extracted with ether. The ether was dried over sodium sulfate and evaporated, leaving an oil which crystallized to colorless plates on standing in an ice box. The crude material melted at about 126°. It was dissolved in cold 10% sodium carbonate solution, cooled in an ice-bath and acidified to the first permanent turbidity with dilute sulfuric acid. Approximately 0.9 g. of white crystals (VI) was thus obtained melting at 127–128.5°. Addition of more sulfuric acid caused the precipitation of about 0.5 g. more of solid material which proved to be mainly starting material. Compound VI was further purified by recrystallization from aqueous methanol giving small white crystals melting at 130–131°. A mixed melting point with a sample synthesized by the method of Fuson, Ullyot and Gehrt[1] showed no lowering.

Summary

1. It has been shown that *p*-bromophenacyl cyanide reacts with methyl sulfate in the presence of potassium hydroxide to yield the O-methyl ether (II). When the alkylating agent was methyl iodide in the presence of sodium ethoxide the C-methyl derivative (III) was obtained.

2. α-Cyanoacetomesitylene when treated with methyl iodide in the presence of sodium ethoxide has been found to yield roughly equal quantities of the O-methylated derivative (V) and the C-methylated derivative (VI).

URBANA, ILLINOIS RECEIVED APRIL 24, 1939

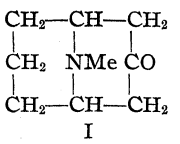
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

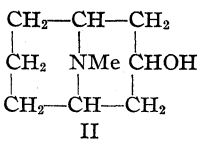
The Validity of the Structure Assigned to Cycloöctatetrene: Pyrolysis of *bis*-Quaternary Ammonium Hydroxides Related to 1,2- and 2,3-Butenes

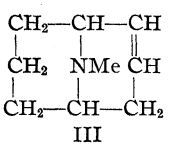
BY CHARLES D. HURD AND LEWIS R. DRAKE

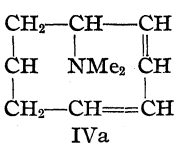
The evidence for the structure of 1,3,5,7-cycloöctatetrene, discovered by Willstätter and Waser[1] and used so widely in theoretical discussions concerning the structure of the aromatic nucleus, rests chiefly on its mode of synthesis from pseudopelletierine and on its hydrogenation to cycloöctane. The hydrogenation evidence does not establish the position of the double bonds at 1,3,5,7 for any cycloöctatetrene should hydrogenate to cycloöctane. In the evidence of synthesis there was the tacit assumption that exhaustive methylation would give rise to conjugate unsaturation; but this was the very feature they were trying to establish. Of course, if other types of unsaturation were present, the structural similarity to benzene would disappear. As is well known, cycloöctatetrene is reactive and displays no such inertness as is found in benzene or diphenylhexatriene,[2] C_6H_5—$(CH=CH)_3$—C_6H_5.

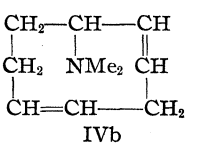
These steps were involved in Willstätter and Waser's synthesis. Pseudo-pelletierine (I) was reduced to II, which was dehydrated to N-methylgranatenine (III). Next, III was converted to a quaternary ammonium salt with methyl iodide, then subjected to a Hofmann degradation. The reaction product was assigned structure IVa,

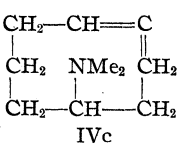

I


II


III

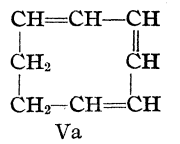

IVa

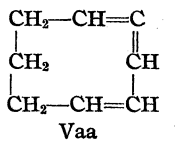

IVb

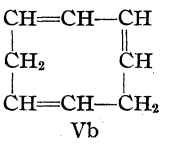

IVc

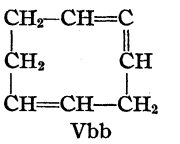
without submitting evidence, however, to show that this cycloöctadiene skeleton must possess 1,3-unsaturation as in (a) to the exclusion of 1,4- or 1,2-unsaturation as in (b) or (c).

From IVa, a cycloöctatriene was prepared by another process of exhaustive methylation. Its structure was listed as Va, but Vaa may have been produced concurrently. Furthermore, if IVb and IVc were involved in the exhaustive methylation, two other isomers would appear, namely, Vb and Vbb.

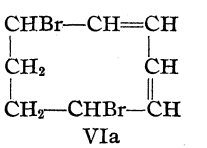

Va

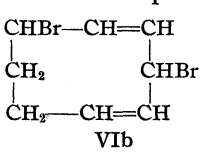

Vaa

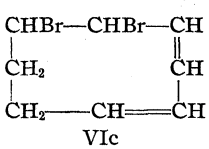

Vb

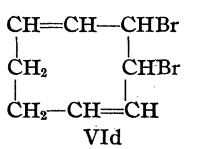

Vbb

The next step was one of bromine addition to convert C_8H_{10} into $C_8H_{10}Br_2$. If all four cycloöctatrienes participated in this reaction, fourteen such dibromides would be anticipated by normal addition at 1,2- or 1,4- or 1,6-positions (four isomers each from Va and Vaa, and three each from Vb and Vbb). Even if Va were the only isomer, as Willstätter and Waser assumed, these four isomers would be reasonable reaction products


VIa


VIb


VIc


VId

but only from VIa would it be possible to synthesize the conjugated cycloöctatetrene, unless molecular rearrangements were assumed. No evidence eliminated VIb, VIc or VId as reaction products and no evidence was submitted to uphold VIa.

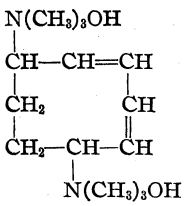
Next, the dibromide (or the dibromide mixture) was heated in benzene with dimethylamine to obtain the *bis-t*-amine, $C_8H_{10}(NMe_2)_2$. Willstätter mentions that this material was not homogeneous but consisted chiefly of an amine which was stable toward acids together with a lesser quantity of an amine which could be hydrolyzed readily. Structures such as C—C—C—NMe_2 or C=C—C—NMe_2 are stable toward hy-

(1) Willstätter and Waser, *Ber.*, **44**, 3433 (1911); Willstätter and Heidelberger, *ibid.*, **46**, 517 (1913)

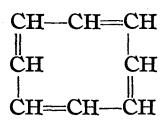
(2) Kuhn and Winterstein, *Helv. Chim. Acta*, **11**, 87 (1928).

drolytic scission, but C—C=C—NMe_2 is a structure which hydrolyzes with acids. It is an ammono analog of the enol ethers and as such it should hydrolyze readily with acids. Structures Vaa and Vbb would yield dibromides which, in turn, would generate the *bis-t*-amines containing the hydrolyzable group C—C=C—NMe_2. It is evident that if Vaa and Vbb are present, this makes a strong case for the presence of all the other isomers.

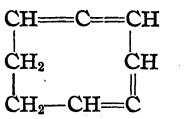
The final step of the synthesis was conversion of the *bis-t*-amine to the *bis*-quaternary ammonium hydroxide, $C_8H_{10}(NMe_3OH)_2$, and pyrolysis of the latter in a Hofmann degradation. The above argument points to the presence of between one and fourteen isomeric quaternary hydroxides. Let us, however, assume the presence of only one of these isomers, namely, the isomer (VII) required by Willstätter and Waser.



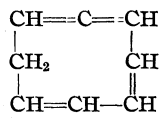
VII



VIIIa



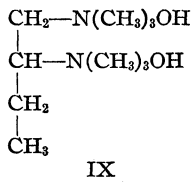
VIIIb



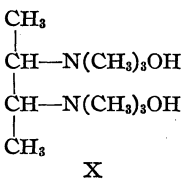
VIIIc

Its breakdown should not necessarily follow an exclusive course leading to 1,3,5,7-cycloöctatetrene (VIIIa). There should be concurrent production of the 1,2,4,5- and 1,2,4,6-isomers (VIIIb and VIIIc, respectively). Of course, other isomers would appear if any of the other fourteen hydroxides entered the reaction.

The question involved may be restated as follows. Must a *bis*-quaternary ammonium hydroxide give rise to conjugate double bonds wherever possible and avoid the production of cumulative double bonds? To obtain evidence on this point it was decided to study the decomposition of some simple *bis*-quaternary bases so that the results would be determined unambiguously. The bases selected for study were the 1,2- and the 2,3-disubstituted butanes, IX and X. The products anticipated from IX by pyrolysis would be methylallene and ethylacetylene, but not 1,3-butadiene. From X one would expect 1,3-butadiene, methylallene and dimethylacetylene.



IX



X

It is possible to analyze either type of gas mixture volumetrically by absorbing ethylacetylene in alkaline potassium iodomercurate solution, 1,3-butadiene in molten maleic anhydride,[3] and methylallene or dimethylacetylene in 82% sulfuric acid. By so doing it was established that IX yielded a mixture containing 44% of ethylacetylene and 56% of methylallene. There was no 1,3-butadiene. The hydrocarbons from X did contain 1,3-butadiene as expected, but it was only to the extent of 42–47% instead of being quantitative. The other 58–53% was a mixture of methylallene and dimethylacetylene. The fact that none of the conjugated hydrocarbon came from IX, and that 1,3-butadiene was not the exclusive product from X casts serious doubt on the structure of Willstätter's cycloöctatetrene.

Experimental Part

Reagents.—Trimethylamine was prepared by the method given in "Organic Syntheses."[4] It was distilled from a Davis column, b. p. 3–4.5°. The synthesis of pure 1-butene and pure 2-butene was described by Hurd and Goldsby.[5] Both of these hydrocarbons were available from this source and were used in the present work. The purity of both was reëstablished, however, by analytical distillation through the Frey–Hepp column. Pure 1-butene also was prepared in the present investigation by pyrolysis of *n*-butyltrimethylammonium hydroxide.

The pure 1-butene was converted into 1,2-dibromobutane by gradual addition of it into a solution of bromine in carbon tetrachloride at −10°. Purification was by distillation through an efficient vacuum-jacketed column. The fraction collected distilled at 165–166°. Similarly, pure 2,3-dibromobutane, b. p. 158–159°, was prepared from pure 2-butene.

***n*-Butyltrimethylammonium Bromide.**—This salt was prepared by mixing 30 g. of *n*-butyl bromide (b. p. 100°) with 12 g. of trimethylamine in a stoppered flask at 0°. After twelve hours, crystals were noticeable. The mixture was then left at room temperature for a week. The nearly solid mass was crystallized several times from butanol, washed a few times with ether, and centrifuged. The salt was deliquescent. In a sealed tube it melted at 197–198°. The yield was 39.7 g. or 92.5%.

Anal. Calcd. for $C_7H_{18}NBr$: Br, 40.8. Found: Br, 40.8, 40.6.

(3) Tropsch and Mattox, *Ind. Eng. Chem.*, **6**, 104 (1934).
(4) "Organic Syntheses," Coll. Vol. I, 1932, pp. 514–519.
(5) Hurd and Goldsby, THIS JOURNAL, **56**, 1813 (1934).

1-Butene.—To 6.65 g. of the bromide dissolved in 30 cc. of water, 3.94 g. of silver oxide was added. The mixture was shaken intermittently for one hour and the silver bromide filtered off. The filtrate was placed in a modified 50-cc. Claisen flask attached in series to a 50-cc. receiver, a small bubbler containing concd. hydrochloric acid, and a 2.5-liter bottle filled with salt solution. The bottle was disconnected at the outset.

The air in the system was displaced by nitrogen, and the contents of the flask heated to incipient boiling. Then the bottle was connected. When all the water was distilled off, the oil-bath temperature was raised slowly to 250°. Vigorous bubbling took place and about 750 cc. of gas was collected in the bottle.

The gas was dried through a soda-lime tube and was liquefied at −80° in the bulb of the Frey–Hepp column.[5] On distillation, 630 cc. of pure 1-butene was collected between −6.0° and −5.6°. There was no 2-butene.

1,2-Butane-bis-(trimethylammonium) Bromide.—A mixture of 22 g. of 1,2-dibromobutane and 10 g. of trimethylamine was left for two weeks at room temperature in a tightly-stoppered flask. The amount of crystals did not increase much after the first week. The excess of trimethylamine was boiled off and absorbed in hydrochloric acid. Then the excess of dibromobutane was decanted and the solid recrystallized from 20 cc. of butyl alcohol, rinsed repeatedly with dry ether, centrifuged, and stored in a vacuum desiccator over sulfuric acid; yield, 4.86 g. or 21%.

Anal. Calcd. for $C_{10}H_{26}N_2Br_2$: Br, 47.87. Found: Br, 47.77, 48.08.

Pyrolysis

Run 1.—A mixture of 4.26 g. (0.0128 mole) of this bromide, 30 cc. of water, and 3 g. (0.0128 mole) of silver oxide was shaken for one hour and the solution was filtered. The filtrate was heated first at 100°, then at 200–250° as described above for the decomposition of butyltrimethylammonium bromide. At the end of the reaction, the apparatus was filled with water to drive over the last portion of gas. In all, 300–310 cc. of gas was obtained.

Run 2.—The same quantities and apparatus were used as before, but this time the solution was allowed to drip into the hot flask (oil-bath at 250°) instead of warming the solution gradually. As before, the apparatus was filled with water at the end of the run. Three hundred thirty cc. of gas was secured.

Analysis.—No 1,3-butadiene was found. It was sought for by passing a sample of the gas through molten maleic anhydride[3] at 100°. Ethylacetylene was determined by absorption[6] in alkaline potassium iodomercurate solution. Methylallene, or a mixture of methylallene and dimethylacetylene, was determined by absorption in 83% sulfuric acid. Air made up 23.0–23.5% of the gas in both runs.

On an air-free basis, run 1 contained 44.5% ethylacetylene and 55.5% methylallene. Run 2 contained 45.5% ethylacetylene and 54.5% methylallene.

2,3-Butane-bis-(trimethylammonium) Bromide.—The same general procedure was used as that for the 1,2-analog. The quantities taken were 32 g. of trimethylamine and 52 g. of 2,3-dibromobutane. As before, a small quantity of oil separated in the first twelve hours only to be replaced by small cubical crystals in another twelve hours. The reaction was left for two weeks. After thorough purification, 4.9 g. (or 6.1%) of the salt was obtained.

Anal. Calcd. for $C_{10}H_{26}N_2Br_2$: Br, 47.87. Found: Br, 46.73, 48.90.

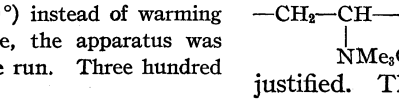
Pyrolysis.—Two runs were performed. Run 1 followed the conditions of run 1 of the 1,2-analog, with 3.72 g. of the salt in 30 cc. of water being treated with 2.6 g. of silver oxide. The volume of gaseous decomposition products was 250 cc. Run 2, with 4.00 g. of the salt, 30 cc. of water and 2.8 g. of silver oxide, corresponded in manipulative detail to run 2 of the 1,2-analog. About 240 cc. of gas was collected.

Gas Analysis.—On an air-free basis runs 1 and 2, respectively, analyzed as follows: 1,3-butadiene 42.5, 47.5; methylallene (or methylallene + dimethylacetylene) 57.5, 52.5. In both runs, there was 45–46% of air present.

Summary

Both 1,2- and 2,3-butane-*bis*-(trimethylammonium) bromides have been prepared from pure specimens of 1,2-dibromobutane and 2,3-dibromobutane. Pyrolysis of the *bis*-quaternary hydroxide from the 1,2-salt gave rise to ethylacetylene and methylallene, but no 1,3-butadiene. Pyrolysis of the bis-quaternary hydroxide from the 2,3-salt yielded 1,3-butadiene and methylallene (or methylallene + dimethylacetylene), the latter being slightly in excess of the 1,3-butadiene.

The assumption that conjugated unsaturation results exclusively during pyrolysis of the



functional group is unjustified. This assumption was made by Willstätter and Waser in their alleged synthesis of 1,3,5,7-cycloöctatetrene. The fact that 1,3-butadiene was not the exclusive product from 2,3-butane-*bis*-(trimethylammonium) hydroxide casts serious doubt on the structure of Willstätter's cycloöctatetrene.

EVANSTON, ILLINOIS RECEIVED MAY 15, 1939

(6) Hurd and Spence, THIS JOURNAL, **51**, 3356 (1929); Hurd and Meinert, *ibid.*, **53**, 294 (1931).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF STANFORD UNIVERSITY]

Carbonium Ions and the Hydrolysis of Alkyl Halides

BY R. A. OGG, JR.

A considerable controversy has developed concerning interpretation of the rates of alkyl halide hydrolysis by neutral water (as distinguished from substitution reaction with hydroxyl ion).[1] Hughes and Ingold assume that the mechanism embodies a slow unimolecular dissociation of the alkyl halide into halide ion and organic cation with an incomplete valence shell (an "open sextet"), followed by the rapid reaction of this cation with water to yield alcohol and hydrogen ion. Olson and Halford, as well as Taylor, conclude that the rate determining step is a bimolecular reaction of a water molecule with alkyl halide to yield halide ion and a cation whose valence shell is completed by coordination of a previously unshared electron pair of a water molecule. The further complications suggested by Hammett do not affect the important distinction between these mechanisms. The author wishes to show that consideration of the energetics of the various reactions allows an unequivocal decision as to the mechanism of methyl halide hydrolysis.

The energy of dissociation of a gaseous methyl halide into gaseous ions has been made accessible to calculation by the determination of the ionization potential of methyl radical.[2] The application of Hess' law in the case of methyl chloride is given below. The energies of reaction are given in kilocalories per mole, roughed off to the nearest whole number (because of experimental uncertainties).

$$\begin{aligned} CH_3Cl(g) &\longrightarrow CH_3(g) + Cl(g) && -75\ ^{3} \\ CH_3(g) &\longrightarrow CH_3^+(g) + e(g) && -258^{2} \\ Cl(g) + e(g) &\longrightarrow Cl^-(g) && +86\ ^{4} \\ \hline CH_3Cl(g) &\longrightarrow CH_3^+(g) + Cl^-(g) && -247 \end{aligned}$$

Similarly, one finds

$$\begin{aligned} CH_3Br(g) &\longrightarrow CH_3^+(g) + Br^-(g) && -238 \\ CH_3I(g) &\longrightarrow CH_3^+(g) + I^-(g) && -229 \end{aligned}$$

The energies of dissociation[3] of CH_3Br and CH_3I are taken, respectively, as 62 and 45 kcal., and the electron affinities[4] of Br and I as 82 and 74 kcal. While the estimated energy effects apply to reactions at absolute zero, for purposes of this discussion they are not significantly different from the reaction energies at moderate temperatures (a few hundred degrees absolute).

To estimate the energy effects for the corresponding processes in aqueous solution, it is necessary to know the energies of solution of the various substances in water. Energies of solution of gaseous methyl halides in water have not been determined. However, the energies of solution of the liquid halides are certainly small, and will be taken as zero. The energy of vaporization of the liquid halide then gives the desired quantity.

If the methyl ion in solution retains its open sextet of valence electrons, as assumed by Hughes and Ingold, then its solvation energy must arise from essentially the same factors contributing to the solvation energy of positive ions of noble gas type—*i. e.*, alkali metal ions. The hydration energy[4] of alkali metal ions is an inverse function of the ionic "size"—*i. e.*, of the effective extension of electron charge density. Since the methyl ion has eight electrons and a nuclear charge distributed over four centers, its spatial extension of electron charge density is certainly greater than that of lithium ion (with only two electrons), and in fact is probably similar to that of sodium ion (ten electrons). Hence the hydration energy of lithium ion safely may be taken as an upper limit for the hydration energy of methyl ion with an open sextet of electrons.

The following hydration energies[4] are used

$$\begin{aligned} Li^+(g) + Cl^-(g) &\longrightarrow Li^+(aq) + Cl^-(aq) + 206 \\ Li^+(g) + Br^-(g) &\longrightarrow Li^+(aq) + Br^-(aq) + 197 \\ Li^+(g) + I^-(g) &\longrightarrow Li^+(aq) + I^-(aq) + 186 \end{aligned}$$

Therefore it is to be assumed

$$\begin{aligned} CH_3^+(g) + Cl^-(g) &\longrightarrow CH_3^+(aq) + Cl^-(aq) + (<206) \\ CH_3^+(g) + Br^-(g) &\longrightarrow CH_3^+(aq) + Br^-(aq) + (<197) \\ CH_3^+(g) + I^-(g) &\longrightarrow CH_3^+(aq) + I^-(aq) + (<186) \end{aligned}$$

(As before, reaction energies are in kilocalories per mole.)

From the above, one may estimate a lower limit for the energy of dissociation of aqueous methyl chloride into aqueous chloride ion and aqueous methyl ion (with an open sextet).

(1) For a recent list of important references, see W. Taylor, THIS JOURNAL, **60**, 2094 (1938).

(2) R. G. J. Fraser and T. N. Jewett, *Phys. Rev.*, **50**, 1091 (1936); *Proc. Roy. Soc.* (London), **A160**, 563 (1937).

(3) N. V. Sidgwick, "The Covalent Bond in Chemistry," G. F. Baker Lectures, Cornell University, 1932.

(4) J. E. Mayer and L. Helmholz, *Z. Physik*, **75**, 19 (1932).

$$CH_3Cl(g) \longrightarrow CH_3^+(g) + Cl^-(g) \quad -247$$
$$CH_3^+(g) + Cl^-(g) \longrightarrow CH_3^+(aq) + Cl^-(aq) \quad +(<206)$$
$$CH_3Cl(aq) \longrightarrow CH_3Cl(l) \quad 0$$
$$CH_3Cl(l) \longrightarrow CH_3Cl(g) \quad -5^5$$
$$CH_3Cl(aq) \longrightarrow CH_3^+(aq) + Cl^-(aq) \quad -(>46)$$

Similarly

$$CH_3Br(aq) \longrightarrow CH_3^+(aq) + Br^-(aq) \quad -(>47)$$
$$CH_3I(aq) \longrightarrow CH_3^+(aq) + I^-(aq) \quad -(>50)$$

(The energies of vaporization[5] of CH_3Br and CH_3I are taken, respectively, as 6 and 7 kcal.)

These figures must be regarded not only as lower limits for the dissociation energies, but as very much below the probable values. It was pointed out above that the "size" of a methyl ion with an open sextet is probably similar to that of a sodium ion. If the hydration energies[4] of the two are assumed to be the same, then the corresponding dissociations of aqueous methyl chloride, bromide and iodide into ions are endothermic by 72, 72 and 74 kcal., respectively.

The unimolecular dissociations postulated by Hughes and Ingold would thus be endothermic by at least some 50 kcal. (and more probably by some seventy) in the case of methyl halides. The activation energies would in consequence be greater than 50 kcal. A unimolecular reaction with a normal temperature independent factor[6] of some 10^{13} sec.$^{-1}$ and an activation energy of 50 kcal. would have a rate constant of only some 10^{-16} sec.$^{-1}$ at 100°. This must be regarded as an absolute upper limit for the rate constant of methyl halide hydrolysis at 100° by the Hughes–Ingold mechanism. Actually, the respective rate constants for the hydrolysis of methyl chloride, bromide and iodide in aqueous solution[7] at 100° are 1.08×10^{-4}, 1.31×10^{-3} and 4.47×10^{-4} sec.$^{-1}$. Thus the actual reactions are more rapid by many powers of ten than is possible by the Hughes–Ingold mechanism. The observed respective activation energies are some 22.7, 21.4 and 23.1 kcal. at 100°, and some 27.7, 26.5 and 28.1 kcal. at 25°—values far lower than the lowest possible limits for the Hughes–Ingold mechanism.

On the other hand, it can be shown that the energetics of the Olson–Halford mechanism are entirely compatible with the experimental data for methyl halide hydrolysis. It is to be noted that a methyl ion coördinated to a water molecule is identical with a proton coördinated to a methyl alcohol molecule—only one electronic structure being possible for $CH_3OH_2^+$. Hence the basic strength of methyl alcohol gives a clue to the energy relations of $CH_3OH_2^+$. For the distribution of protons between methyl alcohol and water molecules the equilibrium constant[8] at 25° is some 0.235—water being the stronger base. It appears unlikely that the transfer of a proton from methyl alcohol to water will involve a large entropy change. If it is assumed that the free energy change is given entirely by the energy of reaction, this latter is equal to $RT \ln (1/0.235)$, which at 298° absolute is only about 1 kcal. Hence it is assumed

$$H_3O^+ + CH_3OH \longrightarrow H_2O + CH_3OH_2^+ \quad -1$$

To estimate the energy of dissociation of aqueous methyl chloride into chloride ion and $CH_3OH_2^+$ the following summation is used.

$$CH_3Cl(aq) + OH^-(aq) \longrightarrow CH_3OH(aq) + Cl^-(aq) \quad +18^9$$
$$2H_2O(l) \longrightarrow H_3O^+(aq) + OH^-(aq) \quad -14^5$$
$$H_3O^+(aq) + CH_3OH(aq) \longrightarrow H_2O(l) + CH_3OH_2^+(aq) \quad -1$$
$$CH_3Cl(aq) + H_2O(l) \longrightarrow CH_3OH_2^+(aq) + Cl^-(aq) \quad +3$$

Similarly it is found

$$CH_3Br(aq) + H_2O(l) \longrightarrow CH_3OH_2^+(aq) + Br^-(aq) + 0$$
$$CH_3I(aq) + H_2O(l) \longrightarrow CH_3OH_2^+(aq) + I^-(aq) + 3$$

Thus dissociation of aqueous methyl halide into halide ion and $CH_3OH_2^+$ is a practically thermoneutral (or slightly exothermic) reaction. This is entirely compatible with the activation energy of the hydrolytic reaction by the Olson–Halford scheme. It is apparent that the reverse reaction (synthesis of methyl halide) must have a considerable activation energy. That is, the slowness of the reactions is due to a "true" activation energy.

It therefore appears that the experimental results of methyl halide hydrolysis are explicable in terms of the Olson–Halford mechanism, but not by that of Hughes and Ingold. The course of the reaction is to be pictured (using say CH_3Cl)

$$H_2O + CH_3Cl \longrightarrow H_2OCH_3^+ + Cl^- \quad \text{(slow)} \quad (1)$$
$$H_2O + H_2OCH_3^+ \longrightarrow H_3O^+ + HOCH_3 \quad \text{(rapid)} \quad (2)$$

Reaction (1) is formally similar to a substitution reaction of alkyl halide with a negative ion[10] in that one electron pair bond is broken and one is formed. Like the negative ion substitution reac-

(5) Landolt–Börnstein, "Tabellen."

(6) L. S. Kassel, "Kinetics of Homogeneous Gas Reactions," A. C. S. Monograph, Chemical Catalog Co., New York, N. Y., 1932.

(7) E. A. Moelwyn-Hughes, *Proc. Roy. Soc.* (London), **A164**, 295 (1938).

(8) H. Goldschmidt and P. Dahl, *Z. physik. Chem.*, **108**, 121 (1924).

(9) R. A. Ogg, Jr., *Trans. Faraday Soc.*, **31**, 1385 (1935).

(10) R. A. Ogg, Jr., and M. Polanyi, *ibid.*, **31**, 604 (1935).

tion, it is undoubtedly attended by Walden inversion.[10]

The dissociation energy of ethyl radical[2] into gaseous ethyl ion and electron is 245 kcal. per mole. If the bond energies are the same as for methyl halides, then the dissociation energies of gaseous ethyl halides into gaseous ethyl radical and halide ions are each some 13 kcal. less than the corresponding values for methyl halides. On the other hand, the "size" of the ethyl ion is undoubtedly greater than that of methyl ion, and in consequence its hydration energy (retaining the "open sextet" structure) must be less than that of methyl ion. Hence the calculated dissociation energies of aqueous ethyl halides into aqueous ethyl ion (with an "open sextet") and aqueous halide ions must be similar in magnitude to the corresponding values for methyl halides.

Only qualitative information is available concerning the rate of hydrolysis of ethyl halides by neutral water. At 100° the hydrolysis of ethyl iodide[11] is definitely slower than that of methyl iodide, but the two rates are of comparable magnitudes. A similar relation may be inferred for the hydrolysis of ethyl bromide and chloride. It thus seems probable that the activation energies for ethyl halide hydrolysis are similar to those for methyl halides, *i. e.*, some 25–30 kcal. From the preceding paragraph it is apparent that this is far less than the value demanded by the Hughes-Ingold mechanism. On the other hand, since the basic strengths of methyl and ethyl alcohols are similar, the dissociation of aqueous ethyl halide into $C_2H_5OH_2^+$ and halide ion is essentially thermoneutral. Thus the observed activation energy for ethyl halide hydrolysis is entirely compatible with the Olson–Halford mechanism.

For various other processes occurring in aqueous solution, in which CH_3^+ and $C_2H_5^+$ may be postulated as intermediates, energy calculations similar to the above indicate that the required activation energies are so large as to rule out the participation of these ions in reactions observable at ordinary temperatures. It is interesting to note the parallelism with the state of protons in aqueous solution. It is now generally recognized that the extremely large hydration energy of a proton is explicable only in terms of coördination with an unshared electron pair of a water molecule, forming H_3O^+. Similarly, methyl and ethyl "ions" in aqueous solution must be regarded as $CH_3OH_2^+$ and $C_2H_5OH_2^+$. Just as the concept of transient existence of "naked" protons has been discredited, so it appears that the concept of transient existence of CH_3^+ or $C_2H_5^+$ with an "open sextet" must be abandoned.

Considerations similar to the above apply to solvents other than water, whose molecules still possess one or more unshared electron pairs. Such solvents are ammonia, amines, sulfur dioxide, ethers, alcohols, carboxylic acids, etc. Since solvation energies of ions in such solvents do not differ radically from those in water, the production of methyl or ethyl ions with an open sextet demands activation energies comparable to those calculated for aqueous solutions, and hence is too slow to contribute to observable reactions. The real ionic intermediates are to be regarded as the coördination complexes of CH_3^+ or $C_2H_5^+$, such as $CH_3NH_3^+$, $CH_3OHCH_3^+$, etc.

Extension of such numerical calculations to higher alkyl halides cannot be made reliably. Bond energies are more uncertain, and appropriate data regarding ionization potentials of higher alkyl radicals are completely lacking. However, it must be borne in mind that solvation energies of larger alkyl radicals (with an "open sextet") are necessarily considerably less than that of CH_3^+. While it is probably true that the ionization potentials of large radicals are also less than that of methyl radical, it seems highly improbable that the difference of ionization potential and solvation energy can decrease sufficiently to make the Hughes–Ingold mechanism energetically feasible in any case. It appears that all "carbonium ions" are to be regarded as coordination complexes with a solvent molecule, and that any reaction calling for participation of ions with an "open sextet" will probably be too slow to be observable under ordinary conditions. The kinetic studies of the hydrolysis of higher alkyl halides are all to be interpreted in terms of the mechanism discussed above for methyl halides —*i. e.*, as a reaction with the solvent molecule, yielding halide ion and $R_3COH_2^+$.

Carbonium ions with an "open sextet" have been postulated freely in mechanisms for various molecular rearrangements. As a typical example, the formation of a mixture of crotyl bromide and methylvinylcarbinyl bromide from either of the pure carbinols and hydrogen bromide[12]

(11) J. Greenspan, S. Liotta and V. K. La Mer, *Trans. Faraday Soc.*, **31**, 824 (1935).

(12) W. G. Young and J. F. Lane, THIS JOURNAL, **60**, 847 (1938).

has been interpreted in terms of resonance between the structures $CH_3—CH=CH—CH_2^+$ and $CH_3—CH^+—CH=CH_2$. If such ions are coordinated with solvent molecules, obviously the possibility of resonance disappears. The following alternative mechanism is entirely in accord with the considerations advanced above

$$CH_3—CH=CH—CH_2OH + HBr \longrightarrow CH_3CH=CH—CH_2OH_2^+ + Br^- \quad (1)$$

$$CH_3—CH=CH—CH_2OH_2^+ + Br^- \longrightarrow CH_3—CH=CH—CH_2Br + H_2O \quad (2)$$

$$CH_3—CH=CH—CH_2OH_2^+ + Br^- \longrightarrow CH_3—CHBr—CH^-—CH_2OH_2^+ \quad (3)$$

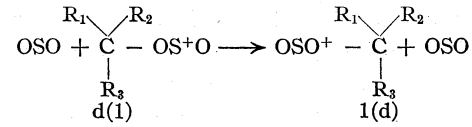
$$CH_3—CHBr—CH^-—CH_2OH_2^+ \longrightarrow CH_3—CHBr—CH=CH_2 + H_2O \quad (4)$$

and similarly for methylvinylcarbinol. It should be noted that reaction (2) (of the usual type accompanied by Walden inversion) gives the normal product, while reactions (3) and (4) yield the rearranged product. Reactions (3) and (4) are similar to those previously postulated to explain the addition of halogens to ethylene linkages.[13]

The various cases in which rapid racemization of optically active carbonium ions has been noted[14] are explicable in terms of an identical exchange reaction of the coördinated ion with the solvent molecules, as, say, in liquid sulfur dioxide.

(13) R. A. Ogg, Jr., THIS JOURNAL, **57**, 2727 (1935).

(14) E. S. Wallis and F. H. Adams, *ibid.*, **55**, 3838 (1933); E. Bergmann and M. Polanyi, *Naturwissenschaften*, **21**, 378 (1933).



The above two examples are typical. It seems legitimate to state that it is never necessary to assume the existence of carbonium ions with an open sextet as intermediates in organic reactions, and that in view of the considerations of reaction energetics advanced above, preference is to be given to mechanisms not involving such ions.

Summary

It is shown that dissociation of a methyl halide (in aqueous solution) into a methyl ion with an "open sextet" and a halide ion is endothermic by at least some 50 kcal. per mole, and more probably by some 70 kcal. On the other hand, reaction with water to yield halide ion and the coordinated methyl ion $CH_3OH_2^+$ is practically thermoneutral. Comparison with the experimental data for methyl halide hydrolysis leads to rejection of the Hughes–Ingold mechanism (involving CH_3^+) in favor of the Olson–Halford mechanism (involving $CH_3OH_2^+$).

It is suggested that carbonium ions with an open sextet never play an appreciable role in observable organic reactions, and that mechanisms employing such ions must be abandoned.

STANFORD UNIVERSITY, CALIF. RECEIVED MAY 2, 1939

[CONTRIBUTION FROM THE PHYSICAL CHEMISTRY LABORATORY, STATE UNIVERSITY OF IOWA]

Physical Studies of Non-aqueous Solvates. III. The Vapor Pressure of Zinc Bromide–Diethyl Ether Solutions

BY H. H. ROWLEY AND FLORENCE V. OLSON[1]

Considerable work has been reported on the preparation and properties of magnesium bromide–diethyl ether systems.[2–4] Extension of the investigation of non-aqueous solvates would naturally include systems resembling the one already mentioned. The zinc bromide–diethyl ether system was chosen for this investigation since zinc belongs to the same periodic group as magnesium and the formulas of the compounds of the two metals are similar. Further, zinc, like magnesium, adds to alkyl halides in an ether medium to form organo-metallic compounds.

One of the first to report in the literature on zinc bromide diethyl etherates was Nickles,[5] who found them to be quite unstable. Raynaud[6] later prepared zinc bromide, using Nickles' method. The two layer system first formed, the lower layer of which was reddish in color, disappeared on further addition of bromine to give a homogeneous, brownish-violet liquid. Removal of excess ether left a

(1) Present address: Women's College of the University of North Carolina, Greensboro, N. C.

(2) B. N. Menschutkin, *Z. anorg. Chem.*, **49**, 34 (1906).

(3) J. Meisenheimer and J. Casper, *Ber.*, **54B**, 1655 (1921); J. Meisenheimer, E. Piper and H. Lange, *Z. anorg. allgem. Chem.*, **147**, 331 (1925).

(4) (a) W. V. Evans and H. H. Rowley, THIS JOURNAL, **52**, 3523 (1930); (b) H. H. Rowley, *ibid.*, **58**, 1337 (1936); (c) H. H. Rowley, *ibid.*, **59**, 621 (1937).

(5) M. J. Nickles, *Compt. rend.*, **52**, 396, 869 (1861).

(6) A. Raynaud, *Bull. soc. chim.*, **39**, 195 (1926).

black liquid stable at 110°, which on analysis corresponded to $ZnBr_2 \cdot (C_2H_5)_2O$. Raynaud claimed verification of this monoetherate by preparing it in a different manner. Sublimed zinc bromide was dissolved in ether and the excess ether removed by heating on a water-bath. The resulting viscous solution was allowed to crystallize in a desiccator containing tallow and concentrated sulfuric acid. Analysis of the solid gave percentages that corresponded to those calculated for the monoetherate.

To check these results and establish other possible diethyl etherates of zinc bromide as well as to learn something of their stability, the vapor pressures of saturated solutions of zinc bromide–diethyl ether solutions were measured over the temperature range −10 to +35°. The wet solids in contact with the saturated solutions were also analyzed at certain temperatures.

Experimental

Apparatus and Materials.—The vapor pressures were measured by the static method using the same apparatus and technique described in a previous paper.[4c] The diethyl ether was of reagent grade, dried, distilled and kept over freshly cut sodium, only the middle third fraction of the distillate being used.

At first, an attempt was made to prepare the solution of zinc bromide in ether by Nickles' method,[5] which was to treat pure zinc turnings in ethyl ether with liquid bromine, cooling when necessary to avoid too violent a reaction. But instead of a colorless two-layer system, like that of magnesium bromide in ether,[2] a yellowish colored two-layer system was first formed, which upon further addition of bromine became a homogeneous purplish-black liquid, as was described by Raynaud.[6]

Another method tried was that of treating a solution of dry hydrogen bromide in ether with zinc turnings. Hydrogen was evolved, and after a short interval a colorless, partially immiscible liquid phase appeared which lasted only as long as the solution was saturated with hydrogen bromide. No solid was precipitated at room temperature from solutions thus prepared.

The method finally used in preparing the solutions was that of adding pure anhydrous zinc bromide to dry ether until a fairly concentrated solution was obtained. The solid zinc bromide was obtained by subliming the C. P. anhydrous product (Baker Analyzed) in a specially constructed Pyrex vessel. During the sublimation and in all subsequent handling of the solutions, the work was carried out in an atmosphere of dry carbon dioxide.

Procedure.—The unsaturated solution, at room temperature, was transferred to the vapor pressure flask, cooled to −78° in carbon dioxide–acetone bath, quickly sealed to the apparatus and evacuated at that temperature with a good oil pump for about thirty minutes. The mercury was then raised in the differential manometer, cutting off the sample flask from the vacuum system, and the sample raised to a sufficiently high temperature to dissolve the solid which was precipitated at the low temperature. The sample was again cooled to −78° and the space above evacuated. In this way, occluded gases could be removed from the sample.

Before readings on the differential manometer were taken, the flask was kept at the desired temperature for several hours, if a solid phase were present at that temperature. If the solution were unsaturated at the desired temperature, known amounts of ether were distilled from the sample until it did contain a solid phase under the conditions desired. Since the solid phases seldom formed of themselves, because of suspended transformation, in order to obtain the stable solid phases it was necessary to cool the samples to fairly low temperatures and then bring them to the desired temperature range and allow them to come to equilibrium.

It was found that a sample which contained considerable solid at 0° might be unsaturated at higher temperatures. Thus as the temperature was raised it was necessary to reduce the amount of ether in the sample. The excess ether was condensed in a calibrated reservoir and the volume recorded. At the end of the measurements all the ether was distilled from the sample into the reservoir, the sample flask was filled with dry air, cut off, and weighed. It was then cleaned, dried and weighed again, and the weight of the pure zinc bromide determined. From the volume and the density of ether at 25°, the moles of ether could be calculated and the mole ratio of diethyl ether to zinc bromide determined for any series of measurements.

The approximate composition of the stable solid phase in equilibrium with the saturated solution at a definite temperature, was determined in the following manner. Saturated solutions were prepared in small flasks, allowed to come to equilibrium and the supernatant solution was poured off quickly. Keeping the temperature as nearly constant as possible, the wet solid was drained for a few minutes, then a sample was weighed, dissolved in water and the total bromide concentration determined gravimetrically as silver bromide.

To check the results of Raynaud,[6] solutions saturated at room temperature were decanted into small evaporating dishes, which were placed in a desiccator containing lard and concentrated sulfuric acid for the adsorption of ether vapor. After a few days, a solid was precipitated, samples of which were taken and analyzed in the manner just described.

Discussion of Results

The vapor pressure study of this system presented difficulties due to the high solubility of zinc bromide in diethyl ether giving rise to viscous, sluggish solutions. Unsaturated solutions at +25°, which would normally contain solid at +15°, could be cooled to 0° and left there for an indefinite time without crystallization occurring. An example of this suspended transformation is shown in Fig. 1, where the logarithm of the vapor pressure is plotted against the corresponding reciprocal absolute temperature. The continuous line at the left in the graph is for the system liquid–

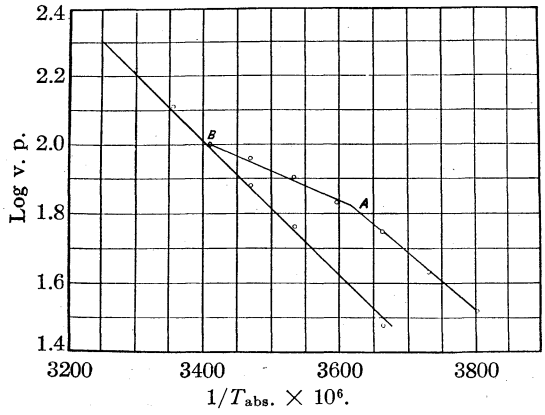


Fig. 1.

vapor, containing no solid. Above point B it represents an unsaturated solution, below B, a supersaturated solution. The other two lines represent the same system when stable solid phases were present with the liquid and vapor phases.

TABLE I

CHANGE OF VAPOR PRESSURE WITH TEMPERATURE FOR THE SYSTEM ZINC BROMIDE–DIETHYL ETHER

Temp. of bath, °C.	$1/T_{abs.} \times 10^6$	Vapor press., mm.	No. of samples	Log v. p.
−10	3802	34 ± 1	4	1.5315
− 5	3731	41 ± 2	4	1.6128
0	3663	57 ± 2	7	1.7559
+ 5	3597	70 ± 4	4	1.8451
10	3534	79 ± 4	4	1.8976
15	3472	89 ± 4	4	1.9494
20	3413	101 ± 2	4	2.0043
25	3356	118 ± 3	5	2.0719
30	3300	156 ± 1	2	2.1931
35	3247	192 ± 1	2	2.2833

Table I lists the data graphed in Fig. 2 for systems of zinc bromide–diethyl ether in which there was a solid, liquid and vapor phase present for the temperature range −10 to +35°. The extreme slowness with which the system attained equilibrium and the persistence of the metastable phases made it difficult to obtain precise vapor pressure measurements. It is to be noted in both Fig. 1 and Fig. 2 that there is a definite change of slope at points A and B. The first break, at point A in both graphs, occurs between 0 and 5°, and the second, at point B, in the neighborhood of 20°. These changes in slope would indicate a change in the nature of the solid phase in equilibrium with the solution. Since there are three sections to the curve, it might be assumed that three distinct solid phases are present in the temperature interval −10 to +35°, the first stable up to about 5°, the second between 5 and 20° and the third stable above 20°.

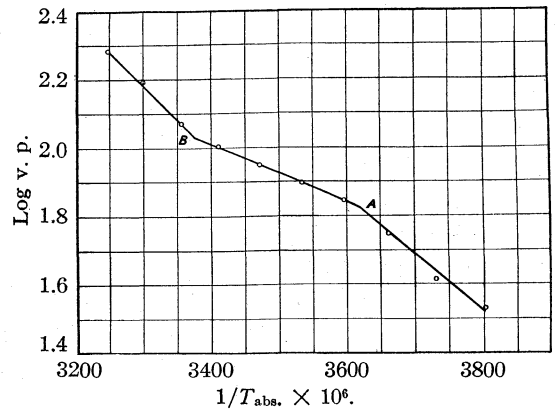


Fig. 2.

These changes in the solid phases could be seen directly. The solid in equilibrium with the saturated solution at 0° crystallized in transparent plates. Between 0 and 5° these disappeared and the solid in equilibrium at 15° was composed of transparent needles. At 25° and above the equilibrium solid was opaque and finely divided so that no crystalline shape was evident.

In order to establish the composition of the solid phase in equilibrium with the solution, samples were analyzed as described. Due to the unstability of the solids and viscosity of the solutions, it was not possible to remove all of the occluded liquid. Hence the "wet solids" were analyzed in an effort to obtain an approximate composition. The results of these analyses at 0, 15 and 25° are summarized in Table II.

TABLE II

ANALYSIS OF "WET SOLIDS" IN EQUILIBRIUM WITH SOLUTIONS

Temp., °C.	No. of samples analyzed	Wt. % $ZnBr_2$
0	5	58.7 ± 0.6
15	3	70.7 ± 0.5
25	6	85.6 ± 1.4

Determinations of zinc bromide in the wet solid at 0° always gave values around 59 wt. %. The theoretical value of zinc bromide in the dietherate, $ZnBr_2 \cdot 2(C_2H_5)_2O$, is 60.3% and that in the trietherate, $ZnBr_2 \cdot 3(C_2H_5)_2O$, is 50.3 wt. %. The value for the zinc bromide in the solid will be lower than that in the pure etherate because the solid was always wet with solution, which contains only 55–57 wt. % of zinc bromide at 0°. Therefore, it can be concluded that the solvate in equilibrium with the solution at 0° is the dietherate.

Likewise, the average value of 70.7 wt. % for the determination of zinc bromide in the solid, stable in contact with the saturated solution at 15°, agrees favorably with the theoretical value, 75.3, of the weight per cent. of zinc bromide in the monoetherate, $ZnBr_2 \cdot (C_2H_5)_2O$. The solubility of zinc bromide at 15° is approximately 68–69 wt. %.

Analyses of the wet solid, stable in contact with the saturated solution at 25°, would vary somewhat according to the extent to which the viscous solution was drained from the solid. The average value of 85.6% indicates that the monoetherate is not stable at this temperature. The solubility of zinc bromide at 25° is approximately 69–70 wt. %.

From these results, it would appear that the transition in the solid phase in the range 0 to 5° is that of the dietherate of zinc bromide to the monoetherate, and the transition of the solid phase in the neighborhood of 20° is that of the monoetherate to the unsolvated zinc bromide.

The results of this investigation do not agree with those of Raynaud.[6] He stated that the solubility of zinc bromide in diethyl ether at 25° was about 45 wt. %; the value found in this work is 69–70 wt. %. He stated further that the monoetherate is stable at room temperature. Part of his work was repeated in this Laboratory and the wet solid formed by allowing a solution to evaporate in a desiccator gave an average value of 86.7 wt. % zinc bromide. With a specially well drained sample this value rose to 90%. The indications in the present work are that the monoetherate, in contact with solution, decomposes in the neighborhood of 20°.

Several possible sources of error may be pointed out in Raynaud's work. As was found in the present study, bromination of zinc in diethyl ether led to the formation of a dark homogeneous liquid. To conclude that this was a pure solution of zinc bromide in ether or to draw any conclusions on the existence of the monoetherate from analysis of this dark liquid certainly was not justifiable. In the present study, a dark liquid was not obtained at any time when pure zinc bromide was dissolved in ether. A further criticism of Raynaud's work is that he mentioned taking no special precautions to exclude moisture in the dissolving of solid zinc bromide in ether. Since zinc bromide hydrolyzes in water, the presence of moisture may have caused the variations in the analyses of the solutions and in the analyses of the solid obtained by allowing the solution to evaporate in a desiccator.

Summary

1. A study of the vapor pressures of the system zinc bromide–diethyl ether over the temperature range −10 to +35° has been made.

2. The existence of the two etherates, the dietherate of zinc bromide, $ZnBr_2 \cdot 2(C_2H_5)_2O$, and the monoetherate, $ZnBr_2 \cdot (C_2H_5)_2O$, has been indicated by (a) breaks occurring between 0 and 5° and in the neighborhood of 20° in the curve obtained by plotting the logarithms of the vapor pressures of the system against the reciprocal of the absolute temperature; (b) analyses of the wet solids in contact with the saturated solutions at 0, 15 and 25°; (c) changes in the appearance of the solids in the ranges 0 to 5° and in the neighborhood of 20°.

3. Disagreements with Raynaud on the system zinc bromide–diethyl ether have been mentioned, and possible sources of error in his work indicated.

IOWA CITY, IOWA RECEIVED APRIL 3, 1939

[CONTRIBUTION FROM THE LABORATORY OF PHYSIOLOGICAL CHEMISTRY, UNIVERSITY OF MINNESOTA]

Changes in pH of Irradiated Egg Albumin Solutions[1]

BY F. W. BERNHART

A change can be observed in the pH of a protein solution after denaturation. The changes in pH produced by the denaturation process vary qualitatively and quantitatively, depending upon the type of denaturation employed. Previous reports in regard to the changes of pH resulting from ultraviolet denaturation of proteins in solutions are at variance. Mond[2] observed decreases of pH after ultraviolet irradiation of egg albumin and serum albumin solutions when the initial pH of the solution was above the protein isoelectric point, and a rise in pH when the initial pH was below the isoelectric point. Clark[3] found that the pH of egg albumin solutions decreased after irradiation when the initial pH was either acid or alkaline with respect to the isoelectric point. Stedman and Mendel[4] found that irradiation caused a drop in the pH, but the initial pH of the solutions was not given. Decreases in the pH of unbuffered distilled water after ultraviolet irradiation led these workers to interpret the drop in pH during irradiation of protein solutions as due to a change in the water. The present investigation was undertaken to examine the validity of these conflicting results.

Methods.—A Burdick air-cooled quartz mercury arc was used as a source of ultraviolet radiant energy. Two quartz mercury arcs, varying greatly in ultraviolet radiant energy output, were used during the investigation. Approximately 20 cc. of the egg albumin solutions were irradiated in quartz test-tubes (20 × 130 mm.), 19.5 cm. from the light source. The irradiation vessels were placed in a constant temperature water-bath held at 25°. Crystalline egg albumin was prepared by the method of Cole[5] and recrystallized twice Salts were removed, using the apparatus described by Bernhart, Arnow and Bratton.[6] About 10 cc. of a concentrated egg albumin solution, stored at 5° and preserved with a toluene paraffin oil layer, was measured accurately and diluted to 100 cc. with distilled water and a definite volume of hydrochloric acid or sodium hydroxide solution. The pH of this solution was measured with the glass electrode. Fresh solutions were prepared from the stock solution immediately before each irradiation. In one series of irradiations a nitrogen atmosphere was obtained by alternately evacuating and bubbling nitrogen through the solution (plus 0.02 cc. of *n*-heptyl alcohol to inhibit foaming) contained in the irradiation tube. The glass tubing employed was then sealed off and the stopper sealed. *n*-Heptyl alcohol (0.02 cc.) in 20 cc. of 0.01 *M* phosphate buffer (pH 6.5 were irradiated for forty-eight hours under nitrogen; this procedure caused no change in the pH of the mixture. In the other series of irradiations free access of air was obtained by fitting the stoppers of the quartz tubes with bent glass tubing. After each irradiation the pH of the solution was again determined.

Results

Change in pH as a Function of Initial pH.—The data obtained after forty-eight hours of irradiation are shown in Fig. 1. The results show

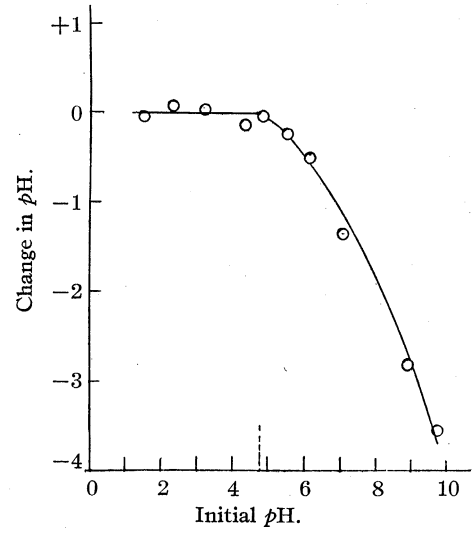


Fig. 1.—Change in pH of egg albumin solutions caused by forty-eight hours irradiation with arc 1W. 0.64 g. egg albumin per 100 cc. solutions irradiated in contact with air. The broken line, pH 4.8, indicates the isoelectric point of egg albumin.

that under the experimental conditions employed, a drop in pH occurs when the initial pH is above the isoelectric point of egg albumin (pH 4.8) and no significant change occurs when the initial pH is below the isoelectric point. A straight line relationship was found between the initial pH of the irradiated solution and the difference in base bound by egg albumin (Cohn[7]) at the pH values

(1) The data in this paper are taken from a thesis submitted by the author (present address: Department of Biochemistry, Tulane University, New Orleans, Louisiana) to the Graduate School of the University of Minnesota in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

(2) R. Mond, *Arch. Ges. Physiol.*, **200**, 374 (1923).

(3) J. H. Clark, *Am. J. Physiol.*, **61**, 72 (1922).

(4) H. L. Stedman and L. B. Mendel, *ibid.*, **77**, 199 (1926).

(5) A. G. Cole, *Proc. Soc. Exptl. Biol. Med.*, **30**, 1162 (1933).

(6) Bernhart, Arnow and Bratton, *Ind. Eng. Chem., Anal. Ed.*, **9**, 387 (1937).

(7) E. J. Cohn, *Physiol. Rev.*, **5**, 349 (1925).

before and after irradiation. This relationship is shown in Fig. 2. The difference in base bound

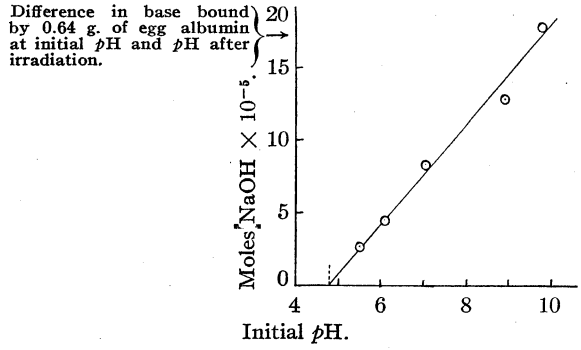


Fig. 2.—The difference in base bound by 0.64 g. egg albumin per 100 cc. at *p*H values before and after irradiation, as a function of the initial *p*H of the irradiated solutions. Experimental data same as Fig. 1.

by the egg albumin is a measure of the strong acid necessary to lower the *p*H to the same extent that it was lowered by irradiation. The data indicate that the photochemical reaction or reactions responsible for the drop in alkalinity of egg albumin solutions irradiated by ultraviolet light are catalyzed either directly or indirectly by the hydroxyl ion concentration of the solution. The change in *p*H observed is correlated with 90 to 98% denaturation of the egg albumin present. The extent of denaturation was determined by bringing the irradiated solution to the isoelectric point, then filtering, washing, drying, and weighing the precipitated protein.

Change in *p*H as a Function of the Time Irradiated.—The results obtained are shown in Fig. 3. The data show that after long periods of irradiation a slight rise in *p*H occurs in solutions whose initial *p*H is below the isoelectric point. Irradiation under nitrogen of a solution (*p*H 6.40) results in a rise of *p*H instead of the drop observed when the solutions are irradiated in air. This indicates that the reaction or reactions responsible for the decreases in *p*H require oxygen.

Discussion.—The data are in agreement with the work of Mond,[2] who concluded that the *p*H values of protein solutions tend to approach the isoelectric point under irradiation. The conclusion of Stedman and Mendel,[4] who believed that the drop in *p*H of irradiated protein solutions is due to a change in the solvent water, is untenable. Assuming the correctness of the methods by which

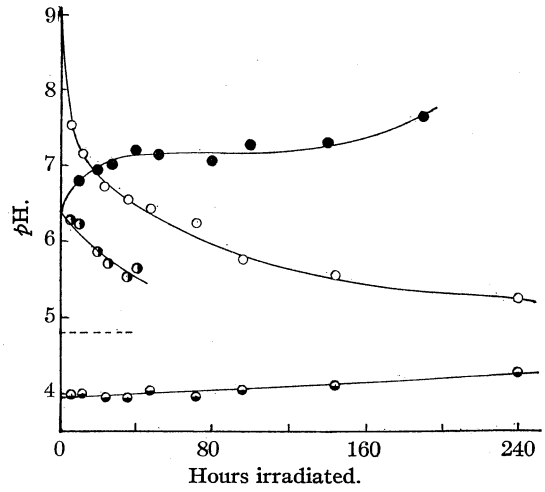


Fig. 3.—The change in *p*H of egg albumin solutions with the time irradiated: ○, 0.81 g. egg albumin per 100 cc., arc 1W, initial *p*H 9.03, irradiated in contact with air; ◒, 0.81 g. egg albumin per 100 cc., arc 1W, initial *p*H 3.94, irradiated in contact with air; ●, 0.76 g. egg albumin per 100 cc., arc 2S, initial *p*H 6.40, irradiated under nitrogen; ◑, 0.76 g. egg albumin per 100 cc., arc 2S, initial *p*H 6.40, irradiated in contact with air.

decreases in *p*H in unbuffered distilled water were found, the extent of the change which they observed corresponds to a very small fraction of the acid formation necessary to reduce the *p*H of a protein–buffer solution. The largest *p*H change of distilled water resulting from ultraviolet irradiation, observed by Stedman and Mendel,[4] is from *p*H 7 to 5.8. The acid necessary to change the *p*H of 100 cc. of distilled water from *p*H 7 to 5.8 is approximately 0.14×10^{-5} mole of hydrochloric acid. In order to change the *p*H of 100 cc. of a solution containing 0.64 g. of egg albumin from *p*H 7 to 5.8, approximately 8×10^{-5} mole of hydrochloric acid is required.

Summary

The change in *p*H caused by ultraviolet irradiation of egg albumin solutions was studied with the glass electrode. The *p*H of egg albumin solutions irradiated in contact with air decreases when the *p*H is above the isoelectric point and rises slightly when the initial *p*H is below the isoelectric point. The *p*H of egg albumin solutions which are alkaline in respect to the isoelectric point increases during irradiation under nitrogen.

NEW ORLEANS, LA. RECEIVED APRIL 24, 1939

[CONTRIBUTION FROM THE DIVISION OF CHEMISTRY, COLLEGE OF AGRICULTURE, UNIVERSITY OF CALIFORNIA]

The Oxidation of Ethyl Disulfide by Hypobromite Ion. The Rate of the Reaction

BY H. A. YOUNG AND M. B. YOUNG

The reaction between ethyl disulfide and hypobromite ion is more complicated than the corresponding one between the disulfide and bromine.[1] Whereas a dilute solution of bromine oxidizes the disulfide quantitatively to ethyl sulfonate, a dilute solution of sodium hypobromite produces some sulfate ion in addition to the sulfonate. In the present investigation, as in the previous ones, the oxidation system consisted of two phases, the solvents being carbon tetrachloride and water. Also, as previously, the primary object of the investigation was the study of the initial reaction between the sulfur compound and the oxidizing agent, particularly with reference to evidence for or against the formation of a "sulfenic" acid according to the reaction

$$RSSR + H_2O = RSH + RSOH$$

Consequently, all of the organic products of the oxidation were not traced, although the principal one, ethyl sulfonic acid, was identified in the manner previously described.[1a]

The possibility of a hydrolytic cleavage of the sulfur–sulfur linkage of disulfides, as described in the above equation, has been the subject of many investigations, the most recent of which have been those of Schöberl and his co-workers.[2]

Stoichiometry

The experiments were carried out as follows. The disulfide was weighed in a weighing ampoule and added to a known volume of carbon tetrachloride in a 1-liter bottle with a tightly fitting ground-glass stopper. The analyzed hypobromite solution, freshly prepared by adding bromine to a solution of sodium hydroxide of known concentration, was then pipetted into the bottle and the mixture shaken violently in a mechanical shaker until samples of the hypobromite layer taken at suitable time intervals showed no appreciable further loss of oxidizing power. A blank experiment containing the same volumes of carbon tetrachloride and hypobromite solutions was run with each experiment, and the results corrected accordingly. The blank corrections were small in every case. The hypobromite was determined iodimetrically by analyzing 10-cc. samples of the aqueous layer; the sulfate was determined gravimetrically as barium sulfate after separation of the carbon tetrachloride layer. Table I is a summary of seventeen experiments.

Examination of the ratio of moles of hypobromite ion used to moles of ethyl disulfide used, column 11, indicates that although the experimental error is larger than might be wished (approximately 2%), there is a variation in this ratio which is too great to be attributed entirely to this cause. From a comparison of the results of Expts. 1, 2, 3, 10, and 11, with those of Expt. 7, and of Expts. 4 and 6, with those of Expt. 9, it is apparent that this variation is independent of the disulfide concentration. In addition, the ratio seems to increase with increased hypobromite ion concentration and decrease with increasing hydroxide ion concentration, other factors remaining constant. These facts indicate that the value of the ratio depends in some manner upon the concentration of hypobromous acid present.

The initial hypobromous acid (Column 7) was obtained using Shilov's[3] value of 2.06×10^{-9} for the dissociation constant of hypobromous acid. In calculating the final concentration of hypobromous acid, it was assumed that the reduction of two moles of hypobromite ion required one mole of hydroxide ion. That this assumed ratio of 2 to 1 is reasonable but possibly somewhat low will be shown by an examination of the equations for the oxidation of disulfide to sulfonic acid and to sulfates. An attempt to measure the ratio during the iodimetric determination of the hypobromite ion was made by using a measured volume of standardized acid and back-titrating with standardized sodium hydroxide solution after the thiosulfate titration. The results obtained for the ratio varied between 2 and 2.5, but the error involved in the method of determination is necessarily large. Fortunately, a value as high as 2.5 does not materially change the conclusion of the present work. The concentrations of hypobromous acid at the end of each experiment, calculated from the above assumption, are given in

(1) (a) Young, THIS JOURNAL, **59**, 811 (1937); (b) Young and Young, *ibid.*, **59**, 812 (1937).

(2) Schöberl, *Ber.*, **70**, 1186 (1937). This is the latest of a series of four papers pertaining to the subject.

(3) Shilov, THIS JOURNAL, **60**, 490 (1938).

TABLE I

SUMMARY OF STOICHIOMETRY EXPERIMENTS

Expt.	G. R_2S_2	Initial R_2S_2	Initial OH^-	Initial BrO^-	Final OH^-	Final BrO^-	Initial HOBr × 10^6	Final HOBr × 10^6	Av. HOBr × 10^6	Moles BrO^- per mole R_2S_2	Moles $SO_4^=$ per mole R_2S_2	M
1	0.1122	0.0612	0.086	0.107	0.059	0.0522	6.21	4.42	5.32	6.03	0.271	12.6
2	.1139	.0620	.086	.103	.057	.0452	5.99	3.96	4.97	6.14	.267	13.5
3	.1296	.0707	.094	.10	.068	.0371	5.32	2.73	4.03	6.05	.230	14.1
4	.2721	.0445	.30	.205	.238	.0474	3.42	1.00	2.21	5.47	.212	9.5
5	.2720	.0445	.56	.23	.49	.0926	2.05	0.95	1.50	5.63		
6	.2275	.0414	.30	.18	.245	.0685	3.00	1.40	2.20	5.77	.257	11.0
7	.1147	.0313	.10	.097	.079	.0555	4.85	3.51	4.18	5.92	.323	10.7
8	.2272	.0620	.312	.100	.276	.0284	1.60	0.51	1.05	5.68		
9	1.3736	.113	.287	.214	.202	.0451	3.73	1.12	2.43	5.72		
10	0.6827	.0558	.10	.0982	.066	.0302	4.91	2.29	3.60	5.82	.262	11.2
11	.8094	.0662	.10	.1061	.057	.0198	5.31	1.73	3.52	5.95	.289	11.5
12	.7002	.0573	.10	.221	.0517	.124	11.0	12.0	11.5	6.76		
13	.7577	.0620	.10	.206	.0490	.104	10.3	13.3	11.8	6.58	.395	13.0
14	.7058	.0578	.10	.176	.0578	.0836	8.80	7.23	8.02	6.47	.371	12.9
15[a]	1.3334	.109	.070	.238	.032	.162	17.0	25.3	21.1	1.82		
16[a]	1.1045	.0903	.10	.222	.064	.150	11.0	11.7	11.4	3.04		
17[a]	1.5203	.124	.10	.244	.031	.106	12.2	17.1	14.6	4.14		

[a] Shaking stopped and solution analyzed before reaction was complete. Values of the ratio of moles of hypobromite used to moles sulfate ion produced are respectively 17.5, 17.0, 17.9.

Column 8. In Column 9 are the average concentrations of the acid.

An examination of the plot of average hypobromous acid concentration against the values of moles hypobromite ion used per mole of disulfide oxidized (Fig. 1) shows that within the limits of experimental error the relationship is a linear one.

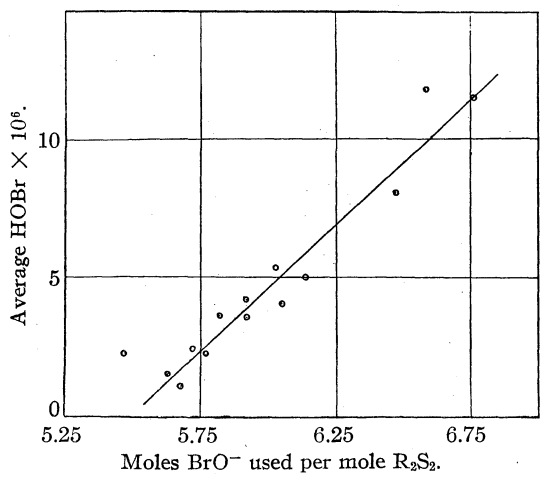


Fig. 1.—Dependence of hypobromite ion requirement upon concentration of HOBr.

In column 12 are given the values of moles of sulfate ion produced per mole of disulfide oxidized, and it is seen that they increase as the hypobromite–disulfide ratios increase. The plot of the values of the sulfate–disulfide ratio against average hypobromous acid concentration is shown in Fig. 2, and again the relationship appears to be a linear one.

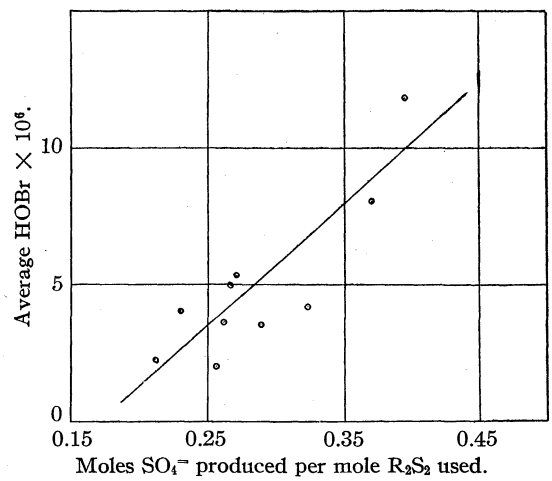


Fig. 2.—Dependence of sulfate production on concentration of HOBr.

The fact that values of the ratio of moles of hypobromite ion used to moles of disulfide used did not increase over those tabulated, even though some of the experiments were allowed to shake for many hours, is evidence that the sulfate ion production is an independent rather than a follow reaction to the production of sulfonate. This conclusion is strengthened by the results of Expts. 15, 16, and 17, in which the reaction was stopped when the values of moles of hypobromite used per mole of disulfide were approximately 2, 3, and 4,

respectively. The resulting values of moles hypobromite used per mole of sulfate ion produced were constant within the limits of error, being 17.5, 17.0, and 17.9, respectively.

The Rate of the Reaction

Experimental.—The rate of disappearance of hypobromite ion during the early stages of the reaction was measured by the following experiments. Freshly prepared hypobromite solutions were pipetted into the reaction vessel, consisting of an indented 500-cc. round-bottomed Pyrex flask, fitted with a mercury-sealed glass stirrer and a side neck of small diameter for withdrawing samples. Freshly prepared solutions of ethyl disulfide, made by dissolving weighed amounts of disulfide in a known volume of carbon tetrachloride, were added by means of a pipet, and the electric stirrer started. The stirring was at constant speed and sufficiently fast to emulsify the two layers. At various times the stirrer was stopped, the carbon tetrachloride layer allowed to settle out, a 10-cc. sample of the water layer removed by means of a pipet, and the hypobromite determined iodimetrically. This procedure of sampling seemed justified, since experiments indicated that there was no decrease in the hypobromite ion concentration when there was no stirring.

The temperature at which the rate experiments were carried out was 25.0 ± 0.1°, maintained by a water thermostat. All reagents were brought to reaction temperature before each experiment by immersion in the thermostat.

Results.—Preliminary experiments showed that the decomposition of hypobromite ion to bromate ion could be neglected if the concentration of hydroxide ion was kept reasonably high. Experiments in which the hydroxide ion concentration at any time became appreciably lower than 0.03 N gave low results for both stoichiometric and rate measurements. Consequently, in the later experiments it seemed advisable to adopt the concentration of 0.03 N as the lower limit for hydroxide ion. That the rate of decomposition of hypobromite ion to bromate ion increases sharply with decreasing hydroxide ion has been shown by Liebhafsky and Makower[4] and more recently by Skrabal and Skrabal.[5]

The experiments indicated that the rate of disappearance of hypobromite ion was proportional to the concentrations of disulfide and hypobromite ion and inversely proportional to the hydroxide ion concentration.

If the stoichiometric relationship may be represented by the equation $L\ BrO^- + L/2OH^- + R_2S_2 \longrightarrow$, where L is a function of the hypobromous acid concentration and is known from the stoichiometry experiments, the following formulation may be made for any one time interval. Let the initial concentrations of hypobromite, disulfide, and hydroxide be a, b, and c, respectively. Then if the volumes of the aqueous layer and of the carbon tetrachloride layer are V and V_1, respectively, and x is the concentration of hypobromite ion at time t, the concentration of disulfide at time t will be $b - \frac{(a-x)}{L}\left(\frac{V}{V_1}\right)$ and that of hydroxide ion will be $c - (a-x)/2$.

The rate law may then be expressed as

$$-\frac{dx}{dt} = \frac{k[x]\left[b - \frac{a-x}{L}\left(\frac{V}{V_1}\right)\right]}{\left[c - \frac{a-x}{2}\right]}$$

or more simply

$$-\frac{dx}{dt} = \frac{k(x)\ (D + Ex)}{F + Gx}$$

where

$$D = b - \frac{a}{L}\frac{V}{V_1} \qquad E = \frac{1}{L}\frac{V}{V_1}$$

$$F = c - \frac{a}{2} \qquad G = \frac{1}{2}$$

Integration of dx between the limits a and x, and of dt between 0 and t leads to the expression

$$kt = \frac{F}{D}\ln\left(\frac{D + Ex}{x}\right) - \frac{G}{E}\ln(D + Ex) - \frac{F}{D}\ln\left(\frac{D + Ea}{a}\right) + \frac{G}{E}\ln(D + Ea)$$

A plot of

$$\left[2.303\frac{F}{D}\log\frac{D + Ex}{x} - 2.303\frac{G}{E}\log(D + Ex)\right.$$

(denoted H) as ordinate against time as abscissa should then be a straight line for each time interval. Because of the variation in V, the results of a single experiment would result in a series of line segments with the initial abscissa of each differing from the final abscissa of the preceding one. If the rate law is correct, translation of each line segment by an amount equal to the summation of the preceding differences should result in a single straight line. That such is the case is shown in Fig. 3, where are plotted the results of two typical experiments. The details of calculation are in Table II.

(4) Liebhafsky and Makower, *J. Phys. Chem.*, **37**, 1044 (1933).
(5) Skrabal and Skrabal, *Monatsh.*, **71**, 251 (1938).

TABLE II

TYPICAL EXPERIMENTS

t	V, cc.	x	$D + Ex$	$\log \frac{-2.303G/E}{D + Ex}$	$\frac{-D + Ex}{x}$	$\log \frac{2.303F/D}{\frac{D + Ex}{x}}$	H	ΔH	Corrn. factor	H, corr.
				Expt. 1						
			Av. HOBr = 2.32×10^{-6}.	$L = 5.8$.	$V_1 = 49.75$.	$F = 0.1468$				
0	190.0	0.0983	0.0359	2.257	0.3653	5.13	7.657			7.657
4	190.0	.0965	.0347	2.553	.360	5.22	7.773			7.773
4	180.0	.0965	.0347	2.696	.360	5.89	8.586	0.813	0.813	
12	180.0	.0934	.0328	2.740	.351	6.10	8.840			8.027
12	170.0	.0934	.0328	2.854	.351	6.92	9.774	0.934	1.747	
24	170.0	.0893	.0304	2.921	.341	7.13	10.051			8.304
24	160.0	.0893	.0304	3.151	.341	8.29	11.441	1.390	3.137	
39	160.0	.0840	.0275	3.264	.328	8.59	11.854			8.717
39	150.0	.0840	.0275	3.482	.328	10.14	13.622	1.768	4.905	
54	150.0	.0798	.0253	3.540	.317	10.43	13.970			9.065
				Expt. 7						
			HOBr = 2.45×10^{-6}.	$L = 5.8$.	$V_1 = 49.75$.	$F = 0.213$				
0	190.0	0.1500	0.0421	2.408	0.2807	4.789	7.197			7.197
6	190.0	.1458	.0393	2.459	.268	4.960	7.419			7.419
6	180.0	.1458	.0393	2.598	.268	5.43	8.028	0.609	0.609	
14	180.0	.1414	.0366	2.657	.259	5.57	8.227			7.518
14	170.0	.1414	.0366	2.765	.259	6.18	8.945	0.718	1.327	
24	170.0	.1369	.0339	2.830	.248	6.39	9.220			7.893
24	160.0	.1369	.0399	3.050	.248	7.10	10.150	0.930	2.257	
36	160.0	.1320	.0312	3.127	.237	7.34	10.467			8.210
36	150.0	.1320	.0312	3.335	.237	8.22	11.555	1.088	3.345	
48	150.0	.1275	.0289	3.409	.227	8.47	11.879			8.534

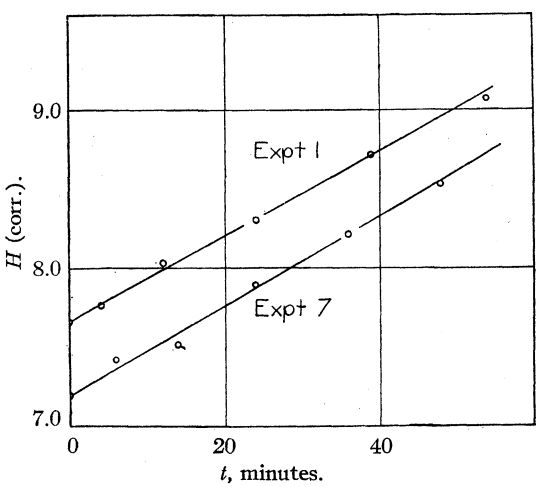


Fig. 3.—Typical rate results. Corrected value of H plotted against time in minutes.

Discussion of Results

An explanation for the above stoichiometric and rate results would be a reaction system which has, as a single rate-determining step, a reaction between disulfide and hypobromous acid. This rate-determining step is probably followed by several rapid reactions, among which must be two competing ones of comparable rates, the first involving hypobromous acid and eventually leading to sulfate ion, the second involving water and leading to sulfonate ion.

Although the authors realize the need for caution in interpreting the results obtained in such a complicated reaction system, it is felt that these experiments seem to prove that the principal rate determining step is not the hydrolysis of the disulfide. The possibility of the establishment of a rapid equilibrium involving water and disulfide as a precursor to further oxidation also seems to be remote, since not only is the solubility of ethyl disulfide in water not materially affected by hydroxide ion, but experiments in which carbon tetrachloride solutions of disulfide were stirred with water for several minutes resulted in water layers which did not reduce hypobromite ion. Any sulfenic acid formed in the latter experiments might reasonably be expected to be in the water layer, and, because of solubility relations, in appreciable quantities.

The conclusion that sulfenic acid formation is not involved in the primary oxidation is in accord with the results of Shinohara and Kilpatrick,[6] who have shown that the rate determining step in oxi-

(6) Shinohara and Kilpatrick, THIS JOURNAL, **56**, 1466 (1934).

dation of cystine by iodine is a simple second order reaction between cystine and iodine (or triiodide ion). Since Shinohara and Kilpatrick worked entirely in acid solution, however, their results do not preclude the possibility of the establishment of a rapid equilibrium involving cystine and water and the formation of a sulfenic acid. But also, the above conclusion is not contradictory to the work of Schöberl and his colleagues. They have shown that symmetrical disulfides which contain a carboxyl group and the sulfur atom attached to the same carbon atom decompose to yield the corresponding sulfhydryl compound, a keto acid, and hydrogen sulfide when heated in alkaline or, in some cases, neutral, solutions.

$$[RCH(COOH)S]_2 + H_2O \longrightarrow RCH(COOH)SH + RCO(COOH) + H_2S$$

For this result, the assumption of an alkaline cleavage of the original disulfide leads to a satisfactory and reasonable mechanism, as they have pointed out. However, the authors feel that there is at present a regrettable tendency in the chemical literature to assume that all disulfides undergo cleavage in alkali. Aside from the evidence of the present paper that such a cleavage is not of importance in the oxidation of ethyl disulfide, Schöberl has pointed out two other disulfides, both of which contain carboxyl groups but only one of which is in the proper position, which do not show any tendency to decompose upon heating with alkali[2] (p. 1187).

If the two over-all reactions for the oxidation of ethyl disulfide are written

$$R_2S_2 + 5\ BrO^- + 2\ OH^- = 2\ RSO_3^- + 5\ Br^- + H_2O$$
$$R_2S_2 + M\ BrO^- + \quad = 2\ SO_4^= + Br^- +$$

values of M may be determined from the stoichiometry measurements of Table I, since it may be readily shown that

$$M = \frac{\left(\frac{BrO^-}{R_2S_2}\right) - 5 + \frac{5}{2}\left(\frac{SO_4^=}{R_2S_2}\right)}{\frac{1}{2}\left(\frac{SO_4^=}{R_2S_2}\right)}$$

where BrO^-/R_2S_2 = moles hypobromite used per mole R_2S_2 used, and $SO_4^=/R_2S_2$ = moles sulfate ion produced per mole R_2S_2 used.

TABLE III

SUMMARY OF RATE EXPERIMENTS

Expt.	Initial BrO⁻	Initial OH⁻	Initial R_2S_2	Initial HBrO × 10⁶	Final HBrO × 10⁶	Av. HBrO × 10⁶	L	k
1	0.0983	0.196	0.0359	2.51	2.14	2.32	5.8	0.027
2	.0994	.098	.0321	5.07	4.69	4.88	6.1	.027
3[a]	.0493	.098	.0321	2.51	1.75	2.13	5.8	.030
4[a]	.0915	.100	.0454	4.57	3.79	4.18	6.0	.029
5[a]	.0912	.100	.0454	0.46	3.84	4.20	6.0	.027
6	.152	.191	.0454	3.98	3.49	3.73	5.9	.026
7	.150	.288	.0421	2.60	2.30	2.45	5.8	.028
8	.0992	.288	.0421	1.72	1.43	1.58	5.7	.029
9[a]	.0730	.288	.0421	1.27	0.97	1.12	5.6	.030
10[a]	.0989	.292	.0650	1.69	1.28	1.49	5.7	.030
11	.0988	.292	.0365	1.69	1.35	1.52	5.7	.031
12	.0977	.392	.0365	1.25	1.04	1.15	5.6	.029

[a] These experiments unfortunately embraced concentration ranges in which D became zero, resulting in a singularity in the integrated expression. However, in the neighborhood of the singularity, the rate constants could be determined by using the simplified rate law—$dx/dt = k(x)(Ex)/(F + Gx)$. Such calculations were made and the rate constants so determined did not differ appreciably from those determined in the usual manner.

Although the values of M (column 14, Table I) vary quite widely, it is observed that, except for Expts. 4 and 5, the values lie between 10.70 and 13.50. The average value of M, 12.1, is at least suggestive of the equation

$$R_2S_2 + 11BrO^- + 6OH^- = 2CH_3COO^- + 2SO_4^= + 11Br^- + 5H_2O$$

Conclusion

1. The oxidation of ethyl disulfide by hypobromous acid involves at least two independent reactions, one of which produces ethyl sulfonate ion and the other sulfate ion.

2. The rate of oxidation has been studied at 25° and the following rate law obtained

$$-\frac{d\ BrO^-}{dt} = \frac{k(R_2S_2)(BrO^-)}{(OH^-)}$$

where k has the value of 0.028 ± 0.002.

3. These experiments give no evidence for the formation of a sulfenic acid by the hydrolysis of the disulfide.

DAVIS, CALIF. RECEIVED APRIL 17, 1939

[CONTRIBUTION FROM MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Reaction of Olefins with Solid Cuprous Halides

BY E. R. GILLILAND, J. E. SEEBOLD, J. R. FITZHUGH[1] AND P. S. MORGAN[2]

That olefins react with cuprous salts in solution has long been known. Berthelot[3] observed that ethylene was absorbed by hydrochloric acid solutions of cuprous chloride. Manchot and Brandt[4] found that ethylene at atmospheric pressure was absorbed by such a solution to the extent of one mole for each mole of cuprous chloride, forming a metastable compound which is empirically $CuCl \cdot C_2H_4$. Ethylene is also known to react with ammoniacal cuprous solutions, several patents[5] having been granted for the recovery of ethylene by absorption in ammoniacal solution.

One case of the reaction of an olefin with a solid cuprous halide has been reported by Tropsch and Mattox.[6] They found propylene did not react. Ethylene was selectively recovered from mixtures of ethylene and ethane and of ethylene and propylene, but in a great deal less than stoichiometric proportion. Chavastelon[7] obtained a similar acetylene compound, $Cu_2Cl_2 \cdot C_2H_2$, and reports equilibrium pressures substantially lower than those for ethylene.

The work reported in this paper summarizes the results obtained employing other systems of olefins and solid cuprous salts.

Experimental

Procedure.—The high variation of the equilibrium pressure of the addition compounds with temperature made it desirable to separate the experimental work into two parts, high pressure and low pressure.

In the high pressure work an accurately known quantity of a powdered cuprous salt was mixed with small mesh pumice and introduced into a steel autoclave. The reactor was then charged with ethylene at about 60 atmospheres pressure for twelve hours at 0°, after which the ethylene was bled from the reactor until the pressure fell just below the vapor pressure of liquid ethylene at 0°. The remaining ethylene was then removed at constant temperature by releasing successive portions of known volume. Sufficient time was allowed between the successive proportions of the gas to obtain pressure equilibrium. These equilibrium pressures were plotted *versus* the volume of the gas withdrawn and the curve gave a plateau at the dissociation pressure of the addition compound; the volume of gas corresponding to the length of the plateau represented the amount of olefin combined with the cuprous salt.

The procedure for measuring the equilibrium dissociation pressure as a function of temperature was identical with that outlined above except that the extraction of gas was discontinued when the constant pressure period was reached. The temperature was then increased in steps, and the corresponding equilibrium pressures were recorded.

The low pressure apparatus was constructed of glass, but the operation was similar to that outlined for the high pressure work.

The operation for the study of mixtures consisted of treating the cuprous salt at constant temperature and pressure with a known gas mixture. Analyses and volume measurements were made of both the unabsorbed portion of the gas and of the gas obtained on decomposing the addition compound.

Pressure measurements were, in general, more accurate than temperature measurements for both the low and high pressure apparatus. Pressure measurements at a given temperature checked to within 3 mm. for the low pressure apparatus, and to within 20 mm. for the high pressure apparatus. Temperatures, however, were read with a calibrated thermometer and are subject to an estimated maximum error of 1 °C.

Results

The results show that such reactions are not limited to ethylene and solid cuprous chloride. Propylene combines mole for mole with solid cuprous chloride yielding a highly dissociative compound which may be written empirically as $CuCl \cdot (C_3H_6)$. Isobutylene forms a similar compound which probably is $CuCl \cdot i\text{-}C_4H_8$, although in this case complete saturation of the cuprous chloride was not obtained, presumably due to the fact that equilibrium was not reached. In one experiment 0.62 mole of isobutylene reacted per mole of solid cuprous chloride in contact with liquid isobutylene at −50°. The molal ratios measured are given in the following table.

TABLE I

Olefin	Mole olefin	Mole CuCl	Mole olefin/mole CuCl
Ethylene	0.186	0.202	0.921
Ethylene	.1468	.150	.979
Ethylene	.1424	.150	.950
Propylene	.01162	.01237	.941
Propylene	.01161	.01237	.940
Propylene	.143	.150	.954
Isobutylene	.0318	.0514	.620
Ethylene	.1328	.1393 (CuBr)	.953

(1) Present address: Standard Oil Co. of La., Baton Rouge, La.
(2) Present address: Ingersoll-Rand Co., New York, N. Y.
(3) Berthelot, *Ann. chim. phys.*, **23**, 32 (1901).
(4) Manchot and Brandt, *Ann.*, **370**, 286 (1909).
(5) French Patent 797,490; British Patent 393,317; U. S. Patent 1,977,659.
(6) Tropsch and Mattox, THIS JOURNAL, **57**, 1102 (1935).
(7) Chavastelon, *Compt. rend.*, **126**, 1810 (1898).

TABLE II

$CuCl \cdot C_2H_4$		$CuCl \cdot C_3H_6$		$CuCl \cdot i\text{-}C_4H_8$		$CuBr \cdot C_2H_4$	
Temp., °C.	Pressure atm. abs.	Temp., °C.	Pressure atm. abs.	Temp., °C.	Pressure atm. abs.	Temp., °C.	Pressure atm. abs.
−42.0	0.0645	−47.0	0.0342	−55.5	0.0165	0.0	17.5
−37.0	.0986	−41	.0710	−46.0	.0394	5.0	23.2
−34.0	.129	−36.0	.0947	−39.5	.0763	10.0	30.7
−28.0	.209	−33.5	.128	−35.5	.121	15.0	42.3
−26.5	.262	−31.1	.168	−33.5	.147	17.0	49.1
−21.0	.382	−25.5	.258	−30.0	.204		
−17.0	.497	−23.0	.392	−26.5	.300		
−14.0	.636	−18.0	.538	−24.5	.352		
− 8.5	.956	−12.0	.960	−18.0	.600		
− 8.0	1.06	− 8.5	1.21	−15.5	.668		
− 7.0	1.15	− 5.5	1.52	−13.0	.761		
0.0	1.95	− 4.5	1.73	−12.3	.795[a]		
12.5	4.25	− 3.0	2.06	− 6.5	.989[a]		
24.0	8.06			− 4.5	1.15[a]		
35.5	15.9			4.8	1.54[a]		
44.0	23.8			6.6	1.62[a]		
61.0	52.5						

[a] Vapor pressures of liquid isobutylene.

The equilibrium data obtained are given in Table II and Fig. 1. The data obtained for the cuprous chloride–ethylene compound agree well with those of Tropsch and Mattox.[6]

At low temperatures where all three olefins (ethylene, propylene and isobutylene) react with cuprous chloride, the equilibrium pressure curves are almost identical. The propylene and isobutylene curves are practically coincident and the ethylene curve shows only a slight deviation from these two, indicating that the reaction is characteristic of the unsaturated structure and is not markedly influenced by molecular weight. At higher temperatures, molecular weight plays a much more important part in the behavior of the olefins toward solid cuprous chloride than does the unsaturated structure in the molecule. Ethylene has been found to combine with solid cuprous bromide mole for mole, according to the formula $CuBr \cdot C_2H_4$, indicating that the reaction is not limited to the chloride. The bromide has been found to have different properties from the chloride, but these may be described and explained on the same basis as the chloride.

A consideration of Fig. 1 shows that a gaseous olefin cannot react with the solid cuprous salts at temperatures higher than correspond to the intersection of the dissociation pressure curve with that of the vapor pressure curve of the olefin in question. These maximum reaction temperatures are approximately 20° for propylene with cuprous chloride and −18° for isobutylene with cuprous chloride. Tropsch and Mattox observed that no propylene was absorbed by cuprous chloride at 23° and 11 atmospheres absolute. This point is very close to the maximum reaction temperature under which condition reaction of the gas would be difficult to observe. Had they operated at a lower temperature reaction no doubt would have been detected.

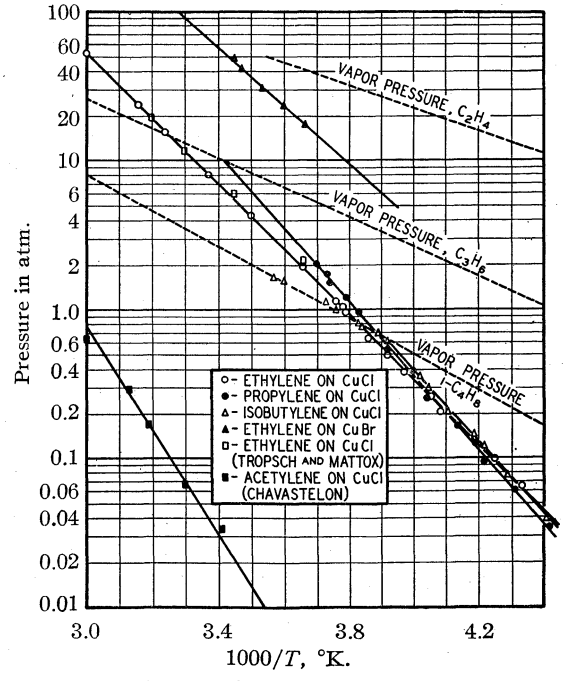


Fig. 1.—Dissociation pressures.

The slopes of the lines of Fig. 1 together with P–V–T data permit the calculation of the heat of reaction at various temperatures. These calculated values of the heat of reaction varied from 10,000 to 11,000 cal. per gram mole at low tem-

peratures down to approximately 7000 cal. per gram mole at the highest temperatures employed.

Under suitable conditions olefins may be recovered from gaseous or liquid mixtures by the use of solid cuprous halides. Consider a gaseous mixture of ethylene and ethane over solid cuprous chloride. Using the Lewis and Randall fugacity rule,[8] the addition equilibrium relation for the mixture can be expressed as

$$yf = f_s$$

where y is the mole fraction of ethylene in the gas phase, f the fugacity of ethylene at the total pressure and temperature of the mixture and f_s the fugacity of ethylene in the equilibrium with the solid complex at the total pressure and temperature. If the difference in volume between the cuprous chloride and the addition compound be neglected, f_s is independent of pressure. Using these assumptions the recovery of ethylene from a given mixture under definite conditions of pressure and temperature may be computed from this equation using the fugacity data given by Lewis and Kay.[9]

Tropsch and Mattox[6] passed a mixture of 60% ethylene and 35% propylene over an excess of cuprous chloride at a pressure of 17.7 atmospheres. They found that "of the 13 liters of ethylene passed only four liters was absorbed, 0.35 mole for each mole of cuprous chloride." Assuming a temperature of 25° the equilibrium value of the recovery calculated as outlined is 4 liters. This calculation is based on an assumed temperature since the authors failed to report the temperature of their observation. These investigators observed that practically no reaction was obtained in the case of a 61% ethylene–35% ethane mixture at 39 atmospheres. The temperature is not reported. Assuming a temperature of approximately 25°, reaction should have proceeded. This is borne out by the success of the present work when dealing with a mixture of ethylene and ethane containing 48% ethylene. Ethylene was recovered from this mixture to the extent of 0.515 mole per mole of cuprous chloride and concentrated to a purity of 98%. This reaction was carried out at 20° and 50 atmospheres absolute pressure. After the reaction had ceased, the ethylene mixture bled from the reactor in successive portions yielded analyses which checked values that were computed by the fugacity method. In similar fashion, ethylene was also recovered from a mixture of hydrogen and ethylene containing 42% ethylene at a temperature of 20°. Here again saturation was not reached, 0.693 mole of ethylene being combined with each mole of cuprous chloride. In like manner, analysis of the gas bled from the reactor checked the equilibrium values calculated. In this case the purity of the removed ethylene was 97%.

Liquid phase reaction was carried out at atmospheric pressure and temperatures lower than that of the intersection of the vapor pressure curve with the addition-compound curve using a mixture of propane and propylene containing 48% propylene, and employing about 50% excess of cuprous chloride. 86% of the propylene was recovered as compared to a computed maximum recovery of 91% for the conditions of the experiment. The liquid mixture was allowed to remain in contact with the solid for about fifteen minutes and the container was not agitated. The purity of the recovered propylene was 98%.

(8) Lewis and Randall, "Thermodynamics," McGraw-Hill Book Co., Inc., New York, 1923.

(9) Lewis and Kay, *Oil Gas J.*, March 29 (1934).

Summary

Ethylene, propylene and isobutylene are absorbed by solid cuprous chloride and ethylene is absorbed by solid cuprous bromide, indicating that the reaction is characteristic of the olefins and the cuprous halides. Except for isobutylene, approximately one mole of olefin is absorbed for one mole of cuprous halide. Olefins have been absorbed from several mixtures and concentrated by the use of these salts and a method for calculating the theoretical maximum recovery is outlined.

CAMBRIDGE, MASS. RECEIVED JANUARY 3, 1939

[CONTRIBUTION FROM THE WILLIAM H. CHANDLER CHEMISTRY LABORATORY OF LEHIGH UNIVERSITY]

Evidence for Ring Structure in Certain Aliphatic Organic Compounds

BY HILTON A. SMITH AND J. P. MCREYNOLDS

In connection with the study of the rate of esterification of organic acids, the postulation has been made that acids with a chain involving four or more carbon atoms have a ring structure. The purpose of this paper is to use this as a basis for explaining a number of properties of organic acids and other organic compounds which might have such a structure.

I. Esterification

The rates of the catalyzed esterification of normal aliphatic acids in methyl alcohol have been studied recently.[1] Figure 1 shows the effect of the length of the carbon chain on the values of the rate constant at 25°. From this figure, it is obvious that increasing the chain length of the acid produces a definite effect when there are less than four carbon atoms in the chain. Starting with butyric acid, however, lengthening of the chain produces no effect. These facts were explained by postulating that the chain of butyric and higher acids was not straight, but that the first four carbon atoms including that in the carboxyl group formed a ring.

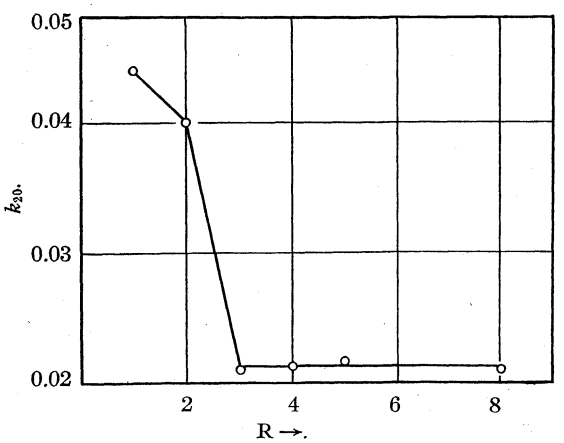


Fig. 1.—Effect of acid chain length on the reaction $CH_3OH_2^+ + RCOOH \rightarrow CH_3COOR + H_3O^+$.

In a subsequent paper[2] it was shown that the rates of the catalyzed esterification of methyl and phenyl substituted acids in methanol substantiated this theory.

(1) Smith, THIS JOURNAL, **61**, 254 (1939).
(2) Smith, *ibid.*, **61**, 1176 (1939).

II. Saponification

The effect of the length of the carbon chain of the acid group on the rate of the alkaline hydrolysis of saturated aliphatic esters was studied by Evans, Gordon and Watson.[3] These workers found that the values of the reaction rate constants decreased with increasing chain length until ethyl butyrate was reached. Further increase in the chain length had no effect. They attributed the decreasing values of k in the early members of the series to an increase in the activation energy of the reaction. This idea has been modified[4] and it has been shown that within experimental error the activation energy does not change with increasing chain length. The change is rather a change in the steric factor in the equation $k = sZe^{-E/RT}$.

Figure 2 shows the effect of the length of the carbon chain on the reaction velocity constants for the saponification of the ethyl esters of normal aliphatic acids at 25°. The data of Smith and Levenson were used for the first three points on this graph, while subsequent points were obtained from the data of Evans, Gordon and Watson.

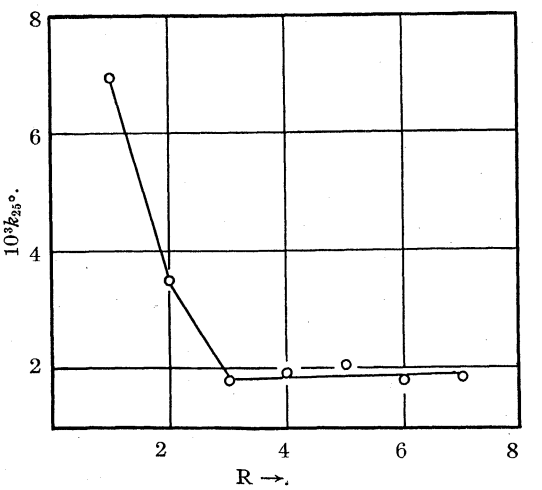


Fig. 2.—Effect of acid radical chain length on the reaction $NaOH + RCOOC_2H_5 \rightarrow RCOONa + C_2H_5OH$.

This figure shows that, as in the case of esterification, the effect of increasing the length of the

(3) Evans, Gordon and Watson, *J. Chem. Soc.*, 1439 (1938).
(4) Smith and Levenson, THIS JOURNAL, **61**, 1172 (1939).

carbon chain is quite different before and after a total of four carbon atoms are present. These results readily may be explained on the basis of the ring theory. The ring will be formed in the ethyl esters of butyric and higher acids.

Evans and co-workers included in their studies the rate of saponification of the ethyl esters of several methyl-substituted acids. Here also the results are readily explainable on the basis of the ring theory. Thus, substitution of a methyl group on the third carbon of butyric acid gives a smaller rate constant than the substitution of a similar group on the second carbon of propionic acid. This is evidenced by the fact that the values of k for ethyl isovalerate are lower than the corresponding values for ethyl isobutyrate.[5] Also the values of k for the saponification of the ethyl ester of methylethylacetic acid are smaller than the corresponding values for isobutyric acid. This shows the effect of the ring formation caused by completion of the four carbon atom chain.

The saponification of the ethyl ester of diethylacetic acid is particularly interesting. This ester gives the lowest values of k and also the highest activation energy of any of the esters studied by Evans, Gordon and Watson. It behaves very similarly to trimethylacetic acid ester. Evans and co-workers were unable to offer any explanation of the results with ethyl diethylacetate. The postulation of a ring structure gives such an explanation. In this ester, there are two rings formed, and the terminal methyl groups are brought into such a position that the screening of the carboxyl group is even greater in the case of the diethylacetate than in that of the trimethylacetate. Evans and co-workers found that branching on the α-carbon atom leads to a lower probability factor in the case of the ethyl esters of isobutyric and trimethylacetic acids. While their conclusion is correct, their low value of the activation energy of isobutyric acid[5] is responsible for their very low value of "s" for this acid.

Hinshelwood and Legard[6] demonstrated that substitution in the α-position often causes an increase in the activation energy. While this increase is found for the esters of trimethylacetic acid, methylethylacetic acid, and isovaleric acid, it is not found for the isobutyric ester. This same effect was found in esterification studies.[7] It may be that in the case of trimethylacetic and diethylacetic acids the reacting molecules must possess an added amount of energy at the time of collision in order to break through the force field set up around the carboxyl group by the several close methyl groups.

(5) In this connection, Evans and co-workers state among other conclusions that "ethyl isobutyrate gives a value of E which is smaller than that for ethyl n-butyrate." This conclusion apparently results from a mistake in calculation. A re-plotting of their reaction rate constants against inverse temperature resulted in an activation energy of 15,000 cal. per mole in each case. These values were checked by the method of least squares. The results gave 15,023 for isobutyric acid and 14,968 for its normal isomer. These are certainly the same within experimental error.

(6) Hinshelwood and Legard, *J. Chem. Soc.*, 587, 1588 (1935).

Acid Dissociation Constants

The dissociation constant of an organic acid may be considered as the representation of an equilibrium between the release of protons by the acid and the reaction between the H_3O^+ ion and the acid radical. The effect of increasing the chain length of the acid may have a different effect on each of these, thus causing a shift in the value of the dissociation constant. The latter reaction is very similar to the catalyzed esterification of an acid with an alcohol. One might, therefore, expect to find much the same results when the effect of chain length on the two properties is studied.

The acid dissociation constants of a number of aliphatic acids have been studied by Dippy.[8] The effect of the length of the carbon chain on the dissociation constant of a normal aliphatic acid is shown in Fig. 3. It will be noted that the general effect of increasing the carbon chain is to lower the value of the dissociation constant. In the case of the shift from propionic to butyric acids, however, there is an increase in the value of K. The recent work of Belcher[9] is in accord with Dippy's findings. Bennett and Moses[10] compared the dissociation constants of propionic, butyric, and heptoic acids; they attributed the high value in the case of butyric acid to the fact that the end methyl in this group, being free to move, occasionally came into close proximity to the carboxyl group and facilitated ionization. Dippy, on the

(7) The activation energy of the catalyzed esterification of isobutyric acid with methyl alcohol was found to be the same as that for normal acids. "E" for the same reaction with methylethylacetic acid was higher. In the case of trimethylacetic acid the activation energy is also greater. The results with this latter acid have not yet been published. In the case of isovaleric acid, the activation energy had about the same value (10,000 cal./mole) as that for normal acids. The value of k at 50° for this acid appears to be somewhat low, and may account for this result. However, this point was checked several times, all runs agreeing within the limits of experimental error.

(8) Dippy, *J. Chem. Soc.*, 1222 (1938).

(9) Belcher, THIS JOURNAL, **60**, 2744 (1938).

(10) Bennett and Moses, *J. Chem. Soc.*, 2364 (1930).

other hand, explains the high dissociation constant of butyric acid by stating that after the proton has left the acid, the anion forms a ring of the type here postulated for the acid itself. The idea that the ring is present in the anion only seems untenable for two reasons. In the first place, the same general effect is found in the study of esterification of the acids, and also of saponification of the corresponding esters. In neither instance is the ion involved in the reaction, but rather the acid or ester molecule itself. In the second place, butyric acid hardly can be regarded as an exception. The dissociation constant of valeric acid is also higher than that of propionic acid, while that of hexoic acid is almost the same. It appears that butyric and higher acids follow one curve, while acids of shorter chain length follow another. Evidently the same effect which is found in butyric acid persists in higher normal acids. These facts can be explained by postulating ring formation for butyric and higher acids both in the undissociated molecule and in the anion. Of course, the ring must be more stable in the anion than in the acid.

Dippy feels that the possibility of explaining the dissociation constants by steric hindrance is rendered less likely by the absence of abnormality in the phenyl-substituted acids.[11] This already has been discussed in connection with the esterification of these acids[2] where it has been shown that the lack of such an abnormality may be readily accounted for by ring structures.

It would appear that the change in the dissociation constants of normal aliphatic acids may be explained on the assumption that increase in the chain length involves two opposing factors. The first may be assigned to a decrease in the ability of the proton to leave the acid when chain length is increased, and results in a decrease in the dissociation constant. This effect becomes smaller with increasing chain length. The second may be due to the fact that the number of effective collisions between the H_3O^+ ion and the COO^- group of the anion is lessened with increasing chain length up to butyric acid. This results in an increase in the value of the dissociation constant. The shape of this curve will be essentially the inverse of that shown in Fig. 1 for the case of esterification. The shape of the curve in Fig. 3 results from the combination of these two curves. The sudden drop in the dissociation constant from octoic to nonoic acids was not explained by Dippy, nor can it be explained here.

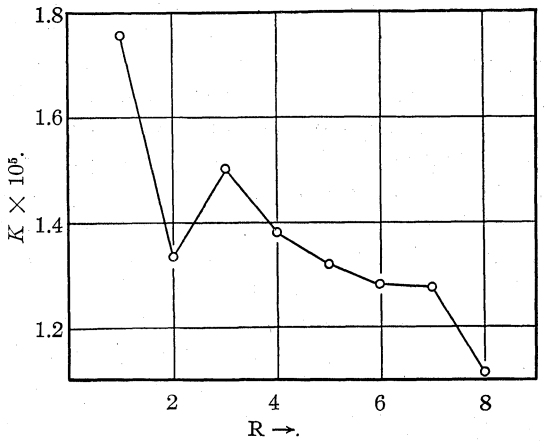


Fig. 3.—Effect of acid chain length on ionization constants.

The high dissociation constants found for isovaleric and diethylacetic acids are readily explainable on the basis of the ring theory; also the fact that isobutyric acid has essentially the same K as propionic acid. The very low value of the dissociation constant for trimethylacetic acid is unexpected, and can be explained only by assuming that some factor comes into play here which decreases the ability of the proton to leave the acid.

Dippy and Lewis[11] also find that the dissociation constant for *cis*-cinnamic acid is considerably higher than that for the *trans* form. This is readily explainable on the basis of the ring theory. In the *cis* isomer the ring will be formed, while in the *trans* isomer this is structurally impossible. For this reason, the solid angle within which H_3O^+ ions may approach the carboxyl group in order to have reaction occur is much greater in the *trans* than in the *cis* form. In fact, it is often found that when organic acids are capable of existing in two geometrical isomers of this type, the *cis* form will have the higher dissociation constant. This generality may be explained by the fact that in the *trans* form the solid angle from which H_3O^+ ions may approach the anion in order to collide with the carboxyl group, is considerably greater than the corresponding solid angle for the *cis* form.

Certain recent evidence may be considered to be opposed to this theory. For instance, dielectric constant data indicate that the length of an amino acid increases regularly with the number of carbon atoms between the charged groups, despite the

(11) Dippy and Lewis, *J. Chem. Soc.*, 1008 (1937).

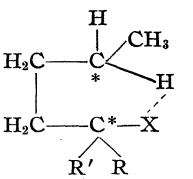
fact that these groups are of opposite sign.[12] Nevertheless, the dipole distances calculated assuming a zig-zag chain structure are considerably larger than those actually found, thus indicating that the charged portions of the molecule actually are closer than might be expected. Then, too, the effect of ring formation has not been observed either for the saponification of the esters of dibasic acids,[13] or in the ionization constants of certain substituted acids.[14] This is, however, not surprising since the effect of substitution of —COOH, —Cl or similar groups gives rise to changes which are of a completely different type and order of magnitude from the effects under consideration here. For instance, substitution of a chlorine atom, or carboxyl group in the alpha position changes the dissociation constant of acetic acid from 1.8×10^{-5} to about 10^{-3}, while the corresponding substitution of a methyl group causes a change which is not only of smaller magnitude (K for propionic acid is approximately 1.3×10^{-5}) but is also in the opposite direction. The work of Ingold[13] when compared with that of Evans, Gordon and Watson[3] also shows that the effects due to increasing chain length are quite different when one is dealing with a dibasic acid as compared to a monobasic acid.

Optical Rotatory Power

The preceding three sections have dealt with the explanation of the effect of the length of the carbon chain of an acid or related compound on certain chemical reactions. The argument may be raised that all of these may be explained on some other basis than that of physical structure. In order to forestall such criticism, a study has been made of the correlation of optical rotatory power of acids and related compounds with their structures as predicted by the ring theory already outlined. This property is known to depend on molecular structure.

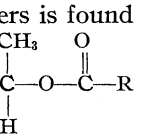
Pickard and Kenyon[15] found evidence of irregularities in optical rotatory power for the series of alcohols EtCHOHR which could be interpreted as evidence for the suggested spiral structure of Frankland.[16] This scheme indicates an irregularity when R = 5 or 6, and again when R = 9 or 10.

The explanation of irregularities in a homologous series of optically active compounds is much more satisfactory when these irregularities are interpreted in the light of a ring formed through a hydrogen bond. The introduction of such a ring into a compound already containing an asymmetric atom should produce certain effects upon the optical activity. (1) The increment of change $\Delta[M]_D$ in the molecular rotation for added CH_2 groups should show a variation when enough groups are added to close a ring. The effect of the added CH_2 group and the effect of the ring closure are superimposed. That ring closure does have a marked effect upon optical activity is well known from the lactones of sugar acids. (2) The introduction of a further CH_2 group after the ring is closed will introduce an asymmetric carbon atom into the ring as shown in I. Due to this increase in the number of asymmetric carbon atoms a change in $\Delta[M]_D$ should be found for the addition of this group. (3) Additional CH_2 groups should show uniform effects. The increment may well be quite small since the change in structure is so far removed from the center of asymmetry that it should show little effect.



I (* asymmetric carbon atom)

The introduction of an asymmetric atom into such a ring does not necessarily demand that such an ester as methyl *n*-valerate be resolvable into optical antipodes. The ring must, by its very nature, be quite unstable. This would prevent isolation of the two diastereoisomers by use of an active resolving agent. A kinetic resolution would occur yielding only one diastereoisomer, followed by immediate racemization upon liberation of the free compound. Thus, the esterification of *n*-valeric acid with an optically active alcohol would direct the structure of the asymmetric carbon in the acid ring preferentially to one or the other possible asymmetric structures.

A sufficiently complete series of esters is found in those of structural formula  (R^1 from CH_3 through C_6H_{13}, and R from CH_3 through C_8H_{17}). The values for the specific rotation were taken from the "International Critical Tables"[17] and converted to molecular rotation through multiplication by one-hundredth of the molecular weight. The molecular rotations are given in Table I. Figure 4 makes use of the data

(12) *Cf.* Cohn, *Ann. Rev. Biochem.*, **4**, 93 (1935).
(13) Ingold, *J. Chem. Soc.*, 2170 (1931).
(14) *Cf.* Westheimer and Shookhoff, THIS JOURNAL, **61**, 555 (1939).
(15) Pickard and Kenyon, *J. Chem. Soc.*, **99**, 45 (1911).
(16) Frankland, *ibid.*, **75**, 368 (1899).
(17) "International Critical Tables," Vol. VII, pp. 360–1.

in this table. In 4 A, $[M]_D$ is plotted against the number of carbon atoms in R (R^1 constant) and in 4 B $[M]_D$ is plotted against the number of carbon atoms in R^1 (R constant).

TABLE I

	$[M]^{20}D$				
Acid	*d*-β-Butyl	*d*-β-Amyl	*d*-β-Hexyl	*d*-β-Heptyl	*d*-β-Octyl
Acetate	29.50	22.31	14.44	13.00	11.76
Propionate	31.01	22.23	15.42	14.40	12.98
Butyrate	31.64	24.92	18.20	18.85	17.90
Valerate	32.74	27.53	20.76	20.52	19.60
Hexoate	32.09		21.68	21.34	20.43
Heptoate	32.31		22.17	21.73	20.79
Octoate	32.28			21.95	21.12
Nonoate	32.16		22.70	22.27	21.49
Dodecoate		28.19			

The essential factor which would be affected by an increase in either R or R^1 according to the treatment under consideration may be called $\Delta[M]_D$ which represents the change in molecular rotation when the number of carbon atoms in the optically active molecule is increased by one.

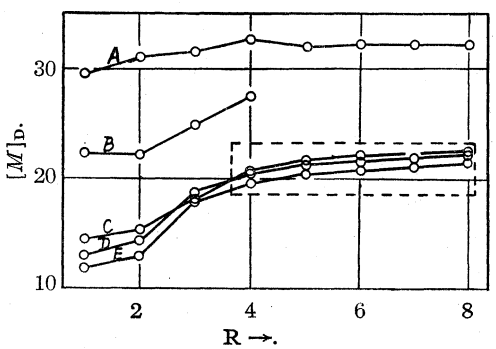
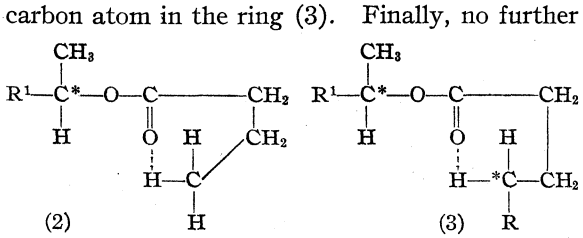


Fig. 4A.—Effect of chain length on molecular rotation of $R^1C(CH_3)(H)-O-C(=O)-R$, R variable: A, *d*-β-butyl; B, *d*-β-amyl; C, *d*-β-hexyl; D, *d*-β-heptyl; E, *d*-β-octyl.

In Fig. 4A the postulated ring structure would predict that $\Delta[M]_D$ for the increase in R from 2 to 3 should show a significant change due to the appearance of a ring structure (2). It would also indicate a significant change in $\Delta[M]_D$ between R = 3 and 4 due to the appearance of an asymmetric carbon atom in the ring (3). Finally, no further marked changes in $\Delta[M]_D$ should appear beyond R = 4. The data plotted in Fig. 4A agree with this treatment with the exception of the $\Delta[M]_D$ between R = 4 and 5 in curve A. Since such an irregularity does not appear in any of the other curves which could be plotted in this range, no explanation can be offered for this apparent irregularity. In Fig. 4B the significant changes in $\Delta[M]_D$ should appear between $R^1 = 1$ and $= 2$ and between $R^1 = 2$ and $= 3$. Substantial agreement is found. The most striking feature of the curves in Figs. 4A and 4B is the exceedingly small effect of changes in either R or R^1 within the areas enclosed within the dotted lines. The esters within this area are of such nature that the ring structure treatment would indicate no significant changes in $\Delta[M]_D$ for additions of CH_2 groups to either the acid (R) or the alcohol (R^1) portions.



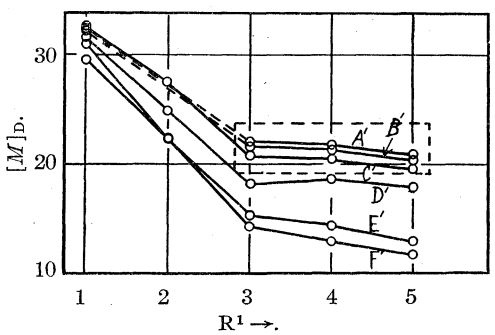


Fig. 4B.—Effect of chain length on molecular rotation of $R^1C(CH_3)(H)-O-O-C(=O)-R$, R^1 variable: A', heptoates; B', hexoates; C', valerates; D', butyrates; E', propionates; F', acetates.

The structure was applied only to acids in the earlier kinetic treatment, but from the above discussion it seems to be independent of the functional group as long as that group contains a donor atom.

In support of this conclusion three homologous series of alcohols are discussed. Data are given in Table II and plotted in Fig. 5. The appearance of the ring should be indicated by $\Delta[M]_D$ from R = 2 to 3, and the asymmetric carbon in the ring by $\Delta[M]_D$ from R = 3 to 4; $\Delta[M]_D$ values for higher R values should be essentially constant. In curve A for γ-isopropyl carbinols $\Delta[M]_D$ values are in good agreement with the theory particularly from R = 4 through higher R

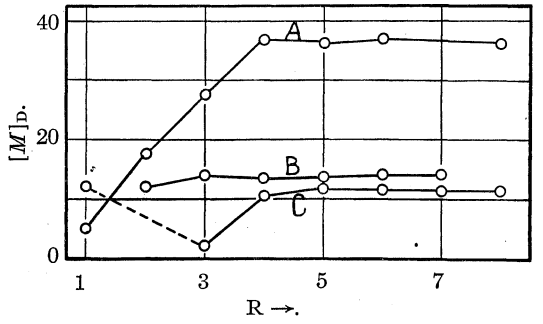


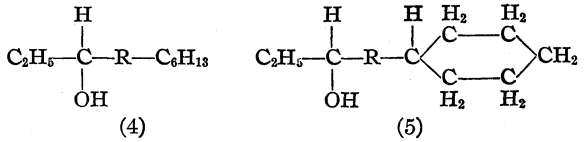
Fig. 5.—Effect of chain length on molecular rotation of *d*-β-methyl, *d*-γ-ethyl, and *d*-γ-isopropyl carbinols: A, isopropyl carbinols; B, methyl carbinols; C, ethyl carbinols.

values. Curve B for *d*-β-methylcarbinols shows the expected trend after R = 4. The Δ[*M*]D values in this series are quite small, and so no significant conclusions may be drawn. Curve C for *d*-γ-ethylcarbinols does not give any information for Δ[*M*]D before the interval R = 3 to 4 since the compound corresponding to R = 2 does not contain an asymmetric atom, and would therefore show an [*M*]D value of zero. The values of Δ[*M*]D beyond R = 3 do show excellent agreement with the postulated effects of a ring structure.

TABLE II

R	[*M*]D R—C(H)(OH)—CH_3	R—C(H)(OH)—C_2H_5	R—C(H)(OH)—$CH(CH_3)_2$
CH_3		12.20	4.95
C_2H_5	12.20		17.47
C_3H_7	13.97	2.28	27.62
C_4H_9	13.42	10.57	36.71
C_5H_{11}	13.73	11.83	36.10
C_6H_{13}	14.06	11.66	36.90
C_7H_{15}	14.02	11.49	
C_8H_{17}		11.62	36.10

An example of the effect of ring formation is seen in the parallel series of alcohols of the type shown in 4 and 5, where R varies from 0 to 2. The optical activity of these series was determined by Kuhn and Biller.[18] The curves for these series as given by Fig. 6 show that very little change takes place in the hexyl, heptyl, and octyl derivatives. This is in agreement with the ring



structure, as the ring is closed and contains the same asymmetric atoms in all three compounds, as

(18) Kuhn and Biller, *Z. physik. Chem.*, **B29**, 1 (1935).

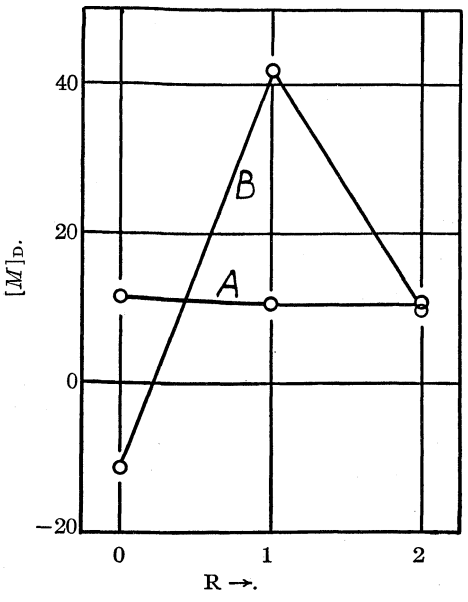
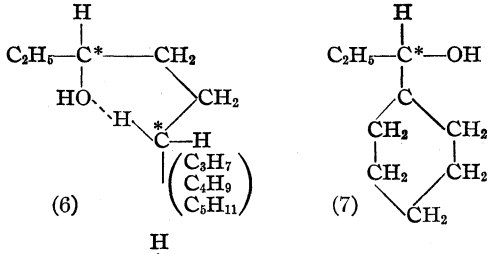
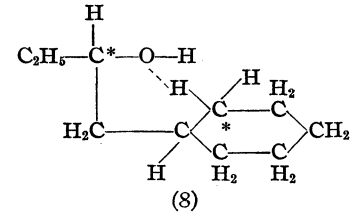
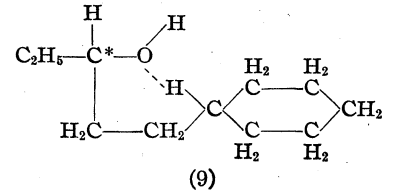


Fig. 6.—[M]D for $C_2H_5CHOHRC_6H_{13}$ and $C_2H_5CHOHRC_6H_{11}$ from R = 0 to R = 2: A, $C_2H_5CHOHRC_6H_{13}$; B, $C_2H_5CHOHRC_6H_{11}$.

is shown in 6. The changes in the cyclohexyl compounds of the same number of carbon atoms arise from a difference in the structure due to ring formation. In the first member, no ring is possible, as shown in 7. In the second case, ring formation is possible, and results in the formation of a second asymmetric atom. This is shown in 8. In the third member, ring formation is also possible. However, in this structure as given by 9, there is

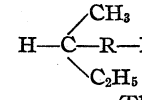






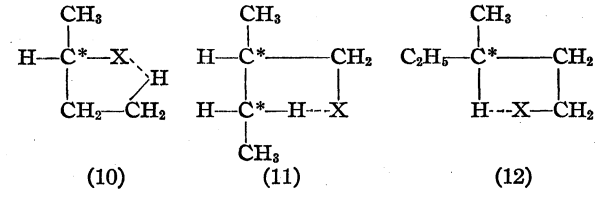
only one asymmetric carbon atom, and the ring structure is much the same as that in the normal series. Figure 6 shows the results of these structures on the optical rotatory power.

That this type of ring formation is quite general seems fairly well supported by the curves in Fig. 7. These represent optical activities of azides, aldehydes, and acids of the general formula



where X is the particular functional group. The values used for acids are by Levene, Rothen and Marker[19]: those for aldehydes by Levene and Rothen[20]; and those for the azides are by the same authors.[21] The three examples of each type contain the same ring structures.

As shown by Fig. 7, the trend of the three curves is quite analogous in all respects, except that the azide curve is inverted. Such inversion offers no difficulties, since an asymmetric carbon may contribute either a positive or negative effect to the total rotation. Whatever structure is used to explain the trend in one series must be used to explain the trend in all three. Possible structures for these series are given by 10, 11, and 12, where X may represent —COOH, —CHO, or $—CH_2N_3$.



(10) (11) (12)

In 10, there is but one asymmetric atom. In 11, there are two such atoms. In 12, there is still the same ring as in 10 and 11, but it contains only one asymmetric carbon.

Unquestionably other data related to optical activity may be explained on the basis of ring structure. However, in most cases, insufficient data are available to warrant further discussion.

It is thus possible to explain not only the effect of the character of the carbon chain on esterification, saponification, and dissociation constants, but also its effect on optical activity, by assuming that certain ring structures may be formed. Probably this type of ring structure may explain other anomalies which now appear in the literature, particularly the peculiar effect which the ethyl group often exerts. This anomaly has been pointed out by Evans and co-workers.[3] The effect of the nature of the carbon chain on the rate of both the base catalyzed[22] and the acid catalyzed[23] prototropy of phenyl alkyl ketones may be explained by the formation of a ring containing four carbons quite as easily as by the three carbon containing ring postulated by the authors. The three-carbon ring must be under a great strain, while that containing four C atoms would be essentially strainless. In this connection, Huggins[24] has pointed out that in general hydrogen bonds are more stable when distances through which the bond operates are small.

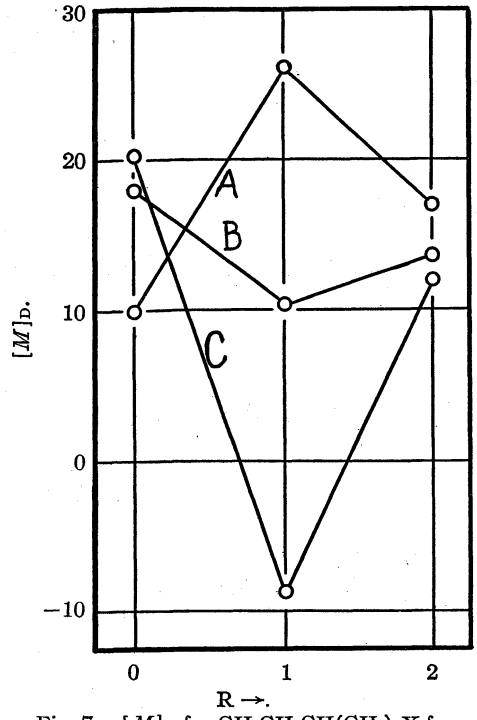


Fig. 7.—$[M]_D$ for $CH_3CH_2CH(CH_2)_nX$ from CH_3 | n = 0 to n = 2: X = COOH, CHO, or CH_2CN_3; A, azides; B, acids; C, aldehydes.

It is probably unnecessary to point out that the ortho effect found in many organic compounds is probably due to this same type of ring formation. That such rings are formed in salicylic acid, *o*-toluic acid, *o*-chlorobenzoic acid, and similar compounds has already been postulated.[25] In all these cases the bonding hydrogen atom completes

(19) Levene, Rothen and Marker, *J. Chem. Phys.*, **1**, 662 (1933).
(20) Levene and Rothen, *ibid.*, **4**, 48 (1936).
(21) Levene and Rothen, *J. Org. Chem.*, **1**, 76 (1936).
(22) Evans and Gordon, *J. Chem. Soc.*, 1434 (1938).
(23) Evans, *ibid.*, 785 (1936).
(24) Huggins, *J. Org. Chem.*, **1**, 407 (1936).
(25) See, for instance, Dippy, Evans, Gordon, Lewis and Watson, *J. Chem. Soc.*, 1421 (1937). It should be noted that these authors postulate that this ring formation takes place only in the anion of the acid. It seems preferable to consider that the bond is also present in the un-ionized acid since reactions such as esterification do not depend on ionization of the acid, but show a marked dependence on the ortho effect.

a six-membered ring similar to that postulated for the normal acids.

Summary

The effect of the character of an alkyl side chain on the processes of esterification and saponification, on acid dissociation constants, and on optical activity has been discussed. It has been shown that ring formation similar to that already postulated to explain the effect of the alkyl chain length of normal aliphatic acids on their velocity of esterification in methanol gives a satisfactory explanation of these phenomena.

The same structure may be used to explain other reactions. It is pointed out that the ortho effect is unquestionably due to the same type of structure.

BETHLEHEM, PENNA. RECEIVED MARCH 2, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

Chlorine. The Heat Capacity, Vapor Pressure, Heats of Fusion and Vaporization, and Entropy

BY W. F. GIAUQUE AND T. M. POWELL

This paper presents the results of a low temperature calorimetric investigation of chlorine. The entropy of chlorine has been calculated previously[1] from band spectrum data and the principal purpose of the present work is to compare the value obtained by means of the third law of thermodynamics with the accurately known spectroscopic value. No difficulty with false equilibrium at low temperatures, such as has been found with a few other substances, was anticipated in the case of a molecule like chlorine. Thus it was expected and has been found that the two methods of obtaining the entropy are in excellent agreement.

The measurements were made in a calorimeter which has been described as Gold Calorimeter II.[2] A detailed description of a similar calorimeter has been given previously.[3]

Chlorine reacts slowly with gold at ordinary temperatures and before the gold calorimeter was used for chlorine the reactivity was investigated by immersing a sheet of gold in liquid chlorine at its boiling point. The sheet had an area of 58.5 cm.^{2} and was boiled in nitric acid, washed in alcohol and heated before weighing after each removal from the chlorine. During the first twenty-four hours the gold lost 0.0140 g. but subsequent immersion for four days caused an additional decrease of only 0.0087 g. Since the calorimetric investigation required that the liquid chlorine be at temperatures near the boiling point for a comparatively short period, the reaction could not occur to any appreciable extent. Moreover, the data on the rate of solution of gold were obtained with undried commercial liquid chlorine whereas the chlorine used to fill the gold calorimeter was carefully dried and purified. Presumably the reaction between gold and very dry chlorine would be much slower than that recorded above. When measurements were not in progress, the chlorine was solidified and kept near the temperature of liquid air.

The resistance thermometer was calibrated during the measurements against a copper–constantan thermocouple with the laboratory designation W.[4] Small corrections to this standard thermocouple were recently determined by Stephenson and Giauque.[5] Following the present research the standard thermocouple was compared with the vapor pressures of hydrogen and agreement with the corrections of Stephenson and Giauque was found.

Preparation of the Chlorine.—The chlorine was prepared by dropping 3 *M* HCl on manganese dioxide. The small amount of hydrogen chloride in the gas was removed by water and the chlorine was dried with concentrated sulfuric acid and finally with phosphorus pentoxide.

Chlorine prepared as above was placed in the calorimeter and measurements of the heat effect associated with premelting in the solid showed it to contain an impurity of about 5 parts in 10,000 on a molal basis. The material was removed from the calorimeter and fractionated in a vacuum jacketed column. Subsequent premelting

(1) Giauque and Overstreet, THIS JOURNAL, **54**, 1731 (1932).

(2) (a) Giauque and Wiebe, *ibid.*, **50**, 101 (1928); (b) Blue and Giauque, *ibid.*, **57**, 991 (1935).

(3) Giauque and Egan, *J. Chem. Phys.*, **5**, 45 (1937).

(4) Giauque, Buffington and Schulze, THIS JOURNAL, **49**, 2343 (1927).

(5) Stephenson and Giauque, *J. Chem. Phys.*, **5**, 149 (1937).

measurements in the temperature range a few degrees below the melting point showed that the liquid-soluble solid-insoluble impurity had been reduced to about 3 moles in 100,000.

The Vapor Pressure of Chlorine.—The vapor pressure of chlorine was measured with a mercury manometer using carbon dioxide as a buffer in the manner described previously[6] for nitrogen tetroxide. The measurements were made with the calorimetric apparatus since it permitted excellent temperature control. A system of capillaries and mixing bulbs was so arranged that the less dense carbon dioxide could not enter the calorimeter or the connecting lines adjacent to it. To guard against slow diffusion a small amount of chlorine was pumped from the calorimeter before each vapor pressure observation. Heat was then added until the desired temperature was reached. The results of two series of observations on the triple point are given in Table I.

TABLE I

TRIPLE POINT DATA FOR CHLORINE (0°C. = 273.10°K.)

Series	% melted	T, °K. Thermocouple	T, °K. Resistance Ther.	$P_{inter.}$ cm. Hg
I	25	172.13	172.111	1.044
I	50	172.12	172.109	1.046
II	7	172.13	172.109	1.052[a]
II	30	172.14	172.120	1.046
II	80	172.11	172.115	1.042
Values accepted		172.12		1.044

[a] This value deviates by more than the error of measurement and is given no weight.

The results starting at the triple point are represented by the equation

Triple point 172.12 to 240.05°K.

$$\log_{10}P_{(inter.\ cm.)} = \frac{-1414.8}{T} - 0.01206\ T + 1.34 \times 10^{-5}\ T^2 + 9.91635 \quad (1)$$

The observed values of the vapor pressure are given in Table II where they are compared with Equation 1. The temperatures are given to thousandths of degrees in order that the high relative accuracy may be used in obtaining temperature coefficients. Near the triple point an error in pressure of 0.001 cm. corresponds to 0.01° and since the accuracy of the pressure measurements is about 0.002 cm. deviations of the order of 0.02° are within the limit of error. At the higher temperatures the larger dP/dT makes temperature measurement the limiting factor. The standard acceleration of gravity was taken as 980.665 cm. sec.$^{-2}$ and for this location g = 979.973 cm. sec.$^{-2}$.

(6) Giauque and Kemp, *J. Chem. Phys.*, **6**, 40 (1938).

TABLE II

VAPOR PRESSURE OF CHLORINE (0°C. = 273.10°K.)

T, °K.	$P_{obsd.}$ inter. cm. Hg	$P_{obsd.} - P_{calcd.}$	$T_{obsd.} - T_{calcd.}$
172.12	1.044	+0.002	−0.02
175.44	1.407	− .001	+ .01
180.38	2.158	+ .002	− .01
185.464	3.250	− .002	+ .008
190.513	4.774	+ .000	− .000
195.513	6.831	+ .002	− .004
200.413	9.507	− .003	+ .005
205.242	12.949	− .001	+ .001
210.000	17.274	− .006	+ .010
215.179	23.251	− .016	+ .013
219.909	30.124	+ .015	− .010
225.104	39.396	− .004	+ .002
229.958	50.042	+ .013	− .005
234.975	63.273	− .018	+ .006
240.050	79.385	+ .002	− .000

dP/dT = 3.3425 cm. deg.$^{-1}$ at 76.000 cm.

From Equation 1 the boiling point was found to be 239.05°K. The values for the melting and boiling points of chlorine are compared with those of previous observers in Table III.

TABLE III

MELTING AND BOILING POINTS OF CHLORINE

M. p., T, °K.	B. p., T, °K.	Observer
....	239.5	Regnault[7] (1863)
171	....	Olszewski[8] (1884)
171.6	239.4	Johnson and McIntosh[9] (1909)
172.2	....	Van der Goot[10] (1911)
....	238.6	Pellaton[11] (1915)
....	238.4	Trautz and Gerwig[12] (1923)
170.8	....	Eucken and Karwat[13] (1924)
172.6	239.15	Harteck[14] (1928)
172.12	239.05	This research

The Calorimetric Data.—The heat capacity results are presented in Table IV and results taken from a smooth curve through the observations are given in Table V. A small pressure of helium gas was used to assist thermal equilibrium in the solid at low temperatures. A correction was applied for vaporization into the small gas space due to changing vapor pressure in the liquid range. This correction was made with the assistance of density measurements on liquid chlorine by Pellaton,[11] who gives the equation

$$D = 1.468 - 2.89 \times 10^{-3}t - 5.3 \times 10^{-6}t^2 \quad (2)$$

(7) Regnault: Landolt, Börnstein and Roth, "Physikalisch-chemische Tabellen," Verlag von Julius Springer, Berlin, 1923.
(8) Olszewski, *Monatsh.*, **5**, 124 (1884).
(9) Johnson and McIntosh, THIS JOURNAL, **31**, 1138 (1909).
(10) Van der Goot, *Tab. Ann.*, 67 (1911).
(11) Pellaton, *J. chim. phys.*, **13**, 426 (1915).
(12) Trautz and Gerwig, *Z. anorg. allgem. Chem.*, **134**, 417 (1923).
(13) Eucken and Karwat, *Z. physik. Chem.*, **112**, 474 (1924).
(14) Harteck, *ibid.*, **134**, 21 (1928).

where t is the centigrade temperature. Since the vapor pressure and heat of vaporization were known accurately, there was no appreciable error involved in the small vaporization correction.

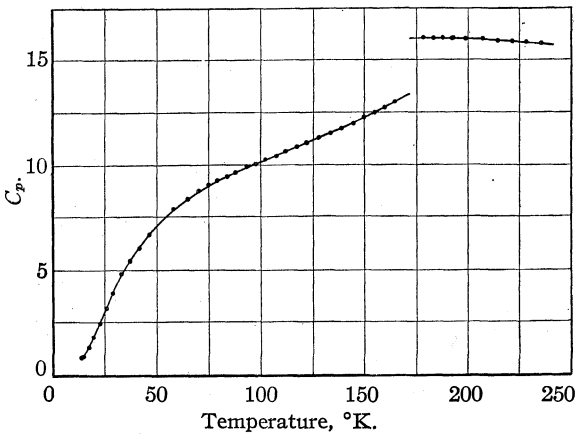


Fig. 1.—Heat capacity in calories per degree per mole of chlorine.

It is estimated that a smooth curve through the data represents the heat capacity to 0.1–0.2% at all temperatures above 35°K. The percentage accuracy decreases near the boiling point of hydrogen due to the rapidly decreasing heat capacity and the rapid decrease in the temperature coefficient of the resistance thermometer in this region.

TABLE IV

THE HEAT CAPACITY OF CHLORINE

0°C. = 273.10°K. Molecular weight, 70.914. 2.3385 moles were in the calorimeter.

T, °K.	ΔT approx.	C_p cal. deg.$^{-1}$ mole^{-1}	T, °K.	ΔT approx.	C_p cal. deg.$^{-1}$ mole^{-1}
14.05	1.1	0.810	118.15	5.4	10.81
15.21	1.0	0.916	123.53	5.2	11.00
17.40	2.7	1.331	128.67	5.0	11.24
19.81	2.0	1.842	134.06	5.7	11.47
22.93	3.9	2.467	139.67	5.4	11.72
26.37	3.0	3.192	145.19	5.2	11.92
29.88	4.0	3.946	150.39	5.0	12.24
33.94	3.2	4.804	155.45	4.8	12.41
37.68	4.2	5.421	160.31	4.6	12.69
42.37	5.1	6.018	164.99	4.5	12.93
47.14	4.4	6.675	172.12	Melting point	
58.59	6.0	7.879	178.98	4.6	16.01
65.42	5.3	8.382	183.75	4.5	16.02
70.50	4.9	8.720	188.40	4.4	15.99
75.25	4.6	8.973	193.21	4.4	15.99
79.71	4.3	9.201	194.08	7.1	15.95
84.06	4.3	9.427	201.50	6.9	15.94
88.66	4.9	9.626	208.63	6.7	15.92
93.47	4.6	9.827	215.90	6.5	15.85
98.06	4.4	10.03	222.82	6.4	15.81
102.92	5.2	10.22	229.73	6.2	15.79
108.06	5.0	10.38	236.77	6.1	15.73
112.99	4.7	10.57	239.05	Boiling point	

TABLE V

THE HEAT CAPACITY OF CHLORINE

Values from curve through observations. 0°C. = 273.10°K. Molecular weight, 70.914.

T, °K.	C_p cal. deg.$^{-1}$ mole^{-1}	Devn., % E. and K. —This research	T, °K.	C_p cal. deg.$^{-1}$ mole^{-1}	Devn., % E. and K. —This research
15	0.89		130	11.29	3.4
20	1.85	1.6	140	11.73	4.3
25	2.89		150	12.20	4.9
30	3.99	4.3	160	12.68	5.5
35	4.97		170	13.17	
40	5.73	8.2	Melting point		
45	6.39		172.12	13.27	
50	6.99	9.0	172.12	16.03	1.4
60	8.00	6.5	180	16.02	1.4
70	8.68	4.8	190	15.99	1.6
80	9.23	3.5	200	15.95	1.9
90	9.71	2.5	210	15.89	2.3
100	10.10	1.5	220	15.84	2.6
110	10.47	2.7	230	15.77	3.0
120	10.87	2.8	240	15.70	3.5

The inaccuracy is estimated to be within 1% at 20°K. but the error may easily be several per cent. at 15°K. In calculating energy 1 calorie (15°) was taken as 4.1832 international joules.

The heat capacity of chlorine has been measured by Eucken and Karwat[13] and their results have been compared with the present work in Table V. The weight of the chlorine used for the heat capacity measurements was found by condensing the material in a steel container with a valve and weighing the liquid at room temperature. 165.829 g. or 2.3385 moles of chlorine were used for the measurements.

The heat of fusion was measured in the usual manner; heat input was started at a temperature somewhat below the melting point and ended several degrees above. The known heat capacity of each phase permitted accurate correction. The results are presented in Table VI.

TABLE VI

HEAT OF FUSION OF CHLORINE

Melting point, 172.12°K. Molecular weight, 70.914

Run	ΔH cal. mole^{-1}
1	1530.5
2	1529.8
3	1531.1
4	1530.7
Average	1531 ± 1
Eucken and Karwat[13]	1615

The heat of vaporization was measured by attaching an absorption bulb, filled with a solution which contained 2 M sodium hydroxide and 1.7 M potassium iodide, to the calorimeter. In order to prevent the solution from being sucked back,

the entrance tube was immersed in a small amount of mercury at the bottom of the absorption bulb. The iodide was added to prevent clogging of the opening when a small portion of the chlorine reacted with the mercury. Heat was introduced so slowly that vaporization could proceed quietly from the surface. The results for the heat of vaporization at the boiling point are given in Table VII.

TABLE VII

HEAT OF VAPORIZATION OF CHLORINE

Boiling point, 239.05°K. Molecular weight, 70.914

Moles evapd.	Time of energy input, min.	ΔH cal. mole^{-1} at 760 mm.
0.16916	40	4881
.17280	40	4884
.17289	40	4876
.17148	40	4874
	Average	4878 ± 4

From vapor pressure equation, $\Delta H = 4851$

The value for the heat of vaporization calculated from the vapor pressure measurements, 4851 cal. mole^{-1}, agrees within the limit of accuracy of the data but is given no weight compared to the reliable calorimetric value. In calculating the heat of vaporization from dP/dT we made use of data of state observations on chlorine gas. Measurements have been made near the boiling point by Eucken and Hoffmann,[15] who also summarize the measurements of other observers. They represent the volume of chlorine gas by the equation

$$V = \frac{RT}{P} + 39 - \frac{8.5 \times 10^8}{T^{2.6}} \text{ cm.}^3\text{/mole} \qquad (3)$$

In many previous researches in this Laboratory the gas volume at the boiling point has been estimated by means of Berthelot's equation of state in order to calculate the heat of vaporization from the vapor pressure. It is of interest to note that in the case of chlorine Berthelot's equation gives a gas volume and therefore heat of vaporization only 0.1% less than Equation (2) at the boiling point. The volume of liquid chlorine at the boiling point was obtained from the density equation of Pellaton[11] mentioned above.

The Entropy of Chlorine.—The calculation of the entropy of chlorine from the calorimetric data is summarized in Table VIII. The correction of the entropy to the ideal gas state was made by means of the thermodynamic equation

$$(\partial S/\partial P)_T = -(\partial V/\partial T)_P$$

and Berthelot's equation of state. The critical constants were taken as $P_c = 76.1$ atm.,[11] $T_c = 417$°K.[11]

$$\Delta S = S_{\text{ideal}} - S_{\text{actual}} = 27RT_c^3P/32T^3P_c$$
$$= 0.12 \text{ cal. deg.}^{-1} \text{ mole}^{-1} \text{ at the boiling point.}$$

We have used Berthelot's equation in preference to Equation (3) in making the above calculation because the data used in obtaining Equation (3) are not sufficiently complete to determine temperature coefficients at the boiling point.

TABLE VIII

THE ENTROPY OF CHLORINE

0–15°K., Debye function $hc\nu/k = 115$	0.331	
15–172.12°K., graphical	16.573	
Fusion 1531/172.12	8.895	
172.12–239.05°K., graphical	5.231	
Vaporization 4878/239.05	20.406	
Entropy of actual gas at boiling point	51.44	
Correction for gas imperfection	0.12	
Entropy of ideal gas at boiling point	51.56	cal. deg.$^{-1}$ mole^{-1}

The calculation of the entropy of chlorine from spectroscopic data has been carried out by Giauque and Overstreet,[1] who have considered the effect of the three isotopic molecular species in considerable detail. We have used their equations and constants to calculate the entropy at the boiling point, 239.05°K. The value for the entropy of the ideal gas at this temperature and 1 atmosphere is found to be 51.55 cal. deg.$^{-1}$ mole^{-1}.

The calorimetric and spectroscopic values of the entropy are compared in Table IX.

TABLE IX

COMPARISON OF CALORIMETRIC AND SPECTROSCOPIC VALUES FOR THE ENTROPY OF CHLORINE

	Entropy in cal. deg.$^{-1}$ mole^{-1}		
	Calorimetric data		
T, °K.	Actual gas	Ideal gas	Spectroscopic
239.05	51.44	51.56	51.55
298.10	...	53.32	53.31

The entropy calculated from spectroscopic data does not include the entropy of isotopic mixing or that due to the nuclear spin of Cl^{35} and Cl^{37} since both of these effects cancel in chemical reactions with a high degree of accuracy. The molecular constants for each of the three isotopic molecular forms of chlorine were of course considered in the calculation. The symmetry number was taken as two in calculating the values given in the last column of Table IX. The value given for the ideal gas at 298.1 was obtained by using the band spectrum data for the gas above the boiling point.

(15) Eucken and Hoffmann, *Z. physik. Chem.*, **B5**, 442 (1929).

The excellent agreement of the entropies calculated from calorimetric and from molecular data supports the third law of thermodynamics and also adds to the substantial evidence that only protons or deuterons may cause molecular rotation in the solid state at the temperatures of liquid hydrogen.

We thank Dr. R. A. Ruehrwein for assisting with the measurements.

Summary

The heat capacity of solid and liquid chlorine has been measured from 14°K. to the boiling point.

The melting and boiling points were found to be 172.12 and 239.05°K., respectively (0°C. = 273.10°K.).

The heat of fusion is 1531 cal. mole^{-1} and the heat of vaporization at the boiling point is 4878 cal. mole^{-1}.

The vapor pressure of liquid chlorine has been measured and the results represented by the equation: triple point 172.12 − 240°K., $\log_{10} P$ (int. cm. Hg) = $-(1414.8/T) - 0.01206\ T + 1.34 \times 10^{-5}\ T^2 + 9.91635$.

The observed triple point pressure was found to be 1.044 cm.

The entropy of chlorine was found to be 51.56 and 53.32 cal. deg.$^{-1}$ mole^{-1} at 239.05 and 298.10° K., respectively, for the ideal gas by means of the third law of thermodynamics.

The data are in excellent agreement with a calculation based on band spectrum data giving 51.55 and 53.31 cal. deg.$^{-1}$ mole^{-1} at the two temperatures.

BERKELEY, CALIF. RECEIVED MAY 1, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, NEW YORK UNIVERSITY]

The Ternary Systems $KBrO_3$–$KClO_3$–H_2O at 25° and $NaBrO_3$–$NaClO_3$–H_2O at 25 and 50°[1]

BY THEODORE SWENSON AND JOHN E. RICCI

These systems have been investigated for the purpose of finding and studying other examples of the type of solid solution previously suggested[2] as a possible addition to the types in the usual Roozeboom classification, namely, the formation of a single incomplete or limited series of solid solutions between two salts without any experimentally measurable degree of mutual solubility for one of the components. Such solid solutions were noted between potassium chlorate and potassium nitrate[3] and between sodium bromate and sodium sulfate.[2] The combinations of potassium bromate and chlorate, and of sodium bromate and chlorate, were therefore studied, as ternary systems with water, using the usual phase rule methods for the investigation of the solubility relationships.

Experimental

High grade (99.9%) potassium bromate was used without recrystallization, while sodium bromate was purified by recrystallization. The chlorates both contained small amounts of the corresponding bromates; this bromate content was in each case determined, by the method described below, and the necessary corrections were then made when the dry chlorates were weighed out for the preparation of the ternary complexes.

The solubility determinations were made according to the usual procedure described in similar investigations, insofar as method of stirring, sampling, filtering, density determination and temperature control are concerned. Starting with complexes of known composition, and analyzing the saturated solutions at equilibrium, the solid phases were then determined by the usual methods of graphical or algebraic extrapolation, besides occasional analyses of wet and centrifuged residues.

The analytical method for the saturated solutions depended on the determination of the combined percentage of the two salts concerned, by evaporation, and iodometric titration of the bromate with thiosulfate, thus allowing the calculation of the percentage of the second salt by difference. This simple scheme involves the difficulty of titrating small quantities of bromate in the presence of large and varying amounts of chlorate. A preliminary investigation of this analytical problem was therefore necessary.

Iodometric Titration of Bromate in Presence of Chlorate.—The determination of bromate by iodometry, in the presence of chlorate, depends on the proper regulation of the acidity, the concentration of iodide, and the time allowed for reaction and titration. Conditions for the differential titration were first given by Junck,[4] chiefly

(1) The material of this paper is taken from the thesis of Mr. T. Swenson presented to the Graduate School of New York University in partial fulfilment of the requirements for the degree of Master of Science.

(2) Ricci, THIS JOURNAL, **57**, 805 (1935).

(3) Toda, *J. Chem. Soc.* (Japan), **43**, 320 (1922).

(4) Junck, *Z. Ges. Schiess Sprengstoffwesen*, **8**, 412 (1913).

from the point of view of the detection and estimation of bromate present as impurity in a chlorate. The literature was reviewed by Taradoire,[5] studying the problem for the same purpose, and employing many refinements in technique for the exact determination of traces of bromate in chlorates. Barneby,[6] studying the general problem of the differential titration of the halogenates in mixtures, described the determination of 0.1 g. of potassium bromate in the presence of 0.1 g. of potassium chlorate. The problem of much larger relative amounts of chlorate, however, such as are found in the present solubility measurements, was not touched upon, and the actual conditions required had therefore to be determined by experiment.

The conditions finally adopted, allowing the titration of up to 0.1 or 0.2 g. of potassium bromate in the presence of as much as 20 g. of sodium chlorate, in a volume of about 100 ml., were the following: sodium iodide, 5 g. (20 ml. of 25% solution), giving a concentration of 0.33 *N* after dilution to 100 ml.; 1.5 ml. of concd. hydrochloric acid (0.18 to 0.2 *N* after dilution); titration with 0.2 *N* sodium thiosulfate to be started one and one-half minutes after addition of the acid, and to be finished in five minutes, inclusive. The above acidity was found to be approximately the minimum for the complete and reasonably fast reaction of the bromate; the large quantity of iodide is required to keep the iodine well in solution. Tests showed these conditions to give complete reaction of the bromate, in the absence of chlorate, with an accuracy of one part in two thousand. When chlorate was added, two corrections had to be made. The first is a constant one depending on the quality and quantity of the chlorate, being caused by the bromate content of the latter. This was therefore determined by previous titration of the chlorate alone according to the method just described and taking account of the second correction too, which is an effect of the slow oxidation of iodide by chlorate under the conditions of the titration. This second effect, which was found to be approximately directly proportional to the chlorate concentration and to the time, was evaluated by measuring the continued liberation of iodine from various initial weights of chlorate, by successive titration with a very dilute thiosulfate solution, and plotting the total volume of thiosulfate used against the time.

Tested on known mixtures, the procedure described, involving two corrections, gave an average error of only one part in two thousand, in six determinations of about 0.2 g. of sodium bromate in the presence of 10 g. of sodium chlorate of known bromate content. The same conditions, moreover, using a 0.02 *N* sodium thiosulfate solution for titration, and applying the time correction indicated, can be used for the detection of quantities as small as 0.001 (±0.0005)% of bromate in chlorate.

Results.—The results of the solubility determinations are shown in Tables I and II, which list the composition of original complexes, the composition (and density, for some) of saturated solutions, and, in the last column, the composition of the solid phase calculated by the extrapolation of tie-lines, on the assumption of an anhydrous solid.

(5) Taradoire, *Bull. soc. chim.*, [5] **4**, 1759 (1937).

(6) Barneby, THIS JOURNAL, **38**, 330 (1916)

TABLE I

SYSTEM $KBrO_3$–$KClO_3$–H_2O AT 25°

Original complex wt. % $KBrO_3$	Original complex wt. % $KClO_3$	Satd. soln., wt. % $KBrO_3$	Satd. soln., wt. % $KClO_3$	Density	Solid phase Wt. % $KClO_3$	Solid phase Formula
	0	7.533	0	1.054	0	$KBrO_3$
19.98	2.00	6.46	2.26		0.46	S.S. I
7.04	4.04	5.75	4.08	1.067	1.10	S.S. I
18.03	3.99	5.63	4.29		2.0	S.S. I
13.11	6.92	4.936	6.546	1.078		S.S. I + S.S. II
6.10	13.95	4.945	6.531	1.078		S.S. I + S.S. II
4.02	15.98	4.02	6.75	1.072	96.0	S.S. II
2.79	9.05	2.79	7.08	1.064	97.2	S.S. II
2.02	20.14	2.07	7.26		98.3	S.S. II
1.01	10.04	1.02	7.60	1.053	99.1	S.S. II
0	...	0	7.895	1.048	100	$KClO_3$

TABLE II

SYSTEM $NaBrO_3$–$NaClO_3$–H_2O

Original complex, wt. % $NaBrO_3$	Original complex, wt. % $NaClO_3$	Satd. soln., wt. % $NaBrO_3$	Satd. soln., wt. % $NaClO_3$	Solid phase Wt. % $NaClO_3$	Solid phase Formula
			25°		
...	0	28.29	0	0	$NaBrO_3$
42.45	12.98	16.46	18.91	−0.15	$NaBrO_3$
25.08	20.99	13.96	24.21	− .70	$NaBrO_3$
27.94	23.06	12.20	28.03	+ .31	$NaBrO_3$
17.98	32.97	8.68	36.75	− .37	$NaBrO_3$
10.84	39.37	7.14	40.98	+ .57	$NaBrO_3$
10.50	39.96	7.00	41.47	2.02	S.S. I
10.01	41.07	6.54	42.62	1.70	S.S. I
10.00	41.97	5.99	43.66	6.84	S.S. I
12.99	41.63	6.05	43.55	24.3	S.S. I + S.S. II (?)
7.10	44.50	5.33	44.64	40.4	S.S. II
5.98	45.64	5.07	44.98	64.2	S.S. II
5.01	46.54	4.49	45.66	71	S.S. II
6.11	52.98	3.79	46.46	83.2	S.S. II
5.03	51.08	3.69	46.56	85.0	S.S. II
3.04	48.50	2.84	47.42	89.4	S.S. II
2.00	49.49	1.89	48.36	91	S.S. II
1.01	50.46	0.96	49.16	98	S.S. II
0.95	56.89	0.79	49.36	98.5	S.S. II
0	...	0	50.07	100	$NaClO_3$
			50°		
...	0	35.50	0	0	$NaBrO_3$
...	...	27.3	10.8	....	$NaBrO_3$
20.0	35.1	11.2	38.9	0.79	$NaBrO_3$ or S.S.
11.1	46.1	7.09	47.7	22	S.S.
8.93	48.1	6.75	48.2	45	S.S.
6.92	50.1	5.80	49.1	68	S.S.
4.99	52.0	4.53	51.1	77	S.S.
3.02	54.0	2.83	53.0	84	S.S.
5.64	74.1	2.62	53.3	91	S.S.
1.39	55.8	1.35	54.4	96	S.S.
0	...	0	55.54	100	$NaClO_3$

Discussion

Both systems reveal solid solution formation. In the potassium salt system there are two series of limited solid solutions, one of potassium chlorate in potassium bromate (S.S. I) with a limit at 3% potassium chlorate, the other with a limit of 5% potassium bromate in potassium chlorate (S.S. II), (both limits estimated from the diagram). The isothermally invariant liquid solution in equilibrium with these two mutually saturated solid solutions has the composition 4.94%

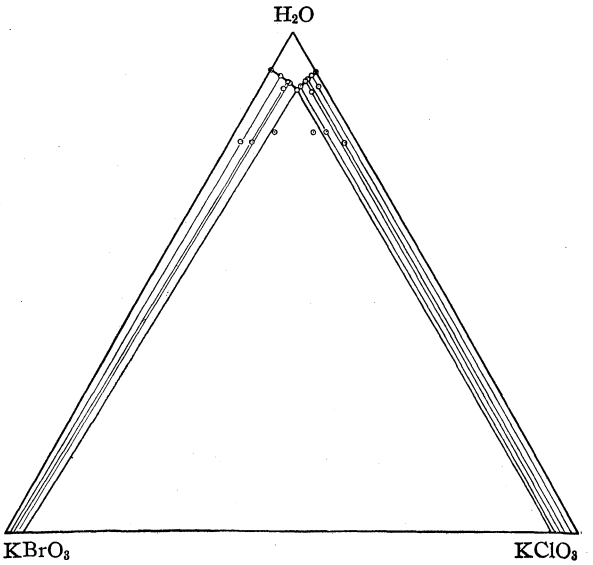


Fig. 1.—System $KBrO_3$–$KClO_3$–H_2O at 25°.

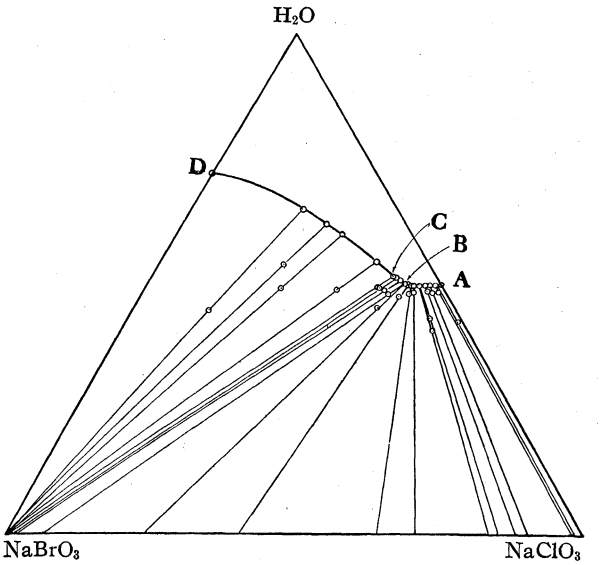


Fig. 2.—System $NaBrO_3$–$NaClO_3$–H_2O at 25°.

potassium bromate and 6.54% potassium chlorate. In one or two experiments the composition of the solid was determined by direct analysis of the dried residue, checking the values obtained by algebraic extrapolation of tie-lines. The time allowed for equilibrium was fourteen days, repeated analysis of saturated solutions having shown this time to be sufficient, when small amounts of solid were used.

The interpretation of the sodium salt system from the data collected is more difficult; perhaps more complete isotherms at both temperatures would be required for a complete interpretation. The chief difficulty in the experiments was the very long time required for the attainment of equilibrium in the formation of the solid solutions here involved; some of the complexes were stirred for periods of one or two months before analysis, some of them still showing small changes going on.

Considering the results at 25°, there is no indication of a break in the solubility curve starting with a solution (point A, Fig. 1) of sodium chlorate alone, until the liquid solution reaches the composition (point B) 6% sodium bromate and 44% sodium chlorate (approximately, as estimated from the diagram). The corresponding solid phase in equilibrium with these liquid solutions changes continuously from pure sodium chlorate, through a wide range of continuous solid solution composition up to 60–65% sodium bromate. A break in the liquid curve at point B (and therefore a corresponding discontinuity in the solid phase) is strongly suggested by the shape of the curve. The solid phase saturating the remaining liquid solutions from B to D seems, however, to be not simply a corresponding solid solution of low sodium chlorate content, but apparently pure sodium bromate over a large part of the curve. For the portion of the curve from D to C (C being an estimated point) the saturating solid is apparently sodium bromate or at most a solid solution of negligible concentration of sodium chlorate in sodium bromate. The appearance of the solid in this region was always quite identical with that of the pure salt, equilibrium was very rapidly attained, and the extrapolation of the tie-lines gave an average algebraic deviation of −0.05% sodium chlorate and an average absolute deviation of 0.41% sodium chlorate, from the point representing pure sodium bromate. Within the experimental variation of the extrapolations, therefore, the phase here is not a solid solution. Beyond C, however, or between C and B, it is possible that a third solid phase is formed, a very finely divided milky solid, slow to settle and slow to come to equilibrium, with compositions, estimated from the disposition of the tie-lines, ranging from very low sodium chlorate content (if not actually pure sodium bromate) to about 5–10% sodium chlorate. This interpretation of three different solid phases would of course involve the existence of two isothermally invariant points for liquid solutions saturated with two adjacent solid phases. These, suggested as points B and C, were not determined; the limits of solid solution com-

position, in view of the slowness in the attainment of equilibrium, would be very difficult to fix.

An alternative possibility is that the two salts form a single solid solution, theoretically continuous from one pure salt to the other, but that the distribution of the salts between the solid and liquid phases is very uneven. The wide divergence of the tie-lines for complexes giving solutions containing approximately 6% sodium bromate (point B) would then simply indicate a marked tendency toward the formation of an isothermally invariant point, because of a tendency toward discontinuity in the solid phase. The observed curvature at the point B, however, suggests actual discontinuity, so that the latter interpretation, while not impossible, seems rather unlikely.

The solid phases are therefore suggested as being pure sodium bromate from D to C, solid solution of some sodium chlorate in sodium bromate (S.S. I) from C to B, and a solid solution (S.S. II) of wide range of proportions of the salts, up to pure sodium chlorate, from B to A. If this interpretation is correct, this system might then be taken as another example of the type of solid solution formation suggested as possible in connection with a study of the system $NaBrO_3$–Na_2SO_4–H_2O[2]; that is, a system in which the miscibility of the salts is such that while solid solutions are formed, a pure salt may still constitute one of the solid phases by itself.

The same general characteristics were noted for the system in the results of a partial isotherm at 50°, also shown in Table II.

Summary

1. In the system $KBrO_3$–$KClO_3$–H_2O, studied at 25°, the two salts dissolve to a limited extent in each other, forming two solid solutions containing up to 3% potassium chlorate in potassium bromate and up to 5% potassium bromate in potassium chlorate.

2. The salts in the system $NaBrO_3$–$NaClO_3$–H_2O studied at 25° (and incompletely at 50°) form a series of solid solutions which, though the evidence is not altogether conclusive, is apparently discontinuous. The solubility curve at 25° appears to be divided into three portions corresponding to the following solid phases: (1) pure sodium bromate, (2) a sodium bromate solid solution containing up to about 5–10% sodium chlorate, (3) a sodium chlorate solid solution containing from 0 to 60–65% sodium bromate.

3. Conditions for the differential iodometric titration of bromate in the presence of very large amounts of chlorate are examined; with proper correction for the slow reaction of chlorate with iodide in acid solution, small amounts of bromate (0.1–0.2 g.) can be determined accurately in the presence of up to 20 g. of chlorate.

NEW YORK, N. Y. RECEIVED MAY 6, 1939

[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY OF THE UNIVERSITY OF CHICAGO]

The Electrostatic Effect of Substituents on the Dissociation Constants of Organic Acids. IV. Aromatic Acids[1]

BY F. H. WESTHEIMER

I

In 1923 Bjerrum[2] advanced the hypothesis that, except for a statistical factor, the effect of a substituent on the ionization constant of an organic acid is electrostatic in origin. Recently, a more satisfactory mathematical formulation of Bjerrum's hypothesis has been advanced by Kirkwood and the author.[3] This treatment differs from the old essentially in that the solute molecules are regarded as cavities of low dielectric constant within the solvent. Shookhoff and the author[4] have applied the new equations with considerable success to a large number of saturated aliphatic acids, and have shown that it will account not only for the ratio of the first to the second dissociation constants of straight-chain dibasic acids, but also, in contrast to the equations of Bjerrum and of Eucken,[5] for the ratio of the dissociation constants of alkylated dibasic acids and for the effect of dipolar substituents on the ionization constants of monobasic acids.

The purpose of the present paper is to apply the new treatment to aromatic acids.

(1) Presented on April 5, 1939, at the Baltimore meeting of the American Chemical Society.

(2) Bjerrum, *Z. physik. Chem.*, **106**, 219 (1923).

(3) Kirkwood and Westheimer, *J. Chem. Phys.*, **6**, 506 (1938); Westheimer and Kirkwood, *ibid.*, **6**, 513 (1938).

(4) Westheimer and Shookhoff, THIS JOURNAL, **61**, 555 (1939).

(5) Eucken, *Z. angew. Chem.*, **45**, 203 (1932).

The equations from which the effect of substituents on the ionization constants of acids can be computed are given below. For dibasic acids

$$\text{Log } K_1/\sigma K_2 = \frac{e^2}{2.303kTRD_E} = \Delta pK$$

and for dipole substituted acids

$$\text{Log } K_1/\sigma K_2 = \frac{eM \cos \zeta}{2.303kTR^2D_E} = \Delta pK$$

In the first equation K_1 and K_2 are the first and second ionization constants of the dibasic acid, e the electronic charge, and R the distance between the ionizable protons. σ, the statistical factor, is equal to four for the dibasic acids and to two in the comparison of hydroquinone with phenol; in the other cases considered in this paper it is unity. In the second equation, K_1 is the dissociation constant of the acid with a polar substituent, K_2 that of the unsubstituted acid, M the dipole moment of the substituent, ζ the angle the dipole makes with the line joining its center with the ionizable proton, and R the distance between the dipole and the proton. D_E, the "effective" dielectric constant, has been evaluated in the previous papers of this series only for spheres and for prolate ellipsoids of revolution in which the substituent and the dipole are at the foci. While neither a sphere nor a prolate ellipsoid of revolution is a good model for aromatic compounds, the ellipsoid will serve as a first approximation for the para substituted benzene derivatives; obviously neither the ortho nor meta compounds can be treated quantitatively. That meta substituted carboxylic acids are, in general, similar to the para, follows from the work of Dippy and Watson.[6] The author is aware of the peculiarities of ortho substituted acids,[7] and hopes to discuss these at a later date.

In the previous publications, the interprotonic or proton–dipole separation has been computed from the known ionization constants, and this length compared with molecular dimensions. In the present instance, it is more advantageous to assume a reasonable distance for the interprotonic or proton–dipole separation, and to compute ΔpK, the difference between the pK values of the two acids (less the logarithm of the statistical factor), a difference which can then be compared with the experimental value. The lengths chosen are, in all cases, reasonable ones. However, variation of 0.2 Å. will, in the case of the benzoic acids, cause a change of ΔpK of 20%. Since the equation employed is not ideally adapted to benzenoid compounds, and since the lengths chosen for R are somewhat arbitrary, values of ΔpK have been given only to the nearest 0.05 unit. The molecular volumes, necessary for the computations, have been estimated from Traube's rule.[8] The internal dielectric constant[3] has been set equal to 2.00, as in previous papers of this series.

(6) Dippy and Watson, *Chem. and Ind.*, **54**, 735 (1935).

(7) *Cf.* Waters, *Phil. Mag.*, [7] **8**, 436 (1929); Hammett, *J. Chem. Phys.*, **4**, 613 (1936).

II

The limited data available for dibasic acids are summarized in Table I.

TABLE I

DIBASIC AROMATIC ACIDS

$V = 190$ Å.^{3} $R = 7.5$ Å. $D_E = 76$

Acid	ΔpK (obsd.)	ΔpK (calcd.)
Terephthalic acid[a]	(0.70)	0.40
Benzoic acid *p*-sulfonamide[b]	0.35	0.40
Benzoic acid *p*-sulfonate		

[a] Due to its insolubility, the first dissociation constant of terephthalic acid has never been measured in water. The estimate in parentheses is that of Kuhn and Wasserman, *Helv. Chim. Acta*, **11**, 44 (1928). [b] The assumption is made that the ionization constant of benzoic acid *p*-sulfonamide is equal to the ionization from the carboxyl group, were it possible to measure it, of benzoic acid *p*-sulfonic acid. The data are given in Landolt–Börnstein, "Physikalisch–chemische Tabellen."

Inspection of this table reveals that the electrostatic effect, while it may not be the exclusive factor, is the major one in determining the effect of a charged group on the strength of an aromatic carboxylic acid.

Since the benzene ring itself introduces complications absent in the aliphatic series, a purely electrostatic treatment will be expected to apply best to the phenylacetic acids, in which a methylene group separates the carboxyl from the ring. The data are collected in Table II. The differences between the dipole moment of the substituents and the hydrogen moment are those given by Smyth[9] for aromatic compounds, and are assumed to be located in the bond between the ring and the substituent. The calculated value for the *p*-methoxy acid has been placed in parentheses because the angle and location of the methoxyl moment is still in doubt.[10] The calculations have

(8) Traube, *Samml. chem. chem.-tech. Vortr.*, **4**, 255 (1899).

(9) Smyth, *J. Phys. Chem.*, **41**, 209 (1937).

(10) Cowley and Partington, *J. Chem. Soc.*, 1257 (1933); Bennett and Glasstone, *Proc. Roy. Soc.* (London), **145A**, 71 (1934); Bennett, *Trans. Faraday Soc.*, **30**, 853 (1934); Hampson and Sutton, *Proc. Roy. Soc* (London), **140A**, 562 (1933); Sutton and Hampson, *Trans. Faraday Soc.*, **31**, 945 (1935).

been made on the assumption that the value of Marsden and Sutton[11] is correct, namely, that the methoxyl moment is at an angle of 76° with the ring to oxygen bond, with the negative end of the dipole toward the ring. While this seems to be the best available estimate, it indicates considerable interaction between the methoxyl group and the ring, causing a complex charge distribution which is poorly represented by a point dipole.

TABLE II

PHENYLACETIC ACIDS

$V = 210$ Å.^{3} $R = 6.6$ Å. $\cos\zeta = 0.90$ $D_E = 10.9$

Acid	ΔpK (obsd.)	ΔpK (calcd.)
p-Chlorophenylacetic acid[a]	0.10	0.15
p-Bromophenylacetic acid[a]	.10	.15
p-Iodophenylacetic acid[a]	.15	.15
p-Nitrophenylacetic acid[a]	.45	.40
p-Methoxyphenylacetic acid[a]	− .05	(− .05)

[a] Dippy and Williams, *J. Chem. Soc.*, 161 (1934); 1888 (1934).

It is apparent that the electrostatic effect alone is adequate to account for the effect of substituents on the ionization constants of phenylacetic acids.

The data for the substituted benzoic acids are summarized in Table III. *p*-Aminobenzoic acid is not included because, since an unknown percentage of the acid is present as a dipolar ion (zwitterion), the value of ΔpK is not known.

TABLE III

BENZOIC ACIDS

$V = 180$ Å.^{3} $R = 5.9$ Å. $D_E = 9.4$

Acid	ΔpK(obsd.)	ΔpK(calcd.)
p-Toluic acid[a]	−0.15	−0.05
p-Fluorobenzoic acid[a]	.10	.25
p-Chlorobenzoic acid[a]	.25	.25
p-Bromobenzoic acid[a]	.25	.25
p-Cyanobenzoic acid[b]	.70	.70
p-Nitrobenzoic acid[a]	.80	.65
p-Anisic acid[a]	− .30	(− .05)
p-Hydroxybenzoic acid[b]	− .25	(− .00)

[a] Dippy and Williams, *J. Chem. Soc.*, 1888 (1934); Dippy, Williams and Lewis, 343 (1935); Dippy and Lewis, 644 (1936). [b] Landolt–Börnstein, "Physikalisch-chemische Tabellen."

Inspection of Table II shows that the electrostatic effect, if not the only one, is at least the major cause of the differences in acidity among the benzoic acids, except for the cases of the hydroxy and methoxy substituted acids.

The close correspondence between the predictions of the electrostatic theory and experiment does not apply to the phenols and anilines. The data for the substituted phenols are presented in Table IV.

TABLE IV

SUBSTITUTED PHENOLS

$V = 160$ Å.^{3} $R = 5.1$ Å. $D_E = 6.5$

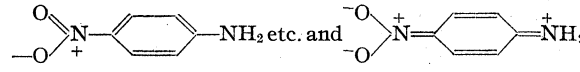
Phenol	ΔpK (obsd.)	ΔpK (calcd.)	$M_{int.}$ in D
p-Cresol[a]	−0.25	−0.10	0.00[b]
p-Chlorophenol[a]	.50	.50	− .03[b]
p-Hydroxybenzaldehyde[a]	1.30	.45	Large[c]
p-Cyanophenol[a]	2.05	1.30	Probably large[d]
p-Nitrophenol[a]	2.80	1.25	0.71[b]
Hydroquinone[a]	−0.70	−0.05	

[a] Landolt–Börnstein, "Physikalisch-chemische Tabellen." [b] Marsden and Sutton, ref. 11. [c] The observed moment in solution of *p*-hydroxybenzaldehyde of 4.19 D (Pearce and Berhenke, *J. Phys. Chem.*, **39**, 1005 (1935)) considerably exceeds 3.20, the moment calculated on the basis of free rotation of both groups. [d] While no value for the interaction moment is available for *p*-cyanophenol, the interaction moment for *p*-cyanodimethylaniline is known. While exceeded by that of *p*-nitrodimethylaniline (1.86 D) it is none the less large (0.71 D).

In the case of the phenols, while the electrostatic theory adequately accounts for the effect of halogen substituents, the effect of the nitro group, for example, in increasing the strength of phenol, is much greater than can be accounted for on the basis of the group moment alone.

It is an interesting and significant fact that, in the majority of cases in which the electrostatic theory is inadequate, the dipole moment of the molecule is not equal to the vector sum of the constituent dipoles. When there is no interaction of the substituent groups, such a summation is valid.[12]

The classical case of interaction of substituent groups is that of para nitroaniline, where the dipole moment of the compound is greater than the absolute sum of the constituent dipoles. Such an enhanced moment has been explained by the assumption that para nitroaniline is a resonance hybrid[13] of the following structures



The last column of Table IV gives the interaction moment for the substituted phenols. The correspondence between the interaction moment and the deviations from the electrostatic theory are apparent.

It is reasonable to assume that resonance is more pronounced in the substituted phenolate ion than

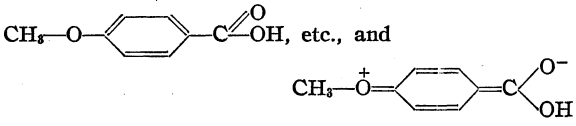
(11) Marsden and Sutton, *J. Chem. Soc.*, 599 (1936).

(12) Höjendahl, *Physik. Z.*, **30**, 391 (1929).

(13) Kumler and Porter, THIS JOURNAL, **56**, 2549 (1934).

in the phenol itself. On this basis, it can be anticipated that, in those cases in which there is interaction of the groups in para positions, the substituent will increase the acid strength of phenol more than can be predicted from a purely electrostatic treatment.

A similar explanation can be advanced to account for the large decrease of acidity caused by a methoxyl or hydroxyl substituent in benzoic acid. The resonating forms of the para methoxy acid are the following



Here it is reasonable to assume that resonance is more important in the acid than in the corresponding ion. As yet, there are no dipole moment data available to support the assumption of resonance in para methoxybenzoic acid. Further, no explanation of the anomalous behavior of hydroquinone can be offered at this time.

Table V contains the data for substituted anilines, regarding anilinium ion as an acid according to the Brönsted definition. Included are the cases of benzidine and *p*-phenylenediamine, in which the substituent is a charged group.

TABLE V

SUBSTITUTED ANILINES

Aniline	V in Å.^{3}	R in Å.	D_E	ΔpK (obsd.)	ΔpK (calcd.)	$M_{int.}$
p-Phenylene-diamine	190	5.6	34	2.90	1.25	
p-Benzidine	250	9.9	94	0.60	0.25	
p-Toluidine	165	5.1	6.2	−0.50	−0.10	0.00
p-Chloroaniline	165	5.1	6.2	.50	.50	.06
p-Bromoaniline	165	5.1	6.2	.35	.50	.05
p-Nitroaniline	165	5.1	6.2	3.45	1.25	.95
p-Anisidine	165	5.1	6.2	− .70	− .10	

While it is at once obvious that the electrostatic equations are quite inadequate to account for the base strength of the substituted anilines, it seems likely that differences in resonance energy can account for many of the observed effects.

Finally, it is interesting to consider the computations in this paper in the light of Hammett's[14] empirical equation

$$\log K = \log K^0 + sr$$

where K is any rate or equilibrium constant for a substituted benzene derivative, K^0 is the corresponding constant for the unsubstituted benzene derivative, s is a constant characteristic of the substituent, and r, a constant characteristic of the reaction, has been set equal to unity for the case of the ionization of substituted benzoic acids. Hammett's equation is of much broader scope than the present treatment, and includes both those effects ascribed to resonance and the purely electrostatic ones. It is interesting that a special value of s was reserved for the *p*-nitro group in aniline and phenol, cases in which the interaction ascribed to resonance is especially large. The present treatment can predict the s values of Hammett's equation with moderate accuracy for those substituents for which no large resonance effects have been observed. The calculated constants are the computed values of ΔpK for the benzoic acids. They have the proper sign, are in the correct sequence and of the right order of magnitude; while the agreement is far from perfect, it is significant that a theoretical treatment based on the electrostatic theory can even approximate these constants.

TABLE VI

VALUES OF s

Para substituent	s (Hammett)	s (calcd.)
CH_3	−0.17 ± 0.05	−0.06
F	+ .06 ± .07	+ .24
Cl	+ .23 ± .04	+ .27
Br	+ .23 ± .04	+ .26
NO_2	+ .78 ± .07	+ .65
CN	+1.00 ± .04	+ .68

Summary

The electrostatic effect of substituents on the dissociation constants of para substituted phenyl acetic acids, benzoic acids, phenol and anilines has been computed by the method of Kirkwood and Westheimer. It is found that the electrostatic effect is the predominant factor in determining the strength of the carboxylic acids with the exception of the para hydroxy and methoxy benzoic acids. The electrostatic effect is an important but subordinate cause of the variation of acidity among substituted phenols and anilinium ions. The difference between the electrostatic and the total effect of a substituent is greatest in those cases in which resonance interaction of the groups has already been indicated by considerations of dipole moment data.

CHICAGO, ILLINOIS RECEIVED APRIL 20, 1939

(14) Hammett, THIS JOURNAL, **59**, 96 (1937).

[CONTRIBUTION FROM THE LABORATORIES OF THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH]

The Free Radicals of the Type of Wurster's Salts

BY L. MICHAELIS, M. P. SCHUBERT AND S. GRANICK

The univalent oxidation products of the aromatic *p*-diamines, or Wurster's salts,[1] are free radicals which may polymerize in a sufficiently concentrated solution and at low temperature or in the solid state.[2] This paper is concerned with their properties, especially their stability and color, in dilute solution where they appear only as free radicals. They are in general much more stable than the corresponding quinone diimines although the latter are not radicals. The absorption spectra of these radicals show a very distinct pattern of bands in the visible range of wave lengths varying according to substitutions of the hydrogen atoms either at the amino groups or at the ring. The influence of substitutions at the amino groups has been described by Piccard. This study will be extended here, and a study of the effect of substitutions at the ring will be added.

1. Stability.—The study of stability in the dissolved state is complicated by the fact that it is impossible to obtain any pure solution of these radicals at all. They exist only in equilibrium with one molecular species at a lower level of oxidation, the diamine, and another at a higher level of oxidation, the diimine. Since the latter are very unstable compounds, liable to undergo irreversible changes, such a system may undergo irreversible changes, which are not directly due to any lability of the radical itself. For this reason the criteria for stability or lability of the radical should be discussed first. Stability in general may be conceived as the reluctance to undergo chemical reactions. One is faced with an obvious ambiguity with respect to the definition and measurement of stability, because the tendency to enter into a chemical reaction depends also on the nature of the substance with which the substance in question is to react. This is true for all reactions except those which are strictly monomolecular such as radioactive decompositions. Among the various chemical reactions which a radical is inclined to undergo there are three types which might be chosen as criteria for stability.

(1) R. Willstätter and J. Piccard, *Ber.*, **41**, 1458 (1908); J. Piccard, *ibid.*, **46**, 1843 (1913); E. Weitz, *Z. Elektrochem.*, **34**, 538 (1928); L. Michaelis, THIS JOURNAL, **53**, 2953 (1931); L. Michaelis and E. S. Hill, *ibid.*, **55**, 1487 (1933).

(2) J. Piccard, *Ann.*, **381**, 351 (1911); *Ber.*, **59**, 1438 (1926).

If we designate, as previously, the three levels of oxidation–reduction by R, S, and T (the diamine, the semiquinone radical, and the diimine), and the dimerized radical as D, the stability of the radical may be measured either by the equilibrium constant of the reversible reaction

$$R + T \rightleftarrows 2S \qquad (1)$$

or by the equilibrium constant of the reversible reaction

$$2S \rightleftarrows D \qquad (2)$$

or (3) by the rate at which the free radical undergoes any irreversible reaction. The kind and rate of such a reaction depends on the solvent and on the nature of the substance with which the radical is to react.

The study of each such reaction will lead to a different notion of the stability of the radical. If we choose the equilibrium constant of reaction (1) as criterion for stability and compare the stabilities of various radicals of the homologous series, not only S is varied but also R and T. If we choose the constant of reaction (2), not only S is varied but also D. So the best comparison available of stabilities of the radicals among themselves seems to be a reaction of the type (3) as standard method, chosen in such a way that only the radical is varied, and the substance with which it reacts is always the same, namely, nothing else but a properly chosen solvent. Thus it seems to be the fairest and most natural method for measuring the stability of the radical just to measure its lifetime in a properly chosen solvent. This criterion of stability is preferable furthermore because the equilibrium constant of reaction (1) cannot be measured (except for diamino-durene) on account of the lability of the quinone diimine, and the process (2) from left to right does not take place to any measurable degree in dilute solution.

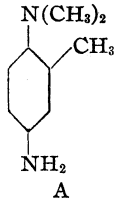
The criterion for stability, then, will be the lifetime of the radical in a properly chosen solvent. There is only one difficulty involved in this procedure which must be first overcome. It is characteristic of the systems to be investigated in this paper that the free radicals (the S forms, Wurster's salts in the present case) are much more resistant to irreversible changes when exposed to a solvent, than are the T forms, the quinone-di-

imines, though the latter are not free radicals. It is known that quinone diimines in all solvents not entirely water free, are very unstable; whereas some of the free radicals such as Wurster's blue, are very stable compounds even in an aqueous solution. Consequently, if in some particular case a radical in a certain solution has only a short lifetime, it cannot be decided directly whether the irreversible disappearance of the radical is due to its own lability, or to the lability of the diimine with which it is in equilibrium. How much of the labile diimine is present in equilibrium with the radical depends on the thermodynamical constant of the equilibrium $R + T \rightleftarrows 2S$. This constant need not show any simple relation to the tendency of the radical to undergo irreversible reactions. Hence we have to find a method to distinguish what may be designated as the *direct*, and the apparent or *indirect*, lability of the radical. The aim is to measure the direct lability of the radical. The lifetime of the radical in a properly chosen solvent will be taken as a measure of its stability provided the lability of the radical under the experimental conditions is a direct one, and not an indirect one. In order to show how this idea can be used in practice we shall describe four typical cases.

First Case.—If a solution of tetramethyl-*p*-phenylenediamine bihydrochloride, about 0.01 *M*, in an aqueous acetate buffer, *p*H 4.6, is oxidized with a very small amount of bromine, say not more than 1 atom of bromine to 50 or 100 molecules of the diamine, the intense blue color of the radical developed is stable for practically any length of time. It is known that the quaternary diimonium compound derived from this diamine is a compound extremely unstable in water. According to Willstätter even in the solid state it readily decomposes with production of formaldehyde. This experiment shows that the amount of the diimonium compound formed under the conditions chosen in equilibrium with the blue radical is vanishingly small, and the radical itself is very stable.

Second Case.—When the same experiment is performed with *p*-phenylenediamine instead of its tetramethylated derivative, the result is quite different. When aqueous acetate buffer is chosen as a solvent, the yellow color of this radical primarily formed on addition of bromine, turns pink in a few minutes. The rate at which this irreversible reaction takes place greatly depends on the initial concentration of the diamine. When this is varied, keeping constant the amount of bromine used for the oxidation, the rate of the irreversible reaction is greatly diminished as the concentration of the diamine is increased. According to reaction (1) the amount of diimine formed is decreased as the concentration of the diamine is increased. This experiment shows that the irreversible reaction is caused essentially by the irreversible changes of the diimine present and that the free radical is much more stable in this solvent than is the diimine. The diimines which have been prepared by Willstätter[3] are all extremely unstable in organic solvents not perfectly water free. When methanol—even containing as much as 20% water—is chosen as a solvent, the life-time of the radical is much longer, but also here the lifetime of the radical is increased as the initial concentration of the diamine is increased. The concentrations of the diamine and of bromine being properly chosen, the lifetime of the radical may be extended to more than a whole day. By extrapolation we may infer that the direct lifetime of this radical is very long, and its apparent lability for the greatest part is due to the fact that the equilibrium constant of the reaction (1) is such as to cause the two steps of oxidation greatly to overlap. This is a case where the direct lifetime proper of the radical can be proven to be quite long, although at first glance the radical may have the appearance of being very labile.

Third Case.—When the same experiment is performed with the diamine (formula A) the radical has a half lifetime of about ten minutes in an aqueous acetate buffer. In this case the lifetime is not influenced at all by varying the initial concentration of the diamine. This radical itself has a restricted lifetime and its breakdown is not caused indirectly by the diimine which may be in equilibrium with it. The direct disappearance of the radical is so fast that the rate of the indirect breakdown, if there be any, plays no role.



A

Fourth Case.—When the same experiment is performed with symmetrical dimethyldiaminodurene, no radical is formed under any conditions. In this case the corresponding diiminium compound, although not perfectly stable for any

(3) R. Willstätter and E. Mayer, *Ber.*, **37**, 1494 (1904); R. Willstätter and A. Pfannenstiehl, *ibid.*, **37**, 4605 (1904); R. Willstätter and H. Kubli, *ibid.*, **42**, 4135 (1909).

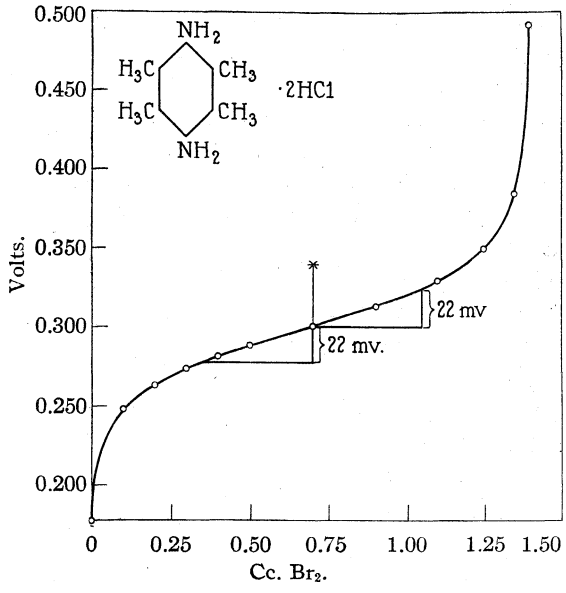


Fig. 1.—Durene diamine bihydrochloride, 50 cc. of 0.001 *M* in a solvent consisting of 8 volumes of methanol + 2 volumes of aqueous acetate buffer of *p*H 4.62 (apparent *p*H of the mixture is 6.21) is titrated with aqueous bromine. Potentials are constant throughout the titration. The titration curve indicates a two-step oxidation with the formation of an intermediate radical (which is yellow). The curve is symmetric, the index potential 22 mv. Hence, the semiquinone formation constant $k = 1.0$; maximum ratio of semiquinone to total substance is 0.33. In this case both the radical and the diimine are stable, at any rate within the period necessary for titration. The initial solution is colorless; it turns yellow during the titration and fades out again at the end-point of titration.

length of time, is yet stable enough to allow a satisfactory potentiometric titration in 80% methanol. The shape of the titration curve confirms that there is no intermediate radical formed at all. Here it is meaningless to speak of the lifetime of the radical. The fact that it is never formed to any measurable extent is itself an expression of its utmost instability, although it must be conceded that here the term "instability" has not precisely the same meaning as in the other cases.

These four examples cover all cases which may be actually encountered. Using critically such tests for stability, the results obtained may be summarized as follows:

The radical derived from *p*-phenylenediamine may be considered as the parent substance. Considering its stability proper according to the above criterion, it is a rather stable compound. Its well-known instability in aqueous solution is essentially an indirect one. Its direct stability can be modified by substitutions. These may be either at the amino groups or at the ring. Considering first compounds with the amino groups unsubstituted, it can be generally stated that substitution of the H atoms in the ring by methyl groups has no influence on the stability exceeding the limits of error of the method. Comparing the compounds not methylated at the ring but methylated at the amino groups, methyl groups appear to increase the stability. The tetramethylamino compound is the most stable of the series. There is, however, no cogent proof that these differences may not be due to differences of the indirect labilities. When both the amino groups and the H atoms of the ring are substituted, the effect largely depends on the particular structure. A methyl group at the ring in ortho position to an unmethylated amino group has sometimes very little effect, sometimes more, and, if any at all, a destabilizing effect. However, if a methyl group is in ortho position to a methylated amino group, it always has a distinct destabilizing effect; two

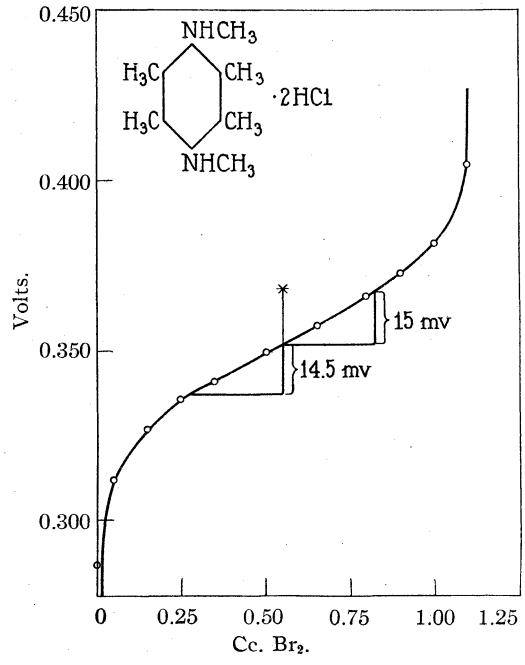


Fig. 2.—Symmetrical dimethyldurene diamine bihydrochloride. Conditions of titration the same as in Fig. 1. Here also a full titration curve is obtained. The index potential is between 14 and 15 mv., indicating that no intermediate radical is formed, in agreement with the fact that no trace of any intermediate colored compound is visible during the titration. The point * in this and all the other curves marks the end of the first step, where 1 atom of bromine per molecule of the diamine has been added.

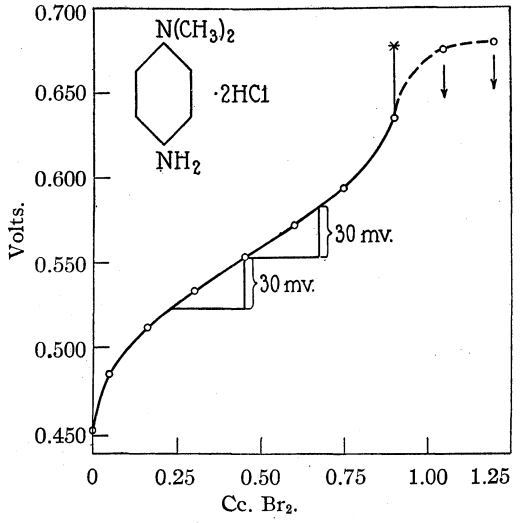
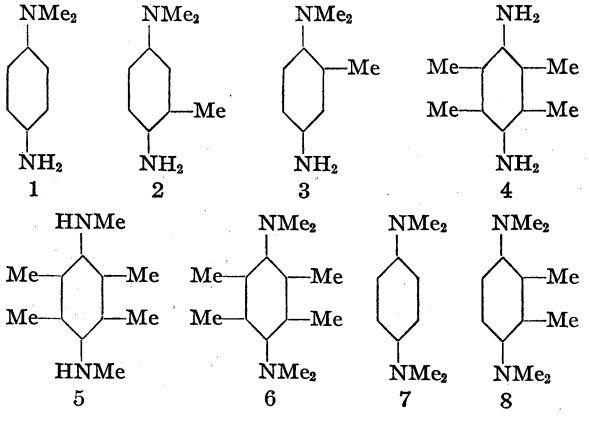


Fig. 3.—Unsymmetrical dimethyl-*p*-phenylenediamine bihydrochloride, 50 cc. of 0.001 *M* solution in a mixture of 8 volumes of methanol and 2 volumes of 0.05 *M* aqueous acetic acid (apparent *p*H of mixture is 3.1) are titrated with aqueous bromine. Potentials are nearly steady only to the end of the first step which is marked with a star (*). During the second step, potentials show considerable drift, as indicated by arrows. Since there is a slight jump at the end of the first step this first step can be treated approximately as a univalent step with no overlapping. The index potential of this univalent step should be 28.6 mv. It is found to be 30 mv., which is in sufficiently good agreement considering the limits of accuracy under the conditions prevailing. Hence, the curve suggests two successive univalent steps of oxidation with no, or very little, overlapping; the first step is reversible; the second step is irreversible due to the spontaneous breakdown of the diimonium compound.

methyl groups, especially if both are ortho to a methylated amino group, decrease the stability to an enormous extent. It may be added that the lifetime of any of these compounds is not affected by diffuse daylight.

To give some examples, the radical derived from 1 (Wurster's red) is a very stable one; 2 is almost as stable; but 3 has a half-lifetime only of less than five minutes in an aqueous solution; the radical derived from 4 is very stable; 5 and 6 do not establish any radicals at all; 7 gives a very stable radical, perhaps the most stable of all; whereas the radical derived from 8 fades out in an aqueous solution within a few minutes.



Substitutions of one single H atom at the ring other than by methyl such as by OCH_3, Cl, SO_3H, all have a distinct destabilizing effect.

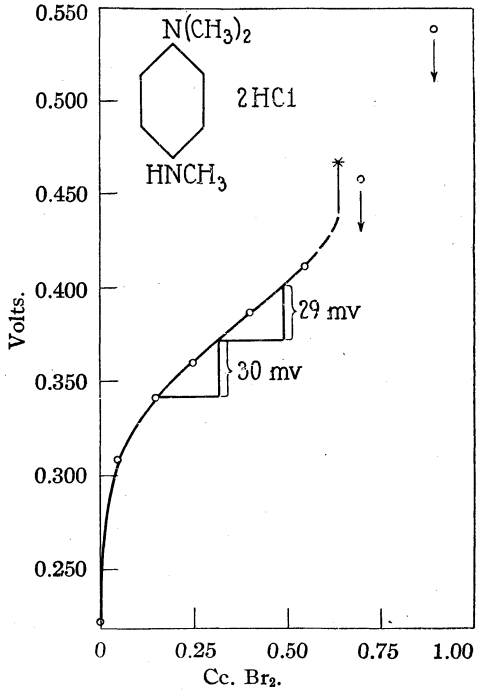


Fig. 4.—Trimethyl-*p*-phenylenediamine dihydrochloride. Conditions of titration similar to those of Fig. 3. Potentials are fairly stable during the first step of oxidation; the index potential corresponds practically to a univalent oxidation (theoretically, 28.6 mv.) and no overlapping with the second step. During the second step of oxidation potentials drift rapidly, showing the instability of the diimine.

The decay of the radical can be observed most easily from the change of its color. In some cases the color simply fades out, in others a new dyestuff may be formed due to condensations. In addition, potentiometric measurements give some indications as to the stability of the radical. If both the radical and the diimine are stable, a potentiometric titration of the diamine with bromine gives a full reproducible potentiometric titration curve up to the end-point of titration. Diaminodurene is the only example of this kind among the

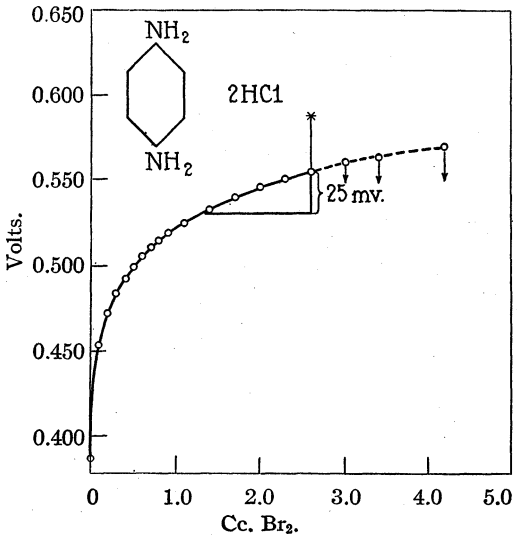


Fig. 5.—*p*-Phenylenediamine dihydrochloride. Conditions of titration similar to those of Fig. 3. The potentials are almost, although not perfectly, steady in the first part of the titration and then begin to drift rapidly.

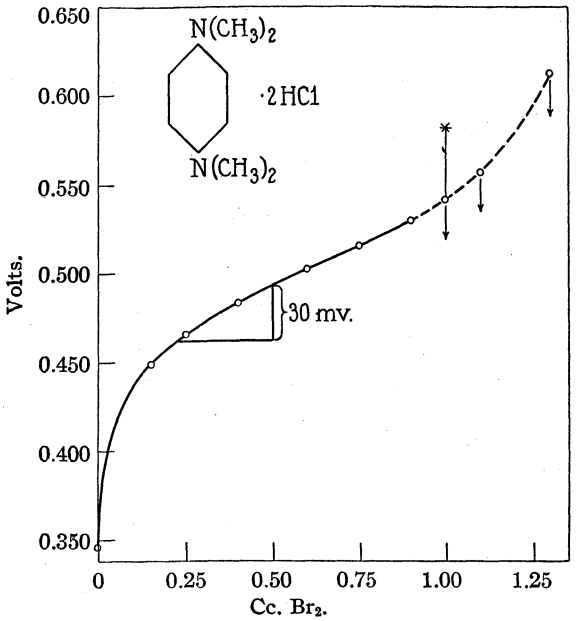


Fig. 6.—Symmetrical tetramethyl-*p*-phenylenediamine dihydrochloride under the same conditions as in Fig. 3. This curve is similar to that of Fig. 3 except that the potentials begin to drift a little earlier.

compounds investigated.[4] If the radical is stable and the diimine is unstable, steady potentials are obtained only in the first stages of the titration as long as there is no appreciable overlapping of the two steps of oxidation. If the radical itself is unstable, the potentials will not be steady even in the first stages of the titration. Many examples of these types of titration curves were obtained, and some are reproduced graphically in the experimental part. Thus a critical discussion of the potentiometric titration curves gives an indication as to the comparative stability of various radicals. The results of the two methods never showed any discrepancy. The limiting case of instability of a radical is the case where no radical is formed at all. If in such a case the diimine happens to be a relatively stable compound, the titration curve should have the shape of a reversible bivalent titration without any intermediate step. Such a case is realized for symmetric dimethyldiaminodurene. If a radical is not formed, and the corresponding diimine compound is not stable either, no steady potentials can be obtained at all during the titration. Such a case is realized in tetramethyldiaminodurene.

2. Absorption Spectra.—The absorption bands for the radicals of the diamines substituted in the amino group, but not in the ring, have been described by Piccard. There are two distinct bands and, if the amino groups are in part or all methylated, a third less conspicuous one toward the shorter wave lengths. Each methyl group substituted in the amino group has a bathochromic effect, displacing the bands toward longer wave lengths. The molar absorption is distinctly greater for the tri- and tetramethyl compounds than for the others. There is scarcely any dif-

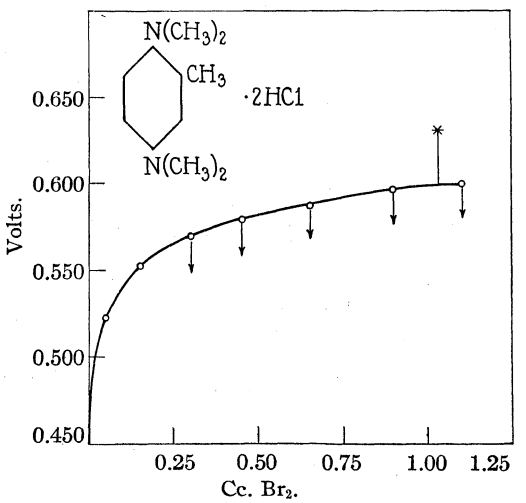


Fig. 7.—Symmetrical tetramethyldiaminotoluene dihydrochloride. Same conditions as in Fig. 3. This curve is one example for a much more unstable radical than Figs. 5 or 6. Potentials drift even in the first stages of titration.

(4) Another example of this kind is symmetrical diphenyl-*p*-phenylenediamine [Michaelis and Hill, THIS JOURNAL, **55**, 1481 (1933)]. Aromatic substituents are not included in the present paper.

ference in the effect of methyl and ethyl; however, carboxymethyl (CH_2COOH) has a stronger bathochromic effect.

Comparing compounds not methylated at the amino groups, the effect of gradually attaching methyl groups at the ring is no bathochromic effect at all, but consists in changing the pattern of the bands as follows (Fig. 8). Without any methyl in the ring the first peak (the one toward the shorter wave lengths) is higher than the second; with one methyl, the two peaks are blurred into one; with two and more methyls, the first peak is decreased in height, the second increased; this effect is greatest in the durene compound.

Comparing the effect of substitutions at the ring in compounds with one or more methyls at the amino groups, the effect of one methyl in the ring consists usually in blurring the pattern; the two bands overlap to a greater extent (Figs. 10, 11, 13). Two methyl groups in the ring make the absorption pattern rather diffuse, (Figs. 9, 13) showing a weak, broad, blurred band. As the bands are blurred the total molar absorption is diminished.

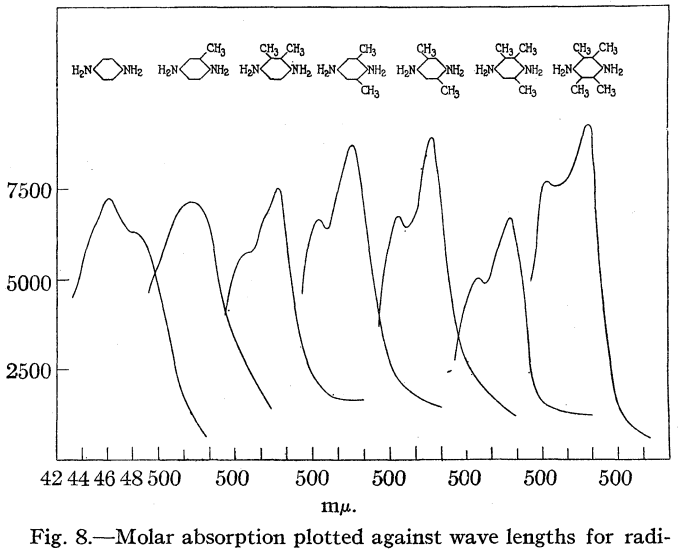
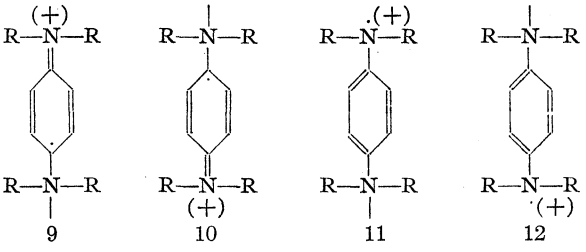


Fig. 8.—Molar absorption plotted against wave lengths for radicals of diamines methylated at the ring, but not at the amino groups. In reality all the curves overlap. All curves should be imagined as displaced horizontally to the left so that the points marked "500 mμ" coincide.

3. Interpretation.—The fact that such radicals are capable of existence at all can be attributed to a particular symmetry of structure resulting in resonance. The molecule has an odd number of electrons; the electrons may be paired in various ways, leaving always one unpaired electron. The odd electron has no fixed place, but there is resonance among various limiting states. Each of them may be considered as contributing a share to the resonating or mesomeric state but none of them can exist as a separate, tautomeric structure for any conceivable length of time. Those two limiting states which may be considered as the main contributors to the resonating state may be symbolized[5] by 9 and 10. There are more configurations of which 11 and 12 are examples.



Resonance among these various structures can take place only if the six carbon atoms of the ring, the two nitrogen atoms and the four atoms attached to the two nitrogen atoms, all are located in one plane. Structures such as 9 or 10 resemble a quinone structure with an odd electron at a carbon atom, while structure 11 or 12 represents a benzenoid structure with an odd electron at a nitrogen atom. Radicals of this type may be designated as semiquinones. The ambiguity as to the benzenoid and the quinonoid structure, or the meriquinoid character which is responsible for the color, lies within a single ring,[6] in contrast to ordinary organic dyestuffs, such as indophenols or triphenylmethane dyes, which are not radicals, and in which this ambiguity is distributed over two (or three) rings. It is the aim of this paper to show that all those radicals showing little stability possess a structure which counteracts a coplanar arrangement such as would be necessary for resonance.

Although not all, yet some of the effects of substitution may be accessible to a rational interpretation at the present time. It is very remarkable that methyl groups in the ring have such a strong destabilizing effect on the radical if the amino groups also are methylated. This effect can be accounted for as follows. In the resonating state, the bond between N and C is

(5) In these formulas letters are atomic kernels, dashes are pairs of electrons, which represent a chemical bond only if they connect two kernels, and the dot is a single electron.

(6) G. Schwarzenbach and L. Michaelis, THIS JOURNAL, **60**, 1667 (1938).

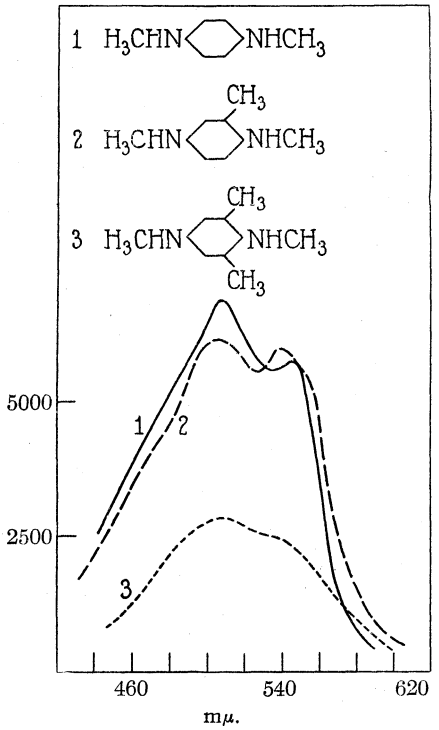
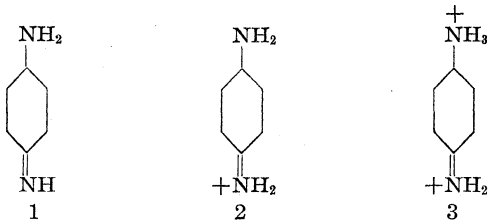


Fig. 9.—Molar absorption plotted against wave lengths for radicals of three symmetrical dimethyl diamines differing by substitution at the ring.

something intermediate between a single and a double bond. The properties of such a quasi double bond will approach those of a double bond and restrict the free rotability of the amino group around this bond as the axis. The two atoms linked by the double bond and the four atoms attached to them must lie in one plane. This plane must be also the plane of the benzene ring. If such a coplanar arrangement requisite for resonance is hampered, stability is diminished.[7]

Some Additional Remarks on the Solvent and on *p*H.—The stability of all of these radicals depends on *p*H. Even the most stable radicals are stable only within a certain *p*H range, which in aqueous solution is usually from *p*H 3.5 to 6. Outside this range all of these radicals become unstable. This is easily accounted for by taking into consideration that among the three possible states of ionization of the radical only formula 2 can exhibit the resonance necessary for the stability. This state, or rather the resonance system of which formula 2 is one of the limiting states, secures whatever stability may be inherent in such an unsaturated compound. A *p*H very suitable

(7) Compare: L. Pauling and G. W. Wheland, *J. Chem. Phys.*, **1**, 362 (1933); E. Hückel, *Z. Physik*, **83**, 632 (1933); *Z. Elektrochem.*, **43**, 752 and 827 (1937).



for stability in most compounds in aqueous solution is 4.6; in 80% methanol it is about *p*H 3 for most of the compounds, and about *p*H 6 for the durene compounds. One easily understandable exception is the radical derived from tetracarboxymethyl-*p*-phenylenediamine, which has its best stability in aqueous solution at *p*H 7. At a lower *p*H, not all of the four carboxyl groups are ionized. If there be any asymmetry with respect to the free electrical charges at these carboxyl groups, resonance will be counteracted.

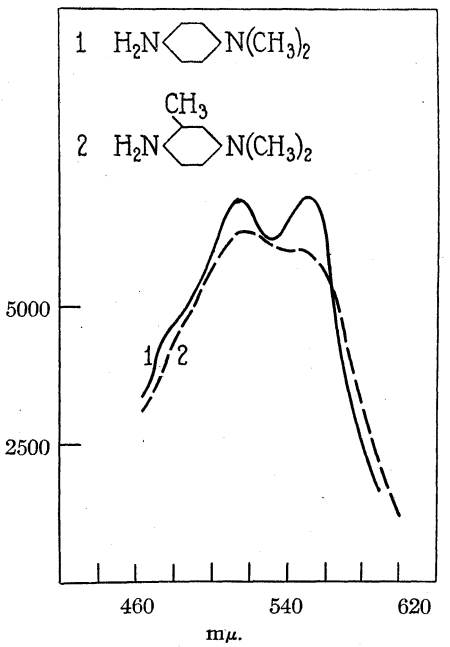


Fig. 10.—Another example of the influence of substitution at the ring upon the pattern of the absorption spectrum.

It has been pointed out before that the radical of *p*-phenylenediamine is very much more stable in methanol than in water. As the amino groups are progressively methylated, the difference of the stability in aqueous and in alcoholic solutions becomes much smaller, and in the tetramethyldiamino compound the radical is perfectly stable both in water and in alcohol. This is quite different from the behavior of the diimines which are all quite unstable in water, and even in alcohol if not

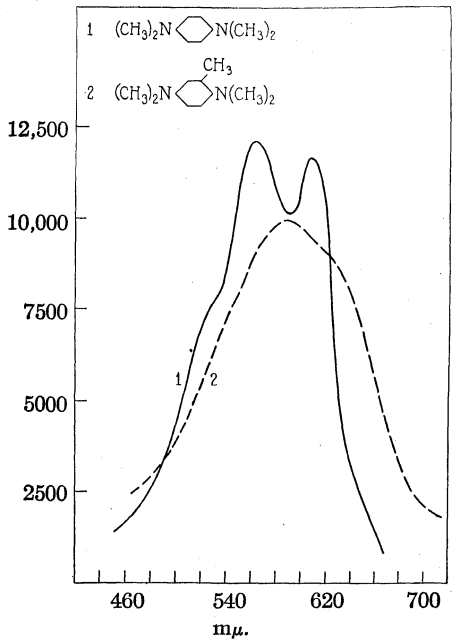


Fig. 11.—A further example of the influence of substitution at the ring upon the pattern of the absorption spectrum.

quite water free; whereas the stability of the radicals in methanol is scarcely diminished even if the alcohol contains 20% of water. The only diimines which in such a solvent have a sufficient stability to allow reproducible potentiometric titration curves throughout both steps of oxidation are the diimine compounds derived from diaminodurene and symmetrical dimethyldiaminodurene.

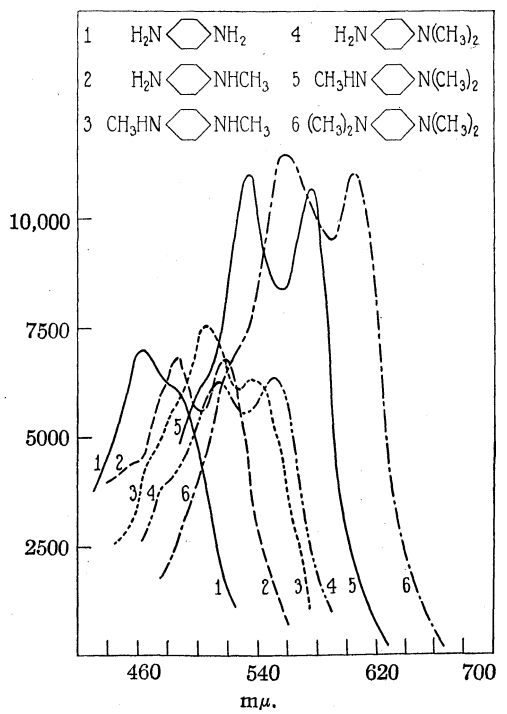


Fig. 12.—Molar absorption plotted against wave lengths for radicals derived from diamines substituted at the amino group but not at the ring. The tetracarboxymethyl derivative is not included in this graph. It is shown in Fig. 13, the last curve, dotted line.

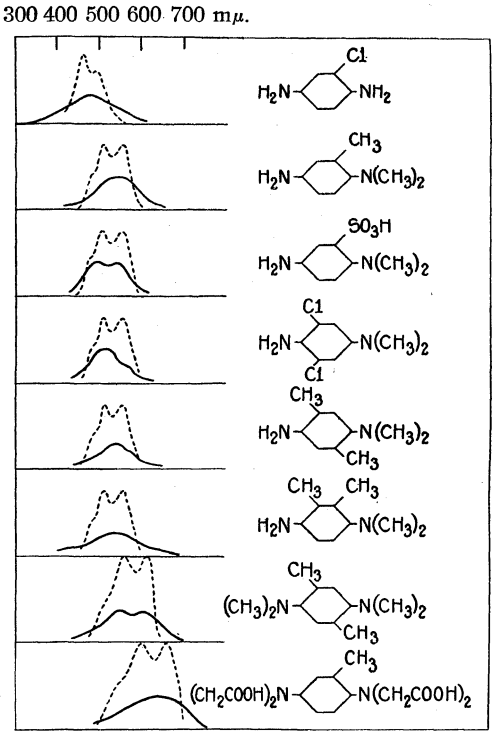


Fig. 13.—Rough sketches of absorption spectra of some compounds substituted at the benzene ring which are not stable enough for accurate measurements of the absorption (drawn out curves). They are obtained by comparing in the hand spectroscope the freshly prepared solutions with those obtained by the homologous, more stable compound with no substitution at the ring. The latter is always plotted in the dashed curve, reproduced from the accurate measurements with the spectrophotometer.

The authors are greatly indebted to Professor Linus Pauling for comments and advice with respect to some of the theoretical discussions.[8]

Experimental

1. Preparation of the Compounds.—All of the *p*-diamines used in this work were prepared as the dihydrochlorides. 1,4-Diaminobenzene, 1,4-diamino-2-methylbenzene and 1-amino-4-dimethylaminobenzene were obtained as commercial preparations and purified by dis-

(8) Professor L. Pauling has drawn our attention to the following analogous case of steric hindrance on resonance: Birtles and Hampson [*J. Chem. Soc.*, 10 (1937)] show that the magnitude of the electric dipole moment of nitrobenzene can be accounted for by resonance due to coplanar arrangement of the NO_2 group and the benzene ring. In nitrodurene this effect of the NO_2 group is strongly diminished.

solving in boiling methanol or boiling methanol containing 10% of water. The solution is decolorized with Darco G. 60 and the hydrochlorides reprecipitated by addition of 5 to 10 volumes of acetone and about 5% volume of concentrated hydrochloric acid.

The symmetrical N,N'-dimethyl derivatives, 1,4-di-(methylamino)-benzene, 1,4-di-(methylamino)-2-methylbenzene, 1-4-di-(methylamino)-2,6-dimethylbenzene and 1,4-di-(methylamino)-2,3,5,6-tetramethylbenzene were all prepared similarly. For example, 12 g. of 1,4-diaminobenzene dihydrochloride in 50 cc. of dry pyridine is heated with 26 g. of toluenesulfonyl chloride at 100° for one and one-half hours. The product is precipitated by pouring the mixture into water and is recrystallized by dissolving in dilute sodium hydroxide solution and adding acetic acid. This ditosyl derivative is methylated in aqueous alkali by the use of excess dimethyl sulfate and the crystalline product is filtered off and washed with dilute alkali. The tosyl groups are removed by warming this product at 90° in a mixture of 30 cc. of acetic acid and 60 cc. of concentrated sulfuric acid until a clear solution results and then for about two hours more. The mixture is diluted with water, made alkaline and extracted with ether. The base is dissolved in 300 cc. of acetone and the dihydrochloride precipitated by the addition of 6 cc. of concentrated hydrochloric acid. It is recrystallized by dissolving in hot methanol and adding 5% volume of concentrated hydrochloric acid and 5 volumes of acetone.

1-Amino-4-methylaminobenzene was prepared from methylacetanilide (55 g.) by nitration in a cold solution of 55 cc. of acetic acid and 110 cc. of sulfuric acid with 19 cc. of fuming nitric acid (d. 1.5); reduction of this nitro compound with stannous chloride in concentrated hydrochloric acid and hydrolysis of the resulting product by heating in this acid mixture under reflux for five hours. The base is separated and the dihydrochloride precipitated from acetone as above.

1-Methylamino-4-dimethylaminobenzene was prepared from 1-amino-4-dimethylaminobenzene by tosylating, methylating and hydrolyzing as for the N,N'-dimethyl derivatives.

A number of the desired compounds were prepared by coupling the appropriate amino compound with diazotized sulfanilic acid, recrystallizing the resulting azo compound and reducing it in boiling water containing a trace of acid by means of zinc dust.[9] By this method there were prepared 1-amino-4-dimethylamino-3-methylbenzene, 1-amino-4-dimethylamino-2-methylbenzene, 1,4-diamino-2,5-dimethylbenzene, 1-amino-4-dimethylamino-2,5-dimethylbenzene, 1,4-diamino-2,6-dimethylbenzene, 1,4-diamino-2,3-dimethylbenzene and 1-amino-4-dimethylamino-2,3-dimethylbenzene.

Pseudocumene was prepared in pure form from a technical product by the method of Jacobsen.[10] The pseudocumene sulfonic acid was recrystallized twice by dissolving in water and adding an equal volume of concentrated hydrochloric acid. The pseudocumene, b. p. 166–167°, obtained from this sulfonic acid was nitrated by the method of Schultz[11] and reduced to pseudocumidine. The subsequent transformation to 1,4-diamino-2,3,5-trimethylbenzene followed the method of Smith.[12]

Most of the N,N'-tetramethyl compounds were prepared either from 1,4-diamino or 1-amino-4-dimethylamino dihydrochlorides by heating with approximately a 50 to 100% excess of methanol in a sealed tube at 150° for eight hours. The free bases were separated in ether or chloroform and distilled at about 1 mm. pressure. In most cases no attempt was made to crystallize the resulting oily bases but these were converted directly in acetone to their dihydrochlorides.

Methylation of diaminodurene with methanol at 150° led, however, to the symmetrical N,N'-dimethyl derivative (m. p. of the base 93°) identical with that obtained by the method described above for preparing N,N'-dimethyl derivatives. This N,N'-dimethyldiaminodurene with nitrous acid in aqueous acid solution gives a dinitroso derivative quite smoothly (m. p. 212°). However, by refluxing diaminodurene in a methanol–water mixture with methyl iodide and sodium carbonate, tetramethyldiaminodurene can be obtained directly (m. p. of the base 67°).

1,4-Tetraethyldiaminobenzene and 1-dimethylamino-4-diethylaminobenzene were prepared from 1,4-diaminobenzene and 1-dimethylamino-4-aminobenzene, respectively, by heating 8 g. of the hydrochlorides in sealed tubes with 15 cc. of absolute ethanol, 1 g. of calcium chloride, 1 g. of cuprous chloride and 1 g. of sodium bromide. The bases are distilled and the hydrochlorides recrystallized from acetone as usual.

2,5-Diaminobenzenesulfonic acid monohydrochloride was prepared by reduction of 2-amino-5-nitrobenzenesulfonic acid with stannous chloride and recrystallization of the product by dissolving in boiling water and precipitating with an equal volume of concentrated hydrochloric acid.

2-Dimethylamino-5-aminobenzenesulfonic acid monohydrochloride was prepared by heating 1-chloro-5-nitrobenzenesulfonic acid with dimethylamine at 100° for two hours and reducing the resulting product with stannous chloride. The tin is removed with hydrogen sulfide and the hydrochloride is recovered by evaporation. It is recrystallized by dissolving in a methanol–water mixture and precipitated with acetone.

The tetracarboxymethyl compounds were prepared as described previously.[13]

2. Compounds not Methylated at the Amino Groups.—The properties of the radicals derived from *p*-phenylenediamine and its homologs substituted at the ring but not substituted at the amino groups are summarized in Table I.

These compounds are more difficult to judge than the others, because they show a greater overlapping of the two steps of oxidation. If the diimine is relatively stable (as in no. 7), the radical is perfectly stable also. If the diimine is very unstable (as in no. 1), it is always obvious that the radical is at least very much more stable than the diimine. The apparent instability of the radical is either in part or entirely an indirect one as can be proved for all these compounds with the "concentration test" described above. Using a higher concentration of the diamine, but

(9) E. Noelting and G. Thesmar, *Ber.*, **35**, 628 (1902).
(10) O. Jacobsen, *Ann.*, **184**, 199 (1877).
(11) G. Schultz, *Ber.*, **42**, 3606 (1909).
(12) L. I. Smith, THIS JOURNAL, **56**, 472 (1934).
(13) L. Michaelis and M. Schubert, *J. Biol. Chem.*, **106**, 331 (1934).

TABLE I

The first column gives the diamine from which the radical is derived by partial oxidation with bromine. All compounds were prepared as bihydrochlorides, except for the two last ones. All compounds mentioned in the table gave satisfactory analyses for N and Cl.

		Color	Lifetime	mμ		Type	Potential behavior in Br_2 titration in solvent indicated[h]
			p-Phenylenediamines				
1	Unsubstituted diamine (1,4)	Yellow (turning blue)	4–8 hrs.	462	479	Sharp	Steady to 75% of 1st step
2	2-Methyl-	Yellow (turning brown)	4–8 hrs.		466	Broad	Steady to 75% of 1st step
3	2,5-Dimethyl-	Yellow (fading out)	2–3 days	452	480	Sharp	Steady to 75% of 1st step
4	2,6-Dimethyl-	Yellow	12 hrs.	452	480	Sharp	
5	2,3-Dimethyl-	Yellow	12 hrs.	452	480	Sharp	
6	2,3,6-Trimethyl-[a]	Yellow	2–3 days	452	480	Sharp	Steady to 70% second step
7	2,3,5,6-Tetramethyl-[a]	Yellow	2–3 days!	452	480	Sharp	Steady throughout both steps
8	2-Methoxy-	Yellow	15 min.	475		Broad	Unsteady
9	2-Sulfonic acid-[b]	Yellow-pink	2–3 sec.	...		....	Unsteady
10	2-Chloro-	Pink-yellow	2–3 min.	475		Broad	Unsteady
11	2,6-Dichloro-	Yellow	2–3 sec.	...		Diffuse	Unsteady
			Monomethyl-*p*-phenylenediamine				
12	Unsubstituted	Orange-pink	1 day	483	516	Sharp	Steady to 100% of 1st step
			Symmetrical Dimethyl-*p*-phenylenediamines				
13	Unsubstituted	Pink	1 day	508	540	Sharp	Steady to 100% of 1st step
14	2-Methyl-	Pink	1 day	505	540	Sharp	Steady to 100% of 1st step
15	2,6-Dimethyl-	Pink	2 hrs.	505	540	....	....
16	2,3,5,6-Tetramethyl-[a]	Colorless	No radical	...	...	....	Steady[c]
			Unsymmetrical Dimethyl-*p*-phenylenediamines (1-Dimethylamino-4-aminobenzene)				
17	Unsubstituted	Red	>7 days[d]	515	550	Sharp	Steady to 100% of 1st step[e]
18	2-Methyl-	Violet-red	5 min.	520		Broad	Unsteady
19	3-Methyl-	Red	2 days!	515	550	....	Steady to 100% of 1st step
20	2,5-Dimethyl-	Violet-pink	1 min.	490	600	Broad	Unsteady
21	2,3-Dimethyl-	Violet-pink	20 sec.	470	510	Broad	Unsteady
22	2-Sulfonic acid	Pink	2 min.	495	530	....	Unsteady
			Trimethyl-*p*-phenylenediamine				
23	Unsubstituted	Purple-red	>7 days	536	578	Sharp	Steady to 90% of 1st step
			Symmetrical Tetramethyl-*p*-phenylenediamines				
24	Unsubstituted	Blue	Weeks!	560	606	Sharp	Steady to 100% of 1st step
25	2-Methyl-	Blue	1 day	590		Broad	Steady to 30% of 1st step
26	2,5-Dimethyl-	Blue	2–3 hrs.	540	560	Diffuse	Unsteady
27	2,3-Dimethyl-	Blue	1 min.	Diffuse		Broad	Unsteady
28	2,3,6-Trimethyl-	No radical formed		...	...	....	Unsteady
29	2,3,5,6-Tetramethyl-	No radical formed		...	...	....	Unsteady
			Miscellaneous *p*-Phenylenediamines				
30	*unsym.*-Dimethyl-diethyl-[f]	Blue	14 days	560	606	Sharp	Steady to 100% of 1st step
31	Tetraethyl-	Blue	14 days	560	606	Sharp	Steady to 100% of 1st step
32	Tetracarboxymethyl-[g]	Blue	14 days	596	645	Sharp	Steady to 80% of 1st step
33	Salt of 2-methyl-tetra-(carboxymethyl)-	Blue	5 min.	Very diffuse spectrum			Unsteady

[a] Dissolved in 8 volumes of methanol + 2 volumes aqueous acetate buffer, *p*H 4.6. [b] Dissolved in aqueous acetate buffer, *p*H 4.6. In all other cases, where no letter is indicated, the solvent is 8 volumes of methanol + 2 volumes of 0.005 *N* aqueous solution of acetic acid. [c] Curve for a simple bivalent oxidation without intermediate step. [d] In absence of O_2, color and intensity change relatively slowly. After five days, the intensity had diminished appreciably, while the intensity of Wurster's blue and the trimethyldiamine had not changed under the same conditions. In aqueous acetate buffer (*p*H 4.6) even in the absence of oxygen, the solution turns to a dirty violet color in one day, the original bands being just visible. [e] Potential jumps to second step, and becomes unstable. [f] Indistinguishable from the tetramethyl compound. [g] Aqueous phosphate buffer at *p*H 7.26. [h] The potentials are, of course, never steady in the strictest sense of the word. There is also a certain arbitrariness in the stage of oxidation where a potential begins to show a distinct drift. The indications in this column can, however, be used for comparative purposes.

the same amount of bromine, the life-time is considerably longer than given in the table.

As the yellow color of these radicals disappears in time it either may be replaced by a different color due to condensation (*e. g.* in no. 1), or simply fade out if such condensations are inhibited owing to substitutions at the benzene ring (as in no. 3 or 7). If a condensation to a colored substance (pink or violet, according to the particular compound) takes place, the lifetime of the radical may be greatly underestimated since its yellow color is superseded by the deeper color of the secondary reaction product. The duration of the yellow color is greatest in pure methanol. However, in order to make possible a variation in *p*H so as to find out its optimum condition, and also in order to make possible the maintenance of a given *p*H during the corresponding potentiometric titration experiment as shown in the last column, the experiments as tabulated were performed in a solvent consisting of 80% methanol and 20% of an aqueous buffer. The latter was chosen so as to give the greatest stability. It was 0.05 *M* aqueous solution of acetic acid, producing in the mixture an apparent *p*H of about 3, for the compounds nos. 1 to 5; it was acetate buffer (*p*H 4.6) producing an apparent *p*H about 6 for compounds nos. 6 and 7.

In order to demonstrate how much the two steps of oxidation overlap in these compounds, the potentiometric titration curve for no. 7 (Fig. 1) may be chosen, which shows steady potentials throughout both steps of oxidation. From this curve it can be derived[14] that the semiquinone formation constant is equal to 1.0. Hence, in the mid-point of titration, where the concentration of the radical is maximum, not more than 33% of the substance exists as radical. When only 0.1 atom of bromine is added to 1 molecule of the diamine, 8% of the substance is present as radical, and still almost 1% as diimine: there is always appreciable overlapping. In aqueous solution the overlapping seems to be even greater, although definite figures cannot be given on account of the instability of the potentials.

So it is evident that the direct stability of the radicals nos. 1 and 7 is much greater than the lifetime in column III seems to indicate. Whether the differences of lifetime within this group are real differences in direct stability or indirectly caused by differences in the stabilities of the diimines, is difficult to decide. There is no doubt that the diimines, although all of them are unstable, differ greatly in stability among themselves according to the number and positions of the methyl groups at the ring which influence the ease and possibility of secondary reactions. For instance, the diimine no. 7 should be, and really is, much more stable than no. 1. It is not certain whether this difference is reflected also in the corresponding radicals.

In contrast, in the compounds 8 to 11, the lifetime of the radical is so short under any condition that the radical itself must be considered as unstable.

3. Compounds Methylated at the Amino Groups (Table I, from no. 12 to the end). **(a) Benzene Derivatives.**—The common feature of these compounds is the fact that the difference between the stability in aqueous and in alcoholic solution is much less conspicuous. This difference becomes smaller as the number of methyl groups at the nitrogen is increased. In the extreme case, for the tetramethylamino compound, the difference between water and alcohol as a solvent vanishes entirely. The fact that these radicals are much more stable in an aqueous solution than the unmethylated ones, may be attributed essentially to the fact that the overlapping of the two steps of oxidation is smaller. As a consequence the indirect lability of the whole system due to the hydrolysis of the diimine in aqueous solution is almost eliminated. Although full potentiometric titration curves cannot be obtained because of the lability of the diimines, such a curve as Figs. 3 and 4 indicates that in spite of the rapid drift of the potentials in the negative direction during the second half of titration, there appears a transient potential jump in the mid-point of titration. This is possible only when the semiquinone formation constant is essentially larger than 16, whereas in the unmethylated diaminodurene mentioned before this constant is 1.0.

The most suitable solvent to combine a sufficient stability of the potentials with a sufficient buffer capacity in order to maintain a constant *p*H during the titration is 8 volumes of methanol and 2 volumes of 0.05 *M* aqueous acetic acid (apparent *p*H of the mixture, 3.1) but the stability is quite satisfactory also in an aqueous acetate buffer *p*H 4.6. Under proper conditions, all of these radicals are stable at least for several days. In the tri- and tetramethylamino compounds the radical does not fade out even over a period of many days; on the contrary, the color increases somewhat, in part due to further oxidation by exposure to the air, and to a slight extent even in the strict absence of oxygen, due to secondary dismutation of the traces of the diimine present. The nature of this peculiar decomposition of the diimine is of no interest for the present purpose.[15] At any rate, all of these radicals are very stable compounds in great contrast to their corresponding diimines.

(b) Compounds Substituted both at the Ring and at the Amino Groups.—A single methyl group at the ring has no, or at least no conspicuous, effect on the stability of the radical, if it is ortho to an unmethylated amino group; however, it has a very decided destabilizing effect when it is ortho to a methylated amino group. This effect is a direct one and is not caused indirectly by the interference of the diimine, as can be shown by the test described before. In the ψ-cumene and durene compounds, no radical is established at all if the amino groups are methylated. This is true whether the corresponding di-

(14) Regarding the method of calculation see Michaelis and Schubert, *Chem. Rev.*, **22**, 437 (1938).

(15) For the understanding of this peculiar process it will suffice to describe the following observations. When a solution of dimethyl-*p*-phenylenediamine in acetate buffer is titrated very rapidly with just enough bromine to cause the red color of the radical to disappear again, and when the colorless solution is allowed to stand, the color of the radical reappears in a short time. The same is true for tri- and for tetramethyl-*p*-phenylenediamines. In the tetra compound there is a remarkable difference insofar as the radical which is secondarily reëstablished is, according to its spectrum, that of the tri, instead of the tetra compound. This again is in conformity with Willstätter's observation that the tetramethyldiimonium compound, even in the solid state, easily loses one methyl group in the form of formaldehyde. The radical itself of the tetramethyl compound (Wurster's blue), has not the slightest tendency to lose a methyl group. This shows once more how much more stable is the radical than the diimonium compound.

imine is stable or labile. In the symmetrical dimethyldiaminodurene, the diimine is rather stable in 80% methanol; in tetramethyldiiminodurene it is extremely labile, yet, in both cases, no radical is formed at all.

Of the many details presented in this table one item is worth special attention. No. 18 is considerably more labile than 17; correspondingly no. 26 is more labile than 25, but no. 26 is much more stable than 18. While in unsymmetrical dimethyldiaminobenzene the introduction of one CH_3 group in the ring ortho to the methylated amino group has a strong destabilizing effect, this effect is smaller for a corresponding substitution in tetramethyldiaminobenzene. In the latter case, the introduction of two methyl groups in the ring is necessary to exert a really strong destabilizing effect. Compare also the difference of this effect according to the position of the two methyl groups (nos. 27 and 28).

4. Absorption Spectra.—Ten cc. of a 0.01 *M* solution of the dihydrochloride in the same solvent as indicated in the tabulation, was mixed with 1 cc. of 0.001 *N* aqueous solution of bromine. The concentration of the radical was calculated according to the amount of bromine added, neglecting the overlapping of the two steps, which causes no appreciable error if the excess of unoxidized diamine is as large as in these experiments. A König–Marten's spectrophotometer was used for the readings.

Summary

The radicals derived from aromatic *p*-diamines as modified by substitutions at the amino groups and at the benzene ring, by univalent oxidation, are compared with each other with regard to stability and color. The stability is measured approximately in terms of the lifetime in a properly chosen solvent. A distinction has to be made as to whether the disintegration is due to the direct breakdown of the radical ensuing from interaction with the solvent, or is caused indirectly by the lability of the diimine with which it always is in equilibrium. The indirect lability is most obvious in compounds not methylated at the amino groups. It may make the radicals appear to be much more labile than they really are. The direct spontaneous lability of the radicals is increased whenever there is a steric hindrance preventing the coplanar arrangement of the molecule necessary for resonance. This is the case when one or two methyl groups substituted in the benzene ring are in ortho position to a methylated amino group. Direct observations of changes in color are supported by potentiometric oxidative titrations of the diamines. The absorption spectra are recorded. It is especially noteworthy that diamino durene forms a very stable radical, but that any methylation of its amino groups entirely prevents the formation of a radical, due to the steric hindrance preventing coplanar arrangement of the molecule.

NEW YORK, N. Y. RECEIVED APRIL 11, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF BIOLOGICAL CHEMISTRY, COLUMBIA UNIVERSITY]

Studies on the Wolff–Kishner Reduction of Steroid Ketones[1]

BY JAMES D. DUTCHER AND O. WINTERSTEINER

In connection with a problem related to the steroid compounds of the adrenal cortex we had occasion, in a practice experiment, to reduce the semicarbazone of cholestanone by the method of Wolff and Kishner. However, the usual agent, sodium ethylate, as well as the benzylate modification described by Ruzicka and Goldberg,[2] yielded not the expected hydrocarbon, cholestane, but α- and β-cholestanol as the sole reaction products. This unusual result prompted us to study the behavior of other ketonic steroids in the Wolff–Kishner reduction, in order to learn whether constitutional or experimental factors were primarily involved.

A search of the literature revealed only two cases in which a similar atypical course of the Wolff–Kishner reduction had been observed. According to Eisenlohr and Polenske,[3] β-decalone semicarbazone yielded, besides the hydrocarbon, 33% of β-decalol. When the experiment was repeated under strictly anhydrous conditions, the yield of alcohol was but little lower, 25%. A complete failure to obtain the normal product had been reported by Reindel and Niederländer,[4] who after treating the semicarbazone of acetyl-nor-lithocholyl methyl ketone with sodium ethylate at 200° were able to isolate only the corresponding carbinol. The formation of secondary alcohols from cyclic steroid ketones

(1) This report is from a dissertation submitted by James D. Dutcher in partial fulfilment of the requirements for the degree of Doctor of Philosophy in the Faculty of Pure Science, Columbia University.

(2) Ruzicka and Goldberg, *Helv. Chim. Acta*, **18**, 668 (1935).

(3) Eisenlohr and Polenske, *Ber.*, **57**, 1639 (1924).

(4) Reindel and Niederländer, *Ann.*, **522**, 218 (1936).

has not, to our knowledge, previously been observed.[5]

Methods.—The usual method of heating the semicarbazones with sodium ethylate in a bomb tube was employed in preference to the benzylate procedure of Ruzicka and Goldberg,[2] since in the latter some benzoic acid is always formed, and this interfered with the isolation of the reduction products in the experiments with bile acids.

In order to obtain quantitative information as to the ratio of carbinols and non-alcoholic products formed, the reaction products were treated with an excess of succinic anhydride in pyridine. The acid succinates of the alcohols can be extracted readily from ether with dilute sodium carbonate solution, a property not possessed by the acid phthalates with which we at first experimented. Both types of acid esters are easily crystallizable and have served in some instances for the identification of the alcohols formed. In the experiments with bile acids the reduced acids had to be converted into the ethyl esters prior to the esterification with succinic acid in order to retain the non-alcoholic products in the ether phase on extraction with sodium carbonate.

Table I summarizes the results obtained with seven ketonic sterols and bile acids. It is immediately apparent from the data that compounds with a semicarbazone group in position 3 are reduced preponderantly to the corresponding C_3-carbinols; semicarbazone groups at positions 7 and 12, on the other hand, do not exhibit this abnormal behavior. Dehydrocholic acid trisemicarbazone and dehydrodesoxycholic acid disemicarbazone consequently yield a high percentage of lithocholic acid (3-hydroxycholanic acid). It is also evident that the observed anomaly is not dependent upon the configuration of carbon atom 5, since it is exhibited by members of both the cholestane and coprostane series.

As was to be expected, the C_3-carbinols produced in the reaction were epimeric mixtures. In accordance with the observations of Windaus[6] on the epimerization of sterols with alkali at high temperature, the epimer with the hydroxyl group in *trans* position to the hydrogen on C_5 is the main product. Thus cholestanone yields chiefly β-cholestanol (dihydrocholesterol) besides some α-cholestanol (*epi*-dihydrocholesterol); coprostanone, on the other hand, gives preponderantly the *epi* compound, α-coprosterol. A small amount of the β-epimer undoubtedly was present but could not be isolated. The ketonic bile acids, which correspond sterically to coprostanone, are reduced to mixtures of α- and β-lithocholic acids, in which the α-epimer likewise preponderates.

The proportion of C_3-carbinol to the normal C_3-methylenic reduction product depends largely on the nature of the ketone reduced and less so on experimental factors. Under standard conditions the saturated C_3-monoketones (cholestanone, coprostanone, dehydrolithocholic acid) give the highest yields of carbinols (70–80%). With the di- and triketo acids the yields of normal reduction product (cholanic acid) are increased, but always fall short of that of the C_3-carbinol (lithocholic acid). No evidence was obtained, in the latter cases, for the presence of polyhydroxy acids which might be formed by an abnormal reduction of the C_7 or C_{12} keto groups. This point was further checked by experiments with 3-hydroxy-12-ketocholanic acid semicarbazone which were thought to provide a better chance for isolating a dihydroxy acid. No compound of this description could be isolated, but some of the original 3-hydroxy-12-ketocholanic acid was recovered besides the normal reduction product, lithocholic acid. The same acid, 3-hydroxy-12-ketocholanic acid, was also invariably found to be present, to the extent of 8–10%, among the reduction products of dehydrodesoxycholic acid disemicarbazone. Since the nitrogen content of the two semicarbazones in question was close to the theoretical value, the possibility that they contained material in which the 12-keto group was left free appears remote. It seems rather that under the conditions of the reaction the semicarbazone group in position 12 undergoes partial hydrolysis, with regeneration of the free ketone.

The reduction of the semicarbazone of the α,β-unsaturated ketone, cholestenone, follows a more complex course. Besides the normal reduction product, Δ_4-cholestene (pseudocholestene), a large proportion of alcohols is formed. One of the steps in the abnormal reaction is probably the formation of the epimeric α,β-unsaturated alcohols, the *allo*-cholesterols. The presence of these com-

(5) After this work had been completed Marker and Lawson [THIS JOURNAL, **61**, 852 (1939)] reported that pregnanol-20(α)-one-3-semicarbazone on reduction by the Wolff-Kishner method yielded almost exclusively pregnanediol-3(α), 20(α), and Marker and Rohrmann [*ibid.*, **61**, 1284 (1939)] reported that the reduction of the semicarbazone of sarsasapogenone, a C_3 ketone (see Marker and Rohrmann, [*ibid.*, **61**, 943 (1939)]), yielded chiefly the carbinol, sarsasapogenin. These results are entirely in harmony with our observations on the reduction of saturated C_3-monoketones.

(6) Windaus, *Ber.*, **49**, 1724 (1916).

TABLE I

WOLFF–KISHNER REDUCTION OF STEROID KETONES

Reaction time eight hours, temperature 200° unless indicated otherwise in Column 1. The melting points in Column 4 are those of the products for which the yield is given; the figures in brackets are the melting points of the pure compounds. When the yield given pertains to a crude fraction, reference is made in Column 4.

Compound reacted	Reaction products	Yield, % of theory	Remarks
Cholestanone semicarbazone (at 180°)	α-Cholestanol β-Cholestanol	90	Weighed as crude carbinol fraction. Both epimers isolated in pure form. Hydrocarbon fraction negligible
Cholestanone semicarbazone (at 200°)	α-Cholestanol β-Cholestanol	75	Weighed as crude succinates. Both epimers isolated in pure form.
	Cholestane	13	M. p. 80° (81°).
Cholestanone semicarbazone + hydrazine	Cholestane	75	M. p. 80–81° (81°).
Cholestanone hydrazone	(α + β)-Cholestanols	82	Weighed as crude succinates.
	Cholestane	15	M. p. 78–80° (81°).
Cholestanone hydrazone + hydrazine	Cholestane	93	M. p. 81° (81°).
Cholestanone ketazine	(α + β)-Cholestanols	75	Weighed as crude succinates.
	Cholestane	18	Crude hydrocarbon fraction.
Cholestanone ketazine + hydrazine	Cholestane	98	M. p. 81° (81°).
Coprostanone semicarbazone (at 180°)	α-Coprostanol	64	M. p. 116–118° (118°).
	β-Coprostanol	Small amount	Indicated by digitonin precipitate. Hydrocarbon fraction negligible.
Cholestenone semicarbazone (at 210°)	α-Coprostanol β-Cholestanol Cholesterol	35	Weighed as crude succinates. Saturated alcohols isolated in pure form; cholesterol indicated by color reaction.
	allo-Cholesterols	Small amount	Isolated as $\Delta_{3,5}$-cholestadiene.
	Δ_4-Cholestene	40	Weighed as crude hydrocarbon fraction. Pure compound (m. p. 79°) isolated.
Cholestenone ketazine + hydrazine	Δ_4-Cholestene	64	M. p. 77° (79°).
Dehydrocholic acid trisemicarbazone	α-Lithocholic acid	38	M. p. 188° (188°).
	β-Lithocholic acid	Small amount	Not isolated.
	Cholanic acid	22	M. p. 161° (164°); part isolated as ethyl ester, m. p. 93° (93°).
Dehydrodesoxycholic acid disemicarbazone	α-Lithocholic acid β-Lithocholic acid	38	M. p. 188° (188°). M. p. 179° (179°).
	Cholanic acid	31	M. p. 164° (164°).
	(α + β)-3-Hydroxy-12-ketocholanic acid	9	M. p. 157°; pure α-epimer (m. p. 164°) and derivatives prepared.
Dehydrolithocholic acid semicarbazone	(α + β)-Lithocholic acid	73	Isolated as crude ethyl lithocholate acid sucinnate, m. p. 140–145° (147°).
	Cholanic acid	7.7	Isolated as ethyl ester, m. p. 93° (93°).
3(α)-Hydroxy-12-ketocholanic acid semicarbazone	(α + β)-Lithocholic acid	70	M. p. 172–176°.
	(α + β)-3-Hydroxy-12-ketocholanic acid	10	M. p. 157° (9 parts α, 1 part β).

pounds, indicated by a strong Rosenheim reaction, was proved by their conversion on acid treatment to the doubly unsaturated hydrocarbon melting at 79° of Schoenheimer and Evans,[7] later shown to be $\Delta_{3,5}$-cholestadiene by Stavely and Bergmann.[8] The *allo*-cholesterols, under the conditions of the Wolff–Kishner reduction, may be partially transformed into the corresponding epimeric β,γ-unsaturated alcohols. Cholesterol could not be isolated as such, but its presence in the digitonin precipitable portion of the carbinol fraction was indicated by a strong Liebermann–Burchard reaction. Reduction of the double bond, as evidenced by the isolation of α-coprosterol and

(7) Schoenheimer and Evans, *J. Biol. Chem.*, **114**, 567 (1936).
(8) Stavely and Bergmann, *J. Org. Chem.*, **1**, 567 (1937).

β-cholestanol, also takes place. Since no saturated hydrocarbons could be found in the hydrocarbon fraction, it appears that double bond reduction does not occur once the keto group has been eliminated.

These results confirm and amplify those of Lettré,[9] who found pseudo-cholestene, cholesterol and a saturated alcohol which he believed to be β-cholestanol, among the reduction products of cholestenone semicarbazone. They also accord with those of Stange,[10] who reduced the disemicarbazone of 3,6-diketocholestene with sodium ethylate and obtained a small amount of Δ_4-cholestene, presumably together with other reduction products. When the 3-monosemicarbazone was subjected to the reaction, cholestanediol-3,6 was obtained.

Influence of Experimental Conditions.—The results discussed so far were obtained under standard conditions. The influence of the reaction time was studied in the case of dehydrodesoxycholic acid. The results recorded in Table II indicate that the proportion of normal and abnormal reduction products does not vary greatly when the period of heating is extended from 4.5 to 8, 10 and 22 hours. No trend is discernible in the figures; the fluctuations observed are probably fortuitous.

TABLE II

REDUCTION OF DEHYDRODESOXYCHOLIC ACID DISEMICARBAZONE; REACTION TIME VARIED

1.0 g. of disemicarbazone yielded the products listed in the percentage given.

Reaction time, hrs.	Cholanic acid		Lithocholic acid		3-Hydroxy-12-keto-cholanic acid	
	Mg.	%	Mg.	%	Mg.	%
4.5	274	38	263	35	71	9
8	238	33	293	39	62	8
10	285	40	224	30	72	9
22	265	36	248	33	64	8

Since the practicable temperature range for the reaction is comparatively narrow (180–210°), the influence of this factor was not systematically investigated. From the first two experiments with cholestanone semicarbazone recorded in Table I it would appear that raising the temperature from 180 to 200° favors slightly the production of the hydrocarbons.

That the addition of 10% of water to the reaction mixture or the exclusion of oxygen do not perceptibly alter the proportion of normal and abnormal reaction products was ascertained in separate experiments with cholestanone semicarbazone.

A profound effect, however, is exerted by the presence of an added excess of hydrazine hydrate. The abnormal reaction is entirely suppressed and a practically quantitative yield of hydrocarbon is obtained. The hydrazone and ketazine of cholestanone, which under standard conditions react in the same way as the semicarbazone to give high yields of carbinol, are also reduced in the normal manner when hydrazine is present.

Among C_3-ketonic steroids of known structure, only the two unsaturated ketones studied by Lettré and by Stange, and a few saturated bile acids previously have been subjected to the reaction. The reduction of the trisemicarbazone of dehydrocholic acid to cholanic acid has been described by Borsche and Hallwass,[11] but no yield was reported, and other products may well have been present. An instance of complete reduction in the presence of hydrazine is found in the paper of Wieland and Kapitel,[12] who obtained good yields of 7-hydroxycholanic acid from the disemicarbazone of 3,12-diketo-7-acetoxycholanic acid. The experiment of Wieland and Jacobi,[13] on the other hand, in which a mixture of the mono- and disemicarbazones of 3,7-diketocholanic acid was reduced to lithocholic acid, can, in the light of our experience, be interpreted as an instance of reduction of the semicarbazone grouping at C_3 to carbinol and that at C_7 to methylene. Fieser,[14] commenting on the anomaly of this result, suggests that the lithocholic acid was formed from the 7-monosemicarbazone by elimination of the C_7-keto group and reduction of the free C_3-keto group to carbinol. In all probability both reactions occurred simultaneously.

In all other instances recorded in the literature, reduction of keto groups other than on C_3 are involved. It is evident from these reports that the reaction proceeds in the normal manner on keto groups at C_6,[15] C_7,[16] C_{12}[16,17] and C_{17}.[18]

(9) Lettré, *Z. physiol. Chem.*, **221**, 82 (1933).

(10) Stange, *ibid.*, **223**, 245 (1934).

(11) Borsche and Hallwass, *Ber.*, **55**, 3324 (1922).

(12) Wieland and Kapitel, *Z. physiol. Chem.*, **212**, 269 (1932).

(13) Wieland and Jacobi, *ibid.*, **148**, 232 (1925).

(14) Fieser, "The Chemistry of Natural Products Related to Phenanthrene," Reinhold Publishing Corp., New York, N. Y., 1937, p. 139.

(15) Sugiyama, *J. Biochem.* (Japan), **25**, 157 (1937); Wieland, Dane and Martius, *Z. physiol. Chem.*, **215**, 15 (1932); Wieland and Dane, *ibid.*, **212**, 41 (1932).

(16) Wieland and Dane, *ibid.*, **210**, 268 (1932); Kawai, *ibid.*, **214**, 71 (1932).

(17) Wieland, Dane and Scholz, *ibid.*, **211**, 261 (1932).

(18) Butenandt, Stoermer and Westphal, *ibid.*, **208**, 149 (1932); Danielli, Marrian and Haslewood, *Biochem. J.*, **27**, 311 (1933).

No satisfactory explanation can be offered at present as to why the C_3-keto group displays this unique resistance to complete reduction. It may be classed with other known differences between the chemical reactivity of C_3-hydroxyl or keto groups and that of similar groups in other positions of the steroid molecule. The C_3-keto groups can be reduced selectively to carbinol catalytically or with sodium and alcohol, and to methylene by the Clemmensen method. Acylation as well as ester saponification proceeds faster at C_3 than at C_7, C_{12}, C_{17} and C_{20}.

For the abnormal reaction the following mechanism is suggested: Wolff[19] believed that the course of the normal reaction from the semicarbazone to the methylene compound proceeded with the intermediate formation of the hydrazone, followed by its decomposition to the methylene compound as shown by Reaction 1. This view is supported by the fact that hydrazones are readily reduced by this method.

Reaction 1

$$>C{=}N{-}NH{-}CO{-}NH_2 \xrightarrow{H_2O} \underset{(I)}{}$$

$$>C{=}N{-}NH_2 + NH_3 + CO_2 \xrightarrow{NaOEt} >CH_2 + N_2$$
$$(II) \qquad\qquad (III)$$

The first step in the abnormal reduction is probably the same as I to II in Reaction 1. The subsequent step, involving the production of a hydroxyl group, can best be explained by the assumption that the hydrazone is hydrolyzed to the free ketone and hydrazine base (II to IV). The regenerated keto group reacts then by oxidation–reduction with sodium ethylate, giving the secondary alcohol and acetaldehyde (IV to V). This reaction can be demonstrated by treating cholestanone itself with sodium ethylate at 180°. The epimeric cholestanols are obtained in good yield. The acetaldehyde which should be formed presumably undergoes further changes such as condensation or oxidation.

Reaction 2

$$>C{=}N{-}NH_2 + H_2O \longrightarrow >C{=}O + H_2N{-}NH_2$$
$$(II) \qquad\qquad (IV)$$

$$>C{=}O + C_2H_5OH \longrightarrow >CH{-}OH + CH_3CHO$$
$$(IV) \qquad\qquad (V)$$

If the postulated equilibrium between free ketone and hydrazine on the one hand and hydrazone on the other actually exists, then the introduction of an excess of hydrazine should keep the concentration of free ketone at a low level and thereby promote the normal reaction (Reaction 1). This is indeed the case, since in the presence of hydrazine the reduction to the hydrocarbon is quantitative. Splitting of the semicarbazone occurs to a measurable extent only at comparatively high temperatures since refluxing with sodium ethylate at 90° does not regenerate the ketone or any other ether-soluble material.

(19) Wolff, *Ann.*, **394**, 86 (1912).

Experimental

The conditions were, in the majority of runs, those customarily employed. The amount of sodium dissolved in absolute alcohol was equal to the weight of the semicarbazone; the temperature was 200° and the reaction time usually eight hours, except in experiments designed to test the influence of the last two variables. Deviations from the standard procedure, such as the addition of hydrazine hydrate, will be referred to in the text.

In the ensuing account, all melting points are uncorrected.

Semicarbazones of Cholestanone and Coprostanone.—These were obtained in quantitative yield as colorless, amorphous powders by refluxing an alcoholic solution of the ketone for two hours with twice its equivalent of semicarbazide acetate. Cholestanone semicarbazone decomposed at 238° after sintering at 227°; coprostanone semicarbazone decomposed at 192° after sintering at 178°.[20]

Anal. Calcd. for $C_{28}H_{49}ON_3$: N, 9.5. Found: N, 9.4, 9.4.

β-Cholestanol Acid Phthalate.—This was prepared by boiling a pyridine solution containing the alcohol and a large excess of phthalic anhydride (10 mols) for one hour. It could neither be extracted with sodium carbonate solution, nor adsorbed on solid sodium carbonate, from its solution in ether or petroleum ether; needles from alcohol, m. p. 160°.

Anal. Calcd. for $C_{35}H_{52}O_4$: C, 78.4; H, 9.7; mol. wt., 537. Found: C, 78.4; H, 9.7; neut. equiv., 535, 536.

α-Coprostanol Acid Phthalate.—This was isolated from the reduction products of coprostanone after treatment with phthalic anhydride in pyridine. It likewise did not possess the desired solubility properties; needles from alcohol, m. p. 218–220°.

Anal. Calcd. for $C_{35}H_{52}O_4$: C, 78.4; H, 9.7; mol. wt., 537. Found: C, 78.3; H, 9.5; neut. equiv., 537.

β-Cholestanol Acid Succinate.—The treatment of β-cholestanol with succinic anhydride in the ratio of 1 to 5 mols in pyridine yielded a mixture of acid ester and di-ester. Only when a ratio of 1 to 10 was employed was the acid ester quantitatively formed; plates from dilute alcohol or ether–methanol, m. p. 171°.

Anal. Calcd. for $C_{31}H_{52}O_4$: C, 76.2; H, 10.7. Found: C, 76.4; H, 10.8.

Reduction of Cholestanone and Coprostanone Semicarbazones.—A mixture of 400 mg. of cholestanone semicarbazone with a solution of 400 mg. of sodium in 15 cc. of absolute alcohol was heated in a bomb tube at 180° for

(20) Dorée and Gardner, *J. Chem. Soc.*, **93**, 1630 (1908).

eight hours. The contents of the tube were poured into water, neutralized with hydrochloric acid and extracted with ether. The ethereal residue (361 mg.) was refluxed with 1.4 g. of succinic anhydride and 5 cc. of pyridine for one hour, poured into water and extracted with ether. The ether layer was then washed several times with dilute sulfuric acid and finally with dilute sodium carbonate solution. The ether, which retained the neutral fraction (hydrocarbon), was washed with water, dried and evaporated, leaving 22 mg. of oily, non-crystallizable material. The sodium carbonate solution was acidified with hydrochloric acid and extracted with ether. This ether solution, containing the acid esters of the alcohols, was washed, dried and evaporated (413 mg.).

The succinates were saponified with methyl alcoholic potassium hydroxide at room temperature, yielding 316 mg. of alcohols; 150 mg. of the latter was treated with digitonin in 80% alcohol, and precipitate and filtrate worked up in the usual manner: 102 mg. of β-cholestanol, m. p. 140°, $[\alpha]_D$ +29° (ethanol); and 27.2 mg. of α-cholestanol, m. p. 181°, $[\alpha]_D$ +34° (ethanol), were thus obtained and identified by specific rotations and mixed melting point determinations with authentic samples. β-Cholestanol[21] has m. p. 141°, $[\alpha]_D$ +28.8° (ether). α-Cholestanol[22] has m. p. 181°, $[\alpha]_D$ +33.95° (alcohol).

Four hundred mg. of coprostanone semicarbazone, reduced under the same conditions, yielded 17.4 mg. of non-crystalline material in the hydrocarbon fraction, and 269 mg. of alcohols. The latter yielded on treatment only a small amount of digitonide which was not worked up. From the digitonin filtrate 225 mg. of α-coprostanol was recovered, m. p. 116–118°, unchanged when mixed with an authentic sample; $[\alpha]_D$ +30° (alcohol); Dorée and Gardner[20] report $[\alpha]_D$ +31.3°.

In another experiment 1.2 g. of the semicarbazone was treated with sodium ethylate (1 g. of sodium in 15 cc. of alcohol) at 200° for ten hours, and the ether-soluble reaction products (1.034 g.) separated with succinic anhydride. The weight of the ester fraction (1.04 g.) indicated that 75% of the sterol portion of the semicarbazone had been converted to alcohols. One hundred mg. of the recrystallized succinate (m. p. 155–160°) was saponified. The precipitate obtained with digitonin yielded 40 mg. of β-cholestanol, m. p. 142°, and the digitonin filtrate 24 mg. of α-cholestanol, m. p. 181–182°.

The hydrocarbon fraction (204 mg.) was recrystallized from alcohol–ether, giving 136 mg. of plates melting at 80°, $[\alpha]_D$ +25° (chloroform); cholestane,[23] m. p. 80°; $[\alpha]_D$ +24.4°.

The lack of effect of water and of oxygen was shown by the following experiment. Each of three bomb tubes (a, b, c) was charged with 300 mg. of the semicarbazone, and with ethylate prepared from 300 mg. of sodium and 5 cc. of absolute alcohol. Tube a served as control; to tube b, 0.5 cc. of water was added; in tube c the air was replaced by nitrogen. After six hours at 200° the contents of the tubes were subjected to the usual fractionation procedure. The weights of the hydrocarbon fractions were (a) 15.7 mg., (b) 14 mg., (c) 10 mg.; those of the carbinol fractions (calculated from the weights of the ester fractions) (a) 252 mg., (b) 252 mg., (c) 241 mg.

Hydrazine hydrate had a marked effect: 434 mg. of the semicarbazone was reduced with sodium ethylate at 200° in the presence of 0.5 cc. of 100% hydrazine hydrate. The crystalline material (330 mg.) obtained by ether extraction of the reaction products yielded on recrystallization 273 mg. (75%) of cholestane, m. p. and mixed m. p. 80–81°.

Reduction of Cholestanone Hydrazone.—The hydrazone was prepared by refluxing 1 g. of the ketone with 1.0 cc. of hydrazine hydrate in 50 cc. of absolute alcohol. Water was added to the hot solution to incipient cloudiness. After standing overnight the hydrazone had precipitated out quantitatively; light yellow needles, m. p. 248° (dec.) after softening at 230°.

Anal. Calcd. for $C_{27}H_{48}N_2$: N, 7.0. Found: N, 7.1.

The reduction of 300 mg. of this compound under standard conditions (300 mg. sodium, 5 cc. alcohol, 200°, eight hours) yielded 280 mg. of ether-soluble material, which was separated into alcoholic (300 mg. of acid succinate) and hydrocarbon (42 mg.) fractions. The crude ester after one recrystallization from dilute alcohol melted at 155–160°, showing that it consisted of a mixture of α- and β-cholestanol acid succinates. The hydrocarbon fraction gave on recrystallization cholestane melting at 78–80°, mixed m. p. with cholestane (m. p. 81°) 80°; yield of alcohols, computed from weight of crude succinates, 80%; of hydrocarbon, 15%.

The same experiment, repeated with the addition of 0.5 cc. of hydrazine hydrate, yielded 260 mg. (93%) of cholestane, m. p. 81°, $[\alpha]_D$ +24.6° (chloroform).

Reduction of Cholestanone Ketazine.—When acetic acid was used to precipitate the cholestanone hydrazone from the above alcoholic solution, the ketazine, an amorphous white powder decomposing at about 200°, was obtained. *Anal.* Calcd. for $C_{54}H_{92}N_2$: N, 3.7. Found: N, 3.8. The reduction of 500 mg. of this compound, carried out under standard conditions, yielded 87 mg. (18%) of hydrocarbon and 477 mg. of acid succinate, corresponding to a 75% yield of alcohols.

When the reduction was carried out in the presence of 0.5 cc. of hydrazine hydrate, 500 mg. of the ketazine yielded 475 mg. (98%) of cholestane, m. p. 82°.

Reduction of Cholestenone Semicarbazone.—The semicarbazone of cholestenone was prepared by the pyridine–alcohol method to be described in the section on bile acids. The amorphous material which formed within an hour after mixing crystallized in clumps of needles after standing at room temperature for twenty-four hours, m. p. 215–235° (dec.).[24] The yield was quantitative.

Anal. Calcd. for $C_{28}H_{47}ON_3$: N, 9.5. Found: N, 9.5.

One and one-half grams of semicarbazone was treated with a solution of 1.5 g. of sodium in 25 cc. of absolute alcohol in a bomb tube at 210° for eight hours. The contents of the tube were poured into water, and the resulting alkaline solution extracted with ether. (Some material remained in the alkaline solution from which it was later extracted with ether after neutralization.) The crude residue (1.08 g.) from the ether was treated with 1.0 g. of

(21) Willstätter and Mayer, *Ber.*, **41**, 2199 (1908).
(22) Windaus and Uibrig, *ibid.*, **47**, 2384 (1914).
(23) Mauthner, *Monatsh.*, **30**, 635 (1909).
(24) Heilbron, Morton and Sexton, *J. Chem. Soc.*, 50 (1928).

succinic anhydride in 5 cc. of pyridine at room temperature for twenty-four hours.[25] The hydrocarbon fraction (500 mg.) after two recrystallizations from acetone–water and one from ether–methanol, yielded Δ_4-cholestene, m. p. and mixed m. p. 79°; $[\alpha]_D$ +65.0° (chloroform).

The virtual absence of saturated hydrocarbons was established in the following way. The material from the mother liquor was dissolved in ether and treated with a solution of bromine in acetic acid, and as much of the dibromide (m. p. 117°) as possible was removed by crystallization. The residue of the mother liquor was dissolved in carbon tetrachloride and treated with acetic anhydride and sulfuric acid according to Anderson and Nabenhauer.[26] The Δ_4-cholestene dibromide was decomposed completely by these reagents. The carbon tetrachloride on evaporation left only 3 mg. of an oily residue, which still gave a positive Liebermann–Burchard reaction.

The acid ester fraction (580 mg.) was saponified with a 20% solution of potassium hydroxide in 50% methanol. On cooling, a crystalline mass formed which was filtered off, washed with dilute methyl alcohol and water and dried *in vacuo*. This crude alcoholic fraction (450 mg.) gave a strongly positive Liebermann–Burchard reaction (presence of cholesterol) and a negative Rosenheim reaction (absence of Δ_4-alcohols). Treatment with 1.0 g. of digitonin in 85% alcohol gave 1.2 g. of digitonide. This, when decomposed with pyridine and ether, yielded 290 mg. of material which on repeated crystallization from 95% ethanol and from aqueous methanol gave a fraction (100 mg.), m. p. 141°. This material gave a negative Liebermann–Burchard reaction and showed no depression of its melting point when mixed with β-cholestanol. The material which remained in the mother liquors still gave an intense Liebermann–Burchard reaction but could not be separated into pure compounds. It probably consisted of cholesterol mixed with some β-coprostanol.

The digitonin filtrate was evaporated to dryness and extracted with ether. The extract after several recrystallizations from aqueous acetone melted at 117–118° and was identified as α-coprostanol. No α-cholestanol could be isolated from the mother liquors.

The acidic fraction (137 mg.), obtained on neutralization of the alkaline solution of the original reaction mixture, showed an intense Rosenheim reaction and contained 4.3% of nitrogen. After recrystallization from boiling 95% ethanol it formed long needles (50 mg.). The Rosenheim reaction was negative. *Anal.* Calcd. for $C_{28}H_{43}ON_3$: C, 76.9; H, 9.9; N, 9.6. Found: C, 77.2; H, 10.0; N, 9.6. This compound is probably identical with a substance of similar properties and composition (C, 77.07; H, 10.19; N, 9.66) which Stange[10] obtained as a by-product from the Wolff–Kishner reduction of Δ_4-cholestenedione-3,6 monosemicarbazone.

Since the residue from the mother liquors (70 mg.) still gave a very strong Rosenheim reaction, indicative of the presence of *allo*-cholesterols, it was dissolved in 50 cc. of alcohol containing a few drops of concentrated sulfuric acid, and the solution boiled for four hours. The solution was then poured into water and extracted with ether. The ether after repeated washings with dilute sodium carbonate solution, yielded 13 mg. of a crystalline residue. On recrystallization from dilute alcohol long needles melting at 78° and exhibiting a specific rotation in benzene, $[\alpha]_D$ −113°, were obtained. $\Delta_{3,5}$-Cholestadiene[7] has m. p. 78–79°, $[\alpha]_D$ −112.5° (benzene).

Reduction of Cholestenone Ketazine in Presence of Hydrazine.—The ketazine was prepared in the same manner as the corresponding compound from cholestanone. It is an amorphous, yellow powder decomposing above 190°. It was dried *in vacuo* at 110° for analysis.

Anal. Calcd. for $C_{54}H_{88}N_2$: N, 3.7. Found: N, 4.0.

The reduction of 500 mg. of the ketazine (500 mg. of sodium, 10 cc. of alcohol, 0.5 cc. of hydrazine hydrate, 200° for eight hours) yielded 490 mg. of ether-soluble material from which no alcohols could be isolated by the succinic anhydride procedure. On recrystallization from aqueous acetone 310 mg. of needles, m. p. 77°, was obtained. Several recrystallizations from alcohol gave Δ_4-cholestene, m. p. and mixed m. p. 78–79°.

Reduction of Dehydrodesoxycholic Acid Disemicarbazone.—The customary method of preparing semicarbazones by refluxing the ketonic compound with an alcoholic solution of semicarbazide acetate proved to be unsatisfactory in the case of the polyketonic bile acids. Although Borsche and Hallwass[11] had used this method for preparing the trisemicarbazone of dehydrocholic acid, we were unable to obtain a preparation with the required nitrogen content, no matter whether their procedure was employed in its original form or whether the conditions were varied in respect to the time of heating and the amounts of reagent used. In the preparation of the semicarbazone of 3-hydroxy-12-ketocholanic acid by this method the yield was very low, and the product was pigmented. Better results were obtained by the use of butyl alcohol as solvent. However, the method of Haller and LaForge,[27] employing semicarbazide acetate in a pyridine–alcohol solution, gave very satisfactory results, especially when the mixture was allowed to stand at room temperature for several days instead of being refluxed for a shorter period.

Five grams of commercial dehydrodesoxycholic acid, m. p. 186°, was dissolved in a mixture of 50 cc. of absolute alcohol and 50 cc. of dry pyridine. To this was added a solution of semicarbazide acetate, prepared by dissolving 5.0 g. of semicarbazide hydrochloride in 15 cc. of water and 5.0 g. of potassium acetate in 50 cc. of absolute alcohol, mixing, and filtering off the precipitated potassium chloride. After the addition of 10 cc. more water the solution was allowed to stand at room temperature for several days. The gelatinous mass which had formed was broken up, poured into a large volume of cold water, filtered and washed as thoroughly as possible to remove pyridine. After drying *in vacuo* at 110° a nearly colorless amorphous product was obtained in theoretical yield; decomposition point 215° after discoloration beginning at 190°.

Anal. Calcd. for $C_{26}H_{42}O_4N_6$: N, 16.7. Found: N, 16.7.

Five grams of disemicarbazone was heated with a solution of 2.0 g. of sodium dissolved in 25 cc. of absolute alcohol at 200° for ten hours. The reaction mixture was

(25) Considerable amounts of pigment and resinous material were formed at 130°.

(26) Anderson and Nabenhauer, THIS JOURNAL, **46**, 1957 (1924).

(27) Haller and LaForge, *J. Org. Chem.*, **1**, 38 (1936).

diluted with water, acidified and extracted with ether. The ether residue was esterified with absolute alcohol and sulfuric acid and fractionated with succinic anhydride as previously described: succinic half-esters, 2.40 g.; cholanic acid ester, 1.58 g.

The neutral fraction (1.58 g.) was crystallized from absolute alcohol, yielding 1.0 g. of ethyl cholanate, colorless needles, m. p. and mixed m. p. 93°. The mother liquors, saponified with potassium hydroxide in methyl alcohol, yielded 200 mg. of crystalline cholanic acid, m. p. 164°. The over-all yield of cholanic acid from the disemicarbazone was 31%.

A small amount of 3-hydroxy-12-ketocholanic acid was isolated from the acid succinate fraction by the following procedure. The esters (2.4 g.) were saponified with alcoholic potassium hydroxide at room temperature for twelve hours. The solution was poured into water, acidified with hydrochloric acid and extracted with ether. The ether solution was washed with water and repeatedly extracted with 0.067 *M* disodium phosphate solution, which was acidified and again extracted with ether. The two ether fractions were again washed, dried and evaporated.

The material remaining in the first ether solution (1.43 g.) was crystallized from aqueous ethyl alcohol. Colorless plates, m. p. 175–177°, were obtained; 100 mg. of this fraction was treated with digitonin in 90% ethyl alcohol; 73 mg. of digitonide was obtained, indicating that the epimeric mixture contained 17.5% of the β-compound. Decomposition of the digitonide yielded material which on crystallization from aqueous ethanol gave colorless plates, m. p. 179°; $[\alpha]_D$ +25.1° (alcohol). β-Lithocholic acid[28] has m. p. 180° and $[\alpha]_D$ +25° (alcohol).

The filtrate from the digitonin precipitation yielded α-lithocholic acid which crystallized from ether–petroleum ether in colorless plates, m. p. 188°. *Anal.* Calcd. for $C_{24}H_{40}O_3$: C, 76.6; H, 10.6. Found: C, 76.7; H, 10.4. $[\alpha]_D$ +33.6° (95% alcohol). α-Lithocholic acid[11] has $[\alpha]_D$ +32.7°. The ethyl ester melted at 92°. Ethyl α-lithocholate[29] has m. p. 92–93°. *Anal.* Calcd. for $C_{26}H_{44}O_3$: C, 77.3; H, 10.9. Found: C, 77.4; H, 10.6. The acetyl derivative melted at 169°. Acetyl α-lithocholic acid[29] has m. p. 169°.

The product recovered from the phosphate solution (0.36 g.), after crystallization from aqueous acetone, melted at 157°. It was shown to be a mixture of α- and β-3-hydroxy-12-ketocholanic acids similar to that obtained by Kyogoku[30] by the biological reduction of dehydrodesoxycholic acid. *Anal.* Calcd. for $C_{24}H_{38}O_4$: C, 74.0; H, 9.8. Found: C, 74.1, 74.1; H, 9.8, 9.9. The acetyl derivative formed needles from aqueous acetic acid; the melting point, 198°, is that reported by Kyogoku, and was not depressed by admixture with authentic α-3-acetoxy-12-ketocholanic acid. *Anal.* Calcd. for $C_{26}H_{40}O_5$: C, 72.2; H, 9.3. Found: C, 72.2; H, 9.2. The acid succinate of the ethyl ester formed colorless prisms or needles from aqueous alcohol, m. p. 170°; $[\alpha]_D$ +96.3° (ethanol); neutralization equivalent found, 517, 529. The melting point was unchanged on admixture with the acid succinate ($[\alpha]_D$ +95.7° in alcohol) prepared from an authentic sample of ethyl α-3-hydroxy-12-ketocholanate.

(28) Reindel and Niederländer, *Ber.*, **68**, 1245 (1935).
(29) Reindel and Niederländer, *ibid.*, **68**, 1969 (1935).
(30) Kyogoku, *Z. physiol. Chem.*, **246**, 99 (1937).

Saponification of the acetyl derivative yielded free α-3-hydroxy-12-ketocholanic acid, m. p. 164°, mixed m. p. 165°.[30] The ethyl ester of this had m. p. and mixed m. p. 132–133°.

The yields of crystalline products from 5.0 g. of semicarbazone were: cholanic acid, 1.13 g., 31%; (α + β)-lithocholic acids, 1.43 g., 38% of the theory; 3-hydroxy-12-ketocholanic acids (90% α-, 10% β-), 0.36 g., 9.2%.

To determine whether the time of reduction influenced the nature or proportion of the products, the following experiment was carried out. Each of four tubes was charged with 1.0 g. of disemicarbazone and 0.75 g. of sodium dissolved in 20 cc. of absolute alcohol. The tubes were placed in the oven at 210° and removed at intervals of 4.5, 8.0, 10.0 and 22 hours. The contents of the tubes were poured into water, acidified and extracted with petroleum ether. The petroleum ether was repeatedly extracted with 0.067 *M* disodium phosphate solution to remove the 3-hydroxy-12-ketocholanic acid present. The residue obtained on evaporating the petroleum ether was then subjected to the succinic anhydride procedure. The distribution of the material in the three fractions is recorded in Table II.

Reduction of 3-Hydroxy-12-ketocholanic Acid.—The acid was prepared by the method of Kaziro and Shimada,[31] m. p. 161° with sintering at 113–115°; $[\alpha]_D$ +110° (alcohol); acetyl derivative, m. p. 198–199°; ethyl ester, m. p. 133°. The semicarbazone, which was obtained in quantitative yield by the pyridine–alcohol procedure, melted at 240° with decomposition.

Two grams of the semicarbazone was reduced under standard conditions. The reaction mixture was diluted with water, acidified and extracted with ether. A small amount of unreacted semicarbazone (80 mg.) collected at the interphase and was removed by filtration. The ether phase was washed with water and extracted with 0.067 *M* disodium phosphate solution. From the material contained in the phosphate solution (229 mg.) 3-hydroxy-12-ketocholanic acid, m. p. 157°, $[\alpha]_D$ +84° (alcohol), was recovered. These properties are those of a mixture of 9 parts of α- and 1 part of β-acid.[30] The acid succinate of the ethyl ester was prepared (m. p. 169°) and identified by mixed melting point determination with the corresponding compound from the pure α-epimer (m. p. 170°); yield of crude acid, 10%.

The residue of the ether solution (1.215 g.) yielded on crystallization from dilute alcohol, lithocholic acid, m. p. 172–176°. Treatment of a small sample with digitonin showed the presence of 18% of β-compound in the epimeric mixture; yield of crude acid, 70%.

Reduction of Dehydrolithocholic Acid Semicarbazone.—Dehydrolithocholic acid (m. p. 140°) was obtained by oxidation of lithocholic acid with chromic acid by the method of Reindel and Niederländer.[28] The semicarbazone was prepared in the usual manner with semicarbazide acetate in alcohol. The colorless, semicrystalline product melted at 230° with decomposition.

Anal. Calcd. for $C_{25}H_{41}O_3N_3$: N, 9.7. Found: N, 9.8.

Five hundred mg. of semicarbazone was treated with 500 mg. of sodium dissolved in 10 cc. of absolute alcohol in a bomb tube at 200° for seven and one-half hours. The

(31) Kaziro and Shimada, *Z. physiol. Chem.*, **249**, 220 (1937).

reaction mixture was worked up in the usual manner. The acid succinate fraction weighed 425 mg., and the cholanic ester fraction 35 mg. This represents a lithocholic acid yield of 73% and of cholanic acid 7.7%. The succinic acid ester melted at 140–145°. For comparison the acid succinate of ethyl α-lithocholate was prepared from an authentic sample of ethyl α-lithocholate. It crystallized from ether–petroleum ether solution in large, hexagonal plates, m. p. 147°; neutralization equivalent calcd. 504; found, 505. On saponification of the succinic ester fraction, m. p. 140–145°, with alcoholic potassium hydroxide, a mixture of α- and β-lithocholic acids was obtained, m. p. 175–177°. Precipitation of a small sample with digitonin showed that approximately 15% of the β-epimer was present.

The neutral fraction on crystallization from absolute alcohol yielded needles of ethyl cholanate, m. p. and mixed m. p. 93°.

Reduction of Dehydrocholic Acid.—Recrystallized dehydrocholic acid, m. p. 236°, was used. The trisemicarbazone was obtained in theoretical yield by the alcohol–pyridine method. The nearly colorless, amorphous product melted above 290° with decomposition. The material was dried *in vacuo* at 110° for analysis.

Anal. Calcd. for $C_{27}H_{43}O_5N_9$: N, 22.0. Found: N, 21.9.

One gram of the semicarbazone was treated with a solution of 1.0 g. of sodium in 15 cc. of absolute alcohol at 200° for eight hours. The highly pigmented contents of the tube were poured into water, acidified with hydrochloric acid and extracted with ether. The residue from the ether solution (525 mg.) was dissolved in 90% acetic acid; 50 mg. of crystalline material, melting at 161°, deposited after prolonged standing. Recrystallization from acetone gave cholanic acid, m. p. and mixed m. p. 164°. The remaining oily material was esterified and the ester fraction (463 mg.) subjected to the succinic anhydride procedure in the usual way. The neutral fraction yielded 100 mg. of ethyl cholanate which after two recrystallizations from absolute alcohol showed m. p. and mixed m. p. 93°. From the sodium carbonate solution 397 mg. of succinic acid esters was obtained. Crystallization from aqueous methanol and aqueous acetone yielded plates melting at 140–145°. This material was therefore similar to the mixture of α- and β-lithocholic ester acid succinates obtained from the reduction of dehydrodesoxycholic acid disemicarbazone. Saponification at room temperature with alcoholic potassium hydroxide yielded, after two recrystallizations from aqueous acetone, colorless plates (250 mg.) of α-lithocholic acid, m. p. and mixed m. p. 188°; $[\alpha]D$ +33.6° (alcohol). The acetate melted at 169°. α-Lithocholic acid[29] has m. p. 188°; $[\alpha]D$ +33.5° (alcohol); acetate, m. p. 169°. The over-all yields from dehydrocholic acid were: cholanic acid, 142 mg., 22%; α-lithocholic acid, 250 mg., 38%.

The majority of the microanalyses reported in this paper were carried out by Mr. William Saschek.

Summary

The products found in the Wolff–Kishner reduction of the semicarbazone of cholestanone, coprostanone, cholestenone, dehydrocholic acid, dehydrodesoxycholic acid, dehydrolithocholic acid and 3-hydroxy-12-ketocholanic acid have been investigated. When the usual conditions are employed, the semicarbazone group at carbon atom 3 yields mainly the corresponding C_3-epimeric carbinols besides smaller amounts of the normal C_3-methylenic reduction products. Semicarbazone groups at C_7 and C_{12} are reduced in the normal manner to methylene. In this way lithocholic acid, in addition to cholanic acid, may be obtained in good yield from the ketonic bile acids. The occurrence of the abnormal type of reduction is not dependent on the configuration of carbon atom 5 in the C_3-ketone used.

The hydrazone and ketazine of cholestanone behave in the same manner as the semicarbazone, yielding on reduction mainly the epimeric cholestanols.

The abnormal reduction to carbinol is completely suppressed by the addition of an excess of hydrazine hydrate to the reaction mixture. Under these conditions a quantitative yield of cholestane was obtained from the semicarbazone, hydrazone and ketazine of cholestanone.

The reduction of cholestenone semicarbazone yields chiefly α-coprostanol, β-cholestanol, and Δ_4-cholestene. Evidence for the formation of *allo*-cholesterol and cholesterol has been obtained. No saturated hydrocarbons are produced in the reaction.

A possible mechanism for the abnormal type of reduction is suggested.

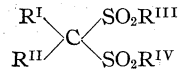
NEW YORK, N. Y. RECEIVED MAY 17, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

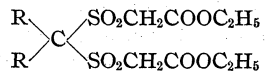
Dialkyl *bis*-(Carbethoxymethanesulfonyl)-methanes

BY R. L. SHRINER, J. M. CROSS AND ELMER H. DOBRATZ

One class of compounds which are useful for their hypnotic and sedative action is that of the dialkyl *bis*-(alkylsulfonyl) methanes represented by the type formula I. To this class belong such



I

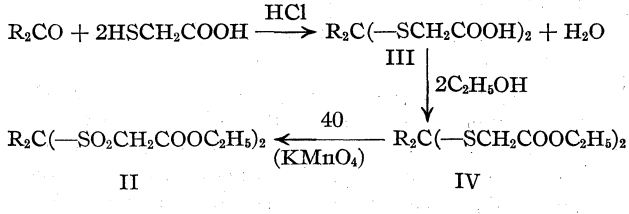


II

well-known compounds as sulfonal, trional and tetronal. These compounds are rather toxic and cannot be used in certain cases of impairment of cardiac or renal function. They also have a very limited solubility in water, tetronal, the most active hypnotic, being only very slightly soluble. Many different alkyl groups have been inserted[1] in an effort to improve the pharmacological action. The effect of introducing other functional groups into the alkyl residues has been studied in a few cases for R^{I} and R^{II} but not at all for R^{III} and R^{IV}. This modification of structure has been made in the present investigation in which the synthesis of a series of dialkyl *bis*-(carbethoxymethanesulfonyl)-methanes of formula II is described.

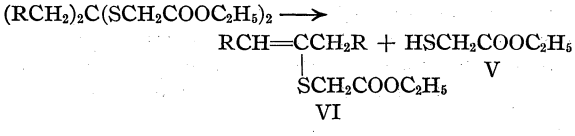
The detoxifying action of a carboxyl or ester group is well known and it was hoped that its presence would eliminate some of the toxic effects. The compounds of formula II should also be more soluble in the alkaline body fluids since they contain two active methylene groups which are capable of forming salts.[2]

These compounds were synthesized by condensing ketones with mercaptoacetic acid in the presence of hydrogen chloride.



The thioketals (III) were then esterified by treatment with absolute alcohol and hydrogen chloride in the presence of anhydrous magnesium sulfate which was used to absorb the water formed, thus preventing excessive hydrolysis of the thioketals. In order to isolate these esters (IV) it was necessary to dissolve the reaction mixture in absolute ether and, after the magnesium sulfate was filtered off, to wash this solution rapidly with ice water and dilute alkali. This removal of the acid was necessary to prevent hydrolysis of the thioacetal linkage in IV. The esters were then obtained in good yields by distilling off the ether and removing the last traces of ether by gentle heating *in vacuo*.

Only the dimethyl thioketal could be distilled *in vacuo* without decomposition. The diethyl, di-*n*-propyl and di-*n*-butyl derivatives were found to split out ethyl mercaptoacetate (V) during distillation with the formation of the corresponding carbethoxymethylmercaptoalkenes (VI), according to the general reaction



The oxidation of the thioketal (IV) to the disulfone (II) proved rather difficult owing to the sensitivity of the compounds to both acids and alkalies. Oxidations by hydrogen peroxide, chromic oxide, and neutral or alkaline permanganate were not successful. The disulfones were finally obtained in yields of 30–40% by adding a carbon tetrachloride solution of the thioketal (IV) to a 10% sulfuric acid solution into which powdered potassium permanganate was sifted so that an excess of permanganate was always present. Although the acid caused some hydrolysis of the thioketal, part of the latter was oxidized to the disulfone. The disulfones corresponding to formula II were prepared in which the alkyl groups were varied from methyl to *n*-butyl. Their analyses and physical properties and the intermediates are given in the experimental part. These sulfones were all soluble in sodium hydroxide solution but insoluble in sodium bicarbonate solution. They were soluble to a limited extent in 2% sodium carbonate solution.

Through the courtesy of the Lilly Research Laboratories the pharmacological action of these

(1) See Fränkel, "Die Arzneimittel Synthese," Verlag von Julius Springer, Berlin, 1927, pp. 526–530.

(2) Ashley and Shriner, THIS JOURNAL, **54**, 4410 (1932).

compounds was studied. It was found that they were comparatively non-toxic as compared to sulfones of type I, which indicates the detoxifying effect caused by the introduction of the carbethoxy group. However, regardless of the mode of administration, oral, intravenous or intraperitoneal injection, none of these disulfones caused hypnosis in the experimental animals. Evidently the presence of the salt forming methylene groups caused too great a shift in the oil–water distribution ratio which is necessary for hypnotic action.

Experimental

Mercaptoacetic Acid.—In order to prepare the thioketals in good yields it was necessary to have the pure anhydrous acid. Eastman Kodak Co. technical mercaptoacetic acid (thioglycolic acid) was mixed with an equal volume of toluene and the mixture subjected to distillation. After the water and toluene had distilled the residual oil was distilled under reduced pressure. The fraction boiling 87–90° at 4 mm. was collected and used.

Dialkyl *bis*-(Carboxymethylmercapto)-methanes (III).—A mixture of 50 g. of the anhydrous mercaptoacetic acid and 50 g. of each of the anhydrous ketones was saturated with dry hydrogen chloride. The flask was stoppered and chilled in an ice–salt mixture until crystallization was complete. The crystals were filtered, washed with petroleum ether, then with cold water and dried in a vacuum desiccator. Table I summarizes their properties.

TABLE I

$R_2C(—SCH_2COOH)_2$

R	M. p., °C. (corr.)	Yield, %	Molecular formula	S Analyses, % Calcd.	Found
CH_3	134–135	82	$C_7H_{12}O_4S_2$	28.57	28.57
C_2H_5	125–126	96	$C_9H_{16}O_4S_2$	25.39	25.11
n-C_3H_7	133–134	92	$C_{11}H_{20}O_4S_2$	22.85	22.56
n-C_4H_9	86–87	94	$C_{13}H_{24}O_4S_2$	20.80	21.01

Dialkyl *bis*-(Carbethoxymethylmercapto)-methanes (IV).—Fifty grams of each of the above acids was dissolved in 600 ml. of absolute ethanol in a two-liter, three-necked flask fitted with a mercury-sealed stirrer and protected by a calcium chloride tube. The flask was immersed in an ice-bath and 75 g. of anhydrous magnesium sulfate was added. Dry hydrogen chloride was passed over the vigorously stirred suspension for six hours. Six hundred milliliters of absolute ether was then added. The magnesium sulfate was removed by filtration and washed with a small amount of absolute ether. The combined filtrate and washings were poured into ice-cold, dilute sodium hydroxide and shaken thoroughly. The ether layer was separated and washed again with ice-cold sodium hydroxide and twice with ice water. An emulsion formed upon washing with ice water. It was broken by adding a few grams of sodium sulfate and shaking thoroughly. After drying over sodium sulfate the ether was distilled and the last traces removed by gentle heating (not over 60°) *in vacuo*. The properties of these esters are summarized in Table II.

Upon distillation *in vacuo* the diethyl, di-*n*-propyl and di-*n*-butyl-*bis*-(carbethoxymethylmercapto)-methanes were found to decompose. After distillation from a Claisen flask the combined fractions obtained from each compound were separated by distillation through a column packed with glass helices.[3]

The lowest boiling fraction from the three compounds was found to boil at 25° at 1.8 mm. and possessed d^{20}_{20} 1.0980; $n^{20}D$ 1.4578. The M_D calculated for ethyl mercaptoacetate was 30.02 and the found value, 29.85. The solid derivatives of this ester mentioned in the literature are the chloromercuri derivatives which Wislicenus[4] mentioned as melting somewhere under 100°, and a nickel complex[5] which melted at 101°. The ethyl chloromercurimercaptoacetate was prepared by adding an alcoholic solution of the ester to an excess of mercuric chloride dissolved in alcohol. The white amorphous reaction

$$HSCH_2COOC_2H_5 + HgCl_2 \longrightarrow ClHgSCH_2COOC_2H_5 + HCl$$

product was removed by filtration and recrystallized from alcohol. Fine, colorless needles melting sharply at 105° were obtained.

Anal. Calcd. for $C_4H_7O_2SHgCl$: S, 9.01; Hg, 56.49. Found: S, 9.12; Hg, 56.59.

For comparison purposes, mercaptoacetic acid was esterified and the properties of the synthetic ethyl ester found to check those recorded above. The chloromercuri derivative was also made and found to melt at 105° and its melting point was not depressed by addition of the above sample.

The second fraction obtained corresponded to the carbethoxymethylmercaptoalkenes (VI). Their properties and analyses are as follows:

3-Carbethoxymethylmercaptopentene-2.—B. p. 78.5° at 2 mm., d^{20}_{20} 1.0127, $n^{20}D$ 1.4797; M_D calcd. 52.82; found, M_D 52.73.

Anal. Calcd. for $C_9H_{16}O_2S$: S, 17.02. Found: S, 17.16.

4-Carbethoxymethylmercaptoheptene-3.—B. p. 90° at 1.8 mm., d^{20}_{20} 0.9838; $n^{20}D$ 1.4749; M_D calcd. 62.06; found, M_D 61.87.

Anal. Calcd. for $C_{11}H_{20}O_2S$: S, 14.81. Found: S, 15.00.

5-Carbethoxymethylmercaptononene-4.—B. p. 108° at 1.8 mm.; d^{20}_{20} 0.9588; $n^{20}D$ 1.4750; M_D calcd. 72.29; found, M_D 72.11.

Anal. Calcd. for $C_{13}H_{24}O_2S$: S, 13.13. Found: S, 13.16.

Dialkyl *bis*-(Carbethoxymethanesulfonyl)-methanes (II).—A solution of 4 g. of each of the above esters in 35 cc. of carbon tetrachloride was added over a period of an hour to 300 cc. of 10% sulfuric acid solution to which was added powdered potassium permanganate at such a rate that the solution was always purple. From 10 to 17 g. of permanganate was required. The mixture was stirred for an additional hour and then sodium bisulfite added until the solution was clear. The carbon tetrachloride layer was

(3) Whitmore and Lux, THIS JOURNAL, **54**, 3448 (1932).
(4) Wislicenus, *Ann.*, **146**, 145 (1868).
(5) Drummond and Gibson, *J. Chem. Soc.*, 3073 (1926).

TABLE II

$R_2C(SCH_2COOC_2H_5)_2$

R	B. p., °C.	Press., mm.	Yield, %	d^{20}_{20}	$n^{20}D$	M_D Calcd.	M_D Found	S Analyses, % Calcd.	Found
CH_3	152–153	1.8	69	1.1368	1.4970	72.26	72.18	22.81	22.92
C_2H_5	162–163	2	65	1.1140	1.4969	81.50	80.80	20.77	20.73
n-C_3H_7	178–179	3	89	1.0758	1.4909	90.74	90.49	19.04	19.06
n-C_4H_9	183–184	3	90	1.0269	1.4862	99.99	99.64	17.58	17.55

separated, washed with water and sodium bicarbonate solution and dried with sodium sulfate. The carbon tetrachloride was evaporated and the residual oil chilled in an ice-bath until it solidified. The sulfones were recrystallized from a mixture of ethanol and water. They were all colorless crystals. Their properties are summarized in Table III.

TABLE III

$R_2C(—SO_2CH_2COOC_2H_5)_2$

R	M. p., °C. (corr.)	Yield, %	Mol. formula	S Analyses, % Calcd.	Found
CH_3	84–85	32	$C_{11}H_{20}O_8S_2$	18.61	18.79
C_2H_5	73–74	41	$C_{13}H_{24}O_8S_2$	17.20	17.08
n-C_3H_7	90–91	37	$C_{15}H_{28}O_8S_2$	16.00	15.82
n-C_4H_9	74–75	42	$C_{17}H_{32}O_8S_2$	14.95	15.07

Summary

A series of dialkyl *bis*-(carbethoxymethanesulfonyl)-methanes has been prepared by oxidizing dialkyl *bis*-(carbethoxymethylmercapto)-methanes. The latter were obtained by esterification of the corresponding acids which were produced by the reaction between mercaptoacetic acid and the simple ketones. These disulfones possessed no hypnotic activity.

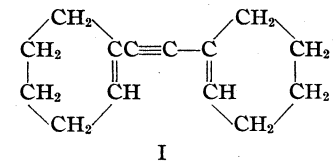
URBANA, ILLINOIS RECEIVED APRIL 28, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

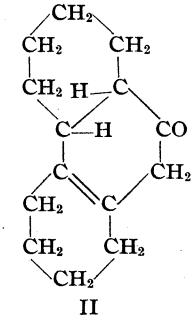
Cyclization of Dienynes. VII.[1] Dehydrogenation of *trans*-Dodecahydrophenanthrene and a Further Study of *trans*-3,4-Dialkyloctalones

BY C. S. MARVEL, RALPH MOZINGO[2] AND E. C. KIRKPATRICK[3]

In an attempt to prepare phenanthrene derivatives[4] it was found that the cyclization of di-Δ^1-cyclohexenylacetylene (I) gave a ketone described as Δ^{11}-dodecahydro-9-phenanthrone (II), which on Clemmensen reduction yielded a hydrocarbon considered to be Δ^{11}-dodecahydrophenanthrene (III). Attempts to dehydrogenate these compounds with selenium did not give phenanthrene or a phenanthrol. The hydrocarbon (III) was converted by this treatment to a compound which appeared to be identical with the *trans-as*-octahydrophenanthrene (IV) reported by van de Kamp and Mosettig.[5] Moreover, reduction of the hydrocarbon (III) gave a product with physical properties which checked closely those of tetradecahydrophenanthrene obtained by the hydrogenation of phenanthrene.[4] These facts seemed to establish the phenanthrene structure and pointed to the conclusion that selenium does not dehydrogenate fused *trans* ring systems.



I



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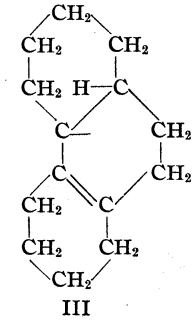


III

Recently, however, Cook, Hewett and Robinson[6] have shown that van de Kamp and Mosettig's *trans-as*-octahydrophenanthrene contains also the *cis*-isomer (V) and the spiran (VI).

(1) For the sixth communication in this series see Pinkney and Marvel, THIS JOURNAL, **59**, 2669 (1937).

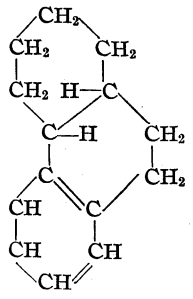
(2) Röhm and Haas Special Research Assistant in Chemistry, 1937–1939.

(3) Solvay Company Fellow in Organic Chemistry, 1937–1938.

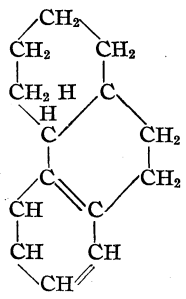
(4) (a) Pinkney, Nesty, Wiley and Marvel, THIS JOURNAL, **58**, 972 (1936); (b) Pinkney, Nesty, Pearson and Marvel, *ibid.*, **59**, 2666 (1937).

(5) Van de Kamp and Mosettig, *ibid.*, **58**, 1062 (1936).

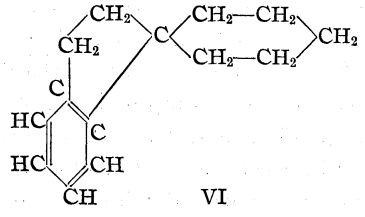
(6) Cook, Hewett and Robinson, *J. Chem. Soc.*, 168 (1939).



IV



V



VI

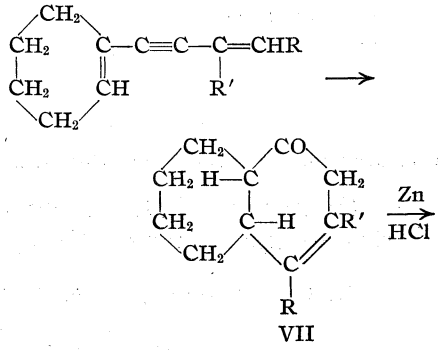
This result coupled with the fact that all comparisons of physical properties in this series had been made on liquids has made it seem desirable to reconsider the structures which have been assigned previously to compounds II and III.

The spiran, cyclohexanespirocyclopentane, has been shown by Clemo and Ormston[7] to be largely decomposed into unidentified fragments when it is heated with selenium although some of it does yield naphthalene, a completely aromatized compound. Since our hydrocarbon (III) is only partially dehydrogenated and not seriously attacked otherwise when heated with selenium, it obviously cannot be the hydrogenated spiran related to VI.

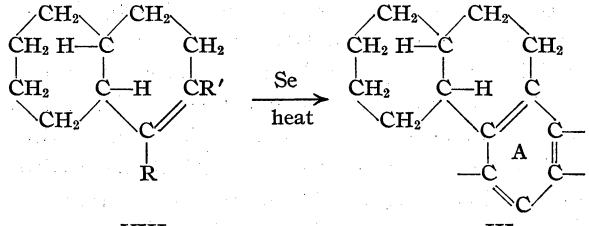
That our hydrocarbon (III) is a phenanthrene derivative has now been established definitely by dehydrogenation over a platinum on charcoal catalyst[8] at 300–320° to give phenanthrene as the only product. This leaves only the question of the position of the double union in the hydrocarbon to be determined.

The fact that dehydrogenation of this dodecahydrophenanthrene with selenium gives octahydrophenanthrene indicates that the double union is at the 11-position. Further evidence of this was sought by ozonolysis of the unsaturated cyclic ketone (II). However, only a mixture of products resulted. These results are similar to those reported by Durland and Adkins,[9] who found that unsaturated hydroaromatic compounds are attacked by ozone–oxygen mixtures at other points as well as at the double bond. Confirmation of the 11-position for the double bond was obtained by hydrogenation of the cyclic ketone (II) over Raney nickel.[10] While this hydrogenation has been reported as giving a non-crystalline alcohol[4b] a solid alcohol has now been obtained. The reduction was more difficult to accomplish than would have been the case if the carbon–carbon double bond had been in an exposed position since a temperature of 185° at 100–200 atmospheres was needed to bring about the addition of hydrogen.

Another case where selenium failed to dehydrogenate a *trans*-bridge has been reported from this Laboratory.[11] An octahydronaphthalene derivative (VIII) was prepared by the following reactions. The structure of the intermediate cyclic

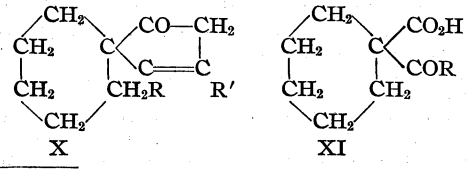


VII



VIII IX

ketone (VII, R = *n*-propyl, R′ = *n*-butyl) was established by ozonolysis to yield a keto acid which could be distilled at 120–125° (2 mm.), without decomposition. If the ring closure had produced a spiran (X), the product of ozonolysis would have been a β-keto acid (XI) and certainly would have decomposed with the loss of carbon dioxide at this temperature. Hence, the hydrocarbon obtained by the Clemmensen reduction of

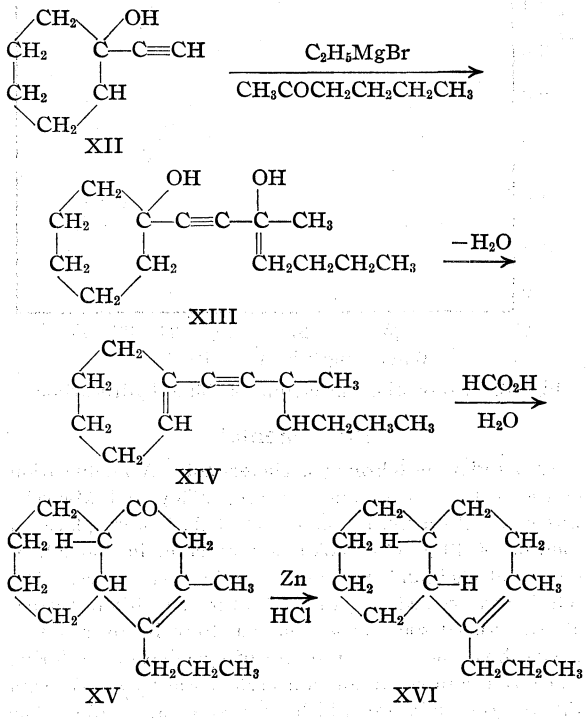


X XI

(7) Clemo and Ormston, *J. Chem. Soc.*, 352 (1933).
(8) Linstead, Millidge, Thomas and Walpole, *ibid.*, 1146 (1937).
(9) Durland and Adkins, THIS JOURNAL, **61**, 429 (1939).
(10) Covert and Adkins, *ibid.*, **54**, 4116 (1932).
(11) Nesty and Marvel, *ibid.*, **59**, 2662 (1937).

the ketone (VII) was assigned the octalin structure (VIII). Attempts to dehydrogenate this hydrocarbon with selenium led to mixtures of hydrocarbons but ultraviolet absorption spectrum evidence indicated no naphthalene derivative. A new aromatic ring (IXA) was apparently formed from the other alkyl groups. It should be noted here that the crude dehydrogenation product was blue in color.

In order more definitely to establish this ring formation from 1,2-dialkyl groups in a Δ^1-octalin derivative, we have now synthesized the compound corresponding to VIII (in which R is *n*-propyl and R′ is methyl) by the following reactions.



When the methyl *n*-propyl octalin (XVI) was heated with selenium, a bluish mixture of hydrocarbons was obtained. Fractional distillation removed the blue color but the colorless product was still a mixture of hydrocarbons. The ultraviolet absorption spectrum of this mixture showed definite bands of the same character and in the same region as the bands shown by tetralin and other hydrocarbons having an alicyclic ring fused to a benzene ring.[12]

Figure 1 shows the ultraviolet absorption curves of the octalin derivative (XIV), its selenium dehydrogenation product and a sample of *trans-as*-octahydrophenanthrene prepared by the method of van de Kamp and Mosettig.[5] Figure 2 shows the curves of the selenium dehydrogenation product from the octalin mixture and for tetralin.[12]

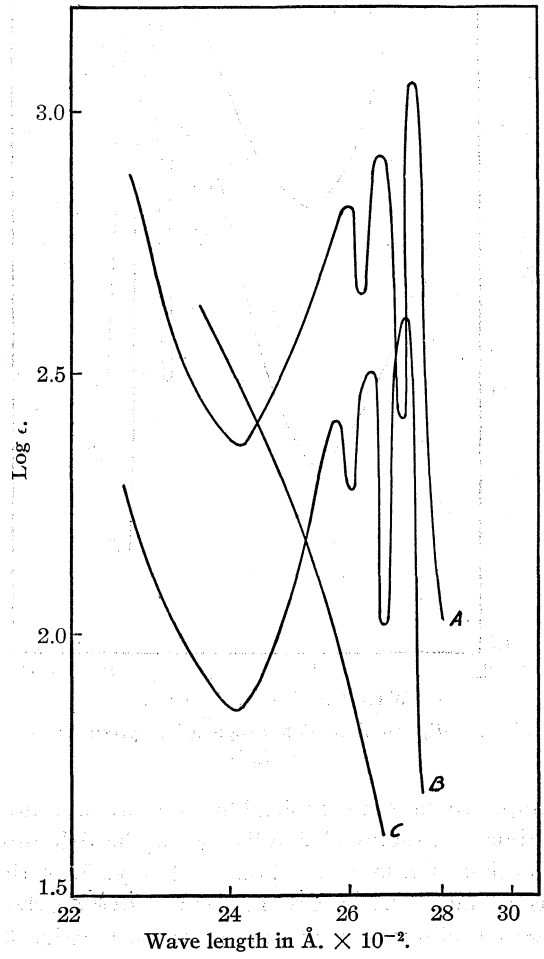


Fig. 1.—*A*, *as*-octahydrophenanthrene; *B*, selenium dehydrogenation products; *C*, octalin derivative (XIV).

The very close similarity between absorption curves B[12a] and A in Fig. 1 shows that they must be produced by the same basic ring structure calculating from Beer's law, the position of B on the log ϵ axis indicates that the concentration of *trans-as*-octahydrophenanthrene in the dehydrogenation product amounts to about 35–40%.

In order to complete the identification of the supposed octalin (XVI), an attempt was made to dehydrogenate it over a platinum–charcoal catalyst to yield the naphthalene in the same way that the dodecahydrophenanthrene (III) had been converted to phenanthrene. However, this at-

(12) Morton and de Gouveia, *J. Chem. Soc.*, 916 (1934).

(12a) To calculate the molal concentration to draw this curve, a molecular weight of 186 was used.

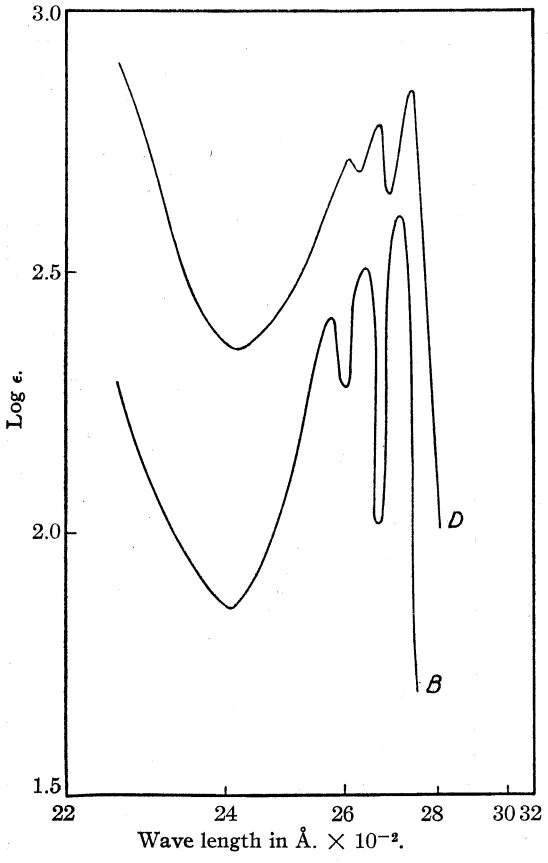


Fig. 2.—*B*, selenium dehydrogenation product; *D*, tetralin.[12]

tempt produced a complex blue mixture of hydrocarbons. Fractional distillation of the dehydrogenation mixture gave about a 19% yield of the deep blue hydrocarbon. This hydrocarbon showed absorption in the ultraviolet (Fig. 3) similar to that shown by known azulene derivatives.[13] The octalin mixture before dehydrogenation gave the characteristic deep blue color with bromine and acetic acid which has been reported for azulene-yielding compounds.[14]

The exact structure of this new azulene has not been established. Its formation, however, shows that the supposed octalin (XVI) contains a hydrocarbon which can be dehydrogenated to give the azulene structure in which a seven-membered ring is fused to a five-membered ring with two carbons in common. Since the ozonization of the ketone (XV) gave evidence of the hydronaphthenone structure, the rearrangement to a seven–five system must have occurred during the Clemmensen[15] reduction. It should be pointed out that no azulenes were noted in the dehydrogenation of the dodecahydrophenanthrene (III) and hence the rearrangement during the Clemmensen reduction must not have occurred in the phenanthrene series.

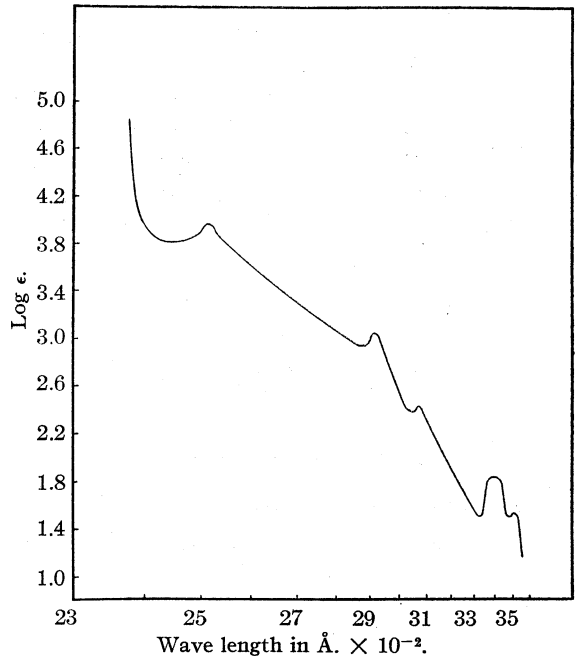


Fig. 3.—Absorption spectrum of blue hydrocarbon.

Experimental

Preparation of 1-Ethynylcyclohexanol.—A modification of the method of Pinkney, Nesty, Wiley and Marvel[4a] was used. In a 2-liter three-necked flask were placed a solution of 40 g. (1.0 mole) of potassium in 400 ml. of *t*-amyl alcohol and 800 ml. of anhydrous ether. The solution was cooled to −15° and saturated with acetylene. To the stirred solution was added dropwise over ten to twelve hours 300 g. (3.0 moles) of cyclohexanone during which time a rapid stream of acetylene was passed through the reaction mixture which was kept at −15°. The solution was stirred for six hours after the addition of all of the cyclohexanone and the acetylene shut off. The reaction mixture was poured into 90 ml. of concentrated hydrochloric acid and 200 g. of ice. The acetylenic alcohol was extracted from the water with ether and fractionated, after removing the unreacted ketone with sodium bisulfite solution. The pure product, b. p. 77–78° (17 mm.), $n^{25}D$ 1.4790, weighed 260 g. (2.1 moles, 69% based on the ketone used).

Preparation of 1-(3-Hydroxy-3-methyl-1-heptynyl)-cyclohexanol.—To the Grignard solution prepared from 79 g. (3.30 gram atoms) of magnesium and 380 g. (3.48 moles) of ethyl bromide in 1.5 liters of anhydrous ether was added with stirring 186 g. (1.50 moles) of 1-ethynylcyclohexanol. The addition was carried out as rapidly as possible without loss of ether and after all the acetylenic

(13) Susz, St. Pfau and Plattner, *Helv. Chim. Acta*, **20**, 469 (1937).

(14) Baber and Smith, "A Research on Eucalypts," Sydney, 1920, p. 417; Haworth, *Ann. Reports*, **34**, 393 (1937).

(15) Clemmensen, *Ber.*, **46**, 1837 (1913).

alcohol had been added the solution was stirred for one hour at room temperature. To the stirred solution was then added 165 g. (1.65 moles) of 2-hexanone and the mixture stirred for two hours. The reaction mixture was poured into 600 g. of ice to which had been added 150 ml. of concentrated hydrochloric acid. The organic layer was separated and the water layer extracted twice with ether. The ether solution was dried over magnesium sulfate, the ether removed and the product fractionated through a modified Widmer column under reduced pressure. The glycol boiled at 124–126° (1 mm.) and did not crystallize on standing. The yields in two runs were 214 g. (61%) and 207 g. (59%), respectively. Some dehydration during distillation evidently occurred because the analysis was high in carbon.

Anal. Calcd. for $C_{14}H_{24}O_2$: C, 75.00; H, 10.71. Found: C, 75.43; H, 10.76.

Dehydration of 1-(3-Hydroxy-3-methyl-1-heptynyl)-cyclohexanol.—Two hundred and seven grams of the glycol was heated to 190–200° with 20 g. of anhydrous potassium bisulfate for thirty minutes. Most of the water which was produced in the dehydration distilled out as it was produced and the remainder was removed under reduced pressure. The residue was fractionated through a Widmer column under reduced pressure. The 1-(3-methyl-3-hepten-1-ynyl)-cyclohexene boiled at 143–148° (21 mm.) and amounted to 154 g. (89%). On standing in the air this hydrocarbon rapidly absorbed oxygen, which accounts for the poor analysis.

Anal. Calcd. for $C_{14}H_{20}$: C, 89.36; H, 10.64. Found: C, 88.14; H, 10.97.

Cyclization of 1-(3-Methyl-3-hepten-1-ynyl)-cyclohexene.—A mixture of 131 g. (0.7 mole) of the dienyne and 900 ml. of 87% formic acid was refluxed for thirty hours. The dark colored mixture was diluted to 2 liters with water and 100 g. of sodium carbonate added to partly neutralize the formic acid. The organic layer was separated and the water layer extracted with ether in portions until the ether no longer became colored. The ether solution was neutralized with sodium bicarbonate and after removal of the ether the product was fractionated under reduced pressure. The first fraction consisted of the dienyne, b. p. 90–93° (1 mm.), and amounted to 15 g. The ketone distilled at 107–108° (1 mm.). The yield after refractionation was 48 g. (38% based on the dienyne not recovered); $n^{25}D$ 1.5022.

Anal. Calcd. for $C_{14}H_{22}O$: C, 81.55; H, 10.63. Found: C, 80.77, 80.60; H, 10.75, 10.64.

The 2,4-dinitrophenylhydrazone, prepared according to the method of Brady,[16] melted at 124–125°.

Anal. Calcd. for $C_{20}H_{26}O_4N_4$: C, 62.18; H, 6.73. Found: C, 61.95; H, 6.85.

Clemmensen Reduction of *trans*-3-Methyl-4-propyl-1,2,4a,5,6,7,8,8a-octahydro-1-naphthalenone.—To a solution of 15 g. of the ketone in 250 ml. of acetic acid were added 100 g. of amalgamated zinc and 90 ml. of 18% hydrochloric acid. The mixture was refluxed one hour and then 60 ml. of concentrated hydrochloric acid added in the course of two hours. The solution was refluxed for twelve hours longer. The organic material was extracted with ether. Fractionation of the ether extract gave 9 g. of hydrocarbon boiling at 115–120° (14 mm.).

Anal. Calcd. for $C_{14}H_{24}$: C, 87.50; H, 12.50. Found: C, 87.20; H, 12.49.

Platinum–Charcoal Dehydrogenation of the Clemmensen Reduction Product.—Four grams of the product from the Clemmensen reduction was passed over platinum–charcoal dehydrogenation catalyst[8] at 300–320°. After repeated passage of the compound over the catalyst until evolution of hydrogen ceased, the product was washed from the dehydrogenation apparatus and subjected to fractional distillation. The lower boiling portion consisted of 0.66 g. of material boiling at 123–128° (20 mm.). An intermediate fraction amounting to 0.32 g. boiling at 128° (20 mm.) to 111° (2 mm.) was colored blue. The fraction boiling at 111–125° (2 mm.) was very dark blue and amounted to 0.75 g. (19% of the theoretical). A brown residue remained.

Azulene Test.—Three drops of the Clemmensen reduction product was dissolved in 10 ml. of acetic acid and enough bromine added to make the solution faintly yellow. After standing for two hours, an intense blue color developed, indicating the presence of a hydroazulene in the reduction product. The blue color was destroyed by allowing the sample to stand in the air for several days.

A similar positive test for azulenes was obtained when the mixture of hydrocarbons obtained in the dehydrogenation was treated with bromine in acetic acid.

Selenium Dehydrogenation of the Clemmensen Reduction Product.—Four grams of the hydrocarbon was heated with 20 g. of powdered selenium under an air condenser for twenty-eight hours at 390–400°. After this time the evolution of hydrogen selenide became slow. The organic material was removed by extraction with ether. After distillation the product, which boiled at 115–123° (17 mm.), amounted to 2.1 g. No attempt was made to fractionate the material, but comparison of the ultraviolet absorption spectrum with *trans-as*-octahydrophenanthrene[5] indicated that the mixture contained about 35–40% of this compound.

In another run the hydrocarbon (15 g.) was heated with selenium (30 g.) for forty-two hours at 390–400°. The product was blue and analyzed for a hydrocarbon.

Anal. Calcd. for $C_{14}H_{24}$: C, 87.50; H, 12.50. Calcd. for $C_{14}H_{18}$: C, 90.32; H, 9.68. Found: C, 88.69; H, 11.41.

Ultraviolet Absorption Spectra.—The spectra were taken with a Bausch and Lomb ultraviolet spectrograph. A hydrogen discharge tube operating on 15,000 volts gave a continuous ultraviolet source and the Hα, Hβ, and Hγ lines served to calibrate the wave length scale of the spectrograph. The pictures were taken with a slit opening 60μ × 5 mm. and a 1.0 cm. quartz cell. Eastman double coated orthochromatic plates were used with a three-minute exposure. The absorption coefficient was determined by comparison with the blackness of a trace due to a 10^{-4} molar solution of naphthalene. The concentrations used were varied from 10^{-2} to 10^{-5} for each sample. Alcohol was used as the solvent.

Ozonization of 3-Methyl-4-propyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-one.—Two ozonolysis reactions were carried out using 10-g. samples of the ketone in carbon

(16) Brady, *J. Chem. Soc.*, 756 (1931).

tetrachloride solution. In the first the reaction was interrupted after six hours and, in the second, after twelve and a half hours. Both gave acidic fractions boiling from 90–180° (1 mm.), but no pure product was isolated. The boiling point changed continuously. The ozonization was not complete in either case. The acidic fraction amounted to 2.1 g. boiling below 100° (1 mm.) and 3.2 g. boiling from 100–180° (1 mm.) with some residue, when the ozonization was carried out for twelve and a half hours. The acid fraction gave no 2,4-dinitrophenylhydrazone.

Preparation of Δ^{11}-Dodecahydro-9-phenanthrone.—This ketone was prepared by the formic acid cyclization of dicyclohexenylacetylene.[4a] The ketone was fractionated to give a fraction boiling at 135–136° (2 mm.) with the refractive index $n^{25}D$ 1.5296. The refractive index of the sample did not vary during distillation.

Hydrogenation of Δ^{11}-Dodecahydro-9-phenanthrone to Tetradecahydro-9-phenanthrol.—A solution of 22.2 g. of the ketone in 120 ml. of ethyl alcohol was hydrogenated at 185° under a pressure of 100–200 atmospheres of hydrogen using Raney nickel[10] as the catalyst. Four hours were required for complete reduction to the saturated alcohol. The product from the hydrogenation was filtered and the solvent distilled. The residue was fractionally distilled through a modified Widmer column. The portion boiling at 136–138° (2 mm.) solidified to a waxy solid on standing for a few hours. The product did not give a sharp melting point and it has not been possible to purify it by recrystallization. The wide melting range indicates that the tetradecahydro-9-phenanthrol is a mixture of *cis–trans* isomers.

Anal. Calcd. for $C_{14}H_{24}O$: C, 80.77; H, 11.54. Found: C, 80.87; H, 11.38.

Δ^{11}-Dodecahydrophenanthrene.—The reduction of Δ^{11}-dodecahydro-9-phenanthrone to the corresponding unsaturated hydrocarbon was carried out by the method of Clemmensen[15] in the manner previously described.[4a]

Dehydrogenation of Δ^{11}-Dodecahydrophenanthrene.—Four and two-tenths grams of Δ^{11}-decahydrophenanthrene was passed repeatedly over platinum–charcoal catalyst[8] until the material was solid. The dehydrogenation product was removed from the apparatus with acetone and filtered. On recrystallization of the solid, after evaporation of the acetone, phenanthrene separated. The noncrystalline portion which remained in the solvent was recovered and again dehydrogenated and the product recrystallized. The phenanthrene amounted to 2.3 g. and melted at 97–98°. No other dehydrogenation product was isolated.

Anal. Calcd. for $C_{14}H_{10}$: C, 94.38; H, 5.62. Found: C, 94.20; H, 5.90.

Summary

1. Evidence has been presented to show that the cyclization of di-Δ^{11}-cyclohexenylacetylene yields Δ^{11}-dodecahydro-9-phenanthrone and not a spiran derivative.

2. Further evidence to support the view that cyclization of dienynes produces ring systems with the *trans*-configuration has been described.

3. Clemmensen reduction of *trans*-3-methyl-4-propyl-1,2,4a,5,6,7,8,8a-octahydro-1-naphthalenone has been found to cause a partial rearrangement of the carbon skeleton to a seven-five fused ring system which yields azulene derivatives on dehydrogenation.

URBANA, ILLINOIS RECEIVED MAY 18, 1939

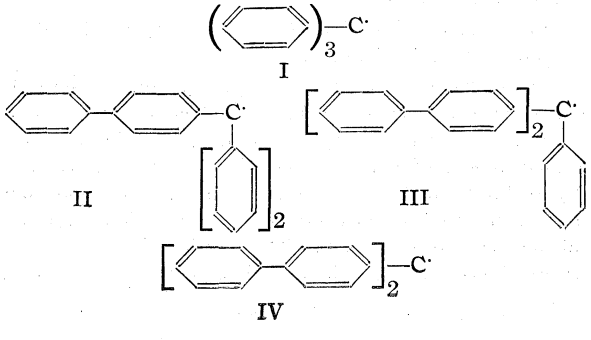
[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Effect of Substitution on the Dissociation of Hexaarylethanes. VII.[1] Meta and Para Phenyl Groups

BY C. S. MARVEL, MAX B. MUELLER AND EMANUEL GINSBERG

A comparison of the degree of dissociation of hexaarylethanes which have phenyl groups substituted for hydrogen atoms in the meta and para positions with respect to their attachment to the ethane carbon atoms is of considerable interest in testing the resonance theory of dissociation of hexaarylethanes.[2]

It has been pointed out previously[2] that in triphenylmethyl (I) the odd electron can resonate among ten positions, in diphenyl-*p*-biphenylmethyl (II), among thirteen positions, in di-*p*-biphenylphenylmethyl (III), among sixteen positions and in tri-*p*-biphenylmethyl (IV) among nineteen positions.



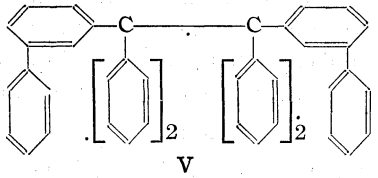
I II III IV

(1) For the sixth communication in this series see THIS JOURNAL, **61**, 77 (1939).

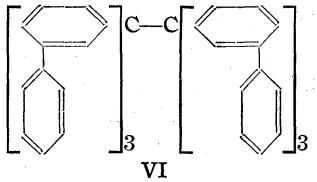
(2) Pauling and Wheland, *J. Chem. Phys.*, **1**, 362 (1933); **2**, 482 (1934); Wheland, *ibid.*, **2**, 474 (1934); Hückel, *Trans. Faraday Soc.*, **30**, 40 (1934); see also Gilman, "Organic Chemistry," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1938, p. 1850.

Accurate measurements[3] have shown that hexaphenylethane and hexa-*p*-biphenylethane dissociate to the extent of 2–3% and 100%, respectively, in one-tenth molar benzene solutions of the ethane at 20°. Hence, the introduction of the para phenyl group has the effect predicted on the resonance theory of increasing markedly the dissociation of the hexaarylethane.

The introduction of a phenyl group into a meta position of triphenylmethyl would not be expected to increase the number of resonance forms. Hence if this factor is the most important one in determining dissociation it would be expected that such ethanes as tetraphenyldi-*m*-biphenylethane (V) and hexa-*m*-biphenylethane (VI) would exhibit approximately the same degree of dissociation as hexaphenylethane.



V



VI

Recently it was reported from this Laboratory that hexa-*m*-biphenylethane (VI) was dissociated to the extent of about 60% in a 2.5% solution in benzene at 25°. We have now prepared the tetraphenyl-di-*m*-biphenylethane (V) and find by measurement of its magnetic susceptibility that it is dissociated to the extent of 11–12% in a 3.6% solution of the ethane in benzene at 25°. A determination of the magnetic susceptibility of the corresponding *p*-biphenyl derivative (II) has also been made under the same conditions. This hydrocarbon exists to the extent of 13–14% as the free radical in a 3.6% solution. As would be expected, the dissociation in 7% solution is only 10%.

It is very significant that the degree of dissociation of the mono-*m*-phenyl and mono-*p*-phenyl derivatives of triphenylmethyl should fall so close together and that hexa-*m*-biphenylethane should be dissociated to the extent of 60% which approaches the complete dissociation shown by the corresponding para isomer. In view of these values it is evident that the number of resonance forms of the free radical must play a rather minor part in determining the degree of dissociation of these hexaarylethanes.

Another interesting fact has been observed in this study of the meta and para phenyl substituted hexaphenylethanes. Whereas Schlenk, Weikel and Herzenstein[4] have shown that progressive substitutions of pairs of *p*-phenyl groups in hexaphenylethane produces a shift in the color of the solution from the characteristic yellow of this hydrocarbon to orange-red, red and violet, the substitution of two phenyl groups in the meta position gives only a yellow-orange color and six phenyl groups in the meta position give only an orange-red color although the dissociations of the two series of ethanes seem to be of the same general order. It is thus evident that the depth of color of a free radical solution is not a reliable index of the degree of dissociation. The color of the free radical solution is partly a characteristic of the groups present and their positions and not of the degree of dissociation alone.

Experimental

Diphenyl-*m*-biphenylcarbinol.—The Grignard reagent was prepared from 30 g. of *m*-bromobiphenyl and 3.4 g. of magnesium in 200 cc. of dry ether. The reaction was started by addition of a little ethylmagnesium bromide. To this Grignard reagent was added, with stirring, 25 g. of benzophenone dissolved in 100 cc. of dry ether during about three hours. The solution was then refluxed and stirred another hour. The reaction mixture was treated with a solution of ammonium chloride and cracked ice and then steam distilled. The solid residue was dissolved in an excess (400 cc.) of petroleum ether (b. p. 90–110°) and dried with calcium chloride. The yellow solution was filtered from the calcium chloride and concentrated. The light yellow solid which separated on cooling was recrystallized from hot petroleum ether. The yield was 32 g. (80%) of white crystals melting at 104–105°.

Anal. Calcd. for $C_{25}H_{20}O$: C, 89.24; H, 6.00. Found: C, 89.24; H, 6.05.

Diphenyl-*m*-biphenylcarbinol Ethyl Ether.—To a solution of 5 g. of the carbinol in 150 cc. of dry ether was added 5 g. of calcium chloride and then dry hydrogen chloride was passed into the mixture until it was saturated. The solution was filtered from the calcium chloride and was concentrated under reduced pressure to a brown viscous sirup. This residue was washed with petroleum ether (b. p. 30–60°) to remove much of the tarry impurity and then dissolved in 100 cc. of hot absolute ethanol. On concentration and cooling 5 g. (94%) of white prismatic needles melting at 78–79° was obtained.

(3) (a) Ziegler and Ewald, *Ann.*, **473**, 163 (1929); (b) Roy and Marvel, THIS JOURNAL, **59**, 2622 (1937); (c) Müller, *et al.*, *Ann.*, **520**, 235 (1935); **521**, 89 (1935).

(4) Schlenk, Weikel and Herzenstein, *Ann.*, **372**, 1 (1910); *Ber.*, **43**, 1753 (1910).

TABLE I

Ethane	t, °C.	% Ethane	$-\chi \times 10^6$ Soln.	$-\chi \times 10^6$ Ethane	$-\chi \times 10^6$ mol.	$-\chi_\alpha \times 10^6$	$\chi_\rho \times 10^6$	α in %	$K = 4\alpha^2 c/(1-\alpha)$
Di-*p*-biphenyl-	26	3.63	0.688 ± 0.001	0.006 ± 0.001	103 ± 18	423	320 ± 18	12.8 ± 0.7	3.76×10^{-3}
tetraphenyl-	26	3.63	.686 ± .001	.004 ± .001	70 ± 18	423	353 ± 18	14.1 ± .7	4.63×10^{-3}
	28	7.24	.676 ± .002	.019 ± .002	167 ± 18	423	256 ± 18	10.3 ± .7	4.73×10^{-3}
Di-*m*-biphenyl-	27	3.63	.690 ± .001	.008 ± .001	140 ± 18	423	283 ± 18	11.4 ± .7	2.93×10^{-3}
tetraphenyl-	26	3.61	.689 ± .001	.007 ± .001	124 ± 18	423	299 ± 18	12.0 ± .7	3.31×10^{-3}

Anal. Calcd. for $C_{27}H_{24}O$: C, 88.97; H, 6.63. Found: C, 88.96; H, 6.55.

Diphenyl - *m* - biphenylchloromethane.—Twenty-five grams of the pure carbinol (or ethyl ether) was dissolved in 100 cc. of hydrogen chloride-free acetyl chloride and the solution refluxed for two hours in an all-glass apparatus. After standing a few hours the dark brown solution was filtered through a sintered glass funnel to remove any tarry material. The filtrate was concentrated and cooled to 0°. The crystals which separated in the course of twenty-four hours were collected and recrystallized from acetyl chloride. The yield was 21 g. (80%) of white crystals melting at 86–87°.

Anal. Calcd. for $C_{25}H_{19}Cl$: Cl, 10.00. Found: Cl, 9.95.

Diphenyl-*m*-biphenylmethyl Peroxide.—A solution of 0.786 g. of diphenyl-*m*-biphenylchloromethane in 25 cc. of dry, thiophene-free benzene was shaken with 3 g. of molecular silver for ten hours in the evacuated measuring apparatus already described. After determining the magnetic susceptibility of the solution, it was transferred as completely as possible to an open beaker. The color disappeared completely within ten minutes. The colorless solution was evaporated to dryness. The slightly colored crystalline residue was recrystallized by dissolving it in 10 cc. of dry benzene followed by the addition of 20 cc. of absolute ethanol. The white crystalline material which separated over a period of twenty-four hours was collected, dried, and weighed: yield, 0.489 g. (66%); m. p. 164–165°.

Anal. Calcd. for $C_{50}H_{38}O_2$: C, 89.55; H, 5.67. Found: C, 89.63; H, 6.01.

***p*-Biphenyl Derivatives.**—These compounds were prepared by the methods of Schlenk.[4,5]

	Found m. p., °C.	Reported[4,5] m. p., °C.
p-Biphenyldiphenylchloromethane	146.5–147	147.5
p-Biphenyldiphenylmethyl peroxide	179–180	180
Di-*p*-biphenylphenylcarbinol	150–151	151
Di-*p*-biphenylphenylchloromethane	131–132	131.5

Magnetic Susceptibility Measurements.—The general procedure used for the determination of the dissociation of hexaarylethane has been described previously.[3b] The results for di-*p*-biphenyltetraphenylethane and di-*m*-biphenyltetraphenylethane are summarized in the table.

Summary

1. Di-*m*-biphenyltetraphenylethane has been prepared in benzene solution.

2. Magnetic susceptibility measurements show that in a 3.6% benzene solution, di-*m*-biphenyltetraphenylethane is 11–12% dissociated while di-*p*-biphenyltetraphenylethane is 13–14% dissociated.

3. It is suggested that the number of resonance forms of the free radical plays a rather minor part in determining the degree of dissociation of an hexaphenylethane.

(5) Schlenk, *Ann.*, **368**, 295 (1909).

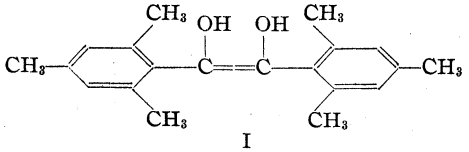
URBANA, ILLINOIS RECEIVED MAY 27, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

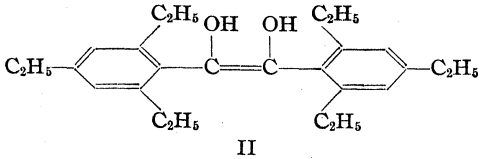
1,2-Diarylacetylene Glycols. II. An Enediol from Hexaethylbenzil

BY REYNOLD C. FUSON, JOSEPH CORSE AND C. H. MCKEEVER[1]

The remarkable stability of the enediol, 1,2-dimesitylacetylene glycol (I),[2] is even more pronounced in its ethyl analog 1,2-di-(2,4,6-triethylphenyl)-acetylene glycol (II).



I



II

The latter, for example, is much more stable in air; it can be exposed to the atmosphere for hours without appreciable change. The methyl compound, on the other hand, is so readily oxidized that it is extremely difficult to purify.

(1) Röhm and Haas Research Assistant.

(2) Fuson and Corse, THIS JOURNAL, **61**, 975 (1939).

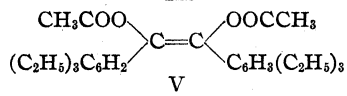
Considerable practical advantage is gained, therefore, by working with the ethyl compound.

The new enediol (II) was made by the action of the binary mixture, Mg + MgI_2,[3] on 2,4,6-triethylbenzoyl chloride and by the method of Thompson[4]—catalytic hydrogenation of the corresponding benzil (III). Both synthetic products melted at 154–155.5° and a mixed melting point showed no lowering.

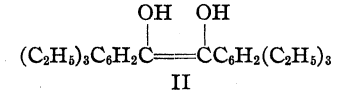
The action of acetic anhydride gave a diacetate (IV), melting at 189–190°—probably the *trans* form. A second diacetate (V) forms when the benzil is hydrogenated in acetic anhydride solution. This isomer—assigned the *cis* configuration—melts at 133.5–134°.

$(C_2H_5)_3C_6H_2COCOC_6H_2(C_2H_5)_3$

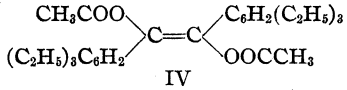
III



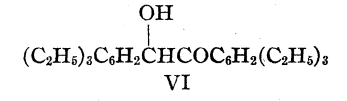
V



II



IV



VI

A mixture of two dibenzoates was formed by the action of benzoyl chloride in pyridine. These melt at 124.5° and 235–236° and presumably possess, respectively, the *cis* and *trans* configurations; treatment with alcoholic potassium hydroxide converts them to the benzil (III).

Like the methyl analog the new glycol (II) can be caused to rearrange slowly to the corresponding benzoin (VI) by heating in a methanol solution containing hydrogen chloride. The benzoin is stable in air and shows no tendency to revert spontaneously to the glycol. In this respect the new enediol and the benzoin appear to differ from ordinary keto–enol pairs; these compounds are not readily interconvertible.

Another property which distinguishes this enediol from ordinary enols is its neutral character. This behavior suggests that vinyl alcohols in general may prove to be neutral substances and that they take on an acidic character only when conjugated with a negative group such as the carbonyl group. This point of view is supported by the observation that in reductone[5] and ascorbic acid[6] the β-hydroxyl group is acidic while the α-hydroxyl group is neutral. The enediol shows infrared absorption maxima at 2.78 and 2.83 μ which may be interpreted to indicate the presence of two hydroxyl groups. Maxima in this region are normally indicative of acidic hydroxyl groups. The double peak observed here is similar to those of compounds in which two hydroxyl groups are held by the same atom. The benzoin, on the other hand, shows a single absorption maximum at 2.85 μ—presumably due to one hydroxyl group.

The authors are indebted to Professors A. M. Buswell and W. H. Rodebush and to Mr. J. R. Downing for the determination and interpretation of the infrared absorption data.

Experimental

2,4,6-Triethylbenzoyl Chloride.—Consistently high yields of this acid chloride were obtained by the thionyl chloride method. This procedure is preferable to that using phosphorus pentachloride[7] since the latter occasionally gave low yields. To 30 g. of 2,4,6-triethylbenzoic acid which had been dried for twelve hours at 60° over phosphorus pentoxide was added, all at once, 21 cc. of thionyl chloride. The reaction started immediately. The mixture was allowed to stand for four hours at room temperature. The excess thionyl chloride was removed under diminished pressure and the acid chloride distilled *in vacuo*. There was obtained 27.5 g. (85% of the theoretical amount) of 2,4,6-triethylbenzoyl chloride, b. p. 108–110° (2 mm.).

1,2-Di-(2,4,6-triethylphenyl)-acetylene Glycol.—A binary mixture of magnesium and magnesium iodide was prepared from 9 g. of magnesium and 46 g. of iodine according to the method of Gomberg and Bachmann.[3] A stream of dry nitrogen was passed through the vessel throughout the period of reaction.

A solution of 32.6 g. of 2,4,6-triethylbenzoyl chloride in 30 cc. of dry ether was added dropwise to the binary mixture. The reaction mixture was stirred for twenty-four hours before nearly all the magnesium had gone into solution. The solution was decanted into a separatory funnel which contained 200 g. of cracked ice and 16 cc. of glacial acetic acid. The ether–benzene layer was separated and washed *rapidly* with three portions of a 10% solution of potassium bicarbonate, once with water, twice with a 5% solution of sodium thiosulfate and twice more with water. The benzene and ether were removed as rapidly as possible under diminished pressure, using a nitrogen-filled capillary tube. The residue was a mixture of white and yellow crystals. The yellow benzil was separated

(3) Gomberg and Bachmann, THIS JOURNAL, **49**, 236) 1927).

(4) Thompson, *ibid.*, **61**, 1281 (1939).

(5) Euler and Martins, *Svensk. Kem. Tidskr.*, **45**, 73 (1933); Norrish and Griffiths, *J. Chem. Soc.*, 2837 (1928).

(6) Reichstein, Grüssner and Oppenauer, *Helv. Chim. Acta*, **17**, 510 (1934).

(7) Fuson and Corse, THIS JOURNAL, **60**, 2063 (1938).

from the mixture by washing with low-boiling petroleum ether. The enediol could be recrystallized by dissolving it in a small amount of ether, evaporating this solution to a small volume and adding low-boiling petroleum ether. There was obtained 8 g. of the enediol, m. p. 148–152° (with decomposition) in an open capillary and 154–155° in a nitrogen-filled capillary.

Anal. Calcd. for $C_{26}H_{36}O_2$: C, 82.05; H, 9.53. Found: C, 81.71; H, 9.79.

The low-boiling petroleum ether solution was allowed to stand at room temperature. After several hours the 2,4,6,-2′,4′,6′-hexaethylbenzil started to crystallize; yield, 5 g. From the potassium bicarbonate washings there was obtained 1.5 g. of triethylbenzoic acid.

The enediol did not dissolve in cold 40% aqueous sodium hydroxide solution. It reduced Tollens' reagent as well as ferric chloride and cupric acetate at 0°, and gave a positive test with 2,6-dichlorobenzeneoneindophenol. Oxidation converts it to the benzil.

The glycol was prepared also by hydrogenation of the benzil on methyl alcohol according to the procedure of Thompson[4] for the methyl analog.

The enediol was recrystallized from ether–petroleum ether mixture. The melting point in an open capillary was 149–151°, with decomposition. In a nitrogen-filled capillary the melting point was 154–155.5°. The melting point of a mixture of this product with the sample prepared from the acid chloride showed no depression.

In later experiments it was found more convenient to use low-boiling petroleum ether as the solvent in the reduction. The enediol precipitated as it was formed. The reaction mixture was filtered and the enediol dissolved in a small amount of ether. This solution was filtered to remove the catalyst and the enediol reprecipitated by evaporating most of the ether and adding low-boiling petroleum ether.

Diacetate (Low-Melting).—When the benzil was hydrogenated in acetic anhydride according to the method of Thompson[4] a diacetate was formed. It crystallized from methyl alcohol in glistening white columns melting at 133.5–134°.

Anal. Calcd. for $C_{30}H_{40}O_4$: C, 77.55; H, 8.68. Found: C, 77.49; H, 8.21.

Diacetate (High-Melting).—One-half gram of the enediol was washed with low-boiling petroleum ether, then added to 3 cc. of acetic anhydride, and the solution refluxed gently for three hours. The light brown reaction mixture was poured into water and heated on the steam cone for a few minutes to decompose the excess acetic anhydride. It was extracted with ether, the ether extracts washed with three portions of a 10% solution of potassium carbonate, then with water. The ether was removed and the solid recrystallized from ethyl alcohol. There was obtained 0.2 g. of white needles which melted at 188–190°, and a very small amount of light yellow oil.

Anal. Calcd. for $C_{30}H_{40}O_4$: C, 77.55; H, 8.68. Found: C, 77.64; H, 8.83.

Dibenzoates.—A mixture of 1.8 g. of the enediol, 30 cc. of pyridine and 5 cc. of benzoyl chloride was refluxed gently for three and one-half hours. The reaction mixture, now red, was allowed to stand at room temperature for three hours, then poured into 100 cc. of water. It was extracted with 70 cc. of benzene, the benzene extract washed three times with a 10% solution of potassium bicarbonate, then acidified with dilute hydrochloric acid, washed several times with large portions of very dilute hydrochloric acid, and finally washed with water. The benzene was removed by an air blast. The white solid which remained was partially soluble in alcohol. It was recrystallized from a benzene–absolute alcohol mixture, m. p. 235–236°.

Anal. Calcd. for $C_{40}H_{44}O_4$: C, 81.6; H, 7.53. Found: C, 81.82; H, 7.82.

The filtrate was evaporated to dryness. There remained 0.8 g. of a compound which crystallized readily from 95% alcohol, m. p. 124–124.5°.

Anal. Calcd. for $C_{40}H_{44}O_4$: C, 81.6; H, 7.53. Found: C, 81.35; H, 7.40.

2,4,6,2′,4′,6′-Hexaethylbenzoin.—To 40 cc. of methyl alcohol saturated with dry hydrogen chloride was added 1.8 g. of the enediol. The solution was refluxed for two and one-half hours. The reaction vessel was stoppered tightly and allowed to stand overnight at room temperature. The reaction mixture was then poured into water and extracted with ether; the ether extracts were washed and dried over calcium chloride. After the ether had been removed, there remained 1.6 g. of a light yellow mixture of compounds. By washing this mixture with small portions of low-boiling petroleum ether the yellow color was removed. From these washings a small amount of 2,4,6,2′,4′,6′-hexaethylbenzil was obtained. The benzoin was recrystallized from low-boiling petroleum ether, m. p. 64–65.5°.

Anal. Calcd. for $C_{26}H_{36}O_2$: C, 82.05; H, 9.53. Found: C, 82.37; H, 9.23.

The benzoin did not reduce Tollens' reagent or copper acetate. It gave a negative test with 2,6-dichlorobenzeneoneindophenol. Oxidation with chromic anhydride, however, converted it to the benzil.

Summary

A new enediol, 1,2-di-(2,4,6-triethylphenyl)-acetylene glycol (II), has been synthesized and characterized.

It yields two diacetates and two dibenzoates, and can be caused to rearrange to the corresponding benzoin.

It is readily oxidized, but is not soluble in aqueous alkali.

URBANA, ILLINOIS RECEIVED MAY 31, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF COLUMBIA UNIVERSITY]

Researcles on Thiazoles. XXIII. The Synthesis of Certain Benzothiazoles Structurally Related to Quinoline Antimalarials

BY H. HERBERT FOX AND MARSTON T. BOGERT

Of the numerous synthetic organic compounds tested as possible antimalarials, Plasmoquine and Atebrine generally have been regarded as among the most useful. The former of these is a 6-methoxy-8-(δ-diethylamino-α-methyl-butyl) aminoquinoline (XXVI), the latter a 2-chloro-7-methoxy-5-(δ-diethylamino-α-methyl-butyl)-aminoacridine (XXVII).

At the time our research was initiated, no work had been reported, at least so far as we could discover, on the synthesis of benzothiazoles structurally related to Plasmoquine, for the purpose of investigating them as possible antimalarials. It was not until the latter part of March, 1938, when most of our work had been completed, that we learned that Knunyantz and Benevolenskaya[1] had been conducting studies also in this field and had found that 6-methoxy-4-(γ-diethylaminopropyl)-aminobenzothiazole and its 2-methyl derivative were devoid of antimalarial effect. It seems unlikely, therefore, that the 6-methoxy-4-(and 7)(β-diethylaminoethyl)-aminobenzothiazoles, described in the following pages, will exhibit any antimalarial properties.

The methods used by us in these syntheses were quite different from those employed by Knunyantz and Benevolenskaya. The latter prepared their benzothiazoles from thiamides by the familiar Jacobson[2] reaction, whereas we utilized the Herz process[3] as applied to *p*-substituted aromatic amines with a free *o*-position. The various steps in our syntheses are shown on the Flow Sheets.

Experimental

Series A

2-Amino-5-methoxyphenylmercaptan (III).—The Herz reaction product (II) was prepared as described by Ast and Bogert,[4] except that it was found possible to reduce by 40% the proportion of sulfur monochloride to *p*-anisidine hydrochloride without loss of yield. As reported by them, it formed a reddish brown microcrystalline solid, melting with decomposition at 168° (corr.), when crystallized from a mixture of ligroin and chloroform.

From the crude Herz reaction product, a clear colorless aqueous solution of the *sodium salt* of the 2-amino-5-methoxyphenylmercaptan was obtained by the Ast and Bogert[4] technique (except that sodium hydroxide was used instead of the bicarbonate), which was likewise followed in the preparation of the corresponding *zinc salt* (IV).

Hydrochloride.—A cold concentrated aqueous solution of the above sodium salt was neutralized carefully with dilute acetic acid. There resulted a yellow precipitate or suspension. The mixture was extracted with ether, the ether extract dried with anhydrous magnesium sulfate and treated with a current of dry hydrogen chloride. The precipitated hydrochloride was collected, dried, and crystallized from a mixture of absolute ethanol and dry benzene. It formed small yellow needles, m. p. in sealed tube, 210–211° (corr.), with decomposition and previous darkening; yield of crude product, 41%, calculated to the initial *p*-anisidine hydrochloride. It was soluble in water, in excess of aqueous caustic alkali, or in alcohol, but not in benzene.

Anal. Calcd. for $C_7H_{10}ClNOS$: C, 43.8; H, 5.3; N, 7.3. Found: C, 43.6; H, 4.9; N, 7.6.

2,2′-Diamino-5,5′-dimethoxydiphenyl Disulfide (V).—A suspension of 3 g. of the zinc salt of the mercaptan (IV) in 100 cc. of concentrated ammonium hydroxide solution was treated for four hours with a vigorous current of air. A red precipitate replaced the suspended salt. The solid material was removed, extracted with alcohol, the alcoholic extract decolorized with Norite, concentrated, treated with three times its volume of water, and allowed to stand. Long yellow needles separated, which were crystallized repeatedly from 25% ethanol, and then melted at 73–73.5° (corr.). The product was insoluble in water or aqueous caustic alkali, but dissolved in the usual organic solvents.

Anal. Calcd. for $C_{14}H_{16}O_2N_2S_2$: C, 54.5; H, 5.2. Found: C, 54.5; H, 4.9.

6-Methoxybenzothiazole (VI).—A mixture of 15.4 g. of the zinc mercaptide (IV), sufficient glacial acetic acid to dissolve it (about a liter), an excess of anhydrous formic acid, and some metallic zinc, was refluxed for four hours. The bulk of the acid was then distilled off, the residue made alkaline with sodium hydroxide and distilled with steam, giving an 82% yield (11.1 g.) of the crude thiazole. Crystallized from petroleum ether, it was obtained in glistening colorless plates, m. p. 72.5–73° (corr.); freely soluble in carbon bisulfide, alcohol, ether, or benzene, moderately soluble in petroleum ether or hot water, and practically insoluble in cold water.

Anal. Calcd. for C_8H_7ONS: C, 58.1; H, 4.3; N, 8.5. Found: C, 58.1; H, 4.1; N, 8.3.

This compound was prepared also from the aminomercaptan hydrochloride (III) and anhydrous formic acid, in the presence of zinc. The yield was 46%. The method

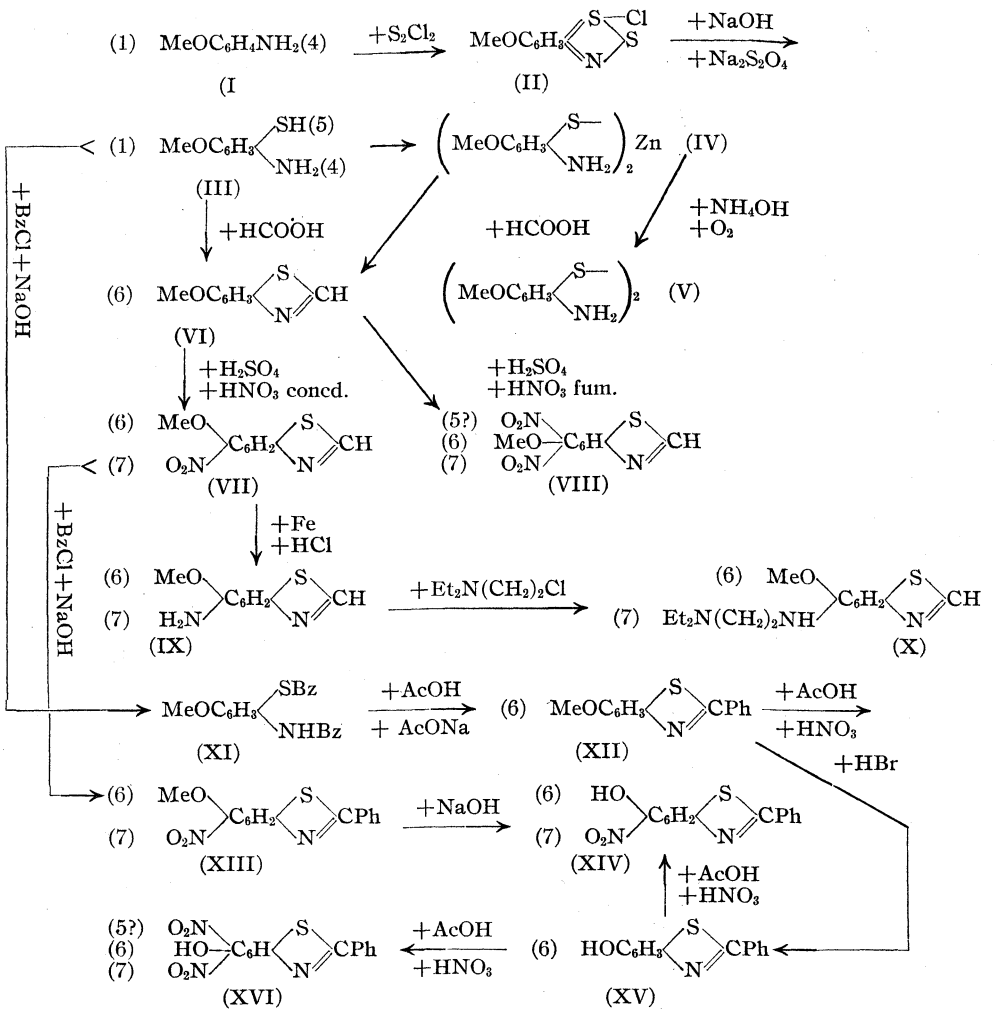
(1) Knunyantz and Benevolenskaya, *J. Gen. Chem.* (*U. S. S. R.*), **7**, 2471 (1937); *C. A.*, **32**, 2119 (1938).

(2) Jacobson, *Ber.*, **19**, 1067 (1886).

(3) Herz, German Patents 360,690, 364,822, 367,346, 367,493 (1914); *Friedlaender*, **14**, 908, 918–923.

(4) Ast and Bogert, *Rec. trav. chim.*, **54**, 917–930 (1935).

FLOW SHEET—SERIES A



was less satisfactory, because the isolation of the pure aminomercaptan hydrochloride was rather troublesome.

6-Methoxy-7-nitrobenzothiazole (VII).—A solution of 1.5 g. of 6-methoxybenzothiazole in 6 cc. of concentrated sulfuric acid was treated gradually with 6 cc. of concentrated nitric acid, the solution being maintained at room temperature for five minutes and then poured upon ice. The precipitated nitro derivative was collected, washed with water, and crystallized from alcohol. The product formed pale yellow plates, m. p. 202–203.5° (corr.); yield, 1.5 g. or 78%. In subsequent runs, the yields were nearly that calculated.

Anal. Calcd. for $C_8H_6O_3N_2S$: C, 45.7; H, 2.9; N, 13.3. Found: C, 45.6; H, 3.1; N, 13.1.

The same product was obtained by treating a solution of the thiazole in concentrated phosphoric acid with a slight excess of fuming nitric acid; but for all of our subsequent work the first method of preparation was preferred.

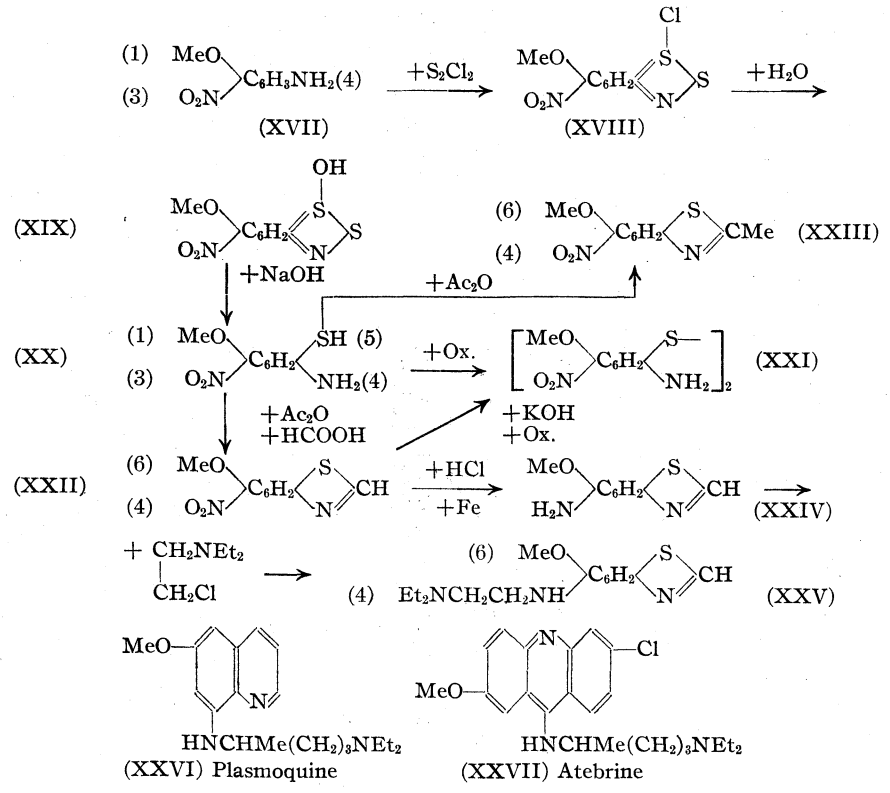
6-Methoxy-5(?),7-dinitro-benzothiazole (VIII).—To a solution of 1 g. of the thiazole (VII) in 6 cc. of concentrated sulfuric acid, there was added dropwise 4 cc. of fuming nitric acid, the mixture being kept for five minutes at 45° and then poured upon ice. The yellow precipitate, when crystallized from alcohol, formed very long needles, of an exceedingly pale yellowish tinge, m. p. 161–162.5° (corr.).

Anal. Calcd. for $C_8H_5O_5N_3S$: C, 37.6; H, 2.0. Found: C, 37.9; H, 2.0.

Since, in what follows, evidence is submitted that the first nitro group is attached to C^7, it seems probable that the second one is on C^5.

6-Methoxy-7-aminobenzothiazole (IX).—A suspension of the corresponding nitro derivative in hot dilute hydrochloric acid was reduced by successive additions of iron powder, and the mixture refluxed until the reaction was complete. The cold mixture was made strongly alkaline with sodium carbonate and filtered hot. As the filtrate cooled, a tan precipitate of the amine separated which was filtered out. The filtrate from this was added to the iron oxide residue and the whole extracted with benzene. The benzene extract was dried over anhydrous sodium sulfate and dry hydrogen chloride passed in, to precipitate the amine hydrochloride. This precipitate was dried, dissolved in water and the aqueous solution made slightly

FLOW SHEET—SERIES B



alkaline with sodium carbonate. The free amine so recovered was added to that obtained from the first alkaline filtrate from the iron oxide, and the whole was purified by solution in dilute acid and reprecipitation by alkali; yield 62%. Purified by repeated crystallization from hot water, it formed tan plates, m. p. 130.5–131.5° (corr.).

Another portion was sublimed *in vacuo*, and the white sublimate crystallized from "Skellysolve D." Nearly white plates were thus secured, m. p. 130–131° (corr.), with previous softening.

Anal. Calcd. for $C_8H_8ON_2S$: C, 53.3; H, 4.5; N, 15.6. Found: C, 53.2; H, 4.6; N, 16.0.

HCl Salt.—Nearly colorless transparent flakes (from alcohol), melting with decomposition and previous darkening at 223–224° (corr.) (sealed tube).

Anal. Calcd. for $C_8H_8ON_2S \cdot HCl$: 0.0992 g. requires 1.055 cc. of 0.434 *N* NaOH. Found: 1.068 cc.

6 - Methoxy - 7 - (β - diethylaminoethyl) - aminobenzothiazole (X).—A mixture of 5 g. of the above amine (IX), 6 g. of β-diethylaminoethyl chloride hydrochloride, and 15 cc. of absolute ethanol was heated at 110° for fifty-six hours under a short air condenser carrying a calcium chloride guard tube, to permit the distillation of the alcohol without ingress of moisture. The reaction product was dissolved in hot water, the reddish-brown solution cooled and a large excess of potassium carbonate added. The solution separated into two layers. The upper viscous dark brown oily one was taken up in ether, the ether solution dried over potassium carbonate, filtered, and the ether boiled off. The residue was distilled at a pressure of about 0.0001 mm. and gave, in addition to some unchanged initial material, a light yellow viscous oily fraction at 140–145°, which darkened rapidly on exposure to the air, and was the compound sought (X); $n^{25}D$ 1.5792.

Anal. Calcd. for $C_{14}H_{21}ON_3S$: C, 60.2; H, 7.6. Found: C, 60.0; H, 7.7.

2 - Benzoylamino - 5 - methoxybenzoylphenylmercaptan (XI) was prepared from the sodium mercaptide (III) and benzoyl chloride, as described by Ast and Bogert[4] and a similar product obtained (m. p. 162–163°, corr.).

2-Phenyl-6-methoxy-benzothiazole (XII), obtained from the foregoing dibenzoyl derivative by the action of acetic anhydride and fused sodium acetate, as described by Ast and Bogert,[4] formed fine long colorless needles, m. p. 114–114.5° (corr.), as reported by them.

2-Phenyl-6-methoxy-7-nitrobenzothiazole (XIII).—To a mixture of 2.4 g. of the above thiazole (XII) with 10 cc. of glacial acetic acid, there was added 2 g. of nitric acid (sp. gr., 1.4) in 4 cc. of glacial acetic acid. There resulted a red solution, which was warmed for a short time at 60°, then cooled and poured into water. The yellow precipitate which formed was collected, washed with water and dried; yield 2.5 g., or 82%. Recrystallized from glacial acetic acid, it formed small yellow needles, m. p. 210–211°.

Anal. Calcd. for $C_{14}H_{10}O_3N_2S$: C, 58.7; H, 3.5. Found: C, 58.6; H, 3.7.

To a hot solution of 2 g. of 6-methoxy-7-nitrobenzothiazole in 5 cc. of benzoyl chloride,[5] an excess of 10% sodium hydroxide solution was added slowly and carefully, and

(5) *Cf.* Reissert, *Ber.*, **38**, 3432 (1905).

the heating continued for a short time longer. The solution was filtered hot and the gummy precipitate thus removed was crystallized repeatedly from glacial acetic acid first and then from ethanol. The purified product formed small yellow needles, m. p. 210–211° (corr.).

Anal. Calcd. for $C_{14}H_{10}O_3N_2S$: C, 58.7; H, 3.5. Found: C, 59.0; H, 3.6.

The product from this second method was apparently identical with that obtained by the direct nitration of the phenylmethoxythiazole (XII) as described above. A mixture of the two melted at 210–211° (corr.).

2-Phenyl-6-hydroxybenzothiazole (XV).—A mixture of 3 g. of 2-phenyl-6-methoxybenzothiazole with 40 cc. of 48% hydrobromic acid was refluxed for six hours, cooled, and made alkaline with dilute sodium hydroxide. A dirty white precipitate separated at first, but soon redissolved, giving a solution with a strong green fluorescence. This solution, after decolorization with Norite, was acidified with excess of dilute acetic acid. A whitish gummy solid precipitated and soon became crystalline. Recrystallized from dilute ethanol, it formed white needles which melted, with previous softening, at 227–227.5° (corr.); yield, nearly that calculated.

Fries and Buchler[6] prepared this compound in much the same way, except that they used glacial acetic acid saturated with hydrogen bromide and heated the mixture for eighteen hours at 100° in sealed tubes. They reported the m. p. of their product as 227°.

2-Phenyl-6-hydroxy-7-nitrobenzothiazole (XIV).—1.01 g. of the above crude hydroxythiazole was nitrated as described by Fries and Buchler.[6] The long orange needles so obtained melted at 170–171° (corr.).

In another experiment, 1 g. of 2-phenyl-6-methoxy-7-nitrobenzothiazole was refluxed for seven hours with an excess of 10% sodium hydroxide solution. The mixture, consisting of a red solution containing a red precipitate, was filtered hot. The red precipitate was extracted by boiling with dry benzene, which recovered a large amount of unchanged initial thiazole. The small quantity of red solid undissolved by the benzene was taken up in hot alcohol, the alcohol solution acidified with hydrochloric acid, decolorized with Norite, and precipitated by careful dilution of the hot solution. Orange needles separated which, when recrystallized from dilute alcohol, melted at 171° (corr.). A mixture of this product with that obtained by the method described in the first paragraph, melted at 170.5–171° (corr.).

Anal. Calcd. for $C_{13}H_8O_3N_2S$: C, 57.3; H, 3.0. Found: C, 57.5; H, 3.0.

2-Phenyl-6-hydroxy-5(?),7-dinitrobenzothiazole (XVI).—A solution of 0.4 g. of 2-phenyl-6-hydroxybenzothiazole in 5 cc. of glacial acetic acid was treated with a solution of 1 cc. of nitric acid (sp. gr., 1.4) in 2 cc. of glacial acetic acid. The red mixture was warmed gently for a short time, then poured into water, the precipitate collected, washed with water, dried, and crystallized from glacial acetic acid. Long fine deep yellow needles were thus obtained, m. p. 194.5–196° (corr.).

Anal. Calcd. for $C_{13}H_7O_5N_3S$: C, 49.2; H, 2.2. Found: C, 49.4; H, 2.4.

(6) Fries and Buchler, *Ann.*, **454**, 240 (1927).

Series B

2-Amino-3-nitro-5-methoxyphenylmercaptan (XX).—The Herz reaction as applied to *p*-anisidine proved very unsatisfactory with *m*-nitro-*p*-anisidine, because of the sensitivity to moisture of the hydrochloride of the latter, and other complications. Recourse was had, therefore, to a modification of the Herz process described in a later German Patent, no. 367,346.[3]

A suspension of 150 g. of *m*-nitro-*p*-anisidine (XVII) in 900 cc. of glacial acetic acid, at 20°, was treated with 440 cc. (750 g.) of previously cooled sulfur monochloride. After being stirred for some time at room temperature, it was heated slowly to 75–80° and maintained at that point until the evolution of hydrogen chloride ceased (about five hours). After a brief additional heating at 90°, the mixture was cooled to room temperature, the orange-yellow precipitate collected, washed with dry benzene, and dried in the air; yield 170 g.

Some of this crude product, purified by crystallization from a mixture of benzene and glacial acetic acid, yielded a yellowish orange microcrystalline solid (XVIII), 1-chloro-4-nitro-6-methoxyisobenzo-1,2,3-dithiazole, which melted with decomposition at 220° (corr.), with previous darkening. However, if heated suddenly at any temperature above 190°, melting and decomposition ensued almost immediately. The compound was soluble in water, alcohol, or glacial acetic acid, but insoluble in benzene. Its aqueous solution, however, soon underwent hydrolysis on standing, with separation of a voluminous flocculent precipitate, which crystallized from absolute ethanol in long yellow needles of the corresponding *hydroxyl derivative* (XIX), which decomposed at 162.5° (corr.) with preliminary darkening; yield, 68%, based on the initial nitroanisidine.

Anal. Calcd. for $C_7H_6O_4N_2S_2$: C, 34.1; H, 2.5. Found: C, 34.3; H, 2.6.

This product easily was converted by caustic alkali into the sodium amino mercaptide (XX), as described for the 2-amino-5-methoxyphenylmercaptide, except that the solution so obtained was blood-red instead of colorless.

The zinc salt, prepared from the aqueous solution of the sodium mercaptide and zinc sulfate, by the Ast and Bogert[4] technique, was obtained in small red needles (from a mixture of ethanol and benzene), freely soluble in ethanol or glacial acetic acid, only slightly soluble in chloroform, and practically insoluble in water or benzene; yield, 40%, calculated to the *m*-nitro-*p*-anisidine.

2,2′-Diamino-3,3′-dinitro-5,5′-dimethoxydiphenyl Disulfide (XXI).—The aqueous alkaline solution of the sodium mercaptide (XX) was acidified with hydrochloric acid. A red flocculent precipitate separated, which was removed, washed with water, and crystallized from ethanol. Beautiful bright red needles were thus obtained, m. p. 171° (corr.).

Anal. Calcd. for $C_{14}H_{14}O_6N_4S_2$: C, 42.2; H, 3.5; mol. wt., 396. Found: C, 42.2; H, 3.7; mol. wt. (Rast), 392.

In the above reaction, the free mercaptan, which separated first, rapidly oxidized in the air to the disulfide. The presence of the mercaptan in the freshly precipitated material was demonstrated easily by its solubility in dilute alkali.

4-Nitro-6-methoxy-benzothiazole (XXII).—All attempts to obtain this thiazole by the action of anhydrous formic acid upon either the freshly precipitated mercaptan (XX), or its zinc salt, proved futile.

To a solution of the sodium mercaptide (XX) obtained by hydrolysis of 100 g. of the Herz reaction product, there was added all at once 140 cc. of crude formic–acetic anhydride, prepared as described by Béhal.[7] The whole was shaken vigorously, and then allowed to stand for five to ten minutes with occasional shaking. A yellow solid precipitated. This was collected, washed with water, and crystallized from dilute ethanol, giving long glistening yellow flat needles, m. p. 150–152°; yield 23.5 g.; or 21%, calculated to the nitroanisidine. Knunyantz and Benevolenskaya,[1] who prepared this compound in another way, gave its m. p. as 151°.

Anal. Calcd. for $C_8H_6O_3N_2S$: C, 45.7; H, 2.9; N, 13.3. Found: C, 45.7; H, 2.8; N, 13.2.

2-Methyl-4-nitro-6-methoxybenzothiazole (XXIII).—A few cc. of the aqueous alkaline solution of the sodium mercaptide (XX) was treated with sufficient acetic anhydride to redissolve the precipitate which first appeared. The solution was warmed and allowed to stand as long as crystals continued to separate. These small yellow needles were removed, washed with water and recrystallized from dilute ethanol. The first recrystallization yielded large intense yellow glistening plates, but all subsequent recrystallizations gave long yellow needles, m. p. 147° (corr.). Knunyantz and Benevolenskaya[1] prepared this compound by a different method and found its m. p. as 149–150°.

Anal. Calcd. for $C_9H_8O_3N_2S$: C, 48.2; H, 3.5; N, 12.5. Found: C, 48.1; H, 3.5; N, 12.4.

4-Amino-6-methoxybenzothiazole (XXIV).—A suspension of 60 g. of the corresponding nitro derivative (XXII) in dilute hydrochloric acid (50 cc. of concentrated acid to 500 cc. of water) was reduced by the gradual addition of 60 g. of iron powder. After refluxing the mixture for two and one-half hours, it was extracted with benzene and the filtered extract distilled. After the removal of the benzene, the residue was crystallized from absolute ethanol, after decolorization by Norite. The crystals obtained varied in form with the rate of cooling, the concentration, and probably other factors, being lightly tinted transparent plates, thick spikes, or long needles in rectangular clusters. The m. p. remained constant at 145.5–146° (corr.), even after the carefully purified material had been sublimed in a vacuum. Knunyantz and Benevolenskaya,[1] who reduced the nitro derivative by stannous chloride and crystallized their product from dilute alcohol, obtained long needles, m. p. 151°.

(7) Béhal, *Ann. chim.*, [7] **20**, 417 (1900).

Anal. Calcd. for $C_8H_8ON_2S$: C, 53.3; H, 4.5; N, 15.5. Found: C, 53.3; H, 4.6; N, 15.3.

Hydrochloride.—Long colorless needles, from concentrated hydrochloric acid, melting with decomposition, in a sealed tube, at 207–209° (corr.) (literature,[1] m. p. 206–208°).

Anal. Calcd. for $C_8H_8ON_2S\cdot HCl$: 0.1 g. requires 1.061 cc. of 0.434 *N* NaOH; found, 1.069 cc.

4-(β-Diethylaminoethyl)-amino-6-methoxybenzothiazole (XXV) was prepared from the foregoing amine and β-diethylaminoethyl chloride hydrochloride in essentially the same way as the 7-(β-diethylaminoethyl) isomer (X) was obtained from the corresponding amine, except that no ethanol was used in the mixture. Distillation of the crude product, at a pressure of 5–6 mm., in an atmosphere of nitrogen, yielded two fractions. One, b. p. 188–215°, consisted mainly of unchanged initial amine; and the other, b. p. 215–217°, was a yellow viscous oil, which darkened rather less rapidly on standing than its isomer (X); $n^{25}D$ 1.5978.

Anal. Calcd. for $C_{14}H_{21}ON_3S$: C, 60.2; H, 7.6. Found: C, 60.2; H, 7.3.

Acknowledgments.—Our grateful thanks are due to E. I. du Pont de Nemours & Co., Inc., of Wilmington, Delaware, and to the National Aniline and Chemical Co., Inc., of New York, for a generous supply of *p*-anisidine and of *m*-nitro-*p*-anisidine, for use in these investigations.

We are indebted also to Mr. Saul Gottlieb, of these Laboratories, who carried out the analyses recorded in this paper.

Summary

1. 6-Methoxy-4(and 7)-(β-diethylaminoethyl)-aminobenzothiazoles have been synthesized from *p*-anisidine in the one case, and from 3-nitro-4-aminoanisole in the other.

2. It was planned to study these compounds as possible antimalarials, but work recently published in Russia, on some closely related benzothiazoles, makes it seem unlikely that they will prove of any value in that direction.

3. From *m*-nitro-*p*-anisidine, 4-amino-6-methoxybenzothiazole is easily prepared.

4. Nitration of 6-methoxy, or of 2-phenyl-6-methoxybenzothiazole, substitutes the H in position 7.

NEW YORK, N. Y. RECEIVED MAY 13, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

Calculation of Base Rate Constants from Acid Rate Constants

BY SAMUEL H. MARON[1] AND VICTOR K. LA MER

For the protolytic equilibrium

$$N + B \underset{k_A}{\overset{k_B}{\rightleftharpoons}} R^- + A \qquad (1)$$

where N is acid substrate which ionizes to yield a proton to a base, B is base (proton acceptor), R^- is conjugate base of N, and A is conjugate acid of B, the equilibrium constant, K, is given by

$$K = \frac{k_B}{k_A} = \frac{[R^-]\,[A]}{[N]\,[B]} \qquad (2)$$

However, the ionization constant of N, K_N, corresponding to the reaction

$$N + H_2O = H_3O^+ + R^- \qquad (3)$$

is given by

$$K_N = [R^-]\,[H_3O^+]/[N] \qquad (4)$$

while the ionization constant of A, K_A, corresponding to the reaction

$$A + H_2O = H_3O^+ + B \qquad (5)$$

is given by

$$K_A = [B]\,[H_3O^+]/[A] \qquad (6)$$

Dividing now (4) by (6)

$$\frac{K_N}{K_A} = \frac{[R^-]\,[H_3O^+]}{[N]} \cdot \frac{[A]}{[B]\,[H_3O^+]} = \frac{[R^-]\,[A]}{[N]\,[B]} = K \qquad (7)$$

by eq. (2). And hence

$$\frac{K_N}{K_A} = \frac{k_B}{k_A} \qquad (8)$$

Knowing any three of the four constants K_N, K_A, k_B, k_A in (8), the fourth may be calculated. It is proposed to apply these equations to the prototropic isomerization of nitroparaffins to calculate k_B from available values of K_N, K_A, and k_A.

The primary and secondary nitroparaffins are acids which react with bases (defined in the general sense of Brönsted[2]) to yield an aci-nitroparaffin ion and a conjugate acid[3] according to the general scheme

$$\begin{matrix} R \\ R' \end{matrix}\!\!>\!CHNO_2 + B \xrightarrow{k_B} \begin{matrix} R \\ R' \end{matrix}\!\!>\!C=NOO^- + A \qquad (9)$$

The mechanism of this reaction has been discussed before.[4] Again, the reisomerization of aci-nitroparaffin to the nitro form has been shown to be, under the proper conditions, a reaction between the aci-nitroparaffin ion and an acid[5] (in the general sense) according to the scheme

$$\begin{matrix} R \\ R' \end{matrix}\!\!>\!C=NOO^- + A \xrightarrow{k_A} \begin{matrix} R \\ R' \end{matrix}\!\!>\!CHNO_2 + B \qquad (10)$$

If (9) and (10) be combined, we have the equilibrium condition:

$$\begin{matrix} R \\ R' \end{matrix}\!\!>\!CHNO_2 + B \underset{k_A}{\overset{k_B}{\rightleftharpoons}} \begin{matrix} R \\ R' \end{matrix}\!\!>\!C=NOO^- + A \qquad (11)$$

with equilibrium constant

$$K = \frac{\left[\begin{matrix} R \\ R' \end{matrix}\!\!>\!C=NOO^-\right][A]}{\left[\begin{matrix} R \\ R' \end{matrix}\!\!>\!CHNO_2\right][B]} = \frac{k_B}{k_A} \qquad (12)$$

Equation (12) is exactly analogous to equation (2), and hence it follows from (8) that

$$K = \frac{k_B}{k_A} = \frac{K_N}{K_A} \qquad (13)$$

where K_N is according to (3) and (4) the constant for the nitroparaffin dissociation

$$\begin{matrix} R \\ R' \end{matrix}\!\!>\!CHNO_2 + H_2O \rightleftharpoons \begin{matrix} R \\ R' \end{matrix}\!\!>\!C=NOO^- + H_3O^+ \qquad (14)$$

and

$$K_N = \frac{\left[\begin{matrix} R \\ R' \end{matrix}\!\!>\!C=NOO^-\right][H_3O^+]}{\left[\begin{matrix} R \\ R' \end{matrix}\!\!>\!CHNO_2\right]} \qquad (15)$$

while K_A is the ionization constant of the acid used and is defined by equations (5) and (6).

The ionization constants K_N of the nitro forms of nitromethane and nitroethane can be obtained from some measurements of Junell.[6] Junell determined what he terms the "scheinbare Dissoziationskonstante" of these two substances by

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(2) Brönsted, *Chem. Rev.*, **5**, 231 (1928).

(3) Pedersen, *Det. Kgl. Videnskab. Selskab. Math.-fys. Medd.*, **12**, 1 (1932) (in English); Junell, *Z. physik. Chem.*, **141A**, 71–90 (1929); Dissertation, University of Uppsala, Sweden, 1935; *Arkiv Kemi*, **11B**, No. 27 (1934); *ibid.*, **11B**, No. 34 (1934); Reitz, *Z. physik. Chem.*, **176A**, 363–387 (1936).

(4) Maron and La Mer, THIS JOURNAL, **60**, 2588 (1938).

(5) Junell, (a) *Arkiv Kemi*, **11B**, No. 30 (1934); (b) *Svensk Kem. Tid.*, **46**, 125–136 (1934); (c) Dissertation, Uppsala, 1935; (d) Maron and La Mer, THIS JOURNAL, **61**, 692 (1939).

(6) Junell,[3] Dissertation, pp. 114–124.

determining at high pH's the total concentration of aci form and calculating the ratio

$$K'_N = [H_3O^+]\,[\text{aci form}]/[\text{nitro form}] \quad (16)$$

The highest H_3O^+ concentration used for the nitromethane measurements was 1.41×10^{-9}, while the highest concentration of H_3O^+ for nitroethane was 5.38×10^{-9}. Now, since the ionization constant of aci-nitromethane is given by Junell[7] as 6×10^{-4} while that of nitroethane has been shown to be 4.1×10^{-5},[8] it follows that the ratios of aci ion to aci acid at equilibrium must be

$$\frac{[R^-]}{[R\,H]} = \frac{6 \times 10^{-4}}{1.41 \times 10^{-9}} = 4.3 \times 10^5 \text{ for nitromethane}$$

and

$$\frac{[R^-]}{[R\,H]} = \frac{4.1 \times 10^{-5}}{5.38 \times 10^{-9}} = 7.6 \times 10^3 \text{ for nitroethane}$$

From these ratios it is seen that compared to the concentrations of aci ion present the concentrations of aci acid are negligible, and hence (16) is essentially

$$K_N' = \frac{[H_3O^+]\,[R^-]}{[N]} = K_N \quad (17)$$

the ionization constants of the nitro forms. For nitromethane Junell reports from five measurements $K_N = (2.6 \pm 0.2) \times 10^{-11}$, while for nitroetnane he gives as a result of four measurements $K_N = (2.7 \pm 0.2) \times 10^{-9}$. These are the values of K_N employed in all calculations.

Table I gives the observed quantities and calculations for nitromethane at 0°. Columns (1), (2) and (3) give the acids used, their ionization constants, and the rate constants, respectively, for the reaction (10)

$$CH_2{=}NOO^- + A \longrightarrow CH_3NO_2 + B$$

These data are due to Junell.[7] Column (4) gives the equilibrium constant K calculated by Eq. (13), while column (5) gives the rate constant, k_B, calculated by (12) for the reaction: $CH_3NO_2 + B \longrightarrow CH_2{=}NO_2^- + A$ where B is the conjugate base of the particular acid.

It is possible to compare several of the calculated values of k_B with observed results. Although no rate data are available for 0°, kinetic measurements are extant for the reaction with the bases H_2O, monochloroacetate, and acetate ions at several temperatures, so that extrapolation to 0° and comparison with the calculated constants are possible. The data available for this purpose are summarized in Table II. A

(7) Junell, Dissertation, ref. 3.

(8) Maron and Shedlovsky, THIS JOURNAL, **61**, 753 (1939).

TABLE I

CALCULATIONS ON NITROMETHANE: Temp., 0.0°C. $K_N = 2.6 \times 10^{-11}$

Acid	K_A obsd.	k_A obsd.	K calcd. $= K_N/K_A$	k_B calcd.	k_B obsd.	K obsd. $= k_B$ obsd./k_A obsd.	K_A calcd. $= K_N K_A/k_B$	Base	p	q	log (k_B/q)	log $(q/p \times K_A)$
H_3O^+	55.5	4500(?)	4.96×10^{-13}	2.24×10^{-9}	1.4×10^{-9} (extr.)	3.11×10^{-13}	83.6	H_2O	1	1	−8.65	1.74
$CHCl_2$—COOH	3.32×10^{-2}	2800	7.83×10^{-10}	2.12×10^{-6}	.....	.....	.....	$CHCl_2COO^-$	1	2	−5.98	−1.18
CH_2Cl—COOH	1.53×10^{-3}	800	1.70×10^{-8}	1.36×10^{-5}	1.1×10^{-5} (extr.)	1.38×10^{-3}	1.88×10^{-3}	CH_2Cl—COO^-	1	2	−5.17	−2.51
CH_2Cl—CH_2COOH	8.0×10^{-5}	290	3.25×10^{-7}	9.43×10^{-5}	.....	.....	.....	CH_2Cl—CH_2COO^-	1	2	−4.33	−3.80
CH_3COOH	1.70×10^{-5}	150	1.53×10^{-6}	2.30×10^{-4}	2.1×10^{-4} (extr.)	1.40×10^{-6}	1.86×10^{-5}	CH_3COO^-	1	2	−3.94	−4.47
$COO^-(CH_2)_2COOH$	2.4×10^{-6}	80	1.07×10^{-5}	8.56×10^{-4}	.....	.....	.....	$COO^-(CH_2)_2$—COO^-	1	4	−3.67	−5.02
$(CH_3)_2AsOOH$	5.7×10^{-7}	210	.....	.....	.....	.....	.....	$(CH_3)_2AsOO^-$	1	2	....	−5.94
$H_2PO_4^-$	4.1×10^{-8}	50	6.34×10^{-4}	3.17×10^{-2}	.....	.....	.....	HPO_4^{--}	2	3	−1.98	−7.11
H_2O	2.1×10^{-17}	1.91×10^{-4} (calcd.)	1.24×10^6	.....	237.6	.....	.....	OH^-	1	1	+2.38	−16.7

TABLE III

CALCULATIONS ON NITROETHANE: Temp., 0.0°C. $K_N = 2.7 \times 10^{-9}$

Acid	K_A obsd.	k_A obsd.	K calcd.	k_B calcd.	k_B obsd.	Base	p	q	log $(q/p\,K_A)$	log (k_B/q)	log (k_A/p)
H_3O^+	55.5	150	4.86×10^{-11}	7.3×10^{-9}	H_2O		1	1	1.74	−8.14	2.18
$CH_2ClCOOH$	1.53×10^{-3}	3.8	1.77×10^{-6}	6.7×10^{-6}	CH_2ClCOO^-		1	2	− 2.51	−5.47	0.58
CH_2ClCH_2COOH	8.0×10^{-5}	1.62	3.38×10^{-5}	5.46×10^{-5}	$CH_2ClCH_2COO^-$		1	2	− 3.80	−4.56	.21
CH_3COOH	1.7×10^{-5}	0.67	1.59×10^{-4}	1.06×10^{-4}	CH_3COO^-		1	2	− 4.47	−4.28	− .174
$COO^-(CH_2)_2$—$COOH$	2.4×10^{-6}	.42	1.12×10^{-3}	4.71×10^{-4}	$(CH_2)_2(COO^-)_2$		1	4	− 5.02	−3.55	− .377
$(CH_3)_2AsOOH$	5.7×10^{-7}	.99	4.74×10^{-3}	4.69×10^{-3}	$(CH_3)_2AsOO^-$		1	2	− 5.94	−2.63	− .004
$H_2PO_4^-$	4.1×10^{-8}	.18	6.59×10^{-2}	1.18×10^{-2}	HPO_4^{--}		2	3	− 7.11	−2.41	−1.046
H_2O	2.1×10^{-17}	3.1×10^{-7} (calcd.)	1.28×10^{-8}	39.1 (obsd.)	OH^-		1	1	−16.7	1.59	.....

TABLE II

RATE CONSTANTS FOR THE REACTION

$$CH_3NO_2 + B \xrightarrow{k_B} CH_2{=}NOO^- + A$$

Temp.	k_B	Reference
	H_2O	
49.91	8.8×10^{-7}	Junell[3]
59.93	2.5×10^{-6}	Junell[3]
69.85	6.8×10^{-6}	Junell[5c]
69.85	7.4×10^{-6}	Reitz[3]
	CH_2ClCOO^-	
11.2	5.1×10^{-5}	Reitz[3]
20.0	1.50×10^{-4}	Pedersen[3]
25.0	2.35×10^{-4}	Reitz[3]
35.0	7.71×10^{-4}	Reitz[3]
	CH_2COO^-	
11.0	8.7×10^{-4}	Reitz[3]
20.0	2.69×10^{-3}	Pedersen[3]
22.0	3.22×10^{-3}	Pedersen[3]
25.0	4.55×10^{-3}	Reitz[3]
35.0	1.38×10^{-2}	Reitz[3]

plot of log k_B *vs.* $1/T$ and extrapolation to 0° yields the constants given in column (6) of Table I. The agreement between calculated and observed results, columns (5) and (6), is good.

In case of the acid H_3O^+ the procedure was reversed and k_A calculated from the values of k_B at 0° measured by Maron and La Mer.[4]

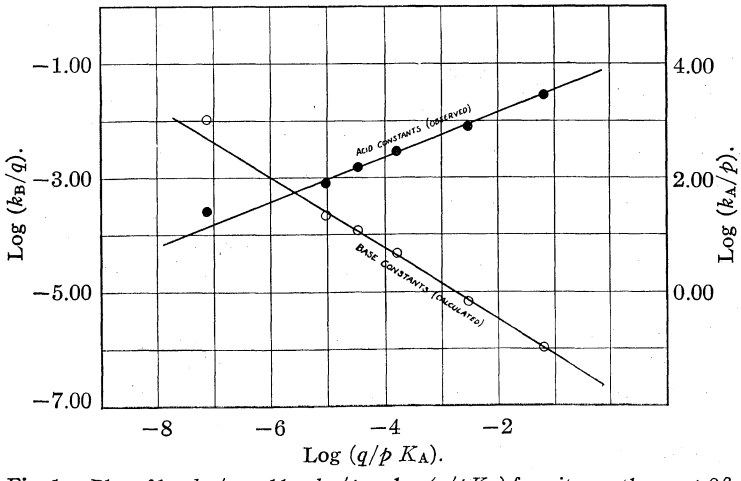

Fig. 1.—Plot of log k_B/q and log k_A/p *vs.* log (q/pK_A) for nitromethane at 0°.

It is possible to make the comparison between observed and calculated constants in two other ways, namely, by calculation of K and K_A from observed data. From equation (13), $K = k_B/k_A$. Using the observed values of k_A and k_B given in columns (3) and (6) of Table I, $K_{obsd.}$ have been calculated and are given in column (7). These values are to be compared with those given in column (4), and calculated from $K_{calcd.} = K_N/K_A$. The agreement again is good. And, finally, also by equation (13), $K_A = K_N k_A/k_B$; values of K_A thus calculated are given in column (8), and again show as good agreement with the observed values of K_A in column (2) as can be expected.

Table III gives the results of similar calculations for nitroethane. These calculations are again based on Junell's values for k_A, and on his value of $K_N = 2.7 \times 10^{-9}$ for nitroethane. Columns (1), (2) and (3) have the same significance as before except that now the reaction involved is

$$CH_3CH_2NO_2 + B \underset{k_A}{\overset{k_B}{\rightleftarrows}} CH_3CH{=}NOO^- + A$$

while columns (4) and (5) give the calculated equilibrium constants of the reaction ($K_{calcd.}$) and the rate constants for the forward reaction (k_B). Unfortunately no extended data on the forward reaction are available to permit comparison of calculated and observed results in this case. The only value of k_B available at 0° is $k_{OH^-} = 39.1$ and due to Maron and La Mer,[4] but no k_A observed is known to permit a calculation of k_B. Hence again the procedure was reversed and the known value of k_{OH^-} was used to calculate the value of k_{H_2O} in column (3).

However, a test of the calculated values of k_B can be obtained in another way. Junell showed that for both nitromethane and nitroethane a plot of log k_A/p *vs.* log (qK_A/p) is essentially linear, as would be expected if the Brönsted relation log $k_A/p = \log G_A + \alpha \log (q/pK_A)$ were obeyed. p and q are the statistical factors to correct the respective measured acid and base constants K_A and K_B to a uniform basis (see ref. 1). The values assigned p and q are given in Tables I and III. On theoretical grounds it may be anticipated that a plot of log k_B/q *vs.* log q/pK_A should also yield a straight line but with slope $= -\beta$ and y intercept $= \log G_B$. Further $\alpha + \beta$ should equal unity. The plot of both log k_A/p and log k_B/q *vs.* log q/pK_A for nitromethane at 0° is shown in Fig. 1. The expected linearity for log k_B/q *vs.* log q/pK_A is verified. Whenever a point is off the curve, the discrepancy is traceable to the corresponding value of k_A, which is also off

the curve. Further, from this plot we obtain $G_A = 8200$, $G_B = 1.98 \times 10^{-7}$, $\alpha = 0.39$ and $\beta = 0.62$, and hence $\alpha + \beta = 0.39 + 0.62 = 1.01$ as against the expected sum of unity.

A similar plot for nitroethane is shown in Fig. 2. Again the linear relation is obtained between log k_B/q and log q/pK_A. In this case $G_A = 32$, $G_B = 1.05 \times 10^{-7}$, $\alpha = 0.36$, $\beta = 0.65$ and $\alpha + \beta = 0.36 + 0.65 = 1.01$.

From the deductions of this paper may be derived another very interesting and quite general relationship. For reactions of the type discussed here, and which lead to an equilibrium, we have in general

$$k_A/p = G_A(q/pK_A)^\alpha \text{ and } k_B/q = G_B(p/qK_B)^\beta$$

where $K_B = 1/K_A$, *i. e.*, the ionization constant for the base conjugate to A. With these equations we obtain finally for log k_B/k_A

$$\log k_B/k_A = [1 - (\alpha + \beta)] \log q/p + \log \frac{G_B}{G_A} - (\alpha + \beta) \log K_A \quad (18)$$

But $k_B/k_A = K$ and $(\alpha + \beta) = 1$. Hence

$$\log \frac{k_B}{k_A} = \log K = \log \frac{G_B}{G_A} - \log K_A \quad (19)$$

However, according to (8) $\log K + \log K_A = \log K_N$. Therefore

$$\log K_N = \log G_B/G_A$$

and

$$K_N = G_B/G_A \quad (20)$$

According to (20) the ratio G_B/G_A should be the ionization constant of the substrate involved in the basic reaction. This relation can be tested easily by utilizing the values of G_B and G_A found at 0° for nitromethane and nitroethane. For nitromethane $G_B/G_A = 1.98 \times 10^{-7}/0.82 \times 10^4 = 2.4 \times 10^{-11}$, as against the observed value of $K_N = 2.6 \times 10^{-11}$. Similarly, for nitroethane $G_B/G_A = 1.05 \times 10^{-7}/32 = 3.3 \times 10^{-9}$ as against the experimental value $K_N = 2.7 \times 10^{-9}$. Considering the uncertainties in drawing the straight lines in Figs. 1 and 2 the agreement is satisfactory.

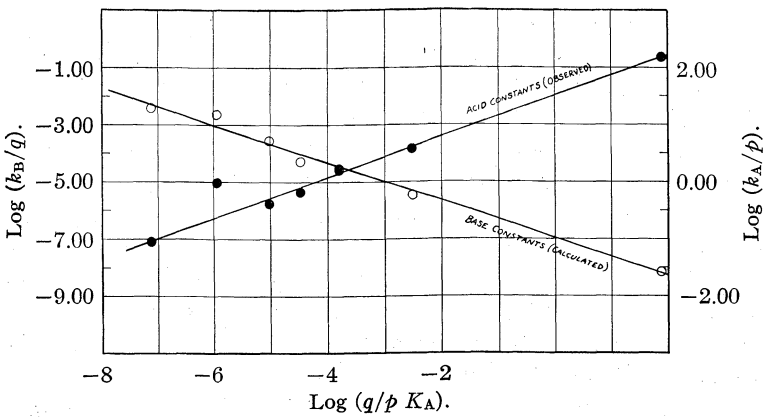

Fig. 2.—Plot of log k_B/q and log k_A/p *vs.* log (q/pK_A) for nitroethane at 0°.

Summary

1. Equations are deduced for calculating rate constants from certain kinetic and thermodynamic data.

2. These equations are applied to calculate the base rate constants for the isomerization of nitromethane and nitroethane to the aci forms.

3. Wherever comparison between calculated and observed values is possible, the agreement is good.

4. The calculated constants obey the Brönsted relation (log $k_B/q = G_B(p/qK_B)^\beta$.

5. An equation is derived relating acid strength of the substrate to the constants G_A and G_B in the Brönsted equations. The equation is shown to be valid for the cases discussed.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF ST. JOHN'S UNIVERSITY]

The Cobalt Ammine Salts of 12-Molybdophosphoric Acid

BY HAROLD A. HORAN

The recent work of Keggin and others[1] has shown that many salts of 12-molybdophosphoric acid are derived from the anion $PMo_{12}O_{40}^{-3}$. The structures of the alkali and ammonium salts have been determined and in general the composition of the anhydrous salts may be represented as $M_3PMo_{12}O_{40}$ while the hydrates have the composition $M_3PMo_{12}O_{40}\cdot 2H_2O$. Many salts of this heteropolyacid with the alkaline earth and heavier metals are known.[2] With the divalent cations the salts generally may be represented by $M_3(PMo_{12}O_{40})_2\cdot xH_2O$, while the salts involving the trivalent cations conform to the general formula $M(PMo_{12}O_{40})\cdot xH_2O$.

The complex cations of the cobaltic and chromic ammine series form characteristic precipitates with 12-molybdophosphoric acid.[3,4] The compositions of these salts have not in general been determined. By analogy to the simple cations we would expect a trivalent complex cation such as the hexammine cobaltic ion to form a salt of the type $[Co(NH_3)_6]PMo_{12}O_{40}\cdot xH_2O$. With the divalent complex cations of the pentammine series we would expect a salt such as $[Co(NH_3)_5X]_3(PMo_{12}O_{40})_2\cdot xH_2O$, where X is Cl, Br, NO_3, etc.

The precipitation of the nitratopentammine salt of 12-molybdophosphoric acid has been proposed for the gravimetric determination of phosphates[4] and as a result of a partial analysis of the salt the formula $[Co(NH_3)_5NO_3]HPMo_{12}O_{40}\cdot H_2O$[5] was suggested. This would indicate salts of the type $[Co(NH_3)_5X](HPMo_{12}O_{40})$, where X is Cl, Br, NO_3, etc. These would be acid salts of the acid, $H_3PMo_{12}O_{40}$. Acid salts of this acid involving the simple mono and divalent cations do not exist.

It is known that the pentammine cations undergo reaction in aqueous solution,[6] namely

$$Co(NH_3)_5X^{++} + H_2O = Co(NH_3)_5(H_2O)^{+++} + X^-$$

The rate and extent of this reaction depend, among other factors, on what X is. Evidence will be presented in this paper to show that due to this reaction the salts formed with the various pentammine cations and 12-molybdophosphate are all of the same composition, namely, $[Co(NH_3)_5(H_2O)]PMo_{12}O_{40}\cdot 4H_2O$. The normal or acid salts mentioned above are not formed. Probably the size of the cation involved is a determining factor in the formation of normal salts of the type, $M_3(PMo_{12}O_{40})_2$, and with large complex cations this structure cannot build up. As for acid salts there is no reason to expect these with the complex cations any more than with the simple ones.

Evidence will also be presented to show that the salt formed with the hexammine cobaltic ion may be represented as $Co(NH_3)_6(PMo_{12}O_{40})\cdot 3H_2O$. It is probable in both cases that part or all of the water of crystallization is lattice water.[7]

Experimental

Materials.—Chloropentammine, aquapentammine and hexammine cobaltic chlorides were prepared and purified by the methods of Biltz.[8] After purification, the salts were washed free of hydrochloric acid with 95% alcohol and finally with small portions of ether. The aquapentammine was air dried, while the chloropentammine and hexammine were dried in an oven, the former at 60° and the latter at 130°. The composition and purity were checked in all cases by Kjeldahl ammonia determinations, and in addition by gravimetric chloride determinations in the case of the aquapentammine and hexammine chlorides. The results were: calcd. for $[Co(NH_3)_5Cl]Cl_2$: NH_3, 34.00. Found: NH_3, 34.15. Calcd. for $[Co(NH_3)_5(H_2O)]Cl_3$: NH_3, 31.72; Cl, 39.62. Found: NH_3, 31.80; Cl, 39.69. Calcd. for $[Co(NH_3)_6]Cl_3$: NH_3, 38.20; Cl, 39.76. Found: NH_3, 38.29; Cl, 39.68.

The nitratopentammine cobaltic nitrate was prepared by the method of Jörgensen.[9] After purification, it was washed thoroughly with 95% alcohol and then with ether. It was dried in an oven at 50°. It was analyzed for ammonia and total ammonia plus nitrate, the former being done by Kjeldahl and the latter by a modified Kjeldahl method.[10] Calcd. for $[Co(NH_3)_5NO_3](NO_3)_2$:

(1) Keggin, *Proc. Roy. Soc.* (London), **144A**, 75 (1934); Bradley and Illingworth, *ibid.*, **157A**, 113 (1936); Santos, *ibid.*, **150A**, 309 (1935); Illingworth and Keggin, *J. Chem. Soc.*, 575 (1935).

(2) Mellor, "Comprehensive Treatise of Inorganic and Theoretical Chemistry," Vol. XI, Longmans Green & Co., London, 1931, p. 663.

(3) Ephraim–Thorne, "Textbook of Inorganic Chemistry," 2d ed., Gurney and Jackson, London, 1934, p. 441.

(4) Furman and State, *Ind. Eng. Chem., Anal. Ed.*, **8**, 420 (1936).

(5) The type expected of a divalent cation $[Co(NH_3)_5NO_3]_3(PMo_{12}O_{40})_2$, was eliminated as a result of the analysis. See H. M. State, Dissertation, Princeton University, 1936.

(6) Lamb and Marden, THIS JOURNAL, **33**, 1873 (1911); Lamb and Fairhall, *ibid.*, **45**, 378 (1923).

(7) Emeleus and Anderson, "Modern Aspects of Inorganic Chemistry," D. Van Nostrand Co., New York, 1938, p. 164.

(8) Biltz, "Laboratory Methods of Inorganic Chemistry," Hall and Blanchard, John Wiley and Sons, Inc., New York, 1909, pp. 173–177.

(9) Jörgensen, *J. prakt. Chem.*, [2] **23**, 227 (1881).

(10) Kolthoff and Sandell, "Textbook of Quantitative Inorganic Analysis," The Macmillan Co., New York, 1936, p. 536.

NH_3, 25.79; NH_3 + NO_3 as N, 33.95. Found: NH_3, 25.70; N, 33.84.

Two standard phosphate solutions were employed. One was prepared and standardized by the method of Furman and State.[4] The other was prepared by weighing out a definite amount of twice recrystallized potassium dihydrogen phosphate (Merck reagent grade) which had been dried to constant weight at 100° and dissolving and making up to a definite volume. The phosphorus content of this solution was checked by double precipitation as magnesium ammonium phosphate and ignition to the pyrophosphate. These solutions will be designated as A and B, respectively. Solution A contained 0.2956 mg. of phosphorus per ml. and solution B contained 0.3196 mg. of phosphorus per ml.

Acid sodium molybdate was prepared immediately prior to use according to Furman and State,[4] using Merck reagent grade molybdic acid. This solution is approximately 1.4 molar.

The potassium permanganate solution used in the molybdenum determinations was standardized against the best obtainable sodium oxalate.

The ferric alum used in the molybdenum determinations was Merck reagent grade. A blank on this and the Jones reductor used was quite small and consistent, 0.10–0.12 ml. of 0.1 *N* potassium permanganate.

The sulfuric acid and sodium hydroxide used were the ordinary C. P. reagents.

Precipitations.—The precipitates were formed, filtered, washed and dried according to the directions of Furman and State.[4] The above-mentioned pentammines were used as precipitants. Solutions of these were prepared immediately prior to use and were approximately 0.025 molar in all cases.

The procedure follows. To the phosphate contained in a volume of approximately 8 ml. and free of nitric and hydrochloric acids but containing approximately 36 milliequivalents of sulfuric acid add 1 ml. of acid sodium molybdate solution for each milligram of phosphorus present. After heating the solution to near boiling, slowly add the pentammine solution. The rates of formation of precipitates increased in the order chloropentammine, nitratopentammine, aquapentammine. This is in agreement with known rates of conversion of the acido ions to the aquapentammine ion. Sufficient precipitant was added in all cases to color the supernatant liquid pink and then an excess of 2–3 ml. in the aqua and nitrato cases. Complete precipitation could not be obtained in the case of the chloropentammine unless an excess of 6–8 ml. of precipitant was used. In all cases the solutions were kept near the boiling point for five to ten minutes to ensure complete precipitation. Longer digestion, fifteen to twenty minutes, was found necessary in the case of the chloropentammine. The volume of solution in all cases was approximately 20 ml. After cooling to room temperature the solutions were filtered through a porous porcelain crucible. The precipitates were washed free of sulfuric acid with 0.3 *N* nitric acid and then once with a small portion of water. The crucibles and contents were washed with 95% alcohol followed by ether. Air was drawn through the crucible for five minutes. The outside of the crucible was wiped with a lintless cloth and the former was placed in an evacuated desiccator over calcium chloride. The crucibles were weighed after thirty minutes. The results of some of the precipitations with the pentammine reagents are given in Table I.

Precipitations were carried out in a similar manner using hexammine cobaltic chloride as the precipitant. This solution was made up approximately 0.025 molar. It was found necessary in these cases to double the amount of sulfuric acid present in order to prevent the precipitation of the molybdate of the ammine. A small excess, 2–3 ml., of precipitant beyond that necessary to color the supernatant liquid orange was used. Table II contains the results of precipitations with the hexammine reagent.

The theoretical weights of precipitate according to the proposed formula for the cobaltic aquapentammine molybdophosphate are given in Table I. Similar data are given in Table II for cobaltic hexammine molybdophosphate.

TABLE I

PRECIPITATIONS OF 12-MOLYBDOPHOSPHATE WITH COBALTIC PENTAMMINE SALTS

Standard soln. used	Volume taken, ml.	Phosphorus taken, mg.	Precipitant used	Wt. of ppt., g.	Theoretical wt.,[a] g.
A	10.01	2.959	Aqua	0.1970	0.1965
A	10.01	2.959	Nitrato	.1961	.1965[b]
A	10.01	2.959	Chloro	.1966	.1965
A	25.01	7.393	Aqua	.4914	.4909
A	25.01	7.393	Nitrato	.4907	.4909[b]
A	25.01	7.393	Chloro	.4901	.4909
B	25.01	7.993	Aqua	.5294	.5307
B	25.01	7.993	Nitrato	.5300	.5307[b]
B	25.01	7.993	Chloro	.5280	.5307
A	49.98	14.77	Aqua	.9790	.9810
A	49.98	14.77	Nitrato	.9795	.9810[b]

[a] The theoretical values are calculated from the amount of phosphorus taken and the formula $[Co(NH_3)_5(H_2O)]PMo_{12}O_{40}\cdot 4H_2O$. [b] The theoretical values in these cases according to the formula proposed by Furman and State[4] are, respectively, 0.1956, 0.4886, 0.5283, 0.9764.

TABLE II

PRECIPITATIONS OF 12-MOLYBDOPHOSPHATE WITH COBALTIC HEXAMMINE CHLORIDE

Standard soln. used	Volume taken, ml.	Phosphorus taken, mg.	Wt. of ppt., g.	Theoretical wt.,[a] g.
B	4.98	1.592	0.1043	0.1047
B	4.98	1.592	.1051	.1047
B	10.01	3.199	.2109	.2105
B	10.01	3.199	.2107	.2105
B	25.01	7.993	.5263	.5258
B	25.01	7.993	.5271	.5258
B	49.98	15.97	1.055	1.051
B	49.98	15.97	1.057	1.051

[a] The theoretical values are calculated from the amount of phosphorus taken and the formula $[Co(NH_3)_6]PMo_{12}O_{40}\cdot 3H_2O$.

Method of Analysis of Precipitates.—Samples for analysis were prepared and dried as mentioned above. Ammonia was determined by distillation from a sodium hydroxide solution into an excess of standard hydrochloric

acid, the excess being titrated with standard sodium hydroxide using methyl red as an indicator.

In the case of precipitates formed using the nitratopentammine reagent, total ammonia plus nitrate determinations were carried out using a modified Kjeldahl method.[10] This method was tested successfully on samples composed of pure potassium nitrate and the molybdophosphate precipitated with the aquapentammine reagent, the combined ammonia and nitrate value being known in these samples.

Molybdenum was determined in samples which were dissolved in a minimum of sodium hydroxide solution and warmed until all ammonia had been expelled. The cobaltic hydroxide thus formed dissolved on the addition of 10 ml. of concentrated sulfuric acid. The solution was evaporated to the fumes of sulfur trioxide and fumed for three to five minutes. This served to destroy any hydrogen peroxide, nitrate and chloride. After dilution the solution was passed through a Jones reductor and the reduced solution was caught under an excess (5-fold) of ferric alum. After the addition of a few ml. of phosphoric acid the solution was titrated with standard potassium permanganate solution. A blank was run on all reagents, including appropriate amounts of cobalt and phosphorus, and the proper correction made. This was never more than 0.12 ml. of 0.1 *N* potassium permanganate solution.

Cobalt and phosphorus determinations were not carried out since the amounts of these constituents are so small that nothing definite would be established by them. Furman and State[4] determined these constituents in the precipitate formed with the nitratopentammine reagent. Their values agree closely with the theoretical values of these constituents on the basis of the formula proposed above for the aquapentammine molybdophosphate.

The precipitates formed using the aquapentammine and chloropentammine reagents were tested qualitatively for chloride. This constituent was found in small amounts. Its presence is probably due to occlusion or post-precipitation.

Results of Analysis.—Some typical results on the precipitate formed using the aquapentammine precipitant follow.[11] Found: NH_3, 4.16, 4.18; Mo, 55.87, 55.91. For the precipitate formed using the nitratopentammine precipitant: Found: NH_3, 4.15, 4.17; Mo, 56.05, 56.15; Total $NH_3 + NO_3$, calcd. as NH_3, 4.16, 4.17. For the precipitate formed using the chloropentammine precipitant: Found: NH_3, 4.19, 4.17; Mo, 55.85, 56.03. The theoretical values according to the proposed formula for the aquapentammine molybdophosphate: calcd. for $[Co(NH_3)_5(H_2O)]PMo_{12}O_{40}\cdot 4H_2O$: NH_3, 4.14; Mo, 55.99; Total N as NH_3, 4.14.

With the precipitate formed using hexammine cobaltic chloride as the precipitant the following are some typical results. Found: NH_3, 4.96, 4.99; Mo, 56.46, 56.63. Calcd. for $[Co(NH_3)_6]PMo_{12}O_{40}\cdot 3H_2O$: NH_3, 5.02; Mo, 56.51.

(11) During the progress of the work which Professor Horan reports in the present paper, he communicated his conclusions regarding the complete aquation of the nitratopentammine salt to us, and these were confirmed by one of us (H. M. S.) and forwarded to Dr. Horan in August of 1938. Although qualitative tests for nitrate may sometimes be obtained, State's quantitative estimations made in 1938 by the Devarda alloy reduction method and subsequent distillation of ammonia gave the same value for total nitrogen as did the direct distillation of the ammonia after adding alkali alone.—[N. H. FURMAN and H. M. STATE.]

Discussion[11]

The results of precipitations and analysis of the salt formed using the nitratopentammine reagent agree closely with those of Furman and State.[4] However, these authors did not determine total ammonia and nitrate and assumed the presence of the latter. The above analysis shows definitely the absence of nitrate. The above results also show definitely that the compound formed with the different pentammine reagents is always the same.

The hexammine and aquapentammine molybdophosphates are similar in composition. The former apparently has three moles of water of crystallization per mole of the salt, while the latter apparently has four. The direct determination of water is not reliable due to decomposition of the salts at temperatures sufficiently high to drive off all of this constituent. We would expect a close similarity between the two salts due to the similar structures of the cations, $Co(NH_3)_5(H_2O)^{+++}$ and $Co(NH_3)_6^{+++}$.

The precipitation of phosphate in the form of such complex compounds is the basis of a satisfactory gravimetric determination of this constituent. Hexammine cobaltic chloride would seem to be the best precipitant. Furman and State[4] claim the nitratopentammine reagent gives the most satisfactory precipitate for analytical purposes. They mention the difficulty of filtering and washing the hexammine precipitate. This difficulty is not apparent except when dealing with very large amounts of precipitate, 1 g. or more, and in such cases the method is scarcely applicable. In view of the comparative ease of preparation and purification as well as stability of solutions, the hexammine precipitant would seem preferable to the nitratopentammine. An additional disadvantage of the nitratopentammine is its low solubility, approximately 8.5 g. per liter. This necessitates the use of large volumes of reagent in many cases, causing unnecessary dilution of the solution. The hexammine reagent easily can be made up ten times as strong as the nitrato reagent. The former has been used successfully in other gravimetric determinations.[12,13]

(12) M. Parks, Dissertation, Columbia University, 1930.

(13) Hynes and others, *Ind. Eng. Chem., Anal. Ed.*, **8**, 356 (1936).

Conclusions

The compositions of the cobaltic pentammine and hexammine salts of 12-molybdophosphoric acid have been determined. The divalent acido cations do not directly form salts with this acid but react with water forming a trivalent ion which then reacts with the molybdophosphate.

The compositions of the cobaltic hexammine molybdophosphate and the cobaltic aquapentammine molybdophosphate are quite similar.

Suggestions have been made concerning the use of hexammine cobaltic chloride as a reagent in the quantitative determination of phosphates.

BROOKLYN, N. Y. RECEIVED MARCH 16, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

The Protium–Deuterium Ratio and the Atomic Weight of Hydrogen

BY JOHN A. SWARTOUT AND MALCOLM DOLE

On the basis of a protium–deuterium ratio in normal water[1] of 5000, the International Committee on Atomic Weights[2] recently changed the accepted atomic weight of hydrogen from 1.0078 to 1.0081; no reference to the source of this ratio, 5000, was given and the Committee apparently overlooked the work of Gabbard and Dole[3] who found 6900 and of Hall and Jones[4] who found 6500. It is the purpose of this paper to demonstrate by a new exchange reaction method the validity of the Gabbard–Dole ratio of 6900, and to point out that the chemical atomic weight of hydrogen is probably closer to 1.0080 than to 1.0081. At the same time we shall also reinvestigate the density of water made from atmospheric oxygen as compared to normal water inasmuch as the published data in the literature vary from 6.0 to 8.6γ[5] for this important constant of nature. We use methods presumably free of isotopic errors, or uncertainties inherent in electrolytic separation, in combustion, in dubious extrapolations or corrections to the data and in isotopic exchange equilibria which are functions of temperature. Furthermore, a modified float method of measuring densities sensitive to $\pm 0.1\ \gamma$ or better and improved techniques throughout increase the reliability of the final observations.

In principle the new method consists in the continued elimination of all the heavy hydrogen from normal water through repeated exchange reactions $H_2 + HOD \rightleftarrows HD + HOH$, without affecting the isotopic composition of the oxygen, until the density of the water has been reduced to a constant minimum value. From the γ-value of this water the protium–deuterium ratio in normal water can be calculated. By burning deuterium-free hydrogen in excess with oxygen of the air, the relative atomic weight of atmospheric oxygen can be calculated from the appropriate combination of the above data.

We have also measured the protium–deuterium ratio in Atlantic Ocean water in order to investigate the influence of the source of the water on this ratio.

Experimental

Preparation of Deuterium-free Water Containing Atmospheric Oxygen.—The deuterium-free water which served as a source of D-free hydrogen was prepared by the fractional electrolysis of water using the cells of Gabbard and Dole.[3] The complete elimination of deuterium was proved by combining the hydrogen from each successive electrolysis with atmospheric oxygen, the hydrogen always being in excess, and by measuring the density of the resulting water. When a minimum value of the density had been attained, the water was assumed to be D-free. Data obtained in this work are given in Table I and plotted in Fig. 1, where the rapidity with which deuterium is eliminated by electrolytic fractionation (factor equal to 5.2) is readily seen. In this plot the diameter of the circles is twice as great as the experimental error.

TABLE I

DATA FOR DENSITIES OF WATER MADE FROM HYDROGEN ON SUCCESSIVE ELECTROLYTIC FRACTIONATION AND ATMOSPHERIC OXYGEN

No. electrolytic fractionations	γ
1	−5.9
2	−7.5
3	−8.9
4	−8.9 ± 0.1
5 (Gabbard and Dole[3])	−9.0 ± 0.3
4 (Hall and Jones[4])	−8.9 ± 0.3

(1) We define the term "normal water" in this paper as signifying purified Lake Michigan water.

(2) G. P. Baxter, O. Hönigschmid and P. LeBeau, THIS JOURNAL, **60**, 737 (1938).

(3) J. L. Gabbard and M. Dole, *ibid.*, **59**, 181 (1937). For references to earlier results see this paper.

(4) N. F. Hall and T. O. Jones, *ibid.*, **58**, 1915 (1936).

(5) γ is defined as the excess density of the water in question over that of normal water in parts per million. A negative sign for γ means that the water is lighter than normal.

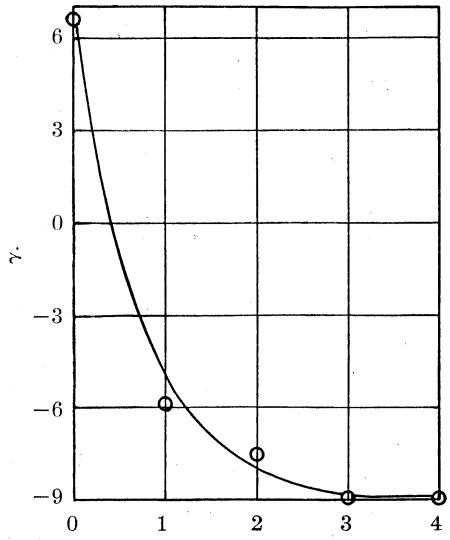


Fig. 1.—Density of water produced from the combustion of hydrogen from successive electrolyses with air oxygen.

Considering the excellent agreement between these independent measurements of the γ-value of D-free water containing atmospheric oxygen, there seems to be little reason to doubt the reliability of our final value of $-8.9\ \gamma$.

Preparation of Deuterium-free Water Containing Normal Oxygen.—In order to prepare water containing normal Lake Michigan oxygen and D-free hydrogen, the D-free hydrogen produced by five electrolytic cells operating at ten amperes current was first purified by passing over hot copper to remove all oxygen, dried over calcium chloride, then bubbled through a sample of Lake Michigan water at 85°. The mixture of water vapor and hydrogen in a ratio of 1:2 was passed through a tube, 60 × 2.8 cm., containing platinized asbestos as a catalyst, and heated to 450°. Following the isotopic exchange, the water vapor was condensed in a water condenser, followed by a carbon dioxide–acetone trap. The exchanged hydrogen was conserved by burning with air over a copper catalyst.

Since equilibrium was reached during the passage of the vapors over the platinum, it was necessary to make a number of runs with each sample in order to reduce the deuterium concentration to a negligible value. The number of repetitions necessary for this was estimated from the equilibrium constant for the reaction at 450° 0.825, which was obtained by extrapolation of the data of Jones and Sherman.[6] According to this calculation, the density of the sample should be within 0.1 p. p. m. of D-free water after seven runs.

In order to test this experimentally, an exploratory set of experiments was made, in which the density of the sample was measured after each equilibration. In these and all following experiments the D-free hydrogen was conserved by using hydrogen from the second electrolysis in the first three runs, that from the third electrolysis in the fourth and fifth runs, and that from the fourth electrolysis in all succeeding runs. The final result of this exploratory set can be given no weight because, first, a portion of the sample was lost during the density measurements; second, the temperature measurements at which floating equilibrium occurred were made with a Beckmann instead of a platinum thermometer; third, no extreme precautions were made in the purification of the samples, being distilled only from alkaline permanganate in Pyrex apparatus; and, fourth, the hydrogen in the final runs may not have been D-free, since no check was made upon it. A 150-ml. sample of normal Lake Michigan water was taken and six runs made. The data for the densities as measured after each equilibrium are collected in Table II and plotted in Fig. 2.

TABLE II

DATA FOR THE DENSITIES OF THE WATER OBTAINED IN THE EXPLORATORY TEST OF THE EXCHANGE FRACTIONATION

Equilibration no.	Δt, °C.	γ
1	−0.024	− 6.2
2	− .036	− 9.2
3	− .047	−12.0
4	− .054	−13.8
5	− .057	−14.5
6	− .057	−14.5

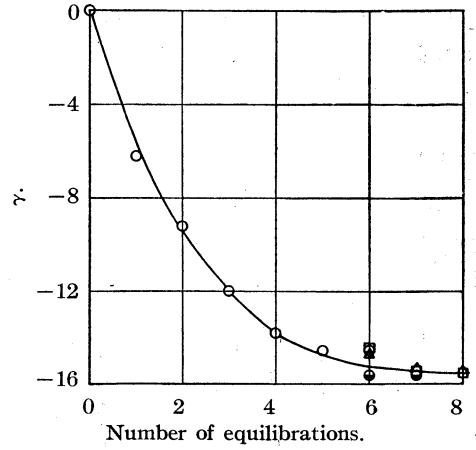


Fig. 2.—Decrease in density for each run through equilibrator: ○, exploratory expt.; □, sample 1; △, sample 2; ◒, sample 3.

Following this work three new sets of experiments were made to determine the concentration of deuterium in three samples of Lake Michigan water. One sample of 300 ml. was taken directly from Lake Michigan while one of 300 ml. and one of 100 ml. were taken from the laboratory distilled water supply. Measurements showed that the laboratory distilled water has the same density as that in the Lake within $\pm 0.1\ \gamma$. Six equilibrations were made on each sample under the same conditions as in the exploratory sample. The original sample and the condensate after each run were weighed to determine any loss of water which might have occurred. In no case was the loss greater than 0.6%. After the sixth equilibration the water was purified and the density determined by the improved method. Repeated exchange equilibrations were then made until the density of the resulting water had been reduced to a minimum value (within the experimental error).

(6) T. Jones and A. Sherman, *J. Chem. Phys.*, **5**, 375 (1937).

TABLE III

DENSITY OF WATERS AFTER EQUILIBRATION WITH D-FREE HYDROGEN

Equilibration no.	γ
Sample 1	
1–6	−14.4
7	−15.4
8	−15.5
Sample 2	
1–6	−14.6
7	−15.2
8	−15.4
Sample 3	
1–6	−15.6
7	−15.6

A blank was run using nitrogen instead of hydrogen in order to make certain that no factor other than the removal of deuterium such as a possible change in the oxygen isotopic ratio caused the decrease in density. Nitrogen was passed through the apparatus in exactly the same way as was the hydrogen. Two evaporations and condensations of normal water were made, then the density was compared to that of the original water. No difference in density could be detected.

A 100-ml. sample of water taken from the Atlantic Ocean 45 miles east of Cape Ann, Massachusetts, was subjected to the same number of equilibrations as was the Lake Michigan water. Table IV gives the results of density measurements made upon this sample.

TABLE IV

DATA FOR THE DENSITY OF DEUTERIUM-FREE ATLANTIC OCEAN WATER

Equilibrations	γ
1–6	−13.6
7	−14.0
Normal ocean water	+ 1.7

From the last value of γ given in Table IV it is evident that normal ocean water is 1.7 p. p. m. heavier than normal Lake Michigan water, and that ocean water from which all deuterium has been removed is 14.0 p. p. m. lighter than normal lake water. This indicates that the difference between normal ocean water and ocean water with no deuterium is equal to: 14.0 + 1.7 = 15.7 p. p. m. Another equilibration might have been made on the ocean water, since the difference between the density of the water after equilibrations six and seven is slightly outside the experimental error, but by analogy to the other experiments seven equilibrations should have been sufficient to remove all the deuterium.

The difference in concentration of the oxygen isotopes in air can be calculated from the difference between the densities of water containing air oxygen and no deuterium (Table I) and water containing normal Lake Michigan oxygen and no deuterium (Table III). The density difference of these two waters is $-15.5 - (-8.9) = -6.6$ γ.

Purification of Water Samples and Density Measurements.—The modified density measuring apparatus employing a platinum resistance thermometer and the new purification techniques were built and worked out by Mr. R. L. Slobod in a study of the isotopic composition of oxygen in carbonate rocks. This work will be submitted shortly for publication. It is sufficient to state here that every attempt was made to reduce all errors in the relative density measurements to less than 0.1 γ; since repeated determinations usually agreed with each other within this range, we believe that our results are reliable, at least as far as the density measurements are concerned, to this small error.

Discussion

The Protium–Deuterium Ratio.—The average value for the difference between the densities of normal Lake Michigan water and water having the same oxygen isotopic content and no deuterium is given by the average of the data of Table III, or -15.5 ± 0.1 γ. From this value the H/D ratio in normal water was found making use of the recent value for the density of pure deuterium oxide recently published by Stokland, Tronstad and Ronaess,[7] 1.10764, and still more recently by Johnston,[8] 1.10763. The mole fraction of deuterium oxide was calculated with aid of the equation published by Swift[9]

$$N_{D_2O} = \frac{9.257 \times 10^{-6}\,\gamma}{1 - 3.3 \times 10^{-8}\,\gamma}$$

Since the H/D ratio is given by the ratio N_{H_2O}/N_{D_2O} (here H_2O refers to pure protium oxide) our final result is 6970/1 or in round numbers 7000 ± for the H/D ratio.

In Table V we have collected for purposes of comparison previous estimates of this ratio.

TABLE V

DENSITY DIFFERENCES BETWEEN DEUTERIUM-FREE WATER AND NORMAL WATER FROM VARIOUS INVESTIGATORS

	Source of water	γ	H/D ratio
This investigation	Lake Michigan	−15.5	6970
	Atlantic Ocean	−15.7	6880
Gabbard and Dole[3]	Lake Michigan	−15.4	7020
Hall and Jones[4]	Lake Mendota	−16.5	6550
Johnston[10]	Columbus, Ohio	−18.3	5900
Morita and Titani[11]	Osaka, Japan	−17.1	6320
Tronstad, Nordhagen,[12] and Brun	Rjukan, Norway	−18.5	5840
Tronstad and Brun[13]	Rjukan, Norway	−20.0	5400

From a study of this table it is evident that our results for both Atlantic Ocean and Lake Michigan water give a smaller amount of deuterium in water than any of the other results. Indeed our

(7) K. Stokland, E. Ronaess and L. Tronstad, *Trans. Faraday Soc.*, **35**, 312 (1939).

(8) H. L. Johnston, THIS JOURNAL, **61**, 878 (1939).

(9) E. Swift, *ibid.*, **61**, 198 (1939).

(10) H. L. Johnston, *ibid.*, **57**, 484, 2737 (1935).

(11) N. Morita and T. Titani, *Bull. Chem. Soc. Japan*, **13**, 419 (1938).

(12) L. Tronstad, J. Nordhagen and J. Brun, *Nature*, **136**, 515 (1935).

(13) L. Tronstad and L. Brun, *Trans. Faraday Soc.*, **34**, 766 (1938).

method of analysis of the water is such that it should give such a minimum value; that is, we know that there is at least as much heavy hydrogen in water as we find because our chief sources of error all tend to make the H/D ratio larger. Thus if we have not eliminated all the deuterium in our preparation of D-free water by either method, if any oxygen of the air leaked into our exchange apparatus, if our D-free water became contaminated in any way with ordinary water, the density of the D-free water would be greater than it should be and the amount of deuterium found correspondingly too small. But the reduction of the density of normal water to a constant minimum value, and the fact that no water was gained or lost in the exchange experiments, seem to rule out the first two possibilities. Five cc. of ordinary water mixed with 100 cc. of our water of γ value equal to -15.5 would produce an error of 1 p. p. m., but we estimate that the amount of ordinary water gained by the light water in the course of a density determination was 0.1 cc. or less since the distilling flask, condenser, receiver, and density measurement tube were always dried out before introducing the light water. The Pyrex float was the only object covered with a film of ordinary water that came into contact with the sample under investigation.

We believe that our method, eliminating as it does all uncertainty in regard to the isotopic composition of the oxygen, yields a reliable result. Furthermore since no great difference was found by us for the H/D ratio in Lake Michigan and Atlantic Ocean water, we disagree with the conclusion of Tronstad and Brun[13] that the varying results of the different investigators indicate varying concentrations of deuterium in waters of different localities. As pointed out before by one of us[14] slight differences in density of water from various natural sources are due primarily to variations in the oxygen isotope ratios. A further indication of the reliability of our H/D ratio is given in the following paragraph.

The Relative Atomic Weight of Atmospheric and Water Oxygen.—From the data of Tables I and III it is evident that the difference in density between normal water and water made from oxygen of the air is 6.6 γ, the latter water being the heavier. In Table VI this value is given along with previous determinations by other investigators.

(14) M. Dole, *J. Chem. Phys.*, **4**, 778 (1936).

TABLE VI

DIFFERENCES IN DENSITY BETWEEN NORMAL WATER AND WATER MADE FROM ATMOSPHERIC OXYGEN AND NORMAL HYDROGEN

	γ
This investigation	6.6
Dole[15]	6.0
Greene and Voskuyl[16]	6.0
Hall and Johnston[17]	6.6
Jones and Hall[18]	6.1
Morita and Titani[19]	7.0
Smith and Matheson[20]	8.6

With the exception of Smith and Matheson's result of 8.6 γ, all the data of Table VI, although obtained by several methods, are in satisfactory agreement. The average of all the data of Table VI excluding the Smith and Matheson figure is 6.4 γ, which when added to 8.9 γ (from Table I) gives 15.3 γ for the difference in density between normal water and deuterium-free water, a value in close agreement with our experimental data of Table III. Thus the data of Table III are consistent with the data of Tables I and VI; this is an important criterion of the accuracy of the γ values from which the H/D ratio is calculated.

The atomic weight of oxygen in the air is 0.000119 atomic weight units greater than the atomic weight of oxygen in water.

The Chemical Atomic Weight of Hydrogen.—Using our new value for the H/D ratio for normal water in calculating the chemical atomic weight of hydrogen by the same method as that of the International Committee on Atomic Weights[2] we obtain 1.0080 instead of the present accepted value of 1.0081.

Note Added to Proof.—Although we had intended to reserve the detailed discussion of the experimental techniques of water purification for the forthcoming publication with Mr. R. L. Slobod, the appearance of the paper by Greene and Voskuyl [THIS JOURNAL, **61**, 1342 (1939)] prompts us to state that possibly the data of Tables I, II, III, and IV may be as much as 0.25 γ too positive because of the fact that in our distilling apparatus there may have been a greater fractionation and decrease in density of our normal water than of our D-free water. We were unsuccessful in an attempt to demonstrate this difference in the distilling properties of the two types of water, probably because the slight difference expected is about equal to our experimental error. Additional

(15) M. Dole, *ibid.*, **4**, 268 (1936).

(16) C. H. Greene and R. J. Voskuyl, THIS JOURNAL, **58**, 693 (1936).

(17) W. H. Hall and H. L. Johnston, *ibid.*, **58**, 1920 (1936).

(18) T. O. Jones and N. F. Hall, *ibid.*, **59**, 259 (1937).

(19) N. Morita and T. Titani, *Bull. Chem. Soc. Japan*, **11**, 403 (1936).

(20) E. R. Smith and H. Matheson, *J. Research Natl. Bur. Standards*, **17**, 625 (1936).

discussion of the work of Greene and Voskuyl, which overlaps ours to a certain extent, will be given later.

Acknowledgments.—We wish to acknowledge gratefully a grant from the Alexander Dallas Bache Fund of the National Academy of Sciences which made possible the use of the platinum resistance thermometer for measuring temperature. We are also indebted to Mr. R. L. Slobod and Mr. J. L. Gabbard for experimental coöperation.

Summary

1. Water containing normal Lake Michigan oxygen and pure protium has been prepared by an exchange reaction in the gas phase: $H_2 + HOD = HD + HOH$. The density of this water has been found to be 15.5 ± 0.1 p. p. m. lighter than normal Lake Michigan water. From this the ratio of hydrogen atoms to deuterium atoms was calculated to be 6970.

2. Water containing normal Atlantic Ocean oxygen and pure protium was prepared by the same method. The difference in density between this and normal Atlantic Ocean water was found to be 15.7 ±0.2 p. p. m., corresponding to a H/D ratio of 6900.

3. Deuterium-free hydrogen was burned with atmospheric oxygen and the density of the water produced was compared with that of water containing normal Lake Michigan oxygen and pure protium. The atmospheric oxygen water was found to be 6.6 p. p. m. heavier, which corresponds to a greater atomic weight of oxygen in air of 0.000119 ± 0.000002 atomic weight units.

4. The chemical atomic weight of hydrogen as calculated from our new H/D ratio is 1.0080 instead of the value of 1.0081 recently adopted by the International Committee on Atomic Weights.

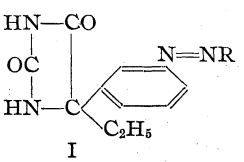
EVANSTON, ILLINOIS RECEIVED MAY 4, 1939

[CONTRIBUTION NO. 155 FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, THE UNIVERSITY OF TEXAS]

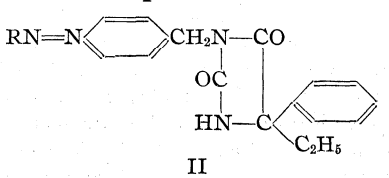
The Synthesis of Colored Derivatives of Nirvanol. II. N-Benzyl Azo Compounds[1]

BY SHIRLEY POWELL LINGO[2] WITH HENRY R. HENZE

Last year there was reported[3] an attempt to convert the soporific called Nirvanol into colored derivatives (I) possessing dyestuff properties. Since it is generally believed that the activity of soporifics is related, at least in part, to the alkyl or aryl groups present in a molecule, it follows that attachment of an azo linkage might so affect the influence of the phenyl group in Nirvanol as to reduce or completely alter its activity. Therefore it was decided to leave intact the phenyl and ethyl groups at the 5-position of the hydantoin nucleus, and to introduce the azo grouping through attachment to a benzyl group linked to the amidic nitrogen of the heterocycle (II).



I



II

In this investigation the sodium salt of Nirvanol was condensed with *p*-nitrobenzyl chloride and the product reduced catalytically to form 3-*p*-aminobenzyl-5-ethyl-5-phenylhydantoin. The latter was diazotized and coupled, in turn, with dimethylaniline, β-naphthylamine, phenol, salicylic acid, α- and β-naphthol, and 1,5-dihydroxynaphthalene, respectively, to form colored azo derivatives. From alkaline solution the dyes derived from phenol, α-naphthol and salicylic acid impart a yellow or orange color, and the 1,5-dihydroxynaphthalene derivative a purple color, to silk or wool. The β-naphthol azo compound is too insoluble in dilute alkali to serve as a dyestuff for these fibers. Likewise, the β-naphthylamine derivative is too little soluble even in concentrated hydrochloric acid to impart color, whereas the azo dyestuff derived from dimethylaniline dyes silk or wool from an acid bath a light purple which is changed to yellow by contact with alkali.

(1) Presented before the Division of Medicinal Chemistry at the 97th meeting of the American Chemical Society, April 3–7, 1939, at Baltimore, Md.

(2) From the Ph.D. thesis of S. P. Lingo in June, 1939.

(3) Spurlock with Henze, THIS JOURNAL, **60**, 3005 (1938).

Experimental

Preparation of *p*-Nitrobenzyl Chloride.—This compound was prepared in satisfactory yield by nitration of benzyl chloride following the procedure of Alway[4]; m. p. 72.5–72.8°.

Preparation of 3-(*p*-Nitrobenzyl)-5-ethyl-5-phenylhydantoin.—A solution of sodium methylate was prepared by action of 23 g. (1 gram atom) of freshly cut sodium with 200 cc. of methanol. To this was added 204 g. (1.0 mole) of Nirvanol[3] (m. p. 198.0–198.5°) dissolved in about 1300 cc. of hot methanol, and the mixture was heated for fifteen hours to accomplish complete reaction. Then, to the clear but slightly yellow colored solution was added 171.5 g. (1.0 mole) of *p*-nitrobenzyl chloride; at first the color of the mixture turned to green, then darkened to a deep brown without turbidity. This solution was heated for seven hours; precipitation of solid material, first noticed at the end of one hour, continued during the next three hours. After standing for twenty-four hours, the solid was separated, washed free of sodium chloride, and dried. The alcoholic solution when diluted with water yielded additional reaction product as well as 9.0 g. of unchanged Nirvanol. The total yield (319 g.) of the nitro compound, of m. p. 170–170.5°, represented 98.5% of the theoretical quantity based on the Nirvanol which reacted. The product was recrystallized from ethyl alcohol and acetone, yielding broad, transparent, colorless needles of m. p. 177.0–177.5° (corr.). The nitrobenzyl derivative is insoluble in water, only slightly soluble in methyl and ethyl alcohols, and is fairly soluble in acetone.

Anal. Calcd. for $C_{18}H_{17}N_3O_4$: N, 12.38. Found: N, 12.16.

The configuration of 3-(*p*-nitrobenzyl)-5-ethyl-5-phenylhydantoin is predicated on the analogous conversion of 5-ethyl-5-phenylhydantoin into 3-methyl-5-ethyl-5-phenylhydantoin.[5]

Preparation of 3-(*p*-Aminobenzyl)-5-ethyl-5-phenylhydantoin.—From 33.9 g. of 3-(*p*-nitrobenzyl)-5-ethyl-5-phenylhydantoin (partially dissolved in 100 cc. of ethanol) was obtained 29.8 g. of the pure amine (96% yield) by reduction using hydrogen under twenty atmospheres pressure with Raney nickel as catalyst at 100°. The 3-(*p*-aminobenzyl) derivative was obtained in the form of colorless, diamond-shaped platelets by adding water to a hot alcohol–acetone solution; m. p. 171.7° (corr.).

Anal. Calcd. for $C_{18}H_{19}N_3O_2$: C, 69.88; H, 6.19; N, 13.59. Found: C, 70.07; H, 6.06; N, 13.53.

Preparation of 3-(Dimethylaniline-*p*-azobenzyl)-5-ethyl-5-phenylhydantoin.—Three and nine-hundredths grams (0.01 mole) of 3-(*p*-aminobenzyl)-5-ethyl-5-phenylhydantoin was dissolved in 100 cc. of water containing 6 cc. of concd. hydrochloric acid; this solution was cooled in ice and treated with a cold solution of 0.69 g. (0.01 mole) of sodium nitrite dissolved in the least volume of water, and the whole mixture allowed to stand for thirty minutes. Then 0.60 g. (0.01 mole) of urea was added to destroy any unreacted nitrous acid and the mixture was stirred during twenty minutes.

To this diazotized solution was added 1.21 g. (0.01 mole) of freshly distilled dimethylaniline causing a yellow color to develop. Ethyl alcohol (about 90 cc.) was added in quantity sufficient to make the solution homogeneous; the solution developed a blood-red color. The addition of about 7 g. of sodium acetate caused an orange-colored solid to separate; the mixture stood overnight.

The solid was filtered, washed with water, and dried in an oven at 105°. The dried material was a very bulky orange powder with a tendency to develop a static electrical charge; yield 4.1 g. (93%). A portion of the solid was dissolved in hot acetone, to which water was added to incipient cloudiness. Set aside to cool, shiny plates separated; filtered, and dried at 105°, 3-(dimethylaniline-*p*-azobenzyl)-5-ethyl-5-phenylhydantoin melts at 228.5–229.0° (corr.). The configuration of this dyestuff is predicated upon the normal tendency of dimethylaniline to form azo derivatives by coupling in the position para to nitrogen. Difficulty was experienced in determining nitrogen by the micro Dumas method until a minute quantity of lead dioxide was added to the sample; neither copper oxide nor potassium chlorate was satisfactory.

Anal. Calcd. for $C_{26}H_{27}N_5O_2$: C, 70.72; H, 6.16; N, 15.87. Found: C, 70.58; H, 6.07; N, 15.73.

Preparation of 3-(β-Naphthylamine-*p*-azobenzyl)-5-ethyl-5-phenylhydantoin.—A solution of 3.09 g. (0.01 mole) of 3-(*p*-aminobenzyl)-5-ethyl-5-phenylhydantoin in 80 cc. of water containing 6 cc. of concd. hydrochloric acid was cooled in ice and diazotized with 0.69 g. (0.01 mole) of sodium nitrite; after twenty minutes the excess of the nitrite was destroyed by addition of 0.60 g. of urea. The diazotized amine was coupled with 1.43 g. (0.01 mole) of β-naphthylamine dissolved in 50 cc. of ethyl alcohol; a bright red solid separated immediately but the mixture was allowed to stand overnight. The product was filtered, washed with water, dried, and then weighed 4.60 g. (99% yield).

The unpurified dyestuff in a melting point tube undergoes a darkening in color and superficial fusion at about 100°, is tarry at about 110°, and is melted with evolution of gas at about 120°. A solution of the azo derivative in glacial acetic acid was poured into ice water to yield a semi-colloidal precipitate that could be coagulated by addition of a few drops of hydrochloric acid. The melting point behavior of the material was unchanged by this treatment. The dyestuff was dissolved in glacial acetic acid, to which some concd. hydrochloric acid had been added, and was reduced by addition of zinc dust. The reduction product was recrystallized from dilute methyl alcohol and from water–acetone mixture; m. p. 170°; mixed melting point with authentic sample of 3-(*p*-aminobenzyl)-5-ethyl-5-phenylhydantoin 171°.

A portion of the original product was heated in an evaporating dish over a free flame until the solid melted to a clear dark red liquid and the evolution of gas had ceased; on cooling a glass-like solid remained. The latter was pulverized and analyzed. Another portion of this heated material was dissolved in glacial acetic acid and reduced with zinc dust and concd. hydrochloric acid. After recrystallization from water–acetone, the melting point was 169°; mixed melting point with an authentic sample of 3-(*p*-aminobenzyl)-5-ethyl-5-phenylhydantoin 170–171°. Qualitative evidence of the recovery of 1,2-diaminonaphthalene from the fusion residue was obtained.

(4) Alway, THIS JOURNAL, **24**, 1060 (1902).
(5) German Patent 611,057

Anal. Calcd. for $C_{28}H_{25}N_5O_2$: C, 72.55; H, 5.44; N, 15.15. Found: C, 72.82; H, 5.39; N, 15.21.

The structural configuration of this azo derivative is predicated upon the usual tendency of β-naphthylamine to couple in the α-position.

Preparation of 3-(Phenol-*p*-azobenzyl)-5-ethyl-5-phenylhydantoin.—This compound could be obtained by coupling the diazotized amine with a solution of phenol in sodium hydroxide and neutralizing the hydrochloric acid formed by means of sodium carbonate, but a slightly better yield of purer product was obtained by proceding similarly to the preparation of the dimethylaniline analog. Thus, 3.09 g. (0.01 mole) of 3-(*p*-aminobenzyl)-5-ethyl-5-phenylhydantoin was diazotized, the excess nitrite decomposed with urea, and to the mixture was added 0.94 g. (0.01 mole) of redistilled phenol, causing the production of a light yellow color. Seven grams of sodium acetate was added and a dull yellow solid separated, but the mixture was allowed to stand overnight before filtration. The solid was washed with water and dried at 105°; the yield was 3.73 g., representing 90% of the theoretical. The dyestuff could be crystallized from acetone–water in the form of clusters of needle-like platelets, m. p. 245–247° (corr.), with gas evolution subsequent to fusion.

Anal. Calcd. for $C_{24}H_{22}N_4O_3$: C, 69.55; H, 5.35; N, 13.52. Found: C, 69.59; H, 5.35; N, 13.46.

The structure assigned to this azo dyestuff is based upon the normal tendency of phenol to couple para to the hydroxyl group.

Preparation of 3-(α-Naphthol-*p*-azobenzyl)-5-ethyl-5-phenylhydantoin.—Diazotization of 3.09 g. (0.01 mole) of 3-(*p*-aminobenzyl)-5-ethyl-5-phenylhydantoin was carried out as usual and the solution poured into one of 1.04 g. (0.01 mole) of α-naphthol in 200 cc. of water containing 4.0 g. of sodium hydroxide. The deep-red colored solution was permitted to stand for one hour before adding a mixture of 15 cc. of concd. hydrochloric acid in 300 cc. of water, with stirring, to precipitate the azo compound. A purple-red flocculent mass was obtained by filtration, which, after washing and drying at 105°, weighed 4.36 g. (94% yield).

The dyestuff behaved as follows upon heating in a melting point tube: began to change color and to sinter at about 120°, formed a tarry sirup at about 140°, had melted sufficiently at 148° to begin a viscous flow down the side of the tube, at about 150° gas evolution began, causing pronounced expansion in volume of the mass. The solid was purified, without change in melting point behavior, by solution in benzene from which it was precipitated by petroleum ether addition. It is a brilliant red substance in finely powdered form, but is much darker in appearance in larger particles. The azo derivative is soluble in the common organic solvents, except petroleum benzine, insoluble in water, and dissolves slowly in 5% sodium hydroxide solution.

Anal. Calcd. for $C_{28}H_{24}N_4O_3$: C, 72.40; H, 5.21; N, 12.06. Found: C, 71.94; H, 5.17; N, 12.17.

The configuration assigned to this compound is based on the usual coupling behavior of α-naphthol, which is para to the hydroxyl group.

Preparation of 3-(β-Naphthol-*p*-azobenzyl)-5-ethyl-5-phenylhydantoin.—The method for preparation of this compound followed that of the phenol derivative. From 3.09 g. (0.01 mole) of the amine and 1.44 g. (0.01 mole) of β-naphthol in alcohol, 4.36 g. (94% yield) of bright red dyestuff was obtained. The product was recrystallized from diluted acetone and from ethyl acetate in the form of dark red crystals, m. p. 212–213° (corr.). Here, too, difficulty was had in analyzing for nitrogen content until a trace of potassium chlorate was incorporated with the sample.

Anal. Calcd. for $C_{28}H_{24}N_4O_3$: C, 72.40; H, 5.21; N, 12.06. Found: C, 72.54; H, 5.22; N, 11.99.

Since it is normal for β-naphthol to form azo compounds by coupling in the α-position, that structure is assigned to this derivative.

Preparation of 3-(1,5-Dihydroxynaphthalene-*p*-azobenzyl)-5-ethyl-5-phenylhydantoin.—Diazotization of 3.09 g. (0.01 mole) of the amine, dissolved in 90 cc. of water containing 7 cc. of concd. hydrochloric acid, was accomplished in the usual manner with 0.76 g. (0.011 mole) of sodium nitrite. The diazotized material was poured into an alkaline solution of 1,5-dihydroxynaphthalene (m. p. 259–260°); the latter was obtained by dissolving 1.60 g. (0.01 mole) in 200 cc. of water containing 4 g. of sodium hydroxide, an amount slightly in excess of that of the hydrochloric acid used for diazotization so that the coupling occurred in basic solution. The development of color was immediate and quite intense, yielding finally a solution so deeply red as to be nearly opaque. The azo dyestuff was precipitated by dropwise addition of the basic solution to a mixture of 300 cc. of water and 20 cc. of concd. hydrochloric acid, utilizing mechanical stirring. A flocculent precipitate resulted, which was filtered, washed, and dried at 105° to a hard, red-black cake weighing 4.85 g. (100% yield).

Attempts at purification of the product were not very satisfactory; in general, an ether solution was shaken repeatedly with water, concentrated, and diluted with petroleum ether to reprecipitate the dyestuff. After drying over calcium chloride, the solid when heated darkened at about 140°, sintered at about 148–158° forming small tarry globules, the latter began a viscous flow at about 168°, and apparently became liquid at about 194°, above which temperature gas evolution caused pronounced expansion; after many and tedious attempts to dissolve out the more soluble portions of material, incipient fusion did not occur below 194° but decomposition with evolution of gas took place at 196°. Material of this latter melting point behavior was analyzed.

Anal. Calcd. for $C_{28}H_{24}N_4O_4$: C, 69.99; H, 5.03; N, 11.66. Found: C, 69.60; H, 5.07; N, 11.51.

The structure of this azo derivative is based upon the behavior of 1,5-dihydroxynaphthalene in coupling in the 2-position in forming azo dyes such as Diamond Black PV.

Preparation of 3-(Salicylic Acid-*p*-azobenzyl)-5-ethyl-5-phenylhydantoin.—A solution was made by dissolving 3.09 g. (0.01 mole) of 3-(*p*-aminobenzyl)-5-ethyl-5-phenylhydantoin in 80 cc. of water containing 7 cc. of concd. hydrochloric acid, cooled in ice and treated with 0.76 g. (0.011 mole) of sodium nitrite dissolved in 5 cc. of cold water. After standing for thirty minutes, the solution of diazonium salt was added with stirring to 1.38 g. (0.01

mole) of salicylic acid dissolved by 4 g. of sodium hydroxide in 200 cc. of water. The azo dyestuff was precipitated by dropping its alkaline solution slowly into a solution of 20 cc. of concd. hydrochloric acid in 300 cc. of water; vigorous stirring caused the separation of a flocculent precipitate. The latter was filtered, washed, and dried *in vacuo* for twenty-four hours. The weight, 4.4 g., represents a yield of 96% of the theoretical.

The resulting dyestuff was a light tan-colored solid which developed an extreme electrical charge when reduced to an amorphous powder by grinding. It exhibited the following behavior when heated: namely, its color deepened at 80–90°, and the solid began to melt at about 110° to a gummy solid. Above this temperature there was progressive softening, and at about 125–130° the material evolved a gas causing much expansion of the mass. No definite melting point or decomposition point could be recognized.

This azo derivative could not be recrystallized from any of the common organic solvents by dilution with water, for such addition of water caused separation of a gum which would not harden subsequently. It fuses in hot water at about 80°. The dyestuff was recrystallized from tetralin, yielding yellow-orange colored microscopic crystals. The latter could be dried at 110° and melted at 133–134°, although darkening occurred at about 125°; gas evolution took place above the melting point. Analysis was made of the recrystallized azo compound.

Anal. Calcd. for $C_{25}H_{22}N_4O_5$: C, 65.49; H, 4.84; N, 12.22. Found: C, 65.88; H, 4.77; N, 12.10.

It is assumed that salicylic acid couples para to the hydroxyl group in forming this derivative in analogy to its behavior in forming Crumpsall Yellow.

Summary

1. Nirvanol has been converted into colored derivatives. The latter contain a substituted aryl-azo-benzyl grouping attached to the nitrogen in the 3-position of the heterocycle.

AUSTIN, TEXAS RECEIVED MAY 8, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE MALTBIE CHEMICAL CO.]

Sulfanilamido Derivatives of Heterocyclic Amines[1]

BY RUSSEL J. FOSBINDER AND L. A. WALTER

Since the discovery by Domagk[2] that compounds containing the sulfanilamido structure are more or less effective in combating streptococcic infections in animals, hundreds of modifications of the parent structure have been prepared and tested for anti-bacterial activity.

This paper describes sulfanilamido derivatives of the pyridine and thiazole series, some of which were prepared before the especially interesting announcement by Whitby[3] that 2-sulfanilamidopyridine was effective against pneumococcic infections.

Through the kindness of Dr. Ralph Mellon and Mr. Frank B. Cooper at Western Pennsylvania Hospital, Pittsburgh, several of the compounds were tested pharmacologically in mice to determine their anti-streptococcic and anti-pneumo-

TABLE I

PROPERTIES OF THE NEW COMPOUNDS AND ANALYTICAL DATA

Compound[a]	M. p., °C.	Formula	% Nitrogen Calcd.	% Nitrogen Found[b]
2-*p*-Nitrobenzenesulfonamido-6-aminopyridine	228–230	$C_{11}H_{10}N_4O_4S$	19.04	18.75
2-Sulfanilamido-6-aminopyridine	204–206	$C_{11}H_{12}N_4O_2S$	21.20	20.93
2-N[4]-acetylsulfanilamido-6-aminopyridine	194–196[c] 237–239	$C_{13}H_{14}N_4O_3S$	18.29	18.19
2-*p*-Nitrobenzenesulfonamido-4-methylthiazole	197–199	$C_{10}H_9N_3O_4S_2$	14.04	13.91
2-N[4]-acetylsulfanilamido-4-methylthiazole	259–260	$C_{12}H_{13}N_3O_3S_2$	13.47	13.17
2-N[4]-acetylsulfanilamidothiazole	256–257	$C_{11}H_{11}N_3O_3S_2$	14.14	13.90
2-Sulfanilamido-4-methylthiazole	236–238	$C_{10}H_{11}N_3O_2S_2$	15.61	15.55
2-Sulfanilamidothiazole	194–196	$C_9H_9N_3O_2S_2$	16.46	16.31

[a] Nomenclature according to Crossley, Northey and Hultquist, THIS JOURNAL, **60**, 2217 (1938). [b] Kjeldahl. [c] Melts, then crystallizes and melts with decomposition at the higher temperature.

TABLE II

PHARMACOLOGICAL ACTIVITY OF THE NEW COMPOUNDS

Compound	Effect: Anti-streptococcic	Effect: Anti-pneumococcic
2-N[4]-acetylsulfanilamido-6-aminopyridine	Slight	None
2-Sulfanilamido-6-aminopyridine	Good	Good
2-Sulfanilamido-4-methylthiazole	Good	Good
2-Sulfanilamidothiazole	Good	Good
2,6-Diamino-3-*p*-sulfonamidophenylazopyridine[a]	None	None
Sulfanilamide	Good	Fair
Sulfapyridine (2-sulfanilamidopyridine)	Good	Good

[a] Mietzsch and Klarer, U. S. Patent 2,148,705.

(1) Presented before the Division of Medicinal Chemistry, A. C. S., Baltimore, April 6, 1939.

(2) Domagk, *Deut. Med. Wochschr.*, **61**, 250 (1935).

(3) Whitby, *Lancet*, **1**, 1210 (1938).

coccic activity as compared to the action of sulfanilamide and sulfapyridine. A sulfonamidophenylazopyridine derivative also tested, is included in Table II.

The observations on chemotherapeutic efficacy are of interest and justify a detailed study of the toxicological properties of the most active compounds. The results seem to indicate that heterocyclic amino compounds, other than 2-aminopyridine, may be coupled with the sulfanilyl radical without great change in physiological activity.

Experimental

2-Aminothiazole and 2-amino-4-methylthiazole were prepared by treating thiourea with α,β-dichloroethyl ether, and with chloroacetone, respectively.[4]

The nitro and acetamino sulfonamides were prepared by treating two moles of heterocyclic amine with one mole of the required sulfonyl chloride in ethyl acetate or dioxane solution, as shown in the following preparation.

2 - *p* - Nitrobenzenesulfonamido - 6 - aminopyridine.—Twenty-one and eight-tenths grams of 2,6-diaminopyridine in 200 cc. of ethyl acetate was poured into a solution of 22.1 g. of *p*-nitrobenzenesulfonyl chloride in 75 cc. of ethyl acetate. The solution was kept in cold water for several hours with an occasional shaking and then let stand overnight at room temperature. The solvent was distilled on a steam-bath and the oily residue shaken with 200 cc. of cold water until it crystallized. The product was filtered off and recrystallized from alcohol with the use of a little decolorizing charcoal. The yield was 22 g. It was soluble in dilute alkalies.

2 - Sulfanilamido - 6 - aminopyridine. 1.—Twenty-two grams of the above nitro compound was stirred with 200 cc. of 10% hydrochloric acid and an excess of finely divided tin. The mixture was kept at 50° for half an hour, filtered while still warm and diluted with water. The tin salts were precipitated with hydrogen sulfide and the filtered solution neutralized with sodium bicarbonate to precipitate the sulfanilamide. The crude material was recrystallized from alcohol, yield 15.5 g. (80%). It was soluble in dilute acids and dilute alkali.

2.—Attempts to hydrolyze the acetyl group from 2-N^4-acetylsulfanilamido-6-aminopyridine by refluxing with 10% hydrochloric acid gave chiefly sulfanilic acid. The acetyl group was removed with practically quantitative yields of the desired sulfanilamide by refluxing with ten times its weight of 5–10% sodium hydroxide for forty-five minutes.

Sulfanilamidothiazoles.—Reduction of 2-*p*-nitrobenzenesulfanilamido-4-methylthiazole with tin and hydrochloric acid as described for the pyridine compound gave only 30% of 2-sulfanilamido-4-methylthiazole.

The acetyl group was hydrolyzed from the 2-N^4-acetylsulfanilamidothiazole by refluxing with ten times its weight of 10% hydrochloric acid for half an hour. The yield of 2-sulfanilamidothiazole was about 70%. Longer refluxing gave a much lower yield. The 2-sulfanilamido-4-methylthiazole was also prepared in this manner. The sulfanilamidothiazoles were soluble in dilute acids and dilute alkali.

Summary

Some 2-sulfanilamido thiazoles and pyridines have been prepared and their chemotherapeutic activity against experimental streptococcic and pneumococcic infections in mice has been determined.

Several of the compounds appear to possess anti-streptococcic and anti-pneumococcic efficacy comparable to sulfanilamide and sulfapyridine, respectively.

NEWARK, N. J. RECEIVED APRIL 18, 1939

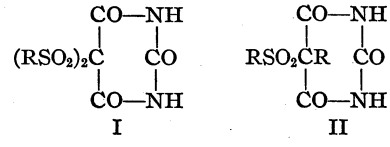
(4) Traumann, *Ann.*, **249**, 36 (1888).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING AT THE UNIVERSITY OF PENNSYLVANIA]

5-Sulfonylbarbituric Acids[1]

BY EDMOND L. D'OUVILLE,[2] FREDERICK J. MYERS AND RALPH CONNOR

α-Sulfonylamides[3] were effective enough as hypnotics to encourage a continued investigation of compounds containing the sulfone group combined with other groups that are present in some of the common hypnotics. Attention was naturally directed toward the synthesis of 5,5-disulfonyl (I) and 5-alkyl-5-sulfonyl (II) derivatives of barbituric acid.



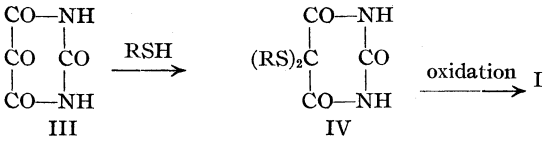
I II

The reactivity of the carbonyl group in alloxan (III) suggested that it might react with thiol compounds to give mercaptols (IV) which could be oxidized to the desired products (I).

(1) A portion of the communication is abstracted from a thesis submitted by Edmond L. d'Ouville in partial fulfilment of the requirements for the degree of Doctor of Philosophy at the University of Pennsylvania in June, 1937.

(2) Chemical Foundation Fellow.

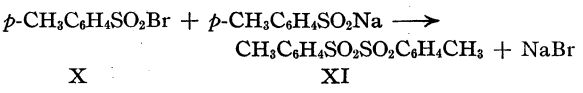
(3) d'Ouville and Connor, THIS JOURNAL, **60**, 33 (1938).



III IV I

With benzyl mercaptan in dry dioxane and using dry hydrogen chloride as a catalyst the product was the hemi-mercaptol, 5-hydroxy-5-(benzylthio)-barbituric acid (V); in glacial acetic acid–acetic anhydride solution 5-acetoxy-5-(benzylthio)-barbituric acid (VI), the acetylation product of V, was formed. Under the conditions tried it was not possible to carry the reaction further to the mercaptol stage. In addition to V, dibenzyl disulfide (VII) was produced; this must involve the reduction of alloxan, presumably to dialuric acid, although the reduction product was not isolated. With *p*-thiocresol in dioxane or glacial acetic acid as solvent and anhydrous hydrogen chloride, sulfuric acid or zinc chloride as catalysts, no condensation with alloxan occurred.

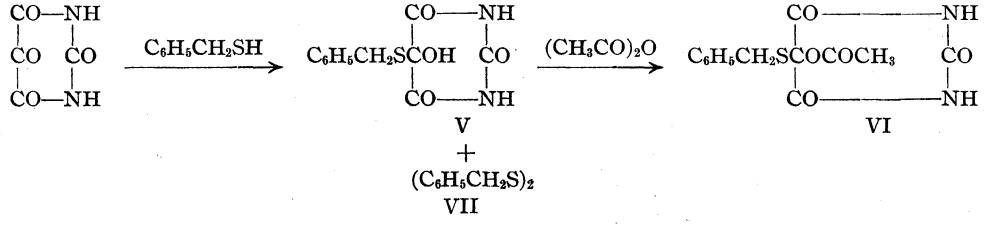
While X was not isolated, di-*p*-tolylsulfone (XI) was obtained; this is evidence for the formation of X since disulfones are readily formed[4] by the reaction of sulfonyl halides with the salts of sulfinic acids. Attempts to avoid the oxidation–re-



X XI

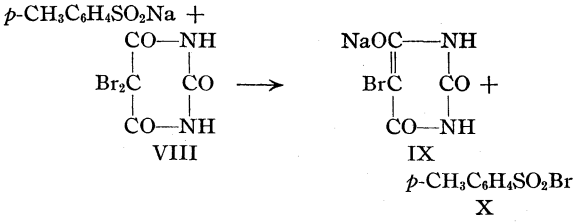
duction reactions in the preparation of disulfonylbarbituric acids were abandoned when the monosulfonyl derivatives (II) had been prepared and found to have properties which indicate that I would probably be very unstable and of no hypnotic value.

5-Ethyl-5-*p*-tolylsulfonylbarbituric acid (XII) and 5-ethyl-5-*p*-tolylsulfonyl-2-thiobarbituric acid (XIII) were prepared by the reaction of sodium *p*-toluenesulfinate with 5-ethyl-5-bromobarbituric acid and with 5-ethyl-5-bromo-2-thiobarbituric acid. Better yields of the metathesis



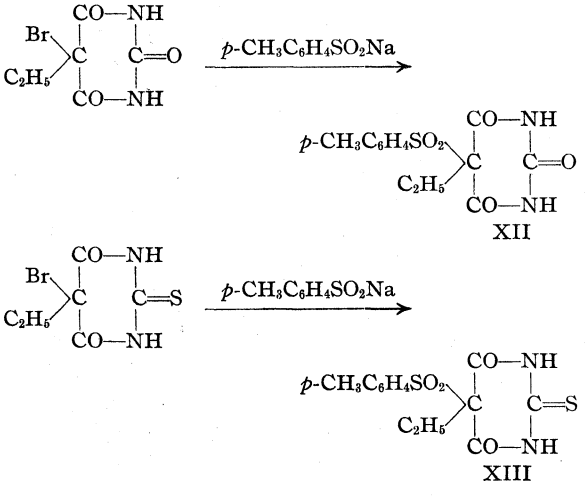
V + $(C_6H_5CH_2S)_2$ VII VI

A second possible synthesis of the disulfonylbarbituric acids was the reaction of 5,5-dibromobarbituric acid (VIII) with salts of sulfinic acid. With sodium *p*-toluenesulfinate a reaction occurred very readily at room temperature but none of the desired product (I, R = *p*-$CH_3C_6H_4$–) was obtained. The reaction appeared to be quite complex and the physical properties of the products made their separation and purification very difficult. The product isolated in the largest amount was the sodium salt of 5-bromobarbituric acid (IX), which was isolated in an amount corresponding to about 40% of the theoretical. The reduction of the dibromobarbituric acid implies that the first step in the reaction is the formation of IX and *p*-toluenesulfonyl bromide (X).



VIII IX X

products were obtained when the reactions were carried out without heating; for example, the yield of XII was 20% at 25° as compared with



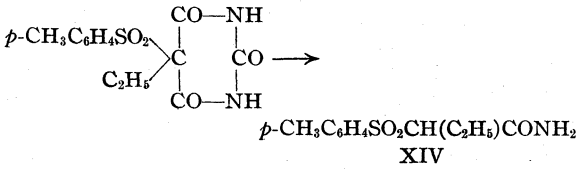
XII XIII

8% at 64°. This influence of temperature has been reported previously[3] and undoubtedly is due to the fact that higher temperatures favor the oxidation–reduction reaction. In the prepara-

(4) Kohler and MacDonald, *Am. Chem. J.*, **22**, 222 (1899).

tion of XII a by-product was the disulfone XI, showing that oxidation–reduction does occur.[5]

The yield of sulfonyl barbituric acid isolated was by no means a true gage of the amount of metathesis. A portion of the metathesis product underwent cleavage to give α-*p*-tolylsulfonyl-*n*-butyramide (XIV).



p-$CH_3C_6H_4SO_2CH(C_2H_5)CONH_2$

XIV

This cleavage of 5-sulfonylbarbituric acids is not surprising in view of other indications that the introduction of a sulfone group into active methylene compounds gives a structure labile to alcoholysis.[7]

It also appears likely that the acidity of the barbituric acids introduces a third complication in these reactions by liberating some of the sulfinic acid from its salt.

The 5-sulfonyl derivatives of the barbituric acids studied were relatively unstable. They dissolved readily in sodium carbonate solution but were slowly converted, even by water alone, to the cleavage product XIV. This, combined with the analytical data, establishes the structures of the products. Of the barbituric acids prepared, XII was the more stable and when pure could be stored satisfactorily in the dark; XIII could not be kept and its melting point was lowered over 35° by standing for three weeks. Preliminary pharmacological tests on XII, carried out through the kindness of Dr. Robert S. Shelton of the Wm. S. Merrell Company, indicated that it was without value as a hypnotic. Because of this report and the instability of the compounds, no further representatives of the series were prepared.

Experimental Part[8]

5-Hydroxy-5-(benzylthio)-barbituric Acid (V).—A mixture of 16 g. (0.1 mole) of alloxan monohydrate, 23 g. (0.19 mole) of benzyl mercaptan and 200 ml. of dioxane was cooled in an ice–salt bath and saturated with dry hydrogen chloride. After standing in the ice–salt bath overnight, the solution was resaturated with hydrogen chloride. White needles began to separate. After two days the solid (22 g., m. p. 135–140 dec.) was removed by filtration and recrystallized successively from alcohol and benzene. The purified product weighed 12.2 g. (46%), m. p. 169–174° dec. It turned deep red if allowed to stand in contact with air.

Anal. Calcd. for $C_{11}H_{10}O_4N_2S$: N, 10.54; S, 11.97. Found: N, 10.51, 10.81; S, 11.88.

Dilution of the mother liquor with water gave 5 g. of dibenzyl disulfide which after one recrystallization from alcohol melted at 70°.

5-Acetoxy-5-(benzylthio)-barbituric Acid (VI).—A mixture of 32 g. (0.2 mole) of alloxan monohydrate, 50 g. (0.4 mole) of benzyl mercaptan, 100 ml. of glacial acetic acid and 40 ml. of acetic anhydride was cooled in an ice–salt mixture and saturated with dry hydrogen chloride. The reaction mixture was kept at 0° for twelve hours and at room temperature for an additional twelve hours; the solid was removed by filtration and washed successively with water, alcohol and ether. The combined washings and mother liquor were diluted to 1.5 liter with water, filtered and the semi-solid residue washed with dilute alcohol. The combined solids weighed 19 g., m. p. 90–100°. Three recrystallizations from alcohol gave 5 g. (9.5%) of a white crystalline solid which turned pink at 190°, later became orange and finally melted with decomposition between 210° and 235°. Dilution of the mother liquors from the recrystallizations gave 4.5 g. of what appeared to be the same product in a less pure state.

Anal. Calcd. for $C_{13}H_{12}O_5N_2S$: N, 9.09; S, 10.39. Found: N, 9.17, 9.34, 9.33; S, 10.25.

Attempted Condensation of *p*-Thiocresol with Alloxan.—Using both glacial acetic acid and dioxane as solvents, reactions were carried out with alloxan hydrate and *p*-thiocresol under conditions similar to those described above. Dioxane was used as a solvent with sulfuric acid and zinc chloride, both alone and together, as catalysts in the cold and at 100°. In all cases no reaction product was isolated and unreacted *p*-thiocresol was obtained.

5,5-Dibromobarbituric Acid with Sodium *p*-Toluenesulfinate.—A suspension of 14.3 g. (0.05 mole) of 5,5-dibromobarbituric acid[9] and 21.4 g. (0.10 mole) sodium *p*-toluenesulfinate dihydrate[10] in 200 ml. of absolute methanol was allowed to stand at room temperature for four days. The crystalline solid (0.8 g.) was removed by filtration and recrystallized from benzene. The purified material became discolored at 200° and melted with decomposition at 207°. An authentic sample of di-*p*-tolyldisulfone[4] behaved similarly, both alone and when mixed with the reaction product.

The methanol filtrate was allowed to stand for seven days at room temperature and the solid that appeared removed by filtration. There was obtained 4.3 g. (38%) of the sodium salt of monobromobarbituric acid. Heating with 40% sulfuric acid solution gave 5-bromobarbituric acid, m. p. 200° (dec.), which was identified by a mixed

(5) Other investigators[6] have reported the formation of sodium benzenesulfonate and the unhalogenated active methylene compound when sodium benzenesulfinate was allowed to react with ethyl α-chloroacetoacetate, ethyl chloromalonate and diacetylchloromethane.

(6) Kohler and MacDonald, *Am. Chem. J.*, **22**, 227 (1899); Otto and Rossing, *Ber.*, **23**, 756 (1890).

(7) For example, the formation[6] of ethyl phenylsulfonylacetate in reactions which should cause the introduction of a phenylsulfonyl group in ethyl malonate and ethyl acetoacetate.

(8) All melting points are corrected.

(9) Biltz and Hamburger, *Ber.*, **49**, 635 (1916).

(10) "Organic Syntheses," John Wiley and Sons, Inc., New York, N. Y., Coll. Vol. I, 1932, p. 479.

melting point with an authentic sample[11] and by conversion with 1:1 hydrochloric acid[9] to 5-chlorobarbituric acid, m. p. 273° (dec.). The latter gave no depression of the melting point when mixed with a sample of 5-chlorobarbituric acid prepared in a similar manner from 5-bromobarbituric acid.

The filtrate obtained after removal of sodium bromobarbiturate gave additional solid material but it appeared to be a mixture that could not be separated. The presence of an additional quantity of sodium bromobarbiturate was shown by the formation of 5-chlorobarbituric acid when a sample of the solid was heated with 1:1 hydrochloric acid.

5-*p*-Tolylsulfonyl-5-ethylbarbituric Acid (XII).—A mixture of 21 g. (0.10 mole) of sodium *p*-toluenesulfinate dihydrate and 20 g. (0.085 mole) of 5-bromo-5-ethylbarbituric acid[12] in 250 ml. of absolute methanol was allowed to stand for eight days at room temperature. The solvent was then removed by evaporation, the residue washed with ether and the solid remaining treated with dilute sodium hydroxide solution. Recrystallization of the alkali-insoluble material from alcohol gave α-*p*-tolylsulfonyl-*n*-butyramide (XIV).[3] Acidification of the alkaline solution with concentrated hydrochloric acid gave a bulky white precipitate which was filtered, dried and recrystallized from alcohol. The yield of pure XII was 5.5 g. (20%), m. p. 200.5–203.5° (dec.).

Anal. Calcd. for $C_{13}H_{14}O_5N_2S$: mol. wt., 310; N, 9.03; S, 10.32. Found: mol. wt., 316, 312; N, 9.08, 9.24; S, 10.25, 10.50.

After the removal of XII, evaporation of the acidic solution gave 12 g. of solid. The material was extremely soluble in water and on ignition charred and gave an alkaline ash. A small portion was refluxed with thionyl chloride[13] but the product was impure, m. p. 58–61°. With *p*-toluenesulfonyl chloride (m. p. 69°) the mixed melting point was 67°.

In another experiment the solid precipitated in the reaction mixture was separated by filtration, washed with water, dried and recrystallized from benzene. The product weighed 2.3 g. (18%), m. p. 204–208° (dec.), and was identified as di-*p*-tolyldisulfone by a mixed melting point.

(11) Back, *Ber.*, **55B**, 3400 (1922).

(12) Aspelund, *J. prakt. Chem.*, [2] **136**, 329 (1933).

(13) Smiles and Hilditch, *J. Chem. Soc.*, **90**, 522 (1907); Sutherland and Shriner, THIS JOURNAL, **58**, 63 (1936).

5-*p*-Tolylsulfonyl-5-ethyl-2-thiobarbituric Acid (XIII).—Twenty-eight grams (0.13 mole) of sodium *p*-toluenesulfinate dihydrate was added to 250 ml. of absolute methanol, the mixture cooled to 5° and 25.6 g. (0.1 mole) of 5-bromo-5-ethyl-2-thiobarbituric acid[14] added. The solution was stirred vigorously and kept below 5° for one and one-half hours. The solution was allowed to come to room temperature and stand for eight days. It was then poured over ice, filtered and the solid washed with water. The product was almost entirely soluble in sodium carbonate solution. This solution was filtered, acidified with concentrated hydrochloric acid and the product recrystallized from dilute alcohol. The yield of pure XIII was 6.5 g. (20%), m. p. 179.9–180°. The product decomposed on standing three weeks, m. p. 141–145°.

Anal. Calcd. for $C_{13}H_{14}O_4N_2S_2$: mol. wt., 326; N, 8.59. Found: mol. wt., 320; N, 8.75, 8.77.

Summary

Attempts to synthesize 5,5-disulfonyl derivatives of barbituric acid were unsuccessful. *p*-Thiocresol did not react with alloxan while benzyl mercaptan gave 5-hydroxy-5-(benzylthio)-barbituric acid in dioxane as a solvent and 5-acetoxy-5-(benzylthio)-barbituric acid in acetic acid–acetic anhydride. Sodium *p*-toluenesulfinate with 5,5-dibromobarbituric acid gave sodium 5-bromobarbiturate, accompanied by oxidation products of the sulfinate.

The reaction at room temperature of sodium *p*-toluenesulfinate with 5-ethyl-5-bromobarbituric acid and with 5-ethyl-5-bromo-2-thiobarbituric acid gave 5-*p*-tolylsulfonyl-5-ethylbarbituric acid and 5-*p*-tolylsulfonyl-5-ethyl-2-thiobarbituric acid. The by-products show that the yields of metathesis products are lowered by oxidation–reduction reactions and by the ease of alcoholysis of the product.

PHILADELPHIA, PENNA. RECEIVED MAY 15, 1939

(14) Prepared by the method of Aspelund[12] for 5-bromo-5-ethylbarbituric acid.

[CONTRIBUTION FROM THE MULTIPLE FELLOWSHIP OF THE COTTON RESEARCH FOUNDATION, MELLON INSTITUTE]

Composition of Cottonseeds. I. Solubility of Nitrogenous Constituents

BY H. S. OLCOTT AND T. D. FONTAINE

Approximately 3,000,000 tons of cottonseeds are produced annually in the United States. At present, after removal of the hulls, the oil is recovered by pressing and the residual meal is used as a source of protein in stock foods. Depending upon the source of the seed and the efficiency of the pressing operation, the protein content of the meal varies from 45 to 55%. Commercial cottonseed meal is adjusted with hull bran to a protein content of 41% .

Inasmuch as proteins are becoming increasingly important as industrial raw materials, it appeared of interest to investigate the possibility of isolating and utilizing the proteins of the cottonseed. The work to be described is part of a general research program along these lines and deals particularly with the efficiency of extraction by aqueous solutions of salts, acids, and alkalies.

The proteins of the cottonseed were first investigated by Osborne and Vorhees.[1] Jones and Csonka[2] subsequently separated and characterized several of the fractions. There has been, however, no detailed study of their solubility behavior.

Experimental

In the procedure used for obtaining cottonseed oil commercially, the meats are first rolled, then cooked for twenty to forty minutes in an atmosphere of steam. After removal of the oil by pressing, the cake is broken and ground. The resultant cottonseed meal of commerce is not suitable for the preparation of protein. The yields are low because of denaturation of the protein by the heat treatment, and the product is dark, the color resulting from a combination of the pigments with the protein. For these reasons, most of the observations recorded refer to cottonseed meal from which the oil was removed by solvent extraction and which was never exposed to a temperature higher than 50°.

Whole cottonseed meats[3] were ground in a burr mill to 16-mesh-size particles, and extracted with ethyl ether in a large continuous extractor of the Soxhlet type for thirty-six to seventy-two hours. Approximately 10 kg. of ground meats could be accommodated in one extraction. The extraction chamber was fitted with a copper coil through which, at the end of the extraction period, warm water (45–50°) was passed to evaporate most of the entrained ether. The residual meal was air-dried, reground in the burr mill, and sieved through a 60-mesh screen to remove most of the hull particles with which the meats were originally contaminated.

One large sample of the light yellow meal so obtained was used for all the determinations. The following analytical data were obtained by the usual methods.

Constituent	Percentage
Water	9.0
Nitrogen	8.6
Lipids	0.5 (ether extraction)
Lipids	2.0 (chloroform extraction)
Ash	7.5

Five-gram portions of the meal were weighed into 8-ounce (240 cc.) centrifuge bottles. Because the meal is difficult to wet, it was stirred up thoroughly with 10 to 20 cc. of the extracting solution. The remainder (total, 200 cc.) was then added, the bottles were shaken thoroughly, and allowed to stand at room temperatures (23 to 28°).

As shown in Table I, continued agitation was unnecessary for complete extraction, and three hours was sufficient time to establish equilibrium. In some series of runs the meal suspensions were allowed to stand for twenty-four hours. The differences between these results and those obtained with the shorter experimental periods were within the limits of error.

In order to determine the amounts of nitrogenous compounds dissolved or peptized, the bottles were centrifuged and aliquots of the supernatant solutions were filtered and analyzed for nitrogen by a semimicro modification of the Kjeldahl–Gunning method (5–20 mg. nitrogen). The results, corrected to 200 cc., are expressed in terms of percentage of total nitrogen.

Table I also illustrates the effect of temperature on the efficiency of extraction by water and by 0.5 normal sodium chloride solution. The differences between the amounts

TABLE I

EFFECT OF TIME AND SHAKING ON EXTRACTION OF ETHER-EXTRACTED COTTONSEED MEAL WITH 0.5 *N* NaCl

Time, min.	% of total nitrogen extracted: Continuous agitation	No agitation
30	75.5	73.6
60	75.5	74.4
90	76.6	76.2
120	77.0	77.3
180	..	78.2
1440	..	78.3[a]

EFFECT OF TEMPERATURE

Temp., °C.	% of total nitrogen extracted: By H_2O	By 0.5 *N* NaCl
0	26.0	55.2
25	28.3	79.7
50	29.8	81.9

[a] See also footnote to Table II.

(1) T. B. Osborne and C. G. Vorhees, THIS JOURNAL, **16**, 778 (1894).

(2) D. B. Jones and F. A. Csonka, *J. Biol. Chem.*, **64**, 673 (1925).

(3) The meats were obtained through the courtesy of the Perkins Oil Company, Memphis, Tenn. They were taken from the mill after dehulling and before rolling.

extracted at 25 and at 50° were sufficiently small to indicate that attempts to carry out the extractions at constant temperature were unnecessary.

An unaccountable variation in the results of different runs prevents the assignment of absolute accuracy within 3 to 5%. However, the duplicability of determinations in a single run was well within 1%. Thus, although the amounts of nitrogen extracted by 0.5 normal solutions of sodium sulfate and sodium sulfite do not differ by more than 0.3%, in the several runs in which they were compared directly, they were invariably efficient in the same order. For this reason, the data in each series of determinations except those of Table II) are those of a single representative run.

A portable glass electrode was used for the determination of *p*H. In the *p*H range above 9, a correction has been applied to the reading, depending upon the concentration of salt present.

Results and Discussion

The principal protein in cottonseed is a globulin. In the experiments of Jones and Csonka,[2] 84.6% of the nitrogen of cottonseed meal was soluble in 10% sodium chloride solution, and an additional 10.3% could be extracted by alkali. The non-protein nitrogen in their extracts amounted to 10.1% of the total. In the present investigation, it was found that 25 to 30% of the nitrogen was extractable with water and that, of this, a large part was present in the form of a hitherto undescribed protein. This fraction has been isolated and will be described in a later publication.

In the discussion which follows, it has been assumed that the water-soluble protein and non-protein nitrogen fractions are soluble in most of the solutions used, and that the variations in amount of nitrogen extracted may be interpreted in terms of the behavior of the globulin and glutelin fractions.

The peptizing activity of a number of inorganic salts is outlined in Table II. In the majority of cases 0.5 normal solutions extracted practically as much nitrogen as could be extracted by higher concentrations. The lyotropic series effect is less marked than that noted by Gortner and his co-workers[4] in the extraction of the proteins from wheat flour.

Sodium and potassium fluorides extracted smaller amounts of protein than did the other neutral salts. The relatively high yields obtained with calcium and magnesium halides as compared with those extracted by sodium dihydrogen phosphate suggest that, at least within a limited range, *p*H is not an important factor in salt peptization. On the alkaline side of neutrality, disodium phosphate and sodium bicarbonate were no more effective extractants than the neutral salts.

In Table III, the effect of concentration on the peptizing activity of sodium chloride and sodium sulfite is outlined in greater detail. The denaturation of cottonseed proteins which have been subjected to the cooking process is shown in the decreased yields from commercial meal.

(4) R. A. Gortner, "Outlines of Biochemistry," 2d ed., John Wiley and Sons, Inc., New York, N. Y., 1938.

TABLE II

EFFECT OF SALTS ON PEPTIZATION OF COTTONSEED PROTEINS

Salt	Percentage of Total Nitrogen Extracted 0.25 *N*	0.5 *N*	1.0 *N*	*p*H[a]
LiCl	53.4	81.2	81.8	6.4
NaF	..	57.5	73.2	7.2
NaCl	51.1	78.2	80.3	6.4
NaBr	59.1	81.5	..	6.4
NaI	68.0	81.9	..	6.4
Na_2SO_4	78.5	81.9	..	6.8
Na_2SO_3	82.8	82.8	82.1	8.3
$NaHCO_3$	..	77.7	..	8.0
Na_2HPO_4	57.9	79.4	..	8.2
NaH_2PO_4	..	28.1	35.6	5.3
Na acetate	..	65.9	78.4	7.0
Na_3 citrate	..	77.0	..	7.4
Na_2 oxalate	67.8	81.7	..	7.1
Na_2 tartrate	55.9	79.2	77.6	6.9
KF	..	54.0	74.7	7.1
KCl	..	78.1	..	6.5
KBr	..	80.5	..	6.5
KI[b]	..	81.9	81.9	6.5
$CaCl_2$	59.1	81.5	81.5	5.1
$MgCl_2$	60.9	82.3	82.9	5.5
$MgBr_2$	62.0	83.5	83.8	5.5
$MgSO_4$	58.9	82.0	82.3	5.7
$BaCl_2$	62.8	77.1	78.9	5.3

[a] *p*H for 0.5 *N* solutions; in general, the values for the other concentrations did not vary by more than 0.1 of a *p*H unit. [b] An interesting phenomenon was observed when, in preliminary trials, calculated amounts of crystalline potassium iodide were added to the meal. Although the salt dissolved immediately upon the addition of water, the amount of protein peptized was never as great as when the salt *solution* was added to the meal. The same results were observed with sodium iodide, but with the chlorides and many of the other salts no differences were detectable.

Time of standing, min.	% of total nitrogen extracted by 0.5 *N* salt solns. KI + H_2O[c]	KI solution[d]
15	67.2	80.4
30	69.6	81.0
60	70.0	81.5
120	70.1	81.9
1440	72.2	81.9

[c] 16.6 g. of KI plus 195.5 cc. of distilled water.
[d] 200 cc. of 0.5 *N* KI.

TABLE III

EFFECT OF SALT CONCENTRATION ON THE EXTRACTION OF PROTEINS FROM COTTONSEED MEAL BY NaCl AND Na_2SO_3

Concn. of salt, normality	Percentage of total nitrogen extracted: Ether-extracted meal with NaCl	Ether-extracted commercial meal with NaCl	Ether-extracted meal with Na_2SO_3
0.0	24.9	7.6	..
.1	28.1	8.4	..
.15	..	..	61.7
.175	..	..	68.5
.2	44.4	..	74.5
.25	..	..	82.8
.3	57.7	21.9	..
.4	71.9	..	..
.5	78.2	37.1	82.8
.75	81.5	..	..
1.0	80.3	41.6	82.1
2.0	79.3	..	..
3.0	78.9	41.2	..
4.0	76.6	..	..
5.0	73.2	38.1	..

Figure 1 illustrates the data outlined in Table IV concerning the solubility of cottonseed proteins in acid and alkali solutions. The results with ether-extracted meal are compared with those obtained in the presence of 0.5 normal sodium chloride solution, with commercial cottonseed meal, and with the behavior of soybean meal as demonstrated by Smith and Circle.[5] The cottonseed proteins differ from those of the soybean in being less soluble in water; the isoelectric range of the most abundant protein is 1.5 to 2 *p*H units higher than that of the soybean protein.

In the presence of 0.5 normal sodium chloride, the amount of protein extracted is constant throughout most of the alkaline range. Only above *p*H 11.0 does the curve rise slightly. Apparently, in the presence of salt, the solubility of the glutelin fraction is depressed. The effect of salt in depressing the *p*H of cottonseed protein solutions, especially in the alkaline range, is marked. The phenomenon also has been noted in experiments with soybean.[5,6]

At least one variable responsible for the difficulty in checking results has been traced to the effect of time on the nitrogenous constituents of cottonseed meal. Over a period of weeks and months, successive runs have demonstrated a gradual slight increase in solubility. The increase could not be correlated with changes in moisture content. A more detailed investigation of these changes is in progress. With soybean, the solubility of the proteins decreases on standing.[5,7]

TABLE IV

EFFECT OF NaOH AND H_2SO_4 ON THE EXTRACTION OF PROTEINS FROM COTTONSEED MEAL

Milli-equivalents of H_2SO_4	Percentage of total nitrogen extracted: Ether-extracted meal *p*H	%	Ether-extracted meal with 0.5 *N* NaCl *p*H	%	Ether-extracted commercial meal *p*H	%
3.60	1.9	23.6	1.5	22.9	1.9	7.2
1.80	2.3	18.1	2.0	24.9	2.3	6.4
1.17	2.9	12.9	2.9	27.1	2.8	5.4
0.81	3.8	13.6	3.8	28.9	3.7	4.8
.45	4.8	18.1	4.7	38.8	4.8	5.6
.18	5.8	22.8	5.6	72.1	5.9	6.8
0	6.9	24.9	6.4	78.2	6.8	7.6
NaOH						
0.10	7.6	32.9	6.9	78.4	7.4	14.6
.21	8.7	73.8	7.5	78.7	8.6	38.1
.31	9.6	85.6	8.8	78.4	..	..
.41	10.4	90.0	9.1	78.7	10.0	55.1
.62	10.7	91.4	9.9	79.5	10.3	60.4
.82	11.1	93.1	10.5	78.4	..	..
1.03	11.4	92.8	10.8	78.0	11.1	64.4
3.09	11.9	92.6	11.5	82.9	11.7	68.4
4.12	12.0	90.9	..	..	..	..

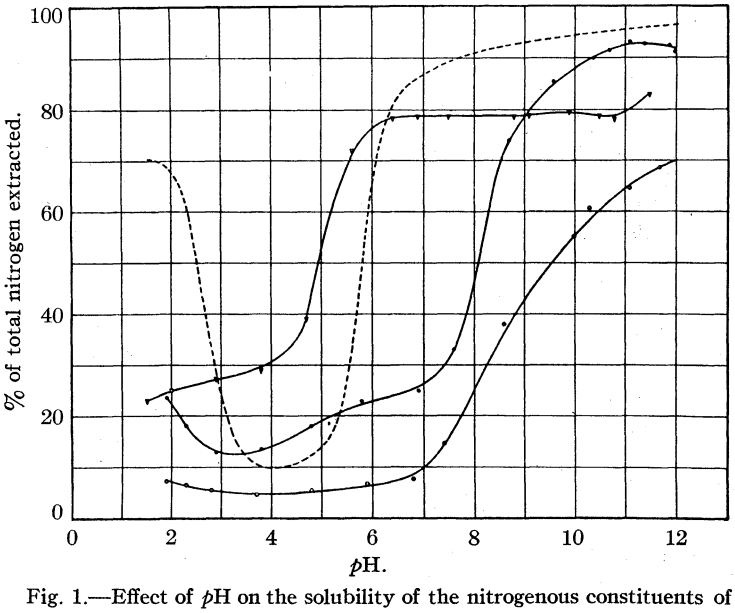


Fig. 1.—Effect of *p*H on the solubility of the nitrogenous constituents of cottonseed meal: —●—●—, ether-extracted cottonseed meal; —▽—▽—, ether-extracted cottonseed meal in 0.5 *N* NaCl; —⊙—⊙—, ether-extracted commercial cottonseed meal; ------, soybean meal.[5]

(5) A. K. Smith and S. J. Circle, *Ind. Eng. Chem.*, **30**, 1414 (1938).

(6) A. K. Smith, S. J. Circle, and G. H. Brother, THIS JOURNAL, **60**, 1316 (1938).

(7) D. B. Jones and C. E. F. Gersdorff, *ibid.*, **60**, 723 (1938).

We are grateful to Dr. R. F. Nickerson for the use of some data obtained in preliminary experiments.

Summary

Cottonseed meats have been ground and extracted with ether. The effect of *p*H and of a number of salts on the extraction of the nitrogenous constituents from the meal is recorded.

PITTSBURGH, PENNA. RECEIVED MAY 22, 1939

[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY OF THE UNIVERSITY OF CHICAGO]

The Pressure–Area and Pressure–Temperature Relations of Expanded Monolayers of Myristic and Pentadecylic Acids

BY GEORGE C. NUTTING AND WILLIAM D. HARKINS

1. Introduction

At 25° when spread on water which contains 0.01 *N* hydrogen ion, margaric ($C_{16}H_{33}COOH$) and higher saturated fatty acids form films which condense rather abruptly at pressures of about 0.5 dyne per cm. to slightly viscous, slightly compressible liquids whose area per molecule extrapolated to zero pressure varies only from about 23 to 24.5 sq. Å.

Lower members, specifically myristic and pentadecylic acids, exhibit a widely different behavior on compression. The limiting area at zero pressure is 46 sq. Å. per molecule. The compressibility is high and the pressure–area plots instead of being linear have a marked concave curvature upward. At a pressure characteristic of the particular acid a break occurs in the pressure–area curve such that the decrement of area per unit increase in pressure increases greatly; that is, the compressibility becomes very high. The curve above the break passes finally into a form characteristic of condensed films. A film which acts in this way is designated below the kink as an expanded film, and above it, until the area per molecule is about 23 sq. Å., as a transition or intermediate film.

The higher fatty acids give similar expanded and intermediate films at higher temperatures. The existence of the expanded state was recognized and investigated by Labrouste[1] and films of this type have been investigated in great detail by Adam and others.[2]

2. Apparatus and Materials

Pressure–area measurements were made with a film balance closely similar to one described by Harkins and Myers.[3] Subsolutions were contained in a shallow trough of stainless steel equipped with a false bottom through which water from a large reservoir was circulated. The trough and film balance were contained in a metal box with a front of plate glass. The top of this box was hollow, and water from the same thermostat was circulated through it in order to keep the temperature the same as that of the trough. This box was surrounded by an air thermostat kept as closely as possible at the temperature of the inner box. Thermocouples were installed just above and just below the film and when the air and the subsolution temperatures were equal it was assumed that the film also was at the same temperature.

In all of the experiments the films were spread on 0.01 *N* sulfuric acid prepared from water redistilled from alkaline permanganate and condensed in tin.

The myristic and pentadecylic acids were generously provided by Professor E. E. Reid of the Johns Hopkins University. The preparation and purification of the acids has been described by Reid and Meyer.[4] The acids were dissolved in purified ligroin (b. p. 60–70°) and spread from a precision pipet devised by Harkins and Anderson.[5] After spreading, a period of from fifteen to forty-five minutes was allowed before compression, during which it was assumed that any micro-crystals present would spread into a monolayer.

3. Pressure–Area Measurements

The pressure–area relations of myristic acid at seven temperatures from 6.7 to 25° are exhibited in Fig. 1 and Table I. So far as is possible, all experimental points are included, except that in the area interval 26–33 sq. Å. of Curve 4 and in a few other places, one-half the points have been omitted in order to avoid too great crowding. The time interval between adjacent points was never less than one minute, and except at the highest temperatures was commonly two to five minutes in the intermediate region. Area decrements also were not uniform but their magnitude may be judged from the curves.

It will be shown later that the rate of compression has a marked influence upon the pressure of

(1) Labrouste, *Ann. Phys.*, **14**, 164 (1920).

(2) N. K. Adam, "The Physics and Chemistry of Surfaces," Clarendon Press, Oxford, England, 1938.

(3) W. D. Harkins and R. J. Myers, *J. Chem. Phys.*, **4**, 716 (1936); G. C. Nutting and W. D. Harkins, THIS JOURNAL, **61**, 1180 (1939).

(4) E. E. Reid and J. D. Meyer, *ibid.*, **55**, 1574 (1933).

(5) W. D. Harkins and T. F. Anderson, *ibid.*, **59**, 2189 (1937).

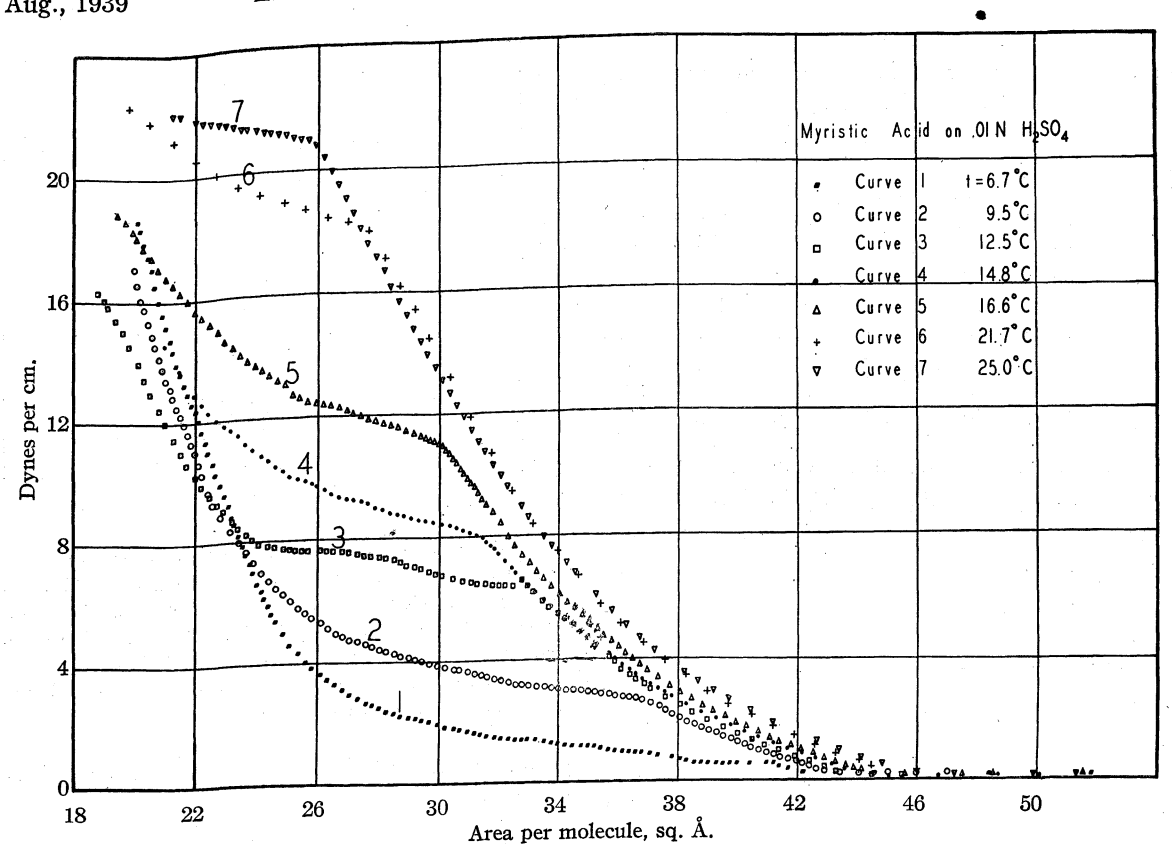


Fig. 1.—Pressure–area relations of myristic acid films. Curve 7 taken at 25° is displaced toward lower pressures and lower areas, especially at the highest temperatures, by the solubility of the myristic acid.

TABLE I

FILMS OF MYRISTIC ACID ON 0.01 *N* SULFURIC ACID

Temp., °C.	Time interval between points, sec.	Area decrements, sq. Å. per mol.	Limiting area, sq. Å. per mol.	Area at kink, sq. Å. per mol.	Press. at kink, dynes per cm.	Total time of expt., min.
6.7	..	...	43.0	41.2	0.58	236
9.5	..	...	44.5	36.9	2.65	293
12.5	..	...	44.5	32.8	6.18	171
14.8	..	...	45.2	31.5	7.95	253
16.7	..	...	45.1	(30.0)	(11.12)	159
	30	0.6	45.4	30.4	10.4	22
	15	1.2	46.5	31.4	10.0	6
21.7	60	0.7	46.9	27.6	18.1	39
25.0	60	0.3	46.4	25.9	20.9	77
	15	1.0	47.0	26.9	21.4	7.5

the intermediate film at any given temperature and molecular area. In the work of Adam and Jessop[6] the rate seems to have been much higher than that used in the present work. In the two investigations the pressures found for the transition Expanded → Intermediate film, are in good agreement, but our molecular areas for the transitions are about 10% lower than theirs. The total time (t) of a compression from the highest to the lowest area varied in our work from 39 minutes at 21.7° to 293 minutes at 9.5°.

The shape of Curve 7 in Fig. 1 is distorted by a spurious effect which causes it to be displaced toward lower areas, and decreases the pressure at the highest pressures. This is due to the solubility of the myristic acid which at 25° removes a part of the material from the film. Since the solubility increases with increase of film pressure as well as temperature the slope of the curve in the intermediate region is much too small.

4. The Rate of Compression

In order to determine the effect of the rate of compression on the form and position of pressure–area curves of expanded and intermediate films a series of experiments was carried out with both pentadecylic and myristic acids at several temperatures. The results are shown in Figs. 2, 3, 4, and 5, and in Tables I and II.

Comparing first the two acids, there is remarkable similarity between the curves for pentadecylic and those for myristic acid at a temperature

(6) N. K. Adam and G. Jessop, *Proc. Roy. Soc.* (London), **A112**, 364 (1926).

TABLE II

FILMS OF PENTADECYLIC ACID ON 0.01 *N* SULFURIC ACID

Temp., °C.	Time interval between points, sec.	Area decrements, sq. Å. per mol.	Limiting area, sq. Å. per mol.	Area at kink, sq. Å. per mol.	Press. at kink, dynes per cm.	Total time of expt., min.
17.9	30	0.25	43.5	41.8	0.5	44
	15	.53	43.8	41.4	.6	11
	15	1.05	43.6	40.8	.7	5.5
21.7	30	0.25	44.6	35.6	4.6	44
	15	.54	45.5	36.4	4.3	12
	15	1.05	45.1	36.1	4.1	5.5
25.0	60	0.3	45.6	33.4	8.4	79
	15	.53	45.9	33.0	8.5	14
	15	1.05	46.1	32.8	8.3	7

11° lower. The principal difference is in the extent of minor irregularities in the intermediate region.

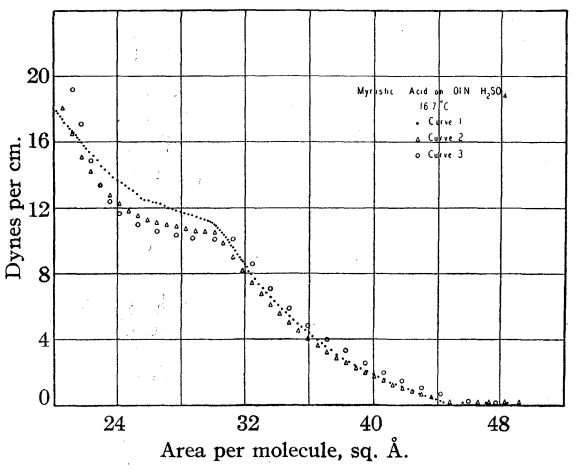


Fig. 2.—Effect of rate of compression on pressure–area relations of myristic acid films. Time of compression from limiting area at zero pressure to 20 dynes per cm.: Curve 1, 159 min.; Curve 2, 22 min.; Curve 3, 6 min.

The general rule is that a decrease in the rate of compression of an intermediate film causes: (1) an increase of molecular area at a given pressure; or (2) an increase of pressure at a given molecular area.

In Fig. 3 this effect is masked in the case of myristic acid by its relatively high solubility at 25° (Curves 1 and 2).

Results in reasonable accord with those reported in this paper for rapid compression have been obtained for myristic acid on 0.002 *N* hydrochloric acid by Dervichian,[7] who used the Wilhelmy method for measuring film pressures. The film was compressed at a very high, constant rate by a motor drive so that the total time of an experiment amounted to only about two or three minutes.

(7) D. G. Dervichian, Thesis, Paris, 1936.

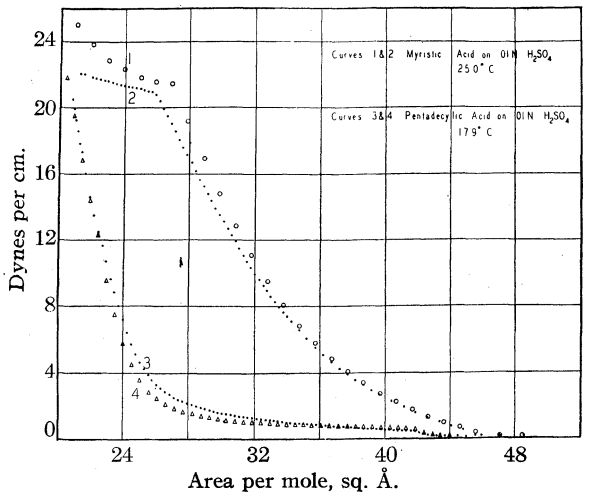


Fig. 3.—Effect of rate of compression on pressure–area relations of myristic and pentadecylic acids. Time of compression: Curve 1, 7.5 min.; Curve 2, 77 min.; Curve 3, 44 min.; Curve 4, 11 min. Curve 2 is depressed below Curve 1 by the solubility of myristic acid at 25°, so these two curves do not give the proper relations due to the effect of time on the film itself.

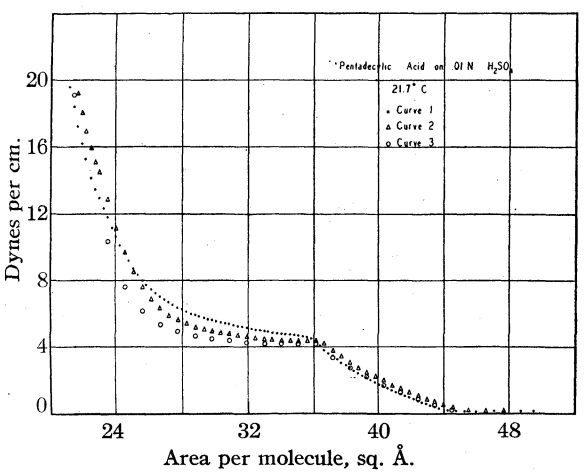


Fig. 4.—Pressure–area relations of pentadecylic acid at 21.7° at different rates of compression. Time elapsed between limiting area at zero pressure and 20 dynes per cm.: Curve 1, 44 min.; Curve 2, 12 min.; Curve 3, 5.5 min.

5. Pressure–Temperature Measurements

Pressure–temperature measurements have been made on monolayers of myristic acid spread on 0.01 *N* sulfuric acid at four molecular areas and on pentadecylic acid films at three molecular areas. Before beginning an experiment the apparatus and subsolution were cooled to the lowest

temperature desired (2° for myristic, 5° for pentadecylic acid), the surface of the subsolution was cleaned thoroughly and the acid was spread from ligroin solution. The area available per molecule at the time of spreading was always considerably greater than the area at which the measurements were to be made. A period of thirty to fifty minutes intervened between spreading and commencement of the slow compression to the selected molecular area. As soon as the temperature above and below the film differed by only a few hundredths of a degree, determinations of the pressure were begun. Several measurements were made at each temperature and the mean value is reported. The temperature interval was not uniform, amounting to 0.2 to 0.3° at the lowest temperatures and about 0.1° near the transition temperature. Temperatures were read to 0.01°. The experiments were performed slowly, and at such a rate that a period of from four to six hours was used in each experiment.

Each curve in Fig. 6 represents the change with temperature of the pressure of a monolayer of either myristic or pentadecylic acid (Table IV) at a definite, constant molecular area, *e. g.*, 33.2 sq. Å. for myristic acid. At the lowest temperature the pressure is also low for any area investigated, and remains constant to ±0.03 dyne per cm., so the f–T relation is given by a line which is almost horizontal, and represents a film of two dimensional vapor and the islands of aggregated molecules with which it is in equilibrium. At 6.5° the myristic acid film begins to exhibit a rapid rise of pressure with temperature, and a value of $(\partial p/\partial T)_a$ of 0.81. The film is here of the intermediate type. The similar change for pentadecylic acid occurs at 17° and the slope is 1.21 for a = 31.3 sq. Å.

This discontinuity between the pressure of the vapor and that of the intermediate film is in all cases rather sharp and for the three pentadecylic acid films is localized in a small temperature interval near 17.2°. The corresponding discontinuity in myristic acid occurs at a temperature about 11° lower.

Any one of the curves which represents an intermediate film approximates a straight line so closely that the derivative of the slope with respect to temperature may be taken as zero. In the curves of Fig. 6, especially those for smaller areas, departures from linearity are evident, but they are as much in one direction as another and the maximum deviation of the experimental points from the best straight line is of the order of 0.05 dyne per cm.

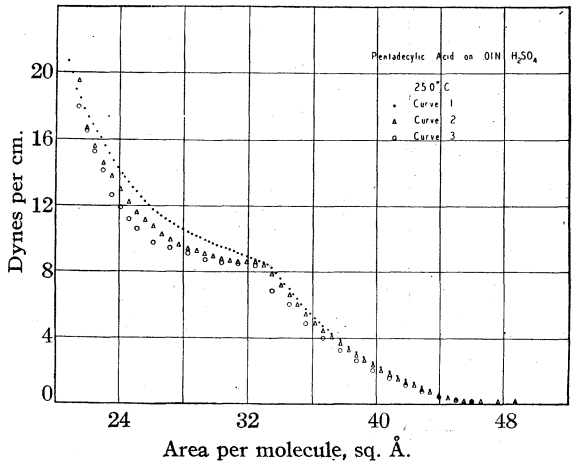


Fig. 5.—Pressure–area relations of pentadecylic acid at 25.0°. Time of compression from limiting area to 20 dynes: Curve 1, 79 min.; Curve 2, 14 min.; Curve 3, 7 min.

The transition Intermediate → Expanded film occurs at a higher temperature and pressure, and seems in some instances to extend over a range of the order of a degree of temperature and a dyne of pressure, but this is dependent upon the rate at which the temperature is increased.

The slope varies from about 0.8 to 1.2 for the intermediate films, but is very much smaller, 0.15 to 0.2, for the expanded films. The f, T relation appears to be linear near the transition region to 0.01 or 0.02 dyne per cm. except where the slope is caused to decrease by the solubility of the film, which increases with both rising temperature and pressure. The solubility effect is exhibited particularly by the myristic acid films above 18°, and especially by the expanded film of this acid at a molecular area of 29.2 sq. Å., since the true positive slope is changed into a fictitious negative one by the increase of solubility.

The slopes $(\partial f/\partial T)_a$ for the intermediate films increase somewhat as the molecular area for a given acid decreases, and are slightly greater for pentadecylic acid, which may be due to the greater solubility of the myristic acid.

The data for the pressure–temperature relations are exhibited in Table III. The temperatures and pressures of transition have been obtained by an extrapolation of the best straight lines which represent the data of the adjacent types of film.

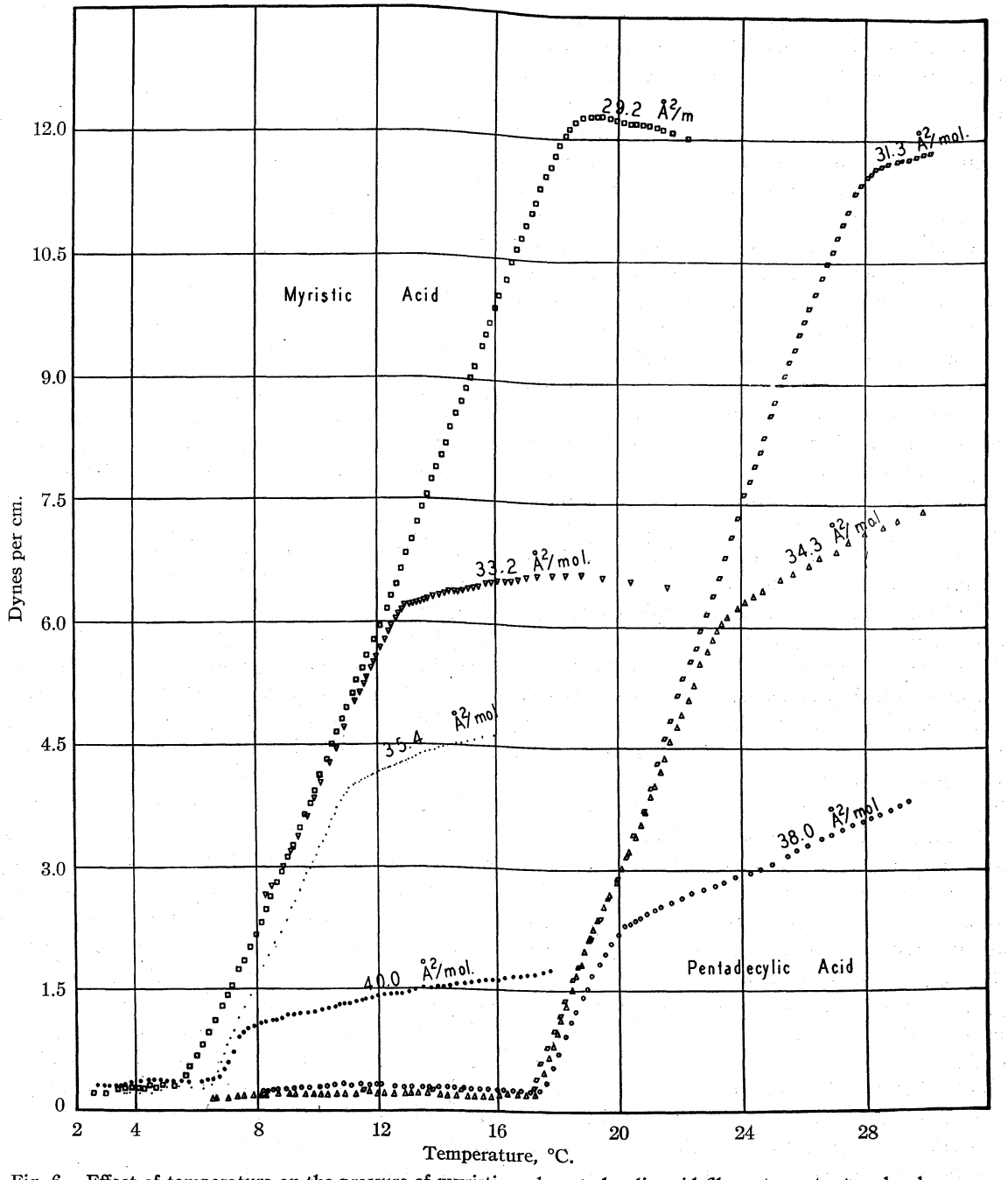


Fig. 6.—Effect of temperature on the pressure of myristic and pentadecylic acid films at constant molecular areas (on 0.01 *N* sulfuric acid).

6. Transformation of an Intermediate into a Condensed Liquid and into a "Plastic Solid" Film

For many years workers in surface chemistry have assumed that the intermediate may be transformed into a condensed film by increase of pressure, but no such transformation could be detected in the pressure–area plots. However, Harkins and Myers[8] discovered by viscosity measurements that pentadecylic acid undergoes a transformation Condensed Liquid → "Plastic Solid" at 21 sq. Å. and about 23 dynes per cm. No well-defined transformation was apparent in the *f*, *a* curves reported in this paper but Boyd and Harkins found that an extremely great in-

(8) W. D. Harkins and R. J. Myers, *Nature*, **140**, 465 (1937).

TABLE III

COLLECTED DATA ON MYRISTIC AND PENTADECYLIC ACID FILMS FROM PRESSURE–TEMPERATURE CURVES OF FIGURE 6

Duration of expt., min.	Area per mol., sq. Å.	Slope of branch Dynes per deg., lower	Slope of branch Dynes per deg., upper	Transition temp., °C.	Transition press., dynes/cm.	Expansion temp.	Expansion press., dynes/cm.
			Myristic Acid				
264	29.2	0.932	−0.068	5.5	0.30	18.65	12.32
246	33.2	.828	.113	..	..	12.70	6.16
271	35.4	.800	.163	6.4	.25	10.95	3.97
336	40.0	.719	.0772	6.8	.40	7.72	1.07
			Pentadecylic Acid				
260	31.1	1.05	.091	17.1	.25	27.8	11.60
340	34.3	0.964	.208	17.2	.20	23.4	6.17
269	38.0	.771	.166	17.5	.25	20.1	2.30

crease in viscosity with pressure occurs at a pressure of 21.2 dynes per cm. if the temperature is 25°. After this the pressure–area data were plotted on a different scale (Fig. 7) which revealed the fact that the two straight lines have their intersection at just this point.

The figure seems also to exhibit several additional kink points, but it is unsafe to assume that they represent phase transformations until this assumption has been tested by determinations of the viscosity of these films. Most of the data obtained thus far indicate that there is probably no definite point at which intermediate films are transformed into condensed liquid films.

7. Relation to Theory

Since additional work, with a theoretical bearing, other than that presented here is in progress in this Laboratory, the general discussion of the theory of the expanded and intermediate states will be deferred until later. However, two connections with theory are of moment here.

Langmuir[9] has proposed that the equation of state of an expanded film may be expressed by a van der Waals expression, simplified to the form

$$(f - f_0)(a - a_0) = kT \qquad (1)$$

Here f and a are, respectively, the measured film pressure and molecular area of the monolayer, and the term $-f_0$ is assumed to represent the spreading coefficient (f_S) of Harkins and Feldman[10] for the hydrocarbon oil which would be formed if the polar groups of the substance of the film were to be replaced by hydrogen atoms. For example, if the film is formed from myristic acid, the spreading coefficient should be that for tetradecane. The value of (f_S) is given by

$$f_S = \gamma_w - \gamma_0 - \gamma_{ow} \qquad (2)$$

in which γ represents the surface on interfacial tension and w and o represent water and oil, respectively.

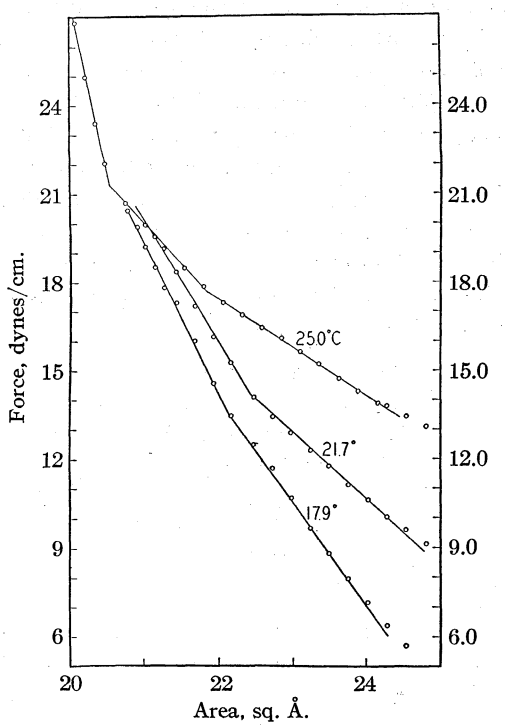


Fig. 7.—Pressure–area relations of pentadecylic acid between 20 and 25 sq. Å. at 25°. Exhibits a phase transition from Condensed Liquid → "Plastic Solid" at 25°, 21.3 dynes per cm., and 20.54 sq. Å. as confirmed by measurements of viscosity.

The values of f_0 which are calculated from the experimental data are seen to vary from 12.3 to 13.0 dynes per cm. for myristic acid, and from 12.4 to 13.5 for pentadecylic acid. While no very accurate determinations of the spreading coefficient have been made, the value for tetradecane obtained by extrapolation from values for the 6 and 8 carbon atom straight chain paraffins

(9) I. Langmuir, *J. Chem. Phys.*, **1**, 756 (1933).

(10) W. D. Harkins and A. Feldman, THIS JOURNAL, **44**, 2665 (1922).

is about 9, while Langmuir's experimental result is 5.7.

Thus the value of f_0 seems actually to correspond much more closely to the spreading coefficients of long paraffin chains of 17 or 18 carbon atoms in length. The value of the spreading coefficient may be given by another form of Eq. (2) which is

$$f_S = w_A - w_{C_0} \qquad (3)$$

in which w_A is the work of adhesion between the oil and water and w_{C_0} is the work of cohesion of the oil. The next paper of this series, which will give values of f_0 for the 13, 15, and 16 carbon atom acids, should make it possible to show more clearly what the relations are. At present it seems likely that the theory in its use of $-f_0 = f_S$ overemphasizes somewhat the attraction between the hydrocarbon chains and the water. Additional determinations of the value of f_S are needed to ascertain the magnitude of this overemphasis.

The values of a_0 for myristic acid (Table IV) are not constant, but increase with temperature from 12.6 sq. Å. at 12.5° to 14.7 sq. Å. at 25°, so the areas are much too small to agree with those of hydrocarbon chains, since the minimum given by films is 20 sq. Å. and the value given by X-rays is not much less than this.

TABLE IV

VALUES OF THE CONSTANTS a_0 AND f_0 IN THE EQUATION OF STATE FOR EXPANDED FILMS OF MYRISTIC AND PENTADECYLIC ACIDS

Temp., °C.	Area range, sq. Å. per molecule	a_0, sq. Å. per mol.	f_0, dynes per cm.	Root-mean-square devn., dynes per cm.
		Myristic Acid		
12.5	28–50	12.6	12.4	0.46
14.9	30–50	12.4	12.3	.46
16.6	28–50	13.4	13.0	.30
21.7	28–50	14.3	12.7	.53
25.0	26–50	14.7	12.7	.61
		Pentadecylic Acid		
21.7	33–48	14.6	13.5	.21
25.0	31–48	12.0	12.4	.16

In section 4 and Figs. 2, 3, 4, and 5, it has been shown that with intermediate films the product fa increases with the time of compression. That is, in the compression of these films there is a process which takes time for its completion, and this process is in the direction of an expansion with time after any given compression. Thus this process does not seem to be a growth either in size or in number of micelles present in the film, since this would be expected to result in a contraction.

In considering the applicability of Equation (1) to expanded films in general it should be kept in mind that no experimental work as yet done subjects the equation to a critical test. This is due to the fact that although the pressure–area curves approximate rectangular hyperbolas, the approach to the asymptotes is so slow that any curves as yet observed cover only a small fraction of the range necessary to give any uniqueness to this special equation. Thus, with myristic acid at 25° the range covered is only from 30 to 50 sq. Å. and from 0 to 20 dynes per cm. Let it be supposed that the asymptotes lie at $f = -11$ dynes per cm., and $a_0 = 16$ sq. Å. Then in order to approach within 1 dyne and 1 sq. Å. of the asymptotes the respective area and pressure must be 400 dynes per cm. and 400 sq. Å., so the observations extend over only a small part of the curve. At other temperatures the conditions for such a test of the equation are not more favorable.

The extent of the hysteresis observed in the f–a relations of the intermediate state make it difficult to apply Langmuir's theory of this state without a more extensive study of the phenomena involved.

8. Summary

1. The effect of temperature upon the pressure (f) at constant molecular area (a) of monolayers of myristic and pentadecylic acid has been determined. The value of the slope $(\partial f/\partial T)_a$ has been found to be of the order of 0.8 to 1.2 for intermediate, and of 0.15 to 0.2 for expanded films.

2. Pressure–area isotherms for myristic acid have been determined at temperatures from 6.7 to 25°.

3. The compression of intermediate films is found to involve a process which takes time for its completion, and in which at constant temperature the pressure increases with time at constant area, or the area with time at constant pressure.

4. At constant temperature an intermediate film seems to undergo a gradual transition into a condensed liquid film by increase of pressure and the resulting decrease of molecular area. The condensed liquid film exhibits a linear pressure–area relation, and in the case of pentadecylic acid at 25° undergoes a sharp transition to a "plastic" solid film at 21.3 dynes per cm. and 20.52 sq. Å. For any long straight chain molecules the molecular area for the transition Liquid → Solid is very much more independent of the material of the film than the pressure.

CHICAGO, ILLINOIS RECEIVED FEBRUARY 27, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF THE GENERAL ELECTRIC COMPANY]

Dependence of Conductance on Field Strength. I. Tetrabutylammonium Picrate in Diphenyl Ether at 50°

BY DARWIN J. MEAD WITH RAYMOND M. FUOSS

I. Introduction

In 1924, Wien[1] showed experimentally that the conductance of electrolytes under high field strengths was abnormal. He first ascribed the effect to a change of the temperature coefficient of conductance with field strength, but subsequent work in his Laboratory[2] showed that the abnormalities were due to an actual failure of Ohm's law for electrolytes.[3] He showed that two effects were present, one quadratic in the field and one linear. The first Wien effect appears in strong electrolytes when the distances the ions move during their relaxation time become of the order of the diameter of the ionic atmosphere Then the retarding effects on mobility of the atmosphere are diminished, with consequent increase of conductance. In weak electrolytes, the conductance is further increased by increased dissociation in the field. The second Wien effect has been treated theoretically by Onsager,[4] who showed that the slopes of the conductance–field curves could be predicted from the dielectric constant and temperature of the solvent and the valence type of the electrolyte.

Because the Wien effects are direct experimental evidence for the existence of the ionic atmosphere and for the pairwise association of ions under their mutual coulomb fields, and also on account of general interest in the behavior of dielectrics under high fields, it seemed worthwhile to study by bridge methods several carefully selected systems in some detail.

Diphenyl ether at 50° was chosen as our solvent on account of its ease of purification, low solvent conductance and high solvent power for substituted ammonium salts, which are convenient 1–1 electrolytes for work in non-aqueous solvents. Its dielectric constant at 50° and 60 cycles is 3.53, which is low enough to give marked ion association. In it, the conductance of tetrabutylammonium picrate satisfies the simple binary association law from below millionth normal up to concentrations of the order of 10^{-4} normal. Consequently the system permitted a test of the theory over a wide range of conductance and concentration. Above 10^{-4} normal, triple ion formation[5] becomes appreciable; in this range a dependence of the Wien coefficient on concentration was observed.

From the initial part of the conductance–field curves, the activity coefficient of the solute can be determined.[4] With our present methods, our precision in activity coefficient is not high, because it is determined as a small difference between two large quantities, one of which depends on an extrapolation, but we can show that our experimental coefficients are in approximate agreement with the values calculated by the limiting law of Debye and Hückel. The present results therefore demonstrate the existence of an ionic atmosphere in a solvent of quite low dielectric constant.

From the linear part of the curves, we find at low concentrations an increase in conductance of 1.6% per kilovolt, which is in good agreement with the theoretical value, 1.32%, calculated by Onsager's theory. Since this theory postulates pairwise association of ions, and explains the second Wien effect as a displacement of this equilibrium in the field, our results give experimental proof of the existence of ionic association.

Further work on different types of electrolytes and on solvents of lower dielectric constant, where still higher field strengths can be studied, is in progress. It will be interesting to see whether the shape (electrical and physical) and size of the ions influence the Wien coefficient and also to study the effect in the range of higher association than pairwise.

II. Materials, Apparatus and Method

Diphenyl ether was purified by recrystallization, after which it was dried first with calcium chloride, and finally with activated alumina. Our highest freezing point was 27.1°. The average solvent conductance was 0.3×10^{-12}; our best value was 0.06×10^{-12}.

Tetrabutylammonium picrate was prepared as described by Fuoss and Kraus,[6] m. p. 89.2–90.0° (corr.).

(1) Wien, *Ann. Phys.*, **73**, 162 (1924).
(2) Wien, *ibid.*, **83**, 327 (1927).
(3) An excellent bibliography is contained in a review by Eckstrom and Schmelzer, *Chem. Rev.*, **24**, 367 (1939).
(4) Onsager, *J. Chem. Phys.*, **2**, 599 (1934).
(5) Fuoss and Kraus, THIS JOURNAL, **55**, 2387 (1933).
(6) Fuoss and Kraus, *ibid.*, **55**, 3614 (1933).

Conductance cells of several types were used. Some determinations were made in the cell described by Deitz and Fuoss,[7] and others in the cell described by Elliott and Fuoss.[8] The former cell showed a pronounced Parker effect at 1000 cycles and was only used for preliminary 60-cycle work. The second cell (cell no. 2) gave results independent of frequency (except for a normal polarization effect) and was used for about half of the work reported in this paper. For the final work, two platinum cells were used, which had two advantages over Elliott's cell: they could be cleaned with hot nitric acid or chrome–sulfuric acid between runs, and they had no movable parts. Cell no. 3 is shown in Fig. 1. The high potential electrode (8.25 cm. long, 2.540 cm. inside diameter, 0.5 mm. wall thickness) was simultaneously the outer cell wall. It and the guard-test combination (outside diameter 2.060 cm.) were sealed to a hollow ring of soft glass, to which were sealed filling tubes. The volume was 25 cc. A shielded lead ran to the test electrode; the shield was connected to the guard electrode, and the shielding was unbroken from cell to bridge. At final balance, the guard and test electrodes are at the same potential, so that except for an insignificant amount of fringing at the glass joint between the guard and test electrodes, the flux is normal over the entire test electrode. The latter condition is essential, because it was necessary to calculate field strength from cell geometry and the voltage applied to the cell. Cell 4 was similar to cell 3, except that the electrode spacing was 0.491 cm., or about twice that of cell 3.

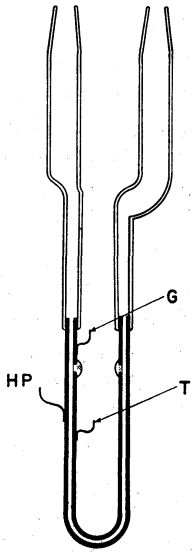


Fig. 1.—Guarded conductance cell.

Cell Comparison and Calculation of Field Strength.—In Fig. 2 are shown conductance–field curves, in which cells 2, 3 and 4 are compared. For convenience in drawing, the ratio of the specific conductance at field strength E to the low voltage conductance is plotted against field strength. Cell 2 had about twice the area and nearly the same spacing as cell 3 (cell constants 0.002727 and 0.004605, respectively), while cells 3 and 4 had about the same area, but quite different spacings (constants 0.004605 and 0.01064). The effect in question is a *linear* field effect; in this case, the average field strength E is given by

$$E = \int_{r_1}^{r_2} E(r)\mathrm{d}r/(r_2 - r_1) = V/(r_2 - r_1) \quad (1)$$

where V is the voltage applied to the high potential electrode. It will be seen that the agreement between the cells checks our calculation of field strength.

Voltage Sources and Scales.—Most of our voltage work was done at 60 cycles; examination with a cathode ray oscilloscope showed that the transformer output was free from harmonics. Some work was done at 500–1500 cycles; here graphical integration of the oscilloscope curves showed the presence of not more than 5% harmonics. The question of harmonics is important, because the second Wien effect is linear in cell voltage and all our voltmeters read mean square voltage. The linear average V was computed from the r. m. s. average V_r by the relations

$$V = (V_{max}/\pi)\int_0^{\pi} \sin x\, \mathrm{d}x = 2\, V_{max}/\pi \quad (2)$$

$$V_r = \left[(V_{max}^2/\pi)\int_0^{\pi} \sin^2 x\, \mathrm{d}x\right]^{1/2} = V_{max}/\sqrt{2} \quad (3)$$

whence

$$V = (2\sqrt{2}/\pi)\, V_r \quad (4)$$

A number of voltage scales were used in order to obtain cross checks. First, the output of the transformer to the cell and bridge network was fed simultaneously to a step-down transformer of known ratio under zero load (potential transformer), and the output voltage of the latter was used as a measure of the cell voltage. The ratio of the potential transformer was determined by

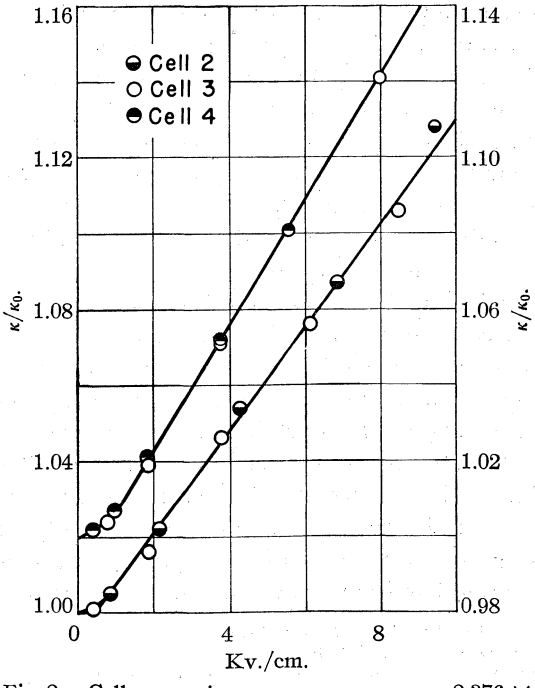


Fig. 2.—Cell comparison: upper curve, $c = 2.376 \times 10^{-5}$; lower curve, $c = 9.64 \times 10^{-5}$.

(7) Deitz and Fuoss, THIS JOURNAL, **60**, 2394 (1938).
(8) Elliott and Fuoss, *ibid.*, **61**, 294 (1939).

A. I. E. E. data relating sparking distance with voltage. Second, an electrostatic voltmeter, also calibrated by spark data, was used. Finally, the calibration of the electrostatic voltmeter was checked by direct determination of the current read on a milliammeter through a voltage insensitive resistor. The resistor was the 100,000 ohm wire wound standard used ordinarily as one arm of our resistance bridge.[9] The voltage calculated from the current and resistance by Ohm's law agreed with that read on the electrostatic voltmeter. The various voltage scales were self-consistent within 2%.

Bridges.—The conductance–field curves were determined using the resistance and Schering bridges which have been described previously.[9,10] Voltages up to 25 kv. were available at 60 cycles by means of transformers on the shop line. In the range 500–2000 cycles, an alternator was used to supply a tapped transformer, whose maximum output was 10 kv.

Low voltage determinations in the audiofrequency range were made on a parallel bridge. The Wagner ground and guard circuits were combined, so that three terminal cells could be used. Two arms of the bridge were reactance-free 10^5 ohm resistors; the other two arms were 10^5 ohm resistors with about 350 $\mu\mu f$ capacity in parallel with each. After obtaining zero-balance, the cell was connected parallel to one of the latter arms, and from the changes in resistance and capacity necessary to restore balance, the conductance and capacitance of the cell could be determined.

Procedure.—Solutions were made up by weight in a dilution flask and the density (1.0440 at 50°) of the solvent was used in calculating normality. (Our highest concentration was about 3×10^{-3} N.) In order to eliminate errors due to sorption effects[11] the cell was filled with successive portions of the same solution from the dilution flask, until the conductance of two consecutive fillings differed by less than 0.1%. Several dilution runs were made, covering the concentration range 10^{-6} to 3×10^{-3} N. For establishing the general conductance concentration curve, the low voltage parallel bridge was used. All electrical measurements were made with the cell in an oil-filled thermostat, maintained at 50 ± 0.02°.

At a series of concentrations, the dependence of conductance on field strength was determined. After the cell came to temperature equilibrium in the thermostat, the conductance at 60 cycles and low voltage was determined, low voltage being defined as a voltage so low that doubling it produced no visible change in bridge setting. Then the conductance was determined at a high voltage, and immediately thereafter again at low voltage. By bracketing the high voltage determinations by low, we were always certain that heating by measuring current was not a cause of the increased conductance. An input of one watt in the platinum cells was sufficient to show a drift in conductance of about 3% per minute. The bridge voltage was applied through a combination of relays and push buttons, and could be turned on or off very quickly; consequently we were able to get reliable readings even at voltages so high that they produced appreciable heating on prolonged exposure. An approximate balance was obtained at high voltage, and then the low voltage conductance was followed until it reached its previous steady state. Then the bridge was set to the approximate high voltage setting first obtained, high voltage was applied for a few seconds, and successive adjustments were made, until a setting was found such that the bridge was in balance when high voltage was flashed on and off. Immediately after this final reading, the low voltage conductance was again checked. A simpler technique was used when the temperature drift caused not more than 1% change in conductance per minute: high voltage was applied at a noted time and the bridge was balanced as quickly as possible. Then the sliding balance was followed and recorded at thirty-second intervals. Extrapolation to zero time gave the true high voltage conductance. For the more dilute solutions, of course, the resistance was so high that temperature drift due to heating by bridge current was negligible.

Polarization.—As anticipated, the apparent conductance varied with frequency. An example is shown in Fig. 3, where the conductance of a 4.22×10^{-4} N solution is plotted against reciprocal root of frequency. A straight line is obtained, which is the normal polarization curve found by Jones and Christian.[12] Several voltage runs were made at 500–1500 cycles. In this range of frequency, the conductance–field curves were less steep than at 60 cycles by about 20% in slope. Further work on the frequency dependence is planned; we expect a decrease of the Wien coefficient with increasing frequency, when the field reverses so rapidly that the ions do not travel far in one cycle, but this effect should not appear until quite high frequencies. The large difference between the slopes at 60 cycles and at 1000 cycles is more likely due to a dependence of polarization on field strength. The question must remain unanswered until more data are available.

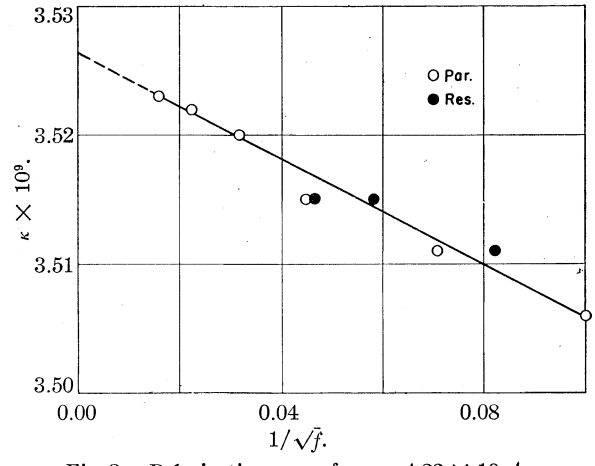


Fig. 3.—Polarization curve for $c = 4.22 \times 10^{-4}$.

Another interesting phenomenon was observed on di-

(9) Fuoss, THIS JOURNAL, **60**, 451 (1938).
(10) Fuoss, *ibid.*, **59**, 1703 (1937).
(11) Cox, Kraus and Fuoss, *Trans. Faraday Soc.*, **31**, 749 (1935).
(12) Jones and Christian, THIS JOURNAL, **57**, 272 (1935).

lute solutions placed in a clean cell, that is, on the initial filling before adsorption was saturated. If high voltage at 60 cycles was left on the cell for a short interval, and then the conductance followed at low voltage, a change with time was noted. For example, a millionth normal solution in the platinum cell was subjected to 25 kv. per centimeter for forty seconds. The conductance measured at low voltage was 15% *lower* than the initial value five minutes after the high voltage was removed; the difference decayed slowly with time, dropping to half value in about twenty minutes. The return behaved like a diffusion mechanism. An increase in cell resistance could not have been produced by heating; these solutions have positive temperature coefficients. Again more information is needed.

Viscosity.—In order to calculate ionic concentrations from conductances, it was necessary to know the limiting mobility. Since extrapolation was impossible, the viscosity of diphenyl ether at 50° was determined, and the limiting conductance calculated by Walden's rule. An Ostwald viscometer was used, whose specifications were as follows: length of capillary 10.0 cm., diameter of capillary 0.0968 cm., average head 20 cm., efflux volume 25 cc. The working volume was 50 cc. Dibenzyl ether (dried over sodium and distilled; b. p. 115–126° at about 1 mm.) was used as the calibrating liquid, and absolute values were based on the data of Bingham and Spooner.[13] At 50°, the viscosity of diphenyl ether was found to be 0.0209 poise.

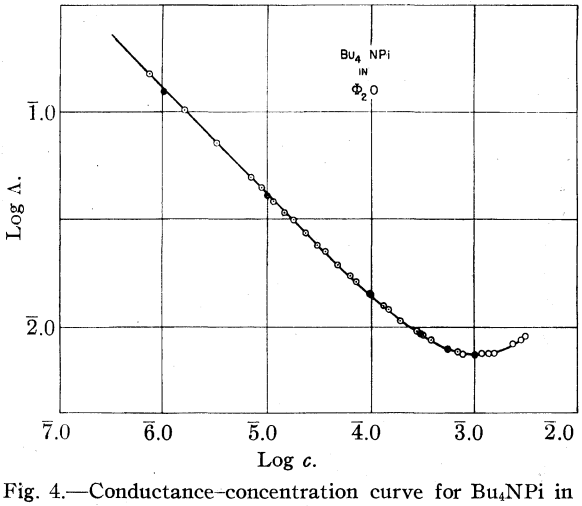


Fig. 4.—Conductance-concentration curve for Bu_4NPi in Ph_2O at 40°.

III. Experimental Results.—In Table I are given the low voltage conductances determined at 1000 cycles on the parallel bridge.

These results are summarized in Fig. 4, where the logarithm of the equivalent conductance is plotted against the logarithm of the concentration. The curve is the normal type expected for a 1–1 salt in a solvent of low dielectric constant.

Typical voltage runs are summarized in Table II. The field strength given is average kilovolts per centimeter, calculated from cell voltage and cell geometry by equations (1) and (4). All data in Table II are for 60-cycle fields; we hope to present data covering higher frequencies in a later paper, after the dependence of polarization on field strength has been studied.

(13) Bingham and Spooner, *J. Rheology*, **3**, 221 (1932).

TABLE I

CONDUCTANCE OF TETRABUTYLAMMONIUM PICRATE IN DIPHENYL ETHER AT 50°, LOW VOLTAGE AT 1000 CYCLES

$c \times 10^4$	$\Lambda \times 10^2$	$c \times 10^4$	$\Lambda \times 10^2$
31.55	0.897	1.308	1.250
28.01	.863	0.941	1.409
23.68	.830	.713	1.614
15.65	.753	.622	1.709
13.82	.746	.4698	1.928
11.74	.750	.3018	2.386
7.745	.749	.2317	2.697
6.729	.764	.1452	3.395
5.771	.792	.0685	4.91
3.781	.853	.0323	7.15
3.116	.908	.01608	10.24
2.737	.954	.01030	12.46
1.446	1.192	.00756	15.06

IV. Discussion and Comparison with Theory

It will be noted in Fig. 4 that the log Λ–log c plot is linear, with slope $(-1/2)$ in the dilute region. This slope corresponds to a simple association of ions pairwise.[14] At about 10^{-3} normal, a minimum appears, due to the association of ion pairs with free ions.[5] In order to obtain the constants for the system, $\Lambda\sqrt{c}\ g(c)$ was plotted against c, as shown in Fig. 5. From the slope and intercept, we obtain $\Lambda_0\sqrt{K} = 1.274 \times 10^{-4}$ and $\lambda_0\sqrt{K}/k = 0.105$, where Λ_0 and λ_0 are the limiting conductances of the types $A^+\cdot B'$ and $A_2B^+\cdot AB_2'$, respectively, and K and k are the corresponding dissociation constants. In ethylene chloride ($\eta_{25} = 0.007853$), Mead[15] found $\Lambda_0 = 57.40$ for tetrabutylammonium picrate at 25°, giving $\Lambda_0\eta = 0.4508$. In tricresyl phosphate ($\eta_{40} = 0.295$), Elliott[8] found $\Lambda_0 = 1.95$, giving $\Lambda_0\eta = 0.575$. Diphenyl either is about intermediate in size between ethylene chloride and tricresyl phosphate, so we take the average of the above values of the $\Lambda_0\eta$ product in order to allow for the deviation from Walden's rule due to size and shape of solvent molecules.[8] Using $\eta\ (Ph_2O)_{50°} = 0.0209$, we find $\Lambda_0 = 24.5$ for tetrabutylammonium picrate in diphenyl ether at 50°. Combining this value with the analysis of Fig. 5, and using the value

(14) Fuoss and Kraus, THIS JOURNAL, **55**, 1019 (1933).

(15) Mead, Kraus and Fuoss, *Trans. Faraday Soc.*, **32**, 594 (1936).

TABLE II

WIEN EFFECT FOR TETRABUTYLAMMONIUM PICRATE IN DIPHENYL ETHER AT 50° AND 60 CYCLES

E	$\kappa \times 10^{10}$
$c = 7.525 \times 10^{-4}$	
0.038[b]	55.75
.094	55.76
.189	55.77
.378	55.81
.755	55.84
1.888	56.24
3.78	57.34
5.85	58.69
8.01	60.57
10.27	62.34
$c = 5.407 \times 10^{-4}$	
0.019[b]	42.25
.094	42.25
.189	42.25
.378	42.28
.755	42.32
1.888	42.67
3.78	43.67
6.12	44.57
8.46	46.22
$c = 5.018 \times 10^{-4}$	
0.038[b]	39.00
.189	39.00
.378	39.01
.755	39.07
1.888	39.36
3.78	40.37
0.018[c]	39.00
.046	39.00
.183	39.01
.366	39.01
.916	39.11
1.83	39.40
2.95	39.92
3.90	40.41
$c = 2.916 \times 10^{-4}$	
0.038[b]	26.94
.189	26.97
0.381	26.96
0.755	27.01
1.87	27.28
3.78	27.99
6.12	28.78
8.46	29.73
11.86	31.23
$c = 9.64 \times 10^{-5}$	
0.042[a]	13.34
.211	13.34
.422	13.35
.843	13.41
2.11	13.63
4.22	14.06
6.83	14.50
9.44	15.05
13.24	15.77
0.038[b]	13.35
.189	13.35
.378	13.36
.755	13.39
1.89	13.56
3.78	13.95
6.12	14.36
8.46	14.76
11.86	15.61
15.07	16.42
$c = 2.376 \times 10^{-5}$	
0.094[b]	6.225
.189	6.225
.378	6.230
.755	6.251
1.89	6.344
3.78	6.542
7.93	6.978
0.046[c]	6.229
.092	6.229
.183	6.230
.366	6.236
.916	6.268
1.83	6.358
3.85	6.550
5.53	6.736
$c = 1.100 \times 10^{-5}$	
0.189[b]	4.219
.378	4.222
.755	4.240
1.89	4.309
3.78	4.435
5.93	4.584
8.01	4.700
$c = 9.87 \times 10^{-6}$	
0.211[a]	3.996
.422	4.003
.843	4.023
2.11	4.103
4.22	4.228
6.83	4.354
9.44	4.549
13.24	4.788
0.189[b]	3.988
.378	4.002
.755	4.018
1.89	4.083
3.78	4.205
6.12	4.325
8.46	4.463
11.86	4.702
$c = 1.030 \times 10^{-6}$	
0.094[b]	1.283
.189	1.283
.378	1.286
.755	1.292
1.89	1.313
3.78	1.350
6.12	1.394
8.46	1.437
11.86	1.505
15.07	1.582
18.88	1.685

[a] Cell 2. [b] Cell 3. [c] Cell 4.

$\lambda_0/\Lambda_0 = 0.82$ found by Bien[16] for the same electrolyte in anisole, we find $K = 2.70 \times 10^{-11}$ and $k = 1.00 \times 10^{-3}$.

From the values of the dissociation constants, we can calculate the corresponding ion sizes, assuming that the association is due entirely to Coulomb forces.[17] For the binary association of tetrabutylammonium ion and picrate ion, we find $a = 5.33 \times 10^{-8}$ cm. This is somewhat smaller than previous values for this salt (5.83×10^{-8} in ethylene chloride[15] at 25°, 5.80×10^{-8} in tricresyl phosphate[8] at 40°, and 5.60×10^{-8} in anisole[16] from −33 to 95.1°); there seems to be a trend of a values with D. For the triple ion equilibrium, we find $a_3 = 7.9 \times 10^{-8}$ cm., which checks Bien's value[16] in anisole at 61.3°. The fact that $a_3 > a$ for picrates has already been discussed.[16]

(16) Bien, Kraus and Fuoss, THIS JOURNAL, **56**, 1860 (1934).
(17) Fuoss, *Chem. Rev.*, **17**, 27 (1935).

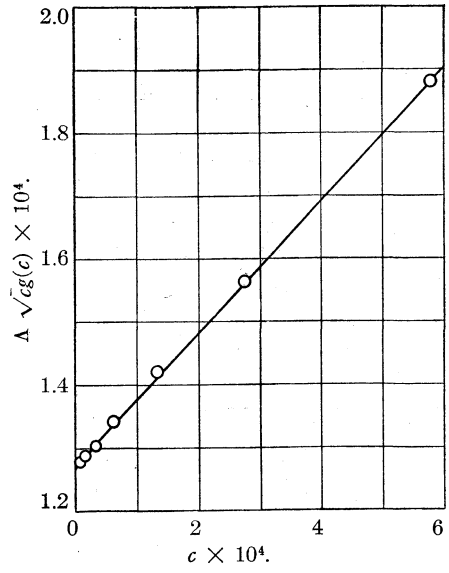


Fig. 5.—Evaluation of dissociation constants by graphical analysis.

We next consider the conductance–field curves. At low concentrations, where the free ion concentration is extremely small, the curve is substantially linear over the whole voltage range studied, as is shown in Fig. 6 for a millionth normal solution. As the concentration increases, the initial part of the conductance–field curve be-

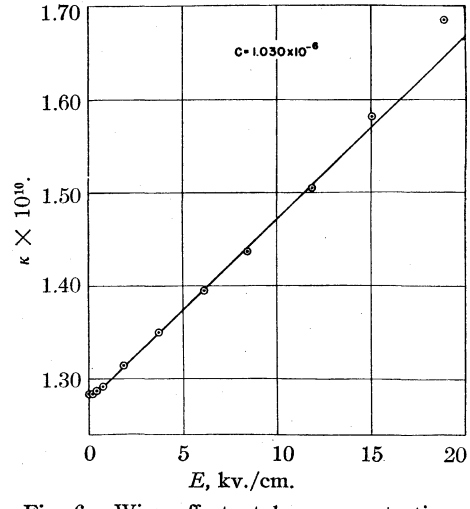


Fig. 6.—Wien effect at low concentration.

comes concave up, and eventually approaches linearity, as is shown in Fig. 7. The curved re-

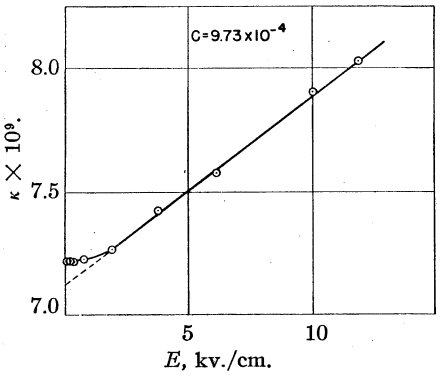


Fig. 7.—Wien effect at high concentration.

gion is due to the presence of an ionic atmosphere and once the ions move so fast in the field that this distribution can no longer be maintained, the curve becomes linear, as predicted by Onsager's theory.[4] Onsager's result, for the case of small degree of dissociation of 1–1 salts (in our case, $K = 2.70 \times 10^{-}$)[11] is

$$\kappa/\kappa_0 = 1 + (\epsilon^3/4Dk^2T^2)\overline{X} \qquad (5)$$

where κ is the conductance at field strength $\overline{X}$, κ_0 is the conductance at zero field strength and the other symbols have their usual meaning. For diphenyl ether at 50°, (5) becomes

$$\kappa/\kappa_0 = 1 + 0.0132\,E \qquad (6)$$

where E is the field strength in kilovolts per centimeter. The data of Table II (see also Figs. 2, 6, 7) all give linear portions at higher field strengths, after the initial concave-up section. The slopes are somewhat higher than predicted by (6), ranging from 1.3 to 1.6% per kilovolt, depending on the concentration. The dependence on concentration is systematic, and therefore, despite the rather large experimental error involved in determining a slope, we believe that it is real. The values of the slope are plotted against concentration in Fig. 8. Below 10^{-4} normal, the slopes are, within our present experimental error, equal to 1.6% per kilovolt, independent of concentration. It is interesting and perhaps significant that the dependence on concentration of the Wien coefficient begins at the concentration where triple ion formation causes the log Λ–log c plot to start to deviate from linearity. The present theory calls for concentration independence of the Wien coefficient. We plan to study systems in solvents of still lower

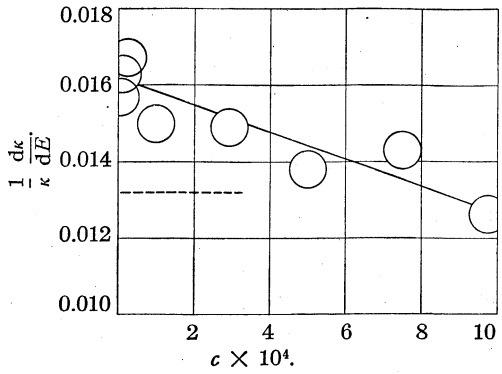


Fig. 8.—Dependence of Wien coefficient on concentration.

dielectric constant, so that the region of complex association can be studied. (It was impossible to work at higher concentrations in diphenyl ether, on account of heating.)

The difference in absolute value between our limiting experimental value of 1.6% at low concentrations and the theoretical value of 1.32% may be due to the dissymmetry of the picrate ion; the theoretical treatment implies a spherical ion. Work in progress on other salts will give information bearing on this question.

If the linear portions of the conductance–field curves are extrapolated to zero field strength, the low voltage conductance is obtained which the ions would have if the activity coefficient were unity.[4] Consequently the ratio of the actual conductance at low voltage to the extrapolated value measures the activity coefficient for the particular concentration involved. We have made the corresponding calculation for the data of Table II; the results are shown in Fig. 9. As abscissa, we used the square root of total *ionic* concentration, which was calculated from

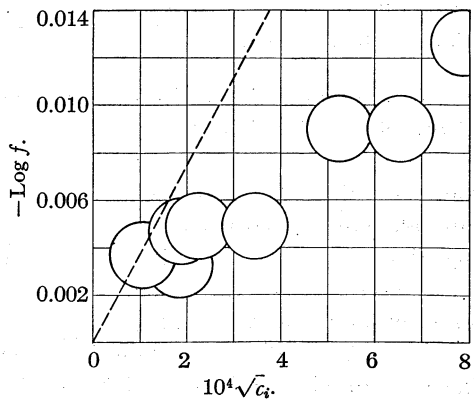


Fig. 9.—Activity coefficients determined by Wien effect.

the stoichiometric concentration and our experimental values of dissociation constants. The dotted line in Fig. 9 is the Debye–Hückel limiting slope, which is given by the following equation for 1–1 salts in diphenyl ether at 50°

$$-\log f = 33.8\sqrt{c_i} \qquad (7)$$

where c_i is total ionic concentration. Considering the large error in the experimental values of f, the results are not disappointing. The fact that we actually find a deviation of the right order of magnitude, which varies in the proper way with concentration, in a solvent of dielectric constant 3.53, is significant, if we recall that K is 2.7×10^{-11}. The highest ionic concentration in Fig. 9 is 6×10^{-7}.

Summary

1. The conductance of tetrabutylammonium picrate in diphenyl ether at 50° has been measured at 1000 cycles and low voltage and at 60 cycles under field strengths up to 15 KV/cm., over the approximate concentration range 10^{-3} to 10^{-6} normal.

2. Onsager's theory of the Wien effect is in good agreement with our data.

3. Deviations of activity coefficients from unity calculated by the limiting law of Debye and Hückel agree in order of magnitude with the experimental values obtained from the conductance curves.

SCHENECTADY, NEW YORK RECEIVED MAY 16, 1939

[CONTRIBUTION FROM THE COAL RESEARCH LABORATORY, CARNEGIE INSTITUTE OF TECHNOLOGY]

The Reduction of Carbon Dioxide by Graphite and Coke

BY MARTIN A. MAYERS

The rates of reaction of monolithic samples of artificial graphite with carbon dioxide and steam at atmospheric pressure and temperatures from 850° have been reported previously.[1] In that work the limiting effect of the diffusion field adjacent to the surface of the sample was eliminated and the measured reaction rates were considered to be true heterogeneous reaction rates and were referred to unit area of the surface exposed to the action of the gas. Later measurements of the reaction with carbon dioxide of artificial graphite and coke in granular form and of monoliths of both artificial and natural graphite have shown that in artificial graphite and in coke, the reaction rate measured depends not only on the surface exposed, but is the total of the contributions of elementary surfaces reached by the oxidizing gas by its perfusion throughout the body of these porous materials. This result suggests a possible explanation of part of the discrepancy between the measurements by this method and those made under high vacuum.[2]

Apparatus and Materials.—Carbon dioxide was withdrawn from a cylinder through a reducing valve, passed through a flowmeter and a purifying train consisting of a heated quartz tube containing reduced copper and copper oxide and a drying tower containing calcium chloride followed by Anhydrone, and then into the furnace. Leaving the furnace the gas stream flowed through a cooling section, and then by way of a three-way stopcock, either direct to the analyzer, or into the large gasometer used in the tests reported before. The gas analyzer was the same one previously described, in which the carbon monoxide is oxidized by iodine pentoxide and its quantity determined by the titration of the iodine liberated which was collected in a condenser cooled by dry ice.

The furnace and sample holder differ from those used in the previous work and are shown in Fig. 1. The smaller diameter of the furnace tube permitted the attainment of high gas velocities without using extremely large volumes of gas. The mullite boat, used as a sample holder, permitted the use of either granular or monolithic samples of carbon. It was streamlined as shown in order to eliminate, as completely as possible, disturbances of the flow across the reacting surface.

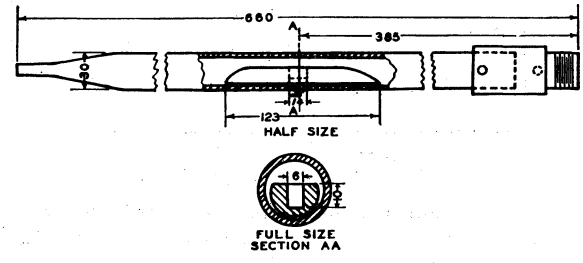


Fig. 1.—Reaction tube and sample boat. All dimensions in millimeters.

Granular samples were prepared for test by crushing coke in a small jaw crusher and by turning off heavy chips of graphite from cylindrical electrodes, and sieving the granular material between standard metal cloth sieves.

(1) M. A. Mayers, THIS JOURNAL, **56**, 70, 1879 (1934).

(2) H. Martin and L. Meyer, *Z. Elektrochem.*, **41**, 136 (1935); Lothar Meyer, *Trans. Faraday Soc.*, **34**, 1056–61 (1938).

The graphite electrodes were of Acheson graphite of spectroscopic grade, and were from the same lot as that used in the work reported previously. The cokes were experimental cokes made from a Pittsburgh Seam coal with controlled rates of heating to 1000°.[3] Table I gives the details of the treatment of the various cokes tested. The boats were filled to the desired depth, shaken down, and uniformly compacted by pressing down the charge with a brass gage block of known dimensions which fitted the depression in the boat. The depth of the sample below the top surface of the boat was then determined by measuring the height of the top of the gage block above the top of the boat by the use of a vernier depth gage reading to 0.02 mm.

TABLE I

LABORATORY COKES MADE FROM PITTSBURGH SEAM COAL (EDENBORN MINE)

Designation	Maximum temp., °C.	Rate of heating, °C./min.
W 85	1000	1.4
W 88	1000	1.4
W 92	1000	21.8
W 93	1000	21.8

Monolithic samples of different thicknesses were cut out of portions of artificial graphite electrode, and from a single mass of foliated Ceylon graphite, to fit the depression in the boat. They were cut out with a sharp knife and finished with a steel file, and then were cemented into the boats so that their top surfaces were not more than 0.5 mm. above the top of the boat. A commercial cement with a sodium silicate base (Insa-lute) was used to seal the samples into the boat. Great care was taken to prevent the cement from coming in contact with the top surface of the sample, and the cement was carefully finished off, after partial drying, to give a smooth contour rising from the boat surface to the surface of the sample.

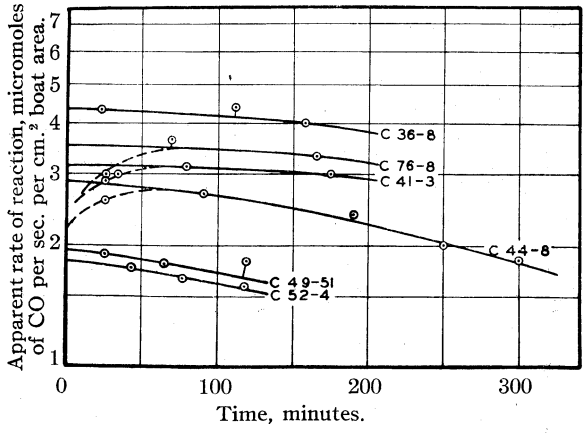


Fig. 2.—Reaction in micromoles of carbon monoxide per second per sq. cm. at various times for several samples of granular graphite.

Procedure and Calculations.—When a boat had been filled as described above, it was introduced into the furnace, and advanced in about fifteen minutes to the center. During this time the furnace was maintained at the temperature at which runs were to be made, and carbon dioxide was passed through the furnace but was not collected. The slow advance of the boat was necessary to prevent breakage of the boat or the mullite furnace tube by thermal shock. Immediately after introducing the boat, and at thirty-five to forty-five-minute intervals thereafter, runs were made in which the gas leaving the furnace was collected and analyzed, the duration of each run being two to three minutes. During the runs, the temperature, the rate of gas flow, and the gas pressure at the inlet and outlet of the furnace were read every minute. Three to six runs were made on each sample.

The rates of reaction measured in several groups of runs at 1000° are plotted in Fig. 2 against the time after the boat was inserted in the furnace. It will be observed that the reaction rates rise to a maximum and then fall off. Since the quantity and approximate condition of the graphite are known only at the time the sample was inserted into the furnace, it is necessary to refer the reaction rate to that time. In performing this extrapolation, the rapidly rising initial portion of the curve is neglected. This is believed to be justified on the ground that this portion of the curve represents a transient condition, while the normal concentration gradients through the body of the sample are being set up. Such an assumption is supported by the fact that this portion of the curve was less pronounced in the measurements on granular samples, when the normal gradient might be expected to be attained more rapidly, than it was in measurements on monolithic samples. The differences in the intercepts at zero time in Fig. 2 are due to differences in the thicknesses of the samples tested, the thickest sample producing the largest reaction.

Theoretical.—In order to interpret these results it is necessary to analyze the conditions under which the reaction takes place. Let the concentration of carbon dioxide in the porous bed be p_1 and that of carbon monoxide be p_2. Since the reaction takes place under a constant total pressure, and these are the only gases present

$$p_1 + p_2 = P \qquad (1)$$

where P is the constant total pressure, atmospheric. Then, if D is the diffusion coefficient, a the void volume in the bed, v the gas velocity in the bed caused by the expansion due to the reaction, μ the reaction rate per unit of carbon crystallite surface, and s the surface of carbon crystallites per unit volume of bed, and if a steady state is reached, p_1 and p_2 must obey the differential equations

(3) Wm. B. Warren, *Ind. Eng. Chem.*, **27**, 72–77 (1935).

$$aD\frac{d^2p_1}{dx^2} + a\frac{d}{dx}(p_1v) - \mu s p_1 = 0$$
$$aD\frac{d^2p_2}{dx^2} + a\frac{d}{dx}(p_2v) + 2\mu s p_1 = 0 \qquad (2)$$

with the boundary conditions

$$dp_1/dx = dp_2/dx = 0 \qquad x = c;$$
$$v = 0, x = c; \text{ and } p_1 = P_1, x = l \qquad (3)$$

where x is the distance below the top of the boat, l is the level of top of the sample, and c is the level of its bottom. Combining (1) and (2), it is found that v satisfies

$$\frac{dv}{dx} = -\frac{\mu s}{a}\frac{p_1}{P} \qquad (4)$$

Eliminating p_1 between (4) and the first of (2), the non-linear equation

$$\frac{d^2v}{dx^2} + \frac{1}{D}v\frac{dv}{dx} - \frac{\mu s}{aD}v = 0 \qquad (5)$$

is obtained, whose solution, by the use of (4), could be used to calculate the total reaction per unit of sample surface by means of the integral

$$R = \int_c^l 2\mu s p_1 dx = 2aPv(l)$$

A general solution to equation (5) has not been found, but a series expansion can be set up[4] for small values of $\mu s/aD(c-l)^2$ in the form

$$R \sim 2\mu s(c-l)\left\{1 - \frac{2}{3}\frac{\mu s}{aD}(c-l)^2 + \frac{2}{3}\left[\frac{\mu s}{aD}(c-l)^2\right]^2 - \ldots\right\} \qquad (6)$$

which, however, converges very slowly. If the coefficient of p_1 in the second of equations (2) were μs instead of $2\mu s$, v would vanish and a simple analytic solution is possible in the form

$$R = 2\sqrt{\mu s aD}\tanh\sqrt{\frac{\mu s}{aD}}(c-l) \sim 2\mu s(c-l)\left\{1 - \frac{1}{3}\frac{\mu s}{aD}(c-l)^2 + \ldots\right\} \qquad (7)$$

Hence, it seems probable that the effect of the non-linearity of equation (5) is merely to change the rate of convergence of R in the neighborhood of $(c-l) = 0$; the similarity between (6) and (7) suggests that near $(c-l) = 0$ there will be a linear relation between $R/(c-l)$ and $(c-l)^2$, and that the value of $2\mu s$, the true rate of formation of carbon monoxide per unit volume of sample, will be given by the intercept of the line at $(c-l)^2 = 0$.

Results

The tests on granular samples of artificial graphite were made on beds of such thickness that this method of plotting gave straight lines, as shown in Fig. 3, in which the reaction rates per unit area at zero time determined from the curves of Fig. 2, divided by the sample thickness, are plotted against the square of the sample thickness. The fact that the experimental results appear to fit straight lines on this plot indicates that the analysis given above may apply to the experimental condition, while the departures from the lines at values of $(c-l)^2$ greater than about 0.4 show that the higher order terms begin to be of influence above the corresponding value of $\mu s/aD(c-l)^2$. The intercepts of these lines, representing the rate of formation of carbon monoxide at 1 atmosphere pressure per unit volume of the bed of granules, can then be plotted as the triangles in Fig. 5, to the coördinates of the Arrhenius equation, showing that the reaction rate has a temperature coefficient corresponding to the heat of activation of 52.3 kcal. The departure of the points from the line corresponds to a probable error of a single determination of about 17%.

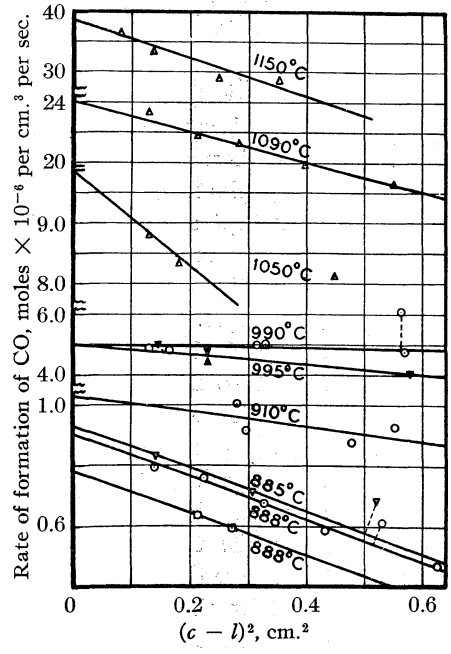


Fig. 3.—Determination of reaction rate per unit volume for granular graphite passing no. 16 and on no. 20 U. S. std. mesh sieves: △, gas velocity 1.9 l./min.; ○, gas velocity 2.5 l./min.; ▽, gas velocity 3.4 l./min.

When the data for monolithic samples are plotted as in Fig. 4 it is observed that the points do not fall on a straight line, but appear to approach

(4) H. G. Landau, to be published.

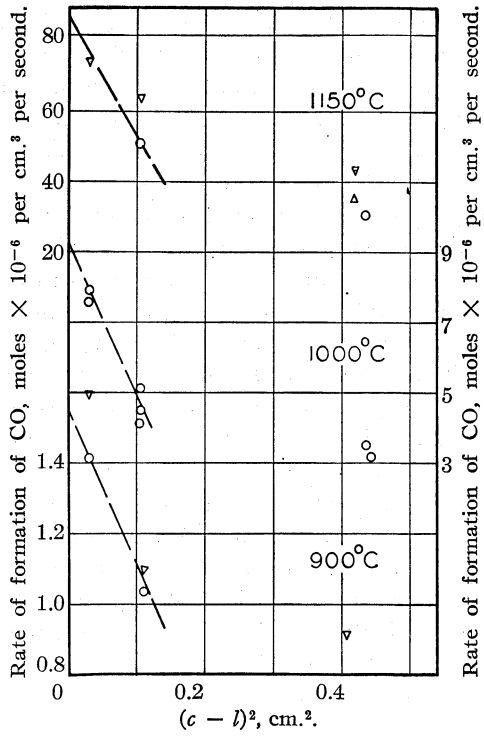


Fig. 4.—Determination of reaction rate per unit volume for monolithic graphite.

a hyperbolic form. This might be taken to indicate that the monolithic samples have a true surface reaction with carbon dioxide, whose value might be obtained by plotting R against $(c - l)$ and reading the intercept at zero thickness. It must be observed, however, that the quantity $\mu s/aD(c - l)^2$ is a function of the porosity, or the void volume of the sample. Comparing samples of the same material packed to different densities, it will be observed that $\mu s/aD$ varies as $(1 - a)/a$. Since the volume of voids of the monolithic samples, determined by comparing their true density determined with helium[5] as the displacing fluid with their apparent densities as shown in Table II, is about 29%, while that for the granular samples may be expected to be about 50%, the value of $\mu s/aD$ for the monolithic sample would be nearly three times that for the granular sample at the same temperature. Since the results for the granular samples departed from the straight line at values of $(c - l)^2$ of about 0.4, those for the monolithic samples may be expected to do so at about 0.13. Because of the difficulty of cutting out thin samples of graphite, there are only two points at each temperature at values of $(c - l)^2$ less than 0.13, but passing straight lines through these points permits making an estimate of the value of $2\mu s$ for the monolithic samples. These values have been plotted on Fig. 5 as circles. The line passing through them corresponds to a heat of activation of about 50.6 kcal. The difference between the heats of activation of the reaction on monolithic and on granular samples indicates the order of the precision of the determination of this quantity, or about ±1.7 kcal. The ratio between the rates of reaction in the two kinds of samples, which is almost constant at a value of 1.58, indicates that the volume of voids in the granular sample is about 55%, corresponding to particles packed to a density of 64%.

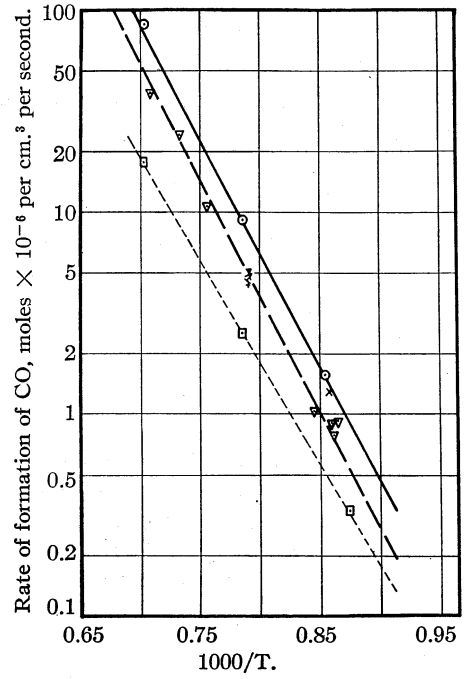


Fig. 5.—Reaction rates per unit volume at various temperatures: ○, monolithic samples of artificial graphite; ▽, artificial graphite −16 +20 mesh; □, natural graphite—read scale in moles × 10^{-6} per sq. cm. per sec. Laboratory cokes: ×, W 85; +, W 88; ⊙, W 92; ø, W 93.

The data on cokes were analyzed by the same methods as described above, and the results are shown by various symbols in Fig. 5. Measurements on natural graphite were made on samples of different orientations with respect to the grain of the sample. The results of these measurements were very erratic, being greatly affected by the quantity of ash exposed, the ash being distributed

(5) H. C. Howard and G. A. Hulett, *J. Phys. Chem.*, **28**, 1082 (1924).

irregularly through the foliated mass from which samples were cut. The results on this material were so erratic as to obscure any differences of reaction rate with orientation of the face or with thickness of the sample that may have been present. The order of magnitude of the reaction rate with this material was, however, the same as that of the monolithic samples, considered as a reaction rate per unit area. These values are also shown in Fig. 5.

Discussion

While the precision of the results is not high, it is great enough to make it certain that the results obtained in this work differ from those previously reported on the same material. The hypothesis that the monoliths of artificial graphite were actually porous, required to correlate the results, was checked by comparing the true density determined by displacement with helium with the apparent density of several samples as shown in Table II. It may be noted that the results of these experiments agree with those previously reported if the correction for volume reaction is not made. Thus it must be concluded that the earlier work is in error because of failure to take account of the perfusion process.

TABLE II

TRUE DENSITIES OF VARIOUS GRAPHITES

Sample, Acheson graphite	True density in g./cc.
Monolith	2.07
Monolith, heat treated at about 2200°	2.08
−16 +20 mesh	2.08
−140 mesh	2.11

APPARENT DENSITIES OF VARIOUS MONOLITHIC SAMPLES OF ACHESON GRAPHITE

Sample	Apparent density in g./cc.
25	1.47
26	1.50
27	1.48
Apparent volume of voids	29%

This result suggests the explanation for some of the discrepancies that exist in the literature concerning this reaction. The present value of the temperature coefficient for the reaction of carbon dioxide with artificial graphite is in approximate agreement with the value that may be calculated from the work of Blakeley and Cobb.[6] It also suggests an explanation of the peculiar temperature coefficient of the reaction rate of artificial graphite with oxygen calculated by Davis and Hottel[7] from their experiments on the burning of carbons in oxygen under conditions in which the diffusion path was fixed and known. From this work both the diffusion coefficient and the specific reaction rate could, theoretically, be calculated, if the reaction took place on a geometrical surface at the end of the diffusion path. However, the reaction rates calculated on this assumption had abnormal temperature coefficients that did not follow the Arrhenius equation, and the reaction rates for different forms of carbon crossed in a peculiar fashion. Davis and Hottel were unable to give an explanation for this behavior; it is suggested, in the light of the results reported here, that the reason for the apparently abnormal behavior may be sought in the perfusion phenomena accompanying the reaction, since the samples used in that work also were porous. The differences in the behavior of the two kinds of carbon for which data are reported probably arise from their having both different porosities and different reactivities, which easily could lead to the change in order of apparent reaction rate that was observed with changes in temperature.

Finally, this work suggests the possibility of partly reconciling the discrepancies observed between determinations of the reaction rates at normal pressures, and those determined in high vacuum.[2] The reaction rates observed at normal pressures, when referred to unit area of the carbon used, are of the order of thousands of times as great as those determined under vacuum. Since, however, the samples tested in the vacuum work[8] had uniform solid surfaces of deposited graphite whose basal planes were parallel to the geometrical surface, the discrepancy must arise in part from the porous nature of the carbons used in the experiments at normal pressures, in almost all of which a large internal surface, which easily could be a thousand times the exposed geometrical surface, was available for reaction. This hypothesis fails to explain, however the large difference in temperature coefficient, which in the vacuum experiments[2] corresponds to a heat of activation of the order of 90 kcal. This extraordinarily high value may be due to the fact that, in the vacuum experiments, only the graphite filament was heated, while the gas was cold.

(6) T. H. Blakeley and J. W. Cobb, *Gas World*, **101**, 452, 498, 612 (1934); *Gas J.*, **208**, 351, 526, 748 (1934).

(7) H. Davis and H. C. Hottel, *Ind. Eng. Chem.*, **26**, 889 (1934).

(8) Lothar Meyer, *Z. physik. Chem.*, **B17**, 385–404 (1932).

Conclusions

Measurements of the rates of reaction of carbon dioxide with both artificial and natural graphite and with several high temperature cokes of known history have been reported. The results have been calculated to give the reaction rates per unit volume of coke or graphite and have been corrected for the perfusion of the reacting gas throughout the body of the porous samples. Because of this manipulation, the results are not particularly precise, errors of the order of 20% being possible.

It is shown that artificial graphites and cokes behave, in reaction, like porous bodies whose internal surface contributes to the reaction rate. The reaction of carbon dioxide with artificial graphite has a temperature coefficient corresponding to a heat of activation of about 52 kcal. That of the reaction with natural graphite is more uncertain because of the marked effect of the mineral impurities which the sample contained, but it appears to be of the order of 44 kcal.

PITTSBURGH, PENNSYLVANIA RECEIVED MAY 31, 1939

[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY, UNIVERSITY OF VIRGINIA]

The Colorimetric Determination of Palladium with *p*-Nitrosodiphenylamine[1]

BY JOHN H. YOE AND LYLE G. OVERHOLSER

The colorimetric methods available for the determination of palladium have been developed in connection with platinum analysis,[2,3] and while they do provide rapid and accurate methods for the determination of quantities of palladium of the order of 0.1 mg., no colorimetric method has been reported that will yield reasonably accurate results with quantities of the order of a few γ. Studies have been made on reagents for the detection and approximate estimation of minute quantities of palladium. *p*-Dimethylaminobenzylidene rhodanine[4] has been used for the detection of palladium, but no application of this reagent for the quantitative determination of the metal has been reported. This reagent is extremely sensitive for palladium but not so nearly specific as *p*-nitrosodiphenylamine. Feigl and Fränkel[5] report that as little as 0.0025 γ of palladium per ml. (1:400,000,000 can be detected by the catalytic effect of palladium on the reduction of nickel salts by sodium hypophosphite. Pierson[6] utilized the reducing action of mercurous chloride for the detection and approximate estimation of minute quantities of the metal by observing the shades of color produced by the adsorbed metal. But there is need of a method that may be used for the determination of minute quantities of palladium and that is not rendered useless by the presence of the other metals frequently accompanying palladium.

p-Nitrosodiphenylamine has been found to react with palladous chloride in neutral and weakly acid solution to give either a deep red colored solution or a purplish-brown precipitate, depending on the concentration of the metal. The reaction is extremely sensitive, permitting the detection of 0.005 γ of palladium by the spot-plate technique, and compares favorably with *p*-dimethylaminobenzylidene rhodanine. The reagent is practically specific for palladium, in the sense that the only other metals forming colored compounds are gold and silver. The sensitivity for gold and silver, however, is much less than for palladium. Oxidizing agents interfere by giving colored solutions; cyanides and iodides prevent the formation of the colored compound. The sensitivity is affected by the *p*H of the solution and the concentration of salts present, but these can be controlled easily.

If the reagent is added in excess to a weakly acidic palladous chloride solution, the palladium is quantitatively precipitated. On the other hand, if a sodium acetate–hydrochloric acid buffer of the proper *p*H and salt concentration is used, a deep red colored solution results which may

(1) This investigation was partly supported by a grant-in-aid from the Carnegie Corporation. It is the first of a projected series based upon studies of inorganic reagents in organic analysis. These studies are being conducted as a coöperative effort in which eight Virginia institutions are participating under the direction of John H. Yoe. Those coöperating with the University of Virginia are: Hampden-Sydney, Mary Baldwin, Randolph-Macon (Ashland), Virginia Military Institute, Virginia Polytechnic Institute, Washington and Lee, and William and Mary.

(2) O. E. Zvyagintzev, *Ann. inst. platine*, 364 (1926).

(3) F. C. Robinson, *Bull. Am. Inst. Mining Met.*, No. 260 (1926).

(4) F. Feigl, P. Krumholz and E. Rajmann, *Mikrochemie*, **9**, 165 (1931); H. Holzer, *ibid.*, **8**, 271 (1930).

(5) F. Feigl and E. Fränkel, *Ber.*, **65B**, 539 (1932).

(6) G. G. Pierson, *Ind. Eng. Chem., Anal. Ed.*, **6**, 437 (1934); *ibid.*, **11**, 86 (1939).

be satisfactorily used for the colorimetric determination of palladium in the range 0.5–50 γ.

This paper presents various aspects of the new reaction, details for the colorimetric method, and procedures for the determination of palladium when accompanied with gold and platinum.

Materials Used

Palladium Chloride.—A stock solution was prepared by dissolving a 1.74-g. sample of palladous chloride (57.5% of palladium) in 85 ml. of hydrochloric acid and diluting to 1 liter with water. This gave a solution 1 *M* with respect to hydrochloric acid and contained 1.003 mg. of palladium per ml. as determined by analysis with dimethylglyoxime. Solutions containing 1 and 10 p. p. m. of palladium, respectively, were prepared by diluting the stock solution with water.

Acids.—Unless otherwise indicated, all acids used in this study were concentrated C. P. reagents.

***p*-Nitrosodiphenylamine.**—The product used was obtained from the Eastman Kodak Company and had a m. p. of 143–144°. A solution of the reagent was prepared by dissolving 50 mg. of the solid in 500 ml. of 95% ethyl alcohol and diluting to 1 liter with water. This solution had a yellowish-orange color and was stable for several months.

Sodium Acetate–Hydrochloric Acid Buffer.—This buffer solution was prepared by adding 240 ml. of 1 *M* hydrochloric acid to 200 ml. of 1 *M* sodium acetate and diluting the mixture to 1 liter with water. The *p*H of the solution, as measured by the quinhydrone electrode, was 1.6. Upon diluting 25 ml. of this buffer to 100 ml. with water a *p*H value of 2.1 was obtained.

Procedure Recommended for the Determination of Small Quantities of Palladium.—The method may be applied successfully to the determination of quantities of palladium not exceeding 50 γ, although it is preferable that the amount present be less than 30 γ. Palladium may be determined in such materials as crude platinum and the various alloys, provided interfering substances are first removed. Directions are given in another section for the separation from platinum and gold, since these metals frequently accompany palladium. Palladium may be determined in the presence of iridium and rhodium, provided the ratio of iridium to palladium and that of rhodium to palladium does not exceed 20 to 1.

Several precautions must be observed in order to obtain reliable results. The palladium should be present as palladous chloride in a solution containing not more than 0.5 mmol. of hydrochloric acid or a total salt concentration of not over 3 mmol. The reagent should be added to all solutions (unknowns and standards) at as nearly the same time as possible (within fifteen minutes), and all the solutions should be at room temperature when the reagent is added. Finally, the matching should be completed within one hour after the addition of the reagent.

Procedure.—Prepare the standard series by using the following increments of palladium in the respective concentration ranges: 0–10 γ, 0.5 γ; 11–25 γ, 1 γ; 26–35 γ, 2 γ; 36–50 γ, 5 γ. Transfer the solutions containing the palladous chloride (standards and unknowns) to 100 ml. volumetric flasks, add 25 ml. of the sodium acetate–hydrochloric acid buffer from a pipet, 2 ml. of reagent from a pipet, and dilute to 100 ml. with water. Before matching the solutions, thoroughly mix and allow them to stand at room temperature for about thirty minutes.

Color matching in our work was done with a roulette comparator[7] using 100-ml. tubes (160 mm.). At the lower palladium concentrations, Corning Filter no. 512 was used advantageously, while filters nos. 585 and 556 were employed at the higher concentrations. In some cases the matching was also carried out in 50-ml. Nessler tubes (220 mm.). The latter method is as sensitive at the lower concentrations but less so at the higher ones, because filters are not applicable. Since the observed color is a mixture of the yellow color of the reagent and that of the red palladium compound, the Duboscq colorimeter is of little use due to the change in the shade of color obtained with different amounts of palladium. The photoelectric colorimeter may be used but no increase in the actual sensitivity is obtained because of the influence of several uncontrollable factors.

Experimental Development of the Procedure

Reaction of *p*-Nitrosodiphenylamine with Palladous Chloride.—The greatest difficulty encountered during the development of the method was the formation of turbid solutions. In unbuffered as well as with biphthalate buffers, turbid solutions always resulted. The sodium acetate–hydrochloric acid buffers were unique because they gave clear red solutions, when buffers having a relatively high salt concentration and a low *p*H were used. If more than 2 ml. of the reagent was used, however, turbid solutions were obtained, even in the presence of the prescribed buffer medium.

A sample of the solid compound was obtained in the following manner: 50 ml. of a solution of palladous chloride containing 50 mg. of palladium was diluted to 500 ml. with water. To this solution was added 50 ml. of a filtered alcoholic solution containing 100 mg. of *p*-nitrosodiphenylamine. The precipitate was filtered off, dried for twelve hours at 110° and analyzed. *Anal.* Calcd. for $C_{24}H_{20}N_4O_2PdCl_2$: C, 50.21; H, 3.51; Pd, 18.59; Cl, 12.35. Found: C, 50.15; H, 3.85; Pd, 18.52; Cl, 12.21.[8]

The composition corresponds to the formula $Pd[C_6H_5NHC_6H_4NO]_2Cl_2$, which is a coördination compound analogous to the other numerous ammino compounds of palladium, exemplified by $Pd(NH_3)_2Cl_2$. Palladous nitrate also reacts with the reagent to give a compound having a similar color which is probably an analogous coördination compound.

The sample analyzed was precipitated from a solution containing an excess of palladium, because the precipitate so obtained was handled more easily than that obtained by using an excess of the reagent. Samples were also prepared by using an excess of reagent, as well as by precipitating the palladium from a sodium acetate–hydrochloric acid buffer under the same conditions used in the colorimetric procedure. In these samples, only palladium was

(7) J. H. Yoe and T. B. Crumpler, *Ind. Eng. Chem., Anal. Ed.*, **7**, 78 (1935).

(8) The authors are indebted to Miss Elizabeth C. Johnson of this Laboratory for the halogen determination.

determined but the values obtained checked that of the compound reported above, leaving no doubt that the samples prepared in the different ways all had the same composition.

The compound appears as a purplish-brown amorphous precipitate which adheres tenaciously to glassware and is very difficult to filter. It loses water slowly when dried at 110°, but if heated above 120° it undergoes a very gradual decomposition. The compound is insoluble in water but moderately soluble in 95% ethyl alcohol, yielding a deep red colored solution. It dissolves in moderately strong hydrochloric, nitric, or sulfuric acid, giving solutions ranging in color from red to yellow. With ammonia and sodium hydroxide, yellow solutions are formed.

Although the composition of the precipitate is satisfactorily constant and has the advantage of a low palladium content, the difficulties encountered in filtering and drying prevent it from having a practical value in gravimetric analysis, especially since other more suitable organic precipitants are available.

The relative absorption curves for solutions of the reagent and of the palladium compound are given in Fig. 1.

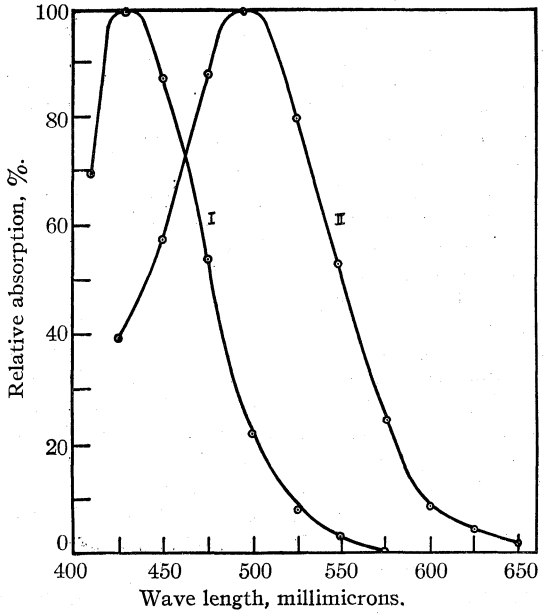


Fig. 1.

The data for the curves were obtained with a photoelectric spectrophotometer.[9] Curve I, the reagent curve, was obtained for a solution prepared by adding 10 ml. of the reagent to 25 ml. of standard buffer solution and diluting to 100 ml. with water (*p*H 2.1). Curve II, the compound curve, was obtained for a solution containing 70 γ of palladium prepared in the same manner as for the colorimetric determination. It will be observed that the maximum for the reagent and that for the compound occur near each other. Consequently, it is difficult to eliminate, by the use of a color filter, the absorption by the reagent.

Effect of Concentration of Salts.—The presence of small amounts of salts, such as sodium chloride, have a marked effect on the reaction when carried out in solutions of low ionic strength. For example, using 5 γ of palladium and a final concentration of hydrochloric acid of 10^{-4} or 10^{-5} *M* it was found that as small a concentration of sodium chloride as 10^{-4} *M* caused a slight decrease in the intensity of the color. With larger amounts of sodium chloride, a corresponding decrease in the red color was observed and with a concentration as great as 1 *M* practically none of the red colored compound formed. Other sodium salts such as the nitrate and sulfate, as well as the corresponding potassium and ammonium salts, exhibit a similar behavior.

Under the conditions recommended, *i. e.*, the use of a buffer with a final salt concentration of 0.05 *M*, the maximum color or sensitivity is not obtainable because of the salt effect. It is necessary to use the buffer to prevent turbidity, and to minimize the effect of additional salts, as well as to control the *p*H. In the buffer system used, the presence of additional salts in amounts to give a final concentration of 0.01 *M* is without effect and the maximum concentration allowable without error is 0.03 *M*.

Effect of Hydrogen-Ion Concentration.—The intensity of the color of the reagent and that of the palladium compound depends upon the *p*H of the solution. The reagent exhibits a yellowish-orange color of maximum intensity at a *p*H of 5 to 6. Above or below these values the intensity of the color decreases, attaining a pale yellow in strongly acidic and basic solutions. The intensity undergoes a pronounced change in the *p*H region in which the determinations are carried out, a change of 0.2 of a *p*H unit giving a difference in color just detectable.

The formation of the colored palladium compound does not occur in strongly acidic or basic solutions. In sodium acetate buffers having a salt concentration of 0.05 *M*, the intensity of the red color increases from a *p*H of 1.7 to 3, where it attains a maximum and then decreases. The change is more pronounced from a *p*H of 1.7 to 3 than from 3 to 5. The maximum sensitivity appears to be at a *p*H of 3, but as the ionic strength of the buffers differed, part of the effect attributed to *p*H may be due to the salt effect. Using 20 γ of palladium, it was found that turbid solutions resulted in all cases where the *p*H was greater than 2.1. Thus the method is limited to a narrow *p*H range, as well as being confined to the sodium acetate–hydrochloric acid buffers. The *p*H of 2.1 was selected for the method as it affords the maximum sensitivity without producing turbid solutions. The solutions are reasonably well buffered. The equivalent of 0.5 ml. of 1 *M* hydrochloric acid may be present without causing any visible change in color intensity and 0.75 ml., which is the maximum allowable, causes no serious error. The latter amount of acid produces a *p*H change of 0.2 unit as measured by the quinhydrone electrode. The presence of equivalent amounts of nitric acid produces a similar effect.

Formation and Stability of Color.—The effect of salts and of the hydrogen-ion concentration on the extent of the development of the color has just been considered. An increase in the amount of salts present or a decrease in the *p*H of the solution causes an increase in the time required for development of the maximum color. Usually, under the conditions giving maximum sensitivity, the development of the color is nearly instantaneous but turbid solutions result. In the colorimetric procedure which

(9) Description of this instrument to be published soon by Barton and Yoe.

yields clear solutions, the development is slow, about thirty minutes being required for the attainment of maximum intensity.

With an increase of temperature, the rate of development increases markedly, but above 50 or 60° the color fades completely. Temperature changes seem to affect only the rate of development and not the final maximum intensity. Although a temperature difference of 5° is noticeable, no special precautions are required other than that the solution be at room temperature when the reagent is added.

All solutions of the colored compound tend to give a precipitate upon aging. Under the conditions used in the method, the clear solutions are reasonably stable for several hours, but upon longer standing they fade and give a precipitate. Because of this limited stability, it is necessary that the reagent be added to all solutions at as nearly the same time as is possible and that the matching be completed within one hour after the addition of the reagent. These conditions are especially important with quantities of palladium exceeding 10 γ.

The colors obtained are satisfactorily reproducible and the order of addition, *i. e.*, reagent to palladium and buffer or palladium to reagent and buffer, has no effect.

Interference of Other Elements.—No reaction between the reagent and any of the following ions was observed. The tests were made on a spot-plate by adding a drop of the reagent to a drop of the solution containing the respective ions (approx. 0.05 mg.). Ions tested: Al^{+3}, As^{+3}, AsO_4^{-3}, $B_4O_7^{-2}$, Ba^{+2}, Be^{+2}, Bi^{+3}, Br^-, CO_3^{-2}, Ca^{+2}, CbO_4^{-3}, Cd^{+2}, Ce^{+3}, Cl^-, Co^{+2}, Cr^{+3}, Cs^+, Cu^{+2}, Dy^{+3}, Er^{+3}, Eu^{+3}, F^-, $Fe^{+2,+3}$, Ga^{+3}, Gd^{+3}, Ge^{+4} (aqueous solution of GeO_2), Hf^{+4}(HfO^{+2}), $Hg^{+,+2}$, I^-, In^{+3}, Ir^{+4}, K^+, La^{+3}, Li^+, Mg^{+2}, Mn^{+2}, MoO_4^{-2}, NO_2^-, NO_3^-, Na^+, Nd^{+3}, Ni^{+2}, OsO_5^{-2}, HPO_4^{-2}, Pb^{+2}, Pr^{+3}, Rb^+, ReO_4^-, Rh^{+3}, Ru^{+3}, S^{-2}, SO_4^{-2}, Sb^{+3}, Sc^{+3}, SeO_3^{-2}, SiO_3^{-2}, Sm^{+3}, $Sn^{+2,+4}$, Sr^{+2}, TaO_4^{-3}, TeO_4^{-2}, Ti^{+4}-(Ti_2O^{+6} or TiO^{+2}), Th^{+4}, Tl^{+3}, Tm^{+3}, UO_2^{+2}, VO^+, WO_4^{-2}, Y^{+3}, Yb^{+3}, Zn^{+2}, Zr^{+4}(ZrO^{+2}).

The auric ion reacts with the reagent to form a purple colored solution. The reaction is not as sensitive as that for palladium, but the presence of gold in amounts exceeding 1 p. p. m.[10] interferes with the method and must be removed.

The first solution of platinic chloride tested yielded a slight red coloration. Later it was found that palladium was present as an impurity, and a subsequent test with a pure solution gave no color reaction. After standing for several hours in direct sunlight, however, platinum does react to give a very faint coloration; after several days an intense red color is formed that may serve as a sensitive test for platinum. Under the conditions of the method, however, platinum does not interfere, except by its color which becomes troublesome at concentrations exceeding 20 p. p. m.

In neutral solution, silver ions react with the reagent to give a red precipitate. The reaction is not sensitive, nor does it occur in acid solution. However, because it is necessary to use a buffer containing hydrochloric acid, silver must be absent to prevent turbid solutions due to silver chloride.

Ceric and bromate ions as well as other strong oxidizing agents interfere. Substances reacting with the palladous ion such as iodide, cyanide, and strong reducing agents, must necessarily be absent.

With the exception of silver and mercurous ions, colorless metallic ions do not interfere. The following were tested at a concentration of 100 p. p. m. and found to be without effect: Al, Cd, Hg^{+2}, Mn^{+2}, Pb, and Zn.

The following colored ions interfere only when present in large enough amounts to produce an interfering color. The ions and limiting concentrations are: Co, 10 p. p. m.; Cu, 50; Fe^{+3}, 30; Ir, 2; Ni, 25; Rh, 2.

Separation of Gold from Palladium.—Gold in excess of 1 p. p. m. must be removed, for it interferes seriously with the method. The removal was attempted unsuccessfully by reduction to the metal with oxalic acid. A single precipitation of the gold resulted in a loss of most of the palladium; a reprecipitation, although improving the separation, did not make it quantitative. Repeated precipitations perhaps would give a satisfactory separation, but such operations are tedious and since another satisfactory method was available, the former method was discarded. Gold may be removed satisfactorily by extraction with either ethyl acetate[11] or ether[12] from a solution containing hydrochloric acid. The following procedure is satisfactory for the removal of gold.

Procedure.—Add sufficient hydrochloric acid to the solution (volume of 15 ml. or less) containing auric and palladous chlorides to give a final concentration of approximately 10%. Transfer the solution to a small separatory funnel, add 10 ml. of ethyl acetate (or ether), shake for a few seconds and draw off the acid layer. Shake the ethyl acetate layer with a few ml. of 10% hydrochloric acid and combine the wash solution with the other acid portion. If necessary, repeat the extraction with another 10-ml. portion of ethyl acetate. Evaporate the solution to dryness on the steam-bath, take up the residue in a few ml. of hydrochloric acid and evaporate almost to dryness (no more than a drop remaining). Add water and determine palladium by the standard procedure.

The results given in Table I were obtained for solutions containing varying amounts of auric and palladous chlorides. The removal of gold has been sufficiently complete to avoid interference in all cases except in the experiments in which the solutions containing 5 mg. of gold

TABLE I

Extractions	Au added, mg.	Pd found: Pd added, γ	Pd found: Ethyl acetate γ	Pd found: Ether γ	Au/Pd
1	1	5.0	4.5	5.0	200
1	5	10.0	10.0	11.0[a]	500
2	10	20.0	19.0		500
1	5	5.0	5.0	6.0[a]	1000
2	10	10.0	9.5	9.5	1000
2	10	5.0	4.5	5.0	2000
2	15	5.0	4.5	5.0	3000
2	20	5.0	4.5		4000
3	50	5.0	5.0	5.5	10000

[a] High results were due to the interference of gold.

(10) This and similar notations refer to a volume of 100 ml. and a solution height of 160 mm.

(11) V. Lenher and C. H. Kao, *J. Phys. Chem.*, **30**, 126 (1926).

(12) F. Mylius, *Z. anorg. Chem.*, **70**, 203 (1911).

were extracted only once with ether and a satisfactory recovery of palladium resulted even where the ratio of gold to palladium was 10,000:1. Ether appears to be the more suitable extractant, yielding slightly higher results in most cases than those obtained with ethyl acetate and if a complete removal of gold is not required it would be preferable. Ethyl acetate is, however, a more efficient extractant; if the most nearly complete removal of gold with the least number of extractions is desired, it is preferable to ether.

Separation of Palladium from Platinum.—Amounts of platinum exceeding 2 mg. produce an interfering yellow color, making it necessary to separate the two metals. The removal of platinum was attempted by precipitation with ammonium chloride. This method was found to be entirely unsatisfactory, resulting in the loss of most of the small amounts of palladium present. Even the use of solutions not saturated with ammonium chloride, and which did not give a quantitative precipitation of platinum, gave unsatisfactory results. The reaction between stannous chloride and platinic chloride in hydrochloric acid and the subsequent extraction with ether[13] or ethyl acetate[14] was also employed. This method was not satisfactory, the loss of palladium perhaps being caused by the presence of hydrated stannic oxide formed in subsequent operations. Palladium could not be precipitated with dimethylglyoxime at such low concentrations. The use of small amounts of nickel as a collector resulted in a partial precipitation of palladium by dimethylglyoxime. The method finally adopted—which involved the precipitation of palladium as the hydrated dioxide as given by Gilchrist and Wichers[15]—gave a very satisfactory separation. This method gives a remarkably clean-cut separation of extremely small amounts of palladium from relatively large amounts of platinum. In our experiments, a small amount of iron was used as a collector, though it was later found that as little as 5 γ of palladium could be separated without the use of a collector. The procedure given is that of Gilchrist and Wichers[15] applied to small quantities of the metals.

Procedure.—Add 0.2 ml. of ferric nitrate (0.2 mg. of iron) to the solution containing platinum and palladium, a few ml. of hydrochloric acid, and approximately 100 mg. of sodium chloride. Evaporate the solution to dryness, add hydrochloric acid, and once more evaporate to dryness. Add 4–5 drops of hydrochloric acid and 40 ml. of water, heat the solution to boiling and add 2 ml. of a filtered 10% sodium bromate solution. Then add dropwise a 10% solution of sodium bicarbonate until cresol red turns pink. (Test a drop of solution on the stirring rod with the indicator.) Add 2 ml. of the sodium bromate solution and boil for fifteen minutes. Filter through a fritted glass funnel or crucible, wash the precipitate several times with a few ml. of a 1% sodium chloride solution, having a *p*H of 6 or 7, dissolve the precipitate in 5 ml. of hydrochloric acid, and wash the filter with water. Evaporate the solution to dryness on the steam-bath, add a few ml. of hydrochloric acid, evaporate almost to dryness (not more than a drop) and take up in water. Determine the palladium in this solution by the standard procedure.

The results obtained by using this procedure for the analysis of solutions containing palladium and platinum were entirely satisfactory. For instance, in an experiment using 20 mg. of platinum and 5 γ of palladium, all the palladium was found. In another set with 20 mg. of platinum and 2 γ of palladium (ratio of Pt/Pd = 10,000), 2 γ of palladium was recovered. The method may be extended to even greater ratios by using larger amounts of platinum.

The method was applied to the analysis of metallic platinum samples. The samples were dissolved in *aqua regia*, the nitric acid removed by repeated evaporation with hydrochloric acid in the presence of sodium chloride and the residues taken up in water. The palladium was then determined. One sample contained 0.09% of palladium; another contained less than 0.002%, this being the limit of sensitivity with a 20-mg. sample.

Several experiments were also run in which palladium was determined in solutions containing the chlorides of palladium, gold, and platinum. The gold was removed by extraction with ethyl acetate and the palladium then determined after separation from platinum by the method given above. Satisfactory results were obtained in all experiments.

Separation of Silver from Palladium.—In the analysis of materials containing silver and "platinum group" metals, silver is usually removed as the chloride and would not be found in the solution prepared for the analysis of palladium. It was of interest, however, to determine whether or not small amounts of palladium might be carried down with the silver chloride. Accordingly, a few experiments were performed in which silver was precipitated as the chloride in the presence of small amounts of palladium. The general procedure followed was to take solutions containing known amounts of silver and palladium, dilute to 100 ml., acidify with nitric acid and precipitate the silver with hydrochloric acid. Each solution was filtered through a fritted glass crucible, the precipitate washed well with very dilute hydrochloric acid and palladium determined in the filtrate by the standard procedure, after the removal of nitric acid by repeated evaporation with hydrochloric acid in the presence of a few mg. of sodium chloride.

The results showed that palladium was lost in the separation. For example, using 20 mg. of silver and 10 γ of palladium only 7.5 γ of palladium was found. In several instances the silver chloride was dissolved in ammonium hydroxide, the filter thoroughly washed and then treated with *aqua regia*. Part of the palladium was recovered by this treatment, indicating that a partial reduction of the palladous ion to the metallic state had occurred. This reduction was probably due to the presence of a small amount of metallic silver formed by the action of light. This does not account, however, for all the palladium lost, and it seems probable that the loss is, at least in part, due to occlusion or adsorption by the silver chloride. Prolonged digestion or a reprecipitation afforded little or no improvement in the separation.

Sensitivity and Accuracy of the Determination.—Using a spot-plate, 0.005 γ of palladium (0.05 ml. of a solution containing 1 part of Pd in 10,000,000) may be detected.

(13) E. Langstein and P. H. Prausnitz, *Chem.-Ztg.*, **38**, 802 (1914).
(14) H. W. Wölbling, *Ber.*, **67B**, 773 (1934).
(15) R. Gilchrist and E. Wichers, THIS JOURNAL, **57**, 2565 (1935).

The paper spot method is sensitive to about 0.01 γ. In solutions of extremely low ionic strength, as little as 1 part of palladium in 300,000,000 parts of solution may be detected in 50-ml. Nessler tubes (220 mm.). Under the conditions in which the determinations are carried out, the concentration limit is 1:200,000,000, using either Nessler tubes or the roulette comparator. This corresponds to 0.25 γ of palladium with the former and 0.5 γ with the latter. The method may be made more sensitive by the use of smaller volumes. For instance, using 2 ml. of solution in small test-tubes which gave a column of liquid 50 mm. in height, 0.04 γ was detectable. With 10 ml. of solution and a column height of 80 mm., 0.1 γ was detectable.

The accuracy of the determination depends upon the concentration of palladium present, the volume of solution used, the method of matching, and the presence or absence of interfering substances. The accuracy reported below for the different amounts of palladium is based on a volume of 100 ml. using a roulette comparator (100 ml. tubes, 160 mm. to mark) with a Corning Filter no. 512 for amounts of palladium up to 20 γ and Filter no. 585 for larger amounts. The accuracy found under the most favorable conditions was as follows: 0.5–10 γ, 0.25 γ; 10.5–25 γ, 0.5 γ; 26–35 γ, 1 γ; 36–50 γ, 2.5 γ.

Acknowledgment.—The authors wish to express their appreciation to Charles J. Barton of this Laboratory for the data used in the relative absorption curves.

Summary

The reaction between *p*-nitrosodiphenylamine and palladous chloride has been described. This reaction is extremely sensitive and nearly specific for palladium. Studies have been made on the effect of salts, of hydrogen-ion concentration, of temperature, and of interfering substances on the color formation and stability of the compound.

The composition of the compound has been determined and found to correspond to the coordination compound $Pd[C_6H_5NHC_6H_4NO]_2Cl_2$. The compound has a purplish-brown color in the solid state but under the experimental conditions used in the colorimetric procedure it forms a red solution.

Relative absorption curves are given for solutions of the reagent and of the palladium compound.

Details are presented for a new colorimetric method permitting the determination of quantities of palladium of the order of a few γ, as well as results of its application. Procedures are also given for the determination of palladium when accompanied by gold and platinum.

UNIVERSITY, VIRGINIA RECEIVED APRIL 1, 1939

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY OF PRINCETON UNIVERSITY]

The Vitrification and Crystallization of Organic Molecules and the Dielectric Behavior of *i*-Butyl and *i*-Amyl Bromides

BY WILLIAM O. BAKER AND CHARLES P. SMYTH

The relation of molecular structure to molecular interaction and rotational freedom in the solid state has been studied by means of dielectric constant and dispersion measurements on a series of molecules of differing shapes. In investigating the connection between the symmetry of the crystal lattice and the symmetry of the molecule, *i*-butyl and *i*-amyl bromides were examined as pear-shaped forms intermediate between the rod-like long[1] chain compounds, and the nearly spherical *t*-butyl halides.[2] Their ready vitrification permitted analysis of both crystalline and glassy behavior.

A capacity bridge coupled to a low-frequency, variable oscillator, and to a vacuum tube, six-stage amplifier was employed for the dielectric measurements in the same general fashion as that already described.[3] Temperatures were obtained from a platinum resistance thermometer. The crystals and glasses were examined over a wide temperature range with a polarizing microscope equipped with a transparent Dewar tube mounted on the stage. The cell containing the material to be measured was inserted in a brass block into which liquid air could be injected at any desired rate.[3] Further the block assembly was suspended in a large Dewar vessel, from the lower portion of which liquid air could be evaporated to provide a very slow rate of temperature change in the cell. The usual care was taken to reduce void formations between the condenser walls by pumping off dissolved gases from the liquid in the cell, by subsequent freezings and meltings, and by slow final freezing from the bottom of the cell upward.

(1) Baker and Smyth, THIS JOURNAL, **60**, 1229 (1938).
(2) Baker and Smyth, to be published.
(3) Smyth and Hitchcock, THIS JOURNAL, **54**, 4631 (1932); **55**, 1830 (1933).

Purification of Materials

The fractionation of these compounds was by a packed column of satisfactory efficiency, elsewhere described.[4]

***i*-Butyl Bromide.**—The Eastman Kodak Co. product was dried over pure calcium bromide, and was fractionally distilled five times; the five fractions in the right boiling range were combined and refractionated. The final criteria for purity were the absence of Maxwell–Wagner polarization on melting, and a low specific conductance for the liquid: b. p. 91.9°; m. p. −118°; $n^{20.0}D$ 1.43440. A separately purified sample gave: b. p. 91.9°; $n^{20.0}D$ 1.43430. Skau and McCullough[5] report for a highly-purified sample, b. p. 91.72°; m. p. −118°. Kharasch and Potts[6] give $n^{20}D$ 1.4355. The tendency for rearrangement to *t*-butyl bromide of this compound was realized, but, under the conditions of distillation, very little should occur,[7] as indicated by the sensitive conductance measurements.

***i*-Amyl Bromide.**—Material of the best Eastman Kodak Co. quality was dried over pure calcium bromide, and thrice fractionated: b. p. 120.5°; m. p. −112°; $n^{20.0}D$ 1.44154. The Landolt–Börnstein "Tabellen" (with $n^{20}D$ from "I. C. T.") give: b. p. 120.65°, m. p. −112.0°, $n^{20}D$ 1.4412.

Experimental Results

Table I contains the dielectric constants ϵ, the specific conductances k (ohm^{-1} cm.$^{-1}$), and the imaginary part of the dielectric constant ϵ'', which is related to the loss factor by $\tan \delta = \epsilon''/\epsilon'$, where ϵ' is the normally recorded dielectric constant, ϵ. The columns of data are headed by the appropriate frequencies in kilocycles, and the temperatures are in °C.

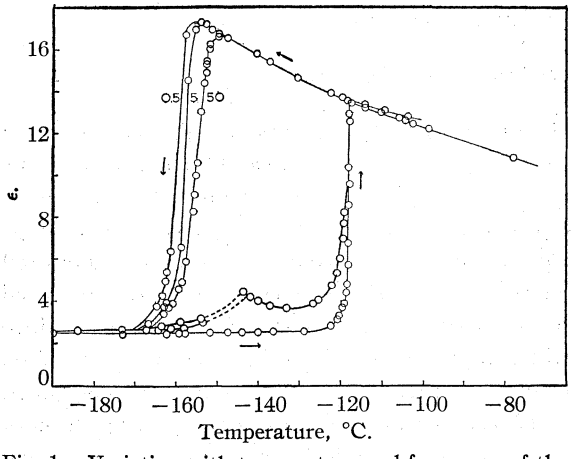


Fig. 1.—Variation with temperature and frequency of the dielectric constant of *i*-butyl bromide.

The data recorded were obtained from at least four separate runs, each of which reproduces the curves of Figs. 1 and 3 exactly. Exceptions, of course, are the cases of those representing partial devitrification, which were dependent on previous treatment, and will be noted later. Values at intermediate temperatures have been omitted for the sake of brevity. The apparent values of ϵ'' for the liquid are too high because of a certain amount of direct current conductance.

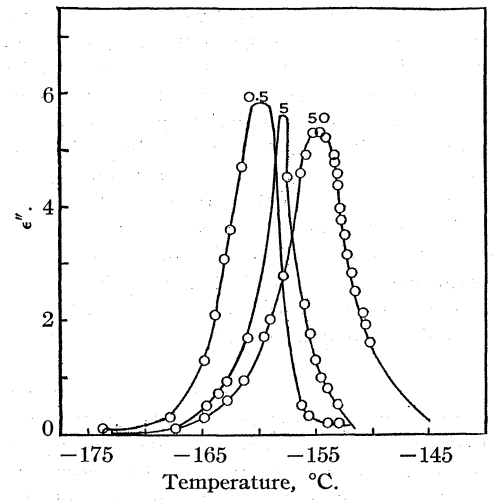


Fig. 2.—Variation with temperature and frequency of ϵ'' for *i*-butyl bromide.

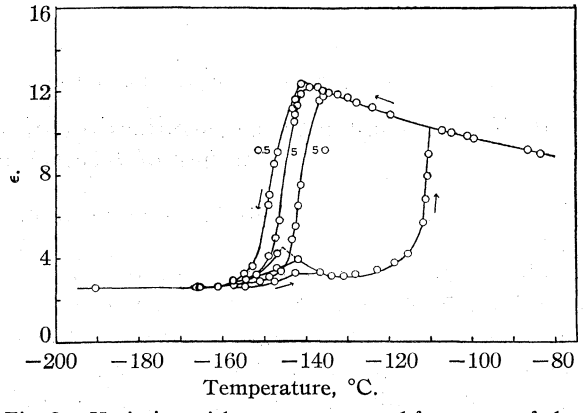


Fig. 3.—Variation with temperature and frequency of the dielectric constant of *i*-amyl bromide.

Discussion of Results

There is still uncertainty about the thermal and optical properties of glasses, about their mechanism of viscous flow, and about the question of their possessing definite vitrification and devitrification temperatures.[8] Commercial glasses, generally used as dielectrics, have been studied as to dielectric constant and loss, and breakdown potential, usually over short temperature ranges.[9]

(4) Baker and Smyth, THIS JOURNAL, **61**, 1695 (1939).
(5) Skau and McCullough, *ibid.*, **57**, 2439 (1935).
(6) Kharasch and Potts, *ibid.*, **58**, 57 (1936).
(7) Michael, Scharf and Voigt, *ibid.*, **38**, 653 (1916).
(8) Richards, *J. Chem. Phys.*, **4**, 449 (1936).
(9) Morey, "The Properties of Glass," Reinhold Publishing Corp., New York, 1938, Chap. XX.

These, like ordinary organic glasses, such as sugars and glycerol, have strong intermolecular bonding, which complicates dielectric interpretations of structure. The simple bromides here investigated, although they have no hydrogen bonds linking the molecules, invariably form clear glasses on cooling.

TABLE I

i-C_4H_9Br

Kc.	50	5	0.5	50	5	0.5	50	5	0.5
t, °C.	ϵ			$k \times 10^{10}$			ϵ''		
				Cooling					
21.6	7.00	7.20	7.73	800	780	760	2.87	28.0	271.0
1.2	7.56	7.72	7.99	530	610	510	1.91	18.5	182.0
− 39.0	8.97	9.06	9.26	270	260	260	0.99	9.40	93.0
− 62.8	10.00	10.09	10.23	210	200	200	.77	7.40	73.0
− 78.3	10.81	10.88	11.00	170	170	160	.62	6.10	60.0
−103.1	12.40	12.47	12.52	108	107	105	.40	3.90	38.0
−106.0	12.63	12.66	12.68	104	100	99.4	.38	3.60	35.5
−107.6	12.75	12.81	12.80	94.7	90.5	89.7	.34	3.20	32.1
−118.3	13.63	13.64	13.64	45.2	43.5	43.5	.16	1.60	15.7
−120.2	13.78	13.82	13.83	40.2	36.7	35.9	.15	1.3	13.0
−122.5	14.01	14.02	14.02	33.5	29.5	29.5	.12	1.1	10.7
−130.8	14.68	14.67	14.67	15.9	10.5	10.6	.06	0.38	3.9
−137.6	15.47	15.52	15.55	14.2	2.3	2.3	.05	.08	0.80
−140.7	15.81	15.87	15.89	21.4	1.2	1.2	.08	.04	.40
−143.1	16.06	16.10	16.12	36.9	0.8	0.70	.13	.03	.30
−145.5	16.29	16.35	16.39	65.3	0.8	.50	.24	.03	.20
−148.1	16.55	16.66	16.65	161.5	1.3	.40	.58	.05	.10
−149.8	16.66	16.82	16.83	350	2.3	.20	1.25	.08	
−150.8	16.73			440			1.60		
−151.7	16.56	17.18	17.19	650	6.0	.40	2.34	.22	.10
−151.8	16.30			790			2.84		
−152.2	16.08			880			3.14		
−152.8	15.63			1050			3.76		
−153.1	15.37	17.28	17.32	1115	14.0	.50	4.02	.51	.20
−153.5	14.45			1287			4.64		
−153.8	14.31			1326			4.77		
−153.9	14.03	17.30	17.33	1350	21.0	.50	4.86	.80	.20
−154.1	13.78	17.28	17.33	1375	23.5	.40	4.95	.85	.20
−154.5	13.08	17.31	17.33	1443	27.3	.80	5.20	.99	.40
−155.0	12.27	17.30	17.31	1475	36.0	.60	5.31	1.30	.30
−155.4	10.63	17.17	17.32	1475	48.4	.80	5.31	1.75	.40
−155.7	10.01	17.17	17.31	1443	49.6	.90	5.20	1.79	.45
−156.3	9.11	16.91	17.31	1364	64.8	1.50	4.91	2.33	.60
−156.5	8.31			1272			4.50		
−158.1		14.61	16.71		126.0	7.80		4.54	2.8
−159.1	4.92			558			2.01		
−159.6	4.61			476			1.72		
[a] −158.2	5.88			822			2.95		
−160.2		6.64			73.6				
−161.2	3.87			259			0.94		
−161.6		4.60	6.44		47.2	13.00		1.70	4.7
−161.8	3.71			238			.86		
−162.5		3.93	5.38		30.5	9.90		1.11	3.6
−162.7	3.51			164.0			.59		
−163.0		3.77	5.01		26.3	8.60		0.95	3.1
−163.2	3.38			133.2			.48		
−163.7		3.53	4.30		19.9	5.90		.72	2.1
−164.7	3.19	3.31	3.79	86.6	13.2	3.60	.31	.48	1.3
−167.7		2.92	3.04		3.3	1.00		.12	0.50
−173.5	2.62	2.66	2.67	7.1	0.7	0.40	.03	.02	.10
−190.3	2.52	2.57	2.58						

[a] Shows complete reversibility at this point.

TABLE I (*Continued*)

Kc 50	5	0.5	50	5	0.5	50	5	0.5
t, °C.	ϵ		$k \times 10^{10}$			ϵ''		
			Warming					
−167.3	2.55	2.58	2.60	3.6	0.6	0.4			
−159.0	2.73	2.89	3.02	26.6	2.8	.6	0.10	1.00	0.20
−153.8	2.98	3.17	3.18	43.5	1.3	.2	.16	0.50	
−144.1	4.45	4.45	4.48	5.3	0.2	.2			
−141.8	4.15	4.15	4.19	3.6	.4	.4			
−139.9	4.00	3.99	4.00	2.2	.4	.5			
−137.0	3.77	3.77	3.79	2.2	.6	.6			
−133.1	3.66	3.66	3.66	2.2	1.1	1.1			
−126.1	3.82	3.84	3.97	3.6	4.3	4.1	.01	.16	1.5
−125.2	3.92	3.95	4.11	5.3	5.7	5.5	.02	.21	2.0
−123.9	4.07	4.10	4.34	7.1	7.6	7.0	.03	.28	2.5
−121.7	4.62	4.68	5.00	14.2	14.7	13.8	.05	.54	5.0
−120.6	5.18	5.26	5.77	19.6	19.6	19.0	.07	.71	6.9
−120.0	5.61	5.69	6.01	23.1	22.2	21.5	.08	.81	7.8
−119.3	6.46	6.59	6.90	26.6	26.7	26.2	.10	.97	9.5
−118.7	7.72	7.95	8.22	31.8	31.4	31.0	.12	1.14	11.2
−118.2	10.04	10.38	10.68	38.5	37.7	37.7	.14	1.36	13.6
−117.9	12.75	12.97	13.09	46.7	45.4	45.5	.17	1.64	16.4
−117.2	13.44	13.47	13.49	52.0	49.6	49.5	.19	1.79	17.8
−114.2	13.28	13.30	13.34	58.7	57.0	57.0	.21	2.05	20.5
− 95.0	11.85	11.91	11.98	141.4	138.3	137.2	.51	4.90	49.4
− 90.4	11.56	11.61	11.71	159.5	157.4	156.0	.57	5.67	56.2
−162.5	2.48	2.48	2.48	7.3					
−158.6	2.50	2.50	2.51	7.3	0.1				
−155.2	2.51	2.52	2.52	10.9					
−151.1	2.54	2.53	2.54	14.4					
−147.5	2.55	2.55	2.55	10.9					
−144.0	2.55	2.55	2.56	7.3					
−140.3	2.55	2.55	2.55	7.3					
−136.5	2.56	2.55	2.55	7.3					
−128.9	2.60	2.61	2.61	7.3	0.2	0.2			
−121.9	2.83	2.87	3.01	10.9	7.3	6.2			
−121.3	2.90	2.95	3.10	14.4	8.4	7.3			
−120.8	2.98	3.02	3.22	14.4	20.2	8.4			
−120.4	3.07	3.13	3.35	14.4	10.5	9.3			
−119.6	3.34	3.41	3.67	18.0	13.0	12.3			
−119.0	3.78	3.90	4.22	21.6	17.0	16.2			
−118.6	4.29	4.44	4.78	25.2	20.5	19.8			
−118.3	5.21	5.43	5.76	28.7	24.8	24.8			
−118.2	5.97	6.27	6.63	28.7	28.4	28.4			
−118.0	6.83	7.19	7.84	36.0	31.7	32.2			
−117.8	8.55	9.57	10.97	50.4	38.5	41.0			
−117.7	12.63	13.44	13.65	57.6	48.6	49.0			
−117.6	13.53	13.53	13.62	64.8	51.2	52.6			
−117.5	13.46	13.45		67.2	55.4				
−114.2			13.45			62.3			
−109.5	13.02	13.01	13.12	98.0	82.0	84.0			
−104.1	12.60	12.61	12.76	123.0	113.0	113.5			
− 98.6	12.19	12.22	12.38	151.3	150.2	150.0			
				i-$C_5H_{11}Br$					
				Cooling					
23.2	5.98	6.01	5.98	35.2	18.3	18.2	0.127	0.67	6.6
5.5	6.36	6.38	6.38	31.8	15.9	15.7	.115	.58	5.7
2.0	6.49	6.52	6.51	28.1	15.5	15.0	.102	.57	5.5
− 18.3	6.92	6.95	6.94	28.3	8.6	8.2	.103	.31	3.0
− 55.7	8.04	8.02	8.05	25.2	2.8	2.8	.100	.10	1.0
− 62.8	8.24	8.25	8.26	24.9	2.2	2.2	.090	.08	0.80

TABLE I (*Continued*)

Kc. / t, °C.	50	5	0.5	50	5	0.5	50	5	0.5
		ϵ			$k \times 10^{10}$			ϵ''	
− 85.6	9.16	9.17	9.18	24.0	0.8	0.9	0.088	0.03	0.40
− 86.4	9.20	9.20	9.21	26.6	.8	.8	.097	.03	.30
− 99.5	9.80	9.81	9.81	35.2	.5	.5	.127	.02	.20
−107.3	10.22	10.24	10.24	17.7	.3	.3	.064	.01	.10
−119.5	10.94	10.97	10.98	9.2	.2	.3	.034	.01	.10
−121.1	11.04	11.06	11.07	23.1	.2	.2	.084	.01	.10
−122.8	11.15	11.19	11.19	24.8	.2	.2	.09	.01	.10
−124.4	11.25	11.29	11.29	30.0	.2	.2	.109	.01	.10
−125.3	11.32	11.35	11.35	30.0	.2	.2	.109	.01	.10
−128.0	11.50	11.56	11.54	43.5	.3	.2	.157	.01	.10
−129.3	11.60	11.65	11.65	55.3	.4	.2	.199	.01	.10
−130.9	11.69	11.76	11.74	73.7	.5	.2	.265	.02	.10
−132.5	11.80	11.87	11.87	111.0			.40		
−133.1	11.85			156.6			.564		
−133.7	11.90			148.9			.536		
−134.2	11.91	11.98	11.98	193.5	1.2	.3	.70	.04	.10
−136.6	11.75	12.08	12.05	410.0	3.2	.3	1.48	.12	.10
−137.5	11.61	12.17	12.13	508.9	4.6	.3	1.86	.17	.10
−138.2		12.18	12.18		7.1	.4		.26	.20
−139.4		12.15	12.16		12.9	.4		.47	.20
−141.5	7.49	12.31	12.31	1008	33.5	.4	3.63	1.21	.20
−141.2	7.58	12.16	12.19	1008	30.0	.4	3.63	1.09	.20
−141.2	7.74	12.09	12.09	1008	28.3	.4	3.63	1.03	.20
−141.6	7.24	11.91	11.90	975	35.2	.3	3.48	1.27	.10
−141.9	6.64	11.71	11.85	922	36.2	.9	3.30	1.31	.30
−142.1	6.47	11.60	11.75	910	38.5	.9	3.28	1.39	.30
−142.5	5.97	11.35	11.62	829	45.2	.9	2.98	1.63	.30
−142.7	5.54	10.92	11.35	739	50.3	1.2	2.72	1.81	.40
−143.3	5.14	10.54	11.24	683	60.4	1.5	2.45	2.17	.50
−143.5	4.86	10.35	11.17	622	62.0	1.5	2.24	2.23	.50
−146.8	3.36	5.81	9.09	258.0	73.4	8.6	0.940	2.64	3.1
−147.7	3.30	4.99	8.47	187.3	61.2	11.4	.680	2.20	4.1
−148.7	3.19	4.32	7.02	153.5	47.0	13.6	.553	1.70	5.0
−149.2	3.10	4.08	6.55	125.3	40.3	13.6	.452	1.46	5.0
−151.1	2.89			62.0			.223		
−152.8		3.18	3.64		13.2	3.8		0.48	1.4
−154.8	2.77	2.97	3.26	30.0	6.1	2.0	.109	.22	0.7
−155.2	2.77	2.92	3.18	30.0	4.8	1.8	.109	.18	.6
−157.5	2.69	2.79	2.90	17.7	2.2	0.8	.064	.08	.3
−164.0	2.60			3.6			.013		
−166.3		2.59	2.58		0.3	.3		.01	.10
−190.5	2.54	2.53	2.55						
				Warming					
−160.8	2.57	2.59	2.61	3.6	0.5	0.4	0.013	0.02	0.20
−154.9	2.62	2.72	2.83	12.5	2.2	.9	.046	.08	.30
−147.2	2.87	3.52	4.19	67.0	15.2	1.2	.241	.55	.40
−142.0	3.31	3.87	3.85	120.6	2.5	0.3	.434	.09	.10
−136.7	3.33	3.33	3.35	24.9	0.3	.2	.09		
−133.5	3.18	3.18	3.18	5.3	.2	.2	.020		
−130.6	3.22	3.23	3.22	2.2	.2	.2			
−129.5	3.28	3.28	3.28	2.2	.2	.2			
−121.3	3.52	3.52	3.54	0.9	.1	.2			
−120.2	3.62	3.62	3.63	.9	.1	.2			
−118.7	3.78	3.79	3.78	.9	.1	.2			
−116.9	4.03	4.04	4.04	.9	.1	.2			
−114.9	4.16	4.20	4.19	.9	.1	.3			
−112.0	5.69	5.76	5.75	.9	.2	.3			
−111.6	6.06	6.19	6.19	.9	.2	.3			
−111.3	6.59	6.67	6.67	.9	.2	.3			

TABLE I (*Concluded*)

Kc	50	5	0.5	50	5	0.5	50	5	0.5
t, °C.		ϵ			$k \times 10^{10}$			ϵ''	
−111.0	7.14	7.20	7.28	0.9	0.2	0.3			
−110.8	7.78	7.92	7.94	.9	.3	.3			
−110.5	9.03	9.22		.9	.2				
−107.9			10.14			.4			
−106.2	10.19	10.18	10.20	2.2	.3	.4			
−105.0	10.12	10.10	10.13	2.2	.3	.4			
−103.9	10.04	10.02	10.04	0.5	.3	.4			
−100.5	9.90	9.87	9.96	3.5	.4	.5			
− 56.5	8.04	8.04	8.05	5.3	2.7	2.7	0.019	0.10	0.10
− 51.1	7.87	7.87	7.87	7.1	3.3	3.2	.026	.12	1.2
− 42.7	7.60	7.61	7.59	7.1	4.4	4.3	.026	.16	1.6
− 31.8	7.29	7.30	7.89	11.4	6.4	6.0	.041	.24	2.2
− 20.9	7.01	7.05	7.04	15.9	10.6	10.0	.058	.39	3.6

Previous dielectric studies on organic glasses over a temperature interval are reviewed in the Landolt–Börnstein "Tabellen."[10] The curves of Figs. 1 and 3 obtained with decreasing temperature resemble those found for liquid and glassy glucose by Thomas,[11] who used the frequency range 92 to 2600 kilocycles. Similar, more detailed studies on glucose,[12] glycerol and several monohydric alcohols[13] by Kobeko and co-workers produced the same sort of marked dispersion and decrease of dielectric constant over a short temperature range, the position of which was determined by the frequency of the applied field. Loss factors of commercial glasses have been measured at high frequencies by Hackel,[14] who used the immersion method of finding a polar liquid mixture with the same dielectric constant as the glass.

Basic postulates of the present report are supported by Hägg's[15] conclusion from X-ray data that organic glasses contain large groups of molecules linked together by strong associative forces. Glycerol glass has been found truly amorphous.[16] X-Ray patterns have been established as valid proofs of the non-crystalline nature of a glass.[17]

The curves of Figs. 1 and 3 obtained on cooling follow the Debye temperature dependence for a polar liquid down to the regions −150 to −165° for *i*-butyl bromide and −135 to −155° for *i*-amyl bromide. In these ranges, there is a gradual, frequency-dependent drop of the dielectric constant to values approaching the square of the refractive index. This apparent rotational freezing differs from ordinary rotational immobilization on solidification in at least two ways. It does not occur sharply and shows no latent heat under the conditions of measurement. The gradual loss of rotational freedom suggests that the individual dipoles are orienting in a viscous medium, for, at a given temperature, it is seen that the molecules may be able to follow quite completely a field of frequency 500, and show little or no rotation in a field of 50,000 cycles.

Mechanically, it was found that *i*-butyl bromide became stiff at about −120°, and *i*-amyl bromide at about −115°. It would seem that, with decreasing temperature and increasing density, enhanced molecular field interaction removes librational freedom even in the absence of a phase change. An artificially increased interaction, such as that caused by high pressures, should then produce the same effect as lowering the temperature. This is confirmed by the experiments of Danforth,[18] who introduced pronounced dispersion at given frequencies in some ten compressible liquids like glycerol and isobutyl alcohol by measuring the dielectric constants under high pressures.

The range of temperature required for the setting of the dipoles with respect to a given frequency in liquids and glasses provides a contrast of the interaction of their molecules with the intermolecular action in crystals which have rotational transitions occurring within a very short or zero temperature interval.[2,3,19] In the latter, the sudden rearrangement of the crystal transition would seem to effect a critical interaction that blocks

(10) See also Tammann, "Der Glaszustand," Verlag L. Voss, Leipzig, 1933.
(11) Thomas, *J. Phys. Chem.*, **35**, 2103 (1931).
(12) Kobeko, *et al.*, *Physik. Z. Sowjetunion*, **4**, 83, 680 (1933).
(13) Kobeko, *et al.*, *J. Tech. Phys. (U. S. S. R.)*, **8**, 715 (1938).
(14) Hackel, *Physik. Z.*, **37**, 160 (1936); *Ann. Physik*, **29**, 63 (1937).
(15) Hägg, *J. Chem. Phys.*, **3**, 42 (1935).
(16) Lark-Horovitz and Miller, *Phys. Rev.*, **47**, 813 (1935).
(17) Warren, *J. Applied Phys.*, **8**, 645 (1937).
(18) Danforth, *Phys. Rev.*, **38**, 1224 (1931).
(19) White and Morgan, *J. Chem. Phys.*, **5**, 655 (1937).

dipole orientation almost completely. However, the curves of Figs. 1 and 3 suggest that the glass slowly contracts with decreasing temperature so that there is a gradual immobilization of dipoles. This may be further evidence for a random molecular arrangement in glasses.

Even before the dipole theory, it was realized that the constituent particles of a dielectric did not all have necessarily the same relaxation time.[20] This concept has been applied to a variety of dielectrics by many workers, and recently Yager[21] has reviewed and extended the method of quantitatively estimating the distribution. The ordinary experimental values represent an average. A rough qualitative idea of the breadth of the distribution may be gained from a calculation of the ideal maximum value of ϵ'' for a given frequency as was done for several compounds by Morgan.[22] An observed maximum value obtained from Fig. 2 or Fig. 4 will deviate the more from the ideal value, which it would have if all the particles had a single relaxation time, the less uniform are the constituent units of the dielectric. The calculation of the ideal $\epsilon''_{max.}$ follows from the observation that the absorption is greatest when $x = 1$ in the Debye expression for ϵ.[23] That is, $\epsilon'' = x(\epsilon_1 - \epsilon_0)/(1 + x^2)$, where $x = \omega\tau(\epsilon_1 + 2)/(\epsilon_0 + 2)$, in which ϵ_1 = dielectric constant at zero frequency, obtained from graphical extrapolation of low frequency values; ϵ_0 = dielectric constant at infinite frequency, obtained from low temperature values of the crystalline solid; $\omega = 2\pi \times$ frequency in cycles; τ = relaxation time of particles. Then, $\epsilon''_{max.} = (\epsilon_1 - \epsilon_0)/2$.

TABLE II

	f, kc.	$\epsilon''_{max.}$ Calcd.	$\epsilon''_{max.}$ Obsd.
i-Butyl bromide	50	7.5	5.3
	5	6.7	5.6
	0.5	4.8	5.9
i-Amyl bromide	50	5.0	3.8
	5	3.9	4.5
	0.5	3.0	5.0

The most uniform relaxation times seemingly are characteristic of the temperature region in which ϵ'' is a maximum for a frequency of 5 kc. as the difference between observed and calculated values, which arises from variation in particle size, is smallest at this frequency for the values in Table II. Figures 2 and 4 confirm this conclusion in showing the 5 kc. dispersion curves to be narrowest, with the sharpest peaks, for, as Yager[21] notes, the narrower the ϵ'' *vs.* temperature peak, the narrower the distribution of relaxation times, and hence of constituent units.

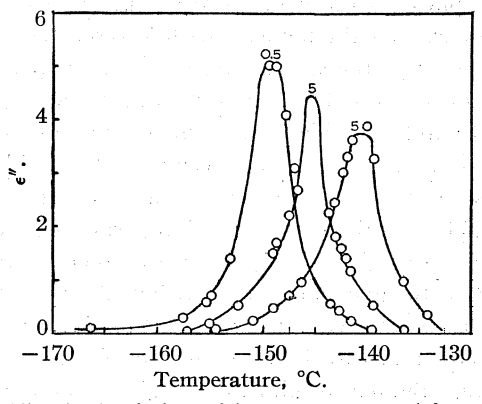


Fig. 4.—Variation with temperature and frequency of ϵ'' for *i*-amyl bromide.

Isobutyl bromide glass appears to be most homogeneous at about −158°, and isoamyl bromide at about −145.5°, whereas a greater variety of agglomerates exists above and below these temperatures. A glass probably contains molecular aggregates[9,15] which must dissociate before molecules can orient to form a crystal lattice. The ordered crystalline state has a lower free energy than the glass, and hence the latter is forced toward the former by a thermodynamic potential that increases with decreasing temperature. It would seem that at just about the temperature of the maximum absorption for 5 kc. in the two glasses, dissociation of the vitreous aggregates has resulted in a maximum homogeneity of particle size. Because of the generally similar behavior of the molecules of the two substances, like relations should obtain for each between the temperature T_i at which the re-ordering enters and the lower temperature T_f of apparent rotational freezing, if temperature difference may be considered as measuring thermodynamic potential. As will be noted below, some devitrification was found to enter at the temperatures of rotational freezing, T_f. The relations found are

i-butyl bromide $T_i(-158°) - T_f(-170°) = 12°$
i-amyl bromide $T_i(-145.5°) - T_f(-160.0°) = 14.5°$

These temperature intervals are, as would be expected, approximately the same, with the larger molecule showing the larger interval.

The portions of Figs. 1 and 3 indicated as ob-

(20) Von Schweidler, *Ann. Physik*, **24**, 711 (1907).
(21) Yager, *Physics*, **7**, 434 (1936).
(22) Morgan, *Ind. Eng. Chem.*, **30**, 273 (1938).
(23) Debye, "Polar Molecules," Chemical Catalog Company, Inc., New York, 1929, p. 94.

tained with rising temperature are next noted. The physical states of *i*-butyl bromide at −175°, and of *i*-amyl bromide at −165°, are those of undercooled liquids (glasses) far below their normal freezing points. Their instability as non-crystalline forms increases with decreasing temperature, but the fruition of this crystallizing tendency is opposed by the increase with lowered temperature of the relaxation times of the molecules. However, around −170° for *i*-butyl and −160° for *i*-amyl bromide, a certain amount of devitrification has occurred, because the dielectric constant–temperature curve from measurements at 0.5 kc. on Fig. 1, was completely reversible with temperature anywhere down to about −167°, while if the glass was cooled below about −167°, and then warmed, the dielectric constant values did not return to those required by the reversible curve. Similar results at a higher temperature were found for *i*-amyl bromide. Moreover, the isotropic glasses began to show scattered areas of double refraction when examined with the polarizing microscope. Because of relaxation effects, the amount of crystal formation observed at −170° for *i*-butyl and −160° for *i*-amyl bromides should depend on the length of time the sample is held at the given temperature after the liquid is cooled. The upper of the two rising temperature curves on Fig. 1 was obtained when the specimen was held near −180° for upwards of thirty minutes. Similar treatment produced the heating curve on Fig. 3. Evidently there was not time for complete crystallization. Presumably, crystallization had proceeded from many nuclei scattered throughout the glass, but there were still vitreous regions when the measurements with rising temperature were begun. Molecules in the crystal lattice of *i*-butyl bromide cannot rotate in the applied field, as the lower curve with rising temperature on Fig. 1 shows, for the dielectric constant is there produced only by atomic and electronic polarization, except in the region of some rotational pre-melting as often observed.[1,24,25] However, molecules still in the glass distributed among the crystal groups should be able to orient as soon as a sufficiently high temperature is reached. For *n*-amyl bromide, as seen in Fig. 3, an increase in dielectric constant is found in about the same temperature region in which it declined on the cooling of the pure glass. For *i*-butyl bromide, the region of increase is shifted to somewhat higher temperatures. A speculation on the reason for this is that, in the sample of *i*-butyl bromide for which the data are graphed, crystallization has progressed so far that the large crystalline groups in a predominantly crystalline lattice inhibit, by their locally oriented force fields, the rotation of the glass molecules dispersed among them. This is consistent with the fact that the maximum dielectric constant on the warming curve of *i*-amyl bromide, although occurring at a lower temperature, is a larger percentage of the true glass value than that for the *i*-butyl bromide. In the curves for both compounds, the dispersion characteristic of the glass is found. Further, the dielectric loss data in Table I for both compounds show a maximum with rising temperature in the region of the temperature of the dielectric constant maximum. This also demonstrates the regaining of partial rotational freedom by those molecules still in the vitreous condition.

Finally, the reason for decrease of the dielectric constant with further temperature rise, as seen on the lower curves of Figs. 1 and 3, is probably that, at the temperature of the maximum, the molecules still in the vitreous state have again acquired sufficiently short relaxation times to crystallize, especially under the orienting influence of numerous crystalline groups. That these latter do predominate is confirmed by the maximum dielectric constant, in the case of *i*-butyl bromide 4.5, instead of the 17.3 of the true glass. As crystallization in the solid state proceeds, the dielectric constant falls to the true crystal value, and then rises again on melting.

The above explanation may be applied to a recent report on the first production of boron trioxide crystals by McCulloch.[26] An ordinary boron trioxide glass held at 250° for three days, after it had stood at room temperature for a much longer period, showed a considerable amount of crystallization as indicated by X-ray analysis. The melting point of a nearly glass-free mass of boron trioxide crystals (99.6%) was found to be 460–470°. The glass at room temperature, 450° below the normal freezing point, may now be regarded as under a large thermodynamic potential tending toward crystallization. Some few very minute crystal nuclei are actually formed, as, indeed, such are found in laboratory glass at

(24) Ubbelohde, *Trans. Faraday Soc.*, **34**, 282, 292 (1938).
(25) Müller, *Proc. Roy. Soc.* (London), **A158**, 403 (1937).
(26) McCulloch, THIS JOURNAL, **59**, 2650 (1937).

ordinary temperatures.[27] However, precisely as here indicated for *i*-butyl and *i*-amyl bromides on Figs. 1 and 3, an increase in temperature to shorten the relaxation time of the molecules facilitates widespread devitrification and is actually essential for a substance with intermolecular bonding like that in boron trioxide. It is suggested that efforts to crystallize organic glasses and sirups might be facilitated by cooling the substance to low temperatures, and then re-warming to a point near, but well below, the melting point of the crystals sought. The dielectric results show mechanically the reorientation that must accompany the crystallization.

The present results, together with those of other work involving a variety of molecular structures,[1,2,4] indicate relations of the structure of the liquid state to the tendency toward glass formation as follows:

a. Moderately unsymmetrical, say pear-shaped, molecules, like *i*-butyl and *i*-amyl bromide, can pack randomly in the liquid with an economical use of volume. Hence, although the molecules are on the whole disordered, their efficient packing permits them to remain in the liquid arrangement far below the normal crystallization temperature. Such substances should vitrify.

b. Long-chain compounds, although they often form viscous liquids, do not generally supercool, as dielectric studies, a sensitive test for supercooling, have shown for several examples including the associated cetyl alcohol. Here, it is probable that the rod-like molecules are already locally, at least, quite well aligned in crystal-like array in the liquid. Random scattering would waste a relatively large volume, and hence would be energetically unfavorable. Indeed, X-ray data indicate alignment along the long axis even in *n*-heptane.[28,29] Hence, when long-chain compounds are cooled to the freezing point, they simply set into the crystal lattice and do not form glasses.

c. Very symmetrical, nearly spherical molecules which form cubic lattices, and especially those which are known to exhibit a rotational freedom in the crystal comparable to that in the liquid,[2,30] in agreement with the above postulates, commonly do not supercool. They may be considered to compose a liquid structure of close-packed spheres, which set into the cubic lattice with little rearrangement and probably no reorientation, and thus have no tendency toward glass formation.

d. As expected, and noted elsewhere,[4] molecules of symmetry intermediate between the pear-shaped and rod-like structures show degrees of supercooling varying with their particular shapes, and very rarely leading to true glass formation.

Extensive inter-molecular bonding in a liquid may so effectively alter the shape of the constituent particles as to require modification of the above conclusions from molecular data alone.

In addition to the data already cited in support of these conclusions, the evidence given by recent work[31] on some pure hydrocarbons may be noted. It was reported that the normal paraffins crystallized readily without supercooling, whereas certain branch-chained paraffins, conforming with the conditions of paragraph above, solidified to glasses. Also, it has been reported[32] that two of the branched heptanes, unlike their other isomers, failed to crystallize even when cooled to 70°K. An efficient but random packing should, therefore, be assigned to their liquid structures.

Summary

The dielectric constants and conductances of isobutyl and isoamyl bromides have been measured with a capacity bridge at frequencies of 0.5, 5 and 50 kilocycles at temperatures from −190 to 30° above their melting points. The substances have also been examined with a polarizing microscope over these wide temperature ranges.

It is found that, when the substances in the liquid state are cooled, they form glasses, which crystallize at low temperatures, their properties depending upon the degree of crystallization brought about by thermal treatment. Examination of these and other, previously studied molecules leads to generalizations as to glass formation. It is concluded that molecules which pack efficiently in the liquid, but which do not form isotropic lattices, should tend to vitrify. The temperature of narrowest distribution of relaxation times may indicate the point at which the vitreous aggregates begin to dissociate.

PRINCETON, NEW JERSEY RECEIVED JUNE 1, 1939

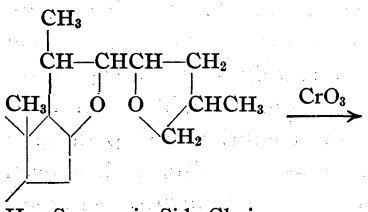
(27) Warren and Biscoe, *J. Am. Ceram. Soc.*, **21**, 259 (1938).
(28) Katzoff, *J. Chem. Phys.*, **2**, 841 (1934).
(29) Pierce, *ibid.*, **3**, 252 (1935).
(30) Smyth, *Chem. Rev.*, **19**, 329 (1936).
(31) Smittenberg, Hoog and Henkes, THIS JOURNAL, **60**, 17 (1938).
(32) Huffman, Parks and Thomas, *ibid.*, **52**, 3241 (1930).

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

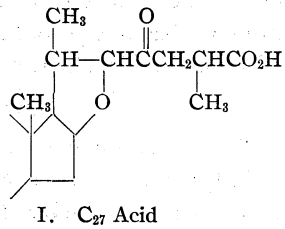
Sterols. LXIX. Oxidation Products of Sarsasapogenin. Sarsasapogenoic Acid and Related Substances

BY RUSSELL E. MARKER AND EWALD ROHRMANN

Fieser and Jacobsen[1] in their investigation of the chromic anhydride oxidation products of sarsasapogenin acetate obtained an acid, $C_{27}H_{42}O_5$, which was designated as sarsasapogenoic acid and which is undoubtedly analogous to an acid obtained by Tschesche and Hagedorn[2] by a somewhat similar oxidation of tigogenin acetate. Tschesche and Hagedorn assigned to this the structure of a γ-keto acid, I.



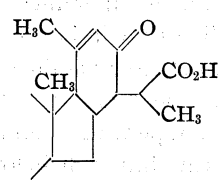
II. Sapogenin Side Chain (Tschesche and Hagedorn[2])



I. C_{27} Acid

It is evident that this structure is based almost entirely upon the assumption that the sapogenin side chain is correctly represented by II.

While Tschesche and Hagedorn[2] found that the C_{27} acid from tigogenin was inert toward hydrogenation and did not react with carbonyl reagents, Fieser and Jacobsen[1,3] found that sarsasapogenoic acid was somewhat more reactive. Treatment with hydroxylamine at 135° yielded a dioxime. Catalytic hydrogenation gave an acid of the probable composition $C_{27}H_{44}O_4$ designated as anhydrotetra-(or di)-hydrosarsasapogenoic acid. When heated with aqueous alcoholic alkali, sarsasapogenoic acid yielded anhydrosarsasapogenoic acid, $C_{27}H_{40}O_4$, a product which was shown to contain an alpha-beta unsaturated ketone grouping[3,4] and to which structure III was assigned.



III. Anhydrosarsasapogenoic acid (Fieser and Jacobsen[3])

Fieser and Jacobsen[3] regarded this structure for anhydrosarsasapogenoic acid as secure and offered it as confirmatory evidence in support of the formulations I and II of Tschesche and Hagedorn.[2]

Inasmuch as most of the available evidence now indicates that the sapogenin side chain is not correctly represented by II,[5] it is evident that the structure of the sapogenoic acid is open to serious question. In conformity with our recently proposed structure IV[5] for sarsasapogenin we believe sarsasapogenoic acid to be a diketo acid best represented by V. The two carbonyl groups in such a molecule would be expected to be sterically hindered, which would explain the difficult formation of a dioxime.[3]

The formation of anhydrotetrahydrosarsasapogenoic acid[3] by catalytic hydrogenation of sarsasapogenoic acid is explained by the conversion of the diketone with loss of water to a tetrahydrofuran derivative, VI. This acid appears to be identical with sarsasapogentic acid[5] which we previously prepared by the oxidation of 3-acetoxydihydrosarsasapogenin (VII). This conclusion is based upon a comparison of the free acids, the methyl esters, the methyl ester benzoates and the 3-dehydro acids.

The suggestion of Fieser and Jacobsen[3] that anhydrotetrahydrosarsasapogenoic acid is a saturated γ-keto acid is hardly in accordance with the properties of known γ-keto acids.

Inasmuch as the identity of anhydrotetrahydrosarsasapogenoic acid and sarsasapogentic acid appears to be conclusive, we propose in order to avoid further confusion that the nomenclature of Fieser and Jacobsen[3] be retained and the term sarsasapogentic acid be discontinued.

The difficulty encountered in purification of the hydrogenation product of sarsasapogenoic acid is

(1) Fieser and Jacobsen, THIS JOURNAL, **60**, 28 (1938).
(2) Tschesche and Hagedorn, *Ber.*, **68**, 1412, 2247 (1935).
(3) Fieser and Jacobsen, THIS JOURNAL, **60**, 2753 (1938).
(4) Fieser and Jones, *ibid.*, **61**, 532 (1939).
(5) Marker and Rohrmann, *ibid.*, **61**, 846 (1939).

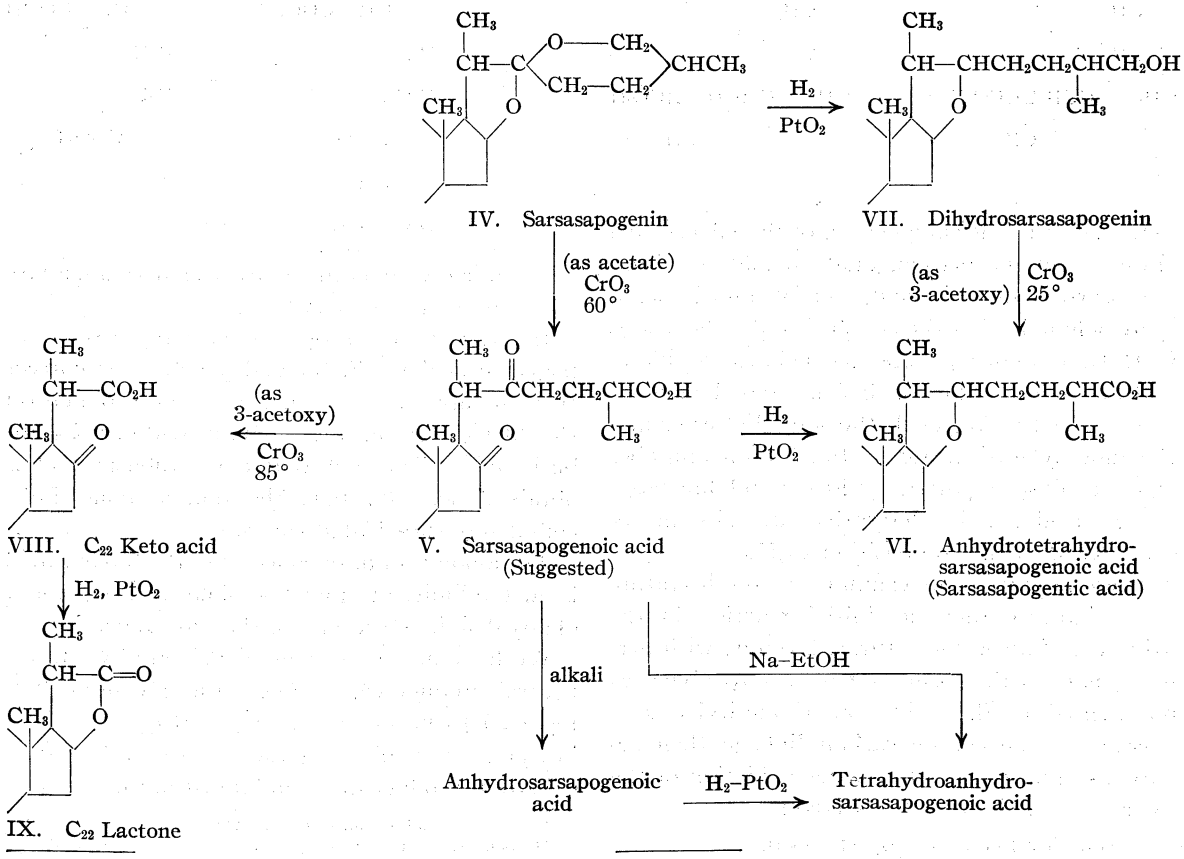
possibly due to the formation of an isomeric mixture which would not be unexpected.

Reduction of sarsasapogenoic acid with sodium and ethanol readily yielded tetrahydroanhydrosarsasapogenoic acid which Fieser and Jacobsen[3] first prepared from anhydrosarsasapogenoic acid by catalytic hydrogenation and by reduction with sodium and *n*-propyl alcohol. Reduction of sarsasapogenoic acid with aluminum isopropylate gave a poor yield of an acidic substance of the probable composition $C_{27}H_{46}O_5$. This reduction product was not studied further.

On mild oxidation with chromic anhydride sarsasapogenoic acid yields 3-dehydrosarsasapogenoic acid, m. p. 163–164°. This acid is very probably identical with an acid of the composition $C_{27}H_{40}O_5$, m. p. 162°, obtained by Jacobs and Simpson[6] by the oxidation of sarsasapogenin with chromic anhydride at 25–30°. The 3-dehydro acid reacts with one mole of bromine to yield a monobromo derivative $C_{27}H_{39}O_5Br$. Sarsasapogenoic acid showed no tendency to react with bromine under similar conditions.

If sarsasapogenoic acid is a γ-keto acid, I, it is obvious that the acid would have to be considered as an intermediate product formed in the oxidation of the sapogenin to the C_{22} lactone (IX). Further oxidation should yield the C_{22} lactone. Fieser and Jacobsen[3] failed to obtain an appreciable neutral fraction when sarsasapogenoic acid acetate was oxidized with chromic anhydride at 95°. By carrying out the oxidation at 85° we were likewise unable to obtain an appreciable neutral fraction. However, a 5% yield of a C_{22} keto acid was obtained. This was identical with the C_{22} keto acid (VIII) previously reported[7] from the chromic anhydride oxidation products of sarsasapogenin acetate. The acid was further identified by its conversion to the C_{22} lactone by catalytic hydrogenation.

Anhydrosarsasapogenoic acid was prepared in 20% yield by allowing sarsasapogenoic acid to stand at 25° for nine hours with aqueous alcoholic potassium hydroxide solution. In preparing anhydrosarsasapogenoic acid by the method of Fieser and Jacobsen,[1] we encountered a more soluble acid (m. p. 184°) having the same composition as the anhydro acid, C_{27}-



(6) Jacobs and Simpson, *J. Biol. Chem.*, **109**, 565 (1935).

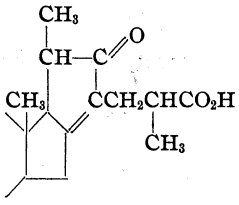
(7) Marker and Rohrmann, THIS JOURNAL, **61**, 1285 (1939).

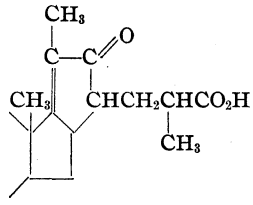
$H_{40}O_4$, m. p. 243°. This isomeric acid on heating with aqueous alcoholic alkali is converted into anhydrosarsasapogenoic acid. This lower melting isomeric acid could not be isolated when the preparation was carried out at 25°, probably due to the presence of unreacted sarsasapogenoic acid which appears to have about the same solubility.

The facile elimination of a molecule of water from sarsasapogenoic acid under the influence of alkali to yield an acid containing an α,β-unsaturated ketone grouping suggests that the reaction involves an intramolecular aldol condensation followed by elimination of a molecule of water.

The fact that anhydrosarsasapogenoic acid gives no semicarbazone under the usual conditions indicates that the carbonyl group is hindered. More difficult to understand is the fact that the acid is not reduced by aluminum isopropylate but this likewise may be attributed to the hindered nature of the group.

At present anhydrosarsasapogenoic acid has not been characterized sufficiently to be assigned a definite structure. However, it seems that the following formulations are the most likely possibilities

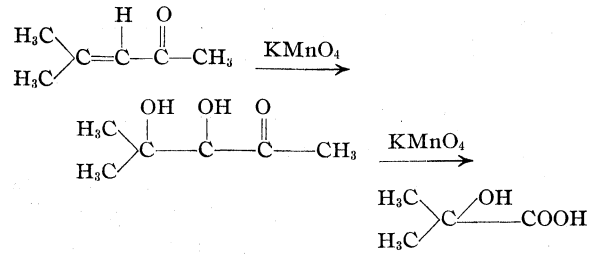




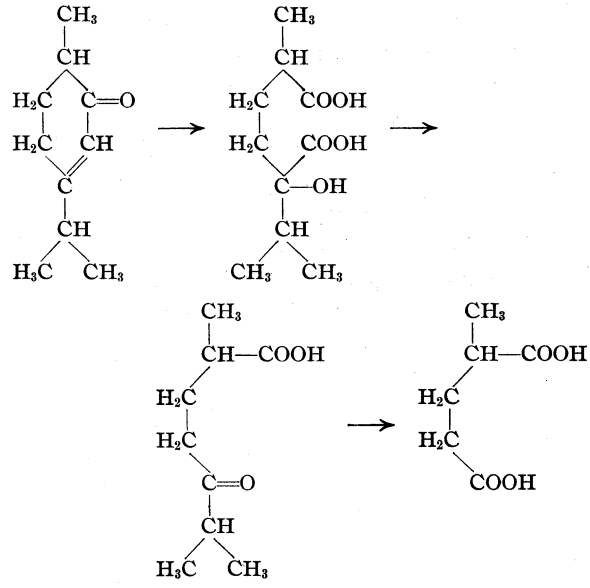
In regard to the composition of the dibasic acid obtained by the permanganate oxidation of anhydrosarsasapogenoic acid,[3] our results indicate quite definitely that the composition of the acid is $C_{27}H_{42}O_7$ and not $C_{27}H_{40}O_7$ as concluded by Fieser and Jacobsen.[3] This conclusion is based on check analyses of the free acid, the dimethyl ester and the dimethyl ester acetate. In addition a number of the analyses reported by Fieser and Jacobsen[3] for the acid and its derivatives are also in accordance with the composition $C_{27}H_{42}O_7$.

There are numerous examples in the literature which indicate that the initial reaction in the oxidation of an α,β-unsaturated ketone with permanganate is the formation of a keto glycol as represented in the oxidation of mesityl oxide.[8] Scission of the carbon–carbon linkage then occurs[9] as indicated, while further oxidation of the hydroxy acid gives further scission.

(8) Harries and Pappos, *Ber.*, **34**, 2979 (1901).
(9) Pinner, *ibid.*, **15**, 591 (1882).



Perhaps a more striking and more pertinent example of the mechanism of permanganate oxidations is afforded by the work of Tiemann and Semmler[10] on the oxidation of carvenone, the reaction going through the stages



A similar case is given by the permanganate oxidation of piperitone.[11]

If structure III proposed for anhydrosarsasapogenoic acid by Fieser and Jacobsen is correct then it appears that permanganate oxidation should yield either a C_{27} tribasic acid or a C_{26} dibasic acid. The fact that a C_{27} dibasic acid is obtained suggests that the double bond links completely substituted carbons.

The amount of data concerning the dibasic acid is far too limited to make possible the assignment of any definite structure for the substance.

We have also investigated incidentally the C_{29} neutral product which Fieser and Jacobsen[1] first reported to be unreacted sarsasapogenin acetate but later[3] recognized as the acetate of a neutral oxidation product of an unknown nature. They

(10) Tiemann and Semmler, *ibid.*, **31**, 2889 (1898).
(11) Simonsen, "The Terpenes," Vol. I, Cambridge University Press, London, 1931, p. 323.

reservedly suggested the substance to be a hydroxysarsasapogenin.

Our analyses of the neutral acetate (m. p. 164°) do not distinguish between $C_{29}H_{44}O_5$ and $C_{29}H_{46}O_5$. In agreement with Fieser and Jacobsen[3] we find that the carbon analyses for the hydrolyzed product (m. p. 217°) are about 0.7% high for the composition $C_{27}H_{44}O_4$.

The neutral acetate readily forms a semicarbazone indicating the presence of a free carbonyl group or possibly of a potential aldehyde group. Reduction of the neutral acetate by the Clemmensen method gave a good yield of tetrahydrosarsasapogenin previously obtained by an analogous reduction of sarsasapogenin.[5] Oxidation of the neutral acetate with chromic anhydride at 80° yielded some of the C_{22} keto acid.[7]

The neutral acetate appeared to be unaffected by catalytic hydrogenation with Adams catalyst in neutral medium while in acidic medium it yielded after hydrolysis a product of the probable composition $C_{27}H_{46}O_4$ or $C_{27}H_{48}O_4$.

The results concerning this neutral substance are difficult to interpret, especially in view of the uncertainty of the analytical data. We feel that the formation of the neutral substance probably represents an important stage of the oxidation of the sapogenin to the various oxidation products. The neutral product was not encountered when the oxidation of sarsasapogenin acetate was carried out at 80–85°.

We wish to thank Parke, Davis and Company for their generous assistance in the various phases of this work.

Experimental Part[12]

Reduction of Sarsasapogenoic Acid. (a) **By Catalytic Hydrogenation.**—Catalytic hydrogenation of sarsasapogenoic acid in acetic acid at 3 atmospheres pressure at 25° with Adams catalyst gave a product which after crystallization from acetone formed white needles, m. p. 180–184°, which agrees with **anhydrotetrahydrosarsasapogenoic acid.**[12] No lactonic material was obtained in the reduction.

Anal. Calcd. for $C_{27}H_{44}O_4$: C, 75.0; H, 10.25. Found: C, 75.0; H, 10.25.

In another preparation the reduction product was crystallized first from acetone and then from aqueous methanol to give flat white needles, m. p. 183–187°. Mixed with a sample of sarsasapogentic acid (m. p. 185–187°) the melting point range was 182–187°.

Anal. Calcd. for $C_{27}H_{44}O_4$: C, 75.0; H, 10.25. Found: C, 74.7; H, 10.2.

(12) Compounds previously reported by Fieser and Jacobsen.

With diazomethane anhydrotetrahydrosarsasapogenoic acid yielded a **methyl ester** which was crystallized from ether–pentane as small white plates, m. p. 125–127°. This gave no depression with a sample of the methyl ester of sarsasapogentic acid (m. p. 123.5–126°).

Anal. Calcd. for $C_{28}H_{46}O_4$: C, 75.3; H, 10.4. Found: C, 75.3; H, 10.3.

Anhydrotetrahydrosarsasapogenoic acid when treated with chromic anhydride in acetic acid at room temperature for one hour gave **3-dehydroanhydrotetrahydrosarsasapogenoic acid** which after treatment with Norite was crystallized from acetone as white needles, m. p. 196–199°. This gave no depression with a sample of 3-dehydrosarsasapogentic acid.[5]

Anal. Calcd. for $C_{27}H_{42}O_4$: C, 75.3; H, 9.8. Found: C, 75.1; H, 9.9.

Anhydrotetrahydrosarsasapogenoic acid with benzoyl chloride in pyridine gave the **methyl ester, benzoate,**[12] m. p. 140–141.5°.

Anal. Calcd. for $C_{35}H_{50}O_5$: C, 76.3; H, 9.15. Found: C, 76.0; H, 9.1.

The methyl ester of sarsasapogentic acid with benzoyl chloride in pyridine yielded a **methyl ester benzoate** which after sublimation in high vacuum at 140–180° was crystallized from methanol as small white plates, m. p. 139–141°. This gave no depression with the methyl ester benzoate of the anhydrotetrahydro acid described above.

Anal. Calcd. for $C_{35}H_{50}O_5$: C, 76.3; H, 9.15. Found: C, 76.2; H, 9.2.

(b) **With Sodium and Ethanol.**—To a boiling solution of 500 mg. of sarsasapogenoic acid in 150 cc. of absolute ethanol was added 12 g. of sodium over a period of two hours. The solution was cooled, diluted with water, acidified with hydrochloric acid and the precipitated solid extracted with ether. The residue remaining upon evaporation of the ether was crystallized from ether–acetone–pentane as small white needles, m. p. 179–181° dec. This gave no depression with a sample of tetrahydroanhydrosarsasapogenoic acid[12] (m. p. 179–181°) obtained by the catalytic hydrogenation of anhydrosarsasapogenoic acid.

Anal. Calcd. for $C_{27}H_{44}O_4$: C, 75.0; H, 10.25. Found: C, 74.9; H, 10.2.

(c) **With Aluminum Isopropylate.**—A solution of 600 mg. of sarsasapogenoic acid and 1 g. of aluminum isopropylate in 30 cc. of isopropyl alcohol was refluxed for fifteen hours. The solvent was then distilled off over a period of one hour. The residual material yielded a product which crystallized from ether–pentane as compact white crystals, m. p. 206–208° dec.

Anal. Calcd. for $C_{27}H_{44}O_5$: C, 72.3; H, 9.9. Calcd. for $C_{27}H_{46}O_5$: C, 71.95; H, 10.3. Found: C, 71.9, 71.9; H. 10.2, 10.3.

3-Dehydrosarsasapogenoic Acid.—To a solution of 500 mg. of sarsasapogenoic acid in 30 cc. of glacial acetic acid was added a solution of 300 mg. of chromic anhydride in 10 cc. of 80% acetic acid. The mixture was allowed to stand at room temperature for thirty minutes. Dilution with water gave a solid which was taken up in ether, treated with Norite and crystallized from ether–pentane as small white plates, m. p. 162–164°.

Anal. Calcd. for $C_{27}H_{40}O_5$: C, 72.9; H, 9.1. Found: C, 72.9; H, 9.2.

With an ethereal solution of diazomethane the acid yielded a **methyl ester** which crystallized from ether–pentane as white needles, m. p. 125°.

Anal. Calcd. for $C_{28}H_{44}O_5$: C, 73.0; H, 9.6. Found: C, 73.0; H, 9.3.

3-Dehydro-4-bromosarsasapogenoic Acid.—To a solution of 1.2 g. of 3-dehydrosarsasapogenoic acid in 30 cc. of acetic acid acidified with a few drops of 48% hydrobromic acid was added 2.7 cc. of 1.05 *M* bromine in acetic acid. The solution was diluted with water and the precipitated solid collected, washed with water and dried. After treatment with Norite the substance was crystallized from acetone to give white crystals, m. p. 188.5–191°.

Anal. Calcd. for $C_{27}H_{39}O_5Br$: C, 61.9; H, 7.5. Found: C, 61.4; H, 7.3.

3-Dehydro-$\Delta^{4,5}$-sarsasapogenoic Acid.—A solution of 800 mg. of the 3-dehydro-4-bromo acid in 20 cc. of dry pyridine was refluxed for six hours. The solution was poured into an excess of dilute sulfuric acid and the precipitated solid taken up in ether. The material was crystallized from acetone–ether as white plates, m. p. 199–201°.

Anal. Calcd. for $C_{27}H_{38}O_5$: C, 73.25; H, 8.7. Found: C, 73.4; H, 8.5.

Oxidation of Sarsasapogenoic Acid Acetate.—A solution of 5 g. of chromic anhydride in 30 cc. of 80% acetic acid was added dropwise with stirring over a period of ninety minutes to a solution of 2.5 g. of sarsasapogenoic acid acetate in 60 cc. of glacial acetic acid at 80–85°. The stirring and heating were continued for an additional two hours after which the mixture was evaporated *in vacuo* to 40 cc. The residue was diluted with water and extracted with ether. The ethereal extract, after thorough washing with water, was washed with 3% sodium hydroxide solution. Evaporation of the remaining ethereal extract gave an insignificant amount of neutral material which was not investigated further.

The sodium hydroxide extract was warmed on the steam-bath for fifteen minutes to hydrolyze any remaining acetates. The solution was then cooled, acidified with hydrochloric acid and the precipitated gum extracted with ether. The ethereal extract was washed with water and the ether allowed to evaporate to a volume of 20 cc. at room temperature over a period of three days. At the end of this time compact white crystals separated. These were collected, washed with ether and crystallized from methanol–ether to give a product, m. p. 287° dec. This gave no depression with an authentic sample of the C_{22} keto acid previously described.[7]

Anal. Calcd. for $C_{22}H_{34}O_4$: C, 72.9; H, 9.5. Found: C, 72.5; H, 9.5.

When shaken with hydrogen (3 atm.) and Adams catalyst in ethanol solution the keto acid yielded a neutral product, m. p. 199–201°. This gave no depression with an authentic sample of the hydroxy lactone of sarsasapogenin.

Anhydrosarsasapogenoic Acid.[12]—A solution of 500 mg. of sarsasapogenoic acid in 5 cc. of ethanol and 10 cc. of 30% aqueous potassium hydroxide solution was allowed to stand at room temperature for nine hours. The solution was then diluted with water, acidified with hydrochloric acid and the precipitated solid taken up in ether. Evaporation of the ether yielded a product which was crystallized from ether–chloroform to give compact white crystals (150 mg.), m. p. 242–244° dec.

Anal. Calcd. for $C_{27}H_{40}O_4$: C, 75.7; H, 9.4. Found: C, 75.4, 75.3; H, 9.2, 9.4.

Catalytic hydrogenation of the anhydro acid in ethanol with Adams catalyst yielded **tetrahydroanhydrosarsasapogenoic acid,**[12] m. p. 179–181°. In another preparation the acid was obtained as white needles, m. p. 194–196°. This gave no depression with the lower melting product.

Anal. Calcd. for $C_{27}H_{44}O_4$: C, 75.0; H, 10.25. Found: C, 74.8; H, 10.1.

When anhydrosarsasapogenoic acid was refluxed with semicarbazide hydrochloride and sodium acetate in 85% ethanol solution for one hour the acid was recovered unchanged. Anhydrosarsasapogenoic acid was also recovered unchanged after refluxing for fourteen hours with aluminum isopropylate and dry isopropyl alcohol.

Anhydrosarsasapogenoic acid was also prepared as described by Fieser and Jacobsen.[1] The filtrate remaining after removal of the anhydro acid yielded a relatively soluble isomeric acid, which crystallized from ethyl acetate–ether as compact white crystals, m. p. 181–184° dec. (gas). The yield was less than that of the anhydro acid.

Anal. Calcd. for $C_{27}H_{40}O_4$: C, 75.7; H, 9.4. Found: C, 75.4; H, 9.4.

A mixture of 500 mg. of this isomeric acid, 60 cc. of 95% ethanol, 2 cc. of water, and 200 mg. of sodium hydroxide was refluxed for two hours. The product was worked up as described for anhydrosarsasapogenoic acid to yield 200 mg. of compact white crystals, m. p. 241–243°. This gave no depression with anhydrosarsasapogenoic acid.

Attempts to prepare a crystalline acetate, methyl ester, or methyl ester acetate of the isomeric acid were unsuccessful. The acid readily reacted with alkaline potassium permanganate at 0°, but no crystalline products were obtained. Catalytic hydrogenation in ether–ethanol at three atmospheres pressure gave a non-crystalline product.

Dibasic Acid.[12]—The dibasic acid was prepared as described by Fieser and Jacobsen.[3]

Anal. Calcd. for $C_{27}H_{40}O_7$: C, 68.04; H, 8.46. Calcd. for $C_{27}H_{42}O_7$: C, 67.74; H, 8.84. Found: C, 67.40, 67.68; H, 8.94, 8.80.

An attempt to prepare a crystalline acetate by heating with acetic anhydride was unsuccessful.

The acid appears to be altered by treatment with periodic acid in methanol solution at room temperature for eighteen hours but no crystalline products were isolated even after sublimation in high vacuum. Treatment of the dibasic acid with chromic anhydride at 20° for fifteen hours in acetic acid gave a gum which did not crystallize even after sublimation in high vacuum.

The acid was recovered unchanged after treatment with semicarbazide acetate under the usual conditions.

When subjected to catalytic hydrogenation in ethanol–ether with Adams catalyst at 3 atmospheres pressure for fourteen hours the acid was recovered unchanged. Hydrogenation in ethanol acidified with hydrochloric acid with Adams catalyst at 3 atmospheres pressure for twenty-four hours gave a sirup which could not be crystallized.

The acid gave a **dimethyl ester,**[12] m. p. 161–162°.

Anal. Calcd. for $C_{29}H_{44}O_7$: C, 69.0; H, 8.79. Calcd. for $C_{29}H_{46}O_7$: C, 68.73; H, 9.15. Found: C, 68.63, 68.58; H, 9.20, 9.21.

Treatment of the dimethyl ester with boiling acetic anhydride for twenty minutes gave a product which was crystallized from ether–pentane to give long white needles of the **dimethyl ester acetate,** m. p. 158–160°.

Anal. Calcd. for $C_{31}H_{46}O_8$: C, 68.10; H, 8.47. Calcd. for $C_{31}H_{48}O_8$: C, 67.85; H, 9.01. Found: C, 67.74, 67.93; H, 8.93, 8.91.

C_{27} Neutral Oxidation Product from Sarsasapogenin.—The neutral fraction obtained in the chromic anhydride oxidation of sarsasapogenin acetate was crystallized from acetone to give white needles, m. p. 162–164°, of a **neutral acetate.**[12]

Anal. Calcd. for $C_{29}H_{44}O_5$: C, 73.65; H, 9.4. Calcd. for $C_{29}H_{46}O_5$: C, 73.4; H, 9.8. Found: C, 73.2; H, 9.7.

Hydrolysis of this product with an excess of ethanolic potassium hydroxide gave the **3-hydroxy compound**[12] which crystallized from acetone as small white plates, m. p. 215–217°.

Anal. Calcd. for $C_{27}H_{42}O_4$: C, 75.3; H, 9.85. Calcd. for $C_{27}H_{44}O_4$: C, 74.9; H, 10.2. Found: C, 75.6, 75.7; H, 10.0, 10.1.

The neutral acetate when treated with semicarbazide hydrochloride under the usual conditions gave a **semicarbazone** which crystallized from acetone as small white needles, m. p. 249–251° dec.

Anal. Calcd. for $C_{30}H_{47}O_5N_3$: C, 68.0; H, 9.0; N, 7.9. Calcd. for $C_{30}H_{49}O_5N_3$: C, 67.75; H, 9.3; N, 7.9. Found: C, 67.5, 67.5; H, 8.9, 8.7; N, 7.6.

Reduction of C_{27} Neutral Oxidation Product. (a) **By Catalytic Hydrogenation.**—A mixture of 1.5 g. of the neutral acetate, 1 g. of Adams catalyst, 100 cc. of glacial acetic acid and 30 cc. of 99% ethanol was shaken with hydrogen at 3 atmospheres pressure at 25° for fourteen hours. The mixture was filtered and the filtrate diluted with water, the precipitated solid was extracted with ether and the ethereal extract washed with sodium carbonate solution. The ether was evaporated and the residue refluxed for twenty minutes with an excess of ethanolic potassium hydroxide. The product was crystallized from methanol–ethanol as white plates, m. p. 215–217°.

Anal. Calcd. for $C_{27}H_{44}O_4$: C, 74.9; H, 10.3. Calcd. for $C_{27}H_{46}O_4$: C, 74.6; H, 10.7. Calcd. for $C_{27}H_{48}O_4$: C, 74.26; H, 11.1. Found: C, 74.6, 74.4; H, 10.7, 10.9.

The neutral acetate was recovered unchanged after shaking with Adams catalyst and hydrogen at 3 atmospheres pressure for six hours at 28° in ethanol solution.

(b) **By Clemmensen Reduction.**—To a boiling solution of 300 mg. of the neutral acetate in 100 cc. of 95% ethanol with 20 g. of amalgamated 20-mesh zinc was added 16 cc. of concentrated hydrochloric acid over a period of nine hours. The solution was decanted into water and the precipitated solid extracted with ether. The ether was evaporated and the residue crystallized from acetone–ethyl acetate to give 200 mg. of compact white crystals, m. p. 191–193°. This gave no depression with a sample of tetrahydrosarsasapogenin.

Anal. Calcd. for $C_{27}H_{48}O_3$: C, 77.1; H, 11.5. Found: C, 76.8; H, 11.5.

Summary

The structure of sarsasapogenoic acid and its transformation products is discussed in terms of the ketone spiro acetal structure for the sapogenin side chain.

STATE COLLEGE, PENNA. RECEIVED MAY 3, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Structure of Gossypol. XXII. Gossypol Ethers and their Reduction Products[1]

BY ROGER ADAMS AND W. R. DIAL[2]

Gossypol hexamethyl ether[3] was one of the most important gossypol derivatives since it served as the compound from which many significant degradation products were obtained.[4] It was assigned the structure I on the basis of its reactions with a drop of sulfuric acid in acetic acid to give gossypol dimethyl ether (II), with phenylhydrazine in glacial acetic acid to give a phenylhydrazone of a gossypol tetramethyl ether (III), which on treatment with methanolic or ethanolic hydrogen chloride reverted to gossypol hexamethyl ether (I) or gossypol tetramethyl diethyl ether (IV).[5]

The study of gossypol ethers has now been extended to a variety of others. Gossypol tetramethyl ether (V)[3] has been ethylated to gossypol diethyl tetramethyl ether (VI), isomeric with IV. This same ether (VI) was also prepared by methylation of gossypol diethyl ether (VII).[5]

The new ether (VI) formed a phenylhydrazone of gossypol dimethyl diethyl ether which with methanolic hydrogen chloride gave back VI or

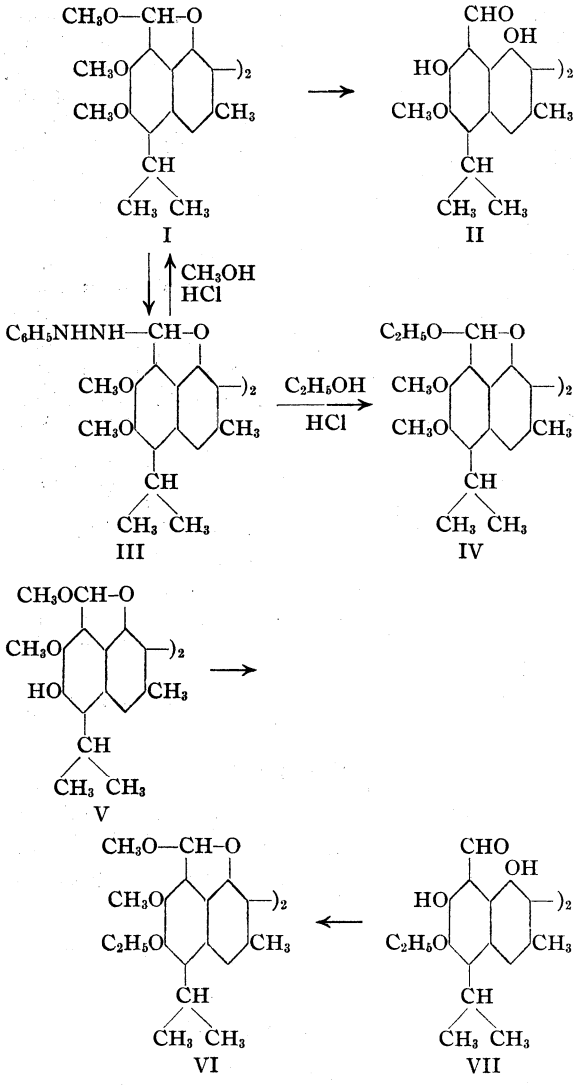
(1) For previous paper see Adams and Baker, THIS JOURNAL, **61**, 1138 (1939).

(2) Dow Chemical Company Fellow, 1936–1939.

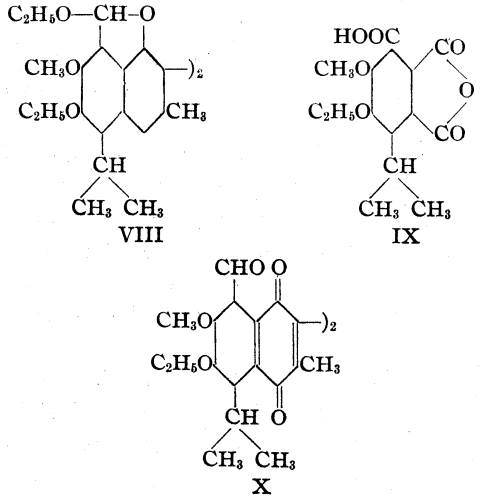
(3) Adams, Geissman and Morris, THIS JOURNAL, **60**, 2967 (1938).

(4) Adams, Morris, Geissman, Butterbaugh and Kirkpatrick, *ibid.*, **60**, 2193 (1938).

(5) Adams and Geissman, *ibid.*, **60**, 2166 (1938).

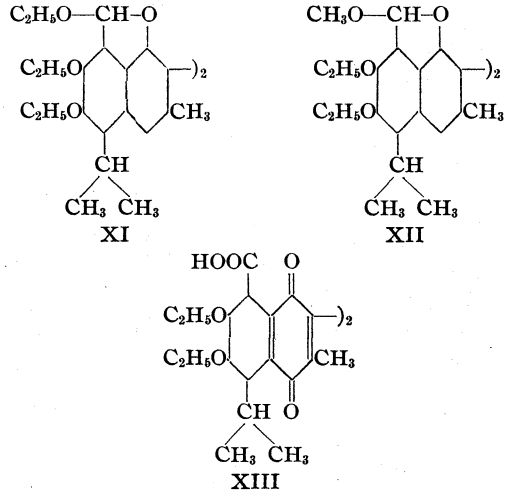


with ethanolic hydrogen chloride gave gossypol tetraethyl dimethyl ether (VIII).

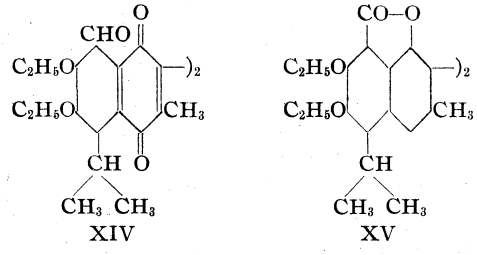


The ether (VI) undergoes reactions similar to gossypol hexamethyl ether. It was dealkylated with a drop of sulfuric in acetic acid[5] to gossypol diethyl ether (VII), and was oxidized with dilute nitric acid to a gossic acid analog (IX)[6] or by chromic acid to a gossypolone derivative (X).

Gossypol hexaethyl ether (XI)[7] was also converted into a phenylhydrazine derivative which on treatment with methanolic hydrogen chloride gave gossypol tetraethyl dimethyl ether (XII) and with ethanolic hydrogen chloride the original ether (XI)

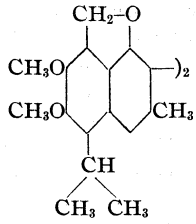


By action of dilute nitric acid on XI, a gossypolonic acid derivative (XIII) resulted[6]; by action of chromic acid XI was converted to gossypolone tetraethyl ether (XIV) and gossylic acid lactone tetraethyl ether (XV).[6]

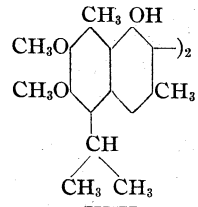


Gossypol hexamethyl ether was unaffected by hydrogen in the presence of platinum catalyst if ethanol or ethyl acetate was used as a solvent, but in acetic acid it was reduced to a new derivative which has been called desoxygossypol tetramethyl ether and has been assigned formula XVI. Formation of such a derivative may be by direct hydrogenolysis of the two acetal methoxyls in gossypol hexamethyl ether or more likely by hy-

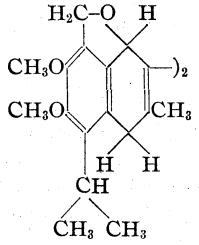
(6) Adams, Morris and Kirkpatrick, THIS JOURNAL, **60**, 2170 (1938).
(7) Morris and Adams, *ibid.*, **59**, 1731 (1937).



XVI



XVII



XVIII

drolysis of the acetal methoxyls, reduction of the two aldehyde groups and subsequent loss of water.

The analyses for this reduction product were more consistent with formula XVII or XVIII but the chemical reactions excluded the latter two possibilities. This substance may be of the nature of gossypol itself for which consistent analyses for its molecular formula, $C_{30}H_{30}O_8$, were practically impossible to obtain.

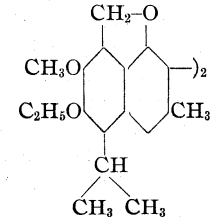
The evidence for structure XVI and against XVII is as follows. The compound gave no color with ferric chloride; it was insoluble in methanolic alkali; it could not be methylated or acetylated; it gave no phenylhydrazine derivative; bromination, nitration, Friedel and Crafts reactions and dealkylation with a drop of sulfuric acid in acetic acid gave no definite products. Neither this product nor gossypol hexamethyl ether with diazotized aniline gave a color; on the other hand, gossylic acid tetramethyl ether which has a free hydroxyl in the same position as is shown in compound XVII did give a color. Diazotized 2,4-dinitroaniline gave a color with all three products. Meyer[8] has shown that diazotized aniline will couple only with phenols and not with phenol ethers whereas diazotized dinitroaniline will couple with both phenols and their ethers. This is evidence for an ether linkage (XVI) in desoxygossypol tetramethyl ether and makes formulas XVII or XVIII unlikely. The infrared absorption spectra[9] of XVI in carbon tetrachloride indicated that no phenolic or alcoholic hydroxyl was present.

(8) Meyer, Isschick and Schlosser, *Ber.*, **47**, 1741 (1914).

(9) The infrared absorption spectra were determined by G. W. McMillan of this Laboratory, to whom we are indebted.

Desoxygossypol tetramethyl ether gave on oxidation with dilute nitric acid gossic acid[6] and with chromic anhydride gossypolone tetramethyl ether. These are the same products as are obtained from gossypol tetramethyl ether with the same reagents.

The gossypol diethyl tetramethyl ether (VI) was reduced under similar conditions with formation of desoxygossypol diethyl dimethyl ether (XIX).



XIX

Gossypol tetramethyl ether (V) was reduced also but no crystalline product was isolated. The crude product must have been the expected desoxy compound for on methylation, crystalline desoxygossypol tetramethyl ether (XVI), and on ethylation, crystalline desoxygossypol diethyl dimethyl ether (XVIII), resulted.

Compounds with this type of ether linkage across the *peri* positions in naphthalene are rare and no very simple compounds of this type have been described with which to compare properties.

Experimental

Gossypol Diethyl Tetramethyl Ether

(a) **Ethylation of Gossypol Tetramethyl Ether.**—A solution of 5.0 g. of recrystallized gossypol tetramethyl ether in a warm mixture of 13 cc. of diethyl sulfate and 22 cc. of benzene was treated with 33 cc. of 20% ethanolic potassium hydroxide added in small portions. The solution was heated for fifteen minutes on the steam-bath and then treated with an additional 13 cc. of diethyl sulfate and 20% ethanolic potassium hydroxide was added until the reaction mixture was alkaline. This was then evaporated to a sludge on the steam-bath with stirring, ethanol being added from time to time until most of the benzene had been removed. The sludge was then cooled and filtered. The solid was washed with ethanol until the filtrates were colorless and then thoroughly with water to remove inorganic salts. The residue (4.0 g.) of gossypol diethyl tetramethyl ether was purified by recrystallizing several times from acetone–methanol mixture and then from benzene–methanol mixture; white microcrystalline powder, m. p. 271–272° (corr.).

Anal. Calcd. for $C_{38}H_{46}O_8$: C, 72.36; H, 7.35. Found: C, 71.99; H, 7.31.

The compound gave an orange color in concentrated sulfuric acid and no color with ferric chloride.

When recrystallized from acetone–methanol mixture alone, the melting point could not be raised above 228–

229° (corr.). The white prisms thus obtained gave *no* melting point depression when mixed in various proportions with the 271–272° form.

Anal. Calcd. for $C_{38}H_{46}O_8$: C, 72.36; H, 7.35. Found: C, 72.47; H, 7.55.

(b) **Methylation of Gossypol Diethyl Ether.**—To a solution of 0.15 g. of gossypol diethyl ether in a mixture of 2 cc. of methanol and 2 cc. of dimethyl sulfate, 3 cc. of 10% methanolic potassium hydroxide was added slowly. The mixture was allowed to stand at room temperature for thirty-six hours and then filtered. The precipitate was filtered and washed with methanol, then with water. The product (0.14 g.) was purified as previously described and gave a crystalline powder, m. p. 271–272° (corr.).

Gossypol Diethyl Ether: Demethylation of Gossypol Diethyl Tetramethyl Ether.—To a solution of 1.0 g. of gossypol diethyl tetramethyl ether (272° form) in 40 cc. of hot glacial acetic acid was added 10 cc. of acetic acid containing ten drops of concentrated sulfuric acid. The solution turned dark red and after heating for fifteen minutes on a steam-bath, it was diluted with 20 cc. of water and cooled. The crude yellow product weighed 0.9 g. It was purified by recrystallization from benzene; yellow needles, m. p. 195–196° (corr.). This product proved to be identical with the diethyl ether of gossypol prepared previously by deëthylation of gossypol hexaethyl ether.[7]

Phenylhydrazone from Gossypol Diethyl Ether.—This was prepared by adding 0.5 cc. of phenylhydrazine to a hot solution of 0.1 g. of gossypol diethyl ether in 3 cc. of glacial acetic acid. After warming for thirty minutes on the steam cone, slender yellow needles of phenylhydrazone separated. These were filtered and washed with methanol; yield, 0.1 g., m. p. 260–261°(corr.). No satisfactory method could be found for the recrystallization of this material.

Anal. Calcd. for $C_{46}H_{50}O_6N_4$: C, 73.22; H, 6.68; N, 7.43. Found: C, 73.07; H, 6.64; N, 7.59.

The same product was obtained from the gossypol diethyl ether formed from gossypol hexaethyl ether.

The phenylhydrazone gives an orange-yellow color in concentrated sulfuric acid and a red color with ferric chloride which changes to orange upon standing. It is insoluble in cold 10% aqueous alkali but soluble in 10% methanolic alkali.

Phenylhydrazone from Gossypol Diethyl Tetramethyl Ether.—A solution of 0.1 g. of the 271–272° form of the above ether in 10 cc. of glacial acetic acid was warmed with 0.8 cc. of phenylhydrazine for thirty minutes on a steam-bath. Upon scratching the side of the flask, 0.95 g. of product separated. After recrystallization from benzene and petroleum ether (b. p. 60–110°), yellow prisms formed, m. p. 268–269° (corr.).

Anal. Calcd. for $C_{48}H_{54}O_6N_4$: C, 73.63; H, 6.95; N, 7.16. Found: C, 73.34; H, 6.71; N, 7.16, 7.25.

The phenylhydrazone gave an orange-yellow color in concentrated sulfuric acid and gave no color with ferric chloride.

The phenylhydrazone prepared in exactly the same manner from the 228–229° form of the ether melted at 268–269° (corr.) and gave no depression when mixed with the phenylhydrazone from the 271–272° form.

The phenylhydrazone can be reconverted to the gossypol diethyl tetramethyl ether by the action of methanolic hydrogen chloride. A suspension of 1.0 g. of the phenylhydrazone in 40 cc. of absolute methanol was treated with dry hydrogen chloride until all of the phenylhydrazone went into solution. The solution was allowed to stand overnight, whereupon the crystalline ether separated. It weighed 0.7 g. and after several recrystallizations from benzene–methanol mixture, melted at 271–272° (corr.) and gave no depression in melting point when mixed with the ether obtained by the ethylation of gossypol tetramethyl ether.

Gossypol Dimethyl Tetraethyl Ether by the Action of Ethanolic Hydrogen Chloride on the Phenylhydrazone from Gossypol Diethyl Tetramethyl Ether.—The same procedure as in the methanolysis was used except for the replacement of methanol by ethanol. After standing overnight 0.75 g. of product separated which was purified by recrystallization from acetone–ethanol mixture; white prisms, m. p. 241–242° (corr.).

Anal. Calcd. for $C_{40}H_{50}O_8$: C, 72.92; H, 7.65. Found: C, 73.19; H, 7.51.

The ether gives an orange color in concentrated sulfuric acid and no color in ferric chloride.

Norgossic Acid Ethyl Methyl Ether: 1-Methoxy-2-ethoxy-3-isopropyl-4,5,6-benzene Tricarboxylic Acid Anhydride-4,5.—Gossypol diethyl tetramethyl ether was treated with dilute nitric acid exactly as was described for the formation of gossic acid from gossypol hexamethyl ether.[5]

The insoluble residue could not be purified but the acid-soluble material amounted to 0.5 g. of crude acid from 2.0 g. of diethyl tetramethyl ether. Purified from toluene, white needles were obtained, m. p. 178–179° (corr.).

Anal. Calcd. for $C_{15}H_{16}O_7$: C, 58.44; H, 5.23. Found: C, 58.39; H, 5.27.

The acid gave no color in concentrated sulfuric acid and no color in ferric chloride.

Gossypolone Diethyl Dimethyl Ether.—To a solution of 2.0 g. of recrystallized gossypol diethyl tetramethyl ether in 50 cc. of boiling glacial acetic acid was added in one portion 10 cc. of a 10% aqueous solution of chromic anhydride. The mixture was allowed to boil for one minute and then poured onto a mixture of 100 g. of ice and 50 cc. of water. The yellow precipitate was filtered with suction, washed with water and air dried. The product was added to 50 cc. of hot methanol and upon cooling yellow platelets separated; yield, 0.8 g. After purification by the recrystallization from methanol, it melted at 185–186° (corr.).

Anal. Calcd. for $C_{36}H_{38}O_{10}$: C, 68.56; H, 6.07. Found: C, 68.20; H, 6.02.

The product gave a brown color in concentrated sulfuric acid which changed to orange upon standing for thirty minutes. It gave no color with ferric chloride.

In this oxidation no evidence of lactone formation was noted.

Phenylhydrazone from Gossypol Hexaethyl Ether.—A solution of 0.1 g. of gossypol hexaethyl ether in 4 cc. of hot glacial acetic acid was treated with 0.5 cc. of phenylhydrazine and the mixture was heated on the steam-bath

for thirty minutes. Upon cooling 0.08 g. of product separated; yellow needles from benzene–petroleum ether (b. p. 60–110°), m. p. 241–242° (corr.).

Anal. Calcd. for $C_{50}H_{58}O_6N_4$: C, 74.05; H, 7.21; N, 6.91. Found: C, 73.91; H, 7.01; N, 6.95.

The product gave an orange color with concentrated sulfuric acid and no color with ferric chloride.

The action of ethanolic hydrogen chloride on this product reconverted it to gossypol hexaethyl ether, m. p. 211–212° (corr.).

Gossypol Tetraethyl Dimethyl Ether.—By treatment of the phenylhydrazone from gossypol hexaethyl ether with methanolic hydrogen chloride in the same manner as described for other phenylhydrazones, 1.5 g. of product was obtained from 2 g. of starting material. It formed white crystals from acetone–methanol, m. p. 206–207° (corr.).

Anal. Calcd. for $C_{40}H_{50}O_8$: C, 72.92; H, 7.65. Found: C, 73.13; H, 7.77.

The product gave an orange color in concentrated sulfuric acid and no color with ferric chloride.

Gossypolonic Acid Tetraethyl Ether.—A suspension of 2.0 g. of gossypol hexaethyl ether in a mixture of 200 cc. of water and 50 cc. of concentrated nitric acid (sp. gr. 1.42) was refluxed for twelve hours. After this time a yellow solid remained in suspension. After cooling the yellow insoluble material was filtered and dissolved in 10% aqueous sodium bicarbonate solution. The bicarbonate solution, after extraction with ether, was filtered and acidified with dilute sulfuric acid. The product weighed 0.5 g. Purified from acetone–methanol mixture, it formed yellow flakes, m. p. 272–273° (corr.).

Anal. Calcd. for $C_{38}H_{42}O_{12}$: C, 66.07; H, 6.13. Found: C, 66.04; H, 6.27.

The product gave a maroon color in concentrated sulfuric acid which changed to brown on standing. It gave no color with ferric chloride. It was soluble in aqueous alkali giving a yellow solution.

The nitric acid filtrate was worked up as described for the dilute nitric acid oxidation of gossypol hexamethyl ether, but no crystalline acid corresponding to gossic acid could be isolated.

Gossypolone Tetraethyl Ether and Gossylic Acid Lactone Tetraethyl Ether.—To a solution of 2.0 g. of gossypol hexaethyl ether in 50 cc. of boiling glacial acetic acid was added 10 cc. of a 10% aqueous solution of chromic anhydride. The mixture was boiled for a minute and then poured onto 100 g. of ice. The insoluble product was filtered and dissolved in 100 cc. of boiling methanol. A yellow insoluble product (0.19 g.) separated almost immediately and proved to be gossylic acid lactone tetraethyl ether. It was purified by dissolving in 8 cc. of boiling acetic anhydride to which was then added slowly a mixture of 3 cc. of glacial acetic acid and 1.5 cc. of water. Upon scratching the walls of the flask, crystals separated. After repetition of this procedure, a white crystalline powder resulted, m. p. 244–245° (corr.).

The methanolic filtrate from the crude gossylic acid lactone tetraethyl ether was concentrated to about 30 cc. and cooled. The precipitate of gossypolone tetraethyl ether (0.5 g.) was purified from methanol; yellow plates, m. p. 146–147° (corr.).

Anal. (Lactone, m. p. 244–245°.) Calcd. for $C_{38}H_{42}O_8$: C, 72.82; H, 6.76. Found: C, 72.54; H, 6.88. (Gossypolone, m. p. 146–147°.) Calcd. for $C_{38}H_{42}O_{10}$: C, 69.28; H, 6.43. Found: C, 69.40; H, 6.55.

The gossypolone gave a brown color in concentrated sulfuric acid and the lactone a yellow color.

The lactone was insoluble in warm aqueous alkali but soluble in warm alcoholic alkali.

Dinitrogossylic Acid Lactone Tetraethyl Ether.—To a solution of 0.08 g. of the gossylic acid lactone tetraethyl ether in 10 cc. of hot glacial acetic acid, 1 cc. of concentrated nitric acid was added. A clear brown solution resulted which was boiled and water added dropwise until crystallization started. After cooling, the product which separated was recrystallized from dilute acetic acid; pale yellow needles, m. p. 266–267° (corr.).

Anal. Calcd. for $C_{38}H_{40}N_2O_6$: N, 3.91. Found: N, 3.72.

Reduction of Gossypol Hexamethyl Ether: Desoxygossypol Tetramethyl Ether.—A solution of 2.0 g. of pure gossypol hexamethyl ether (m. p. 223–225°) in 200 cc. of warm (50°) glacial acetic acid was placed in a reduction bottle together with 0.1 g. of platinum oxide catalyst and shaken with hydrogen at room temperature under three atmospheres pressure. After four hours, the solution was filtered to remove the platinum and the filtrate was poured into 800 cc. of water. The white flocculent precipitate was filtered, washed with water until free of acid and dried in air. The 1.9 g. of white amorphous product was triturated with warm methanol. A gummy mass was at first obtained which became crystalline upon standing for a few minutes. The methanol-insoluble material was filtered and weighed 1.5 g. After recrystallization from acetone–methanol mixture, it melted at 261–263° (corr.), with decomposition.

Anal. Calcd. for $C_{34}H_{38}O_6$: C, 75.28; H, 7.01; 4 OCH_3, 22.8; mol. wt., 542. Calcd. for $C_{34}H_{42}O_6$: C, 74.73; H, 7.69; 4OCH_3, 22.7; mol. wt., 546. Found: C, 74.75, 74.49, 74.31, 75.08, 74.44, 74.90, 74.65; H, 7.49, 7.37, 7.56, 7.46, 7.39, 7.42, 7.29; OCH_3, 26.0, 26.8; mol. wt. (b. p. elev., $CHCl_3$), 529.

The compound is insoluble in alkali (aqueous or alcoholic) and gives no ferric chloride color and no color with Dimroth's pyroboroacetate reagent. It gives a brilliant green color with concentrated sulfuric acid.

The compound is soluble in ether, benzene and acetone. It is slightly soluble in acetic acid or methanol and insoluble in ligroin.

Attempts to reduce gossypol hexamethyl ether in alcohol or ethyl acetate resulted in the recovery of the unchanged ether.

Phenylhydrazine, acetic anhydride and sodium acetate, pyridine and acetic anhydride, methanolic dimethyl sulfate and alkali, all resulted in recovery of unchanged starting material.

Attempted demethylation with glacial acetic acid and a drop of sulfuric acid gave no results.

Nitration with various strengths of nitric acid gave only amorphous products. The same was true of bromine, attempted Friedel and Crafts reactions with acetyl chloride, and of hydriodic acid.

Aniline and 2,4-dinitroaniline were diazotized in glacial acetic acid with butyl nitrite and sulfuric acid according to the method of Meyer.[8]

Each of the solid diazonium sulfates was dissolved in 6 parts of cold glacial acetic acid and 1 cc. of each of these solutions was added to a solution of 15 mg. of the compound to be tested in 5 cc. of glacial acetic acid. Diazotized aniline gave no color with gossypol hexamethyl ether or desoxygossypol tetramethyl ether; it did give a color with gossylic acid tetramethyl ether. Diazotized 2,4-dinitroaniline, on the other hand, gave a color with all three products.

Oxidation of Desoxygossypol Tetramethyl Ether to Gossic Acid—A suspension of 0.18 g. of desoxygossypol tetramethyl ether in a mixture of 15 cc. of water and 5 cc. of concentrated nitric acid (sp. gr. 1.42) was refluxed for fourteen hours whereupon all the material went into solution. After cooling, about 30 mg. of insoluble acidic material was filtered. This could not be purified. The dilute nitric acid filtrate was neutralized with sodium carbonate, then acidified to congo red with sulfuric acid, saturated with sodium chloride and extracted several times with ether. The ether extracts were dried with anhydrous magnesium sulfate and then petroleum ether (b. p. 60–110°) added. The ethyl ether was evaporated whereupon brown needles separated from the petroleum ether. The product was purified from toluene, yield 0.08 g. Upon sublimation (2 mm. at 180°) and then recrystallization from toluene, white needles were obtained, m. p. 185–186° (corr.). Mixed with an authentic sample of gossic acid the melting point was 185–186° (corr.).

Anal. Calcd. for $C_{14}H_{14}O_7$: C, 57.15; H, 4.76. Found: C, 57.27; H, 4.78.

Oxidation of Desoxygossypol Tetramethyl Ether to Gossypolone Tetramethyl Ether.—To a solution of 0.21 g. of desoxygossypol tetramethyl ether in 15 cc. of boiling glacial acetic acid was added rapidly with vigorous stirring 2 cc. of 10% aqueous solution of chromic anhydride and the mixture was allowed to boil for one minute. It was then poured onto a mixture of 30 g. of ice and 10 cc. of water. The product was filtered with suction and the yellow residue was washed with water and air dried. This was added to 10 cc. of warm methanol and the gummy material first formed gradually became crystalline. Recrystallized from methanol, 0.1 g. of yellow plates, m. p. 154–155° (corr.), was obtained. Mixed with an authentic sample of gossypolone tetramethyl ether the melting point was 154–156° (corr.).

Anal. Calcd. for $C_{34}H_{34}O_{10}$: C, 67.77; H, 5.64. Found: C, 67.73; H, 5.81.

Reduction of Gossypol Tetramethyl Diethyl Ether to Desoxygossypol Tetramethyl Ether.—Gossypol tetramethyl diethyl ether[5] which has two acetal ethoxy groups was reduced in the same manner as described for the hexamethyl ether. Upon recrystallization of the product from acetone–methanol, white plates were obtained, m. p. 261–263° (corr.). Mixed with the product obtained by the reduction of gossypol hexamethyl ether, it melted at 261–263° (corr.).

Anal. Calcd. for $C_{34}H_{38}O_6$: C, 75.28; H, 7.01. Found: C, 74.62; H, 7.57.

Reduction of Gossypol Diethyl Tetramethyl Ether: Desoxygossypol Diethyl Dimethyl Ether.—Gossypol diethyl tetramethyl ether[5] which has two methoxy groups as acetal linkages was reduced as previously described for the hexamethyl ether. From 1.2 g. of starting material, 0.6 g. of desoxy compound was obtained; white plates from acetone–methanol mixture, m. p. 240–242° (corr.).

Anal. Calcd. for $C_{36}H_{42}O_6$: C, 75.76; H, 7.42. Found: C, 75.28; H, 7.58.

Reduction of Gossypol Tetramethyl Ether: Desoxygossypol Dimethyl Ether.—Gossypol tetramethyl ether[3] which has two acetal methoxyls was reduced in the same manner as described for the hexamethyl ether but no crystalline material was obtained. The crude tan amorphous desoxygossypol dimethyl ether thus obtained weighed 1.5 g. and had a very indefinite melting point. That this material was a reduction product similar to that obtained by the reduction of gossypol hexamethyl ether was demonstrated by methylation and ethylation.

A solution of 1.5 g. of crude product in 20 cc. of methanol was treated with 5 cc. of dimethyl sulfate. To this mixture was added 16 cc. of a 20% solution of potassium hydroxide in methanol and then heated on a steam-bath for five minutes. Another 5 cc. of methyl sulfate and 16 cc. of 20% methanolic potassium hydroxide was added and the solution evaporated with stirring to a thick sludge. About 20 cc. of methanol was added and the mixture was cooled and filtered. After washing with methanol until the washings were colorless and washing with water to remove potassium salts, 0.5 g. of a cream-colored crystalline material remained on the filter. This after four recrystallizations from acetone–methanol mixture melted at 262–263° (corr.). The white platelets thus obtained proved identical with the desoxygossypol tetramethyl ether already described, mixed m. p. 262–263° (corr.).

Anal. Calcd. for $C_{34}H_{38}O_6$: C, 75.28; H, 7.01. Found: C, 74.67; H, 7.01.

By treatment of the amorphous desoxygossypol dimethyl ether with diethyl sulfate and 20% potassium hydroxide in ethyl alcohol desoxygossypol diethyl dimethyl ether was obtained. It formed white crystals, m. p. 240–242° (corr.) and gave no depression in the melting point when mixed with the sample prepared by the reduction of gossypol diethyl tetramethyl ether.

Summary

1. A number of new ethers of gossypol are described—two gossypol tetraethyl dimethyl ethers and gossypol diethyl tetramethyl ether. These had properties similar to gossypol hexamethyl ether. They could be oxidized to analogous products.

2. Gossypol hexamethyl ether was reduced in glacial acetic acid with hydrogen to desoxygossypol tetramethyl ether and an analogous compound was obtained by the reduction of gossypol diethyl tetramethyl ether. The desoxy compounds oxidize to products similar to those from gossypol hexamethyl ether.

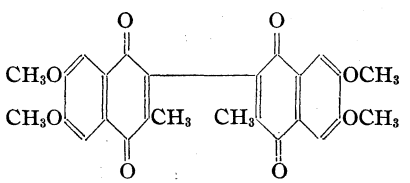
URBANA, ILLINOIS RECEIVED MAY 31, 193

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Structure of Gossypol. XXIII. Attempts to Prepare Desapogossypolone Tetramethyl Ether. Condensation of Hexadiene-2,4 with Dibenzoylethylene[1]

BY ROGER ADAMS AND T. A. GEISSMAN

The completion of the verification of the postulated structure for gossypol is dependent either on the degradation of gossypol to a substance of known structure which will establish the positions of the methyl groups and the linkage between the naphthalene nuclei or on the synthesis of one of the supposed β,β-binaphthyl degradation products of gossypol. The former procedure has thus far met with failure. Attempts are now being made to synthesize desapogossypolone tetramethyl ether (I) and the initial series of reactions studied is described in this communication.

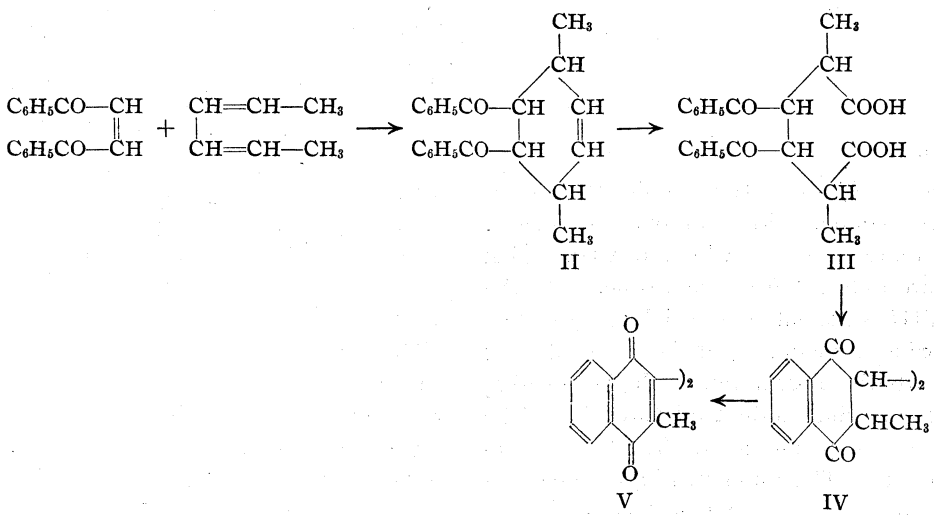


I

In order to test the feasibility of the method, the synthesis of the methoxyl-free analog of desapogossypolone tetramethyl ether was undertaken. *trans*-Dibenzoylethylene and hexadiene-2,4 were condensed to give product II. It was planned to oxidize the double bond in II to give the dibasic acid (III). This, in turn, was to be cyclicized either directly or indirectly to IV which should oxidize to the desired compound (V).

The initial reaction of the dibenzoylethylene and the diene proceeded without difficulty but all the oxidation reactions of II resulted in complete degradation of the molecule or in substances different from the dibasic acid (III) desired. A description of the results actually obtained is given here, along with a description of studies made on the conversion of the adduct (II) by methods which appear to be general for compounds of this type into the fully aromatic derivative (XIX) and the benzofuran (XVI).

The Diels–Alder reaction between hexadiene-2,4 and dibenzoylethylene results in a good yield of a mixture of two products in a ratio of 10:1. These are unquestionably *cis–trans* isomers and each was converted into a dibromide. Merely the higher melting compound, obtained in larger amounts, was further studied. It was oxidized by means of (a) ozone, (b) potassium permanganate, (c) osmium tetroxide and chlorates, and (d) by other specific reagents, such as Prévost's reagent and the action of acetates on the dibromide (XIII), but in no case were satisfactory results obtained. The conclusion drawn from these experiments was that the reactivity of the hydrogen atoms on the carbons *alpha* to the carbonyl groups was so great that these reagents did not confine their action to the double bond.



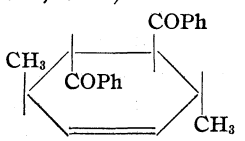
II III IV V

Upon oxidation of the adduct with monoperphthalic acid in an ether–chloroform solution,

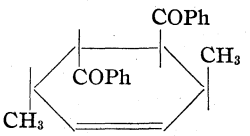
(1) For previous paper in this series see Adams and Dial, THIS JOURNAL, **61**, 2077 (1939).

a smooth consumption of one atom of oxygen was observed and the product was a fairly good yield of a mixture of two isomeric oxido compounds. Of the two oxido compounds, one could be separated easily in a pure state by virtue of its extreme insolubility in methanol, while the other was contaminated with what appeared to be a third substance and was difficult to purify.

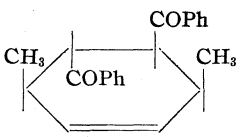
The stereochemical possibilities in these compounds may be deduced with reasonable certainty on the following considerations. Assuming that the benzoyl groups are *trans* in the adducts, the following configurations are to be expected (VI, VII, VIII).



VI

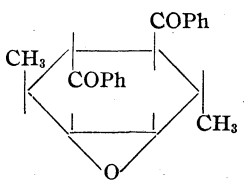


VII

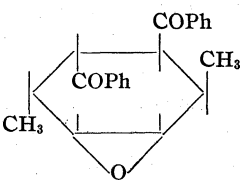


VIII

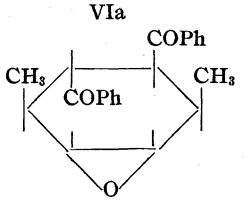
The oxido compounds derived from these three adducts would be



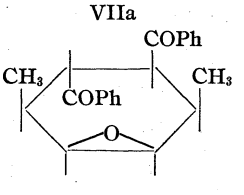
VIa



VIIa



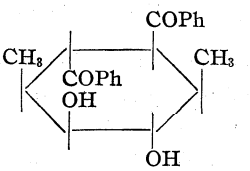
VIIIa



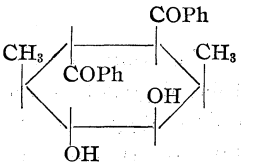
VIIIb

The symmetry of VI or VII precludes the formation of more than one oxido compound from each. These are represented by VIa and VIIa which obviously are different from each other. As the structure VIII is the only one which can give two different oxido compounds, it is assumed that this represents the more abundant higher-melting isomer in the original adduct mixture (II). The lower-melting compound must then have structure VI or VII. The lower-melting oxido compound may be assigned structure VIIIb and the higher-melting VIIIa on the basis of the relationship of the oxido group to the two methyls.

Since the formation of a glycol from an oxide leads to the *trans*-glycol, it would be expected that both VIIIa and VIIIb would give a mixture of the same two glycols (IX and X).



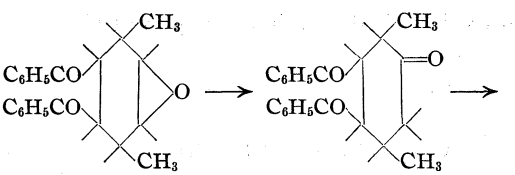
IX

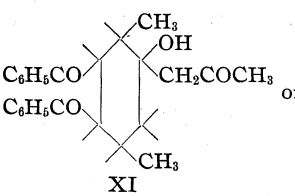


X

Upon hydrolysis of the oxides in acetone solution this was found to be the case, but different proportions of the glycols were obtained from each oxide. From the lower-melting oxide, the higher-melting glycol and from the higher-melting oxide, the lower-melting glycol predominated. The glycols had similar solubility characteristics and were difficult to separate.

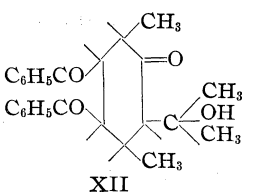
In the preparation of glycol from a low-melting fraction of oxide a third substance was isolated in one run which appeared to be an addition product of one molecule of acetone to the oxide. The structure was not determined but it may possibly be one of the following two, XI and XII, on the assumption that the glycol has rearranged to a ketone and then condensed with acetone. The structure XII is preferred since the compound does not give ketone derivatives (the benzoyl groups in other compounds of the series do not form ketone derivatives) and gives no iodoform on treatment with sodium hypobromite in dioxane solution.





XI

or

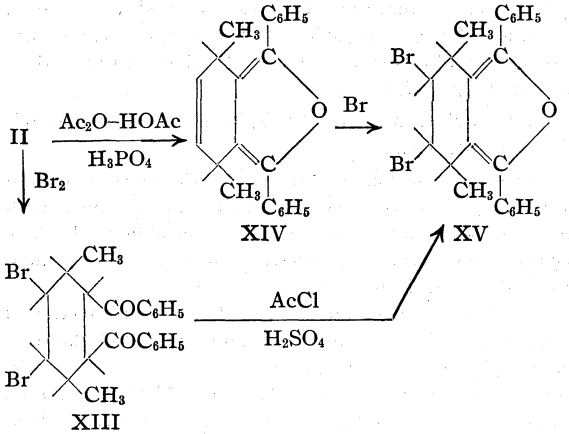


XII

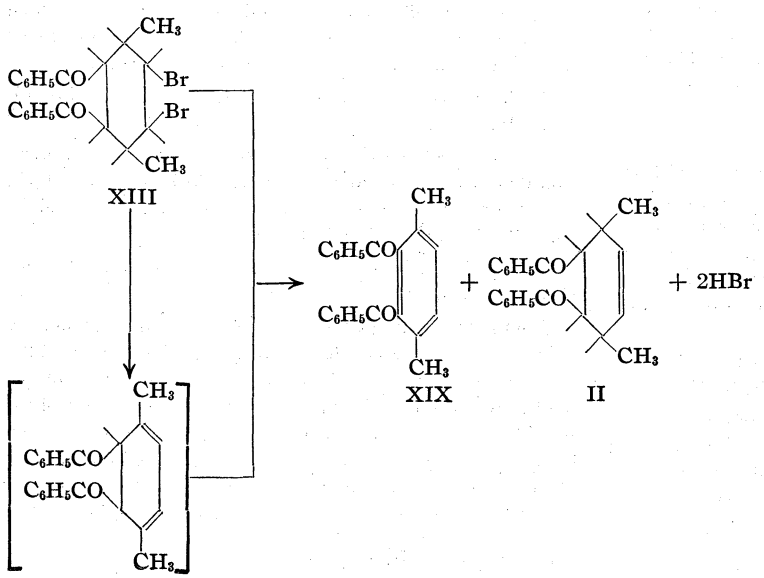
The dibromide (XIII) of the higher-melting adduct of hexadiene-2,4 and dibenzoylethylene upon treatment with sodium acetate rearranged to an isomeric dibromide, probably a stereoisomer of the original compound.

The conversion of the adduct (II) and its dibromide (XIII) into derivatives of isobenzofuran can be accomplished readily by treatment with

dehydrating agents under the proper conditions. When the adduct (II) is treated with a mixture of acetic acid, acetic anhydride and a trace of phosphoric acid it is converted smoothly into the dihydrobenzofuran derivative (XIV). The adduct dibromide (XIII) when treated with acetyl chloride containing sulfuric acid is dehydrated in good yield to the corresponding dibromo derivative (XV). Bromination of XIV under suitable conditions also yields XV.

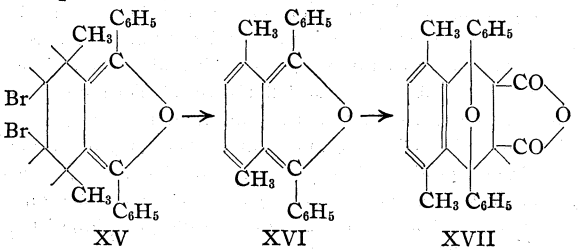


Attempts to convert the adduct (II) into the fully aromatic compound (XIX) by treatment of the dibromide (XIII) with pyridine led to the formation of a mixture of the desired benzene derivative (XIX) and the original adduct. Apparently the dihydrobenzene formed as a direct result of the removal of two molecules of hydrogen bromide from the dibromide (XIII) reacts as shown below to debrominate a molecule of the dibromide and becomes aromatized

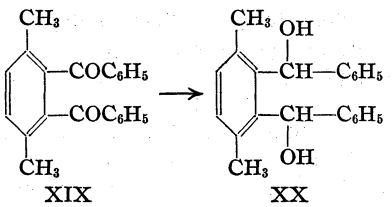


The formation of the benzene derivative (XIX) was accomplished in good yield by treatment of the dihydrobenzofuran (XIV) with two moles of bromine in the presence of sodium acetate.

The dibromotetrahydrobenzofuran (XV) was unchanged by boiling with sodium acetate in acetic acid, but on treatment with dry pyridine it was converted smoothly into the benzofuran (XVI). The latter compound reacted with maleic anhydride instantly in the cold to give the addition product (XVII).



Since other studies in this Laboratory have indicated that certain benzofurans of the type of compound XVI can be obtained by reduction of the dibenzoylbenzenes corresponding to XIX with zinc dust in alcoholic alkali, an attempt was made to form XVI from XIX in this way. None of the benzofuran (XVI) was produced, however, the product being a colorless compound which may be the *o-bis*-(α-oxybenzyl) derivative (XX)



A further study of diene additions to diaroylethylenes and their reaction products is under way.

Experimental

Preparation of Hexene-2-ol-4.—The Grignard reagent prepared from 305 g. of ethyl bromide and 64 g. of magnesium in 1500 cc. of dry ether was cooled in an ice-bath, and 160 g. of crotonaldehyde (in a little ether) was added dropwise with vigorous stirring at such a rate as to keep the solution at 15–20°. After the aldehyde was added stirring was continued for one-half hour while the solution was allowed to come to room temperature. The mixture was decomposed with iced ammonium chloride solution, the ether layer separated, and worked up in the usual manner. There was ob-

tained 188 g. (83%) of hexene-2-ol-4, b. p. 55° (15 mm.). Reiff[2] reports 85–87° (120 mm.) and 133–134° (760 mm.).

Hexadiene-2,4.—A mixture of 75 g. of hexene-2-ol-4 and 5 cc. of 48% hydrobromic acid was distilled slowly through a short column, the outlet temperature of which was maintained by controlling the rate of distillation at 85–95°. The distillate was separated from the water formed and dried over calcium chloride. It boiled at 79–83°; yield, 41 g. (67%).

This method is faster and more convenient than that described by Kyriakides.[3]

3,6-Dimethyl-4,5-dibenzoylcyclohexene-1,2 (II).—A mixture of 60 g. of dibenzoylethylene, 56 cc. (41 g.) of hexadiene-2,4 and 75 cc. of toluene was heated on the steam-bath for eighteen hours (under reflux). The solvent was evaporated in a stream of air and to the residual sirup while still hot was added 150 cc. of methanol. On cooling, the solution set to a crystalline mass. The product was collected by suction and washed with methanol. The crude product was a cream-colored crystalline material weighing 63 g. Recrystallized from acetone–methanol, it formed stout, colorless needles, weighing 53 g., m. p. 136–137°.

Anal. Calcd. for $C_{22}H_{22}O_2$: C, 82.97; H, 6.97. Found: C, 82.66, 83.09; H, 7.00, 6.83.

From the methanol mother liquors from two preparations with a total of 90 g. of dibenzoylethylene there was obtained by concentration 10.5 g. of a low-melting crystalline compound. After repeated recrystallization from methanol there was obtained 6.5 g. of white needles, m. p. 86–88°. This is an isomeric adduct.

Anal. Calcd. for $C_{22}H_{22}O_2$: C, 82.97; H, 6.97. Found: C, 82.73; H, 7.09.

Dibromides of Addition Products

(1) **Of High-Melting Adduct (XIII).**—To a solution of 3.18 g. of adduct (m. p. 136°) in 25 cc. of glacial acetic acid, was added dropwise with cooling a solution of 1.60 g. of bromine in 16 cc. of acetic acid. The bromine was decolorized instantly. The solution was poured into water, the dibromide extracted with chloroform, the chloroform solution concentrated to a small volume, diluted with ethanol, and concentrated again until crystallization began: white crystals, m. p. 169–170°; yield 3.94 g.

Anal. Calcd. for $C_{22}H_{22}O_2Br_2$: C, 55.23; H, 4.60. Found: C, 55.52; H, 4.64.

This dibromide is converted by means of sodium acetate to another dibromide, presumably stereoisomeric with the first. A mixture of 2 g. of the dibromide, 2 g. of anhydrous sodium acetate, 15 cc. of acetic acid, 1 cc. of acetic anhydride was refluxed for five hours. The solution was poured into water. The product crystallized from methanol as white needles, m. p. 202.5–203°, with decomposition; yield, 0.6 g.

Anal. Calcd. for $C_{22}H_{22}O_2Br_2$: C, 55.23; H, 4.65; Br, 33.43. Found: C, 55.66; H, 4.98; Br, 33.15.

(2) **Of Low-Melting Adduct.**—The bromination was carried out essentially as described for the high-melting adduct. The dibromide forms pearly-white leaflets from chloroform–ethanol, m. p. 152°, with decomposition.

Anal. Calcd. for $C_{22}H_{22}O_2Br_2$: Br, 33.43. Found: Br, 33.41.

3,6-Dimethyl-4,5-dibenzoylcyclohexene Oxide-1,2 (VIIIa and VIIIb).—Phthalmonoperacid was prepared according to the directions of Böhme.[4]

To a cold (0°) solution of 31.8 g. of adduct in 100 cc. of chloroform was added a liter of phthalmonoperacid (0.32–0.34 molar in available oxygen), and the solution stored at 0°.

After the oxidation was complete (about five days), as shown by no further drop in titer, a deposit of white prisms was present in the solution. The solution was decanted from this material which was collected, washed with ether, and dried. The oxide (VIIIa) weighed 7.0 g., and after recrystallization from acetone–methanol formed white needles, m. p. 187.5–188°.

Anal. Calcd. for $C_{22}H_{22}O_3$: C, 79.04; H, 6.59. Found: C, 79.28; H, 6.79.

The ether solution was washed with aqueous sodium bisulfite to remove excess oxidizing agent, then with aqueous sodium hydroxide to remove phthalic acid. The solution was dried over sodium sulfate and evaporated under diminished pressure.

The residual solid was recrystallized from methanol and by successive concentrations and removal of the fractions which were, in turn, recrystallized there was obtained the following: 6.6 g., m. p. 148–150°, and 9.7 g., m. p. 146–149°. The first crop after several crystallizations from methanol gave colorless prisms, m. p. 154–155°.

Anal. Calcd. for $C_{22}H_{22}O_3$: C, 79.04; H, 6.59. Found: C, 78.81; H, 6.58.

3,6-Dimethyl-4,5-dibenzoylcyclohexanediol-1,2 (IX and X) from High-melting Oxide.—A solution of 1 g. of the higher melting oxide (m. p. 187°) in 20 cc. of acetone and 5 cc. of 25% sulfuric acid was refluxed for thirty minutes. The solution was poured into water and extracted with chloroform. The oil obtained on evaporation of the chloroform solidified on triturating with ether and petroleum ether; yield 0.62 g.; m. p. about 160°. On crystallization from a mixture of ether–petroleum ether (b. p. 30–60°) first a small amount of product was obtained which separated in colorless prisms. These were recrystallized from dilute methanol, white needles, m. p. 212–213°.

Anal. Calcd. for $C_{22}H_{24}O_4$: C, 74.96; H, 6.87. Found: C, 74.91; H, 6.94.

The filtrates from the ether–petroleum ether crystallization deposited a second product in colorless rosets which, after purification from ethyl acetate–petroleum ether (b. p. 30–60°), melted at 173–175°.

Anal. Calcd. for $C_{22}H_{24}O_4$: C, 74.96; H, 6.87. Found: C, 75.20; H, 6.99.

From Low-Melting Oxide.—In place of pure low-melting oxide, either of the two low-melting fractions, m. p. 148–150° or 146–149°, described under the preparation of the oxides, was used. The procedure followed for hydrolysis was identical with that for the high-melting oxide. From 3.1 g. was obtained as a main product 1.7 g. of high-melting glycol which was purified to its proper melting point of 212–213° with dilute methanol. From the ether–petro-

(2) Reiff, *Ber.*, **39**, 1603 (1906); **41**, 2739 (1908).

(3) Kyriakides, THIS JOURNAL, **36**, 987 (1914).

(4) Böhme, *Ber.*, **70**, 379 (1937).

leum ether filtrates was obtained 0.35 g. of low-melting glycol which on crystallization from the same mixed solvent melted at 173–175°.

From one run of oxide purification was not carried to the extent previously described but merely three fractions were separated, one of high-melting oxide, a second primarily of low-melting, and a third fraction presumably chiefly low-melting oxide. When the last fraction and the mother liquors were hydrolyzed together with sulfuric acid in acetone, a new product (XII) was obtained. It was purified with methanol, white prisms, m. p. 187–188°. A mixed melting point showed it to be different from the high-melting or low-melting oxide.

Anal. Calcd. for $C_{25}H_{28}O_4$: C, 76.53; H, 7.14. Found: C, 76.12; H, 7.19.

The cause of the difference of results in the run just described and the others that were made may be due to the fact that the peracid ether solution was less dry in this experiment. The composition corresponds to a compound from one molecule of oxide and one of acetone.

1 - Hydroxy - 2 - acetoxy - 3,6 - dimethyl - 4,5 - dibenzoylcyclohexane.—In an attempt to cleave the glycol by means of periodic acid, four 1-g. runs of the low-melting oxide were allowed to stand for three hours with various concentrations of one molar periodic acid (1–10 equivalents) in 20 cc. of glacial acetic acid. After pouring into water, extracting with ether, washing, and evaporating the solvent, an oil resulted which crystallized on scratching. It was purified from ether–petroleum ether (b. p. 30–60°), then from dilute methanol; yield, 0.77 g. from the four runs, flat leaflike needles, m. p. 207°.

Anal. Calcd. for $C_{24}H_{26}O_5$: C, 73.06; H, 6.65. Found: C, 72.92; H, 6.58.

Apparently any oxidation products of the oxide or glycol produced from it could not be isolated and merely the monoacetate of the glycol resulted.

The same product could be obtained merely by heating 1 g. of the low-melting oxide, 15 g. of acetic acid and 5 cc. of 25% sulfuric acid on a steam cone for fifteen minutes. Dilution to cloudiness and cooling caused the product to separate. By boiling the compound with 15 cc. of methanol and 15–20 mg. of sodium for fifteen minutes, there was obtained from the reaction mixture 0.2 g. of solid which on purification from dilute methanol melted at 212–213° and proved to be identical with the higher-melting glycol.

Oxidation of Lower-Melting Oxide with Periodic Acid in Acetone Solution.—A solution of 1.0 g. of oxide (low-melting form) in a mixture of 20 cc. of acetone and 5 cc. of 1 *M* periodic acid was refluxed for thirty minutes. The solution was poured into water, extracted with chloroform and the solvent removed under reduced pressure. The residual sirup crystallized on scratching with ethyl acetate–ligroin, and yielded 0.82 g. of crystalline material. After several recrystallizations from benzene, in which the compound is difficultly soluble, the product melted at 177–178° with decomposition.

Anal. Calcd. for $C_{24}H_{26}O_5$: C, 73.06; H, 6.65. Found, C, 73.88, 73.27; H, 6.91, 6.97.

It may also be recrystallized from dilute acetone.

The same product is obtained by oxidizing the glycol with periodic acid in acetone.

Oxidation of the Glycol (M. p. 212°) with Lead Tetraacetate.—A suspension of 1.35 g. of lead tetraacetate in a solution of 1.05 g. of glycol in 10 cc. of acetic acid was shaken at room temperature for four hours and allowed to stand for two days. A crystalline precipitate formed, weight 0.63 g. Upon recrystallization from benzene it formed white needles, m. p. 170–170.5°, with decomposition.

Anal. Found: C, 69.93, 70.69, 69.96; H, 6.42, 6.41, 6.41.

α,α' - Diphenyl - β,β' - (3,6 - dihydro - 3,6 - dimethylbenzo)-furan (XIV).—A solution of 10 g. of the adduct (II) in a mixture of 80 cc. of glacial acetic acid, 40 cc. of acetic anhydride and 0.5 cc. of sirupy (85%) phosphoric acid was refluxed for twenty minutes. The solution was poured into water, extracted with chloroform and the solvent removed under reduced pressure. The residue crystallized on triturating with warm methanol. It weighed 9.0 g. and melted at 100–107°. Recrystallized from methanol it formed silky white needles or stout prisms melting at 114–115°. Occasionally the needle form separated first and changed into the prism form on standing in the solution.

Anal. Calcd. for $C_{22}H_{20}O$: C, 87.95; H, 6.70. Found: (prisms): C, 88.16; H, 6.94; (needles): C, 88.29; H, 6.92.

α,α' - Diphenyl - β,β' - (3,4,5,6 - tetrahydro - 4,5 - dibromo-3,6-dimethylbenzo)-furan (XV).—This compound can be obtained in either of two ways: (a) by bromination of the dihydrobenzofuran (XIV) or (b) by dehydration of the adduct dibromide (XIII).

(a) **Bromination of the Dihydrobenzofuran (XIV).**—To a cold solution of 2.0 g. of the dihydrobenzofuran in 15 cc. of glacial acetic acid was added, slowly and with cooling, a solution of 1.07 g. (1 mol) of bromine in 10 cc. of acetic acid. The bromine was decolorized instantly, and before all was added the addition compound began to separate. After precipitation was complete the product was collected, washed with acetic acid and water and dried. It weighed 2.10 g. and melted at about 165°, with decomposition. Recrystallized from *n*-butanol it formed pale yellow needles, m. p. 168–170°, with decomposition.

Anal. Calcd. for $C_{22}H_{20}OBr_2$: C, 57.39; H, 4.35. Found: C, 57.01; H, 4.50.

(b) **Dehydration of Adduct Dibromide.**—The dibromotetrahydrobenzofuran is most conveniently prepared by this procedure. After preliminary experiments on the pure adduct dibromide, it was found unnecessary to isolate and purify the adduct dibromide and that good results were obtained by dehydration of the crude product obtained by bromination of the adduct.

A solution of 5.0 g. of bromine in 50 cc. of acetic acid was added slowly to a well-cooled solution of 10 g. of the adduct (II) in 50 cc. of acetic acid. The faintly yellow solution was poured into water containing a little sodium bisulfite, extracted with chloroform and the solvent removed under reduced pressure. To the crystalline residue was added 50 cc. of acetyl chloride and five drops of concentrated sulfuric acid and the mixture heated under reflux. The dibromide went into solution rapidly and the solution assumed a brown-red color. After about

ten minutes of refluxing, yellow crystals began to separate and soon a heavy crystalline precipitate filled the liquid. The color of the solution slowly faded and at the end of thirty minutes had become a pale greenish-yellow. The mixture was cooled and filtered and the product washed with acetic acid and with water. There was obtained 11.4 g. of faintly yellow crystals, m. p. about 165°, with decomposition. Recrystallized from *n*-butanol it formed tiny, pale yellow needles, m. p. 168–170°, with decomposition, identical with the material obtained in (a).

α,α′-Diphenyl-β,β′-(3,6-dimethylbenzo)-furan (XVI).—A solution of 2.0 g. of the dibromotetrahydrobenzofuran in 10 cc. of dry pyridine was refluxed for thirty minutes. The solution, almost colorless at the start, became a bright yellow and after ten to fifteen minutes crystals of pyridine hydrobromide separated from solution. The solution was poured into water and the oil which separated soon crystallized. The crude product, which contained a trace of bromine, weighed 1.46 g. and melted at about 115–120°. The benzofuran was separated from unchanged dibromo compound by virtue of its ready solubility in cold ether, in which the dibromo compound is practically insoluble. Removal of the ether and recrystallization of the bright yellow crystalline residue from methanol gave bright yellow needles, m. p. 129–131°.

Anal. Calcd. for $C_{22}H_{18}O$: C, 88.53; H, 6.10. Found: C, 88.26; H, 6.27.

The benzofuran appeared to be somewhat unstable, considerable loss occurring on recrystallization. In the reaction with maleic anhydride described below the first ether extract of the crude product was used, giving a good yield of the addition product based on the original dibromotetrahydrobenzofuran.

1,4 - Endoxo - 1,4 - diphenyl - 5,8 - dimethyl - 1,2,3,4-tetrahydronaphthalene - 2,3 - dicarboxylic Anhydride (XVII).—Treatment of a solution of the benzofuran (XVI) in ether or benzene with a solution of maleic anhydride caused immediate precipitation of the addition product as fine white needles. The compound was best prepared by treating 2.0 g. of the dibromotetrahydrobenzofuran with pyridine as described above, and extracting the crude, dried product with ether. An ether solution containing an excess of the calculated amount of maleic anhydride was added and the addition product began to crystallize immediately. After cooling the solution in ice, the product was collected and washed thoroughly with fresh ether. It formed tiny white needles weighing 1.10 g. (70% over both steps). After recrystallization from glacial acetic acid from which it formed tiny white plates the compound melted at 310–312° with some decomposition.

Anal. Calcd. for $C_{26}H_{20}O_4$: C, 78.79; H, 5.05. Found: C, 78.85; H, 5.04.

The compound dissolves readily in methyl alcoholic potassium hydroxide but only with difficulty in aqueous alkali.

1,2-Dibenzoyl-3,6-dimethylbenzene (XIX).—This compound was obtained (a) by treatment of the adduct dibromide (XIII) with pyridine, (b) by treatment of the adduct (II) with bromine in pyridine solution, (c) by treatment of the dibromotetrahydrofuran (XV) with one mole of bromine in acetic acid containing sodium acetate, and (d) by treatment of the dihydrobenzofuran (XIV) with two moles of bromine in acetic acid containing sodium acetate. Only method (d) gave satisfactory results but method (a) is also described since it involved the unusual reaction mentioned previously which led to the formation of some of the original adduct (II).

(a) A solution of 2.0 g. of the high-melting adduct dibromide (XIII) in 10 cc. of dry pyridine was heated for twenty hours on the steam-bath. Crystalline pyridine hydrobromide separated during the heating. The solution was poured into water and extracted with ether. After washing the ether solution with dilute hydrochloric acid and water and drying, it was evaporated under reduced pressure. The oily residue crystallized on triturating with an ether–petroleum ether mixture and the solid was collected; yield 0.30 g. Upon recrystallization from methanol it formed white, flat prisms, m. p. 144–145°.

Anal. Calcd. for $C_{20}H_{18}O_2$: C, 84.08; H, 5.74. Found: C, 83.82; H, 5.82.

The ether–petroleum ether filtrate yielded on evaporation 0.40 g. of the original adduct (II), bromine-free.

(d) To a solution of 1.0 g. of the dihydrobenzofuran (XIV) and 1.5 g. of anhydrous sodium acetate in 5 cc. of hot acetic acid was added a solution of 1.0 g. of bromine in 10 cc. of acetic acid. The bromine was absorbed instantly and sodium bromide separated. The solution was refluxed for thirty minutes and diluted to cloudiness with water. The product separated on cooling. It weighed 0.83 g., melted at 140–143°, and contained no bromine (Beilstein test). Recrystallized from methanol it formed white prisms, m. p. 143–145°, shown by mixed melting point to be identical with the compound obtained by method (a).

Methods (b) and (c) gave inferior yields of the same compound.

1,2-*bis*-(α-Oxybenzyl)-3,6-dimethylbenzene (XX).—A solution of 1 g. of the benzene derivative (XIX) in a solution of 2 g. of sodium hydroxide in 20 cc. of alcohol was boiled until a deep yellow-brown color appeared. About 0.5 g. of zinc dust was added in portions to the boiling solution and heating was continued for fifteen minutes on the steam-bath.

The nearly colorless solution was poured into water and the gummy precipitate crystallized from dilute methanol. After several recrystallizations from 50% methanol the compound was obtained as tiny white prisms melting at 149–151°. The substance was somewhat unstable and showed a tendency to decompose when dried at 100°.

Anal. Calcd. for $C_{22}H_{22}O_2$: C, 82.97; H, 6.97. Found: C, 83.74; H, 6.68.

Summary

1. The addition of hexadiene-2,4 to *trans*-dibenzoylethylene has been described.

2. An unsuccessful attempt has been made to convert the cyclohexene derivative so obtained into an analog of one of the degradation products of gossypol, namely, desapogossypolone tetramethyl ether.

3. The oxidation of the cyclohexene derivative with perphthalic acid to the corresponding cyclo-

hexene oxides, and the stereochemistry of these oxides and certain of their derivatives, are described.

4. Various transformation products of the cyclohexene derivative have been described, among them the corresponding dibenzoylxylene and α,α'-diphenyl-β,β'-(3,6-dimethylbenzo)-furan. It is believed that the methods described are general for the preparation of compounds of these types.

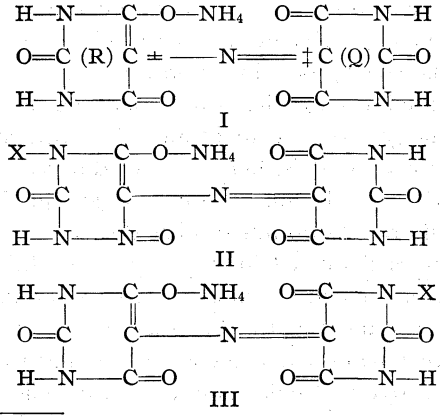
URBANA, ILLINOIS RECEIVED MAY 31, 1939

[CONTRIBUTION FROM JONES CHEMICAL LABORATORY, UNIVERSITY OF CHICAGO]

Structure of the Murexides and the Alloxantines[1]

BY N. M. WINSLOW[2]

The structure of the dye murexide (I) was established independently by Stieglitz,[3] Moehlau,[4] and Piloty.[5] Acid hydrolysis of the dye gives uramil and alloxan in semiquantitative yields. Hydrolysis should, therefore, provide a means of distinguishing isomeric N-substituted murexides of general structures II and III.[6] Hydrolysis of II should give N-substituted uramil and alloxan, while similar treatment of III should give uramil and N-substituted alloxan. However, if II and III exist in tautomeric equilibrium, or if resonance occurs between the two forms, then any preparative procedure calculated to yield either II or III would give the same mixture of the two, and hydrolysis of the product would yield four products: N-substituted uramil, N-substituted alloxan, uramil, and alloxan. The present investigation is concerned with the two isomeric N-phenylmurexides, 1-phenylmurexide (II, X = C_6H_5) and 1′-phenylmurexide (III, X = C_6H_5).



I

II

III

(1) A part of a dissertation submitted by the author in partial fulfilment of the requirements for the degree of Doctor of Philosophy at the University of Chicago in 1936. The investigation was carried out under the direction of the late Professor Julius Stieglitz.

(2) Present address: Lakewood, Ohio.

(3) Stieglitz, *Am. Chem. J.*, **31**, 661 (1904).

(4) Moehlau, *Ber.*, **37**, 2686 (1904).

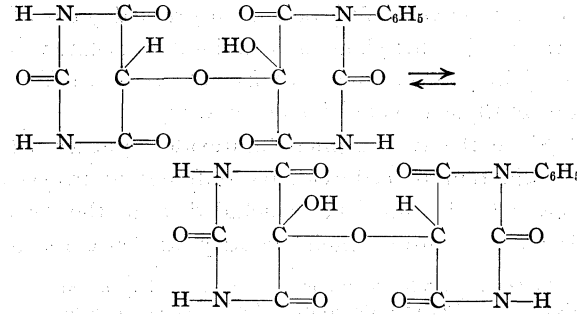
(5) Piloty, *Ann.*, **333**, 22 (1904).

(6) The murexides decompose without melting. A study of absorption spectra should furnish confirmatory evidence.

1-Phenylmurexide was prepared readily from 1-phenyluramil and alloxan in ammonium carbonate solution. When the dye was hydrolyzed within forty-eight hours of its preparation, 1-phenyluramil and alloxan, the latter determined as alloxantine, were recovered in yields representing 70 and 56%, respectively, of the theoretical.

The synthesis of 1′-phenylmurexide in a manner analogous to the method used for the preparation of 1-phenylmurexide was attempted without success, due to the relative insolubility of uramil in ammonium carbonate solution and the instability of the murexide in alkali sufficiently strong to dissolve uramil. There remained the alternative method of preparing the corresponding 1′-phenylalloxantine and treating this compound with ammonia.

Pure 1′-phenylalloxantine was prepared by the condensation of N-phenylalloxan with dialuric acid in hot aqueous solution. But chemical purity, as established by elementary analysis, was not the only requirement of 1′-phenylalloxantine intended for use in the preparation of 1′-phenylmurexide; it must also maintain its tautomeric identity. Quite obviously if a tautomeric equilibrium existed, treatment of the alloxantine with ammonia would give only a mixture of 1-phenylmurexide and 1′-phenylmurexide.



When 1′-phenylalloxantine was hydrolyzed with aqueous potassium acetate, dialuric acid, pre-

cipitated immediately as the potassium salt, was obtained in 98% yields. This quantitative yield of potassium dialurate showed that 1′-phenylalloxantine maintained its identity under the conditions of preparation, a conclusion in entire agreement with the results of Stieglitz and Nightingale,[7] obtained with 1-methylalloxantine and 1′-methylalloxantine.

In this connection it was of interest to study the isomeric 1-phenylalloxantine, prepared by heating 1-phenyluramil with alloxan solution containing hydrochloric acid. Hydrolysis of the pure material with sodium acetate produced 74.5% of the theoretical yield of N-phenyldialuric acid, giving additional confirmation of the views of Stieglitz and Nightingale regarding the asymmetrical structure of alloxantines and the maintenance of identity by isomeric N-substituted alloxantines. One further observation lends strong support to the conclusion of these authors. When 1-phenylalloxantine, which presumably is hydrolyzed to N-phenyldialuric acid and alloxan, was treated with potassium acetate, potassium dialurate was obtained.[8] However, it was precipitated slowly, as contrasted with immediate precipitation when 1′-phenylalloxantine was treated with potassium acetate, and the total amount obtained was approximately 67% of the theoretical. Their explanation of the formation of potassium dialurate from the hydrolysis of the methylalloxantine prepared from alloxan and methyluramil, as the result of a slow inter-(or intra-?)-molecular oxidation and reduction, thus was fully confirmed by our own work with the alloxantine prepared from the alloxan and phenyluramil.

By treatment of 1′-phenylalloxantine, which had been shown to maintain its identity under the conditions of preparation, with ammonia, 1′-phenylmurexide was obtained. Hydrolysis of this dye gave 96.5% of the theoretical yield of uramil. N-Phenylalloxan could not be isolated as a hydrolysis product because of its instability under the acid conditions of hydrolysis.

Since the two N-phenylmurexides synthesized by different procedures gave different hydrolysis products, it must be concluded that the two isomers maintain their identity at least for a limited length of time. Both resonance and rapid tautomerism between the two are ruled out, but this conclusion in no way precludes the probability that each of the dyes will in the course of time be transformed into identical equilibrium mixtures which would give identical hydrolysis products.

Similar results have been obtained with two other pairs of isomeric N-substituted murexides: Stieglitz and Slimmer,[3] later Stieglitz and Eckstein,[9] and finally Stieglitz and Tartar,[10] prepared the two isomers 1,3-dimethylmurexide and 1′,3′-dimethylmurexide; hydrolysis of the former yielded dimethyl uramil and alloxan, while uramil and dimethylalloxan were obtained from the latter as hydrolysis products. More recently,[11] the isomers 1,3-diphenylmurexide and 1′,3′-diphenylmurexide were prepared and similarly shown to yield different hydrolysis products.

These investigations were undertaken in connection with the Stieglitz theory of color production in organic molecules.[12] It is the fundamental concept of this theory that color of organic molecules is due to partial absorption of white light by vibration of electrons held in proper restraint between their own atomic nucleus in a reducing group (the auxochrome) and a nearby strongly positive group (the chromophore). For example, in the structure (I) of the dye murexide, it is, in particular, the pair of electrons indicated by—in $C^{\pm}$, held in loose restraint in the reducing uramil group R, which are attracted both by the positive nucleus of $C^{\pm}$ itself and by the alloxan group Q whose oxidizing power may be considered centered in $C^{\ddagger}$. According to the views of Stieglitz, the color-producing vibrations of these electrons are intra-atomic, that is, between the different energy levels of an atom ($C^{\pm}$), rather than interatomic, that is, between two different atoms ($C^{\ddagger}$ and $C^{\pm}$), leading to tautomeric equilibrium.

While results obtained with the N-substituted murexides discussed above do not establish the source of color in the molecules, they are in complete agreement with the Stieglitz theory. On the other hand, early theories[13] holding that the color of dye molecules is due to electronic movements involved in tautomeric equilibrium are

(7) D. N. Nightingale, "Studies in the Murexide and Alloxantine Series," Doctoral Dissertation, University of Chicago, 1928; *cf.* Nightingale, THIS JOURNAL, **59**, 806 (1937).

(8) The potassium salt of N-phenyldialuric acid is soluble in water.

(9) Unpublished results, University of Chicago, 1905.

(10) H. V. Tartar, "The Constitution of Murexide and the Theory of Dyes," Doctoral Dissertation, University of Chicago, 1920.

(11) R. M. Cole, Doctoral Dissertation, University of Chicago, 1936.

(12) Stieglitz, *Proc. Natl. Acad. Sci.*, **9**, 303 (1923); *J. Franklin Inst.*, **198**, 35 (1924).

(13) Armstrong, *Proc. Chem. Soc.*, **2**, 27 (1888); Baeyer, *Ann.*, **354**, 153 (1907); Willstaetter, *Ber.*, **41**, 1458, 3245 (1908).

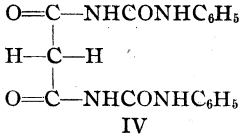
definitely disproved. Resonance involving the valence bonds of the central nitrogen atom in the murexide molecule is also eliminated as the source of color. Nothing is indicated concerning the bonds of other atoms in the molecules.

The results are of more recent interest in connection with the theory of resonance. If the structure (I) of the parent substance is correct, an N-substituted murexide would be expected to exist as a resonance hybrid of II and III. The fact that three different isomeric pairs of N-substituted murexides have been shown to maintain their identity presents an interesting problem.

Experimental

Preparation of Intermediate Compounds.—N-Phenylbarbituric acid was prepared by refluxing a mixture of malonic acid (50 g.), phenylurea[14] (64 g.), acetic anhydride (100 cc.) and dry chloroform (700 cc.) for twenty-four hours. The chloroform was removed by distillation, and from the dry residue a 40% yield of N-phenylbarbituric acid was obtained by extraction with cold aqueous sodium carbonate.

The material undissolved by cold aqueous sodium carbonate contained a small amount of symmetrical acetylphenylurea, but consisted chiefly of malonyl dimonophenylurea (IV):



IV

This compound was obtained in the pure condition by recrystallization from acetone.

Anal. Calcd. for $C_{17}H_{16}O_4N_4$: C, 60.00; H, 4.71; N, 16.20. Found: C, 60.02; H, 5.11; N, 16.21.

The malonyl dimonophenylurea was dissolved in 500 cc. of 0.6 *M* sodium carbonate by digestion for one hour on a steam-bath. Chilling of the solution precipitated about 25% of the phenylurea originally used in the preparation, and the addition of hydrochloric acid gave an additional 20% yield of N-phenylbarbituric acid.

For the purposes of this investigation, N-phenylbarbituric acid prepared as described proved to be sufficiently pure, melting from 254.5 to 258.5°. A pure sample, obtained by recrystallization from dioxane, melted at 262°. The recorded[15] melting point is 262°.

1-Phenyluramil was prepared from a solution of sodium phenylviolurate obtained by digestion at 50° of N-phenylbarbituric acid (5 g.) with 100 cc. of water containing sodium nitrite (1.5 g.). The solution was reduced with hydrogen sulfide, acidified with 50 cc. of concentrated hydrochloric acid, warmed to 45°, and filtered from precipitated sulfur. 1-Phenyluramil crystallized slowly after the addition of four volumes of alcohol; yield 1.7 g.

Anal. Calcd. for $C_{10}H_9O_3N_3$: N, 19.18. Found: N, 19.25.

(14) Davis and Blanchard, THIS JOURNAL, **51**, 1791 (1929).

(15) Macbeth, Nunan and Traill, *J. Chem. Soc.*, **129**, I, 1252 (1926).

N-Phenylalloxan was prepared by oxidation at 0° of 1-phenyluramil (0.50 g.) with 2 cc. of nitric acid (sp. gr. 1.42). The reaction mixture was dried *in vacuo*, and N-phenylalloxan was recovered by extraction with ether and precipitation from the ether solution with four volumes of ligroin. Yields varied from 60 to 90% of the theoretical.

Anal. Calcd. for $C_{10}H_8O_5N_2$: C, 50.95; H, 3.36; N, 11.66. Found: C, 50.65; H, 3.31; N, 11.94.

Preparation of Alloxantines.—1-Phenylalloxantine was prepared by heating at 50° for six hours a suspension of 1-phenyluramil (1 g.) in a solution of alloxan monohydrate (0.9 g.)[16] in 12 cc. of water containing 1 cc. of concentrated hydrochloric acid. The product was collected on a filter, washed with cold water and dried *in vacuo;* yield 1.4 g.

Anal. Calcd. for $C_{14}H_{10}O_8N_4$: N, 15.47. Found: N, 15.50.

A solution of dialuric acid was obtained by reduction of alloxan monohydrate (1.00 g.) dissolved in 12.5 cc. of water with hydrogen sulfide at 98°. When the hot solution, filtered from the precipitated sulfur, was mixed with a hot solution of N-phenylalloxan (0.50 g.) in 6 cc. of water, 1′-phenylalloxantine crystallized over a period of about ten minutes. The product was washed with cold water, alcohol, and ether; yield 0.8 g.

Anal. Calcd. for $C_{14}H_{10}O_8N_4$: N, 15.47. Found: N, 15.42.

Preparation of Murexides.—1-Phenylmurexide was prepared by mixing a solution of alloxan monohydrate (2 g.) in 10 cc. of water with a solution of 1-phenyluramil (2 g.) in 10 cc. of 20% ammonium carbonate solution. The mixture was heated for thirty minutes at 50° in an atmosphere of hydrogen. The product was purified by repeated extraction with 15-cc. portions of 95% alcohol; yield 1.1 g.

Anal. Calcd. for $C_{14}H_{12}O_6N_6$: N, 23.33. Found: N, 23.57.

1′-Phenylalloxantine (1.5 g.) suspended in absolute benzene at 50°, was converted to 1′-phenylmurexide by passing a stream of dry ammonia gas through the suspension for three hours. The murexide was purified by washing with benzene and heating in air for ten hours at 50°; yield 1.5 g.

Anal. Calcd. for $C_{14}H_{12}O_6N_6$: N, 23.33. Found: N, 23.71.

Hydrolysis of Alloxantines and Murexides.—A suspension of 1-phenylalloxantine (0.500 g.) in 19 cc. of water containing sodium acetate (0.35 g.) was heated on a steam-bath until the alloxantine dissolved. From the clear hydrolysate, acidified with 1 cc. of 50% acetic acid, basic lead N-phenyldialurate[17] was precipitated by the addition of 0.600 g. of lead acetate [$Pb(C_2H_3O_2)_2 \cdot 3H_2O$]; yield 0.455 g., theoretical 0.611 g.

Anal. Calcd. for $C_{10}H_8O_6N_2Pb$: N, 6.32; Pb, 46.73. Found: N, 6.67; Pb, 46.50.

1′-Phenylalloxantine was hydrolyzed in the same manner as 1-phenylalloxantine except that potassium acetate was

(16) Biltz and Heyn, *Ann.*, **413**, 60 (1917); *J. Chem. Soc.*, **112**, I, 289 (1917).

(17) This compound was also prepared from N-phenyldialuric acid obtained by reduction of N-phenylalloxan with hydrogen sulfide at 98°.

Anal. Calcd. for $C_{10}H_8O_6N_2Pb$: N, 6.32; Pb, 46.73. Found: N, 6.91; Pb, 46.74.

used instead of sodium acetate. When the hydrolysate was chilled in ice, potassium dialurate was obtained; yield 0.247 g. from 0.500 g. of 1′-phenylalloxantine, theoretical 0.252 g.

Anal. Calcd. for $C_4H_3O_4N_2K$: N, 15.38. Found: N, 15.48.

1-Phenylmurexide (1.000 g.), suspended in 100 cc. of oxygen-free water by the passage of a slow stream of hydrogen, was hydrolyzed with 16 cc. of approximately molar hydrochloric acid added a few drops at a time over a period of forty-five minutes. The solid material remaining when the color of the solution had been completely discharged was brought upon a filter and identified as 1-phenyluramil by its qualitative reactions and nitrogen content; yield 0.427 g., theoretical 0.605 g. From the filtrate from the 1-phenyluramil, concentrated at room temperature to 5 cc., alloxantine was obtained by reduction with stannous chloride; yield 0.205 g., theoretical 0.364 g.

Hydrolysis of 1′-phenylmurexide (1.000 g.) by the procedure used for the hydrolysis of 1-phenylmurexide yielded 0.383 g. of uramil; theoretical 0.397 g. Due to the instability of N-phenylalloxan[18] in acid solution, only traces of 1,1′-diphenylalloxantine could be obtained from the filtrate from the uramil by reduction with stannous chloride.

(18) 1,1′-Diphenylalloxantine was obtained in 73% yields by reduction of a freshly prepared acid solution of N-phenylalloxan with stannous chloride. When the acid solution was allowed to stand for forty-five minutes before reduction, the yield was only 1.5%.

Anal. Calcd. for $C_{20}H_{14}O_8N_4$: N, 12.79. Found: N, 12.87.

Summary

1. The isomers 1-phenylmurexide and 1′-phenylmurexide maintain their identity at least for a limited length of time under certain experimental conditions. 1-Phenylalloxantine and 1′-phenylalloxantine also maintain their isomeric identities.

2. These phenylmurexides constitute the third pair of isomeric N-substituted murexides for which maintenance of identity has been established. The importance of this fact in connection with the theories of color production and resonance in organic molecules has been discussed.

3. The following compounds not described in the literature have been prepared: 1-phenylmurexide, 1′-phenylmurexide, 1-phenylalloxantine, 1′-phenylalloxantine, 1,1′-diphenylalloxantine, 1-phenyluramil, N-phenylalloxan, and malonyl dimonophenylurea.

RECEIVED FEBRUARY 23, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF PHYSICAL CHEMISTRY, HARVARD MEDICAL SCHOOL]

The Influence of Ionic Strength and *p*H on Electrophoretic Mobility

BY BERNARD D. DAVIS AND EDWIN J. COHN

Electrophoretic mobilities are generally determined in the presence of buffer solutions. It seemed of importance to investigate further the influence of the valence of the buffer and of the ionic strength of the solution. Tiselius has noted[1,2] the effect of ionic strength and of the valence of inorganic cations, and work in this Laboratory had indicated that the ionic strength of the buffer has a very profound influence on electrophoretic mobility. The influence of these variables also has been studied by Abramson[3] and by Smith,[4] who observed the movements of particles of quartz or collodion coated with egg albumin in an electric field. The latter studied especially the dependence of the isoelectric point upon the nature and concentration of neutral salts.

In the present investigation we have used the moving boundary method and have chosen horse carboxyhemoglobin as the protein to be investigated since it is a well characterized protein whose other properties have been investigated extensively.[5–9] Mobility has been determined from *p*H 5.65 to 7.2. Hemoglobin was therefore present as cation in most of these systems, whereas most of the other blood proteins would be present as anions. The ionic strengths vary from 0.02, the concentration often used by Tiselius, to ionic strengths characteristic of physiological systems. Two sets of buffers were employed, namely, phosphates in which monovalent and bivalent anions, and citrates in which bivalent and trivalent anions, are present. The measurements reported demonstrate the great influence

(1) A. Tiselius, Dissertation, Upsala, 1930.

(2) A. Tiselius, *Trans. Faraday Soc.*, **33**, 524 (1937).

(3) H. A. Abramson, "Electrokinetic Phenomena and their Application to Biology and Medicine," Chemical Catalog Co., Inc., New York, 1934.

(4) E. R. B. Smith, *J. Biol. Chem.*, **108**, 187 (1935); *ibid.*, **113**, 473 (1936).

(5) R. M. Ferry and A. A. Green, *ibid.*, **81**, 175 (1929).

(6) E. J. Cohn and A. M. Prentiss, Loeb Memorial Vol., *J. Gen. Physiol.*, **8**, 619 (1927).

(7) J. L. Oncley, THIS JOURNAL, **60**, 1115 (1938).

(8) R. M. Ferry, E. J. Cohn and E. S. Newman, *ibid.*, **60**, 1480 (1938).

(9) M. Richards, *J. Biol. Chem.*, **122**, 727 (1938).

of the type of buffer and of the ionic strength of the solution both upon the observed electrophoretic mobility and upon the apparent isoelectric point of the protein.

Materials and Methods.—The carboxyhemoglobin of the horse employed in these experiments was twice recrystallized from aqueous solution by the method of Ferry and Green.[5,10] The crystals were then repeatedly triturated with distilled water, and centrifuged from the resulting saturated hemoglobin solutions to free them from salt. Solutions saturated with the hemoglobin after the crystals had been washed from three to five times in this manner, were employed in these studies.[11] The desired solutions of hemoglobin in buffer were dialyzed in cellophane bags against identical buffer solutions for from twelve to twenty-four hours at about 3°. This practice, employed by Tiselius,[1] minimizes the disturbances at the protein–buffer interface. The pH and the conductivity of the two solutions were found to be identical within the limits of experimental error.

The phosphate buffer solutions of known ionic strength and pH were those generally employed in this Laboratory.[12,13] Using the data of Hastings and Van Slyke,[14] which give the concentrations of primary, secondary and tertiary citrate at the successive stages in the titration of 0.1 M citric acid with sodium hydroxide, graphs were prepared from which could be read the concentration of citrate necessary to produce a solution of given pH and ionic strength. The pH values of all solutions were checked electrometrically after dialysis, and it is these values that are recorded in the tables.

The apparatus used consists of a U-tube connected through side-arms to large buffer chambers, at the bottom of which Ag–AgCl electrodes, coils of no. 18 wire 1.5 cm. in diameter and 4.5 cm. long, were immersed in reservoirs of 20% potassium chloride. The content of the U-tube below the tops of the stopcocks was about 15 cc.; the potassium chloride reservoir up to a level several mm. above the electrode, 30 cc. on each side; the rest of the buffer chamber and vertical column of the U-tube had a volume of 125 cc. on each side, ample to ensure a run of many hours without contamination by the transport of potassium chloride or electrode products. The diameter of the U-tube was 0.95 cm. The design of the electrode was largely adopted from Tiselius,[1,15] the U-tube was that previously used in investigations in this Laboratory.[16,17] The sharp boundary of the hemoglobin was read directly.

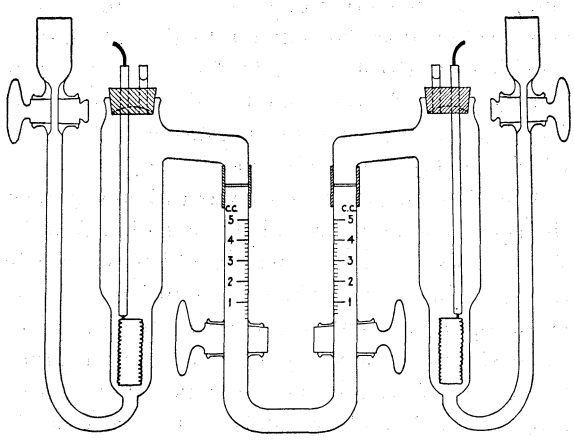


Fig. 1.

The top of each buffer chamber was closed with a two-holed rubber stopper, slightly hollowed on the under side to prevent the trapping of air bubbles. Through one hole of the stopper was passed the glass sealed electrode lead, and through the other a tube for the introduction and leveling of the buffer. The various solutions were evacuated and brought to the temperature of the bath before introduction, in order to remove dissolved air which would later form bubbles injurious to the boundary. When the protein, buffer and hydrochloric acid solutions had been introduced in the proper positions the assembled apparatus was immersed up to the side arms in a glass-walled thermostat at 25 ± 0.1°. The buffer solutions were carefully leveled in the tubes above the buffer chambers by addition of appropriate amounts of solution; the stopcocks were then opened and buffer solution slowly added to one chamber and removed from the other until one hemoglobin column was raised above the optical irregularities of the U-tube near the stopcock. A potential of 110 v. was applied to the electrodes and the movement of the protein in the field directly observed from time to time. The electrodes in successive experiments were alternated in polarity in order to keep them coated with silver chloride.

The determination of the mobility in units of cm.²/volt-sec. involved measurements of the rate of migration in cc./hour, of the conductivity of the buffer, and of the current flow. These quantities are related in the following formulas

$$IR = eq \quad (1)$$

$$M = ueq \times 3600 \quad (2)$$

$$u = M/3600\,IR \quad (3)$$

where M = rate of migration (cc./hour); u =

(10) A. A. Green, *J. Biol. Chem.*, **93**, 495 (1931).

(11) Many of these preparations were the same ones used by Ferry, Cohn and Newman[8] for their study.

(12) E. J. Cohn, THIS JOURNAL, **49**, 173 (1927).

(13) A. A. Green, *ibid.*, **55**, 2331 (1933).

(14) A. B. Hastings and D. D. Van Slyke, *J. Biol. Chem.*, **53**, 269 (1922).

(15) Since completion of most of these measurements Tiselius has perfected a new electrophoretic cell, and these measurements have been confirmed with this apparatus at 25°. The symbol ◐ in Fig. 2 represents measurements with the new Tiselius apparatus.[2]

(16) E. J. Cohn, J. Gross and O. C. Johnson, *J. Gen. Physiol.*, **2**, 145 (1919).

(17) L. Reiher, *Kolloid Z.*, **40**, 327 (1926).

mobility (cm.²/volt-sec.); I = current (amperes); R = specific resistance of buffer (ohms cm.); e = potential drop in U-tube (volts/cm.); and q = cross section of U-tube (sq. cm.). The cross section does not enter into the calculation, provided the U-tube is calibrated in cc. Current leakage through the joints and stopcocks was found to be negligible by measuring the current while the stopcocks were closed.

The advancing boundary, except when very near the isoelectric point, remained sharp indefinitely, showing less spreading than would be caused in the same interval of time by diffusion. On reversal of the current, the receding boundary became diffuse. Since the difference in conductivity and therefore the difference in potential drop at the boundary interface was very small, the influence of the hemoglobin concentration on its own mobility, whereby velocity increases with concentration, would appear the most probable explanation of the difference in velocity and diffuseness of the advancing and receding boundaries. The measurements reported are for the advancing boundary.

Influence of Hemoglobin Concentration.—The reproducibility of these electrophoretic measurements upon carboxyhemoglobin solutions may be illustrated by a series of experiments in which the hemoglobin concentration was varied systematically, the ionic strength of the buffer and the pH being maintained constant. The hour by hour readings in the seven experiments carried out at pH 5.93 at ionic strength 0.05 and hemoglobin concentrations from 1.67 to 13.3 g. per liter are recorded in Table I. They demonstrate the agreement between duplicate experiments, and the constancy of the rate of electrophoretic migration throughout the experiments. The current, which was always measured with a standardized Weston ammeter, generally increased slightly during the first period. The value when the current flow had become sensibly constant was employed in estimating the mobilities in absolute units recorded in Table I. The current flow, I, varied to be sure with the ionic strength, but the product of the current and the resistance, R—which measures the potential drop—did not vary systematically with pH or ionic strength.

The average mobility at each hemoglobin concentration is given at the bottom of Table I. There would appear to be a definite effect of the hemoglobin concentration upon mobility. This

TABLE I

INFLUENCE OF CARBOXYHEMOGLOBIN CONCENTRATION UPON ELECTROPHORETIC MOBILITY AT 25° IN PHOSPHATE BUFFERS OF IONIC STRENGTH 0.05 AND pH 5.93

Expt....	92	96	86	98	88	91	99
Time in hours	Carboxyhemoglobin concentration 1.67 g./liter		3.3 g./liter		6.7 g./liter	13.3 g./liter	
	Migration in cc.						
1.0	0.42	0.46	0.42	0.46	0.44	0.48	0.52
2.0	.84	.90	.84	.92	.90	1.02	1.06
3.0	1.24	1.32	1.28	..	..	1.52	..
4.0	..	1.74	..	1.78	1.84	..	2.10
5.0	2.06	2.16	2.20	2.24	2.30	2.58	2.64
6.0	2.46	2.60	2.64	2.68	2.74	3.08	3.14
IR	2.43	2.48	2.38	2.41	2.43	2.39	2.37
	Mobility (Migration per hour × IR × 3600) × 10^5						
1.0	4.8	5.1	4.9	5.3	5.0	5.6	6.1
2.0	4.8	5.0	4.9	5.3	5.1	5.9	6.2
3.0	4.7	4.9	5.0	...	...	5.9	...
4.0	...	4.9	...	5.1	5.3	...	6.1
5.0	4.7	4.8	5.1	5.2	5.3	6.0	6.2
6.0	4.7	4.8	5.1	5.2	5.3	6.0	6.1
Av.	4.7	4.9	5.0	5.2	5.2	5.9	6.2
	4.8		5.1		5.2	6.1	

was not only true at pH 5.93, but in other experiments. Thus at an ionic strength of 0.02 and a pH of 7.11, alkaline to the isoelectric point, when the hemoglobin was moving as an anion, its mobility was -1.6×10^{-5} cm.²/volt-sec. in a solution of 0.3% with respect to hemoglobin (Expt. 81) but -2.3×10^{-5} cm.²/volt-sec. in a 1% hemoglobin solution (Expt. 80).

The observed increase in mobility with increase in hemoglobin concentration may well be associated with interaction of the protein dipolar ions with each other[18] or with buffer ions.[19] Tiselius,[20] working with serum proteins, has explained boundary irregularities at high protein concentration as due to the effect of the protein on the transport of the buffer ions, causing a shift of pH at the boundaries. In the range of hemoglobin concentration here described, all boundaries were sharp and all mobilities reasonably constant. In several experiments with hemoglobin concentrations below 0.1% at ionic strength 0.05, the boundary became convex and then diffuse. The hemoglobin concentration was maintained at 1% in studying the influence of ionic strength.

(18) E. J. Cohn, T. L. McMeekin, J. D. Ferry and M. H. Blanchard, *J. Phys. Chem.*, **43**, 1 (1939).

(19) Smith[4] has found that the mobility of egg albumin decreases with increasing protein concentration. She measured mobility of the protein adsorbed on quartz particles, and her observations may be related to this difference in technique, or to the far smaller effects of egg albumin on the dielectric constant of solvents.[21]

(20) A. Tiselius, *Biochem. J.*, **31**, 313, 1464 (1937).

(21) J. L. Oncley, unpublished work.

Influence of *p*H and Ionic Strength.—Observations on the influence of *p*H on the mobility of hemoglobin were early reported by Michaelis and Airila.[22] The influence of ionic strength on the mobility of carboxyhemoglobin is shown in Table II. The mobilities in phosphate buffers are graphically represented in Fig. 2, those in citrate buffers in Fig. 3. It will be noted that protein mobility is extremely sensitive not only to *p*H and ionic strength, but also to the valence and nature of the ions present; an effect noted also by others.[1,3,4,23] This sensitivity to the nature and strength of the ionic atmosphere (Fig. 2) would appear to be nearly as important as *p*H in

TABLE II

ELECTROPHORETIC MOBILITY OF 1% CARBOXYHEMOGLOBIN IN PHOSPHATE AND CITRATE BUFFERS AT 25°

Expt.	Concn. of salt mole/liter	Mole fraction K_2HPO_4	*p*H	Electrophoretic mobility $u \times 10^5$
		Phosphate, $\Gamma/2 = 0.02$		
52-III	0.0182	0.0424	5.65	10.3
55-III	.0180	.0550	5.81	9.3
60-IV	.0156	.140	6.22	6.5
53-IV	.0140	.230	6.49	4.4
54-IV	.0110	.395	6.82	1.8
80-V	.0093	.566	7.11	− 2.3
68-V	.0088	.616	7.18	− 3.0
57-IV	.0088	.616	7.21	− 3.1
		Phosphate, $\Gamma/2 = 0.05$		
61-IV	0.045	0.0535	5.68	6.7
63-IV	.0375	.165	6.21	4.0
62-IV	.032	.283	6.52	2.1
67-V	.0263	.444	6.82	− 0.2
69-V	.0235	.550	7.00	− 2.2
		Phosphate, $\Gamma/2 = 0.10$		
50-III	0.088	0.068	5.69	3.8
48-IV	.084	.088	5.79	3.5
49-III	.084	.088	5.79	3.4
89-VI	...	...	6.42	0.7
59-IV	.051	.477	6.83	− 1.1
		Phosphate, $\Gamma/2 = 0.15$		
75-V	0.129	0.080	5.72	2.5
77-V	.110	.176	6.12	1.1
73-V	.100	.249	6.30	0.3
74-V	.089	.341	(6.60)	− 1.0
76-V	.074	.500	6.82	− 2.2
		Citrate, $\Gamma/2 = 0.02$		
45-III	0.00481		5.92	4.9
47-IV	.00481		5.91	4.9
42-III	.00380		6.50	2.4
46-IV	.00380		6.55	2.3
71-V	.00358		7.09	− 1.3
		Citrate, $\Gamma/2 = 0.10$		
44-III	0.02403		5.68	2.0
64-V	.02035		6.10	0.7
41-III	.01821		6.56	− 0.5
65-V	.01821		6.54	− 0.6
		Citrate, $\Gamma/2 = 0.20$		
78-V	0.04384		5.77	0.2
79-V	.03718		6.31	− 1.3

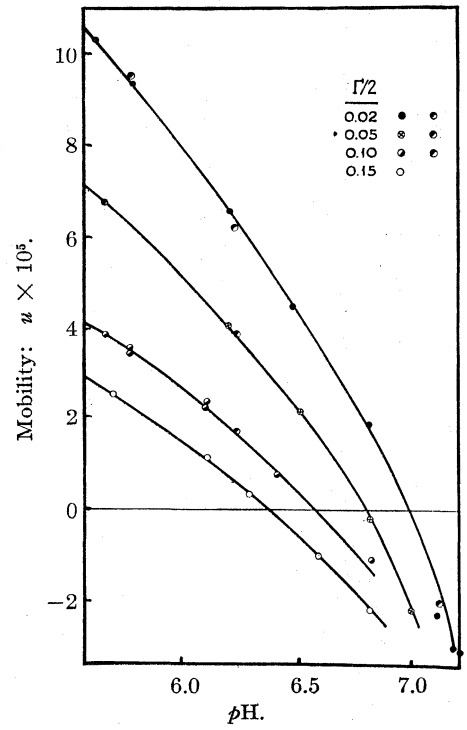


Fig. 2.—Phosphate buffers.

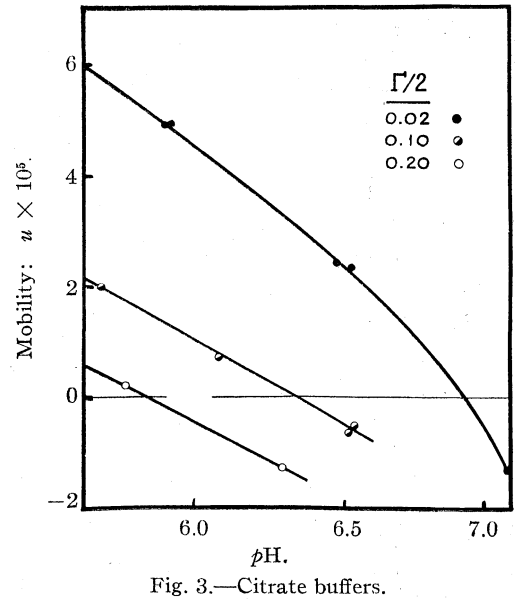


Fig. 3.—Citrate buffers.

(22) L. Michaelis and Y. Airila, *Biochem. Z.*, **118**, 144 (1921).

(23) L. S. Moyer and H. A. Abramson, *J. Biol. Chem.*, **123**, 391 (1938).

determining the optimal conditions for the electrophoretic separation of proteins.

The effect of ionic strength[24] and ionic species on the apparent isoelectric point is shown in Fig. 4, the conditions at which there is no mobility being graphically estimated from Figs. 2 and 3. As might be expected on theoretical grounds, mobility in citrate and phosphate buffers appears to approach the same value at low ionic strengths.

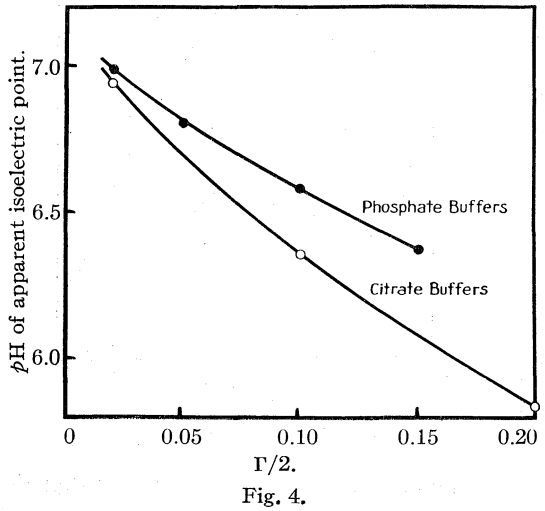


Fig. 4.

In order to analyze further the measurements of electrophoretic mobility that are reported, it seemed desirable first to consider them from the points of view that have been developed for ions of ordinary valence. Two generalizations may first be made: that the greater the valence, the greater the net charge and therefore the greater the mobility. On the other hand, the greater the valence the more the mobility will diminish from that which would obtain in infinitely dilute solution.

The mobility of an ion is given, following Onsager's theory, by an equation of the form

$$u = u_0 - (\alpha u_0 + \beta)\sqrt{\Gamma/2} \qquad (4)$$

in which u is the mobility at ionic strength $\Gamma/2$, u_3 the mobility at infinite dilution and α and β constants depending, respectively, on the relaxation and on the electrophoretic migration of the ionic atmosphere. The former effect is a complicated function of the valence and mobilities at infinite dilution of all ions present.

This equation, valid only in very dilute solution, has been extended by Shedlovsky to the case of more concentrated solutions[25-27] as follows

$$u = u_0 - (\alpha u_0 + \beta)\sqrt{\Gamma/2} + B(\Gamma/2) - \alpha B(\Gamma/2)^{3/2} \qquad (5)$$

The third term is small, in part because of the exponent of the ionic strength, in part because α is small in comparison with β (0.22 and 28.9, respectively, for a univalent ion at 25°). The empirical constant B for simple ions often has been found to be nearly equal to $(\alpha u_0 + \beta)$. Neglecting the third term in the above equation, we may write

$$u = u_0 - A'\sqrt{\Gamma/2} + B'(\Gamma/2) \qquad (6)$$

Values of u_0, A' and B' estimated from the observed mobilities by this equation show no significant variation with ionic strength, and are given in Table III. As in the case of simple ions the values of A' are close to those of B' and it is therefore possible to use for interpolation the still simpler equation for the influence of ionic strength

$$u = u_0 - A'(\sqrt{\Gamma/2} - \Gamma/2) \qquad (7)$$

TABLE III

CONSTANTS DEFINING THE MOBILITY OF CARBOXYHEMOGLOBIN IN PHOSPHATE AND CITRATE BUFFERS VARYING IN pH AND IONIC STRENGTH AT 25° IN TERMS OF EQUATIONS (6) AND (7)

	Three constant equation			Two constant equation	
pH	u_0	A'	B'	u_0	$A' = B'$
		Phosphate Buffers			
5.65	18.5	66.7	66.7	18.5	66.8
5.8	16.6	59.2	56.5	17.1	62.7
6.0	14.5	53.0	49.7	15.0	56.8
6.2	12.6	48.4	45.9	12.9	51.5
6.4	10.2	41.6	38.9	10.6	45.1
6.6	7.9	35.3	31.9	8.4	39.4
6.8	5.6	20.9	29.3	5.9	33.1
		Citrate Buffers			
5.8	9.57	34.7	30.4	10.37	41.2
6.0	8.54	32.4	27.5	9.37	39.4
6.2	7.38	29.3	23.7	8.34	37.3
6.4	6.14	26.1	20.0	7.18	34.8

For the studies in phosphate and citrate buffers, deviations in linearity of u_0 in pH over this pH range are scarcely greater than the experimental error. The straight lines drawn in Fig. 5 for phosphate and citrate, respectively, are given by the equations

$$u_0 - 4.0 = 11.0\ (7.00 - p\text{H}) \qquad (8)$$
$$u_0 - 4.0 = 5.5\ (7.00 - p\text{H}) \qquad (9)$$

It would, however, not be safe to estimate isoelectric points by extrapolation of these equations.

(24) The possibility that the change in mobility with ionic strength might partly be due to differences in heat production was tested in one experiment with high conductivity (acetate) by the introduction in series of a resistance which halved the potential drop, but which did not sensibly influence the mobility.

(25) T. Shedlovsky, THIS JOURNAL, **54**, 1405 (1932).

(26) D. A. MacInnes and T. Shedlovsky, *ibid.*, **54**, 1429 (1932).

(27) T. Shedlovsky and A. S. Brown, *ibid.*, **56**, 1066 (1934).

Indeed their use would imply a higher isoelectric point for hemoglobin in the presence of very small concentrations of citrate than of phosphate ions. Rather linearity would appear to depend on the almost linear combining capacity of carboxyhemoglobin for acid and base over this pH range, one of the reasons for the choice of these particular systems for this study. For the evidence would appear to be conclusive[28-30] that the changes in net charge of the carboxyhemoglobin molecule over this pH range is ascribable to the imidazole ring of histidine. There are 32 or 33 histidine residues in horse hemoglobin on the basis of a molecular weight of 66,800, of which 12 or more dissociate at reactions acid to the isoelectric point. We thus estimate a large number of imidazole groups dissociating over this pH range. The values of A' in Table IV vary only from 20 to approximately treble this value. Moreover, in the systems containing phosphate buffer A' as well as u_0 is linear in pH (Fig. 5) and is given over the range investigated by the relation

$$A' - 27.6 = 29.0\ (7.00 - p\mathrm{H}) \qquad (10)$$

whereas in the systems containing citrate buffer the relation appears more complicated.

Although the above equations are useful for interpolation, their significance is doubtful. If the valence be assumed to reach approximately 12 at the most acid pH investigated, on the basis of the titration curve of hemoglobin,[30] far higher values of u_0 and A' should be expected.

Moyer and Abramson[23] have employed an equation for the electrophoretic mobility of proteins of the form

$$u = u_0[1/(1 + \kappa r)] \qquad (11)$$

Taking the radius of hemoglobin as 27 Å., u_0 may be estimated by this equation as

$$u_0 = u(1 + 9\sqrt{\Gamma/2}) \qquad (12)$$

The values of u_0 calculated by means of our data and equation (12) vary with ionic strength. Thus for the four phosphate ionic strengths investigated at pH 5.65, this equation yields 23.37, 20.78, 15.22 and 12.15; whereas equation (7) yields 18.38, 18.51, 18.45 and 18.54. At other reactions also values of u_0 calculated by equation (7) are essentially independent of ionic strength, whereas those calculated by means of equation (12) show wide variations.

(28) B. German and J. Wyman, Jr., *J. Biol. Chem.*, **117**, 533 (1937).
(29) J. Wyman, Jr., *ibid.*, **127**, 1 (1939).
(30) E. J. Cohn, A. A. Green and M. H. Blanchard, THIS JOURNAL **59**, 509 (1937).

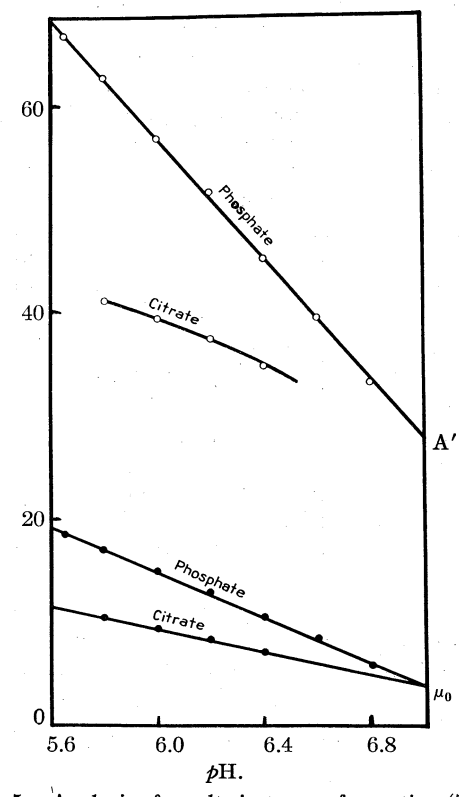


Fig. 5.—Analysis of results in terms of equation (7).

In the electrophoretic term of the Onsager equation, as generally employed, there is omitted a factor of $1/(1 + \kappa r)$, which would take into account as a first approximation the finite size of the ion[31] (p. 325). For dilute solutions of small ions κr is small in comparison with unity, but for proteins this is not the case. Including the above factor but omitting the relaxation term in α. equation (4) becomes

$$u = u_0 - \beta\sqrt{\Gamma/2}/(1 + (r/3)\sqrt{\Gamma/2}) \qquad (13)$$

To use equation (13) for extrapolation to infinite dilution, we have again taken r for carboxyhemoglobin as 27 Å. Values of u_0 and β estimated by means of this equation for the phosphate and citrate systems investigated are recorded in Table IV. These values of u_0 are satisfactorily constant and independent of ionic strength at each pH. They are moreover appreciably greater than the estimates of u_0 derived from either equation (7) or (12).

Not only is u_0 more than half again as great as estimated by means of equation (13) but β is nearly five times as great as A' of equation (7). Whereas A' is approximately of the magnitude

(31) D. A. MacInnes, "The Principles of Electrochemistry," Reinhold Publishing Corporation, New York, 1939.

TABLE IV

CONSTANTS DEFINING THE MOBILITY OF CARBOXYHEMOGLOBIN IN PHOSPHATE AND CITRATE BUFFERS VARYING IN *p*H AND IONIC STRENGTH AT 25° IN TERMS OF EQUATION (13)

*p*H	u_0	β	β/u_0
	Phosphate Buffers		
5.65	30.78	325.4	10.57
5.8	28.84	308.6	10.71
6.0	25.71	280.3	10.91
6.2	22.62	253.4	11.21
6.4	19.17	222.7	11.62
6.6	15.83	194.5	12.29
6.8	12.11	163.1	13.47
	Citrate Buffers		
5.8	17.70	197.5	11.16
6.0	16.63	191.9	11.54
6.2	15.36	183.7	11.96
6.4	13.85	172.8	12.48

to be expected of a univalent or bivalent ion, the values of β from equation (13) approach those that might be expected for decavalent ions, and this, as we have seen, is approximately the mean valence of the hemoglobin at the greatest acidities studied.

Since the apparent isoelectric point is different for each solvent (Fig. 4), it seemed desirable to consider mobility at fixed *p*H intervals from that *p*H at which there was no mobility in a buffer of the same ionic strength. Applying the same equations to the measurements under these conditions yields the constants in Table V. The values of all the constants are smaller when computed in this way. Moreover, the ratios (A'/u_0) and (β/u_0) would appear to be more nearly independent of the nature of the buffer, as might be expected if both were largely dependent upon the net charge of the protein.

TABLE V

CONSTANTS DEFINING THE MOBILITY OF CARBOXYHEMOGLOBIN IN PHOSPHATE AND CITRATE BUFFERS AT CONSTANT *p*H INTERVALS FROM APPARENT ISOELECTRIC POINTS

	Equation (7)			Equation (13)		
δ *p*H	u_0	A'	A'/u_0	u_0	β	β/u_0
	Phosphate Buffers					
0.1	1.74	5.54	3.20	2.08	27.2	13.32
.2	3.30	10.49	3.20	5.28	51.8	9.82
.4	5.89	18.3	3.11	9.33	90.1	9.66
.6	8.43	26.1	3.10	13.37	128.7	9.63
.8	10.86	33.7	3.11	17.22	166.2	9.65
	Citrate Buffers					
0.1	1.13	3.57	3.16	1.39	12.22	8.78
.2	1.94	5.89	3.07	2.43	21.02	8.67

The quantity u_0 estimated from measurements in systems containing buffer may well have no significance for salt-free solutions. Indeed values of u_0 independent of the nature of the buffer are not quite realized on the basis of these measurements and of any of the equations considered. Whether this failure depends upon the form of these equations, upon the approximate method of estimating equal net charges for comparison or upon ion association between protein and buffer must await further investigation. The results do not preclude the latter interpretation, especially for buffers with polyvalent anions, and such association, if it occurs, must be taken into account as well as the electrostatic forces between buffer ions, protein ions and protein dipolar ions.

We are indebted to R. M. Ferry and W. C. Morro for certain of the measurements confirming our earlier results with the new Tiselius apparatus, and to J. D. Ferry and G. Scatchard for considering with us implications of the alternative methods of analyzing electrophoretic measurements.

Summary

1. The electrophoretic mobility of carboxyhemoglobin has been studied at 25° in phosphate and citrate buffers, varying in *p*H from 5.65 to 7.2, and in ionic strength from 0.02 to 0.20.

2. Over this range the influence of ionic strength upon mobility is of the same order as that of *p*H. Corrections for the influence of electrostatic forces both in diminishing mobility and in changing the isoelectric point are considered.

3. Whereas the computations attempted on the basis of these results do not preclude ion association, they yield constants for the effect of the buffers at constant *p*H, and at constant *p*H intervals from the isoelectric condition.

4. Carboxyhemoglobin has a net charge due to the dissociation of twelve or more imidazole groups at the most acid reactions investigated.

5. Not only mobility but diminution in mobility due to electrostatic forces is a function of the net charge, and therefore increases with distance from the isoelectric condition.

BOSTON, MASS. RECEIVED APRIL 8, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE INSTITUTE OF TECHNOLOGY, UNIVERSITY OF MINNESOTA]

Thermodynamic Significance of Polarographic Half-Wave Potentials of Simple Metal Ions at the Dropping Mercury Electrode

BY JAMES J. LINGANE[1]

The electrodeposition of simple (hydrated) metal ions at the dropping electrode is a chemically reversible process when the resulting metal is soluble in mercury, and may be represented by

$$M^{n+} + ne + Hg \rightleftharpoons M(Hg) \qquad (1)$$

where M(Hg) represents the amalgam formed on the surface of the mercury drops.[2] Heyrovsky and Ilkovic[3] have pointed out that if the foregoing reaction takes place reversibly the dropping electrode should be subject only to concentration polarization, and accordingly its potential at every point on a discharge wave should be given by

$$E_{d.e.} = E_a^0 - \frac{RT}{nF_y} \ln \frac{C_a \gamma_a}{C_0 \gamma_s} \qquad (2)$$

where C_a is the concentration of the amalgam formed on the surface of the mercury drops, C_0 is the concentration of the metal ions in the depleted layer of solution *at the surface* of the drops, γ_a and γ_s are, respectively, the activity coefficients of the metal in the amalgam and the metal ions in the solution, and E_a^0 is the standard potential of the amalgam, that is, the e. m. f. of the cell: Reference electrode / $M^{n+}(a = 1)$/M(Hg)$(a = 1)$ (I).

When an excess of an indifferent electrolyte is present so that the migration current is eliminated, the reducible metal ions reach the surface of the dropping electrode only by diffusion.[2,4] Representing the concentration of the reducible metal ions in the body of the solution by C, the current at any point on the polarographic wave by i, and the diffusion current by i_d, we have the relations[2,3]

$$i_d = KC \qquad (3)$$
$$i = K(C - C_0)$$

or

$$C_0 = \frac{i_d - i}{K} \qquad (4)$$

and

$$C_a = ki \qquad (5)$$

The validity of eq. 3, in which K is the diffusion current constant, has been amply demonstrated.[2,4] The theoretical significance of K and the factors which influence it have been discussed in detail by Ilkovic[5] and Lingane and Kolthoff.[4] Equation 5 is simply a statement of the fact that the concentration of the amalgam at every point on the wave must be proportional to the current.

By substituting the foregoing relations into eq. 2 we obtain

$$E_{d.e.} = E_a^0 - \frac{RT}{nF_y} \ln \frac{\gamma_a k K}{\gamma_s} - \frac{RT}{nF_y} \ln \frac{i}{i_d - i} \qquad (6)$$

The half-wave potential is defined[3] as the value of $E_{d.e.}$ at the midpoint of the wave, and since the last log term becomes zero when $i = i_d/2$ eq. 6 may be written

$$E_{d.e.} = E_{1/2} - \frac{RT}{nF_y} \ln \frac{i}{i_d - i} \qquad (7)$$

and hence the half-wave potential is given by

$$E_{1/2} = E_a^0 - \frac{RT}{nF_y} \ln \frac{\gamma_a k K}{\gamma_s} \qquad (8)$$

It should be mentioned that the observed value of $E_{d.e.}$ includes a small iR drop in the solution. However, with concentrations of supporting electrolyte greater than about 0.01 M the resistance of a polarographic cell is generally less than 1000 ohms, and hence the iR drop is usually less than 0.001 v. per microampere, which is negligibly small.

When the resulting metal is not soluble in mercury it is simply deposited in the solid state on the surface of the dropping electrode, and in such a case the reduction of the metal ions will be given by

$$M^{n+} + ne \rightleftharpoons M(s) \qquad (9)$$

If this reaction would take place reversibly it readily can be derived that the equation of the polarographic wave should be

$$E_{d.e.} = E_M^0 - \frac{RT}{nF_y} \ln \frac{K}{\gamma_s} + \frac{RT}{nF_y} \ln (i_d - i) \qquad (10)$$

where E_M^0 is the ordinary standard potential of the metal. Quite obviously the curve of this equation is not symmetrical about the half-wave point, and therefore in this case the half-wave potential has no particular thermodynamic significance. The difficulty of obtaining reproduci-

(1) Present address: Department of Chemistry, University of California, Berkeley, California.

(2) For a detailed review of the fundamental principles of the polarographic method see I. M. Kolthoff and J. J. Lingane, *Chem. Rev.*, **24**, 1–94 (1939).

(3) J. Heyrovsky and D. Ilkovic, *Coll. Czech. Chem. Commun.*, **7**, 198 (1935).

(4) J. J. Lingane and I. M. Kolthoff, THIS JOURNAL, **61**, 825 (1939).

(5) D. Ilkovic, *Collection Czech. Chem. Commun.*, **6**, 498 (1934); *J. chim. phys.*, (*France*) **35**, 129 (1938).

ble electrode potentials in the classical manner with metals that are insoluble in mercury (*e. g.*, metals of group VI in the periodic classification, the iron group, arsenic, vanadium, etc.) is well known, and chemical polarization and passivity phenomena are common in this group. Hence the reduction of such metals according to eq. 9 is in most cases probably not a reversible process. For these reasons the following discussion will be confined to those metals that are soluble in mercury, and whose ions are reduced at the dropping electrode according to eq. 1.

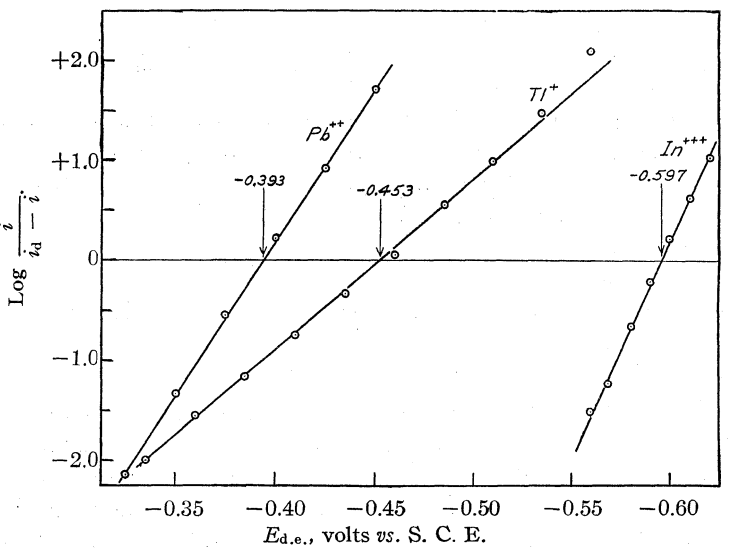


Fig. 1.—Log plots of observed current–voltage curves of thallous and lead ions in 0.1 *N* potassium chloride, and of indium ions in 1 *N* potassium chloride. The slopes of the three lines are Tl^{+} 0.059 v., Pb^{++} 0.033 v., and In^{+++} 0.023 v.

Equation 7 has been verified experimentally by Tomes[6] and Kolthoff and Lingane.[2] By plotting $E_{d.e.}$ against log $i/(i_d - i)$ a straight line results, whose slope is equal to $2.3RT/nF_y$, and the value of $E_{d.e.}$ corresponding to a value of zero for the log term is the half-wave potential. This is demonstrated in Fig. 1, where the plots have been constructed from experimental current–voltage curves obtained by the writer, in the electrolysis of 0.002 *M* solutions of thallous, lead, and indium ions in the presence of an excess of potassium chloride. The current–voltage curves were obtained with the apparatus previously described.[2,4] As predicted by eq. 7, the experimental points fall on straight lines. The observed slopes of the three lines are, respectively, 0.059, 0.033, and 0.023 v. for the thallous, lead, and indium ions, in good agreement with the theoretical values which are 0.059, 0.030, and 0.020 v. for the discharge of uni-, di-, and trivalent ions. It is evident that eq. 7, and the fundamental assumption that the dropping electrode is subject only to concentration polarization in the discharge of metal ions according to eq. 1, are essentially correct.

(6) J. Tomes, *Coll. Czech. Chem. Commun.*, **9**, 12, 81, 150 (1937).

By setting the second differential of eq. 7, *i. e.*

$$\frac{d^2E}{di^2} = \frac{RT}{nF_y}\left(\frac{1}{i^2} - \frac{1}{(i_d - i)^2}\right)$$

equal to zero, it is found that the curve of eq. 7 has a point of inflection when $i = i_d/2$. The polarographic wave is therefore symmetrical about the half-wave point, and $E_{1/2}$ coincides with the true inflection point of the curve.[3]

It has been found experimentally[2,3] that the half-wave potential is entirely independent of the geometrical characteristics of the particular capillary that is used, the rate of flow of mercury, and the drop time. Therefore, it is evident from eq. 8 that the product kK is constant and independent of these factors. Although both k and K are individually dependent on the properties of the capillary, the rate of mercury flow, and the drop time, the effect of these factors on k must be inversely proportional to their effect on K, so that the product kK remains constant. It is also an experimental fact[2,3] that the half-wave potential is constant and independent of the concentration of the reducible metal ions, provided that the composition of the solution with respect to foreign salts, *i. e.*, γ_s, is kept constant. It is evident, therefore, that the half-wave potential is a characteristic property of the reducible ions, and it has definite thermodynamic significance.

Influence of the Concentration of Supporting Electrolyte on the Half-Wave Potential.—Since the activity coefficient, γ_s, of the reducible metal ions decreases with increasing ionic strength, it is to be expected from eq. 8 that $E_{1/2}$ should be shifted somewhat to more negative values with increasing concentration of supporting electrolyte. This is actually observable experimentally, as shown by the data in Table I obtained by the writer.

TABLE I

HALF-WAVE POTENTIALS OF THALLOUS, ZINC, CADMIUM, AND LEAD IONS IN VARIOUS CONCENTRATIONS OF SUPPORTING ELECTROLYTE

Half-wave potentials in volts referred to the saturated calomel electrode at 25°.

Supporting electrolyte	Tl^+	Zn^{++} $E_{1/2}$	Pb^{++}	Cd^{++}
0.02 *N* KNO_3	−0.451	−0.988		−0.572
0.1 *N* KNO_3	.459	0.997	−0.388	.578
1 *N* KNO_3	.477	1.012	.405	.586
0.02 *N* KCl		−0.988	− .377	− .578
0.1 *N* KCl	−0.459	0.995	.396	.599
0.25 *N* KCl	.466		.402	
1 *N* KCl	.480	−1.022	.435	.642

These data were obtained by the manual method of measurement and with the cells that have already been described,[2,4] and $E_{d.e.}$ was measured directly against an external saturated calomel reference electrode during the electrolysis. The concentration of the metal ions was 5×10^{-4} *M* or smaller, the current at the half-wave point was less than 2 microamp., and hence the correction for the *iR* drop in the solution was negligibly small. The $E_{1/2}$ values are reproducible to about ±2 mv.

The negative shift of the $E_{1/2}$ values with increasing ionic strength is of the order of magnitude predicted by eq. 8, when potassium nitrate is used as supporting electrolyte. The half-wave potential of thallous ions is the same in potassium nitrate and potassium chloride media at the same ionic strength, but with the other metal ions the negative shift is considerably greater in potassium chloride than in potassium nitrate solutions, due to complex ion formation between the divalent metal ions and chloride ions. It is well known that the half-wave potentials of metal ions are shifted to more negative values by complex formation.[2,3] In potassium nitrate solutions there is no appreciable complex formation, and only the ionic strength effect is operative.

Thermodynamic Interpretation of the Half-Wave Potential.—In order to interpret the half-wave potentials thermodynamically, it is convenient to compare them with the ordinary standard potentials of the metals. Consider the cell $M(s)/M^{n+}/M(Hg)$ two phase (II), in which the left electrode is the solid metal, and the right electrode is its saturated two-phase amalgam. Let $a_{satd.}$ be the activity of the metal in the saturated liquid amalgam in contact with a solid phase which may be either the pure metal, or a solid compound, or solid solution, of the metal and mercury. The e. m. f. of this cell is given by

$$E_{II} = E^0_a - E^0_M - \frac{RT}{nF_y} \ln a_{satd.} \qquad (11)$$

where E^0_M is the ordinary standard potential of the metal, that is, the e. m. f. of the cell: Reference electrode/$M^{n+}(a = 1)$/M(s) (III).

If we express the composition of the amalgam in terms of mole fraction of the metal, *N*, and designate the *solubility* of the metal in mercury by $N_{satd.}$ and the corresponding activity coefficient by $\gamma_{satd.}$, we obtain from eq. 11

$$E^0_a = E^0 + E_{II} + \frac{RT}{nF_y} \ln N_{satd.}\, \gamma_{satd.} \qquad (12)$$

By substituting this expression for E^0_a into eq. 8 we find that the difference between the half-wave potential of a metal ion and its ordinary standard potential is given by

$$E_{1/2} - E^0_M = E_{II} + \frac{RT}{nF_y} \ln N_{satd.}\, \gamma_{satd.} - \frac{RT}{nF_y} \ln \frac{\gamma_a kK}{\gamma_s} \qquad (13)$$

The first two terms on the right side of this equation are thermodynamic terms, but the last term involves the kinetics of the electroreduction.

In the case of metals which do not form solid compounds or solid solutions with mercury, *e. g.*, zinc, E_{II} is zero. In general, however, when the metal forms a solid compound or solid solution with mercury, E_{II} is equal to $-\Delta F/nF_y$, where ΔF is the free energy increase in the formation of the solid M_xHg_y, according to the reaction

$$xM(s) + yHg(l) \rightleftharpoons M_xHg_y(s) \qquad (14)$$

It is evident, therefore, that the difference between $E_{1/2}$ and E^0_M depends on three distinct factors; the affinity of the metal for mercury (ΔF of reaction 14), the solubility of the metal in mercury, and the kinetic term *kK*.

A comparison of the half-wave potentials and the ordinary standard potentials of several metal ions is given in Table II. The values of $E_{1/2}$ given for the first four metal ions are the values obtained with 0.1 *N* potassium nitrate as the supporting electrolyte (Table I). The $E_{1/2}$ values of sodium and potassium ions were taken from the compilation given by Heyrovsky and Ilkovic[3]; they were obtained by using tetra-substituted alkylammonium salts as the supporting electrolyte.

It will be noted that the difference between $E_{1/2}$ and E^0_M is greatest in the case of the alkali metals, due to their great affinity for mercury. In these cases the difference is due chiefly to the large value of E_{II}, and the second and last terms in eq. 13 are of subordinate importance. On the

TABLE II

COMPARISON OF HALF-WAVE POTENTIALS AND STANDARD ELECTRODE POTENTIALS OF SEVERAL METAL IONS

The values of $E_{1/2}$ and E^0_M are in volts with respect to the saturated calomel electrode at 25°.

Ion	$E_{1/2}$	E^0_M	$E_{1/2} - E^0_M$	E_{II}	$N_{satd.}$	$\gamma_{satd.}$	kK, calcd.
Tl^+	−0.459[a]	−0.582	+0.123	+0.003[c]	0.435[i]	7.75[j]	0.025
Pb^{++}	− .388[a]	− .372	− .016	.006[d]	.0143[k]	0.717[k]	.033
Cd^{++}	− .578[a]	− .647	+ .069	.051[e]	.0953[i]	.216[l]	.0025
Zn^{++}	− .997[a]	−1.008	+ .011	0[f]	.0638[m]	.756[m]	.011
Na^+	−2.12[b]	−2.961	+ .84	.780[n]	.0538[g]	1.28[g]	.005
K^+	−2.14[b]	−3.170	+1.03	1.001[h]	.0254[h]	5.52[h]	.036

[a] In 0.1 N KNO_3; see Table I. [b] Heyrovsky and Ilkovic, ref. 3. [c] Richards and Daniels, THIS JOURNAL, **41**, 1732 (1919). [d] Gerke, *ibid.*, **44**, 1684 (1922). [e] Hulett, *Trans. Am. Electrochem. Soc.*, **7**, 333 (1905). [f] Clayton and Vosburgh, THIS JOURNAL, **58**, 2093 (1936). [g] Bent and Swift, *ibid.*, **58**, 2216 (1936). [h] Bent and Gilfillan, *ibid.*, **55**, 3989 (1933). [i] Teeter, *ibid.*, **53**, 3917, 3927 (1931). [j] Lewis and Randall, "Thermodynamics," p. 267. [k] Hoyt and Stegeman, *J. Phys. Chem.*, **38**, 753 (1934). [l] Hildebrand, "Solubility of Non-Electrolytes," Reinhold Publishing Corp., New York, 1936. [m] Pearce and Eversole, *J. Phys. Chem.*, **32**, 209 (1928). [n] Bent and Forziati, THIS JOURNAL, **58**, 2220 (1936).

other hand, in the case of thallium E_{II} is negligibly small, but the solubility of thallium in mercury is large, so that the difference between $E_{1/2}$ and E^0_M is determined practically entirely by the last two terms in eq. 13.

The solubilities of the various metals in mercury at 25° are listed in the sixth column of the table, in terms of mole fraction, and the corresponding activity coefficients are given in the seventh column. The values of $\gamma_{satd.}$ are based on infinite dilution ($\gamma_a = 1$) as the standard state.

The last column contains approximate values of kK for the various metals calculated by means of eq. 13 from the observed differences between $E_{1/2}$ and E^0_M, and the experimental values of E_{II}, $N_{satd.}$, and $\gamma_{satd.}$ given in the table. In this calculation it was assumed that the activity coefficient of the univalent ions is 0.8, and that of the divalent ions 0.5, at an ionic strength of 0.1 M in potassium nitrate solutions.[7] Since we had no exact knowledge, *a priori*, regarding the concentration of the amalgams formed on the surface of the mercury drops, it was assumed that the concentrations of the amalgams were so small, under the usual conditions of a polarographic experiment, that γ_a was equal to unity. Because of this uncertainty the calculated values of kK can only be considered as approximations, but they are sufficiently accurate to indicate at least the order of magnitude of the constant k.

Although the observed values of $E_{1/2} - E^0_M$, and E_{II}, vary from a few millivolts up to one volt, and the activities of the saturated solutions of the metals in mercury vary widely from 0.01 in the case of lead up to 3.5 in the case of thallium, the calculated values of kK are all of the same order of magnitude. Unfortunately, no independent experimental method for determining k has yet been discovered, so that a more direct test of eq. 13 is not possible at the present time. However, the uniformity of the various calculated values of kK constitutes good indirect evidence of the validity of eq. 13.

The diffusion current constant K for the metal ions in Table II is of the order of magnitude of 5 microamp. per millimole per liter, with capillaries of the usual dimensions.[2,4] Hence the apparent value of k, from the data in Table II, is of the order of 0.005 mole fraction per microamp. for most of the metals. If we express the composition of the amalgams in volume concentration units, the apparent value of k is of the order of 300 mmol. per liter per microamp. This rather large value of k indicates that the deposited metal atoms remain close to the surface of the drop during its life, and that diffusion into the body of the drop is relatively slow. At the present time our knowledge of the diffusion processes in the mercury drops is so meager and incomplete that any attempt at a more detailed interpretation of these results at this time would be pure conjecture.

(7) J. Kielland, THIS JOURNAL, **59**, 1675 (1937).

Summary

The equation of the current–voltage curves in the electrodeposition of metal ions at the dropping mercury electrode has been discussed. When the reduced metal is soluble in mercury the dropping electrode is subject only to concentration polarization.

Experimental data have been presented which demonstrate that the half-wave potentials of metal ions are shifted somewhat to more negative values with increasing ionic strength of the solution.

The characteristics of the half-wave potential have been discussed, and an equation was derived relating the half-wave potentials to the ordinary standard potentials of the metals. The difference between the polarographic half-wave potential of a simple metal ion and the ordinary standard potential of the metal was shown to be a function of three distinct factors: (1) the affinity of the metal for mercury; (2) the solubility of the metal in mercury; and (3) the kinetics of the diffusion processes in the solution and in the mercury drops.

MINNEAPOLIS, MINN. RECEIVED MAY 12, 1939

[CONTRIBUTION FROM THE AVERY LABORATORY OF CHEMISTRY, UNIVERSITY OF NEBRASKA]

Mutarotation of Tetramethyl-α-d-glucopyranose and Tetramethyl-α-d-mannopyranose

BY B. CLIFFORD HENDRICKS AND ROBERT E. RUNDLE

In a previous paper,[1] a study of the complexity of the mutarotation of *d*-galactopyranose was reported. In this communication a study of the analogous glucose and mannose sugars is presented.

The mutarotation of tetramethyl-α-*d*-glucopyranose has been investigated by Purdie and Irvine,[2] Lowry and co-workers[3-5] and Böeseken and Couvert[6] in water and other solvents. These workers, however, gave direct attention to the reaction order of the sugars' mutarotations at only one temperature. The mutarotation of tetramethyl-α-*d*-mannopyranose has been previously reported,[7] though only incidentally.

A systematic study of the unmethylated α-*d*-glucose[8] does not support the reported[9] complex mutarotation of α-*d*-glucose. The authors proposed to learn whether methylation and mutarotation at or near 0° would give evidence of mutarotation complexity.

Since there is a paucity of data upon tetramethylmannose they prepared and followed the mutarotation of tetramethyl-α-*d*-mannopyranose also.

The two sugars were prepared as indicated in a previous paper.[10] The properties of the tetramethyl-α-*d*-glucopyranose used were: initial rotations, $[\alpha]^0D$ +104.0; $[\alpha]^{25}D$ +104.0; equilibrium rotations: $[\alpha]^0D$ +80.4; $[\alpha]^{25}D$ + 84.8 and m. p. 92.5–93.5°. The constants for the tetramethyl-α-*d*-mannopyranose used were m. p. 49–50°; initial rotations: $[\alpha]^0D$ +11.5; $[\alpha]^{25}D$ +6.3; equilibrium rotations: $[\alpha]^0D$ +2.5 and $[\alpha]^{25}D$ −0.2.

TABLE I

MUTAROTATION OF TETRAMETHYL-α-*d*-GLUCOPYRANOSE AT 25°

2.4298 g. of sugar in 25 ml. of water

Time Min.	Sec.	Rotation obsd.	$(k_1 + k_2) \times 10^3$ calcd.
7	15	19.60	
9	0	19.49	
11	15	19.32	9.00
13	50	19.15	8.57
20	30	18.71	8.84
25	0	18.46	8.75
34	50	17.98	8.70
49	0	17.42	8.75
62	25	17.02	8.78
88	15	16.50	8.81
104	0	16.25	9.17
125	0	16.07	9.20
∞		15.75	
			Av. 8.86 ± 0.34

TABLE II

MUTAROTATION OF TETRAMETHYL-α-*d*-GLUCOPYRANOSE AT 1.0°

2.819 g. of sugar in 25 ml. of water

Time Min.	Sec.	Rotation obsd.	$(k_1 + k_2) \times 10^3$ calcd.
9	15	25.32	
10	45	25.30	
18	10	25.24	0.754
25	30	25.18	.644
32	30	25.12	.786
40	50	25.03	.864
58	20	24.90	.829
81	45	24.82	.670
166	30	24.26	.709
255	0	23.78	.707
293	0	23.62	.693
424	0	23.14	.661
575	0	22.64	.660
646	0	22.46	.651
748	0	22.18	.662
∞		20.68	
			Av. 0.715 ± 0.149

(1) Hendricks and Rundle, THIS JOURNAL, **60**, 3007 (1938).
(2) Purdie and Irvine, *J. Chem. Soc.*, **85**, 1070 (1904).
(3) Lowry and Richards, *ibid.*, **127**, 138 (1925).
(4) Jones and Lowry, *ibid.*, 720 (1926).
(5) Richards, Faulkner and Lowry, *ibid.*, 1733 (1927).
(6) Böeseken and Couvert, *Rec. trav. chim.*, **40**, 354 (1921).
(7) Drew, Goodyear and Haworth, *J. Chem. Soc.*, 1237 (1927).
(8) Isbell and Pigman, *Bur. Standards J. Research*, **18**, 141 (1937).
(9) Worley and Andrews, *J. Phys. Chem.*, **32**, 307 (1928).
(10) Hendricks and Rundle, THIS JOURNAL, **60**, 2563 (1938).

TABLE III

MUTAROTATION OF TETRAMETHYL-α-d-MANNOPYRANOSE AT 25°

1.3911 g. sugar in 25 ml. of water

Time Min.	Sec.	Rotation obsd.	$(k_1 + k_2) \times 10^3$ calcd.
10	15	0.75	
11	15	.70	
12	25	.69	
14	00	.66	15.8
15	30	.63	18.6
20	00	.59	15.1
29	00	.48	18.1
36	50	.43	17.4
45	15	.38	18.3
51	20	.37	16.7
80	00	.30	
∞		−.28	
			Av. 17.1 ± 2.0

TABLE IV

MUTAROTATION OF TETRAMETHYL-α-d-MANNOPYRANOSE AT 0.0°

0.807 g. of sugar in 20 ml. of water

Time Min.	Sec.	Rotation obsd.	$(k_1 + k_2) \times 10^3$
10	30	0.48	
12	10	.42	
13	30	.41	
65	0	.35	1.39
91	30	.34	1.08
131	0	.30	1.15
263	0	.20	1.14
585	0	.07	1.19
∞		.02	
			Av. 1.19 ± 0.20

The experimental method followed and technique used were as described in a communication[1] previously cited. In this paper, as there stated, the rotation velocity constant, $k_1 + k_2$, is considered an index of the character of the mutarotation.

Results listed in Tables I, II, III and IV are representative of the results of the numerous experiments made.

The "thermal mutarotation" of tetramethyl-α-d-glucopyranose, using the procedure described previously,[1] was followed over a period of fifteen hours after a temperature change of from 25 to 0°. The calculations from the data for twenty-two observations gave a velocity constant, $(k_1 + k_2) \times 10^3$, of 0.640 ± 0.135. The deviations were random in their distribution with no more indication of trends than that shown in Table II. However, due to smaller changes in specific rotation during mutarotation, the experimental error is larger for methylated sugars. This is especially true for observations for the "thermal mutarotation" of the tetramethylglucose.

Discussion of Results

For purposes of ready comparison the constants of the three methylated sugars are tabulated with their unmethylated analogs in Table V. The data for the latter sugars are taken from the publication of Isbell and Pigman.[8] Those for the methylated galactose are from the paper previously listed.[1]

The mutarotation velocity constants for the methylated glucose show but slightly more variability than do those for the unmethylated sugar, probably due to experimental error. That agreement and the small variation of the velocity of mutarotation constants for the "thermal mutarotation" experiment give no support to the suggested[9] second order type of mutarotation for α-d-glucopyranose. Likewise the mutarotation of tetramethyl-α-d-mannopyranose is as truly of the first order as that of α-d-mannopyranose itself. It should be noted that there is as good an agreement between the heats of activation for the methylated sugars, 16,970 ± 260, as with those of the non-methylated sugars, 17,000 ± 300. These deviations are of about the same order as that introduced by the experimental error.

TABLE V

Sugar	$(k_1 + k_2) \times 10^3$	$(k' + k_2) \times 10^3$	Heat of activation, Q[b]
α-d-Glucopyranose	0.74 ± 0.05 at 0.2°	6.32 ± 0.14 at 20°	17,200
Tetramethyl-α-d-glucopyranose	.72 ± .15 at 1.0°	8.86 ± .34 at 25°	16,963
α-d-Galactopyranose[a]	.93 ± .02 at 0.0°	8.03 ± .04 at 20°	17,100
Tetramethyl-α-d-galactopyranose	.91 ± .06 at .0°	12.1 ± 1.7 at 25°	16,720
α-d-Mannopyranose	2.16 ± .15 at .1°	17.3 ± 0.2 at 20°	16,700
Tetramethyl-α-d-mannopyranose	1.19 ± .20 at .0°	17.1 ± 2.0 at 25°	17,230

[a] The constants for galactose are given only for the second slower phase of its complex mutarotation.

[b] $2.0326 \log \frac{(k_1 + k_2)}{(k_1' + k_2')} = \frac{Q}{1.9864}\left(\frac{1}{T_2} - \frac{1}{T_1}\right)$

Summary

The mutarotations of the tetramethylpyranose forms of both α-d-glucose and α-d-mannose have been investigated at the temperatures 0.0 and 25°.

Neither sugar shows a mutarotation of other

than the first order within the precision limits of the experimental technique used.

The heats of activation of these methylated sugars show a marked agreement with the heats of activation of analogous non-methylated sugars.

LINCOLN, NEBRASKA RECEIVED MAY 31, 1939

[CONTRIBUTION FROM THE COLLEGE OF PHARMACY, UNIVERSITY OF CALIFORNIA]

Sulfophenylarsonic Acids and Certain of their Derivatives. II. *p*-Sulfonamidophenylarsonic Acid

BY J. F. ONETO AND E. L. WAY

In this paper, which is a continuation of our studies of sulfophenylarsonic acids and their derivatives, a number of compounds have been described, two of which (*p*-sulfonamidophenylarsonic acid and *p*-sulfonamidophenylarsine oxide) should be of pharmacological interest.

The preparation of *p*-sulfonamidophenylarsonic acid was effected by application of the Bart reaction to sulfanilamide.

p-Sulfonamidophenylarsine oxide was prepared by two methods: (A) hydrolysis of *p*-sulfonamidophenyldibromoarsine with ammonium hydroxide; (B) interaction between *p*-chlorosulfonylphenyldichloroarsine and ammonium hydroxide. The oxide was converted to *p*-sulfonamidophenylarsonic acid by oxidation with hydrogen peroxide in alkaline solution.

p-Chlorosulfonylphenylarsonic acid, obtained by partial hydrolysis of *p*-chlorosulfonylphenyltetrachloroarsine, reacts with aniline to form *p*-sulfonanilidophenylarsonic acid. This reaction is now being studied in the preparation of substituted anilide and amide derivatives of *p*-sulfophenylarsonic acid.

Experimental Part

***p*-Sulfonamidophenylarsonic Acid.**—This acid was prepared by application of the Bart reaction to sulfanilamide (*p*-aminobenzenesulfonamide). It crystallizes from water in colorless, glistening needles, yield 25%. The acid is somewhat soluble in alcohol and in acetic acid; insoluble in acetone.

Anal. Calcd. for $C_6H_8O_5NAsS$: As, 26.66. Found: As, 26.51.

When heated for two hours under reduced pressure at 185–190°, the acid loses one molecule of water to form the anhydride.

Anal. Calcd. for $C_6H_5O_4NAsS$: As, 28.47. Found: As, 28.36.

The crystalline silver salt of *p*-sulfonamidophenylarsonic acid was obtained when 0.7 g. of the acid dissolved in 10 cc. of boiling water was treated with an excess of 0.25 *N* silver nitrate solution; yield 0.7 g.

Anal. Calcd. for $C_6H_7O_5NAsSAg$: As, 19.31; Ag, 27.81. Found: As, 19.39; Ag, 27.50.

In a second procedure the acid was obtained when 2 g. of *p*-sulfonamidophenylarsine oxide (obtained by treating *p*-chlorosulfonylphenyldichloroarsine with ammonium hydroxide) dissolved in 10 cc. of 10% sodium hydroxide was oxidized with 3 cc. of 30% hydrogen peroxide by heating on the steam-bath for one-half hour. The hot solution was acidified, whereupon the acid crystallized on cooling; yield 0.7 g.

The acid thus obtained was converted to the corresponding dibromoarsine; mixed m. p. 190–191°.

***p*-Sulfonamidophenyldiiodoarsine.**—A hot solution consisting of 1.7 g. of *p*-sulfonamidophenylarsonic acid in 25 cc. of water was treated with 15 cc. of 50% hydriodic acid. The diiodoarsine crystallized on cooling; yield, after recrystallizing from glacial acetic acid, 1.8 g.; m. p. 192–193°.

Anal. Calcd. for $C_6H_6O_2NAsSI_2$: As, 15.45; I, 52.35. Found: As, 15.36; I, 52.70.

***p*-Sulfonamidophenyldibromoarsine.**—A solution prepared from 2 g. of *p*-sulfonamidophenylarsonic acid, 20 cc. of 30% hydrobromic acid and a trace of hydriodic acid was saturated with sulfur dioxide. The resulting crystalline precipitate was recrystallized from glacial acetic acid; yield 2 g.; m. p. 191–192°.

Anal. Calcd. for $C_6H_6O_2NAsSBr_2$: As, 19.16. Found: As, 19.26.

***p*-Sulfonamidophenyldichloroarsine. (A).**—A solution consisting of 2 g. of *p*-sulfonamidophenylarsonic acid, 10 cc. of 37% hydrochloric acid and a trace of hydriodic acid was saturated with sulfur dioxide. The resulting dichloroarsine was recrystallized from glacial acetic acid; yield 1.5 g.; m. p. 176–177°.

Anal. Calcd. for $C_6H_6O_2NAsSCl_2$: As, 24.81. Found: As, 24.85.

(B).—Two grams of *p*-sulfonamidophenylarsonic acid was ground in a mortar with 12 cc. of phosphorus trichloride. After standing for one-half hour, the mixture was treated with ice water and the resulting crude dichloroarsine removed by filtration. The crude dichloroarsine was purified by dissolving in hot 10% hydrochloric acid and precipitating the crystalline substance by the addition of concentrated hydrochloric acid; yield 1.4 g.; mixed m. p. 176–177°.

(C).—One gram of *p*-sulfonamidophenylarsine oxide was dissolved in 10 cc. of hot 10% hydrochloric acid. The crystalline dichloroarsine was precipitated by the

addition of an excess of concentrated hydrochloric acid; yield 0.8 g.; mixed m. p. 176–177°.

p-Sulfonamidophenylarsine Oxide. (A).—Three and one-half grams of *p*-sulfonamidophenyldibromoarsine was boiled with 20 cc. of 27% ammonium hydroxide. The mixture was then chilled in ice and the crude oxide removed by filtration; yield, 1.8 g. after recrystallizing from 2% phosphoric acid.

Anal. Calcd. for $C_6H_6O_3NAsS$: As, 30.32; N, 5.67. Found: As, 30.21; N, 5.67.

(B).—Seven grams of crude *p*-chlorosulfonylphenyldichloroarsine was treated with 20 cc. of concentrated ammonium hydroxide. After standing for one hour the mixture was acidified with dilute sulfuric acid and the resulting oxide purified as above; yield 2.2 g.

One-half gram of the oxide was converted to the corresponding dichloroarsine by method (C) outlined under *p*-sulfonamidophenyldichloroarsine; mixed m. p. 176–177°.

p-Chlorosulfonylphenyldichloroarsine.—This substance was prepared by the method of Barber[1] using phosphorus trichloride and phosphorus pentachloride. The yield from 5 g. of sodium *p*-sulfophenylarsonic acid[2] after several recrystallizations from glacial acetic acid was 1 g.; m. p. 84–85°. This substance is soluble in most organic solvents.

Anal. Calcd. for $C_6H_4O_2AsSCl_3$: As, 23.30; Cl, 33.09. Found: As, 23.42; Cl, 32.87.

(1) Barber, *J. Chem. Soc.*, 2047 (1930).
(2) Oneto, THIS JOURNAL, **60**, 2058 (1938).

p-Chlorosulfonylphenylarsonic Acid.—Five grams of *p*-chlorosulfonylphenyldichloroarsine was dissolved in 10 cc. of warm chloroform and saturated with chlorine. The mixture was chilled in ice and the unstable, crystalline *p*-chlorosulfonylphenylarsine tetrachloride removed by filtration. The tetrachloroarsine was hydrolyzed to the corresponding *p*-chlorosulfonylphenylarsonic acid by treating with ice water. The crude acid was dried in vacuum over calcium chloride and recrystallized from ethyl acetate; yield 1.5 g.

Anal. Calcd. for $C_6H_6O_5AsSCl$: As, 24.93. Found: As, 24.89.

p-Sulfonanilidophenylarsonic Acid.—A mixture consisting of 5.3 g. of *p*-chlorosulfonylphenylarsonic acid and 12 cc. of aniline was heated on a water-bath for one-half hour. The resulting mass was treated with 40 cc. of 5% sodium hydroxide. The alkaline layer, which separated on standing, was treated with concentrated hydrochloric acid until acid to congo red paper, whereupon the *p*-sulfonanilidophenylarsonic acid precipitated in a crystalline form; yield, after recrystallization from water, 5 g.

Anal. Calcd. for $C_{12}H_{12}O_5NAsS$: As, 20.97. Found: As, 20.66.

Summary

The preparation and properties of *p*-sulfonamidophenylarsonic acid and a number of its derivatives have been described.

SAN FRANCISCO, CALIF. RECEIVED MAY 31, 1939

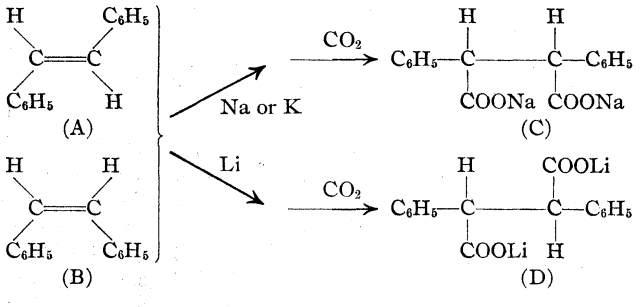
[CONTRIBUTION FROM THE CHEMICAL LABORATORY, UNIVERSITY OF TORONTO]

Addition of Alkali Metals to the Stilbenes

BY GEORGE F. WRIGHT

Introduction

In 1928 Schlenk and Bergmann[1] presented evidence to show that when alkali metals were added to ethylenes, the configuration of the adduct depended on the metal added and not upon the geometric isomer which was used. Thus, the addition of sodium or potassium to either stilbene (A) or isostilbene (B) gave, after carboxylation, the salt of *meso*-diphenylsuccinic acid (C), whereas addition of lithium to either geoisomer under similar conditions gave the salt of *dl*-diphenylsuccinic acid (D). They further demonstrated that, under conditions not conducive to the addition reaction, isostilbene was isomerized by sodium to stilbene.



While such a directed addition is not impossible from stereochemical considerations, it would seem improbable that two metals as similar as are sodium and lithium should orient themselves so specifically that mixtures of diastereomers would not be formed. The observations of Schlenk and Bergmann have not been questioned; indeed Bachmann and Pence[2] assumed, on the basis of color, that addition of lithium or sodium to 1,2,3,4-dibenzanthracene yielded each a characteristic diastereomer. However Jeanes and Adams[3]

(1) Schlenk and Bergmann, *Ann.*, **463**, 98 (1928).
(2) Bachmann and Pence, THIS JOURNAL, **59**, 2339 (1937).
(3) Jeanes and Adams, *ibid.*, **59**, 2608 (1937).

found that sodium, potassium and lithium all added to phenanthrene to give *trans* dimetalated dihydrophenanthrenes. In contrast, therefore, to the findings concerning stilbene, these latter authors find that the configuration of the adduct is independent of the alkali metal used to form it.

Inspection of the experimental data of Schlenk and Bergmann reveals a contradiction concerning their supposed *dl*-diphenylsuccinic acid. This substance was reported by many workers and was finally resolved by Wren and Still.[4] The resolvable acid melts at 183°, resolidifies and again melts at 222°. The melting point of the carboxylated organolithium compound, which Schlenk and Bergmann designated as the *dl*-isomer, was 241°. It will be shown in the present work that the apparent anomaly is eliminated on the basis that Schlenk and Bergmann never obtained any acid other than the *meso*-diphenylsuccinic acid. Although the latter acid ordinarily melts at 229°, it has been found that melting points of 242,[5] 245,[6] and 252°[7] may be obtained. The variation seems to be dependent on the rate of heating. Since a substance having such an indefinite melting point is obviously unsuited for mixed melting point determination, the fact that Schlenk and Bergmann observed a depression on admixture of their two supposed isomers is of little consequence. Likewise their further identification is unconvincing since, of the two methyl esters which they obtained by diazomethane treatment of the acids, the one derived from their supposed *dl*-isomer melted over a 22° range.[8] The extremely questionable evidence upon which these authors base their specific modes of alkali metal addition to ethylenes made it seem advisable to re-investigate the problem.

The addition of the alkali metals to the stilbenes was therefore reëxamined, giving attention to three variables: 1, configuration of the stilbene; 2, choice of metal and 3, choice of solvent. Table I lists the series of experiments carried out to allocate the effect of each of these factors. The resulting organometallic compound was characterized by conversion to the *s*-diphenylsuccinic acids. In no case was a pure diastereomer isolated, although the presence of both isomers could not be demonstrated when the initial yield was low, owing to the difficulty encountered in isolating the *dl*-acid from a mixture with other impurities. Even under favorable circumstances of high yield the reported percentages of *dl*-isomer must be regarded as questionable; on the other hand, the method employed, that of Anschütz and Bendix[6] involving separation by means of barium salt solubilities, gave reliable yields of pure *meso* acid. Both acids, after separation, were identified by conversion to the methyl esters and by mixed melting point determination of the latter with authentic samples.

Reference to Table I shows that *meso*-diphenylsuccinic acid was always obtained regardless of the geometric isomer, or the metal used. This substantiates the claim of Schlenk and Bergmann that *cis*- and *trans*-stilbene give the same product, but disproves their postulate that sodium and lithium orient differently. Although the table shows only the exception (expt. 2) all other experiments yielded impure *trans*-stilbene as recovered ethylene, regardless of the geoisomer originally used. The solvent medium was found to exert a profound effect. In non-coördinating solvents like petroleum ether and benzene, the organometallic compounds were insoluble; the yields were poor. Much better yields were obtained in coördinating solvents like ethyl ether and glycol dimethyl ether in which the organoalkali compounds were soluble. Of greatest significance is the fact that the ratio of diastereomers varies with the solvent used.

Since isostilbene reacted only slightly, and stilbene not at all in 60–70° petroleum ether, even when the reactive sodium–potassium liquid alloy was used, the addition was studied in benzene. Reaction could not be initiated with sodium or lithium unless a small amount of chlorobenzene was added. This unavoidable contaminant may have contributed to the impurity of the carboxylated product; it was found impossible with the methods at hand to isolate *dl*-diphenylsuccinic acid from the poor yield of comparatively low melting crude substance (Table I, expts. 3–8). It can, however, be stated with certainty that the reddish precipitates, obtained with lithium from stilbene or isostilbene, as well as the brownish-black precipitates of disodium compound from

(4) Wren and Still, *J. Chem. Soc.*, **107**, 449 (1915).
(5) Sonn and Schellenberg, *Ber.*, **50**, 1517 (1917).
(6) Anschütz and Bendix, *Ann.*, **259**, 91 (1890).
(7) Roser, *ibid.*, **247**, 152 (1888); Ruheman and Naunton, *J. Chem. Soc.*, **101**, 50 (1912).
(8) Although the matter has not been re-investigated in the present study, it should be noted that Schlenk and Bergmann obtained two acids, both melting at 296°, by the action of sodium and lithium on *s*-diphenyldimethylethylene. They claim these acids to be different, but the results obtained in this present work would indicate that the acids are identical.

TABLE I

PREPARATION OF DIPHENYLSUCCINIC ACIDS

Expt.	Stilbene, moles	Iso-stilbene, moles	Metal atoms Na	K	Li	Solvent	Time of reaction, hrs.	Products: Crude % yield	Crude M. p., °C.[a]	Separated diastereomers: meso- % of crude	meso- M.p., °C.[a]	dl- % of crude	dl- M. p., °C.[a]	Remarks
1	0.1		0.4	0.4		60–70° pet. ether	24	None						
2		0.1	.4	.4		60–70° pet. ether	24	0.4	220–229	90	229	Not found		0.08 mole isostilbene recovered unchanged
3	.01		.02			Benzene	24	.4	200–210					Reaction initiated with 0.05 cc. chlorobenzene
4	.01		.02			Same	144	2.0	205–220					Same
5	.01		.02			Same	312	4.8	200–205	50	223	Not found		Same
6		.01	.02			Same	600	18.0	206–208	>61	229	Not found		Same
7		.01			0.02	Same	800	0.3	200–204					Same
8	.01				.02	Same	2900	.6	223	90	229	Not found		Same
9	.01				.02	Ethyl ether	3	45.0	208	55	229	26	180–200	
10	.01				.02	Same	22	61.0	205–215					
11		.01	.02			Glycol dimethyl ether	1.5	65.0	214–215					
12	.01		.02			Same	2	73.0	213–215	93	224	Not found		
13	.01		.02			Same	1	72.0	214–215	76	229	Not found		Sodium compound treated with dry hydrogen for 1 hr.
14	.01				.02	Same	2	48.0	208–210	78	220	Not found		
15	.01		.02			Same	2	39.0	214–217					Treated with dry hydrogen and Raneynickel for 1 hr.
16	.05		.25			Same	2	74.0	212	94	229	0.3	180–200	

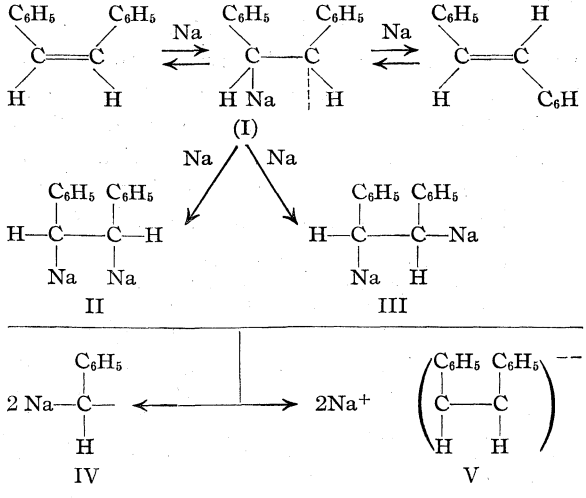
[a] All of these melting points were taken with slow (6°/min.) heating of the bath.

these two geoisomers, all gave *meso*-diphenylsuccinic acid upon treatment with carbon dioxide. Thus in a non-coördinating solvent, from which the organometallic compound precipitates as it is formed, no specific orientation of either sodium or lithium, can be found. Some significance can perhaps be attached to the higher yields from expt. 2 over expt. 1 and expt. 6 over expts. 3, 4 and 5 as indicating that isostilbene is more reactive than stilbene.

Since these results contradicted those of Schlenk and Bergmann, their experiments using lithium and stilbene in diethyl ether were repeated. Instead of an acid melting at 241° as they reported it was found that a mixture of *meso*- and *dl*-diphenylsuccinic acids was obtained when the impure product was subjected to separation through the barium salts. The proportion (55%) of *meso*-diphenylsuccinic acid isolated from the mixture is much more accurate than that of the *dl*-acid. The organometallic compound formed a reddish-brown solution in the ethyl ether. The yield, not reported by Schlenk and Bergmann, was found to be fair, especially over a twenty-four-hour reaction period (expts. 9, 10).

When glycol dimethyl ether[9] was used as a solvent, even better yields were obtained than with ethyl ether, while the reaction period was likewise shorter (expts. 11–16). The solutions of organometallic compounds were so dark that a color difference between organosodium and lithium was difficult to distinguish. The carboxylated product melted higher than that obtained from benzene or ether and, in spite of the careful separation through the barium salts, no *dl*-diphenylsuccinic acid could be isolated until a larger experiment was carried out (expt. 16), wherein 0.3% of the impure *dl*-diphenylsuccinic acid was isolated and identified. The ratio of diastereomers produced is, therefore, found to be different in benzene, ether, and glycol dimethyl ether, although the ratio of isomers is evidently independent of the metal used.

The possible steps in the addition reaction may be outlined according to the following diagram



(9) Scott, Walker and Hansley, THIS JOURNAL, **58**, 2442 (1936).

The first step involves random addition of sodium atoms to the ethylene linkage to give I; if this step were reversible the observed isomerization of isostilbene to stilbene would be expected.[10] The further addition of sodium atoms, with or without Walden inversion to give the pair of diastereomers II and III, is remindful of halogen addition to stilbene, if atomic addition is presumed to cause formation of two dibromostilbenes regardless of the isomer used. The possibility that I → II + III is an equilibrium reaction, or that II and III might dissociate to give a free radical of type IV is exceedingly improbable, but may be discounted further by the fact that the reaction mixture was unaffected by hydrogen, with or without a catalyst (Table I, expts. 13, 15). Finally, a dissociation into sodium cation and organic anion, II and III → V, was suggested by Schlenk and Bergmann, and especially favored by Jeanes and Adams,[3] who considered the sodium ion to be solvated. The ionic hypothesis would explain isomerization in the ethers, though not in benzene, but, unless the ether contributed greatly to anion deformation, it is not clear why different ethers should give different ratios of diastereomers. A better explanation might be afforded if it were assumed that the amorphous ion were subjected to the further influence of the reactant used for characterization. This possibility could not be tested heretofore, because all reactants other than carbon dioxide caused a reversion to stilbene.

Schlenk and Bergmann have shown that the vicinal diorganometallic compound when treated with methyl iodide does not react to give the dimethyl derivative but, instead, reverts to the parent ethylene. In the present investigation it has been found that dimethyl sulfate, unlike methyl iodide, reacts as a methylating agent. The ratio of diastereomers thus obtained is quite different from that produced in the same solvent by the carboxylation reaction. The absolute configuration of the 2,3-diphenylbutanes has not yet been established, but about twice as much low melting isomer as high melting isomer was produced. The ratio of diphenylsuccinic acids in the same solvent, glycol dimethyl ether, was about 300:1. On the basis of two reactions of different type (carboxylation and methylation) it can thus be stated that formation of diastereomeric mixtures is a function of the characterizing reactant. The dependence of stereochemical configuration in the adduct upon the nature of the augend to which the organometallic compound has been added has previously been encountered in the case of geoisomeric Grignard reagents.[11]

(10) Schlenk and Bergmann, *Ann.*, **463**, 1 (1928).

Experimental Part

Addition of Sodium or Lithium in Benzene.—A solution of 1.80 g. (0.01 mole) of stilbene or isostilbene in 25 cc. of benzene was placed in a nitrogen-filled Schlenk tube together with 0.02 mole of sodium or lithium, cut into about 50 pieces. After two sharp glass rods were added the tubes were sealed and shaken for periods of one to ten days. Since no apparent reaction took place, the tube was opened under nitrogen, and 0.02 g. of chlorobenzene was added. Reaction commenced in several hours. The precipitate was reddish-brown when lithium was used and reddish-black with sodium, the supernatant liquid being colorless. The reaction mixture was carboxylated by opening the tube under nitrogen, then by means of a sharp-pointed nichrome rod inserted through the straight arm of the tube breaking the bottom so that the contents dropped into a sidearm Erlenmeyer flask which was attached to the bole of the Schlenk tube by a rubber stopper. The Erlenmeyer flask contained a large excess of crushed dry-ice, which had been freed of water crystals by violent shaking of the flask under water-pump vacuum, atmospheric pressure being eventually restored by carbon dioxide evolution. The excess of sodium was decomposed by adding water to the carbon dioxide-filled flask. The water layer was separated from the benzene layer containing impure stilbene, and, after shaking with charcoal, was filtered and acidified with 12% hydrochloric acid to yield diphenylsuccinic acid.

Addition of Sodium and Lithium in Ethers.—The technique employed heretofore for preparation of organolithium compounds[12] was utilized, a stopcock having been sealed to the bottom of a three-necked flask. When glycol dimethyl ether[13] was used as solvent a conical flask[11] was found unsatisfactory when sodium was employed because the metal agglomerates to a solid lump after the reaction has started and thus interferes with the stirrer. No such difficulty was encountered with lithium. Reaction started immediately upon addition of the stilbene; protection from the air was afforded by a blanket of nitrogen rather than a stream of this gas over the reaction mixture. Upon completion of the reaction the contents of the flask were drained from unused metal through the stopcock into dry-ice. The carboxylated mixture was freed of the ether by evaporation at 70 mm. pressure and the residue processed as before.

Separation and Identification of the Diastereomeric Diphenylsuccinic Acids.—This method of Anschütz and Bendix was checked using equal mixtures of *meso*- and *dl*-diphenylsuccinic acids, the latter having been prepared by isomerization of the *meso* acid with barium hydroxide at 200°. The *meso* acid was recovered in 85% yield, m. p. 229°, while 70% of the *dl*-acid, m. p. 180–222°, was obtained.

(11) Wright, *J. Org. Chem.*, **1**, 457 (1936).

(12) Gilman, Zoellner and Selby, THIS JOURNAL, **54**, 1957 (1932).

(13) Furnished by courtesy of the Roessler and Hasslacher Chemicals Division, E. I. du Pont de Nemours and Company.

In a typical experiment, 1.56 g. of crude diphenylsuccinic acid was dissolved in ammonia, the excess having been boiled off, and treated with 70 cc. of warm barium hydroxide solution saturated at 25°. The solution was then treated with dry-ice until precipitation was complete, the precipitate being then treated with 1:3 hydrochloric acid. The residue, weighing 0.33 g., melted at 160–210°. It was crystallized from hot water to melt at 180–210° (wt. 0.03 g.) and was identified as *dl*-diphenylsuccinic acid by conversion with diazomethane to the dimethyl ester, m. p. 176–177° after two crystallizations from propanol-1. The filtrate from the barium carbonate precipitation was acidified to yield *meso*-diphenylsuccinic acid, m. p. 226°, weight 0.86 g. This was crystallized from acetic acid or propanol-1 to melt at 229–230° (m. p. 238° when placed in bath 10° below this melting point) and was identified by diazomethane treatment in propanol-1 as the dimethyl ester, m. p. 221–222° after crystallization from the same solvent. This ester was hydrolyzed by twelve hours of boiling with a 1:1 mixture of acetic acid and 12% hydrochloric acid. The product, m. p. 232°, was dissolved in ammonia, filtered and re-acidified with hydrochloric acid to melt at 241° (bath initially at 226°). Repeated crystallization failed to raise the melting point. The melting point of the pure *meso*-diphenylsuccinic acid when quickly heated evidently misled Schlenk and Bergmann to assign a diastereomeric configuration to the identical compound.

Methylation of 1,2-Diphenylethanedisodium.—The organodisodium compound prepared over a three-hour period as before from 1.80 g. (0.01 mole) of isostilbene and 0.46 g. (0.02 mole) of sodium in 30 cc. of glycol dimethyl ether was stirred and maintained at 25° while 2.52 g. (0.02 mole) of freshly distilled dimethyl sulfate in 10 cc. of glycol dimethyl ether was added over a twenty-minute period. After the color was completely bleached, the remaining ball of sodium (0.13 g., 0.006 mole) was removed. The reaction mixture was distilled at 40° (10 mm.) to recover the ether; the remainder was mixed with water and the oil which separated was taken up in benzene and treated with an excess of bromine. After evaporation of the benzene at 20 mm., the remainder was steam distilled. The distillate, extracted with ether and the latter evaporated, furnished an oil which was dissolved in hot ethanol. On cooling, 0.46 g. of 2,3-diphenylbutane separated, m. p. 115°. This was identified, after crystallization from 2 cc. of petroleum ether (b. p. 60–70°) m. p. 124°, by mixed melting point with a sample obtained from Dr. C. F. H. Allen and prepared by reduction of 2,3-diphenylbutadiene-1,3.[14] Evaporation of the crystallizing liquors left 0.04 g. more of the solid isomer together with an oil which distilled at 132–134° (6 mm.), wt. 1.14 g. On the basis of the crude products 21% of the solid isomer and 53% of the liquid isomer were obtained.

(14) Allen, Eliot and Bell, *Can. J. Research*, **17**, 75 (1939).

When the experiment was repeated using stilbene, the yields of solid and liquid diastereomers of 2,3-diphenylbutane were 20 and 45%, respectively.

Nitration of the 2,3-Diphenylbutanes.—A stirred suspension of 0.11 g. (0.0005 mole) of 2,3-diphenylbutane (m. p. 124°) in 3 cc. of acetic anhydride was chilled to 0° while a nitrating mixture of 2 cc. of nitric acid (sp. gr. 1.52) and 2 cc. of acetic anhydride was added over a one-minute period. After fourteen hours the precipitate was filtered off, wt. 0.10 g. (65% of theoretical), m. p. 249°. When crystallized from 7 cc. of benzene this melted at 256°, same on recrystallization from benzene.

Anal. Calcd. for $C_{16}H_{16}N_2O_4$: C, 64.0; H, 5.37; N, 9.33. Found: C, 64.5; H, 5.37; N, 9.50.

The experiment was repeated using the liquid isomer. No precipitate appeared following the nitration, so the reaction mixture was poured into ice and water, and alkali was added to *p*H 6. The precipitate was taken up in ether; after evaporation the latter was crystallized from ethanol to yield a crude dinitrodiphenylbutane, m. p. 121–122° in 40% yield. This was recrystallized from ethanol to melt at 133°. None of the much less soluble high melting diastereomer, which is insoluble in the nitrating mixture, was detected in this latter nitration.

Anal. Calcd. for $C_{16}H_{16}N_2O_4$: C, 64.0; H, 5.37; N, 9.33. Found: C, 64.2; H, 5.31; N, 9.42.

Oxidation of the 2,3-Di-(*p*-nitrophenyl)-butanes.—Both of the dinitro compounds were recovered unchanged after boiling with potassium permanganate in acetic acid, but when 0.05 g. (0.00016 mole) of either dinitro compound was boiled in 1.5 cc. of acetic acid with 0.160 g. of chromic anhydride, a 90% yield of *p*-nitrobenzoic acid, m. p. 238–239°, was obtained and identified by mixed melting point.

Thanks are due Miss Joan Romeyn for carrying out the microanalyses reported here.

Summary

1. It has been found, contrary to previous reports, that the addition of alkali metals to stilbene gives a mixture of diasteromers.

2. When *s*-diphenylethanedisodium is treated with dimethyl sulfate a good yield of 2,3-diphenylbutane may be obtained.

3. The isomerization which results in a mixture of diastereomers is thought to occur chiefly when the organoalkali compound is characterized as the derivative and, therefore, the mixture of isomeric products is not indicative regarding configuration of the organometallic compound.

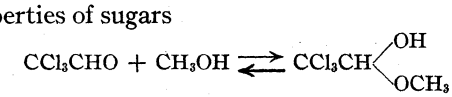
TORONTO, ONTARIO, CANADA RECEIVED MAY 4, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, No. 196]

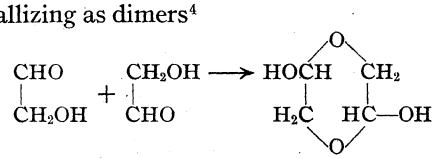
The Chemistry of the Tetrose Sugars. IV.[1] The Structure of a Methyl-*d*-erythroside.[2] The Mutarotation of *d*-Arabinose Oxime

BY ROBERT C. HOCKETT AND CARL W. MAYNARD, JR.[3]

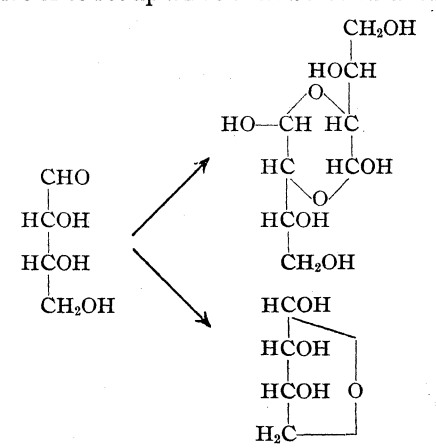
The universal affinity between carbonyl compounds and alcohols, which often impels the reversible formation of hemiacetals, underlies many of the most characteristic physical and chemical properties of sugars



Glycolaldehyde and the trioses manifest this affinity by *inter*molecular hemiacetal formation, crystallizing as dimers[4]



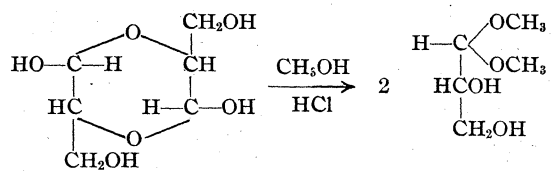
The pentoses and hexoses satisfy similar affinities by *intra*molecular addition of alcohol to aldehyde, yielding cyclic hemiacetals. The predilection in all these cases for a six-membered ring would render difficult a prediction whether the tetroses, on crystallizing, would tend rather to dimerize or to set up a five-membered furanose ring



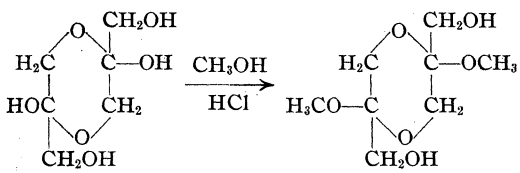
The observation that *l*-erythrose is monomeric in dilute aqueous solution[5] does not solve this question; the trioses are dissociated under like conditions.

On condensation of sugars with methanol containing hydrogen chloride, three types of behavior have been observed.

(1) The dimeric cyclic hemiacetal, glyceraldehyde, is converted into a monomeric open-chain dimethyl acetal



(2) The dimeric hemiacetal, dihydroxyacetone, is converted directly into the dimeric methyl glycoside[6]



(3) Finally, the more stable products obtained by such treatment of the monomeric inner hemiacetal, glucose, are the methyl pyranoside and the methyl furanoside.

Although isolation of a particular type of methyl derivative does not justify any conclusion regarding the preferred structure of the free sugar, it does provide *prima facie* evidence for the existence of the corresponding sugar form and provides some insight into the habits of the compound.

The first objective of the present study was to learn how *d*-erythrose would condense with meth-

(1) Number III of this series, THIS JOURNAL, **60**, 278 (1938).

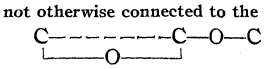
(2) This paper was read before the Division of Organic Chemistry at the Milwaukee meeting of the American Chemical Society, September, 1938. It is taken from a thesis submitted by Carl W. Maynard, Jr., to the Graduate School of the Massachusetts Institute of Technology in partial fulfilment of the requirements for the degree of Doctor of Philosophy in July, 1938.

(3) Cellulose Research Fellow during 1937–1938.

(4) Fischer and Taube, *Ber.*, **60**, 1704 (1927); *cf.* Bergmann and Miekeley, *ibid.*, **54**, 2152 (1921); *cf.* Fischer and Baer, *ibid.*, **63**, 174 (1930), for formulation as dioxane derivatives.

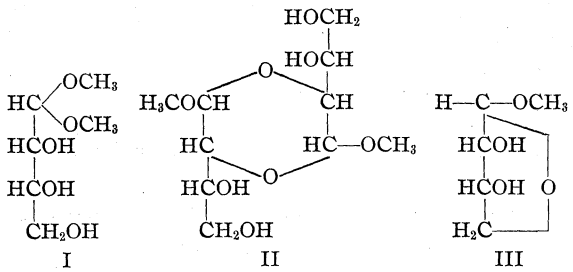
(5) Deulofeu, *J. Chem. Soc.*, 2973 (1932).

(6) We have not succeeded in finding anywhere an accurate definition of the term glycoside. The definition of Beilstein (Beil., Vol. XXXI, p. 11) is not valid since discovery of the true acetals of the higher sugars [Montgomery, Hann and Hudson, THIS JOURNAL, **59**, 1124 (1937)]. Our concept of a glycoloside provides that within such a compound a carbon atom be joined through oxygen to another carbon which is otherwise linked to the first and also through oxygen to a third carbon not otherwise connected to the first.



More concisely, a glycoside is a monocyclic mixed acetal. This definition includes the methyl glycoloside of Fischer and Baer[4] and analogous derivatives of the three-carbon sugars which are very similar in properties to the prototype, methyl glucoside. It excludes levoglucosan and arabinose dimethyl acetal, which are dicyclic and noncyclic, respectively.

anol containing 1% hydrogen chloride, the possible products being represented as follows[7]



I II III

To determine the structure of the product, both the methylation procedure and the method of cleavage oxidation[8] were employed (Fig. 2).

d-Erythrose diacetamide, obtained from *d*-arabinose by a modification of the Wohl degradation,[9] was hydrolyzed partially with sulfuric acid. The erythrose thus freed was treated with methanol containing about 1% hydrogen chloride and the methyl erythroside obtained was separated from the non-volatile nitrogenous compounds by distillation in a relatively high vacuum. On further methylation and oxidation with nitric acid, inactive dimethoxysuccinic acid was obtained, indicating that the product of condensation with methanol was a methyl-*d*-erythrofuranoside (III).

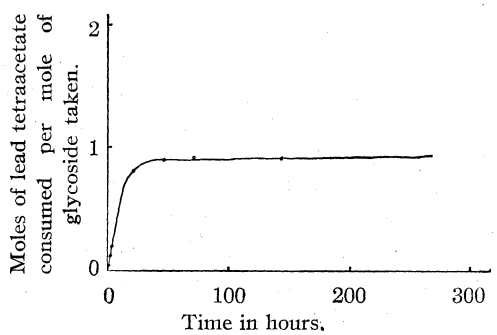


Fig. 1.—Oxidation of methyl-*d*-erythroside by lead tetraacetate.

This methyl-*d*-erythrofuranoside furnished us with a glycoside containing only two free hydroxyl groups, and those of known position and configuration, rendering possible a direct test of certain conclusions drawn by McClenahan and the senior author[8] from relatively indirect evidence, concerning the relative rates of oxidation of *cis* and *trans* glycols by lead tetraacetate. It was found that one mole of the glycoside consumes only one mole of this oxidant and that the rate of the reaction is the relatively rapid one found in the previous study to be characteristic of *cis* glycols (Fig. 1).

Moreover, after lead tetraacetate oxidation of this glycoside, the further action of strontium hypobromite yielded a crystalline salt closely resembling strontium D′-methoxydiglycolate. The latter was reported by Jackson and Hudson[8] and by McClenahan and Hockett[8] as a product of the action either of *excess* periodic acid or of lead tetraacetate (*two* moles) upon alpha-methyl-*d*-pentopyranosides, followed by treatment with strontium hypobromite. The present product showed the same composition and similar crystal habit, but differed optically, showing specific rotation $-8.94°$[13] as compared with a recorded value of $+55.0°$ for the beta and $-56.6°$[13] for the alpha isomer. This was considered evidence that our methyl-*d*-erythrofuranoside was a mixture containing about 58% of the alpha and 42% of the beta form (Fig. 2).

Data are included concerning the mutarotation of *d*-arabinose oxime and the hydrolysis of *d*-erythrose diacetamide by 0.100 *N* sulfuric acid (Table I and Fig. 3).

Experimental Part

***d*-Arabinose.**—This sugar was prepared from calcium gluconate by the procedure of Hockett and Hudson[10] modified for larger scale production.

***d*-Arabinose Oxime.**[5,11]—The method of preparation was almost the same as that described for *d*-xylose oxime.[12] The product crystallized readily from the reaction mixture, on cooling, in a yield of 86%. Recrystallized from about 70% ethanol as thin rectangular plates, washed with absolute ethanol, and dried at 50°, it showed m. p. 136–137° and rotated[13] $-13.5°$ at equilibrium (c, 2.0544; l, 2; H_2O).

The substance showed a mutarotation which was followed quantitatively. The change was found to be very nearly unimolecular.

Tetraacetyl-*d*-arabonic Nitrile.[11]—The *d*-arabinose oxime was acetylated using acetic anhydride and either fused sodium acetate or pyridine as the catalyst. In the former case, the procedure was just as described for *d*-xylose oxime,[12] dry dioxane being used as a diluent to prevent the reaction from becoming too vigorous In the second case 50 g. of pulverized oxime was suspended in 200 cc. of Eastman practical pyridine and 200 cc. of C. P. acetic anhydride

(7) *Cf.* Swan and Evans, THIS JOURNAL, **57**, 200 (1935); Felton and Freudenberg, *ibid.*, **57**, 1637 (1935).

(8) Jackson ond Hudson, THIS JOURNAL, **58**, 378 (1936); **59**, 994 (1937); Maclay and Hudson, *ibid.*, **60**, 2059 (1938); Hockett and McClenahan, *ibid.*, **60**, 2061 (1938); **61** 1667 (1939).

(9) Hockett, *ibid.*, **57**, 2265 (1935).

(10) Hockett and Hudson, THIS JOURNAL, **56**, 1632 (1934).

(11) *Cf.* Wohl, *Ber.*, **26**, 744 (1893); Ruff, *ibid.*, **31**, 1573 (1898).

(12) Hockett, THIS JOURNAL, **57**, 2265 (1935).

(13) All rotations quoted in this paper represent specific rotations of the D line of sodium at 20°; c is concentration in grams per 100 cc. of solution; and l is the tube length in decimeters.

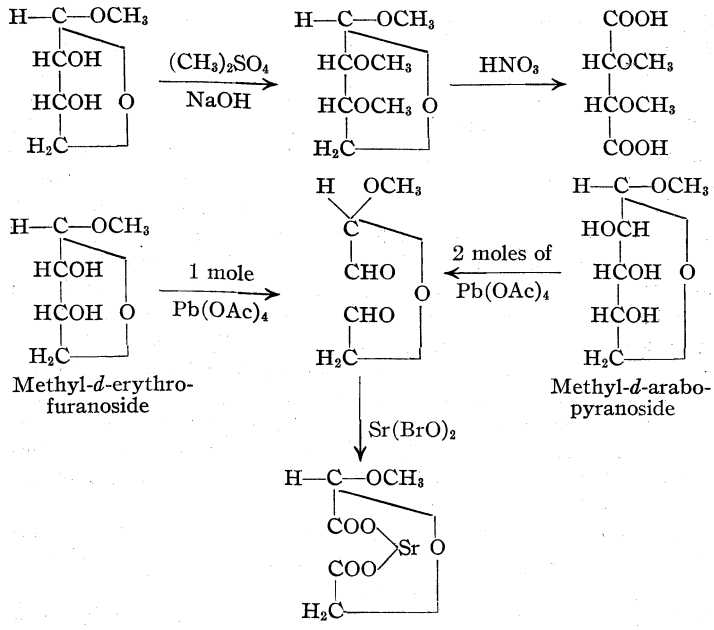


FIG. 2.

was added in three portions with cooling under the tap. The mixture was refrigerated overnight, warmed on a steam-bath for an hour, cooled, and poured upon about 500 g. of cracked ice. After refrigeration overnight, the precipitated gum had become a white solid which was washed free of pyridine with water and dried at 60° *in vacuo;* yield by either procedure, 63%. Recrystallized from absolute ethanol to constant properties, the compound melts 120–121° (corr.) and rotates −3.3° (*c*, 2.824; *l*, 2, $CHCl_3$).

Hydrolysis of *d*-Erythrose Diacetamide.—A sample of 2.0003 g. of purified *d*-erythrose diacetamide was dissolved to a volume of 50.0 cc. with 0.100 *N* sulfuric acid. This solution was poured into a 200-cc. flask submerged in a bath of rapidly boiling water and the time was noted. At noted intervals, the whole solution was cooled rapidly and its rotation read in a 4-dm. polarimeter tube. The results are represented by Fig. 3. The curve corresponds approximately to the unimolecular law; *k* (minutes and logarithms on base 10) = 0.0175. Hydrolysis was not yet complete after the last observation as demonstrated by the isolation of some unchanged *d*-erythrose diacetamide. The data could not be used to calculate a more reliable figure for the specific rotation of *d*-erythrose, owing to lack of a sample of pure sugar with which to standardize a method of estimating *d*-erythrose.[12]

***d*-Erythrose.**—Nine grams of *d*-erythrose diacetamide was heated for seventy-five minutes with 189 cc. of approximately 0.6 *N* sulfuric acid in a boiling water-bath (see Fig. 3). After concentration to about 50 cc., the solution was extracted with ether for eight hours in a continuous extractor to remove acetic acid. The aqueous layer was then treated with barium hydroxide solution to remove sulfuric acid quantitatively, decolorized with carbon, and filtered. The colorless filtrate was concentrated in a vacuum at less than 50°, to a thick sirup which was dried by distilling dry methanol from it.

TABLE I

MUTAROTATION OF *d*-ARABINOSE OXIME IN WATER

Concentration 0.5136 g. in 25.0 cc. solution; tube length 2 dm.; temperature 20 ± 0.5°.

Time after making soln., min.	$[\alpha]^{20}D$	$k_1 + k_2$
0	−84.0[14]	
6.9	−83.4	0.0006
14.9	−82.7	.0006
20.6	−81.75	.0007
21.7	−81.05	.0009
28.1	−80.0	.0009
53.1	−77.2	.0008
72.1	−74.7	.0009
104.1	−70.8	.0009
108.7	−70.0	.0009
128.8	−67.4	.0009
177.8	−60.7	.0010
196.8	−59.00	.0010
442.0	−37.1	.0011
589.7	−29.1	.0012
777.7	−23.2	.0011
897.5	−20.65	.0011
1,072.5	−17.90	.0011
1,169.5	−16.87	.0011
1,374.5	−15.17	.0012
	−13.50	

(14) Determined by extrapolation of the nearly straight line obtained by plotting log $(r_t - r_\infty)$ against time.

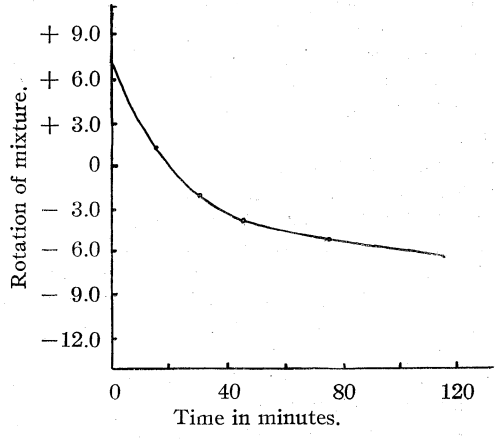


Fig. 3.—Hydrolysis of erythrose diacetamide by 0.1 *N* sulfuric acid.

Methyl-*d*-erythroside.—The erythrose described in the previous paragraph was dissolved in 100 cc. of a 1% solution of hydrogen chloride in dry methanol. The rotation in a 1-dm. tube immediately after homogenizing was −0.08°; this changed to −0.13° in about twenty minutes at room temperature and then remained constant, even though the solution was warmed on a steam-bath. The

power to reduce Fehling's solution disappeared during the same interval. The hydrogen chloride was removed with an excess of silver carbonate, and after filtration the solution was saturated with hydrogen sulfide and refiltered. The filtrate was concentrated under reduced pressure to a thick sirup. On reducing the pressure to 1–2 mm. and heating with an oil-bath, a light yellow liquid came over between 78–98° which showed a rotation[13] of −5.34° in chloroform (*c*, 3.372; *l*, 1), −5.93° in water (*c*, 3.372; *l*, 1), and $n^{20}D$ 1.5318. On another occasion, the distillate was collected in two portions, of which the first rotated −2.25° (*c*, 2.223; *l*, 2; $CHCl_3$) and the second was virtually inactive. The difference is likely due to varying proportions of the alpha and beta forms.

Dimethyl-methyl-*d*-erythroside.—An undistilled sample of methyl-*d*-erythroside weighing between 2 and 3 g. was washed with a little water into a 500-cc. three-necked flask, where, with vigorous mechanical stirring, it was treated first with 18 cc. of freshly distilled dimethyl sulfate and then with 80 cc. of 60% sodium hydroxide added very slowly drop by drop until the vigor of the reaction had slackened and then at an increased rate.[15] The mixture was warmed on a water-bath to 75° and treated with 32 cc. more of dimethyl sulfate added gradually. Finally the water-bath was maintained at boiling for half an hour. The solution was diluted with water, and extracted with 240 cc. of chloroform in four portions which were combined, dried with sodium sulfate, filtered and concentrated free from solvent. The product was distilled at 1–2 mm. with a bath temperature of 135–145°; yield, 0.194 g.

***meso*-Dimethoxysuccinic Acid.**—The 0.194 g. of dimethyl-methyl-*d*-erythroside was treated with 5 cc. of nitric acid (sp. gr. 1.2) at 85–90° for five hours. Freed from most of the nitric acid by distillation under reduced pressure, and redistillation after adding water, the resulting sirup crystallized rapidly on cooling. The large rosets, after recrystallization from a small volume of acetone and drying at 55°, weighed 0.189 g., melted from 146–152°,[16] and were inactive optically (*c*, 3.144; *l*, 2; H_2O).

Anal. Calcd. for $(COOH)_2C_2H_2(OCH_3)_2$: neut. equiv., 178; OCH_3, 34.83. Found: neut. equiv., 180; OCH_3, >31.85.

Strontium D′-Methoxy-diglycolate.—A sample of 0.83 g. (0.0062 mole) of freshly distilled methyl-*d*-erythroside was dissolved in 45 cc. of dried chloroform (calcium chloride) and stirred mechanically in a 250-cc. flask while 3.32 g. (0.0075 mole) of crystalline lead tetraacetate was added. Stirring was continued for one and one-half hours; then the nearly insoluble lead diacetate was removed by filtration and the chloroform was distilled out under reduced pressure. The residue, after solution in water, was treated with hydrogen sulfide to remove lead. After filtration and aeration, the solution was concentrated under reduced pressure to a sirup which was dried and freed from acetic acid by distilling sulfur-free toluene from the flask several times. The product was diluted to 125 cc. with water and treated with 7 g. strontium carbonate and 1 cc. of bromine in the dark at room temperature for twenty-four hours. The mixture was shaken several times during the first hour. The excess bromine was removed by aeration, the excess carbonate was filtered, soluble halides were removed with silver carbonate and, after filtration, silver was removed as the sulfide. After another filtration and aeration, and adjustment of the *p*H slightly to the alkaline side with strontium hydroxide, the solution was concentrated under reduced pressure to 5 cc. Alcohol was added to turbidity (between 2 and 3 cc.) and the solution refrigerated for an hour, whereupon a crop of fine white needles appeared, which were eventually filtered, washed with 50% alcohol and dried in air; yield 0.1085 g. These crystals showed a specific rotation[13] of −8.94° (*c*, 0.447; *l*, 2; H_2O). On addition of one molecular equivalent of 0.1 *N* hydrochloric acid, the rotation became too small to read. Since the beta form of strontium D′-methoxydiglycolate rotates +55.0° and the alpha form −56.6°, and the corresponding free acids, +11.9 and −11.5°, respectively, the particular sample of methyl erythroside employed evidently contained about 58% of the alpha isomer and 42% of the beta.

Anal. Calcd. for $C_5H_6O_6Sr \cdot 3H_2O$; H_2O, 17.8. Found: (loss in wt. at 105° *in vacuo*), 17.1. Calcd. for $C_5H_6O_6Sr$: Sr, 35.1. Found: Sr, 35.9.

Rate of Oxidation of Methyl-*d*-erythroside by Lead Tetraacetate.—A sample of 0.0923 g. (0.00069 mole) of distilled and dried methyl-*d*-erythroside was dissolved in a little less than 50 cc. of aldehyde-free glacial acetic acid in a 100-cc. glass-stoppered volumetric flask, brought to 20°, the time noted and 50.0 cc. of 0.1222 *N* lead tetraacetate solution in acetic acid was added. After making up to 100.0 cc. and mixing, the solution was placed in a 20° room. At intervals, 10-cc. samples were removed and the unconsumed lead tetraacetate estimated by the method of Hockett and McClenahan.[8] The results obtained are shown by Fig. 1. The reaction was very nearly monomolecular, the value of *k* being 0.025 (hours and logarithms on base 10).

Summary

1. *d*-Erythrose sirup has been obtained by the hydrolysis of *d*-erythrose diacetamide prepared from *d*-arabinose by a modification of the Wohl degradation.

2. *d*-Erythrose has been found to condense with methanol containing 1% hydrogen chloride in about twenty minutes at room temperature to give a mixture of α- and β-methyl-*d*-erythrofuranosides.

3. The methyl-*d*-erythrofuranoside mixture has been purified by vacuum distillation.

4. The methyl-*d*-erythrofuranoside mixture has been converted by methylation to dimethyl methyl-*d*-erythrofuranosides which are separated from other substances by high vacuum distillation.

5. Oxidation of the methyl-*d*-erythrofuranoside mixture with nitric acid yielded inactive dimethoxysuccinic acid, proving the presence and nature of the ring.

6. Oxidation of the methyl-*d*-erythrofuranoside

(15) West and Holden, THIS JOURNAL, **56**, 930 (1934).

(16) *Cf.* Purdie, *J. Chem. Soc.*, **79**, 957 (1901).

mixture with lead tetraacetate in chloroform followed by strontium hypobromite, yielded partially racemized strontium D-methoxy-diglycolate, proving independently the presence and nature of the ring and showing the proportion of alpha and beta forms in the mixture used.

7. The rate of oxidation of methyl-*d*-arabinofuranoside by lead tetraacetate, as well as the amount of oxidant consumed, have been found to be in close agreement with the predictions previously made for a substance of this structure.

8. The rate of hydrolysis of *d*-erythrose diacetamide by 0.100 *N* sulfuric acid has been measured.

9. The rate of mutarotation of *d*-arabinose oxime has been measured.

CAMBRIDGE, MASS. RECEIVED JUNE 2, 1939

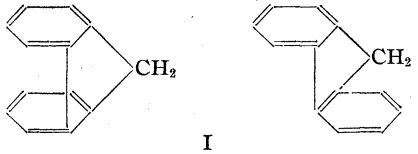
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF TRINITY COLLEGE]

The Structure of Fluorene

BY WARREN C. LOTHROP

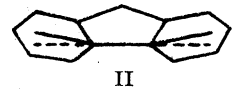
Although fluorene has been a familiar compound for many years, it has not excited the interest which has so enlarged our knowledge of the comparable tricyclic hydrocarbons anthracene and phenanthrene. Indeed a recent review of the chemistry of fluorene[1] indicates how little is known of its reactions and how much uncertainty still attaches to its structure.

Since 1925 when Kuhn and Jacob[2] proposed a space formula for fluorene (I) based on Kaufler's formula for diphenyl, in order to explain



I

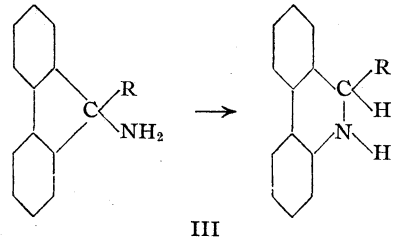
their claimed separation of two forms of 9-aminofluorene, there has been extensive investigation of the possibility of stereoisomerism of 9-substituted fluorenes. All such attempts have failed or been disproved,[3] so that the existence of such extreme forms as pictured in (I) seems unlikely if not impossible. Whether or not the two aromatic rings are inclined at a slight angle to the plane of the five-membered ring[4] cannot be stated with certainty yet, but the evidence does seem to indicate that the rings are bent away from the coaxial diphenyl bond with a distortion of the valence angles from the benzene rings by 12°,[5] to give a planar structure (II) as pictured by Pinck and Hilbert[6] where the five-membered ring is a nearly regular pentagon



II

This formula is probable from dipole measurements[5,7] and X-ray studies[8] and is further supported by the failure of fluorenone-4-carboxylic acid to close a fourth ring,[4a] the distance being too great to be bridged.

That such a planar configuration as (II) would be in a condition of some strain is to be anticipated and has been used[6] to account for the ready enlargement of the five-membered ring in the Stieglitz rearrangement of amines of the type (III) to yield phenanthridines:



III

It has been suggested further[5] that this internal strain could be relieved at least partially by a preferred arrangement of the double bonds according to the argument of Mills and Nixon[9] so that a definitely preferred bond structure (IV) should most nearly represent fluorene

(1) Rieveschl and Ray, *Chem. Rev.*, **23**, 287 (1938).

(2) Kuhn and Jacob, *Ber.*, **58**, 1432 (1925).

(3) Cook and Iball, *Chemistry & Industry*, 467 (1936), give a critical review of the stereochemistry of fluorene.

(4) (a) Mills, Palmer and Tomkinson, *J. Chem. Soc.*, **125**, 2365 (1924); (b) Iball, *Z. Krist.*, **94**, 397 (1936).

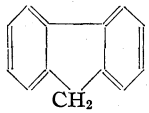
(5) Hughes, LeFèvre and LeFèvre, *J. Chem. Soc.*, 202 (1937).

(6) Pinck and Hilbert, THIS JOURNAL, **59**, 8 (1937).

(7) Bergmann, Engel and Hoffmann, *Z. physik. Chem.*, **17**, 92 (1932).

(8) Hengstenberg and Mark, *Z. Krist.*, **70**, 283 (1929).

(9) Mills and Nixon, *J. Chem. Soc.*, 2510 (1930).



IV

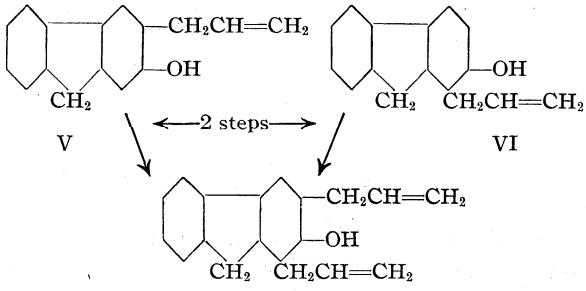
Auwers and co-workers[10] have given the only evidence as to the chemical nature of the double bonds and on the basis of refractive studies they declared that the aromatic rings of fluorene must be classed as similar to naphthalene and anthracene although they do not attempt a quantitative comparison. Others,[11] while not going as far, have distinguished fluorene from diphenyl by considering it as "quasi-aromatic" and more to be compared to dibenzocyclopentadiene. This view is disputed by Ruiz[12] and Mangini[13] with however little evidence aside from the special reactivity of fluorene at positions 2 and 7 which correspond to the active 4,4′-positions in diphenyl.

Evidence favoring formula IV is scant but may be found in the ring closures of γ-2-fluorylbutyric acid[14] and of *o*-(2-fluoryl)-benzoic acid[15] both of which take place into the 3-position. As similar ring closures in the case of 2-substituted naphthalene would be into the 1-position, analogy would seem to indicate that the double bond in fluorene is located entirely between positions 2 and 3 as shown in IV.

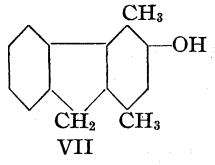
Another reaction indicating preference for position 3 may be found in the reported formation of 2,3-diacetofluorene,[16] while the special reactivity[17] of a bromine atom at 3 must have significance.

From the above discussion it is evident that the problem of the bond structure of fluorene is similar to that of naphthalene, anthracene, hydrindene and tetralin and like them should be susceptible to attack by the methods used by Fieser and Lothrop,[18] which depend on the Claisen rearrangement of allyl ethers and the diazo coupling of hydroxyl derivatives.

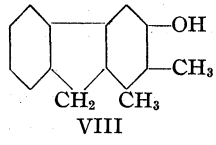
A preliminary investigation of the rearrangement of the allyl ethers of 2-hydroxyfluorene and 3-hydroxyfluorene gave ambiguous results. From the pyrolysis of the former, two isomeric substances were obtained corresponding undoubtedly to compounds V and VI, both of which yielded 1,3-diallyl-2-hydroxyfluorene on pyrolysis of their respective allyl ethers. This indicates apparently that the aromatic ring in fluorene is more benzenoid than naphthoid, for such behavior would be impossible in the latter case. Pyrolysis of the allyl ether of the previously unreported 3-hydroxyfluorene, however, yielded only an unworkable gum.



So that there might be no doubt regarding the chemical activity of a hydroxyl group in position 3, derivatives were synthesized by unambiguous methods in which both ortho positions were successively blocked by methyl groups. The allyl ethers of these test compounds (VII and VIII) rearranged smoothly and the free hydroxyfluorenes coupled readily in alkaline solution with diazotized aniline, proving conclusively that there is little or no fixation of the double bonds in the Mills–Nixon formulation (IV) and that fluorene



VII



VIII

is more like benzene, tetralin and hydrindene, than like naphthalene, anthracene and phenanthrene. The special reactivity of positions 2 and 7 is probably to be ascribed to the greater directive influence of the phenyl group as compared to the benzyl group, and the hydrocarbon is closely related to diphenyl although form IV may be favored slightly.

The preparation of the needed derivatives of 3-hydroxyfluorene was accomplished by the method employed originally by Ullmann and co-workers[19] for the preparation of 3-methoxyfluorenone. This consisted of the internal coupling of diazotized *o*-aminobenzophenone derivatives obtained

(10) Auwers and Frühling, *Ann.*, **422**, 220 (1920); Auwers and Krollpfeiffer, *ibid.*, **430**, 264 (1923).

(11) Goss and Ingold, *J. Chem. Soc.*, 1268 (1928); Anatakrishnan and Hughes, *ibid.*, 1607 (1935).

(12) Ruiz, *Añal. asoc. quìm. argentina*, (a) **16**, 170 (1928), (b) **17**, 42 (1929).

(13) Mangini, *Ricerca sci.*, **7**, I, No. 5–6 (1936).

(14) Koelsch, THIS JOURNAL, **55**, 3885 (1933).

(15) Barnett, Goodway and Watson, *Ber.*, **66**, 1876 (1933).

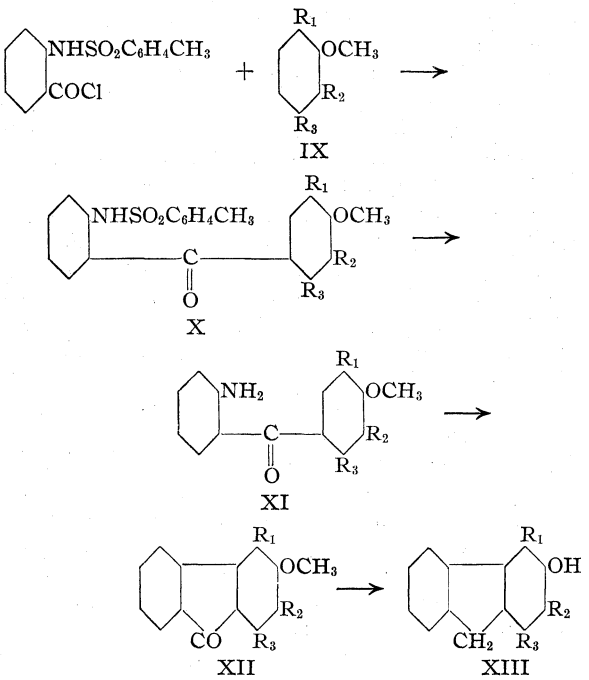
(16) Dziewonski and Kleszcz, *Roczniki Chem.*, **12**, 172 (1932); *cf.* ref. 1, p. 365.

(17) Miller and Bachman, THIS JOURNAL, **57**, 2443 (1935).

(18) Fieser and Lothrop, *ibid.*, (a) **57**, 1459 (1935); (b) **58**, 749, (c) 2050 (1936); (d) **59**, 945 (1937).

(19) Ullmann and Bleier, *Ber.*, **35**, 4273 (1902).

by sulfuric acid hydrolysis of the products formed in the Friedel–Crafts synthesis between the appropriate anisole derivative and the *p*-toluenesulfonamide of anthranilic acid chloride. Refluxing of acetic acid solutions of the resultant methoxyfluorenones with red phosphorus and hydriodic acid gave the desired hydroxyfluorenes directly, since demethylation and reduction were thus effected simultaneously. The general method is indicated below



Experimental Part

2-Hydroxyfluorene.—This compound was obtained in 57% yield from 2-aminofluorene by diazotization and subsequent hydrolysis as described by Ruiz.[12a] After treatment of its alkaline solution with norite and precipitation with acid, it was crystallized in white plates from 50% acetic acid, m. p. 169°.

2-Alloxyfluorene.—A solution of 8.5 g. of 2-hydroxyfluorene in 150 cc. of anhydrous acetone was refluxed for twenty-four hours with 7.7 g. of allyl bromide and 9.25 g. of finely powdered anhydrous potassium carbonate. A white solid product, completely insoluble in 1 *M* sodium hydroxide, was precipitated when the reaction mixture was poured into water; it was crystallized in gleaming white plates from dilute alcohol, m. p. 95–96°. The yield was 10.3 g. or 99%.

Anal. Calcd. for $C_{16}H_{14}O$: C, 86.44; H, 6.34. Found: C, 86.30; H, 6.38.

1-Allyl and 3-Allyl-2-hydroxyfluorene (VI and V).—Pyrolysis of 6.0 g. of 2-alloxyfluorene at 235–238° for five minutes gave a solid product, m. p. 83–84°, which was soluble in alkali but only with great difficulty. It was separated into two products by repeated fractional crystallization from petroleum ether. Compound A crystallized in fine, cream-colored needles, m. p. 87–88°, and represented about 60% of the whole. Compound B crystallized in thick, pale-brown needles, m. p. 111–112°, and represented about 25% of the material recovered.

By analogy with the melting points of pseudo-cumenol (m. p. 70°) and hemi-mellitenol (m. p. 81°) it seemed likely that Compound A was 3-allyl-2-hydroxyfluorene (V) and Compound B was 1-allyl-2-hydroxyfluorene (VI). This is in agreement with the preferred reactivity of position 3 previously cited; however, no proof of structure was attempted.

Anal. Calcd. for $C_{16}H_{14}O$: C, 86.44; H, 6.34. Found for A: C, 86.30; H, 6.18. Found for B: C, 86.16; H, 6.03.

The allyl ethers of both A and B were prepared without difficulty in 70–75% yields and were crystallized from 80% alcohol in nearly colorless plates. The allyl ether of A melted at 44–45° while that of B melted at 82–83°.

Anal. Calcd. for $C_{19}H_{18}O$: C, 87.00; H, 6.90. Found for allyl ether of A: C, 87.30; H, 7.12. Found for allyl ether of B: C, 87.12; H, 7.16.

1,3-Diallyl-2-hydroxyfluorene.—Pyrolysis of the allyl ethers of either A or B gave the same dark oil, which was purified by vacuum distillation, b. p. 170° at 3 mm. The distillate solidified in small clumps of fine yellow needles and crystallized from petroleum ether in fine, cream-colored needles, m. p. 58°.

Anal. Calcd. for $C_{19}H_{18}O$: C, 87.00; H, 6.90. Found: C, 86.96; H, 7.09.

3-Methoxyfluorenone (XII where R_1, R_2 and R_3 are H atoms).—This compound, described by Ullmann and Bleier,[19] was obtained as an orange-yellow solid, m. p. 92–94°, which was not purified further.

3-Hydroxyfluorene (XIII where R_1, R_2 and R_3 are H atoms).—A solution of 8.5 g. of the crude 3-methoxyfluorenone in 75 cc. of glacial acetic acid was refluxed for eighty hours with 1.0 g. of red phosphorus and 60 cc. of constant boiling hydriodic acid. The crude product dissolved in ether and filtered to remove excess phosphorus was extracted with small portions of cold, dilute alkali containing a trace of sodium hydrosulfite to remove iodine and any unreduced hydroxyfluorenone. This method served to eliminate the impurities without apparently effecting any loss of the much less acidic hydroxyfluorene, which was recovered as a white solid. It was crystallized from dilute alcohol in cream-colored plates, m. p. 136–137°. The yield was 4.9 g. or 66%. The **benzoate** crystallized from dilute alcohol in fine plates, m. p. 128°.

Anal. Calcd. for $C_{13}H_{10}O$: C, 85.66; H, 5.54. Found: C, 85.36; H, 6.14. Calcd. for $C_{20}H_{14}O_2$ (benzoate): C, 83.89; H, 4.92. Found: C, 83.52; H, 5.27.

2-(4-Toluenesulfonamido)-benzoyl Chloride.—The acid chloride was prepared from anthranilic acid as described by Miller and Bachman.[17]

2,5 - Dimethyl - 4 - methoxy - 2′ - (4 - toluenesulfonamido)-benzophenone (X where R_1 and R_3 are CH_3 groups and R_2 is a H atom).—To a vigorously stirred mixture of 20.4 g. of powdered aluminum chloride and 45.5 g. of the above acid chloride in 200 cc. of carbon disulfide, 20.0 g. of the methyl ether of *p*-xylene[18c] was added drop-

wise at room temperature, and the resulting dark red complex gradually warmed on the steam-bath. Refluxing was continued for six hours and the reaction allowed to stand overnight. Treatment of the mixture in the usual manner gave 4.2 g. of unchanged methoxyxylene and a white product which crystallized well from 600 cc. of 95% alcohol after treatment with norite. The yield of thick, pale yellow blades, m. p. 140–141°, was 35.0 g. or 71%.

Anal. Calcd. for $C_{23}H_{23}O_4NS$: C, 67.45; H, 5.67; N, 3.42. Found: C, 67.03; H, 5.69; N, 3.52.

The corresponding **methylamine** derivative was prepared in 99% yield by treatment of an alkaline solution of the above compound with dimethyl sulfate. It crystallized in gleaming white plates from alcohol, m. p. 168–169°.

Anal. Calcd. for $C_{24}H_{25}O_4NS$: C, 68.08; H, 5.95; N, 3.31. Found: C, 68.55; H, 6.34; N, 3.16.

2,5-Dimethyl-4-methoxy-2′-aminobenzophenone (XI where R_1 and R_3 are CH_3 groups and R_2 is H).—When 12 g. of the above sulfonamide was mixed with 35 cc. of concentrated sulfuric acid a clear red solution resulted in a few hours but reaction was complete only after three days of standing at room temperature. The mixture was poured into excess ammonia and the product filtered and crystallized from dilute alcohol in bright yellow needles, m. p. 102–104°. The yield was 7.5 g. or 99%.

Anal. Calcd. for $C_{16}H_{17}O_2N$: C, 75.27; H, 6.70; N, 5.48. Found: C, 74.97; H, 6.46; N, 5.46.

1,4-Dimethyl-3-methoxyfluorenone (XII where R_1 and R_3 are CH_3 groups and R_2 is H).—Several trials indicated that while this compound could be obtained in one step by the diazotization of the diluted sulfuric acid hydrolysis solution of the above amine in the manner described by Ullmann and Bleier,[19] the yields were low (36%) and the product difficult to purify. The most satisfactory results were obtained when the crude aminobenzophenone (7.5 g.) was dissolved in 1 liter of cold water containing 260 cc. of concentrated hydrochloric acid and treated with 8.0 g. of sodium nitrite. The clear orange solution was filtered, warmed on the steam-bath for five hours, and the bright yellow product which separated was recovered by filtration. It was three times extracted by suspension at 100° in 50-cc. portions of 3 *N* potassium hydroxide and after thorough washing with water crystallized from dilute alcohol in bright yellow needles, m. p. 140–141°. The yield was 5.85 g. or 84%.

Anal. Calcd. for $C_{16}H_{14}O_2$: C, 80.64; H, 5.92. Found: C, 80.78; H, 6.12.

2,5-Dimethyl-4-methoxy-2′-hydroxybenzophenone.—Acidification of the alkaline extracts above gave a substance which crystallized from alcohol in yellow prisms, m. p. 94–95°, and which weighed 0.1 g. Its **acetate** crystallized from alcohol in white prisms, m. p. 81–82°.

Anal. Calcd. for $C_{16}H_{16}O_3$: C, 74.99; H, 6.28. Found: C, 75.17; H, 6.65. Calcd. for $C_{18}H_{18}O_4$(acetate): C, 72.50; H, 6.07. Found: C, 72.45; H, 6.34.

1,4-Dimethyl-3-hydroxyfluorenone.—This compound was a product of incomplete reduction in the reaction described below, or could be obtained directly by the demethylation of its methyl ether with 48% hydrobromic acid. It crystallized from glacial acetic acid in fine, brilliant yellow needles, m. p. 223–224°, and gave an intensely red solution in alkali. The **acetate** separated from dilute acetic acid in pale yellow needles, m. p. 133–134°.

Anal. Calcd. for $C_{15}H_{12}O_2$: C, 80.36; H, 5.40. Found: C, 80.62; H, 5.75. Calcd. for $C_{17}H_{14}O_3$(acetate): C, 76.67; H, 5.29. Found: C, 76.72; H, 5.69.

1,4-Dimethyl-3-hydroxyfluorene (VII).—A solution of 3.9 g. of 1,4-dimethyl-3-methoxyfluorenone in 125 cc. of glacial acetic acid was refluxed for sixteen hours with 30 cc. of hydriodic acid (b. p. 127°) and 0.5 g. of red phosphorus. The product was recovered and purified in the manner already described for 3-hydroxyfluorene, being finally crystallized from ligroin in long, flesh colored needles, m. p. 180–181°. The yield was 2.58 g. or 87%. The acetate crystallized from alcohol in cream-colored plates, m. p. 100°.

Anal. Calcd. for $C_{15}H_{14}O$: C, 85.70; H, 6.71. Found: C, 85.69; H, 6.72. Calcd. for $C_{17}H_{16}O_2$(acetate): C, 80.94; H, 6.38. Found: C, 81.28; H, 6.45.

1,4-Dimethyl-2-benzeneazo-3-hydroxyfluorene.—When an alkaline solution of 0.1 g. of the hydroxyfluorene above in 10 cc. of 2 *N* sodium hydroxide and 5 cc. of water was treated at 0° with a slight excess of a freshly prepared solution of benzene diazonium chloride, an orange-brown precipitate immediately appeared. It was crystallized from glacial acetic acid in fine brown needles, m. p. 183–184°.

Anal. Calcd. for $C_{21}H_{18}ON_2$: C, 80.24; H, 5.76. Found: C, 80.34; H, 5.59.

1,4-Dimethyl-3-alloxyfluorene.—A mixture of 1.1 g. of (VII), 1.0 g. of powdered anhydrous potassium carbonate and 0.7 g. of allyl bromide in 25 cc. of acetone, was refluxed for forty-five hours and poured into water. The oily product was recovered by ether extraction and crystallized from dilute alcohol in fine white needles, m. p. 54–55°. The yield was 1.06 g. or 82%.

Anal. Calcd. for $C_{18}H_{18}O$: C, 86.40; H, 7.23. Found: C, 86.68; H, 7.29.

1,4-Dimethyl-2-allyl-3-hydroxyfluorene.—This compound was obtained in 62% yield by the pyrolysis of the above alloxyfluorene under nitrogen at 215°. It was difficultly soluble in alkali and crystallized from glacial acetic acid in nearly colorless plates, m. p. 150–151°.

Anal. Calcd. for $C_{18}H_{18}O$: C, 86.40; H, 7.23. Found: C, 86.66; H, 7.34.

vic-*o*-Xylenol Methyl Ether (IX where R_1 is H and R_2 and R_3 are CH_3 groups).—Several different attempts showed that this compound may be prepared best from 2-amino-3-methylanisole[20] by its conversion into 2-bromo-3-methylanisole[21] and subsequent treatment of the Grignard reagent of the latter with dimethyl sulfate. The yields for the last two procedures, however, were improved materially. In the Sandmeyer reaction the cuprous bromide solution was added at 0° instead of 60° and the diazonium complex allowed to decompose by standing at room temperature for two hours. The yield of product, b. p. 122–127° at 18 mm., m. p. 37–38°, was 80% compared with the reported 44%.[21]

(20) Gibson, *J. Chem. Soc.*, **123**, 1269 (1923); Hodgson and Beard, *ibid.*, **127**, 498 (1925).

(21) Short, Stromberg and Wiles, *ibid.*, 319 (1936).

The conversion of the bromide into the desired xylenol methyl ether was effected in 79% yield by the use of two moles of dimethyl sulfate instead of one[21] and subsequent treatment as described elsewhere.[22] The over-all yield from 118 g. of *m*-cresol was 26.3 g. of vic-*o*-xylenol methyl ether.

The preparation of the compounds listed below was accomplished by procedures exactly like those recorded above; therefore repetition of details is omitted.

2,3 - Dimethyl - 4 - methoxy - 2′ - (4 - toluenesulfonamido)-benzophenone (X where R_2 and R_3 are CH_3 groups and R_1 is H).—Was obtained from alcohol in 33% yield as nearly colorless needles, m. p. 136–138°.

Anal. Calcd. for $C_{23}H_{23}O_4NS$: C, 67.45; H, 5.67; N, 3.42. Found: C, 67.43; H, 5.90; N, 3.50.

The corresponding **methylamine** derivative was prepared with difficulty due to the great insolubility of the above sulfonamide in alkali. It crystallized from dilute alcohol in white needles, m. p. 160°.

Anal. Calcd. for $C_{24}H_{25}O_4NS$: C, 68.08; H, 5.95; N, 3.31. Found: C, 68.05; H, 6.25; N, 3.37.

2,3 - Dimethyl - 4 - methoxy - 2′ - aminobenzophenone (XI where R_2 and R_3 are CH_3 groups and R_1 is H).—This was obtained in 95% yield and crystallized from dilute alcohol in pale yellow needles, m. p. 144–145°.

Anal. Calcd. for $C_{16}H_{17}O_2N$: C, 75.27; H, 6.70; N, 5.48. Found: C, 75.58; H, 7.05; N, 5.29.

1,2-Dimethyl-3-methoxyfluorenone (XII where R_2 and R_3 are CH_3 groups and R_1 is H) was obtained in 63% yield by the use of much larger volumes of solutions due to the extreme insolubility of the amine hydrochloride. It crystallized from glacial acetic acid in brilliant yellow needles, m. p. 178–179°.

Anal. Calcd. for $C_{16}H_{14}O_2$: C, 80.64; H, 5.92. Found: C, 80.90; H, 6.22.

2,3-Dimethyl-4-methoxy-2′-hydroxybenzophenone was formed as a by-product in the above reaction to the extent of 10%. It separated from dilute alcohol in yellow prisms, m. p. 135–136°. Its **acetate** also crystallized from dilute alcohol in white prisms m. p. 97–98°.

Anal. Calcd. for $C_{16}H_{16}O_3$: C, 74.99; H, 6.28. Found: C, 74.79; H, 6.50. Calcd. for $C_{18}H_{18}O_4$(acetate): C, 72.50; H, 6.07. Found: C, 72.80; H, 6.35.

(22) *Org. Syntheses*, **11**, 66 (1931).

1,2 - Dimethyl - 3 - hydroxyfluorenone.—This compound separated from acetic acid in orange needles, m. p. 258–259° dec. The **acetate** was obtained from the same solvent in long yellow needles, m. p. 137–138°.

Anal. Calcd. for $C_{15}H_{12}O_2$: C, 80.36; H, 5.40. Found: C, 80.36; H, 5.59. Calcd. for $C_{17}H_{14}O_3$(acetate): C, 76.67; H, 5.29. Found: C, 76.99; H, 5.48.

1,2-Dimethyl-3-hydroxyfluorene (VIII), formed in 74% yield was obtained in fine white needles from benzene–ligroin, m. p. 212–213° dec. The **acetate** separated from dilute acetic acid in white needles, m. p. 146–147°.

Anal. Calcd. for $C_{15}H_{14}O$: C, 85.70; H, 6.71. Found: C, 85.82; H, 6.98. Calcd. for $C_{17}H_{16}O_2$(acetate): C, 80.94; H, 6.38. Found: C, 81.22; H, 6.68.

1,2 - Dimethyl - 4 - benzeneazo - 3 - hydroxyfluorene.—The extreme insolubility of the hydroxyfluorene in alkali at 0° necessitated the addition of 5 cc. of dioxane. The coupling product crystallized from glacial acetic acid in fine clusters of brown needles, m. p. 201° dec.

Anal. Calcd. for $C_{21}H_{18}ON_2$: C, 80.24; H, 5.76. Found: C, 80.32; H, 6.02.

1,2-Dimethyl-3-alloxyfluorene was obtained in 76% yield from alcohol as white plates, m. p. 102–103°.

Anal. Calcd. for $C_{18}H_{18}O$: C, 86.40; H, 7.23. Found: C, 86.62; H, 7.56.

1,2-Dimethyl-4-allyl-3-hydroxyfluorene.—Pyrolysis of the above allyl ether at 230° gave a yield of 78% of pale yellow needles, m. p. 135–136°, from glacial acetic acid.

Anal. Calcd. for $C_{18}H_{18}O$: C, 86.40; H, 7.23. Found C, 86.44; H, 7.53.

Summary

Methods which have been useful for the location of double bonds in other aromatic hydrocarbons have been applied to fluorene, with the result that the latter may be said to be benzenoid rather than naphthoid. Fluorene has been found to possess no considerable fixation of bonds as might be expected if the Mills–Nixon effect were operating and it is suggested that the special reactivity of positions 2 and 7 may be ascribed to the superior directive properties of the phenyl group.

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Native Lignin[1] I. Its Isolation and Methylation

BY F. E. BRAUNS

The experiments reported in the present paper deal with isolated native lignin. Inasmuch as the term "native lignin" has very often been misused in the lignin literature, its meaning in the present investigation is explained briefly. It is a general belief that lignin as it occurs in the plant material is insoluble in organic solvents and cannot be extracted by them without the use of a mineral acid as a catalyst. It is true that it occasionally has been noted that, on extraction of wood with alcohol, some lignin goes into solution. It seems that Klason[2] isolated a product by hot alcohol extraction which he considered to be lignin, but he did not even carry out a test for the presence of methoxyl groups in his product. Moreover, Freudenberg[3] has observed that on extraction of wood with hot alcohol–benzene some low molecular members of the lignin series are removed along with the resins, but the quantity was so small that he discarded the fraction. On the other hand, Hägglund,[4] in his "Holzchemie," says: "The native lignin of the wood is not soluble in organic solvents without the addition of acids." There is little doubt that the principal part of the lignin can be isolated from wood only by the use of strong mineral acid, cuprammonium hydroxide, or by organic solvents in the presence of mineral acids. In the method where alcohols are used without mineral acids,[5] high temperatures (up to 185°) must be applied; the lignin obtained on distillation of the solvent is a black pitchlike product and can no longer be considered identical with native lignin.

Native or unaltered lignin can be obtained only if one can succeed in isolating it by the use of an indifferent solvent and without the application of an elevated temperature. The present investigation deals with the isolation of such a lignin. It has been found during the last fifteen years that a large number of lignin preparations are soluble in methyl or ethyl alcohol and that almost all, except those prepared by extraction of the cellulose with mineral acids, are also soluble in dioxane. If lignin is to be extracted in an unchanged state, these solvents should be the most suitable ones. Furthermore, it has been found possible to extract a small amount (about 2 to 3%) of the lignin present in wood by using such solvents without the application of a high temperature. *The term "native lignin," therefore, means a lignin isolated in such a way that the solvent does not react with the lignin or alter it in any way.*

When sprucewood meal is allowed to stand for three to four days in 96% ethyl alcohol and is then filtered and the clear light brown filtrate evaporated under reduced pressure, a resinous residue is obtained which is washed with distilled water and ether. With the removal of the resins by the ether, the native lignin is obtained as a very finely divided light cream-colored powder, which is precipitated repeatedly from its solution in dioxane into ether until a constant methoxyl content is obtained. This powder gives the typical lignin color reactions: a deep purple with phloroglucinol and hydrochloric acid and a bluish-green with phenol and hydrochloric acid. The native lignin has a methoxyl content of 14.8%. This seems to be low, considering that the methoxyl content of lignin as it occurs in wood has always been assumed to be about 17.3%; furthermore, it is a well-known fact that the methoxyl content of sprucewood lignin, isolated according to Klason, Willstätter, or Freudenberg, varies between 14.5 and 17%, depending upon the conditions of preparation. A methoxyl content of about 17% has been calculated also for spruce lignin by Fuchs[6] from the lignin and the methoxyl contents of the wood, on the obviously incorrect assumption that all the methoxyl in the wood is combined with the lignin. It has been shown by Ritter and his coworkers,[7] and more recently by Hägglund and Sandelin,[8] however, that 0.56% of the total methoxyl content (4.6%) in sprucewood is attached to carbohydrate material. When this part was taken into consideration, Hägglund[4]

(1) Presented in part at the Baltimore meeting of the American Chemical Society, April, 1939. This is the first of a series of papers on this subject; future papers will clarify many of the points raised herein.

(2) Klason, "Beiträge zur Kenntnis der chemischen Zusammensetzung des Fichtenholzes," Berlin, 1911, pp. 34–36.

(3) Freudenberg, *et al.*, *Ber.*, **69**, 1415 (1936).

(4) Hägglund, "Holzchemie," Leipzig, 1939, p. 205.

(5) Aronovsky and Gortner, *Ind. Eng. Chem.*, **28**, 1270 (1936).

(6) Fuchs, "Die Chemie des Lignins," Berlin, 1926, p. 76.

(7) Kurth and Ritter, THIS JOURNAL, **56**, 2720 (1934); Ritter and Barbour, *Ind. Eng. Chem., Anal. Ed.*, **7**, 238 (1935); Harris, Sherrard and Mitchell, THIS JOURNAL, **56**, 889 (1934).

(8) Hägglund and Sandelin, *Svensk Kem. Tid.*, **46**, 83 (1934).

(pp. 199, 299) calculated a methoxyl content of 14.8% for lignin. This is exactly the amount found during this investigation.

The first questions to be answered are, of course: "Is this native lignin really lignin, or is it some other methoxyl-containing constituent of the wood, and to what extent is this part of the lignin identical with the principal part of the lignin in wood?" The color reaction with phloroglucinol and hydrochloric acid is not decisive, for there are many other compounds in wood which give the same reaction. In a very recent article Wiechert[9] claims to have shown that this coloration, at least as far as beech lignin is concerned, has no relation to the lignin. Without going into further details, it can be asserted positively that this phloroglucinol color reaction is typical at least of spruce lignin[10]; the mechanism of this reaction is the subject of an investigation now in progress.

There are two other typical lignin reactions—the reactions of lignin with phenol and with thioglycolic acid. The isolated native lignin condenses with phenol in the presence of hydrochloric acid with the formation of a phenol lignin having a methoxyl content of 11.5% which is identical with the same derivative prepared from Willstätter or Freudenberg lignin.[11] Inasmuch as Willstätter lignin is obtained in nearly quantitative yield and the two phenol lignins are apparently identical, it would seem that isolated native lignin has the same chemical properties as the total lignin in the wood. This is further shown by the preparation of the thioglycolic acid derivative of the isolated native lignin with a methoxyl content of 10.5%. This content is in agreement with that found by Holmberg[12] for a tetrathioglycolic acid lignin from sprucewood which is obtained in an almost quantitative yield, but about 1% lower than that found by Ahlm and Brauns.[13] To what extent the phenol and the thioglycolic acid derivatives of the isolated native lignin are identical with corresponding lignin derivatives obtained directly from wood in a quantitative yield will be shown later. If it is possible to prove that this native lignin behaves chemically in a manner similar in every respect to the total lignin, it is obviously an ideal product for a chemical study of the lignin problem.

(9) Wiechert, *Papier-Fabr.*, **37**, 17, 30 (1939).
(10) Brauns and Brown, *Ind. Eng. Chem.*, **30**, 779 (1938).
(11) Buckland, Brauns and Hibbert, *Can. J. Research*, **13B**, 61 (1935).
(12) Holmberg, *Ing. Vetenskaps Akad. Handl.*, **103**, 64 (1930).
(13) Ahlm and Brauns, THIS JOURNAL, **61**, 277 (1939).

The first experiment carried out with the isolated native lignin was the action of 42% hydrochloric acid and of 72% sulfuric acid. In preliminary experiments it was found that in both cases about 5 to 8% of the lignin could not be recovered. Native lignin gives with supersaturated hydrochloric acid a bright emerald-green color similar to that observed at the beginning of the preparation of Willstätter spruce lignin; with native lignin the green color is much brighter (purer) and lasts much longer than with wood meal. A part of the lignin dissolves in the hydrochloric acid, and it can be recovered from the filtrate on evaporation.

With 72% sulfuric acid a bluish-green coloration appears at the beginning, lasts only a short time, and soon changes to black. From the clear, colorless filtrate of the sulfuric acid treatment, after removal of the acid with barium carbonate, a white, crystalline product is obtained. The ease with which it crystallizes and the fact that it is optically inactive indicate that it is not a carbohydrate, even though it reduces Fehling solution quite strongly. A further investigation of this crystalline product is in progress. The behavior of the native lignin after treatment with mineral acids resembles that of Willstätter and Klason lignins. The methoxyl contents of these lignins vary from 15.2 to 16%, the same range as that given in the literature for those lignins isolated directly from sprucewood by these methods in a quantitative yield.

The presence of free hydroxyl groups in the native lignin is shown by its acetylation and methylation. With pyridine and acetic anhydride an acetylated native lignin is obtained having a methoxyl content of 11.8%.

Methylation of native lignin with diazomethane in anhydrous dioxane solution gives a partially methylated, nearly white lignin, with a methoxyl content of 21.4%. However, when the methylation with diazomethane is carried out with a suspension of the dry product in anhydrous ether, the methylation seems to stop at about 18.3%, but on further methylation in dioxane solution a final methoxyl content of 21.4% is obtained. The product with 18.3% methoxyl is completely soluble in dilute sodium hydroxide solution, indicating that an acidic hydroxyl group in the lignin molecule is still free; if the lignin were in part completely methylated and in part completely unmethylated, only a portion would be alkali solu-

ble. It should be noted that this partially diazomethane-methylated native lignin still gives the bright purple color reaction with phloroglucinol and hydrochloric acid, whereas on complete methylation with diazomethane this color fails to appear.

A quantitative yield of a lignin with the same methoxyl content (21%) is also obtained when sprucewood meal is methylated with diazomethane and the lignin is isolated according to Klason with 72% sulfuric acid.[10] When the diazomethane-methylated native lignin is treated with 72% sulfuric acid under the same conditions as those used in the Klason method, a partially methylated Klason lignin with a methoxyl content of 21.15% is obtained, which has the same appearance as that isolated directly from diazomethane-methylated sprucewood. The experiment with the methylated native lignin and 72% sulfuric acid has not been followed quantitatively; it is therefore possible, or even probable, that in this case, as in the experiment with the unmethylated native lignin, a small fraction is split off the lignin. A larger amount of the diazomethane-methylated product has been prepared, and an investigation of the fraction split off will soon be started.

A spruce lignin with a methoxyl content of about 21% is also obtained when Willstätter or Freudenberg lignin is methylated in cyclohexanol suspension with diazomethane.[14] As these lignins are isolated in a nearly quantitative yield, it shows that the isolated native lignin, on methylation with diazomethane, behaves in the same way as the lignin which remains in the wood after extraction of the soluble native lignin.

The diazomethane-methylated native lignin still has some free hydroxyl groups, as acetylation with pyridine and acetic anhydride gives an acetylated, partially methylated native lignin with a methoxyl content of 18.9%.

When sprucewood meal is extracted with methanol, using 2% hydrochloric acid as a catalyst, so-called methanol lignin is obtained.[15] By using other alcohols, such as ethyl, butyl, or amyl in the presence of hydrochloric acid, it is found that lignin forms condensation products with these alcohols. In the case of methanol, the reaction could not immediately be established, since the lignin itself contains methoxyl groups. As a matter of fact, when Friedrich[16] first prepared his so-called "primary lignin" by hydrolysis of wood with hydrochloric acid followed by extraction with ethyl alcohol, he believed that native spruce lignin had a methoxyl content of approximately 21%. Hägglund and Urban[15c] later ascertained the presence of ethoxyl groups in Friedrich's "primary lignin."

It was therefore of interest to determine whether isolated native lignin would react with alcohols in the presence of hydrochloric acid. When native lignin is dissolved in methanol, a yellow-brown solution is obtained which, on addition of a solution of anhydrous hydrochloric acid in absolute methanol, immediately turns to a deep wine-red, indicating that a reaction takes place almost instantly. When the concentration of the hydrochloric acid is so chosen that a 2% methanol solution is used and the solution refluxed for four to five hours, about 35% of the lignin separates out as a resin, which is insoluble in dioxane. Its methoxyl content is 20.85%. From the methanol solution a methanol lignin with a methoxyl content of 21.5% is isolated. This methoxyl content agrees exactly with that of methanol lignin prepared under the same conditions directly from sprucewood.[15] The large amount of polymerized methanol lignin formed is undoubtedly due to the relatively high concentration of hydrochloric acid, for when a concentration of only 0.5% is used the same change in color of the solution occurs, but all the lignin remains in solution; the methoxyl content of the isolated methanol lignin in this case is 20.9% and does not change when the treatment with 0.5% methanol–hydrochloric acid is repeated. This observation is in direct contradiction to an experiment recently reported by Hibbert and co-workers,[17] in which it is claimed that "an acetylated, carefully purified oak lignin (8.7% OCH_3, 35% $COCH_3$) [is] reconverted into its primary building units by refluxing it with anhydrous ethanol containing 2% hydrogen chloride." The methoxyl content of this oak lignin, calculated on the acetyl-free lignin, is then about 13.5%, a rather low content for an oak lignin, for which a methoxyl content of 21.8% is given in the literature[4] (p. 229). The discrepancy between the behavior of isolated native spruce lignin and

(14) Brauns and Hibbert, *Can. J. Research*, **13B**, 78 (1935).

(15) (a) Klason, *Tek. Tid., Avd. Kem.*, **23**, 55 (1893); (b) Holmberg and Runius, *Svensk Kem. Tid.*, **37**, 89 (1925); (c) Hägglund and Urban, *Cellulosechem.*, **8**, 69 (1927); **9**, 49 (1928); (d) Brauns and Hibbert, *Can. J. Research*, **13B**, 28 (1935).

(16) Friedrich and Diwald, *Monatsh.*, **46**, 31 (1925); Friedrich and Brüda, *ibid.*, **46**, 600 (1925).

(17) Peniston, McCarthy and Hibbert, THIS JOURNAL, **61**, 530 (1939).

Hibbert's acetylated oak lignin toward alcohol and hydrogen chloride can be explained only by the fact that the latter was decomposed in its preparation, as is shown by its low methoxyl content. The fact that a part of the native lignin becomes insoluble when treated with a 2% methanol–hydrogen chloride solution may also explain the assumption made by Hägglund[4] (p. 190) that a condensation of the lignin takes place in the solid phase through the mineral acid and for this reason not all the lignin can be extracted in such a way from the wood.

The question now arises as to how methanol and alcohols in general react with lignin in the presence of mineral acids. It has generally been assumed that in this reaction an oxygen ring, such as the furan or pyran ring, is opened with the formation of a new alkoxyl group and a new hydroxyl group. Hägglund and Urban,[15c] using butyl and amyl alcohols, agree with the opinion of Holmberg and Runius[15b] that these so-called alcohol lignins are probably acetals and that, on a basis of a molecular weight of approximately 400 for lignin, a half-acetal is formed[4] (p. 190). It will be pointed out later that, on a basis of a molecular weight of 840, a true acetal is obtained. If the alcohol is bound in an acetal-like manner, it should be possible to split off these groups with acids. When methanol lignin from isolated native lignin is treated with 72% sulfuric acid according to Klason, the methoxyl content decreases from 20.9 to 16.4% (which is the methoxyl content of Klason lignin from sprucewood); in other words, those methoxyl groups introduced by the treatment with methanol and hydrochloric acid are split off again. This is an experimental support for Hägglund's and Holmberg's assumption that in the reaction of alcohols with lignin in the presence of acids acetal-like compounds are formed.

Methanol lignin prepared directly from sprucewood is soluble in sodium hydroxide solution[15b] and can be acetylated or methylated. The same is true of methanol lignin from isolated native lignin. In both cases acetylated or partially methylated methanol lignins, which are insoluble in caustic soda solution, are obtained. The acetylated product has a methoxyl content of 16.9%, the diazomethane-methylated product 25.36%, and the corresponding derivative prepared directly from spruce[15d] 24.9%. A partially methylated lignin with a methoxyl content of 24.4% is obtained when the diazomethane-methylated native lignin is treated with methanol and hydrochloric acid. On remethylation of this product with diazomethane, the methoxyl content increases to 25.45% or to the same value as that of diazomethane-methylated methanol lignin. In other words, isolated native lignin gives partially methylated lignin derivatives with the same methoxyl content regardless of whether it is first methylated with diazomethane and then treated with methanol and hydrochloric acid, or whether this process is reversed.

On further methylation of the diazomethane-methylated native lignin and of the methanol native lignin, two different lignin derivatives fully methylated with regard to dimethyl sulfate are obtained, the first with a methoxyl content of 31.3% and the second with a methoxyl content of 33.0%.

Formulas for Lignin and its Derivatives

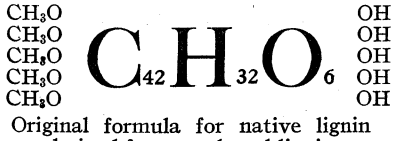
The results of these experiments show a far-reaching agreement with those of the corresponding products obtained in an almost quantitative yield directly from sprucewood. Based on these earlier results, an empirical formula (I) for the lignin building unit[18] was proposed.[19] As was later found by Hägglund[19c] and Holmberg,[19d] this formula is in good agreement with the experimental results of other lignin investigators, and the question arises as to how the experimental results obtained from isolated native lignin fit into this formula.

It must be recalled that this formula was developed on the assumption found at that time in the literature, namely, that "native lignin" has a methoxyl content of 17.3% and that one new methoxyl group is formed in the lignin molecule on reaction with methanol and hydrochloric acid; it was also based on the assumption that one methoxyl group was introduced into the lignin building unit on methylation with diazomethane. The assumptions, however, were proved to be in error (this indicates again how cautious one has to be in making assumptions in lignin chemistry) for the methoxyl content of the isolated native lignin is found to be only 14.8%, which is in

(18) The term "lignin building unit" was used by Brauns and Hibbert in 1933 for a unit with a molecular weight of approximately 840. In his recent publications, Hibbert uses the same term for one with a C_9 group only. In order to avoid confusion it would seem to be advisable to use the term "lignin building stone" for the C_9 groups as has already been done by Freudenberg ("Tannin, Cellulose, Lignin," Berlin, 1933, p. 134).

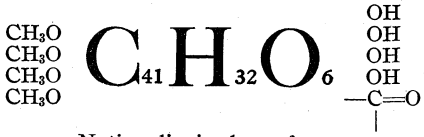
(19) (a) Brauns and Hibbert, THIS JOURNAL, **55**, 4720 (1933); (b) Sarkar, *J. Indian Chem. Soc.*, **12**, 547 (1935); (c) Hägglund, *Svensk Papperstidn.*, **39**, 347 (1936); (d) Holmberg, *Papier-Fabr.*, **36**, 218 (1938); (e) Freudenberg, *ibid.*, **37**, 28 (1939).

agreement with that calculated by Hägglund. In the methylation of the isolated native lignin either with diazomethane or with methanol and hydrochloric acid, two partially methylated lignin derivatives with *almost* the same methoxyl contents are obtained. They differ, however, from each other in that the diazomethane-methylated product is insoluble in sodium hydroxide, whereas the methanol derivative is soluble, and also in that their behaviors toward 72% sulfuric acid are dissimilar. With this reagent the methoxyl content remains unchanged in the case of diazomethane-methylated isolated native lignin (IV), whereas that of methanol lignin is decreased to 16.4%. On the other hand, when diazomethane-methylated isolated native lignin (IV) is treated with methanol and hydrochloric acid (VII) and methanol native lignin is methylated with diazomethane (VI), products with the same methoxyl contents are obtained. It is obvious that with diazomethane an acidic hydroxyl group is methylated which remains free in the methylation with methanol and hydrochloric acid. On the other hand, in both cases one hydroxyl group is methylated either by diazomethane or by methanol and hydrochloric acid. Finally, there is a third hydroxyl group in the native lignin which is only methylated by methanol and hydrochloric acid. In other words, three methoxyl groups are introduced into the lignin molecule when diazomethane and methanol–hydrochloric acid are both used, and two when only one of these reagents is used. The fact that with methanol–hydrochloric acid two methoxyl groups are introduced which are split off again with 72% sulfuric acid indicates that these groups are present in an acetal-like form as proposed by Holmberg. The presence of a carbonyl group in the isolated native lignin is proved by the reaction with phenylhydrazine whereby a hydrazone is formed.



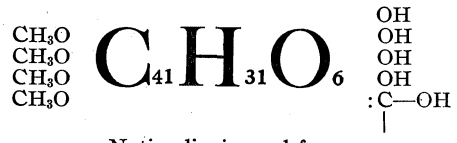
Original formula for native lignin derived from methanol lignin

I



Native lignin keto form

II

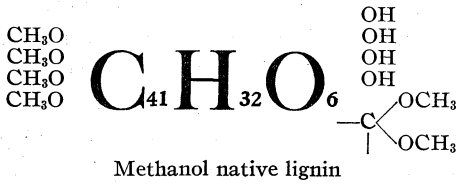


Native lignin enol form

III

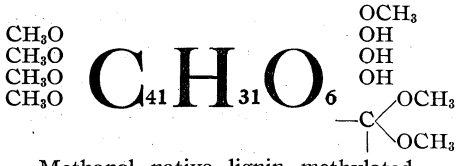
Native lignin methylated with diazomethane

IV



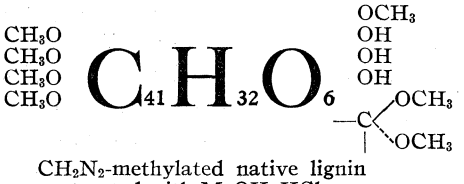
Methanol native lignin

V



Methanol native lignin methylated with diazomethane

VI



CH_2N_2-methylated native lignin treated with MeOH–HCl

VII

To return now to the development of the empirical formula (I), it is evident that this formula, insofar as methanol lignin is concerned, remains unchanged. With regard to the native lignin, however, all that has to be changed is that one methanol molecule has to be taken out because the calculation was based on the entrance of only one methoxyl group on methylation with methanol and hydrochloric acid, whereas actually two enter the lignin building unit forming a dimethylacetal with the carbonyl group. This carbonyl group is easily enolizable. The empirical formula for native lignin would then be as given in Formula II in its keto form and in formula III in its enol form with a molecular weight of around 840.

In Table I the methoxyl contents of the various derivatives of native lignin and, for comparison,

TABLE I

NUMBER OF GROUPS

	Lignin derivative	Mol. wt.	CH_3O	OH or acetyl	Calcd. MeO	Found MeO	MeO found for corresponding comp. by other investigators
1	Native lignin (N.L.)	838.3	4	4 OH	14.80	14.8	14.8[a]
2	N.L. acetylated Keto form	1006.3	4	4 Ac	12.33	..	..
	Enol form	1048.3	4	5 Ac	11.84	11.8	..
3	N.L. methylated with CH_2N_2	866.3	6	3 OH	21.48	21.4	21.2[b]
4	N.L. methylated with CH_2N_2 and acetylated	992.3	6	3 Ac	18.76	18.9	..
5	Methanol N.L.	884.3	6	4 OH	21.00	20.9	21.6[c]
6	Methanol N.L. acetylated	1052.3	6	4 Ac	17.7	16.92	17.8[c]
7	Methanol N.L. methylated with CH_2N_2	898.3	7	3 OH	24.17	25.36	24.8[c]
8	Methanol N.L. methylated with CH_2N_2 and acetylated	1024.3	7	3 Ac	21.20	22.7	21.4[c]
9	N.L. methylated with CH_2N_2 and treated with MeOH–HCl	(After remethylation with CH_2N_2) 898.3	7	3 OH	24.1	25.4 24.4	24.8[c]
10	No. 3 methylated with Me_2SO_4 + NaOH	908.3	9	...	30.74	31.3	30.3[d]
11	No. 5 methylated with Me_2SO_4 + NaOH	940.3	10	...	33.00	33.1	32.3[c]
12	Phenylhydrazone of N.L.	928.3	4	4 OH	13.36	13.4	..

[a] Calculated by Hägglund[9] for native spruce lignin. [b] Diazomethane-methylated Willstätter lignin. [c] MeO content of derivatives of methanol lignin directly isolated from sprucewood.[16d] [d] Willstätter lignin methylated with CH_2N_2 followed by Me_2SO_4 and NaOH.

those calculated on the basis of the formula are given.

It can be seen that in those cases (1, 2, 3, 4, and 11) where neither alkali nor acid is used, the values found for the methoxyl contents agree very well with those calculated, whereas in those cases where the native lignin has come into contact either with alkali, as in 9 and 10, or with acid (HCl), as in 5, 6, 7, and 8, the methoxyl contents vary somewhat. This discrepancy may be explained by the possibility that a methylene oxide group[20] has been split off with the formation of free phenolic hydroxyl groups. Such a reaction seems to be indicated especially in the treatment of diazomethane-methylated native lignin with methanol and hydrochloric acid. When native lignin, completely methylated with regard to diazomethane and containing methoxyl groups which are stable even to 72% sulfuric acid, is treated with methanol–hydrochloric acid, a partially methylated methanol native lignin (VI) is obtained with almost the calculated methoxyl content (24.4 instead of 24.1%). On remethylation of this product with diazomethane, the methoxyl content increases to 25.4% or to the same value as the diazomethane-methylated methanol lignin.

It is a well-known fact that lignin as it occurs in wood is dissolved when heated with a bisulfite solution. When isolated native lignin is heated with sodium bisulfite solution containing 1 g. of sodium oxide and 4.5 g. of sulfur dioxide per liter for twelve to fourteen hours at 125°, it goes completely into solution, giving lignosulfonic acid. In a recent paper[11] it was shown that when sprucewood meal is treated with diazomethane until the lignin has a final methoxyl content of 21%, this wood can no longer be pulped with bisulfite solution. Similar results have been obtained by Hägglund and J. Holmberg[21] and by Klingstedt.[22] This has been explained by the fact that in the lignin molecule a hydroxyl group capable of methylation with diazomethane is present which is essential for rendering the lignin soluble in a bisulfite cook; by blocking this hydroxyl group with methoxyl, this reaction can no longer take place. Freudenberg, on the other hand, showed that, when sprucewood is methylated with diazomethane to a methoxyl content of from 18 to 19% for the lignin, the lignin in this wood can be dissolved completely by a bisulfite cook. How can this discrepancy be explained? It is shown in the present investigation that on methylation of native lignin with diazomethane two methoxyl groups are introduced in the lignin molecule having a molecular weight of 840. Since one of these hydroxyl groups is also methylated by methanol and hydrochloric acid, it is evident that this hydroxyl group is an enolic one and that the

(20) The presence of a methylene oxide group in lignin has been established definitely by Freudenberg, *et al.* [*Ber.*, **72**, 217 (1939)] in contrast to Hibbert and co-workers [*ibid.*, **71**, 734 (1938)], who believe that the formaldehyde obtained in the distillation of lignin with mineral acids is derived from carbohydrate material in the lignin.

(21) Hägglund and Holmberg, unpublished work. See ref. 4, p. 149.

(22) Private communication.

second group is a phenolic one. As already mentioned, on partial methylation of native lignin in ether suspension with diazomethane, only one hydroxyl group in the lignin building unit is methylated, and since the phenolic hydroxyl is more acidic than the enolic, it is very probable that the former is the first to be methylated. Such a partially diazomethane-methylated native lignin has a methoxyl content of 18.3% (that calculated for a native lignin with five methoxyl groups is 18.14%) and with its unchanged carbonyl group it should still be soluble in bisulfite solution. An experimental proof of this statement will be carried out soon. Since Freudenberg methylated his sprucewood to a methoxyl content for the lignin of 18 to 19% only, it is quite understandable how, in his methylated wood, the lignin is dissolved with bisulfite. This would mean that instead of a "phenolic or an enolic hydroxyl" group being responsible for the reaction of the lignin with bisulfite liquor,[10] it is in reality an easily enolizable carbonyl group.

Since a partially methylated lignin with the same methoxyl content is obtained from diazomethane-methylated sprucewood, it follows that in wood the keto form of the lignin is either already present in its enolic form or it is slowly enolized. The long period of time required to reach a final methoxyl content in the diazomethane-methylation of sprucewood may indicate that the keto group is slowly enolized during the methylation.

Experimental[23]

Isolation of Native Spruce Lignin.—Black sprucewood meal (100- to 150-mesh) is extracted first with cold water, then with ether, and finally with alcohol at room temperature in a percolator until the alcohol drains off colorless. The alcohol solution is distilled off under reduced pressure, whereupon a finely divided creamy precipitate separates out in addition to a resinous material. This is washed with water and ether until the material becomes solid and powdery. It is filtered, dissolved in dioxane, and precipitated by pouring the solution into distilled water. Should a colloidal solution be formed, the addition of a few grams of sodium sulfate will coagulate it. The precipitate is filtered again, dried and redissolved in dioxane to give a 10% solution and the centrifuged and filtered dioxane solution dropped slowly into absolute ether with vigorous stirring. The native lignin separates out as a fine powder. This precipitation process is repeated until the methoxyl content remains constant. The product is washed after each purification with ether and finally with petroleum ether. The lignin so obtained is a very light cream-colored powder. It is soluble in 4% sodium hydroxide solution, methanol, ethanol, dioxane, and pyridine, and insoluble in water, ether, benzene, and petroleum ether. It reduces Fehling solution and when dissolved in dioxane with phloroglucinol–hydrochloric acid gives the typical purple color reaction.

Anal. C, 63.62; H, 6.20; MeO, 14.7; after another precipitation from dioxane into benzene, C, 63.89; H, 6.07; MeO, 14.9, 14.6; another preparation gave C, 63.85; H, 6.19; and MeO, 14.8.

Acetylation of Native Lignin.—One gram of native lignin is dissolved in 15 cc. of dry pyridine, 12 cc. of acetic anhydride is added and the mixture allowed to stand at room temperature for two days. It is then poured over cracked ice and the creamy colored precipitate filtered. It is washed well with distilled water and dried in a desiccator over sulfuric acid and sodium hydroxide. It is then dissolved in dioxane, the solution centrifuged and filtered, and the product precipitated as a light cream-colored powder by pouring the solution drop by drop into dry ether. After washing with ether and petroleum ether it is dried. Its solubilities in organic solvents are the same as those of native lignin but it is no longer soluble in cold sodium hydroxide. *Anal.* Found: MeO, 11.9 and 11.7.

Methylation of Native Spruce Lignin with Diazomethane in Dioxane.—Twenty-five grams of native lignin is dissolved in 100 cc. of dioxane, and diazomethane prepared from 20 cc. of nitrosomethylurethan is passed into the solution. A vigorous nitrogen evolution takes place. After standing overnight a sample of the product is precipitated by dropping 5 cc. of the centrifuged solution into dry ether. The product is washed as usual and has a methoxyl content of 20.9%. After two more methylations, each with diazomethane from 10 cc. of nitrosomethylurethan, the methoxyl content is constant. The diazomethane-methylated native lignin is an almost white powder. It still reduces Fehling solution but no longer gives the color reaction with phloroglucinol and hydrochloric acid. It is soluble in alcohol, dioxane, acetone, and pyridine but insoluble in benzene, ether, petroleum ether and alkali solutions. *Anal.* Found: MeO, 21.4, 21.54, and 21.4.

Acetylation of Native Spruce Lignin Premethylated with Diazomethane.—Diazomethane-methylated native lignin is acetylated as described for acetylated native lignin. It is isolated as a cream-colored powder.

Methylation of Native Spruce Lignin Premethylated with Diazomethane with Dimethyl Sulfate and Sodium Hydroxide.—Diazomethane-methylated native spruce lignin (2.5 g.) is dissolved in 25 cc. of acetone and methylated twice at 20° with 25 cc. of dimethyl sulfate and 35 cc. of sodium hydroxide solution (30%) keeping the mixture only slightly alkaline. After eight hours of stirring, the acetone is distilled off under reduced pressure, whereupon the methylated lignin separates as an orange-colored solid material. This is filtered, thoroughly washed with distilled water, and dried in a desiccator. It is then redissolved in dry acetone, centrifuged, and a part of the solution dropped into dry ether with vigorous stirring, whereupon the methylated lignin is precipitated as a cream-colored powder. It is washed with ether and petroleum ether and dried. For the

(23) Many of the analyses were made by Dr. M. A. Buchanan of The Institute of Paper Chemistry.

analysis it is dried in an Abderhalden drier at 100° over phosphorus pentoxide at 10 mm. for several hours. It has a methoxyl content of 30.2%. It is remethylated as before and has then a final methoxyl content of 31.3%. In the final purification the product is precipitated once from its acetone solution into distilled water and twice from its dioxane solution into ether.

Phenylhydrazone from Native Spruce Lignin.—To a solution of 0.5 g. of native spruce lignin in 5 cc. of dioxane, 1 g. of phenylhydrazine is added and the mixture heated for two hours on a water-bath at 80°. It is allowed to stand overnight at room temperature, centrifuged, and the clear deep red solution precipitated into dry ether with vigorous stirring. It separates out as a lemon-yellow product and after another precipitation has a methoxyl content of 13.5%, which remains practically unchanged after a second treatment with phenylhydrazine.

Methanol Spruce Lignin from Isolated Native Lignin.—Ten grams of native spruce lignin is dissolved in 200 cc. of absolute methanol, and 50 cc. of methanol containing 1.25 g. of hydrochloric acid are added. The original yellow-brown color of the solution turns immediately to a cherry-red color. The mixture is refluxed for two and one-half hours, the methanol solution distilled off under reduced pressure, and the reddish-brown residue taken up in 100 cc. of methanol–acetone mixture (1:1). This solution is filtered and dropped into 2 liters of distilled water with vigorous stirring, whereupon the methanol lignin separates as a light brown flaky precipitate. It is filtered, washed well with distilled water, and dried. The yield is almost quantitative. It is twice precipitated from its dioxane solution into dry ether and shows then the same properties as the methanol lignin directly prepared from sprucewood.[15d] The acetylation of methanol spruce lignin from isolated native lignin and its methylation with diazomethane and with dimethyl sulfate and sodium hydroxide are carried out in the same way as that described for the isolated native spruce lignin. The methoxyl contents are given in the table.

Treatment with Methanol and Hydrochloric Acid of Isolated Native Spruce Lignin Premethylated with Diazomethane.—This reaction is carried out under the same conditions as those observed in the preparation of methanol spruce lignin from isolated native lignin. The product so obtained has almost the same methoxyl content (24.4%) as the corresponding derivative prepared directly from sprucewood (24.7%), but on remethylation of the former with diazomethane the methoxyl content increases to 25.4% or the same as the diazomethane-methylated methanol lignin from native lignin.

Summary

1. An unchanged native lignin has been isolated from black spruce by an extraction with indifferent organic solvents without the use of acids or alkali. It has a methoxyl content of 14.8%.

2. Methylation of this lignin with diazomethane indicates that two methoxyl groups are introduced into the lignin building unit of a molecular weight of 840. One of these methoxyl groups is attached to a phenolic hydroxyl group, the second to an enolic hydroxyl group.

3. In the reaction between methanol and native lignin in the presence of 0.5% anhydrous hydrochloric acid, a methanol lignin is formed combining two new methoxyl groups in an acetal-like form to a carbonyl group.

4. The presence of a carbonyl group has been proved by the formation of a phenylhydrazone.

5. A molecular size of the lignin building unit of approximately 840 has been confirmed.[18]

6. The presence of a phenolic hydroxyl group in the lignin building unit has been shown by methylation with diazomethane of the original lignin and of the methanol lignin, and by the solubility of the native lignin and its methanol derivative in sodium hydroxide solution, from which it is reprecipitated by carbon dioxide.

7. The isolated native lignin is completely soluble in bisulfite but it becomes insoluble in this solvent when fully methylated with respect to diazomethane, by which the enolized carbonyl group is methylated.

APPLETON, WISCONSIN RECEIVED MAY 19, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, No. 194]

The Rearrangement of Certain Derivatives of Toluene by the Action of Aluminum Chloride

BY JAMES F. NORRIS AND HOWARD S. TURNER[1]

Many investigations have shown that derivatives of benzene which contain only alkyl groups undergo disproportionation and rearrangement when heated with aluminum chloride. We have not found reports of any study of the rearrangement of alkyl groups in aromatic compounds which contain, in addition to these groups, an atom or group of a different type. The influence of the nature of a substituent on the reactivity of a particular atom or group in a compound has been studied for several years in this Laboratory and it was of interest to extend the study to include the influence of different classes of substituents on the change of position of an alkyl group brought about by the action of aluminum chloride. Further, if rearrangement took place the process might be used as a means of preparing from a readily accessible compound an isomer which is formed to a small extent during nitration, chlorination, etc. For example, if *m*-chlorotoluene or *m*-cresol could be formed from their isomers, the method might make available compounds which are now obtained by indirect methods.

In this paper are described the results of the study of heating with aluminum chloride the following: *o*-, *m*- and *p*-chlorotoluene, *o*-, *m*-, and *p*-nitrotoluene, *p*-cresol, and *p*-dimethylaminotoluene. The effects of change in temperature, time, and the molecular ratio of the aluminum chloride to the second reactant were studied in certain cases. Appreciable rearrangement was observed only with the chlorotoluenes and *p*-cresol. The addition compounds formed from the amines and aluminum chloride were stable at the temperatures used. In the case of the limited number of compounds studied, it appears that the ortho and para orienting groups methyl, hydroxyl, and chlorine produce in a methyl radical sufficient reactivity to permit a change of position of the latter in the molecule. The meta orienting nitro group stabilizes a methyl radical so that it does not migrate under the conditions that affect the other class of compounds.

p-Chlorotoluene was studied first because a preliminary experiment showed that it underwent both rearrangement and disproportionation and resembled *p*-xylene in its behavior. The products resulting from disproportionation indicated that the methyl radical and not the chlorine atom was involved in the change. It has been shown that bromobenzene, when heated at its boiling point with aluminum chloride, yields benzene and *p*-dibromobenzene,[2] but the conditions used in our experiment were much less drastic.

The main difficulty to be overcome in the case of the chlorotoluenes was the quantitative determination of the amount of each isomer in the rearranged product. After the investigation of chemical procedures, which proved to be inadequate, a physico-chemical method was adopted. The amount of the para compound in the mixture, which contained only the isomers, was determined by the freezing point lowering of *p*-chlorotoluene produced by the mixture; this was a measure of the sum of the *o*- and *m*-chlorotoluenes present. A modified form of the Swietoslawski differential ebullioscope[3] was used to determine the percentages of the ortho and of the meta compounds in the mixture. The temperature of the vapor from a rapidly boiling mixture which contained a fixed percentage of the para isomer was determined, and its position on a plot previously prepared was noted. This plot was made by determining the temperature of the vapor of a series of mixtures which contained a definite percentage of the para compound and varying percentages of the other isomers. The change in vapor temperature with change in composition was sufficient to give results accurate within a few per cent. The results are given in the table.

An examination of the table leads to the following conclusions: (a) *p*-chlorotoluene undergoes rapidly both rearrangement and disproportionation when heated with aluminum chloride at 100°; (b) from expts. 1 and 2 it is seen that when heated for half an hour a large change in the molecular

(1) From the thesis of Howard S. Turner presented in partial fulfilment of the requirements for the degree of Doctor of Philosophy, 1936.

(2) Dumreicher, *Ber.*, **15**, 1867 (1882); Coposarow, *J. Chem. Soc.*, **119**, 442 (1921).

(3) M. W. Swietoslawski, *Bull. soc. chim.*, **49**, 1567 (1931) (Fig. 4).

TABLE I

REARRANGEMENT OF CHLOROTOLUENES BY ALUMINUM CHLORIDE IN THE PRESENCE OF HYDROGEN CHLORIDE

In each experiment 16 g. of chlorotoluene was used. Experiments 1–10 refer to the para compound; in experiment 11 the meta and in experiment 12 the ortho compounds were used.

Expt.	Mole ratio $CH_3C_6H_4Cl$ to $AlCl_3$	Time, hours	Temp., °C.	G. from final distn.	Wt. % of fractions in prod. recov. I up to 158°	II 158 to 163°	III residue	% rearranged prods. in fraction II	% recov. prods. other than chlorotoluenes	% compn. of fraction II Ortho	Meta	Para
1	1	0.5	100	12.9	8.5	68.3	23.2	41.8	31.7	21.5	20.3	58.2
2	10	.5	100	13.4	6.7	71.6	21.7	36.5	27.4			63.5
3	1	4	100	12.5	35.2	32.8	32.6	85.8	67.2	50.4	35.4	14.2
4	10	4	100	14.2	13.9	65.2	20.9	74.7	34.8	30.2	44.5	25.3
5	10	36.5	50	14.5	5.5	69.7	24.8	23.4	30.3			76.6
6	1	2.5	100	12.2	24.0	45.0	33.0	80.6	55.0			19.4
7	10	36.5	70	10.2	23.4	40.0	36.2	64.3	60.0			35.7
8	10	72	54	14	15.5	60.2	20.9	53.9	39.8			46.1
9	1	36.5	55	14	10.9	65.5	23.6	67.8	34.5	29.3	38.5	32.2
10 Para	10	4.25	96	14.5	18.3	56.8	24.9	73.4	43.2	24.8	48.6	26.6
11 Meta	10	4.25	96	14.5	9.4	77.5	13.1	50.8	22.5	32.9	49.2	17.9
12 Ortho	10	4.25	96	15	8.9	83.4	7.7	21.6	16.6	78.4	17.1	4.5

The figures in the column headed "% recovered products other than chlorotoluenes" were calculated from the weights of fractions I, II and III. It is probable that small amounts of the chlorotoluenes were not separated from fractions I and III; for this reason the values of the percentages of recovered products other than chlorotoluenes are presumably too great. The results are comparable, however.

ratio of the chlorotoluene to aluminum chloride has little effect, whereas in four hours the larger proportion of aluminum chloride produced a much greater increase in disproportionation than in rearrangement. This difference also was observed in the case of the xylenes[4]; (c) it is seen from expts. 1, 6 and 3 (mole ratio 1:1) that increase in time results in approximately equivalent increases in the amounts of both rearrangement and disproportion. When less aluminum chloride was used in expts. 2 and 4 (mole ratio 10 to 1) increase in time produced a much larger increase in rearrangement than in disproportionation; (d) increase in temperature (expts. 5 and 7) from 50 to 70° doubled the disproportionation and increased rearrangement 2.8 times; (e) of the three isomers (expts. 10, 11 and 12) the ortho is the most stable under the conditions used; the para is the least stable. Of the original isomer in the rearranged product the ortho compound yielded 78.4%, the meta 49.2% and the para 26.6%. It would be possible to prepare *m*-chlorotoluene from the para compound.

Attempts made to produce rearrangements of the three nitrotoluenes by aluminum chloride and hydrogen chloride were unsuccessful. The temperature used varied from 100 to 150°, the time from half an hour to two hours and the molecular ratios of aluminum chloride to nitro compound were 1 to 1 and 2 to 1. At the lower temperature the nitro compound was recovered unchanged; at the higher temperatures tars were formed.

Since there was such a marked difference between the activating influence of a chlorine atom and a nitro group on a methyl radical joined to a benzene ring, it appeared desirable to study the influence of a dimethylamino group. It has been shown[5] that dimethylaniline is recovered unchanged after being heated at 250° for ten hours. The amine is converted into methyl chloride and aniline hydrochloride when heated with hydrogen chloride.[6] These facts were considered in the experiments with *p*-dimethylaminotoluene. The compound of the latter with aluminum chloride in the absence or presence of hydrogen chloride was so stable that it suffered no appreciable change on heating.

A preliminary experiment has been made with *p*-cresol. When the compound (0.19 mole) was heated at 200° for one and one-half hours with aluminum chloride (0.38 mole), rearrangement took place. The meta isomer which was formed in appreciable quantities was identified by the melting point of the trinitro derivative.

Experimental

Details of an Experiment.—The apparatus used in most of the experiments consisted of a round-bottomed flask provided with an inlet tube through which hydrogen chloride (1 to 2 bubbles per sec.) was passed, a mechanically driven stirrer and a reflux condenser fitted with a calcium chloride tube. The flask containing the reactants was placed in a glycerol bath which was heated by a

(4) Norris and Vaala, THIS JOURNAL, **61**, 2131 (1939).

(5) Giraud, *Bull. soc. chim.*, [3] **1**, 691 (1888).

(6) Lauth, *Ber.*, **6**, 677 (1873).

refluxing liquid for the desired time. There appeared to be little or no solution of the aluminum chloride in the chlorotoluene. The mixture was treated with ice and hydrochloric acid and distilled with steam. In certain cases the separation of the organic liquid was difficult. If a partial emulsion was formed this was separated, and treated with a little water and calcium chloride. The dense aqueous solution helped in the separation of the two liquids. The product was dried with calcium chloride and distilled very slowly through a 13-turn Davis column.

Compounds Used.—The *p*-chlorotoluene was made from *p*-toluidine and distilled through a 12-turn Davis column; a cooling curve showed that it melted at 7.2° (6.2 to 7.5° in the literature). The ortho and para compounds obtained from the Eastman Kodak Company were fractionated with the Davis column[7]; the ortho isomer was collected at 158.7–158.9° at 754 mm. (literature 159.15 at 760 mm.); the meta compound boiled at 161.8–162° at 768 mm.

The nitrotoluenes were obtained from the Eastman Kodak Company; the para compound melted at 51–53°; the meta at 15–16°; and ortho at −6°. The *p*-dimethylaminotoluene (Kahlbaum) melted at −30.5° (thermometer not calibrated). The *p*-cresol (Eastman Kodak Company) melted at 32.5° (literature 33.5°). Merck pure sublimed aluminum chloride was used.

Methods of Analysis for the Chlorotoluenes.—The amount of the para compound in a mixture containing only the three isomers was found by determining the lowering of the freezing point of pure *p*-chlorotoluene produced by the mixture. The freezing point constant for *p*-chlorotoluene was determined by using *m*-chlorotoluene as solute; two determinations gave 5.92 and 5.97 as the constant. The determinations were made in the apparatus previously described.[4] The method was tested by the analysis of a mixture of known composition, para 50%, meta 33.3%, ortho 16.7%; found 47.8 and 49.8% para.

The determinations of the amounts of the ortho and the para isomers in the mixtures were made in a Swietoslawski differential ebullioscope a drawing of which is included in the reference already given. The apparatus is designed to record the temperature of a boiling liquid and that of the vapor from the liquid, which is condensed and returned to the flask in which the liquid is boiling. Tests of the apparatus designed with a boiling flask of 5-cc. capacity showed that the temperatures of the vapor could be reproduced more accurately than those of the liquid; as a consequence the vapor temperatures were used in the determinations. The apparatus was heavily insulated by cork. In order to operate at a constant and reproducible pressure, the end of the reflux condenser was connected with a 5-gallon (20-liter) bottle which contained 5 lb. (2.5 kg.) of calcium chloride to keep the air at a constant content of moisture. The bottle was placed up to its neck in a large container filled with water. The bottle was connected to a 1-liter flask kept in a thermostat. When a determination was to be made the pressure in the apparatus was adjusted so that the surfaces of the mercury in the two arms of the manometer were at the same level. This arrangement kept the pressure so nearly constant that the temperatures of the vapor during an experiment varied less than 0.005°. In duplicate determinations the temperatures checked within 0.01°.

With this apparatus the temperatures of the vapor from mixtures of varying composition of the three isomers were determined. In each case 11 g. of the mixture which contained 9 g. of the para isomer was used; the amounts of ortho and meta isomers were varied from 2 g. ortho and 0 g. meta to 0 g. ortho—2 g. meta. Determinations on eleven mixtures gave data for a curve that deviated only slightly from a straight line. The difference in the temperatures of the vapors from the two mixtures which varied most in composition was 0.52°. In each case five observations at different time intervals were made of the temperature of the vapor, and the values were averaged. The difference between the several single observations in the case of a particular mixture varied from 0.001 to 0.004°. An analysis was made of a mixture of known composition: calcd., *o* 16.7%, *m* 33.3%, *p* 50%; found, *o* 15.2%, *m* 34.8%, and *p* 48.8%.

In the analyses of the mixtures produced by rearrangement, the product obtained as the result of heating the chlorotoluene with aluminum chloride was distilled with steam and the volatile material was weighed. After drying, the mixture was distilled very slowly through a 12-turn Davis column and separated into three fractions: I up to 158°, II 158–163°, III residue. The percentage of the para isomer in fraction II was next determined. The weight of the mixture that contained 2 g. of the ortho and para compounds was calculated, weighed and taken for analysis. The weight of the para isomer in this sample was calculated and enough of the para compound was added so that the resulting mixture contained 9 g. of para and 2 g. of a mixture of ortho and meta chlorotoluenes. The temperature of the vapor from this mixture when it was boiled in the ebullioscope was determined as before. The position of the temperature on the plot gave the percentages of the ortho and of the meta compounds in the mixture.

An experiment was made with *p*-chlorotoluenes to determine to what extent a more careful fractionation of the mixture before analysis would affect the percentages of the isomer in the fraction boiling at 158–163°. The three fractions obtained with the Davis column were refractionated through a Fenske column[8] (15 theoretical plates). The analyses of the fraction boiling between 158 and 163° showed that the product of the first distillation contained 75.2% of the ortho and meta isomers and after the second distillation 80.6%. As a result of the second distillation the weights of the first and third fractions decreased and the middle fraction increased. As stated in the note in the table the percentages of disproportion given are too great. We were particularly interested in rearrangement and did not carry out the additional fractionation on the experiments reported.

In order to determine what products had been formed as the result of disproportionation, the low boiling fractions from all the experiments were combined and fractionated through a Fenske column equivalent to 13 theoretical plates. About 75% of the material boiled

(7) H. S. Davis, *Ind. Eng. Chem., Anal. Ed.*, **1**, 61 (1929).

(8) M. R. Fenske, Quiggle and Tongberg, *Ind. Eng. Chem.*, **24**, 408 (1932).

between 132.2 and 132.4° and was shown to be chlorobenzene by converting it into *p*-bromochlorobenzene which melted at 65–66°.

The original fractions boiling above 168° were combined and distilled through the Fenske column. There were obtained the following fractions: 2 g. at 170–180°, 6.8 g. at 180–185°, 5.3 g. at 185–187.6°, 8.5 g. at 187.6–192°, 0.9 g. at 192–200° and a small residue. The known chloroxylenes boil from 186.6 to 191.5° and the dichlorotoluenes from 198–206°. It appeared probable that the methyl radical and not the chlorine had migrated. This conclusion was strengthened by the results of the determination of the density of the mixture of the two fractions which boiled between 187.6 and 192°; it was found to be 1.052^{25}_{25}. The density of 2,4-dichlorotoluene is 1.246^{20}_{20} and of 1,2-dimethyl-4-chlorobenzene is 1.069^{15}_{15}. Since the densities of the isomers of these compounds differ but little, it is highly probable that the high-boiling fraction contained chloroxylenes.

Experiments with the Nitrotoluenes.—Equal molecular quantities of aluminum chloride and *o*, *m*, and *p*-nitrotoluenes were heated at 104° for two hours. The chloride dissolved and an oil was formed in each case. After decomposition with water a small amount of tar and the nitrotoluene used was recovered. When *p*-nitrotoluene was heated at 115, 125, and 150° for one hour the amount of tar was increased but no isomers were formed. Similar results were obtained when the meta compound was heated at 115° for one hour. Tests for an amine in the products formed were negative. The result was not changed when 2 molecular quantities of aluminum chloride were used.

Summary

1. It was shown that when the chlorotoluenes are heated with aluminum chloride and hydrogen chloride rearrangement and disproportionation take place.

2. The extent to which these changes occur is determined by the temperature, time of heating and the molecular ratio of aluminum chloride to the chlorotoluene.

3. Under certain fixed conditions the stabilities of the isomers are ortho > meta > para.

4. Under certain conditions the mixture of the isomers obtained from *p*-chlorotoluene consisted of ortho, meta and para in the ratio 1–2–1.

5. Under the conditions used to cause the rearrangement of the chlorotoluenes, the isomeric nitrotoluenes and *p*-dimethylaminotoluene were not affected.

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The Rearrangement of the Xylenes by Aluminum Chloride

BY JAMES F. NORRIS AND GORDON T. VAALA[1]

In certain Friedel and Crafts reactions in which a variety of substances are condensed with alkyl derivatives of benzene, the orientation of the alkyl groups in the products obtained is not the same as that in the hydrocarbons from which they were produced. Much work has been done on the rearrangement and disproportionation of such hydrocarbons, but the conditions used have been such that the results cannot be taken as a guide in Friedel and Crafts reactions, when it is desired either to avoid or to take advantage of the rearrangement. The isomeric xylenes were of particular interest because it was found that under certain conditions the chief product of the methylation of benzene was 1,2,4-trimethylbenzene and under other conditions a high yield of 1,3,5-trimethylbenzene was formed.[2] It appeared probable that xylenes were intermediate products. It was important to determine, if possible, whether the change in conditions led primarily to different orientation or to secondary rearrangements. In the earlier work it was shown that the three xylenes underwent appreciable rearrangement when they were heated with aluminum chloride at 55° for ten minutes.

This paper contains the results of a detailed study of the rearrangement of the xylenes. The following factors were investigated: the time, the temperature, the molecular ratio of hydrocarbon to aluminum chloride, the effect of the presence of varying amounts of ferric chloride, and the presence or absence of hydrogen chloride. The results were such that they have been of value in the control of several Friedel and Crafts condensations, which will be described in papers to be published later.

In determining the percentages of the three

(1) From the thesis of Gordon T. Vaala, submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy, 1936.

(2) Norris and Rubinstein, THIS JOURNAL, 61, 1163 (1939).

isomers in the rearranged product, the freezing point method of Norris and Rubinstein was used for *p*-xylene. An improved apparatus was used, which facilitated the work and has been used in other investigations. The freezing point method when applied to *o*-xylene involved work at inconveniently low temperatures. A method of analysis based on oxidation of the mixture of the xylenes was developed and tested with synthetic mixtures. It was shown that the corresponding dibasic acids could be determined with an accuracy of about 90%.

The results of the experiments are given in the form of tables.

TABLE I

REARRANGEMENT OF *m*-XYLENE AT 50° IN THE PRESENCE OF HYDROGEN CHLORIDE

Mole ratio $1C_6H_4(CH_3)_2$ to $1AlCl_3$. The hydrocarbon used boiled at 139.2–139.5° and was shown by analysis to contain 1% *p*-xylene and less than 1% *o*-xylene.

Time, hours	Weight xylene used, g.	% recovered hydrocarbons	% xylenes in recovered hydrocarbons	% isomers in recovered xylenes Ortho	Meta	Para
0.5	85	92	100	..	..	3
1.5	65	94	100	16	77	7
5	53	95	88	14	74	12
18	85	95	85	16	69	15
30	43	93	84	16	69	15
48	43	87	80	16	67	17
75	43	89	72	16	65	19

TABLE II

REARRANGEMENT OF THE XYLENES IN THE PRESENCE OF HYDROGEN CHLORIDE

Mole Ratio $1C_6H_4(CH_3)_2$ to $1AlCl_3$

Xylene	Temp., °C.	Time	% xylenes in recovered hydrocarbons	% isomers in recovered xylenes Ortho	Meta	Para
Ortho	50	5 hrs.	94	40	55	5
Meta	50	5 hrs.	88	14	74	12
Para	50	5 hrs.	83	14	76	10
Ortho	94	15 min.	84	38	46	16
Meta	94	15 min.	100	18	72	10
Para	94	15 min.	90	16	31	53

A comparison of the results in Table II with those of Norris and Rubinstein shows that at 55° for ten minutes the para isomer gave 3.4 times as much rearranged products as did the ortho; at 50° for five hours 1.5 times, and at 94° for fifteen minutes 0.75 times. The percentage rearrangements of *m*-xylene under the two conditions used were approximately the same.

TABLE III

EFFECT OF MOLECULAR RATIO OF HYDROCARBON TO ALUMINUM CHLORIDE ON REARRANGEMENT OF *m*-XYLENE AT 50° IN THE PRESENCE OF HYDROGEN CHLORIDE

Moles xylene to moles $AlCl_3$	Time, hours	% xylenes in recovered hydrocarbons	% isomers in recovered xylenes Ortho	Meta	Para
1	48	80	16	67	17
5	50	90	13	68	19
100	50	100	..	..	4

TABLE IV

EFFECT OF FERRIC CHLORIDE ON THE REARRANGEMENT OF *m*-XYLENE AT 50° FOR 20 HOURS IN THE PRESENCE OF HYDROGEN CHLORIDE

1 mole xylene ratio moles $AlCl_3$ to $FeCl_3$	% isomers in recovered xylenes Ortho	Meta	Para
1 to 0	16	69	15
1 to 0.03	16	69	15
0.5 to 0.5	17	68	15

TABLE V

EFFECT OF HYDROGEN CHLORIDE ON THE REARRANGEMENT OF *m*-XYLENE AT 50° FOR 50 HOURS

Mole ratio 1 xylene to $1AlCl_3$

	% xylenes in recovered hydrocarbons	% isomers in recovered xylenes Ortho	Meta	Para
With HCl	80	16	67	17
No HCl	96	14	71	15

The conclusions from the results of the investigation can be used in the preparation of compounds by the Friedel and Crafts reaction and be used as a guide in the discovery of the structure of the compounds obtained. They furnish an explanation of the formation of pseudocumene when benzene is methylated at 0°; the orientation is ortho and para, as might be expected. At 100° the chief product is mesitylene in which the orientation is meta. In the simultaneous acylation and methylation of benzene by esters which is carried out best at about 100°, the orientation of the alkyl groups is largely meta.

A preliminary experiment has been made on the rearrangement of commercial pseudocumene with the thought that the reaction might be used as a convenient and cheap way of preparing mesitylene. A sample of pseudocumene (b. p. 169–171°) which was analyzed by sulfonation and found to contain 8.5% mesitylene, was heated with 2 moles of aluminum chloride at 94° for one hour. The recovered mixture of hydrocarbons contained 18% of mesitylene.

The fact that aluminum chloride produced a rearrangement of the xylenes led to a study of the condensation of methyl alcohol with pure *m*-xylene. The molecular ratios were 1.25 hydrocarbon, 0.25 methyl alcohol, and 0.75 aluminum chloride, the time five hours and temperature 110°; the yield of mesitylene boiling at 163.8° to 165.2° was 84%. After sulfonation and hydrolysis the yield was 80% of mesitylene which boiled

at 164–164.8° and gave a yield of 99.5% of the tribromo derivative which melted at 224–225° before crystallization.

A similar experiment was carried out but the time of heating was reduced to one and one-half hours and dry air was passed through the reacting mixture to remove the hydrogen chloride. In this case the yield of mesitylene boiling at 164.2–164.8° after sulfonation was 90% of the theoretical. With technical xylene at 90° for five hours, the yield of mesitylene was 34% and that of pseudocumene 37%.

Experimental

Details of an Experiment.—The aluminum chloride was placed in a 500-cc. round-bottomed flask fitted with a spiral return condenser, a motor-driven stirrer and a tube, leading to the bottom of the flask, through which dry hydrogen chloride was passed (1 bubble in two seconds). This tube contained a T through which the hydrocarbon could be introduced from an attached separatory funnel. The flask was heated in an oil-bath at the desired temperature, and the hydrocarbon, previously heated, was introduced. At the end of the desired time the product was cooled rapidly, decomposed by ice and hydrochloric acid in a flask, and distilled with steam. In certain experiments hydrogen chloride was not passed through the reactants.

Merck reagent anhydrous aluminum chloride was used in all experiments. The *m*-xylene was furnished by the du Pont Company. All temperatures are corrected; they were determined with a calibrated thermometer graduated in 0.2°.

Analytical Methods.—After the hydrocarbon had been heated with aluminum chloride the product was decomposed by ice and hydrochloric acid and distilled with steam. The weights of hydrocarbon used and of the mixture which distilled gave data for the percentage of hydrocarbon recovered.

The product was dried, distilled slowly through a 13-turn Davis column,[3] and the temperature observed on a calibrated Anschütz thermometer with graduations of 0.2°. The material was collected in three fractions: I up to 137°; II 137–144°; III above 144°. The residue in the flask was redistilled in a 10-cc. flask and any material boiling at 137–144° was added to fraction II and higher boiling material, to fraction III. The sum of the weights of fractions I and III and the weight of fraction II were used in calculating percentage recovered xylenes.

Quantitative Determination of *p*-Xylene.—The lowering of the freezing point of pure *p*-xylene produced by a sample of the mixture gave data for calculating the percentage of compounds other than *p*-xylene in the mixture. The solvent was prepared from Eastman Kodak Co. pure *p*-xylene by distillation through a 13-turn Davis column; the fraction used boiled at 137.5–137.6° and melted at 13.0°. The freezing point constant was determined with toluene (b. p. 110.4–110.5°) and found to be 42.5 (value in literature, 43). The method was tested by analyzing two known mixtures which contained I 8% para, 10% ortho, and 82% meta xylenes, and II 20% para and 80% meta xylenes. Mixture I was found to contain 8.3% and mixture II 20.4% *p*-xylene.

In determining freezing points, a very convenient modification of the Hortvet cryoscope[4] was used. The apparatus consisted of a tall 1-liter vacuum bottle, insulated with a metal case and covered with a tightly fitting cork with a central opening for a metal tube 4 cm. in diameter and 20 cm. long. This tube served as an air jacket for a test-tube (18 × 2.5 cm.) which was fitted to it by a cork. The cooling was accomplished by passing dry air through a 4-mm. metal tube which extended to the bottom of the vacuum bottle where 500 cc. of ether had been placed. The tube ended in a loop which was pierced with pin holes to permit the formation of a stream of air bubbles. The evaporation of the ether produced by drawing air through it caused a lowering of the temperature which could be held within 0.10° at temperatures from 20 to −10°. In making the freezing point determinations the bath was held at 8 ± 0.1°, and the solution was supercooled about 0.3°. Determinations checked within 2%.

Quantitative Determination of *o*-Xylene.—A method was developed for the oxidation of the three xylenes to the corresponding phthalic acids, which gave sufficiently high yields to make the method useful for quantitative determinations. *o*-Xylene gave 89.4% of an acid which was shown by titration to be 98.6% dibasic; the corresponding figures with *p*-xylene were 88.3 and 97.4% and with *m*-xylene 91.3 and 98%.

The method was as follows: 4 cc. of the xylene, measured in a calibrated pipet, was placed in a 500-cc. flask fitted with a motor-driven stirrer through a mercury seal, a reflux spiral condenser, and a dropping funnel. The flask was heated to 120° and 3.8 cc. of bromine added drop by drop. Next, 10 cc. of a saturated solution of sodium hydroxide diluted with an equal volume of water was added. After the solution was refluxed for one hour, 100 cc. of a 5% solution of potassium permanganate (one-third the theoretical amount) was added. After heating for fifteen minutes, another 100 cc. was added and after one hour, 130 cc. The total time of refluxing was six hours. The cooled solution was treated with sulfur dioxide and filtered. The filtrate and washings from manganese dioxide were concentrated to about 150 cc. and poured into a 25% excess of concentrated hydrochloric acid. In a few minutes the hot solution was filtered; the precipitated isophthalic and terephthalic acids were washed with cold water, dried, and weighed. The filtrate and washings were evaporated to dryness, the residue powdered and transferred to a 500-cc. round flask with a long neck. Into the latter was placed a test-tube through which water flowed. The flask, surrounded and covered by asbestos, was placed on an iron gauze and asbestos and heated by a flame to such a temperature that a thermometer placed in the jacket just above the gauze registered 180–190°; the phthalic anhydride sublimed slowly. At the end of from two to three hours the anhydride collected as a compact crystalline mass on the cooled test-tube. The latter was withdrawn, the

(3) H. S. Davis, *Ind. Eng. Chem., Anal. Ed.*, **1**, 61 (1929).

(4) Hortvet, *J. Ind. Eng. Chem.*, **13**, 203 (1921).

anhydride dissolved in 200 cc. of neutral alcohol and titrated with 0.1 *N* sodium hydroxide solution. To test the purity of the acid it was recovered and converted into phthalic anhydride. The quantitative isolation of the anhydride in this way was tested with a weighed sample which was converted into the salt, liberated and sublimed, and titrated. The recovery was 95.7%. In a second test a mixture of 1 g. each of the three phthalic acids gave a recovery of *o*-phthalic acid of 97%.

We were unable to find a quantitative method for the separation of isophthalic and terephthalic acids. As a consequence, the percentage of *m*-xylenes in the mixtures analyzed was considered to be the difference between the weights of the mixed xylenes and the sum of the ortho and para isomers. In several experiments the weight of *m*-xylene was calculated from the weights of the *p*-xylene and of the isophthalic and terephthalic acids obtained. The result checked within less than 1% the value obtained.

Summary

1. The effect of aluminum chloride on the three xylenes was studied under different conditions.

2. It was found that (1) change in temperature affects the relative proportions in which the isomers are formed; (2) rearrangement takes place much more rapidly than the decomposition of the hydrocarbons and yields a mixture approaching that present in commercial xylene; (3) decrease in the molecular ratio of aluminum chloride decreases the rate of rearrangement and the percentage decomposition; (4) the presence of ferric chloride had little or no effect and (5) hydrogen chloride did not affect rearrangement but appeared to increase decomposition.

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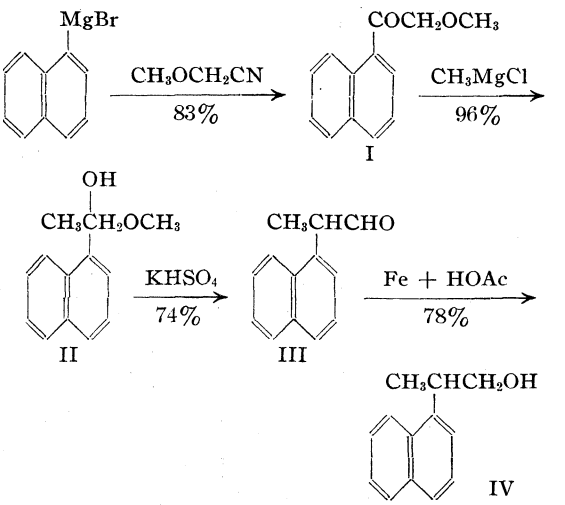
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Synthetic Experiments in the Chrysene Series

BY LOUIS F. FIESER, LLOYD M. JOSHEL[1] AND ARNOLD M. SELIGMAN[2,3]

The goal of the present work was the development of a synthesis of 5-methylchrysene which would be capable of application as well to the synthesis of 4,5-dimethylchrysene, both hydrocarbons being desired as possible models of the carcinogenic 3,4-benzpyrene.[4] The scheme selected for investigation required 2-(α-naphthyl)-propionaldehyde (III) as an essential intermediate, and a method for the preparation of the aldehyde was found which is very satisfactory for the case at hand and which should be capable of other applications. The remainder of the plan could not be realized, for a rearrangement was encountered in the final stages of the synthesis.

In the most satisfactory procedure for preparing the intermediate aldehyde, α-naphthylmagnesium bromide was condensed with methoxyacetonitrile to give the keto ether I and this by interaction with methylmagnesium chloride was converted into the carbinol ether II in over-all yield of 80%. It is not practical to reverse the order of the two Grignard reactions, for when methylmagnesium chloride was added to methoxyacetonitrile ac-



cording to Gauthier[5] and the resulting methoxyacetone condensed with α-naphthyl Grignard reagent, the over-all yield of II was only 12%. Carbinol ethers analogous to II have been synthesized similarly by Bradsher and Schneider[6] from 2-iodobiphenyl and cyclized with acids to phenanthrene derivatives. Our methyl-methoxymethyl-α-naphthylcarbinol (II) in the next step was distilled over potassium bisulfate, when methyl alcohol was liberated and the chief product was 2-(α-naphthyl)-propionaldehyde (III). This

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(3) The procedures for the synthesis of 2-(α-naphthyl)-propionaldehyde and the corresponding alcohol were worked out originally by A. M. Seligman and the further experiments were all conducted by Dr. L. M. Joshel.

(4) Fieser and Seligman, THIS JOURNAL, **60**, 170 (1938).

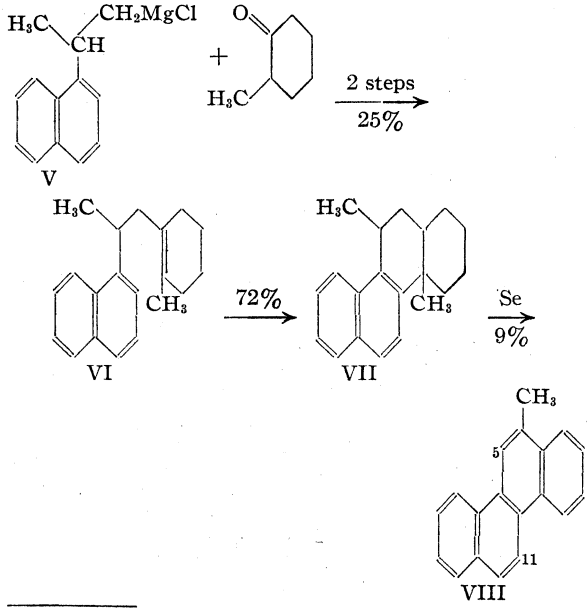
(5) Gauthier, *Ann. chim.*, [8] **16**, 318 (1909).

(6) Bradsher and Schneider, THIS JOURNAL, **60**, 2960 (1938).

is probably formed by dehydration of II to the enol ether, $Ar(CH_3)C{=}CHOCH_3$, and acid hydrolysis to the enol form of the aldehyde. A small amount of the enol ether indeed escaped hydrolysis under the conditions used and was isolated as a by-product on purifying the aldehyde through the bisulfite compound. It is convertible into the aldehyde in good yield by hydrolysis with dilute hydrochloric acid.

2-(α-Naphthyl)-propionaldehyde, a liquid substance characterized as the crystalline semicarbazone, was reduced in good yield with iron powder and dilute acetic acid to the alcohol IV. Certain of the standard methods for conversion to the chloride or bromide gave mixtures of wide boiling range, but treatment of the alcohol with phosphorus pentachloride in benzene afforded a homogeneous chloride in fair yield. The chloride seems to have the expected normal structure, for carbonation of the magnesium derivative gave a substance corresponding in properties to the known β-(α'-naphthyl)-butyric acid.[7]

In one attempt to obtain 5-methylchrysene use was made of the Bogert–Cook synthesis and Cook's device of introducing a 2-methyl group in the alicyclic ring to suppress spiran formation, for this has been shown to give good results in the synthesis of chrysene itself.[8] The Grignard reagent (V) from 2-(α-naphthyl)-chloropropane was condensed with 2-methylcyclohexanone and the carbinol (oil) was dehydrated with potassium bisulfate. This gave an unsaturated hydrocarbon of composition corresponding to VI, which was cyclized with aluminum chloride in carbon bisulfide solution at 0° to the dimethyloctahydrochrysene VII. Dehydrogenation with sulfur gave no pure product, but with either selenium or palladium charcoal there was obtained an oily product from which a homogeneous hydrocarbon was isolated in low yield through the trinitrobenzene derivative. The hydrocarbon, m. p. 159–159.8°, corr., has the expected composition but corresponds in properties to 6-methylchrysene (VIII), recently synthesized by Newman.[9] A direct comparison of the hydrocarbon, picrate (m. p. 170–170.6°, corr.), and trinitrobenzene derivative (m. p. 189.8–190.6°, corr.) with samples kindly made available by Dr. Newman established the identity of the substances, for the melting points are the same and there is no depression on mixing.

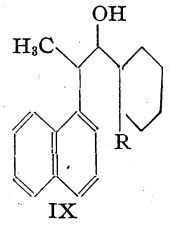


While it is not likely that Newman's synthesis could give anything but the expected 6-methylchrysene, there is analogy for the occurrence of a rearrangement in the dehydrogenation of a substance of the structural type involved in the present synthesis. Haworth[10] observed the para migration of a methyl group in the dehydrogenation of a 4-methyl-1,2,3,4-tetrahydrophenanthrene, but noted that rearrangement occurs only if the methylated ring is completely saturated. The nuclear methyl group of our hydrocarbon VII occupies a similar position in a saturated ring, and the case differs from that studied by Haworth only in that the para position is blocked. The most plausible interpretation of the present observation is that the methyl group migrates from C_5 to the ortho position 6. W. E. Jones and Ramage[11] recently investigated the dehydrogenation of certain decahydrochrysenes which normally should give 5-methylchrysene and 5,11-dimethylchrysene. They found the methyl groups to be largely eliminated from these positions with the formation of chrysene, but obtained from both starting materials small amounts of a methylchrysene, m. p. 151° (uncorr.?) which they tentatively regard as the 5-isomer. The apparently uncorrected melting points of their hydrocarbon, its picrate, and trinitrobenzene derivative are from 4 to 10° below the corrected melting points for corresponding compounds of the 6-methylchrysene series.

Before the above experiments were completed

(7) Radcliffe, Sherwood and Short, *J. Chem. Soc.*, 2293 (1931).
(8) Cook, Haslewood and A. M. Robinson, *ibid.*, 667 (1935).
(9) Newman, THIS JOURNAL, **60**, 2947 (1938).
(10) Haworth, Mavin and Sheldrick, *J. Chem. Soc.*, 454 (1934).
(11) W. E. Jones and Ramage, *ibid.*, 1853 (1938).

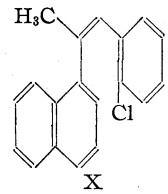
other possible synthetic routes were explored. 2-(α-Naphthyl)-propionaldehyde (III) was condensed with cyclohexylmagnesium chloride and the resulting carbinol IX (R = H) was submitted



IX

to cyclodehydration, both with phosphorus pentoxide and with potassium bisulfate, followed by aluminum chloride. In a closely analogous case, Perlman, Davidson and Bogert[12] obtained from benzylcyclohexylcarbinol a mixture of *as*-octahydrophenanthrene and the isomeric spiran. In our experiments the crude cyclization product on dehydrogenation with selenium afforded a hydrocarbon mixture from which there were separated as the trinitrobenzene derivatives small amounts of substances having the composition of a methylchrysene and of a spiran, respectively. Neither substance was obtained in large enough amounts for satisfactory purification and identification. Spiran formation was effectively suppressed by employing 2-methylcyclohexylmagnesium chloride in the synthesis, but the homologous carbinol (IX, R = CH_3) on cyclodehydration and selenium dehydrogenation gave a mixture containing chrysene and, in one experiment, a small amount of a substance which was not fully purified but which appeared from the analysis to be a methylchrysene. The partial loss of the methyl group corresponds to the experiences of W. E. Jones and Ramage,[11] and this synthesis clearly is not practical.

Another trial was inspired by Hewett's[13] successful utilization of a general synthetic method described in the patent literature.[14] 2-(α-Naphthyl)-propionaldehyde was condensed with the Grignard reagent from *o*-chlorobromobenzene and the crude carbinol was dehydrated by distillation over potassium bisulfate. The product was a liquid of the expected composition but boiled over a considerable range, and it presumably consisted of a mixture of the geometrical isomers of the structure X. Attempts to cyclize this sub-



X

stance by fusion with potassium hydroxide alone[13] or in quinoline solution[14] gave only tars. The Grignard reagent from *o*-bromoiodobenzene was tried in the synthesis in the hope of obtaining a halide which would undergo cyclization more readily, but the carbinol was low in halogen content and no hydrocarbon was obtained on putting the crude material through the remaining steps of the above process.

Experimental Part[15]

Methoxymethyl α-Naphthyl Ketone (I).—The **methoxyacetonitrile** required was conveniently prepared by the action of cuprous cyanide on chloromethyl ether according to Gauthier.[16] Previous reports give the yield as 60–70%[16] and 74%[17]; by using a fused salt-bath to distil completely the product from the reaction mixture we obtained a yield of 81.6% of redistilled product, b. p. 120–120.6°.

A solution of 68 g. of methoxyacetonitrile in 300 cc. of benzene was dropped with stirring into a Grignard solution from 230 g. of α-naphthyl bromide and 27.5 g. of magnesium in 500 cc. of ether and 150 cc. of benzene. The mixture was refluxed for one-half hour and allowed to stand overnight. After decomposition with dilute hydrochloric acid the mixture was steam distilled for one hour and the residue taken up in ether, dried, and distilled. The ketone distilled as a viscous yellow oil, b. p. 144–146° (1 mm.) or 172° (4 mm.); yield 159.5 g. (83%).

Anal. Calcd. for $C_{15}H_{12}O_2$: C, 77.98; H, 6.04. Found: C, 77.77; H, 6.47.

The **semicarbazone,** prepared by refluxing a solution in alcohol with semicarbazide hydrochloride and sodium acetate, was crystallized from benzene and then from alcohol and formed colorless needles, m. p. 166.4–167.8°.

Anal. Calcd. for $C_{14}H_{15}O_2N_3$: N, 16.33. Found: N, 15.87, 15.94.

Methyl-methoxymethyl-α-naphthylcarbinol (II). (a) From the Ketone I.—A solution of 244 g. of the ketone in 500 cc. of ether was added during one hour to the Grignard reagent from 35 g. of magnesium and excess methyl chloride. The mixture was refluxed for one and one-half hours, allowed to stand overnight, and decomposed with acid. The ether layer was washed and dried and the product distilled, giving 254 g. (96.4%) of carbinol, b. p. 138–142° at 1.5 mm. The distillate partially crystallized in the receiver; a sample crystallized from petroleum ether in colorless prisms, m. p. 56.4–60.4°. The material analyzed was purified merely by distillation.

(12) Perlman, Davidson and Bogert, *J. Org. Chem.*, **1**, 288 (1936).

(13) Hewett, *J. Chem. Soc.*, 1286 (1938).

(14) British Patent 459,108; French Patent 807,704; American Patents 2,109,518, 2,109,833 [*C. A.*, **31**, 4136, 5814 (1937); **32**, 3168, 3629 (1938)].

(15) All melting points are corrected. Microanalyses by Lyon Southworth, Herbert S. Wight†, and the Arlington Laboratories.*

(16) Gauthier, *Compt. rend.*, **143**, 831 (1906).

(17) Henze and Rigler, THIS JOURNAL, **56**, 1350 (1934).

*Anal.** Calcd. for $C_{14}H_{16}O_2$: C, 77.70; H, 7.46. Found: C, 77.69; H, 7.70.

(b) From Methoxyacetone.—In one trial the yield of **methoxyacetone**[5,17] from methoxyacetonitrile (67 g.) and methylmagnesium halide was 31% (b. p. 114°). Twenty-six grams of this reagent was added to a stirred Grignard solution from 70 g. of α-naphthylmagnesium bromide, and on proceeding as above there was obtained 26 g. (41%) of distilled carbinol.

2-(α-Naphthyl)-propionaldehyde (III).—A mixture of 160 g. of the carbinol II and 15 g. of fused potassium bisulfate was heated in a Claisen flask at 165–180° for one-half hour, allowing the volatile products to escape, and the residue was distilled at 2–4 mm. pressure. The clear distillate was stirred mechanically or shaken with 250 cc. of saturated sodium bisulfite solution, when a white precipitate of the addition product soon formed. After cooling, this was collected and washed with alcohol and ether. The aldehyde is conveniently stored in the form of this derivative; it is best liberated by shaking the bisulfite compound with aqueous sodium carbonate solution and extraction with ether. In the experiment cited there was obtained 83.5 g. (61%) of colorless aldehyde, b. p. 130–132° (2 mm.).

The **semicarbazone** formed colorless needles from alcohol, m. p. 203–204°.

*Anal.** Calcd. for $C_{14}H_{15}ON_3$: C, 69.72; H, 6.27. Found: C, 69.95; H, 6.09.

On recovering the material in the alcohol–ether washings of the bisulfite compound there was obtained 23.4 g. (16%) of the **enol methyl ether** of the aldehyde as a pale yellow, unsaturated oil, b. p. 120–122° (1.5 mm.).

Anal. Calcd. for $C_{14}H_{14}O$: C, 84.81; H, 7.12. Found: C, 84.49; H, 7.19.

A 5.6-g. portion of this ether was refluxed with 50 cc. of 20% hydrochloric acid for three and one-half hours and the oil was extracted with benzene, washed, dried and distilled, giving 4.8 g. of crude aldehyde, b. p. 116–119° (1.5 mm.). On purification through the bisulfite compound and redistillation, 4.2 g. (81%) of pale yellow aldehyde, b. p. 117–119° (1.5 mm.), resulted. On this basis the total yield of pure aldehyde obtainable from the carbinol is 74%.

2-(α-Naphthyl)-propanol-1 (IV).—A mixture of 83.5 g. of the pure aldehyde III, 300 cc. of acetic acid, 300 cc. of water, and 200 g. of iron powder was heated with stirring on the steam-bath for seven hours. The solution was filtered hot and the filter cake was washed well with water and then with ether. The filtrate and washings were diluted with water and extracted with ether, and after evaporation of the solvent the remaining oil was refluxed for one-half hour with 15 g. of sodium hydroxide in 30 cc. of water and 50 cc. of alcohol to hydrolyze any acetate. The alcohol was then washed and dried in ether and distilled; it was obtained as a yellowish, viscous oil, b. p. 144–147° (3 mm.); yield 66.3 g. (78.5%).

The **3,5-dinitrobenzoate,** prepared by warming the alcohol with dinitrobenzoyl chloride, crystallized from alcohol in small, colorless needles, m. p. 125.5–126.5°.

*Anal.** Calcd. for $C_{20}H_{16}O_6N_2$: C, 63.17; H, 4.24. Found: C, 63.16; H, 4.22.

Attempts to obtain a homogeneous halide from the alcohol II by the use of hydrobromic acid, phosphorus tribromide, thionyl chloride with pyridine or with dimethylaniline, or by the action of phosphorus pentachloride or tribromide on the acetate, all failed. Also unsuccessful were attempts to prepare the chloride by the condensation of naphthalene with allyl chloride[18] in the presence of sulfuric acid or anhydrous hydrogen fluoride; with the latter condensing agent (five hours at room temperature) there was obtained 13% of a halogen containing compound, but this had a wide boiling range (110–130° at 1 mm.). A satisfactory transformation of the alcohol was accomplished as follows.

2-(α-Naphthyl)-1-chloropropane.—A solution of 94 g. of the alcohol IV in 500 cc. of dry benzene was treated with 125 g. of phosphorus pentachloride, the vigorous reaction ensuing being controlled by external cooling. After refluxing for two hours the solution was cooled, water was added, and the benzene layer was washed, dried, concentrated, and treated with phosphorus pentoxide. Three distillations gave a mobile, yellowish liquid, b. p. 114–116° (1 mm.); yield 58 g. (56%). A sample shaken with 90% sulfuric acid and distilled was obtained in an almost colorless condition.

Anal. Calcd. for $C_{13}H_{13}Cl$: C, 76.28; H, 6.40. Found: C, 76.45; H, 6.41.

On preparing the Grignard reagent from 2.9 g. of the chloride and 0.4 g. of magnesium the reaction started promptly but about half of the metal remained unattacked after refluxing for several hours. On adding solid carbon dioxide and recovering the product in the usual way the acidic fraction afforded 1.1 g. (36%) of crude acid, m. p. 80–95°, on crystallization from benzene–ligroin. The recrystallized material formed colorless prisms, m. p. 108–108.6°, corresponding to the description of β-(α'-naphthyl)-butyric acid reported by Radcliffe, Sherwood and Short[7] (m. p. 108°).

2-(α-Naphthyl)-1-(2'-methylcyclohexenyl)-propane (VI).—Difficulty was again experienced in effecting the conversion of 2-(α-naphthyl)-1-chloropropane (31.8 g.) into the Grignard reagent (with 4 g. of magnesium in ether–benzene), and titration showed only 40% active reagent. No better results were obtained on forming the reagent in the presence of 1 mole of ethyl bromide. The cooled solution was treated with 21 g. of 2-methylcyclohexanone, kept at room temperature for one hour, refluxed for three hours, stirred overnight, and then decomposed with ammonium chloride solution. The neutral portion was distilled, and after a large fore-run, 11.8 g. (27%) of a yellow, viscous oil was obtained at a bath temperature of about 250° (2 mm.). The carbinol could not be obtained crystalline.

For dehydration, 16.1 g. of the carbinol was heated with 25 g. of potassium bisulfate at 200° for one and one-quarter hours. After two distillations the hydrocarbon was obtained as a yellow, viscous oil boiling at about 200–225° (2 mm.); yield 14.2 g. (94%). The substance crystallized readily when triturated with methanol at −70° but melted below room temperature.

Anal. Calcd. for $C_{20}H_{24}$: C, 90.85; H, 9.15. Found: C, 90.59; H, 9.53.

(18) Truffault, *Compt. rend.*, **202**, 1286 (1936); **207**, 676 (1938).

5,10a-Dimethyl-*as*-octahydrochrysene (VII).—A solution of 13.5 g. of the olefin VI in 135 cc. of carbon bisulfide was treated at 0° with 15 g. of aluminum chloride in portions and stirred at 0° for twenty-one hours. The solution was decanted, washed with water, dried and evaporated, and the residue was distilled from a little sodium. Redistillation gave 9.7 g. (72%) of a viscous, almost colorless oil, b. p. about 220–240° (2 mm.). Tests with bromine and alkaline permanganate indicated that some unsaturated material was still present, but the tests were still positive after a further treatment with aluminum chloride as above at room temperature.

Anal.† Calcd. for $C_{20}H_{24}$: C, 90.85; H, 9.15. Found: C, 91.37; H, 8.94.

6-Methylchrysene (VIII).—The octahydride (2 g.) was heated with selenium (4.8 g.) at 320° for twenty-four hours and the product extracted with benzene, distilled, treated with norite in benzene, and distilled over sodium. The resulting oil yielded a crude but crystalline trinitrobenzene derivative from benzene, and after passing a benzene solution of this material through a tower of alumina the recovered hydrocarbon crystallized from benzene–alcohol as colorless plates, m. p. 141–148° (167 mg.). The combined product from two such runs was crystallized several times from ethyl acetate–alcohol and gave 165 mg. of colorless, fluorescent needles, m. p. 159–159.8°.

Anal. Calcd. for $C_{19}H_{14}$: C, 94.18; H, 5.82. Found: C, 94.19; H, 5.90.

The melting point of the hydrocarbon was not depressed by admixture with a sample of 6-methylchrysene synthesized by Newman.[9] This was true as well of the **picrate,** which crystallized from benzene–alcohol in orange needles, m. p. 169.8–170.2°, with previous softening, and of the **trinitrobenzene derivative.** The latter derivative, which has not been described before, was obtained from our hydrocarbon as yellow needles, m. p. 188.5–189.5°, from benzene–alcohol, and from Newman's sample of hydrocarbon as yellow needles, m. p. 189.8–190.6°.

Anal. Calcd. for $C_{25}H_{17}O_6N_3$: C, 65.93; H, 3.76. Found: C, 65.83; H, 4.02.

On heating 0.5 g. of the octahydride with 50 mg. of 30% palladium charcoal for sixteen hours at 310°, with the addition of 150 mg. more catalyst at intervals, the gas evolution was only 25% of the theoretical amount. The mixture was extracted with benzene and the hydrocarbon precipitated as the trinitrobenzene derivative. After recovery as before, one crystallization from benzene–ligroin gave 17 mg. of colorless needles, m. p. 145–150°; on recrystallization the substance melted at 154–158° and gave no depression when mixed with the above sample.

1-Cyclohexyl-2-(α-naphthyl)-propanol (IX, R = H).—A solution of 7.3 g. of freshly distilled 2-(α-naphthyl)-propionaldehyde in 40 cc. of ether was added to the ice-cold Grignard reagent from 5.8 g. of cyclohexyl chloride and 1.3 g. of magnesium. After one hour in the ice-bath, and one and one-half hours at room temperature, the mixture was refluxed for one hour and decomposed with ammonium chloride solution. The ether solution was washed and dried and the solvent displaced with petroleum ether, from which the carbinol crystallized in two crops as colorless needles, m. p. 55–58°; yield 6.5 g. (61%). On recrystallization the substance melted constantly at 59–61°.

Anal. Calcd. for $C_{19}H_{24}O$: C, 85.03; H, 9.00. Found: C, 84.64; H, 9.69.

Cyclodehydration of IX and Dehydrogenation.—For dehydration and ring closure the above carbinol (IX, R = H) was either heated with phosphorus pentoxide at 150° for thirty minutes or heated with potassium bisulfate at 160–180° for one hour, followed by treatment of the resulting oil with aluminum chloride in carbon bisulfide at 0° for twenty-four hours. In either case the oil was then heated with selenium at 320° for twenty-four hours and the product isolated as the trinitrobenzene derivative. The crude derivative from 2 g. of carbinol amounted to 363 mg. and melted at 90–100°. Fractional crystallization from alcohol gave 50 mg. of an orange substance, m. p. 232–235° with previous softening, having the composition of a **methylchrysene–trinitrobenzene.**

Anal.† Calcd. for $C_{25}H_{17}O_6N_3$: N, 9.23. Found: N, 9.27.

A yellow substance was also separated in small amounts from the mixture; this melted at 107–109° and the nitrogen content is that of a derivative of the **spiran** (or octahydride).

Anal.† Calcd. for $C_{25}H_{25}O_6N_3$: N, 9.07. Found: N, 9.09.

The preparation of **1-(2′-methylcyclohexyl)-2-(α-naphthyl)-propanol-1 (IX, R = CH_3)** from 2-methylcyclohexyl chloride[19] (6.6 g.) and the aldehyde III (7 g.) was conducted as before, the product remaining after evaporation of the washed and dried ether extract being a viscous yellow oil which failed to crystallize (stereoisomerism?); yield 8.3 g. (77%). In one trial 3 g. of the crude carbinol was dropped slowly with stirring and ice cooling into 6 cc. of 90% sulfuric acid and the dark, viscous mass was extracted with benzene. After washing with 85% sulfuric acid and water, and removing the solvent, a yellow, viscous oil (1.4 g.) distilled at a bath temperature of about 240° (2 mm.). This was heated with selenium as above and the purified product afforded 239 mg. of an orange mixture of trinitrobenzene derivatives, m. p. 155–162°, which could not be separated by crystallization. After decomposing the complex (alumina tower), crystallization from benzene–methanol afforded 42 mg. of **chrysene,** m. p. 242–248°, which gave no depression when mixed with an authentic sample, and, from the more soluble fraction, 36 mg. of another substance as colorless needles, m. p. 98–100°. After two recrystallizations this largely fused at 105.5–106.5°, but the melt became clear only at 165°. The trinitrobenzene derivative formed orange needles, m. p. 165–167°, from alcohol. The composition of the hydrocarbon is that of a methylchrysene.

Anal. Calcd. for $C_{19}H_{14}$: C, 94.18; H, 5.82. Found: C, 94.11; H, 5.88.

In another experiment 2.95 g. of the carbinol IX (R = CH_3) was dehydrated with potassium bisulfate at 180° and the oil (2 g.) treated at 0° with aluminum chloride in carbon bisulfide (nineteen hours). The material (1.35 g.) was then dehydrogenated and a crystalline trinitrobenzene derivative was separated and reconverted to the

(19) Sabatier and Mailhe, *Compt. rend.*, **140**, 841 (1905); von Auwers and Dersch, *J. prakt. Chem.*, **124**, 232 (1930).

hydrocarbon, giving 22 mg. of chrysene as the sole homogeneous product.

1 - (*o* - Chlorophenyl) - 2 - (α - naphthyl) - propene (X).—An ethereal solution of 3.2 g. of the aldehyde III was added at 0° to the reagent from 4.2 g. of *o*-chlorobromobenzene and 0.6 g. of magnesium and the temperature was slowly raised from 0° to the boiling point. The product was collected as a viscous oil (5.3 g.) which was heated with 7.5 g. of potassium bisulfate at 170–180° for one hour and distilled twice, giving a light yellow oil, b. p. 150–180° (1 mm.); yield 3.1 g. (64%).

Anal. Calcd. for $C_{19}H_{15}Cl$: C, 81.86; H, 5.42. Found: C, 81.27; H, 5.66.

In various experiments this olefin was refluxed with potassium hydroxide in quinoline for three hours, stirred with potassium hydroxide at 250–260° for seven minutes, or at 250–300° for twenty minutes, but this resulted only in tars or in oils from which no crystalline trinitrobenzene derivative could be isolated. The carbinol was also fused with potassium hydroxide under various conditions without successful result.

When *o*-bromoiodobenzene was used in the synthesis the distilled carbinol contained only 13.0% of halogen, as compared with the theoretical value of 23.4%. No satisfactory product was obtained on dehydration and alkali fusion.

Summary

A convenient method of preparing 2-(α-naphthyl)-propionaldehyde has been found in the condensation of α-naphthylmagnesium bromide with methoxyacetonitrile followed by a methyl Grignard reaction on the resulting methoxymethyl α-naphthyl ketone and acid dehydration of the carbinol. The aldehyde can be reduced smoothly to the alcohol and the latter converted into the chloride.

With these intermediates readily available, an attempt was first made to synthesize 5-methylchrysene by the Bogert–Cook method, but there was obtained instead a hydrocarbon identical with Newman's 6-methylchrysene. Apparently in analogy with the para migration of a methyl group attached to a saturated ring observed by Haworth, an ortho methyl migration occurs in the dehydrogenation.

Various other possible methods of utilizing the same intermediates for the synthesis of 5-methylchrysene were explored without success, the difficulty being associated in part with the ready loss of methyl from the 5-position, as observed by W. E. Jones and Ramage.

CONVERSE MEMORIAL LABORATORY
CAMBRIDGE, MASSACHUSETTS RECEIVED JUNE 8, 1939

[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY OF THE UNIVERSITY OF CHICAGO]

The Oxygen Effect in the Reaction of Cyclopropane with Bromine and with Hydrogen Bromide

BY M. S. KHARASCH, M. Z. FINEMAN AND F. R. MAYO

Previous papers from this Laboratory[1–3] have shown that the brominations of toluene and phenanthrene are markedly accelerated by traces of oxygen and peroxides. These and similar observations with other hydrocarbons[4] have led us to reëxamine the reactions of cyclopropane with bromine and with hydrogen bromide.

Previous Work

The literature on the reaction of cyclopropane with bromine and hydrogen bromide is meager, although a great deal of work has been done with substituted cyclopropanes.[5] Gustavson[6] states that at ordinary temperatures cyclopropane reacts with bromine quite slowly in the dark, and rapidly in sunlight. He noted that propyl bromide, more highly brominated products, and large quantities of hydrogen bromide were formed in addition to trimethylene bromide. Ogg and Priest[7] have investigated several vapor phase reactions of cyclopropane. At 250° iodine yielded 1,3-diiodopropane and light had no effect on the reaction. At room temperature under intense illumination, bromine added to give mostly 1,3-dibromopropane and a little hydrogen bromide. At 220° in the dark, large proportions of hydrogen bromide were formed. Hydrogen bromide gave little indication of reaction at 300°.

Experimental Part

The cyclopropane used in this work was obtained from the Ohio Chemical Company. It boiled at −33.5 to

(1) Kharasch, Margolis, White and Mayo, THIS JOURNAL, **59**, 1405 (1937).
(2) Kharasch, White and Mayo, *J. Org. Chem.*, **2**, 574 (1938).
(3) Kharasch, White and Mayo, *ibid.*, **3**, 33 (1938).
(4) Kharasch, Hered and Mayo, unpublished work.
(5) (a) Farmer, *J. Chem. Soc.*, **123**, 3341 (1923); (b) Demjanow and Dojarenko, *Ber.*, **56B**, 2200 (1923); (c) Nicolet and Sattler, THIS JOURNAL, **49**, 2066 (1927); (d) Bone and Perkin, *J. Chem. Soc.*, **67**, 118 (1895); (e) Gustavson, *J. prakt. Chem.*, [2] **62**, 270 (1900).
(6) Gustavson, *ibid.*, [2] **62**, 273 (1900).
(7) Ogg and Priest, THIS JOURNAL, **60**, 217 (1938).

−33° and was completely absorbed by concentrated sulfuric acid. The method of preparation excluded the possibility of the presence of propylene and similar impurities.[8] Analytical reagent grade bromine was used. It was dried with anhydrous calcium bromide and distilled in an all-glass apparatus. Only the middle fraction which boiled at 58.7° at 751 mm. was used.

Difficulty was experienced in obtaining consistent results in the study of the addition of bromine and hydrogen bromide to cyclopropane until the apparatus shown in Fig. 1 was devised for eliminating dust and water from the reaction.

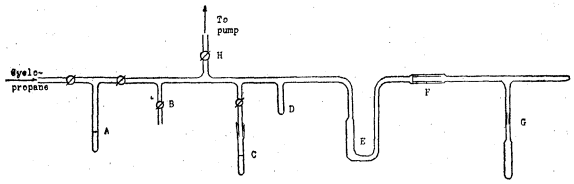


Fig. 1.

A was calibrated to contain 1.56 g. of liquid cyclopropane at the temperature of a solid carbon dioxide–acetone bath. The tube C was calibrated (by titration) to contain 0.288 or 2.62 g. of liquid hydrogen bromide at a similar temperature and was attached to the system through a ground glass connection. To avoid contact of bromine with stopcock and joint lubricant, bromine was weighed out in a tube which was then sealed onto the line at D. After the tube containing hydrogen bromide or bromine was attached to the system, the tube was cooled in liquid nitrogen and the whole system was evacuated to about 10^{-5} mm. through the line H. By suitable manipulations of stopcocks, cyclopropane was introduced into A, any excess hydrogen bromide or cyclopropane was removed from the calibrated tubes by cautious evacuation, and the reactants were degassed.[3] They were then distilled successively through phosphorus pentoxide and a glass wool plug in tube E, and finally through glass filter cloth in tube F, into the reaction tube G. Any added substances had been previously placed in G before it was sealed onto the system and kept cold during the above procedures. For experiments in the absence of oxygen (indicated by − in the oxygen column of the tables), the system was then evacuated once more to remove traces of uncondensed gases and tube G was sealed off at the constriction. For experiments in the presence of oxygen, the degassing operation was omitted and oxygen was admitted through stopcock B until its pressure in the line was 22 cm. before tube G was sealed off. Since this tube was at the temperature of liquid nitrogen it was estimated that the oxygen pressure would increase to about one atmosphere at room temperature.

For the dark reaction, the bomb tubes were allowed to stand in an iron pipe at room temperature. In the photochemical studies (indicated by + in the "light" column in the tables) the reaction tubes were immersed in water kept at 20 ± 5° and only the liquid phase was exposed to light from a 300-watt incandescent lamp at a distance of approximately ten centimeters.

(8) Hass, McBee, Hinds and Gluesenkamp, *Ind. Eng. Chem.*, **28**, 1178 (1936).

After reaction, the bomb tube was immersed in liquid nitrogen and opened. A tube was then sealed on so that the low-boiling contents would distil into water or aqueous potassium iodide solution at room temperature. The remainder was washed into the same solution. Unreacted bromine or hydrogen bromide was then determined by titration.

Reaction of Cyclopropane with Bromine.—In Table I are summarized the experiments which demonstrate the effect of various substances on the interaction of bromine and cyclopropane. The first two experiments show that the reaction of cyclopropane and bromine in the dark is very slow, and that oxygen has an accelerating effect on the reaction. It is remarkable, however, that in the absence of oxygen the photochemical reaction is extremely slow (47% reaction in two hundred hours), while in the presence of oxygen the reaction is complete in about two hours. Peroxides exert an effect similar to that of oxygen. Another striking observation is the inhibition of the photochemical oxygen-catalyzed reaction by ethyl alcohol and isoamyl nitrite.

TABLE I

THE ADDITION OF BROMINE TO CYCLOPROPANE[a]

Added substances[b]	Conditions Oxygen	Conditions Light	Reaction time	% reaction[c]	Remarks
None	−	−	52 days	13	2% HBr found
None	+	−	53 days	20	2% HBr found
None	−	+	200 hrs.	47	Checked. 8.3% HBr evolved
None	+	+	1.9 hrs.	100	Checked
None*	+	+	2.0 hrs.	100	
Ascaridole, 0.03	−	+	3.2 hrs.	100	
Bz_2O_2, 0.03	−	+	3.5 hrs.	100	
Bz_2O_2, 0.03	+	+	2.1 hrs.	100	
Ethanol, 0.05	+	+	64.0 hrs.	100	
i-AmONO, 0.1	+	+	204 hrs.	37	2% HBr found
Water, 0.1	+	+	1.7 hrs.	100	
Water, 0.1	−	+	76.7 hrs.	100	Checked. Two phases
HBr, 0.1	+	+	2.1 hrs.	100	

[a] In all cases the mole ratio of bromine to cyclopropane was 1:10, except the one marked with an asterisk when it was 1:2. Experiments in concentrated solution were not carried out because bromine seems to act as an inhibitor for chain reactions under such conditions. [b] Quantities expressed in moles per mole of bromine used. [c] Complete reaction was assumed when color faded to a faint yellow tinge.

Because of the small quantities of materials used in our study, we were unable to isolate any reaction product other than 1,3-dibromopropane. That other materials are formed was indicated by the formation of hydrogen bromide and small quantities of a material boiling lower than 1,3-dibromopropane.

Reaction of Cyclopropane with Hydrogen Bromide.—Two distinct types of reaction mix-

tures were used in the study of the reaction of cyclopropane and hydrogen bromide. In one group of experiments, equimolecular quantities of the reactants were used, in the second, a tenfold excess of cyclopropane. These procedures yielded strikingly different results as shown in Table II.

TABLE II

THE ADDITION OF HYDROGEN BROMIDE TO CYCLOPROPANE

Added substances[a]	Conditions Oxygen	Light	% reaction	Remarks
None[b]	−	−	8	
None[b]	−	+	11, 12	
None[b]	+	−	81	
None[b]	+	+	99, 99	
Bz_2O_2, 0.03[b]	−	+	74	
$(C_6H_5)_2NH$, 0.03[b]	+	+	91	
Catechol, 0.03[b]	+	+	28, 41, 43[c]	Catechol not completely dissolved
Catechol, 0.03[b]	+	−	41, 50[c]	
Catechol, 0.03[b]	−	+	41, 43[c]	
Water, 0.1[b]	−	−	87	Two phases
None[d]	−	−	55, 66[e]	
None[d]	−	+	70[e]	
None[d]	+	−	67, 73[e]	
None[d]	+	+	74, 76[e]	
Thiocresol, 0.03[d]	−	+	90	Mixture became warm in a few minutes
Catechol, 0.03[d]	−	−	97[b]	
Water, 0.03[d]	−	−	94	
Acetic acid, 0.03[d]	−	−	87	

[a] Quantities expressed in moles per mole of hydrogen bromide used. [b] Mole ratio of hydrogen bromide to cyclopropane was 1:10; the reaction time was two hours. [c] Odor of product indicated formation of propyl ether of catechol. [d] Mole ratio of hydrogen bromide to cyclopropane was 1:1; the reaction time was four hours. [e] Addition products combined and found to be *n*-propyl bromide.

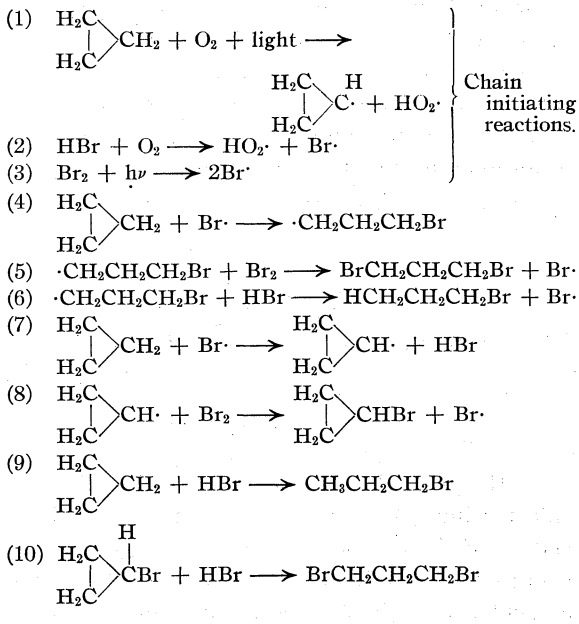
Thus, when excess cyclopropane was used, and oxygen was removed from the system, a slow reaction took place in the dark (8% in two hours), and only a slight increase was observed upon illumination (11% in two hours). However, in the presence of oxygen a tremendous increase in the reaction velocity was noted. Thus, in two hours a yield of 81% of normal propyl bromide was obtained in the dark and nearly 100% in the light. The effect of benzoyl peroxide on the rate of reaction was similar to that of oxygen. Antioxidants appear to overcome partially the accelerating effect of oxygen, but duplicate experiments show that in illuminated reactions in the absence of oxygen, catechol accelerates the reaction. Since water has the same effect (in the dark), it seems likely that catechol may accelerate the reaction by one mechanism while inhibiting it by a second.

On the other hand, when equimolecular quantities of cyclopropane and hydrogen bromide are used, oxygen and illumination have no significant effect on the rate of reaction. Water, acetic acid, thiophenol and catechol accelerate the addition reactions in the absence of oxygen.

Discussion

It is evident from our experiments that pure cyclopropane and pure bromine do not react appreciably in the dark, and only very slowly in the light. The observations recorded in the literature regarding the ring cleavage by bromine must therefore apply to an oxygen-catalyzed photochemical reaction. A careful study of our data indicates that we are dealing with a chain reaction similar to the oxygen-catalyzed photochemical brominations of phenanthrene[2] and toluene.[1,3] In support of this one may cite the following facts: (1) minute amounts of oxygen or peroxides are effective in bringing about a rapid reaction; (2) traces of inhibitors markedly retard the reaction.

The following schematic representation is suggested for the bromination of cyclopropane (a dot is used to represent an unpaired electron)



The low-boiling materials observed by us could have been formed in reactions 6, 8 and 9. Reaction 7 readily explains the formation of hydrogen bromide. The relative ineffectiveness of light in the absence of oxygen is surprising for one might expect a fairly large concentration of

bromine atoms from equation 3. This suggests that the active entity responsible for the chain reaction may not be the bromine atom but a free radical of the type $\cdot BrO_2$. The latter is a possibility which we are keeping in mind.

From the standpoint of the thesis developed in this paper, an attractive explanation is at once available to account for the fact that cyclopropylamine does not react with bromine, although the ring is easily cloven by nitrous acid.[9] The amino group is an inhibitor in reactions involving bromine atoms. The stability of the ring, therefore, is to be ascribed to the chain-breaking mechanism of the amino group, rather than to the inherently greater stability of the ring in cyclopropylamine. The same explanation applies to the resistance toward cleavage of cyclopropyl cyanide.[5c] The effect of groups on the stability of the cyclopropane ring is, therefore, not necessarily related to ease of cleavage of the ring with bromine.

The oxygen effect in the reaction of hydrogen bromide and cyclopropane, when the latter is used in large excess, is readily correlated with our bromine atom chain mechanism. The free bromine atoms are formed by equations 1 or 2. The formation of normal propyl bromide by the chain mechanism is indicated by equations 4 and 6, by a different mechanism in equation 9.

The ineffectiveness of light and oxygen on the rate of reaction of equimolecular quantities of hydrogen bromide and cyclopropane is suggestive of an ionic mechanism different from an atom or free-radical chain reaction. Furthermore, the fact that substances such as thiocresol, catechol, acetic acid, and water have an accelerating effect lends some support to the idea that the mechanism is ionic in character. These substances are all capable of combining with a proton and thereby causing dissociation of the hydrogen bromide molecule into a bromide ion and a positively charged fragment. The cleavage of the cyclopropane ring by ions would not be expected to be photochemical. The accelerating effect of hydroxylic compounds indicates that the contribution of an atom mechanism to the rate of reaction is insignificant in concentrated hydrogen bromide solutions.

(9) Kishner, *Chem. Zentr.*, **72**, II, 579 (1901); **76**, I, 1703 (1905).

Summary

1. The reaction of bromine with a ten-fold excess of cyclopropane is greatly accelerated by the combined effect of oxygen and light.

2. The reaction of hydrogen bromide with a ten-fold excess of cyclopropane is greatly accelerated by oxygen and only slightly accelerated by light.

3. Organic peroxides have an effect similar to that of oxygen.

4. A chain mechanism involving bromine atoms is suggested for each addition reaction.

5. The addition of hydrogen bromide to an equivalent quantity of cyclopropane is not significantly affected by oxygen or light, but is accelerated by hydroxylic compounds. For this effect a competing non-atomic mechanism is suggested.

CHICAGO, ILLINOIS RECEIVED MAY 22, 1939

[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY OF THE UNIVERSITY OF CHICAGO]

Chlorinations with Sulfuryl Chloride. I. The Peroxide-Catalyzed Chlorination of Hydrocarbons

BY M. S. KHARASCH AND HERBERT C. BROWN[1]

In the past the use of sulfuryl chloride as a chlorinating agent has depended upon the dissociation of the compound, under the experimental conditions, into its components—sulfur dioxide and chlorine. That is, the sulfuryl chloride served as a source of *molecular* chlorine, and it has been used almost exclusively for the chlorination of aromatic nuclei in the presence of halogen carriers.[2] The utilization of sulfuryl chloride in this way offers little advantage over the use of gaseous chlorine; for this reason sulfuryl chloride has not been generally adopted in the laboratory for carrying out such chlorinations.

In the course of investigations on the chemical properties of free radicals in solution, which are now being carried out in this Laboratory, it was found that in the presence of certain catalysts (such as organic peroxides) sulfuryl chloride can serve as a source of chlorine *atoms*. Using this procedure,

(1) Eli Lilly Fellow, 1938–39.

(2) (a) Tohl and Eberhard, *Ber.*, **26**, 2940 (1893); (b) Silberrad, *J. Chem. Soc.*, **119**, 2029 (1921); (c) **121**, 1015 (1922); (d) Silberrad, Silberrad and Parke, *ibid.*, **127**, 1724 (1925).

it is possible to chlorinate *in the dark* many types of compounds (paraffin hydrocarbons, side-chains of aromatic hydrocarbons, aliphatic acids, aldehydes, and ketones, etc.) far more rapidly and conveniently than is possible by the use of elementary chlorine and light.[3]

General Procedure

$$RH + SO_2Cl_2 \xrightarrow[\text{peroxide}]{\Delta} RCl + SO_2\uparrow + HCl\uparrow$$

The sulfuryl chloride is mixed with the compound to be chlorinated (Note 1) in a round-bottomed flask, and a small amount of benzoyl peroxide (Note 2) is added (0.001 to 0.005 mole of peroxide per mole of sulfuryl chloride). The flask is connected to an efficient reflux condenser (Note 3), preferably by a ground-glass joint, and the entire mixture is refluxed gently. Evolution of gases (hydrogen chloride and sulfur dioxide) begins at once. When these gases are no longer given off, the reaction is complete (Note 4). The reaction mixture is fractionated without further treatment (Note 5).

As previously stated (Note 3), the yields obtainable by this method vary with the efficiency of the reflux condenser. Without using any particular precautions, yields of 80% (based on the available chlorine utilized) are obtained easily. If a trap kept at $-10°$ is connected to the condenser, and the trapped material is returned to the reaction flask periodically, the yields can be made quantitative.

Notes

(1) The molar ratio of sulfuryl chloride to organic compound which is used depends upon the same factors that operate in ordinary chlorinations: relative cost of materials, ease of separation of the higher chlorinated products, etc. In this work, we have usually used a large excess of hydrocarbon in carrying out the chlorination because in most of the preparations we were interested primarily in observing the point of attack of the reagent, not in obtaining the maximum possible yield.

(2) Benzoyl peroxide was used in most of this work. Most other peroxides tested (*e. g.*, lauroyl peroxide) act similarly. On the other hand, ascaridole gives poor results. Apparently, it decomposes far too rapidly to be used as a catalyst in this reaction.

(3) In this paper the chlorination of hydrocarbons is discussed. The chlorination of many types of oxygen derivatives by this method is under investigation, and the results will be reported shortly.

(3) The yield of product depends upon the efficiency of the reflux condenser. An inefficient condenser permits the gases evolved to carry off an appreciable quantity of the volatile reactants.

(4) The progress of the reaction is followed easily if the gases evolved are led through a gas wash bottle connected by tubing to the top of the reflux condenser. The time required to carry out a reaction varies with the compound to be chlorinated, the rate of heating, and the amount of peroxide added; however, in most cases, the reaction can be completed in from one to two hours for reaction mixtures which contain one mole of sulfuryl chloride, one to three moles of hydrocarbon, and 0.002 mole of peroxide.

(5) The results reported in this paper were obtained with the use of a short fractionating column, 25 cm. in length, the inner tube of which (9 mm.) was packed with a spiral of no. 18 silver wire coiled to two turns per centimeter.

Chlorination of Paraffin Hydrocarbons

The study of the action of sulfuryl chloride on paraffin hydrocarbons and their halogen derivatives has been neglected almost completely. The only report in the literature dealing with this subject is a patent covering the chlorination of methane with sulfuryl chloride at 300° in the presence of a catalyst such as carbon.[4]

In the absence of catalysts and light, sulfuryl chloride does not react with **cyclohexane**[5] to an appreciable extent at temperatures as high as its boiling point. Even in the presence of light, the chlorination of the hydrocarbon with sulfuryl chloride is very slow. For example, a mixture of the two compounds, strongly illuminated[6] and refluxed, reacts no more than 25% in six hours.

Most of the materials whose catalytic activity was investigated affect the rate of chlorination but slightly. In contrast, the effect of a trace of peroxide is amazing. The addition of 0.001 mole of benzoyl peroxide to the reaction mixture causes *complete reaction in from fifteen to thirty minutes in the dark*. The results of these studies are listed in Table I.

In these experiments, 0.6 mole of the hydrocarbon and 0.2 mole of sulfuryl chloride were refluxed, usually for six hours unless the reaction was complete before that time.

(4) McKee and Salls, U. S. Patent 1,765,601 (1930).

(5) Cyclohexane was selected because of its simple structure and availability, and its reactions with sulfuryl chloride under various conditions were studied intensively.

(6) A 300-watt lamp, placed 10 cm. from the flask, was used to illuminate the reaction mixture.

The extent of reaction was calculated from the amount of chlorocyclohexane isolated upon fractionation of the reaction mixture. Except where stated otherwise, the reaction was carried out with complete exclusion of light.

TABLE I

CHLORINATION OF CYCLOHEXANE WITH SULFURYL CHLORIDE

Catalyst	Reaction time, hours	Yield, %
CuCl, 0.2 mole	6	20
S, 0.01 mole	6	0
I, 0.01 mole	6	0
PCl_5, 0.01 mole	6	5
Slow stream HCl	3	0
Slow stream SO_2	3	0
Slow stream O_2	3	0
No catalyst	6	0
Animal carbon, 5 g.	6	30
No catalyst, light[a]	6	25
Animal carbon, 5 g., light	6	75[b]
Benzoyl peroxide, 0.001 mole	1/2	80
Lauroyl peroxide, 0.001 mole	1/4	80

[a] For intensity of light, see footnote 6. [b] Reaction was not complete in less than six hours.

The study of the chlorination of a number of paraffin hydrocarbons and their halogen derivatives was undertaken to determine the generality of this method of chlorination and to compare the results thus obtained with those reported for the photochemical chlorination of these compounds with chlorine gas.

In general, the results are similar. Secondary hydrogen atoms are substituted by chlorine more readily than primary, and the presence of a halogen substituent increases the difficulty of further substitution. This deactivating effect is especially strong upon the carbon atom holding the substituent,[7] and decreases with increasing distance from it.

The experimental results are summarized in Table II.

Chlorination of Side-Chains in Aromatic Hydrocarbons

As stated previously, the use of sulfuryl chloride as a chlorinating agent has been restricted largely to the chlorination of aromatic nuclei in the presence of halogen carriers.[2] However, the isolation of benzyl chloride from the chlorination of toluene has been reported several times. Dubois[8] reports that toluene and sulfuryl chloride react slowly at 115° to form benzyl chloride and chlorotoluene, and Wohl[9] patented the preparation of benzyl chloride in 50% yield by the action of sulfuryl chloride on toluene at 130°. Tohl and Eberhard[2a] state that a refluxing mixture of toluene and sulfuryl chloride does not react. More recently, this statement has been questioned, and it has been reported that toluene and sulfuryl chloride do react in the dark at the temperature of reflux.[2d]

We find that pure peroxide-free **toluene** shows no sign of reaction with sulfuryl chloride after six hours of refluxing in the dark. In the light,[6] however, a slow reaction takes place which is not complete in less than seven hours.[10] Benzyl chloride is formed. In the presence of a small amount of added peroxide, a vigorous reaction occurs in the dark and nearly quantitative yields of benzyl chloride can be obtained in fifteen minutes. In the presence of excess sulfuryl chloride further chlorination of the side-chain occurs and benzal chloride is formed. The introduction of a third chlorine atom into the side-chain either does not take place or occurs so slowly that for all practical purposes the reaction may be neglected. For example, a mixture of **benzal chloride,** sulfuryl chloride, and benzoyl peroxide was refluxed for twenty hours without any reaction being observed. This result is a confirmation of the conclusion previously drawn from the inertness of *sym*-tetrachloroethane and chloroform: the accumulation of two chlorine atoms upon a carbon atom prevents further substitution upon that atom (by this method of chlorination).

Derivatives and homologs of toluene are chlorinated readily by sulfuryl chloride and peroxide with but few exceptions. Thus ***p*-chlorotoluene, ethylbenzene, isopropylbenzene,** etc., are easily and smoothly chlorinated in the side chain. On the other hand, neither ***o*-nitrotoluene** nor ***p*-nitrotoluene** can be chlorinated in this way.

Diphenylmethane is another compound which does not undergo the peroxide-catalyzed chlorination with sulfuryl chloride. Furthermore, this compound strongly inhibits the reaction between sulfuryl chloride and cyclohexane. This inhibitory ability must be a property of the substance itself; careful purification of the hydrocarbon does not alter its behavior.

(7) The presence of two or more chlorine atoms upon a carbon atom completely prevents further substitution on that carbon atom by this method. Thus, neither chloroform nor *sym*-tetrachloroethylene could be chlorinated. That this inactivity is not due to the presence of inhibitors is shown by the fact that these compounds can be used as solvents in the chlorination of other substances.

(8) Dubois, *Bull. acad. roy. Belg.*, **42**, 126 (1876).

(9) Wohl, German Patent 139,552 (1903); 160,102, 162,394 (1905).

(10) The reaction mixture contained 0.6 mole of toluene and 0.2 mole of sulfuryl chloride.

TABLE II

CHLORINATION OF ALIPHATIC HYDROCARBONS AND THEIR HALOGEN DERIVATIVES

Compound chlorinated	Moles taken: Compound	SO_2Cl_2	Peroxide	Reacn. time, hr.	Yield chlor. prods., %[a]	Products[b] %	Compound	B. p. °C.	Mm.	$n^{20}D$
Cyclohexane	0.8	0.6	0.001	1.5	100	72	Chlorocyclohexane	66–68	62	1.462
						28	Dichlorocyclohexane			
Cyclohexane	1.8	.6	.001	1.5	98	89	Chlorocyclohexane			
						11	Dichlorocyclohexane			
n-Heptane	3.0	.75	.001	1.0	90	15	1-Chloroheptane	156–159		1.428
						85	*s*-Chloroheptane			
n-Propyl chloride	0.6	.2	.002	4.0	85	60	1,2-Dichloropropane	96–99		
						40	1,3-Dichloropropane	121–125		
n-Butyl chloride	2.5	1.0	.001	3.0	85	25	1,2-Dichlorobutane	121–123		1.441
						50	1,3-Dichlorobutane	131–133		1.444
						25	1,4-Dichlorobutane	77–79	62	1.455
						No	1,1-Dichlorobutane			
Propylene chloride	10.0	2.5	.005	1.5	80	15	1,1,2-Trichloropropane	131–133		
						48	1,2,2-Trichloropropane	122–124		
						37	1,2,3-Trichloropropane	155–158		
Ethylene chloride	0.3	0.3	.002	2.5		70	1,2,2-Trichloroethane	113–114		1.4708
sym-Tetrachloroethane	.2	.4	.002	6.0	None					
Chloroform	.22	.2	.005	3.0	None					
n-Propyl bromide	3.0	.75	.001	2.5	90	50	1-Bromo-2-chloropropane	116–117		1.4746
						30	1-Bromo-3-chloropropane	68–70	62	1.4950
						20	Higher b. unidentified			
						No	*n*-Propyl chloride			

[a] The total yield was calculated from the chlorinated reaction mixture before separation into the individual components. [b] Yields are calculated from the rectification graphs.

This method of chlorination with sulfuryl chloride promises to be of special value in the chlorination of side-chains of aromatic hydrocarbons containing reactive nuclei. The photochemical chlorination of the side-chains of such molecules usually leads to impure products due to simultaneous nuclear substitution. By the use of sulfuryl chloride and a peroxide, however, it is possible, in some cases, to prevent entirely the chlorination of the nucleus and obtain a pure product, containing halogen in the side-chain only.

For example, the chlorination of the side-chain of ***m*-xylene** with chlorine gas and sunlight to form *m*-xylyl chloride is accompanied by the formation of at least 10% of 4-chloro-*m*-xylene under the most favorable conditions.[11] The separation of the two products by fractionation is difficult. Chlorination of *m*-xylene with sulfuryl chloride and peroxides yields only *m*-xylyl chloride. The purity of the product was ascertained from the refractive index, and a comparison of the analytical data for side-chain and total halogen. In spite of reports to the contrary,[2a] pure sulfuryl chloride and *m*-xylene do not react at the reflux temperature[12] of the mixture.

***t*-Butylbenzene** is another compound whose chlorination is better effected by the use of sulfuryl chloride than by the ordinary photochemical method. As a matter of fact, the side-chain of this hydrocarbon is so unreactive toward the halogens that it is impossible to obtain the halogen derivatives directly. Conditions under which reaction occurs with the halogens lead only to nuclear substitution products.[13] However, by the use of a peroxide and sulfuryl chloride, the side-chain can be chlorinated with ease.

On the other hand, the nuclei of **fluorene** and **β-methylnaphthalene** are extremely reactive, and the reaction, to produce nuclear substitution products,[14] occurs so readily that the method cannot be used for the chlorination of the side-chains of these molecules.

The experimental results are summarized in Table III.

Experimental Part

Materials.—The sulfuryl chloride was obtained in large quantities from the Hooker Electrochemical Company. The other materials used in this work were chiefly Eastman Kodak Co. chemicals or commercial products. Several of the substances used were prepared by standard methods.

(11) King and Merriam, *Proc. Nova Scotian Inst. Sci.*, **18**, 276 (1933–34); *C. A.*, **29**, 6214 (1935).

(12) The difficulties encountered in proving this fact illustrate the extreme caution needed in working with peroxide-catalyzed reactions. A test run which was made in the dark with *m*-xylene and sulfuryl chloride in the absence of added peroxides showed a vigorous reaction. The product formed, however, was *m*-xylyl chloride, not the 4-chloro-*m*-xylene which nuclear chlorination would have produced. The reagents were tested and found to be peroxide free. Further investigation disclosed that the solvent (acetone) which had been used to rinse the reaction flask, was the source of the peroxide impurity.

(13) Salibil, *Chem. Ztg.*, **35**, 97 (1911); *Chem. Zentr.*, I, 1581 (1911).

(14) The products formed in the reaction between sulfuryl chloride and such reactive hydrocarbons will be reported in a later communication.

TABLE III

CHLORINATION OF SIDE-CHAINS OF AROMATIC HYDROCARBONS

Compound chlorinated	Moles taken: Cpd.	SO_2Cl_2	Peroxide	Reacn. time, hr.	Yield chlor. prods., %[a]	%	Products[b] Compound	Physical constants B. p. °C.	Mm.	$n^{20}D$
Toluene	0.6	0.2	None, light	7.0		75	Benzyl chloride	96–99	62	1.5390
Toluene	.4	0.2	0.0003	0.25		80	Benzyl chloride			
Toluene	.4	1.6	.003[c]	6.0	85	10	Benzyl chloride			
						90	Benzal chloride	104–105	30	1.5503
Benzal chloride,	.2	0.4	.002	20	None					M. p.
p-Chlorotoluene	.4	.2	.001	0.25		70	*p*-Chlorobenzyl chloride	114–117	30	29°
Ethylbenzene	.8	.2	.001	0.25	85	Chiefly	α-chloroethylbenzene	90–93	30	
Isopropylbenzene + 0.75 mole of benzene	1.5	.3	.001	1.5	95	90	α-Chlorocumene			
						10	β-Chlorocumene	95–99	21	
m-Xylene + 0.7 mole of carbon tetrachloride	1.0	.3	.001	0.5		80	*m*-Xylyl chloride	101–102	30	1.5345
m-Xylene + 0.3 mole of carbon tetrachloride	0.2	.1	None	6.0	None					
t-Butylbenzene	.6	.3	0.001	0.2		70	β-Chloro-*t*-butylbenzene	119–120	30	1.5253
o-Nitrotoluene	.6	.2	.001	2.0	No chlorination but decomposition of SO_2Cl_2					
p-Nitrotoluene	.2	.4	.005	4.0	No chlorination but decomposition of SO_2Cl_2					
Diphenylmethane	.2	.22	.002	2.0	Less than 20% chlorination and decomposition of SO_2Cl_2					
Fluorene	.3	.1	None	Reacn. on warming		Nuclear chlorination				
β-Methylnaphthalene	.3	.1	None	Reacn. on warming		Nuclear chlorination				

[a,b] See notes on Table II. [c] Added in three equal portions at one-hour intervals.

n-Propyl bromide and *n*-butyl chloride were synthesized according to the general procedures described in "Organic Syntheses." Diphenylmethane was prepared by the action of aluminum amalgam on benzyl chloride and benzene.[15] *t*-Butylbenzene was prepared conveniently by the treatment of a mixture of 40 moles of benzene and 4 moles of *t*-butyl chloride with 10–15 g. of aluminum chloride for four hours at room temperature. The yield of purified product was 80%.

Although in the experiments reported in this paper the materials were purified by distillation or recrystallization before use, such purification is not necessary: the commercial products undergo this peroxide-catalyzed chlorination readily. In some cases in which impure materials were used, an inhibition period of from fifteen to thirty minutes was observed. However, no noticeable diminution of the yield occurred. It appears that the impurities which cause the inhibition are removed or deactivated by continued refluxing with sulfuryl chloride and peroxides.

Solvents.—The use of a solvent or a diluent is advantageous in a few cases, as in the chlorination of solid materials and in lowering the reaction temperature,[16] so the applicability of a number of solvents was tested.

A mixture containing 0.3 mole of toluene, 0.2 mole of sulfuryl chloride, and 0.3 mole of the solvent (diluent in this case) was treated with 0.001 mole of benzoyl peroxide and refluxed. The course of the reaction was followed by the rate of evolution of the gases, and by the loss in weight of the reaction flask.

The following solvents were found applicable: methylene chloride (40°), chloroform (61°), carbon tetrachloride (77°), benzene (80°), chlorobenzene (132°), and *o*-dichlorobenzene (180°).

Carbon tetrachloride was used in the chlorination of a number of aromatic hydrocarbons (Table III).

Chlorination of Aliphatic Hydrocarbons.—The chlorination of the aliphatic hydrocarbons and their halogen derivatives when treated with sulfuryl chloride and peroxides according to the general procedure outlined, proceeds smoothly, and the experimental conditions in the individual cases need not be described. However, it may be worthwhile to call attention to the following observation. The chlorination of volatile compounds (*e. g.*, *n*-propyl chloride, b. p. 46.8°) is rather slow, due to the slow rate of decomposition of the benzoyl peroxide at the temperature of reflux. This rate can be increased in two ways—by using a less stable peroxide (*e. g.*, lauroyl peroxide) or by raising the boiling point of the reaction mixture. The latter can be accomplished most conveniently in the laboratory by adding a suitable diluent of relatively high boiling point (chlorobenzene or *o*-dichlorobenzene).

(15) *Org. Syntheses*, **15**, 34 (1934).

(16) The solution must be kept refluxing throughout the reaction so that the vapors of the boiling solution may keep the oxygen of the air, which strongly inhibits the reaction, away from the reaction mixture. By using a low-boiling solvent, it is possible to accomplish this at a lower temperature and thus minimize the possibilities of secondary reactions of sulfuryl chloride with the compound.

Chlorination of Side-Chains.—The chlorination of the side-chains of aromatic hydrocarbons according to the general procedure also proceeds smoothly in most cases. However, certain of the preparations require special techniques or raise points of interest, and therefore should be discussed further.

Toluene reacts readily when an excess of the hydrocarbon is treated with benzoyl peroxide and sulfuryl chloride. The identity of the chief product was established as benzyl chloride by preparing the quaternary ammonium salt with dimethylaniline (m. p. 115–116°). On the other hand, when the hydrocarbon is treated with an excess (1:4) of sulfuryl chloride, the reaction does not go to completion, but ceases after only two parts of the sulfuryl chloride have been utilized to form benzal chloride. In order to determine the cause of this inactivity the following experiments were carried out.

In a 200-cc. round-bottomed flask were placed 36.8 g. of toluene (0.4 mole), 54.0 g. of sulfuryl chloride (0.4 mole), and 0.5 g. of benzoyl peroxide (0.002 mole). Upon refluxing this mixture a vigorous reaction took place, complete in less than half an hour. Another portion of sulfuryl chloride (0.4 mole) and benzoyl peroxide (0.002 mole) was added, and the refluxing was continued. In this case, the reaction required three hours to reach completion. No further reaction was observed after a third portion of sulfuryl chloride and peroxide was added and the treatment was repeated. The product isolated was benzal chloride.

Benzal chloride (Eastman Kodak Co.) was distilled under reduced pressure, and a fraction boiling between 104–105° at 30 mm. was collected. A reaction mixture made up of 32.2 g. of this material (0.2 mole), 54.0 g. of sulfuryl chloride (0.4 mole), and 0.5 g. of benzoyl peroxide (0.002 mole) was refluxed for twenty hours. The loss in weight of the flask was less than 10% of the theoretical. The reaction mixture was fractionated, but beyond the fact that the last portion of the reaction mixture distilled up to 108° (30 mm.), no evidence of reaction was observed.

In a flask were placed 18.4 g. of toluene (0.2 mole), 16.1 g. of benzal chloride (0.1 mole), and 27.0 g. of sulfuryl chloride (0.2 mole). Benzoyl peroxide was added (0.002 mole), and the mixture was refluxed. Reaction began at once, and was complete in twenty minutes.

These experiments indicate that the inability of sulfuryl chloride to chlorinate toluene completely to benzotrichloride must be due to the inactivity of benzal chloride toward the reagent, and not to any chain-breaking property of the molecule.

The chlorination of **ethylbenzene** yields the α-chloro derivative as shown by the ease of hydrolysis of the compound isolated, and by the formation of acetophenone by the action of cupric nitrate upon the compound.[17] A small amount of β-chloroethylbenzene is probably formed also, but its presence could not be demonstrated by the method used.[18]

In a sealed tube were placed 14.0 g. of chloroethylbenzene (0.1 mole), and 20 g. of pyridine (0.25 mole). The mixture was heated at 115–120° for six hours. The tube was then opened, and the styrene and excess pyridine were removed under reduced pressure. The residue was extracted twice with an alcohol–ether mixture. However, the quaternary ammonium salt of β-chloroethylbenzene could not be isolated.

The chlorination of **isopropylbenzene** also indicates that the substitution of chlorine in the side-chain takes place predominantly at the α-position. In this case, the analysis of the reaction mixture is simplified by the fact that the α-chloro derivative is a tertiary chloride, readily decomposed by heating into an olefin and hydrogen chloride.

The reaction was carried out according to the general procedure. In order to minimize disubstitution, a 5:1 ratio of hydrocarbon to sulfuryl chloride was used (1.5 mole cumene, 0.3 mole sulfuryl chloride). Benzene was used as a solvent to keep the temperature moderate throughout the reaction. After the reaction was complete, the benzene and excess isopropylbenzene were carefully removed under reduced pressure (21 mm.). The weight of the residual liquid indicated a yield of 95%. This material was refluxed under reduced pressure until hydrogen chloride was no longer given off, and was then fractionated. β-Phenylpropylene passed over between 59 and 62° (21 mm.). Between 95 and 100°, 2.5 g. of β-chloroisopropylbenzene was collected. This represents approximately 10% of the total product.

***t*-Butylbenzene** was prepared by the Friedel–Crafts synthesis. The measurement of the refractive index of the product ($n^{20}D$ 1.4927) and its unreactivity toward bromine demonstrate the absence of alpha hydrogen atoms, and establish the purity of the product.

The hydrocarbon, 5.0 g., was treated with 1 cc. of a 5% solution of bromine in carbon tetrachloride. The mixture was illuminated by a 300-watt lamp for twenty-four hours. No reaction was evident.

In another experiment, the hydrocarbon was treated with bromine and ascaridole,[19] but no reaction occurred.

Chlorination of the hydrocarbon with sulfuryl chloride proceeded with a rapidity that is especially surprising in view of the general unreac-

(17) Fischer and Schmitz, *Ber.*, **39**, 2210 (1906). The acetophenone was identified in the form of its phenylhydrazone.

(18) α- and β-chloroethylbenzene cannot be separated by fractionation.

(19) Kharasch, Margolis, White and Mayo, THIS JOURNAL, **59**, 1405 (1937).

tivity of the side-chain toward other reagents. A product was isolated by fractionation (b. p. 119–120° at 30 mm., $n^{20}D$ 1.5253) which was identified as β-chloro-*t*-butylbenzene by the preparation of the anilide of β,β-dimethylhydrocinnamic acid,[20] m. p. 122–123°.

The action of **diphenylmethane** toward sulfuryl chloride is different from that of any of the other hydrocarbons whose chlorinations have been described. Not only is this compound incapable of undergoing the usual peroxide-catalyzed reaction with sulfuryl chloride, but it is capable of inhibiting the chlorination of other hydrocarbons by this method.

It is probable that this peculiar action is not due to the hydrocarbon itself, but to some product formed by a reaction of sulfuryl chloride with the compound. When diphenylmethane is mixed with sulfuryl chloride (no peroxide added), and the mixture is permitted to stand at room temperature, the originally clear solution becomes cloudy within a few minutes, reddening upon longer standing. After some time (one to three days), a red oil separates.

In a round-bottomed flask were placed 33.6 g. of diphenylmethane (0.2 mole), 30 g. of sulfuryl chloride (0.22 mole), and 0.5 g. of benzoyl peroxide (0.002 mole). The mixture was refluxed. No evolution of gas occurred during the first thirty minutes, but the solution became red in color. Upon continued refluxing, a slow reaction occurred, as was shown by the gas given off. Examination disclosed that this gas contained free chlorine, indicating decomposition of the sulfuryl chloride. After three hours, reaction had ceased. The reaction mixture was fractionated under reduced pressure. It consisted chiefly of unchanged diphenylmethane. Less than 20% of the product distilled in the temperature range of benzhydryl chloride (156–162 at 13 mm.). No sulfuryl chloride was recovered; it was probably completely dissociated into sulfur dioxide and chlorine.

A number of other experiments were carried out in which the conditions (temperature, solvents, peroxide, ratio of reagents, etc.) were altered, but with the same result. Since sulfuryl chloride is ordinarily stable under the conditions used in these experiments, the dissociation of the reagent must be due to the catalytic action of some substance formed in the reaction mixture.

The following experiment illustrates the inhibiting effect of diphenylmethane on the chlorination of other hydrocarbons.

(20) The general procedure recommended by Underwood and Gale, THIS JOURNAL, **56**, 2117 (1934), was followed with one exception. The Grignard reagent could not be prepared with the usual commercial magnesium activated according to the procedure recommended. Using sublimed magnesium and a crystal of iodine, the reaction occurred without difficulty.

Two reaction mixtures were made up. Both contained 5 g. of sulfuryl chloride and 5 g. of toluene plus a few grains of benzoyl peroxide. To one was added 5 cc. of chlorobenzene; to the other, 5 cc. of diphenylmethane. The flasks containing the mixture were placed in a hot-water bath simultaneously. The first mixture reacted vigorously while the second showed no signs of reaction after two hours.

Triphenylmethane, however, is chlorinated without difficulty.

In a reaction flask were placed 8.4 g. of triphenylmethane (0.033 mole), 13.5 g. of sulfuryl chloride (0.1 mole), and 0.1 g. of lauroyl peroxide (0.0005 mole). The mixture was refluxed for thirty minutes. The excess sulfuryl chloride was removed, and the reaction product was twice recrystallized from ligroin (90–100°). There was isolated 5.7 g. of material, m. p. 111–112°, which was identified as triphenylmethyl chloride by the fact that the melting point of a mixture with a known sample of triphenylmethyl chloride was not depressed.

The **nitrotoluenes** do not undergo the peroxide-catalyzed reaction with sulfuryl chloride. This inactivity is probably due to inhibitory (chain-breaking) properties of the nitro groups. For example, the chlorination of cyclohexane is slowed down markedly by the addition of a small amount of *p*-nitrotoluene.

Inhibition of the Reaction.—It has been pointed out that the reaction between sulfuryl chloride and hydrocarbons is markedly catalyzed by small amounts of peroxides.[21] The reaction is equally sensitive to small quantities of other substances. For example, the addition of iodine or sulfur, in moderate excess over the amount of peroxide added, will completely inhibit the reaction. A slow stream of oxygen through the reaction mixture also inhibits the reaction.[16] A number of substances were tested for their effect on the reaction.

A mixture of 168 g. of cyclohexane (2.0 moles) and 270 g. of sulfuryl chloride (2.0 moles) was made up. To 21.9 g. of this mixture (containing 0.1 mole each of cyclohexane and sulfuryl chloride) there was added 0.001 mole of benzoyl peroxide and 0.01 mole of the substance whose inhibitory properties were being tested. The mixture was refluxed for one hour (unless the reaction was complete before that time), and the extent of the reaction was estimated from the loss in weight of the reaction flask.

Under these conditions, the following substances inhibit the reaction: iodine, sulfur, *p*-nitrotoluene, thionyl chloride, phosphorus trichloride, and isoamyl nitrite. A slow stream of oxygen passing

(21) We have not made any attempt as yet to measure the smallest quantity of peroxide capable of completely chlorinating one mole of hydrocarbon. In one experiment, however, 0.0003 mole of benzoyl peroxide was sufficient catalyst to chlorinate completely one mole of toluene.

through the reaction mixture also prevents reaction.

On the other hand, the addition of acetyl chloride, acetic acid, and benzophenone has no noticeable effect upon the rate of the reaction.

Reaction of Benzoyl Peroxide with Sulfuryl Chloride.—In developing the mechanism of this reaction between sulfuryl chloride and hydrocarbons to be described later in this paper, it became of interest to study the action of benzoyl peroxide on sulfuryl chloride itself. It was found that at 70–80° benzoyl peroxide reacts slowly with sulfuryl chloride to form chlorobenzene, according to the equation

$$(C_6H_5CO)_2O_2 + SO_2Cl_2 \xrightarrow{\Delta} 2C_6H_5Cl + SO_2 + 2CO_2$$

Sulfuryl chloride (0.4 mole) and benzoyl peroxide (12.1 g., 0.05 mole) were placed in a round-bottomed flask, and 0.4 mole of benzene was added as a diluent. The mixture was refluxed for twenty-four hours, and then fractionated; chlorobenzene, 8.0 g., was isolated (b. p. 128–131°), and identified by means of its nitration product, 2,4-dinitrochlorobenzene (m. p. 50–51°). Since the amount of chlorobenzene isolated represents 70% of the theoretical yield, it is evident that the equation above represents the main reaction. A few grams of higher-boiling material was also formed. This was fractionated under reduced pressure and the presence of benzoic acid and diphenyl demonstrated. These are the usual products of the decomposition of benzoyl peroxide in benzene.[22]

Mechanism of the Reaction

It is evident that this reaction between sulfuryl chloride and hydrocarbons has those characteristics which are commonly ascribed to chain reactions. Among these properties, the most significant is probably the sensitivity of the reaction to small traces of other substances—the rate is increased tremendously by small amounts of peroxides, and completely inhibited by small quantities of sulfur, iodine, and oxygen. Furthermore, the similarity of the results obtained in this reaction with those obtained by photochemical chlorination is also significant, and points to an identical reactive intermediate—the chlorine atom.

The decomposition of peroxides to form free radicals appears to be well established.[23] These free phenyl radicals are known to remove halogen from molecules containing reactive halogen. Based upon these facts, the following chain mechanism for this reaction is advanced tentatively.

$$C_6H_5CO{-}OO{-}COC_6H_5 \longrightarrow 2C_6H_5- + 2CO_2 \quad (1)$$
$$C_6H_5- + SO_2Cl_2 \longrightarrow -SO_2Cl + C_6H_5Cl \quad (2)$$
$$-SO_2Cl \longrightarrow SO_2\uparrow + Cl- \quad (3)$$
$$Cl- + RH \longrightarrow R- + HCl\uparrow \quad (4)$$
$$R- + SO_2Cl_2 \longrightarrow RCl + -SO_2Cl \quad (5)$$

It may be that the reaction proceeds through an alternative mechanism involving a direct attack of the chlorine atom upon the hydrocarbon, forming the alkyl chloride and liberating a *hydrogen atom* to carry on the chain. This mechanism, which we consider very unlikely, may be indicated as follows:

$$Cl- + RH \longrightarrow RCl + H- \quad (4')$$
$$H- + SO_2Cl_2 \longrightarrow HCl\uparrow + -SO_2Cl, \text{ etc.} \quad (5')$$

The chain could be broken by the following steps

$$R- + R- \longrightarrow R{-}R \quad (6)$$
$$R- + Cl- \longrightarrow R{-}Cl, \text{ etc.} \quad (7)$$
$$H- + H- \longrightarrow H_2 \quad (6')$$
$$H- + Cl- \longrightarrow HCl, \text{ etc.} \quad (7')$$

In addition, traces of impurities could break the chain by combining with the reactive intermediates, the atoms or free radicals. Those substances which have been shown capable of inhibiting the reaction probably operate in this manner.

These considerations indicate why peroxides are effective catalysts in this reaction. Furthermore, they suggest that any substance capable of removing a chlorine atom from sulfuryl chloride should also catalyze the reaction between sulfuryl chloride and organic compounds. This conclusion has been verified in a number of cases.[24] However, benzoyl peroxide remains the most convenient catalyst for general use in this reaction.

Summary

1. A trace of an organic peroxide induces a reaction between sulfuryl chloride and organic compounds

$$RH + SO_2Cl_2 \xrightarrow[\text{peroxide}]{\Delta} RCl + SO_2\uparrow + HCl\uparrow$$

By the use of this procedure, it is possible to chlorinate *in the dark* many types of organic compounds more rapidly and conveniently than can be done by the use of elementary chlorine and light.

2. The study of the chlorination by this method of cyclohexane, *n*-heptane, *n*-propyl chloride, *n*-butyl chloride, ethylene chloride, propylene chloride, *sym*-tetrachloroethylene, chloroform, and *n*-propyl bromide leads to the following generalization: (a) Substitution takes place on a secondary carbon atom in preference to a primary. (b) A second chlorine atom tends to substitute as

(22) Lippmann, *Monatsh.*, **7**, 522 (1886).

(23) Hey and Waters, *Chem. Rev.*, **21**, 186 (1937).

(24) These results will be reported in a later communication.

far from the first chlorine atom as possible. (c) Substitution of a second chlorine atom upon a carbon atom already holding a halogen substituent is difficult; a third chlorine atom cannot be introduced. (d) A bromine substituent is not displaced.

3. The chlorination of side-chains of aromatic hydrocarbons proceeds readily as shown by a study of the chlorination of toluene, *p*-chlorotoluene, ethylbenzene, isopropylbenzene, *t*-butylbenzene, *m*-xylene, and triphenylmethane. The study of the chlorination of toluene, with an excess of sulfuryl chloride, reveals that in this case also the substitution of chlorine upon a carbon atom ceases with the introduction of the second chlorine atom. Both ethylbenzene and isopropylbenzene chlorinate chiefly in the alpha position of the side-chain. Diphenylmethane and the nitrotoluenes cannot be chlorinated by this method.

4. This method of chlorination is of particular value for the chlorination of side-chains in molecules containing reactive nuclei. Thus, *m*-xylene is chlorinated in the side-chain without the simultaneous formation of any nuclear-substituted products; and *t*-butylbenzene reacts readily to form β-chloro-*t*-butylbenzene, a compound which cannot be prepared by the direct action of chlorine upon the hydrocarbon.

5. The characteristics of the reaction indicate that the slow decomposition of the peroxide at the reaction temperature initiates a chain reaction involving chlorine *atoms*.

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The Magnetic Properties of Myoglobin and Ferrimyoglobin, and their Bearing on the Problem of the Existence of Magnetic Interactions in Hemoglobin

BY DONALD S. TAYLOR

Myoglobin, or muscle hemoglobin, was first isolated in crystalline form by Theorell,[1a] who showed that it is very similar to hemoglobin but that it has certain important differences. The minimum molecular weight calculated from the iron analysis is 17,000,[1a] a value agreeing with that calculated from hemoglobin analyses. Theorell[1b] investigated the sedimentation velocity of crystallized myoglobin, and found two components, with molecular weights of 34,000 for the principal one and 68,000 for the secondary one. A redetermination by Polson[2] in the same laboratory gave the value 17,000, leading to the conclusion that there is only one iron atom, and therefore only one heme group per molecule. The oxygen saturation curve found for myoglobin[1e] is a rectangular hyperbola rather than a sigmoid curve as is found for hemoglobin. It has a much higher affinity for oxygen than hemoglobin has[1e] and thus acts as an oxygen reservoir for the muscle. Its oxygen equilibrium is much less affected by change in acidity than is that of hemoglobin.[1e] Myoglobin forms compounds analogous to those of hemoglobin, and is very easily oxidized to brown ferrimyoglobin[3] (metamyoglobin). The absorption spectra[1c] of myoglobin and its derivatives are very similar to those of the analogous hemoglobin substances, but the band positions are slightly shifted.

The magnetic studies of myoglobin are then of interest for the information they give about the structural chemistry of the myoglobin series, and also for the opportunity offered to make a comparison between this series in which the hemes are located on individual molecules (or at least are physico-chemically independent as judged by the oxygen equilibrium study[1e]) and the hemoglobin series in which there are four hemes per molecule with a large physico-chemical interaction effect (calculated to be about 6000 calories per mole according to the theoretical analysis of the oxygen equilibrium by Pauling[4]). In particular this comparison should shed light on the question as to

(1) H. Theorell, *Biochem. Z.*, (a) **252**, 1 (1932); (b) **268**, 47 (1934); (c) **268**, 55 (1934); (d) **268**, 64 (1934); (e) **268**, 73 (1934).

(2) T. Svedberg, *Nature*, **139**, 1051 (1937). Note added in proof: Dr. Theorell has informed us in a private communication that Polson worked with cow myoglobin, so that the reported differences from values obtained by Theorell on horse myoglobin may be real. However, the discussion or conclusions given here are not changed by this new information.

(3) The nomenclature adopted here is analogous to that proposed by Pauling and Coryell[5] for hemoglobin substances.

(4) L. Pauling, *Proc. Natl. Acad. Sci.*, **21**, 186 (1935).

whether magnetic interactions occur between the hemes in hemoglobin. The postulate of interaction was advanced by Pauling and Coryell[5] because the magnetic moment of ferrohemoglobin (calculated from the magnetic susceptibility assuming no interaction) is somewhat higher than expected for ferrous ion. It was thought that this might be caused by a slight tendency for the magnetic moments of the four hemes in a molecule to orient together when a magnetic field is applied. In myoglobin we have the hemes on separate molecules, so that no magnetic interaction can occur in dilute solution. The magnetic moment calculated for myoglobin from the susceptibility must then be the true magnetic moment of the heme group conjugated to globin, a value different from that found for hemoglobin if magnetic interaction does occur.

In the work that is to be described it will be shown that the magnetic properties of the iron in myoglobin (from horse heart muscle) in both the ferrous and ferric forms are to within the limits of experimental error equal to those of the corresponding hemoglobin substances.

Experimental Part

Preparation of Myoglobin Solutions.—Three myoglobin preparations were made, which will be designated as myoglobins I, II, and III. The first preparation was a pioneer preparation using the material from one heart. The last two yielded sufficient quantities for magnetic measurements. The method used in the preparations is essentially that described by Theorell[1a] with modifications as suggested by Morgan.[6] The procedure will be described here, as some variations were introduced.

Horse hearts were obtained from the animals less than two hours after death and placed in ice for the trip to the laboratory. They were then washed well with water and freed from fat as thoroughly as possible, and the meat was finely ground. An amount of water about equal to half the weight of the meat was added and the mixture allowed to stand about twenty hours in the cold room. A reddish extract was then obtained by squeezing out the liquid in a large press. It was found that additional myoglobin solution was obtained if the meat was again extracted in the same way.

The red liquid which was obtained rapidly darkened due to auto-oxidation to ferrimyoglobin when the reducing action of the tissues was no longer effective.

The *p*H was adjusted to 7.00 by addition of 1 *N* potassium hydroxide with rapid stirring. The solution was mixed at room temperature with one-fourth its volume of a saturated solution of basic lead acetate. This substance caused precipitation of the globulins in the form of a dense white glutinous mass which was easily removed by centrifuging. The *p*H was again adjusted to 7.00 by addition of 1 *N* potassium hydroxide, and 210 g. of potassium dihydrogen phosphate and 300 g. of potassium monohydrogen phosphate were added to each liter of solution, this being enough to give a solution approximately 3 molar in phosphate and buffered at about *p*H 6.6. The precipitate of lead phosphate and hemoglobin which then formed was filtered off. The myoglobin was obtained by repeatedly dialyzing this solution against saturated neutral ammonium sulfate solution. The first nearly colorless precipitate (albumins) was filtered off and discarded. The myoglobin finally precipitated as a brownish solid mixed with considerable albuminous material. Dialysis was carried out in cellophane casings in the cold room.

The crude myoglobin precipitate thus obtained was purified somewhat by several treatments involving redissolution in water and dialysis against saturated neutral ammonium sulfate until precipitation took place. No effort was made to get absolutely pure crystals since the only requirement for this work was the preparation of a hemoglobin free solution of sufficiently high myoglobin concentration.

All processes were carried out in the cold room or in the refrigerator except for the short periods for filtration and handling. Chemically pure reagents were used throughout except for some impure ammonium sulfate used in preparation II, it being thought that the inorganic iron present would not be carried through the purification process. Some seemed to have been carried through, however, and this rendered certain measurements on this solution valueless, as will be pointed out later.

For preparation II eleven hearts were obtained and the final step yielded 130 ml. of dark brown solution concentrated enough for magnetic measurements. In preparation III twelve hearts (45 pounds, 20 kg.) were used but only about 100 ml. of solution of slightly lower concentration was obtained. (From concentrations given later it can be calculated that in all about 15 g. of myoglobin was obtained.) The solutions were adjusted to *p*H 7.0 and kept in the refrigerator until used.

Standardization of Solutions.—Spectroscopic examination of solutions obtained in the manner described above indicated that all of the myoglobin was in the form of ferrimyoglobin. A Van Slyke–Neill[7] oxygen-capacity determination on solution III gave zero oxygen capacity, which also indicated the substance to be entirely in the ferric form, as Theorell[1c] has pointed out.

The concentration of the solutions was determined in the following manner. To 10 ml. of solution 0.15 g. of sodium hydrosulfite ($Na_2S_2O_4$) was added to reduce the ferrimyoglobin completely. The carbon monoxide capacity of the solution so obtained was then determined by the method of Van Slyke and Hiller[8] using the Van Slyke–Neill blood gas apparatus. Calculations from equilibrium data showed that the carbon monoxide affinity of myoglobin is not enough different from that of hemoglobin to affect the completeness of saturation when carried out in the manner recommended for hemoglobin. One-ml. solution samples were used, corrections being

(5) L. Pauling and C. D. Coryell, *Proc. Natl. Acad. Sci.*, **22**, 210 (1936).

(6) V. E. Morgan, *J. Biol. Chem.*, **112**, 557 (1936).

(7) D. D. Van Slyke and J. M. Neill, *J. Biol. Chem.*, **61**, 523 (1924).

(8) D. D. Van Slyke and A. Hiller, *ibid.*, **78**, 807 (1928).

made for retention on the walls of the transfer pipet and for change in the meniscus level on standing. The Van Slyke gas pipet had been calibrated previously. A volume of 0.25 ml. of acid ferricyanide reagent was used and correction for solubility of carbon monoxide in the sample and dissolved gases in the reagent was determined as is customary by analysis carried out on 1 ml. of water.

From the amount of carbon monoxide chemically bound as determined in this way the concentration of myoglobin was calculated in terms of moles of heme iron per liter. The gasometric determinations were carried out at least three times, and the agreement was thoroughly satisfactory.

Measurement of Magnetic Properties of Solutions.—The general technique used in the magnetic measurements by the differential Gouy method has been described elsewhere.[9] The standardized tube was surrounded by an air thermostat at 25°. The Δw values which are given below represent the mean of two determinations of the observed force in milligrams on the tube containing the sample when in a standard magnetic field. The two determinations were made in fields of different strengths and converted to a common basis by an empirically determined factor.

Each sample of myoglobin solution was treated in the following way. Twenty-five ml. of solution was placed in the tube and the value of Δw of the ferrimyoglobin ($\Delta w_{\mathrm{Mgb}^+}$) was measured. The solution was then reduced by the addition of 0.3 g. of sodium hydrosulfite and the Δw measured, which on the addition of an experimentally determined correction of +0.09 mg. for the diamagnetism of the added hydrosulfite gives the Δw for ferromyoglobin (Δw_{Mgb}). This solution was then removed from the tube, treated with 0.1 g. of sodium hydrosulfite and saturated with carbon monoxide by stirring in a dark stoppered flask with pure carbon monoxide. The solution so obtained was returned to the tube in the dark or diffuse daylight, and the Δw was measured, which on addition of a total correction of +0.12 mg. for diamagnetism of hydrosulfite gives Δw for carbonmonoxymyoglobin ($\Delta w_{\mathrm{MgbCO}}$). Enough of solution II was available to run four sets of measurements as described above and enough of solution III to run three sets of measurements. Averages of the values obtained were used in calculations.

Calculations.—The molal susceptibilities (χ_m) of the paramagnetic iron atoms in any compound x were calculated by means of the following equation, which holds for determinations made in the manner described.

$$\chi_m \times 10^6 = \frac{(\Delta w_x - \Delta w_{\mathrm{MgbCO}})}{m} 18.60 \qquad (1)$$

Here m is the molar concn. of heme iron and 18.60 is the apparatus constant determined by standardization with air and water.

In using Equation (1) we are assuming that the iron in carbonmonoxymyoglobin is in a diamagnetic state, and that therefore $\Delta w_{\mathrm{MgbCO}}$ may be used to correct for the diamagnetism of the solutions. This assumption is partially justified by the very close chemical similarity between carbonmonoxyhemoglobin and carbonmonoxymyoglobin. The magnetic results obtained by making this assumption agree so well with results for hemoglobin that we do not hesitate to accept them. If carbonmonoxymyoglobin were paramagnetic its magnetic moment would be due to unpaired electrons, of which there would necessarily be at least two. These two unpaired electrons would give a magnetic moment of at least 2.83 Bohr magnetons, an amount which would certainly cause a large difference in the calculated results for the free ferrous and ferric forms from results for the corresponding hemoglobin compounds arrived at in the same manner.

Magnetic moments μ in Bohr magnetons were calculated assuming Curie's law in the form

$$\mu = 2.84 \sqrt{\chi_m T} \qquad (2)$$

Experimental Results

All important experimental and calculated values are collected in Table I. It is to be noticed that the value of $\Delta w_{\mathrm{Mgb}^+} - \Delta w_{\mathrm{MgbCO}}$ for solution II is noticeably low. We ascribe this to the presence of inorganic iron in some form which undergoes increase in susceptibility on reduction. However, the value for solution III compares favorably with hemoglobin values, and since in this case care was taken to avoid contamination with inorganic iron we use this value to calculate the susceptibility of ferrimyoglobin. For ferromyoglobin measurements inorganic iron can have no effect, since the change in going from ferromyoglobin to carbonmonoxymyoglobin, the addition of carbon monoxide, would not change the susceptibility of the inorganic iron, but only that of the heme iron. In taking the difference we calculate the paramagnetic susceptibility of the heme iron independently of the other constituents of the solution. The close check between results for the two solutions indicates the precision that was obtained for even these rather dilute solutions.

The mean value of the molal susceptibility (χ_m) of ferromyoglobin is accordingly found to be $12{,}400 \times 10^{-6}$, corresponding to a magnetic moment of 5.46 Bohr magnetons; the value of the molal susceptibility of ferrimyoglobin (solution III) is found to be $14{,}200 \times 10^{-6}$, corresponding to a magnetic moment of 5.85 Bohr magnetons.

Experiments made on a very dilute solution of

(9) C. D. Coryell, F. Stitt and L. Pauling, THIS JOURNAL, **59**, 633 (1937).

TABLE I

EXPERIMENTAL DATA AND CALCULATED RESULTS

	Concn., m	Δw_{Mgb^+}	Δw_{MgbCO}	Δw_{Mgb}	Ferromyoglobin	Ferrimyoglobin
			Solution II			
	0.00437	+0.68	−2.28	+0.93		
	.00437	+ .85	−2.38	+ .94		
	.00438	+ .73	−2.25	+ .84		
		+ .77	−2.29	+ .88		
Av.	.00437	+ .76	−2.30 ± 0.04	+ .90 ± 0.4		
			$\Delta w_{Mgb^+} - \Delta w_{MgbCO}$ = +3.06 mg.			
			$\Delta w_{Mgb} - \Delta w_{MgbCO}$ = +3.20 mg.		$\chi_m = 12{,}300 \times 10^{-6}$	
			Solution III			
	0.00352	+0.92	−2.21	+0.48		
	.00350	+ .68	−2.23	+ .38		
	.00354	+ .59	−2.31	+ .29		
Av.	.00352	+ .73 ± 0.13	−2.25 ± 0.04	+ .38 ± 0.06		
			$\Delta w_{Mgb^+} - \Delta w_{MgbCO}$ = +2.98 mg.			$\chi_m = 14{,}200 \times 10^{-6}$
			$\Delta w_{Mgb} - \Delta w_{MgbCO}$ = +2.63 mg.		$\chi_m = 12{,}500 \times 10^{-6}$	
				Mean χ_m	$12{,}400 \times 10^{-6}$	$14{,}200 \times 10^{-6}$
				μ	5.46	5.85

ferrimyoglobin recovered from carbonmonoxymyoglobin III indicated that the formation of ferrimyoglobin hydroxide is accompanied by a decrease of magnetic susceptibility to approximately 8000×10^{-6}, very much like that attending the formation of ferrihemoglobin hydroxide.[9] These experiments were not of sufficient accuracy to allow quantitative conclusions to be made. A similar experiment also indicated that ferrimyoglobin fluoride has a susceptibility somewhat greater than that of ferrimyoglobin itself.

Discussion

The value $12{,}400 \times 10^{-6}$ for the molal magnetic susceptibility found for ferromyoglobin is to within experimental error equal to that of $12{,}290 \times 10^{-6}$ reported by Taylor and Coryell[10] for ferrohemoglobin. The susceptibility found for ferrimyoglobin is also to within the experimental error equal to that of ferrihemoglobin reported by Coryell, Stitt and Pauling.[9]

The values of the magnetic moments obtained for ferromyoglobin and ferrimyoglobin may be interpreted in the same manner as for ferrohemoglobin[5] and ferrihemoglobin,[9] leading to the conclusion that the iron atoms are held to the porphyrin by essentially ionic bonds.

Since myoglobin has one (or possibly two chemically independent) hemes per molecule as contrasted with the four of hemoglobin, the existence of interaction between the hemes of hemoglobin might lead to some difference in the magnetic moments observed for the two substances. That no difference greater than the experimental error is observed for either the ferrous or ferric forms of these substances is a strong indication that there is little or no magnetic interaction between the hemes in hemoglobin. We believe, therefore, that 5.44 Bohr magnetons is the magnetic moment of ferroheme conjugated with globin, and that 5.80 Bohr magnetons is the magnetic moment of ferriheme conjugated with globin. Magnetic titrations carried out by Coryell, Pauling, and Dodson[11] on systems involving the transformation of ferrohemoglobin to oxyhemoglobin and to nitric oxide hemoglobin also failed to give evidence for magnetic interactions between the hemes in ferrohemoglobin. These measurements would not be expected to be so sensitive as those described in this study.

That the observed moment of ferromyoglobin and ferrohemoglobin is considerably higher than that calculated for spin alone (4.92 for ferrous ions) may possibly be explained by assuming that the difference is due to orbital contribution to the moment. This contribution seems to be greater than that usually found for ferrous ions (0.2–0.3 Bohr magnetons). However, it should be remembered that the ferrous ion in the heme compounds is surrounded by the nitrogen atoms of the rigid planar heme group, and the closeness of approach of the nitrogen atoms to the iron atom is so restricted by the porphyrin structure that the separations may be greater than they would be

(10) D. S. Taylor and C. D. Coryell, THIS JOURNAL, **60**, 1177 (1938).

(11) C. D. Coryell, L. Pauling and R. W. Dodson, *J. Phys. Chem.*, in press (1939).

if the groups were free to move radially; and hence the orbital moment might not be quenched so much as it is in simpler compounds. A large amount of orbital contribution to the moment is also observed in the case of ferrihemoglobin cyanide and hydrosulfide,[9] which, however, have only one unpaired electron per iron atom.

Summary

The magnetic moments of the iron atoms in ferromyoglobin and ferrimyoglobin have been determined to be 5.46 and 5.85 Bohr magnetons, respectively. The magnetic moments indicate that the iron atoms are held by essentially ionic bonds in ferromyoglobin and ferrimyoglobin. The agreement of the magnetic moments with those calculated for the analogous hemoglobin compounds leads to the conclusion that magnetic interactions do not occur between the four hemes of hemoglobin.

PASADENA, CALIF. RECEIVED MAY 24, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

Activity Coefficients of Barium and Strontium Carbonates in Aqueous Solutions of Alkali Chlorides

BY ERNEST HOGGE AND HERRICK L. JOHNSTON

Townley, Whitney and Felsing[1] have computed activity coefficients of strontium and barium carbonates in alkali chloride solutions from solubility measurements in carbon dioxide-free, aqueous solutions at 25 and at 40°. We have been unable to check the calculations recorded in their tables and, while details of their computations are not given, it appears that they incorrectly computed the mean ion molality and have misinterpreted (K_2')'s taken from tables of MacInnes and Belcher[2] as stoichiometric second dissociation constants of carbonic acid in salt solutions whereas these K's are in reality the products of the stoichiometric constants by the square of the mean activity coefficients of hydrochloric acid in the same solutions.[3] Correction for the activity coefficients of hydrochloric acid is important in the higher concentrations of the salt solutions employed by Felsing and co-workers.

We have accordingly recalculated the activity coefficients and obtained results that differ from those of T., W. and F. by as much as 100% in the higher salt concentrations. We employed the same equation used by T., W. and F. to correct for hydrolysis of carbonate ion, namely

$$\frac{x^2}{C - x} = \frac{k_w}{k_m'} \qquad (1)$$

with C set equal to *total* carbonate concentration in solution (equal as well to divalent metal ion concentration); x, to the concentration of bicarbonate ion; $(C - x)$ to that of carbonate ion; k_w to the stoichiometric ionization constant of water in the salt solutions and k_m' to the correct stoichiometric second ionization constant of carbonic acid in the solutions. The latter is computed from MacInnes and Belcher's tabulations of pK_2' [2] by the relationship

$$\log k_m' = -pK_2' - 2 \log \gamma_{HCl} \qquad (2)$$

In solving equation (1) for x, necessary in the eventual computation of the mean molality of barium (or strontium) and carbonate ions and the evaluation of the activity coefficients of barium (or strontium) carbonate, we employed the following sources of data.

Values of C are taken from Tables I and II of Townley, Whitney and Felsing. These are smoothed values of their solubility measurements in potassium, sodium and lithium chloride solutions, respectively.

The values of k_w are taken from the data of Harned and co-workers[4] who have determined the

(1) Townley, Whitney and Felsing, THIS JOURNAL, **59**, 631 (1937).

(2) (a) MacInnes and Belcher, *ibid.*, **55**, 2630 (1933); (b) **57**, 1683 (1935).

(3) The above misinterpretation is easily made for MacInnes and Belcher refer to their (K_2')'s as "apparent second ionization constants" and use them, without correction, as the stoichiometric constants in constructing their Tables V and VI. For their own purpose this use was justified for they were employed in computing a small correction term in solutions of relatively low ionic strength and neglect of the factor γ^2_{HCl} was without significance. The correct interpretation was further clouded by a misprint in equation (12) of MacInnes and Belcher's first paper (ref. 2a) which is, however, given in correct form as equation (3) of their second paper (ref. 2b). The latter equation shows clearly the dependence on γ^2_{HCl} in relating (K_2') to the stoichiometric constant

$$\left(K_2 \frac{\gamma_{HCO_3^-}}{\gamma_{H^+}\,\gamma_{CO_3^=}}\right)$$

(4) (a) Harned and Hamer, THIS JOURNAL, **55**, 2194 (1933); (b) Harned and Copson, *ibid.*, **55**, 2206 (1933); (c) Harned and Mannweiler, *ibid.*, **57**, 1874 (1935); (d) Harned and Cook, *ibid.*, **59**, 2304 (1937).

degree of water dissociation in each of the three chlorides and at, or near, both 25 and 40°.

Values of k'_m were computed, for potassium chloride solutions, by use of equation (2) with pK'_2 taken from the tables of MacInnes and Belcher[2a,b] and γ_{HCl} from Table IV of Harned and Hamer.[4a] Interpolations were made by graphical methods. MacInnes and Belcher's measurements at 38° were assumed valid at 40°.

For sodium and lithium chlorides evaluation of k'_m is, of necessity, less exact. Reliable values of γ_{HCl} in these solutions are available[4b,c] but MacInnes and Belcher's determinations of pK'_2 are limited to potassium chloride solutions and no determinations of similar accuracy are available for sodium and lithium chlorides. We corrected for this as follows

$$k'_m \text{ equals } \left(K_2 \frac{\gamma_{HCO_3^-}}{\gamma_{H^+}\ \gamma_{CO_3^-}}\right)$$

where K_2 is the true thermodynamic dissociation constant, whence

$$\log (k'_m)_{NaCl} - \log (k'_m)_{KCl} = \log \left(\frac{\gamma_{HCO_3^-}}{\gamma_{H^+}\ \gamma_{CO_3^-}}\right)_{NaCl} - \log \left(\frac{\gamma_{HCO_3^-}}{\gamma_{H^+}\ \gamma_{CO_3^-}}\right)_{KCl}$$

and a similar relationship holds for the ratio of $(k'_m)_{LiCl}$ to $(k'_m)_{KCl}$. Further, $\gamma_{CO_3^-}$ can be set equal to $\gamma^4_{HCO_3^-}$ as an approximation.[5,6] A similar relationship has held in other solutions of similarly related mono-, di- and trivalent ions.[7]

We may therefore write

$$\log (k'_m)_{NaCl} = \log (k'_m)_{KCl} + \log (\gamma_{H^+}\ \gamma^3_{HCO_3^-})_{KCl} - \log (\gamma_{H^+}\ \gamma^3_{HCO_3^-})_{NaCl}$$

and reduce this to the form

$$\log (k'_m)_{NaCl} = \log (k'_m)_{KCl} + 4 \log \frac{(\gamma_{HCO_3^-})_{KCl}}{(\gamma_{HCO_3^-})_{NaCl}} \quad (11)$$

by the not unreasonable assumption that $(\gamma_{H^+})_{KCl}$ bears to $(\gamma_{H^+})_{NaCl}$ very nearly the same ratio as $(\gamma_{HCO_3^-})_{KCl}$ to $(\gamma_{HCO_3^-})_{NaCl}$.

The final term in equation (3) is evaluated from Table XII of Walker, Bray and Johnston,[6] and is considered to be the same at 25 and at 40°. The influence of this correction alone affects the activity coefficients of the carbonates to the extent of about 10% at the higher ionic strengths in aqueous lithium chloride.[8]

Finally, the values of x obtained from equation (1) were employed to yield values of $(1/m_\pm)$, by the relationship $m_\pm = \sqrt{C(C-x)}$, and a plot was made of log $(1/m_\pm)$ *vs.* $\sqrt{\mu}$ for the several solutions. Extrapolation to $(\mu = 0)$ gave the limiting values listed in Table I.

(5) This approximation should be quite good at low ionic strengths (to 0.1 or 0.2 μ) where the mean activity coefficient of the alkali bicarbonate should be given rather accurately by an expression of the type

$$\log \gamma_{25°} = \frac{-0.504\sqrt{\mu}}{1 + A\sqrt{\mu}} \quad (3)$$

[Debye and Hückel, *Physik. Z.*, **24**, 185 (1923)], where A is a constant related to the "mean ion size," and that of the alkali carbonate by the expression

$$\log \gamma_{25°} = \frac{-1.008\sqrt{\mu}}{1 + A\sqrt{\mu}} \quad (4)$$

Since it is fair to conclude that carbonate and bicarbonate ions will differ little in size (Ref. 6) the A's can be set equal and it follows that

$$\log \gamma_{M_2CO_3} = 2 \log \gamma_{MHCO_3} \quad (5)$$

and

$$\log \gamma_{CO_3^-} = 4 \log \gamma_{HCO_3^-}$$

At ionic strengths above 0.1 or 0.2 the mean activity coefficients of the electrolytes require the addition of a linear term in μ, to correct for the influence of the ions on the dielectric constant of the medium. This leads to equations of the type

$$\log \gamma_{MHCO_3} = \frac{-0.504\sqrt{\mu}}{1 + A\sqrt{\mu}} + B_{MHCO_3}\mu \quad (6)$$

$$\log \gamma_{M_2CO_3} = \frac{-1.008\sqrt{\mu}}{1 + A\sqrt{\mu}} + B_{M_2CO_3}\mu \quad (7)$$

[Hückel, *ibid.*, **26**, 93 (1925), also cf. Harned, THIS JOURNAL, **48**, 326 (1926), and Åkerlöf, *ibid.*, **48**, 1160 (1926)], whence

$$\log \gamma_{M_2CO_3} = 2 \log \gamma_{MHCO_3} + (B_{M_2CO_3} - 2B_{MHCO_3})\mu \quad (8)$$

and the extent to which the approximation we use is in error is determined by the magnitude of the term in μ.

Walker, Bray and Johnston (ref. 6) claim to have shown that log $\gamma_{CO_3^-} = 4 \log \gamma_{HCO_3^-}$ for several of the alkali carbonate–bicarbonate mixtures in alkali chloride solutions but the proof that they offer appears rather to confirm only the experimental accuracy of their determinations of ϕ/ϕ_0 (defined as $\gamma_{CO_3^-}/\gamma^2_{HCO_3^-}$) arrived at both from equilibrium and cell measurements. However, their data for the potassium salts can be shown to confirm the above simple relationship in the following manner.

Combination of equations (6) and (7) with the definition of (ϕ/ϕ_0), and the introduction of activity coefficient of the metal ion leads correctly to the result

$$\log \phi/\phi_0 = \frac{-\sqrt{\mu}}{1 + A\sqrt{\mu}} + 4B_{MHCO_3}\mu + (6B_{M_2CO_3} - 12B_{MHCO_3})\mu \quad (9)$$

$$= 2 \log \gamma_{MHCO_3} + (6B_{M_2CO_3} - 12B_{MHCO_3})\mu \quad (10)$$

Disappearance of the last term in (10) leads to the assumed relationship $\gamma_{M_2CO_3} = \gamma^2_{MHCO_3}$ or $\gamma_{CO_3^-} = \gamma^4_{HCO_3^-}$. Walker, Bray and Johnston's data for the potassium salts are quite accurately reproduced by the equation

$$\log \phi/\phi_0 = \frac{-\sqrt{\mu}}{1 + 1.72\sqrt{\mu}}$$

over the *whole* concentration range (*i. e.*, to $\mu = 2.5$) which is equivalent to equation (9) with *both* of the terms in μ removed (*i. e.*, implies that equations (3) and (4) yield the correct activity coefficients for the potassium salts in chloride solutions even to μ greater than 2). A similar experimental simplification does not hold for their measurements on *sodium* salts which may mean only that B_{MHCO_3} is not negligible in the *sodium* salt solution. Accurately, this would permit us to use the simplification log $\gamma_{CO_3^-} = 4 \log \gamma_{HCO_3^-}$, with full confidence above $\mu = 0.1$ or 0.2 only within the potassium chloride parentheses of our equation (11). However, it does not appear to us reasonable that sensible error is introduced by using the simplifications for sodium chloride as well.

(6) Walker, Bray and Johnston, THIS JOURNAL, **49**, 1235 (1927).

(7) McDowell and Johnston, *ibid.*, **58**, 2009 (1936); Johnston and Leland, *ibid.*, **60**, 1439 (1938).

(8) In the treatment by Townley, Whitney and Felsing this correction for sodium and lithium salt solutions was neglected—*i. e.*, they considered the change of the stoichiometric ionization of *water* with the variation in salt solutions but not the change in the stoichiometric ionization of carbonic acid.

TABLE I

LIMITING VALUES OF $(1/m_{\pm})$ AT $\mu = 0$

Carbonate	Temp., °C.	$(1/m_{\pm})_{\mu=0}$
$SrCO_3$	25	43,680
$SrCO_3$	40	44,170
$BaCO_3$	25	22,180
$BaCO_3$	40	19,110

Values of $(1/m_{\pm})$ were read from the curve for convenient values of μ and used to obtain γ by the relationship

$$\gamma = \left(\frac{1}{m_{\pm}}\right)_{\mu=m} \Big/ \left(\frac{1}{m_{\pm}}\right)_{\mu=0} \qquad (12)$$

Values of γ so computed are listed in Tables II and III.

The absolute accuracy of these values is probably not better than $\pm 2\%$, but the relative values for each salt at a given temperature should be somewhat more accurate than this figure, and for this reason the third figure as given in the values of γ is included.

TABLE II

MEAN ACTIVITY COEFFICIENTS OF BARIUM CARBONATE IN AQUEOUS SALT SOLUTIONS

Ionic strength	25° LiCl	25° NaCl	25° KCl	40° LiCl	40° NaCl	40° KCl
0.001	0.905	0.925	0.936	0.916	0.916	0.919
.002	.863	.893	.909	.881	.879	.885
.005	.780	.835	.855	.814	.807	.819
.01	.685	.760	.795	.737	.727	.744
.02	.555	.663	.711	.627	.615	.637
.03	.460	.585	.649	.543	.535	.557
.04	.391	.524	.600	.478	.474	.497
.05	.342	.473	.558	.421	.420	.455
.07	.275	.398	.491	.357	.363	.403
.10	.214	.326	.415	.293	.302	.355
.15	.161	.253	.335	.227	.244	.304
.20	.131	.210	.283	.186	.208	.269
.30	.100	.161	.219	.138	.167	.230
.50	.075	.115	.176	.094	.120	.194
.70	.064	.070	.158	.070	.110	.174
1.00	.048	.073	.132	.051	.098	.157

TABLE III

MEAN ACTIVITY COEFFICIENTS OF STRONTIUM CARBONATE IN AQUEOUS SALT SOLUTIONS

Ionic strength	25° LiCl	25° NaCl	25° KCl	40° LiCl	40° NaCl	40° KCl
0.001	0.854	0.913	0.924	0.839	0.918	0.888
.002	.794	.871	.893	.772	.884	.852
.005	.682	.796	.832	.657	.817	.753
.01	.573	.713	.764	.551	.742	.665
.02	.451	.598	.673	.435	.632	.561
.03	.382	.509	.607	.372	.561	.494
.04	.335	.442	.554	.328	.487	.446
.05	.305	.395	.511	.298	.438	.413
.07	.269	.333	.442	.256	.370	.366
.10	.239	.276	.373	.210	.299	.320
.15	.210	.206	.304	.182	.218	.271
.20	.189	.162	.263	.161	.166	.238
.30	.160	.122	.217	.136	.118	.206
.50	.139	.097	.184	.110	.080	.177
.70	.132	.082	.170	.096	.063	.175
1.00	.130	.082	.161	.083	.052	.183

Summary

The mean activity coefficients of barium and strontium carbonates in aqueous solutions of the alkali chlorides, published originally by Townley, Whitney and Felsing,[1] have been recomputed. The recomputations correct for: (1) improper evaluation of the mean molalities; (2) misinterpretation of constants published by MacInnes and Belcher[2] and (3) differences in the degree of carbonic acid dissociation in the several alkali halides. The latter correction was made with the aid of Walker, Bray and Johnston's[6] observations concerning the activity coefficient ratio of carbonate and bicarbonate ions in alkali chloride solutions. The influence of the above corrections affects barium carbonate activity by some 40% at unit ionic strength, and about doubles the values for strontium carbonate.

Tables of the corrected values are given, for 25 and 40°.

COLUMBUS, OHIO RECEIVED MAY 2, 1939

[CONTRIBUTION FROM THE GEOPHYSICAL LABORATORY, CARNEGIE INSTITUTION OF WASHINGTON]

Phase Equilibrium Relations in the System, Na_2SiO_3–Li_2SiO_3

BY F. C. KRACEK

The experimental investigation reported upon in this article is a continuation of the work of this Laboratory on phase equilibrium relations in silicate systems involving one or more alkalies. The system described is a binary section within the ternary system, Na_2O–Li_2O–SiO_2, which is now under investigation, in preparation for a study of the mineralogically more interesting relationships of the sodium and lithium aluminosilicates.

The two metasilicates, Na_2SiO_3 and Li_2SiO_3, cocrystallize in two series of solid solutions with intermediate compound formation, one series extending from Na_2SiO_3 to $NaLiSiO_3$, while the other, a limited series, is at the Li_2SiO_3 end of the system, with Na partially replacing Li in crystalline Li_2SiO_3.

The freezing point relations in this and several other binary systems of silicates were investigated by Wallace[1] in Tammann's laboratory, by the method of cooling curves, supported by microscopic examination. It is now well realized that the results of cooling curve thermal analysis must be interpreted with care, even with rapidly crystallizing substances; with silicates, the arrest temperatures are always found to be too low in comparison with the equilibrium values as determined by quenching.[2] The reason for this lies in the reluctance with which most silicates crystallize. Although, in the system under discussion, the crystallization is comparatively rapid, the temperatures as determined by cooling curves are below the equilibrium values by as much as 72° for mixtures at the Na_2SiO_3 end of the system.

Wallace concluded from his data that mixtures of the two components crystallize together in a complete series of solid solutions with a minimum on the freezing curve between 40 and 50% Li_2SiO_3, and noted that, under the microscope, the crystalline phase changed at about 20 to 30% Li_2SiO_3 from Na_2SiO_3-like to Li_2SiO_3-like aspect. As no measurements of the refractive indices are presented, these observations have only qualitative value at the present time.

(1) R. C. Wallace, *Z. anorg. Chem.*, **63**, 1 (1909).

(2) E. S. Shepherd, G. A. Rankin and F. E. Wright, *Am. J. Sci.*, **28**, 293 (1909).

Experimental Details

The mixtures of sodium and lithium metasilicates employed in this work were synthesized by fusing together pure silica, sodium and lithium carbonates in the required proportions. The fusions were made in platinum crucibles. The reagents used were: (1) purified quartz, first converted to cristobalite by heating in a gas furnace at about 1500° to enhance its reactivity in the fusions. It left a residue of 0.03% after evaporation with hydrogen fluoride and sulfuric acid. (2) Reagent grade $Na_2CO_3 \cdot H_2O$, converted to sodium carbonate by drying at about 250° in an atmosphere containing carbon dioxide. Analysis by E. G. Zies gave 0.001% of $Fe_2O_3 + Al_2O_3$, 0.001% of CaO, and negligible amounts of other impurities. (3) Reagent grade lithium carbonate, stated to contain 0.003% $Fe_2O_3 + Al_2O_3$ and only a trace of Na.

A standardized method of fusing the mixtures was employed for the reason that, unless special precautions are taken, the lithium carbonate present, on melting in air, corrodes platinum with the formation of a greenish to black deposit which tends to crawl over the surface of the crucible. Experiments show that the attack is not caused by the lithium carbonate itself, as fusions of this carbonate in a carbon dioxide atmosphere have no appreciable action on platinum. Another reason for exercising special care in making the fusions is that mixtures of sodium carbonate and lithium carbonate begin to melt as low as 510°,[3] and when silica is present, vigorous bubbling and mechanical losses may occur at very low temperatures.

The procedure adopted is to heat the mixtures in covered crucibles over a small Méker burner to incipient fusion until a large part of the carbon dioxide in the charge is driven off. The temperature is then raised slowly to complete the fusion. The carbon dioxide from the burner provides a sufficiently inert atmosphere to prevent the corrosion of the crucibles. In order to expel the carbon dioxide completely, the charges must be heated finally in a carbon dioxide-free atmosphere, such as that of an electric furnace; access of oxygen to the charges at this stage is no longer harmful because the alkali is now well incorporated in the melt. Precaution must, however, be taken to avoid excessive volatilization of the alkali. Instead of heating to a high temperature, and allowing the carbon dioxide to escape by diffusion and bubbling, the desired result may be accomplished more safely by crystallizing the melt, which causes the carbon dioxide to be forced out during the last stages of the crystallization. For this purpose the crucibles are alternated between two electric furnaces, one kept at a temperature high enough to produce complete melting, the other at a temperature sufficiently lower to allow the melt to crystallize. About five successive crystallizations and remeltings suffice to expel the carbon dioxide completely from the mixtures in this system.

(3) W. Eitel and W. Skaliks, *Z. anorg. allgem. Chem.*, **183**, 263 (1929).

TABLE I

EQUILIBRIUM DATA[a] FOR THE SYSTEM Na_2SiO_3–Li_2SiO_3

Composition in weight, per cent. Na_2SiO_3	Li_2SiO_3	Refr. index of quenched glass ± 0.003	Temperature, degrees, °C. ± 0.5° Liquidus g + c	Liquidus g	Solidus c	Solidus c + g	Peritectic Below	Peritectic Above	Ref. no.
Primary Phase: Solid Solution, Na_2SiO_3 to $NaLiSiO_3$									
100.0	0.0	1.517		1089		1089			574
90.0	10.0	1.527	1022	1024	975	983			664
85.0	15.0	1.528	987	988	919	927			783
				987h					
80.0	20.0	1.529	954	955	882	892			665
76.5	23.5	1.529	930	931	863	868			782
				925h					
73.1	26.9	1.530	905	907	851	854			725
70.0	30.0	1.532	885	886	848	849			666
67.5	32.5	1.534	869	870	848	849			741
66.0	34.0	1.534	861	862	847	848			745
64.0	36.0	1.536	851	853	845	..			736
64.0	36.0	1.537	851	852	845	846			779
62.0	38.0	1.536	846	847	845	846			744
61.2	38.8	1.538	846	847	845	..			781
60.7	39.3	1.539	..	..	845	..	846	848	
Primary Phase: Li_2SiO_3 Limited Solid Solution									
60.7	39.3	1.539	848	848	845	..	847	848	778
60.0	40.0	1.538	852	855	845	846	847	848	667
59.0	41.0	...	860	862	846	847	847	..	777
57.57	42.43	1.539	872	873	847	..	847	..	737
57.57	42.43	1.539	872	874	846	..	..	848	742
57.57	42.43	1.540	872	873	847	..	847	848	776
57.0	43.0	1.540	877	878	..	..	847	848	780
50.0	50.0	1.542	931	935	..	..	846	848	668
40.0	60.0	1.545	998	1004	..	..	846	848	669
				1005h					
30.0	70.0	...		1072h	..	..	847	..	670
20.0	80.0	...		1125h	..	..	..	848	671
15.0	85.0	...		1147h	860	880			793
10.0	90.0	...		1169h	970	990			672
5.0	95.0	...		1185h	1077	1092			792
0.0	100.0	1.557		1201		1201			602

[a] All preparations were pre-crystallized for quenching. Under the headings "Liquidus" and "Solidus" the letter "c" denotes crystals alone, and "g" glass alone, in the quenched samples. "c + g" or "g + c" denotes the presence of both glass and crystals; "h" denotes determinations by heating curve thermal analysis.

Slight losses of alkali by volatilization occur in spite of the precautions, particularly from mixtures of more than 70% lithium metasilicate. These losses, which may be as much as 0.1% of the total weight of the charge, appear to be mainly due to lithium oxide. To compensate for them a small excess of lithium carbonate is weighed out in preparing the mixtures, in accordance with a previously determined estimate. This method of compensating for the losses was found to be preferable to the alternative one of adding a small amount of the desired constituent after the mixture had been prepared, as it avoids a number of additional reheatings.

The compositions of the mixtures are known from the initial and final weights during the synthesis. They were in all cases within 0.10% of the desired values. Any departure toward ternary compositions could have been detected under the microscope by the presence of more than traces of residual glass in quenches from temperatures which are below the lowest point on the solidus in the binary system, but above the eutectics in the ternary system.

The liquidus and solidus relations were determined mainly by quenching in mercury. It was found, however, that in compositions of more than 60% lithium metasilicate, the equilibrium at the liquidus cannot be satisfactorily quenched, because of rapid crystallization of lithium metasilicate. The quenching determinations in this region were supplemented by heating curves, where use was made of a special technique which was described in an earlier paper,[4] and in which a thimble crucible with a centrally reëntrant sheath for a differential thermocouple provides an accurately centralized location of the junction in the melting charge.

The temperatures were measured by calibrated Pt *vs.* 90 Pt–10 Rh thermocouples connected to a shielded potenti-

(4) F. C. Kracek, N. L. Bowen and G. W. Morey, *J. Phys. Chem.*, **41**, 1183 (1937).

ometer system. The conversion of the thermocouple readings to degrees was made with the aid of standard tables.[5] The furnaces used in the quenching work were thermostatically controlled with a precision of ±0.3 to 0.5° at the various required temperatures. In short runs (up to three hours) the precision was somewhat closer, but in long runs it approached the value given.

Equilibrium in the various charges was reached in approximately one hour, but two hours were usually allowed in the study of the liquidus relations. For the solidus the runs lasted a day or more in testing certain questions that arose during the course of the work.

Experimental Results

The essential thermal measurements are presented in Table I, as determined by quenching, and, for a few of the preparations, by heating-curve thermal analysis. The latter determinations are distinguished by the letter "h." The quenching results are presented by listing the two nearest temperatures determined above and below the transformation point in question for each composition, rather than by giving a detailed abstract of the experimental record.

The Phase Equilibrium Diagram

Figures 1 and 2 represent the phase equilibrium relations in the system (at atmospheric pressure). Instead of a complete series of solid solutions with a minimum on the liquidus, as outlined by Wallace,[1] there is an incongruently melting intermediate compound, $NaLiSiO_3$, and two series of solid solutions. One of these series extends from Na_2SiO_3 to $NaLiSiO_3$; the other is a Li_2SiO_3-rich solid solution, the composition limits of which lie between 83 ± 3 and 100% Li_2SiO_3.

The compound, $NaLiSiO_3$ (42.43% Li_2SiO_3), at its incongruent melting point of 847 ± 1°, decomposes into a melt, containing 39.3 ± 0.2% of Li_2SiO_3, and the above-mentioned Li_2SiO_3-rich solid solution. The extent of the peritectic line giving the compositions of these phases is determined by the measurements on the liquidus, on the one hand, and by a search with the microscope, on the other hand, for the presence of two kinds of crystals in quenches from below the peritectic, in compositions near the Li_2SiO_3 end of the system. At 85% Li_2SiO_3, only Li_2SiO_3-like crystals were found; at 80%, in addition to these, there was present a small quantity of $NaLiSiO_3$. The position of the solidus curve for the Li_2SiO_3-rich solid solutions, as determined by quenching, must be regarded as only approximate, because of the difficulty of quenching the interstitial glass.

Above the peritectic, the liquidus for the Li_2SiO_3-rich solid solutions rises smoothly to the melting point of Li_2SiO_3 at 1201 ± 1°.[6]

Between Na_2SiO_3 and the end of the peritectic line the liquidus and solidus relations are as illustrated in Figs. 1 and 2, the crystalline phase being

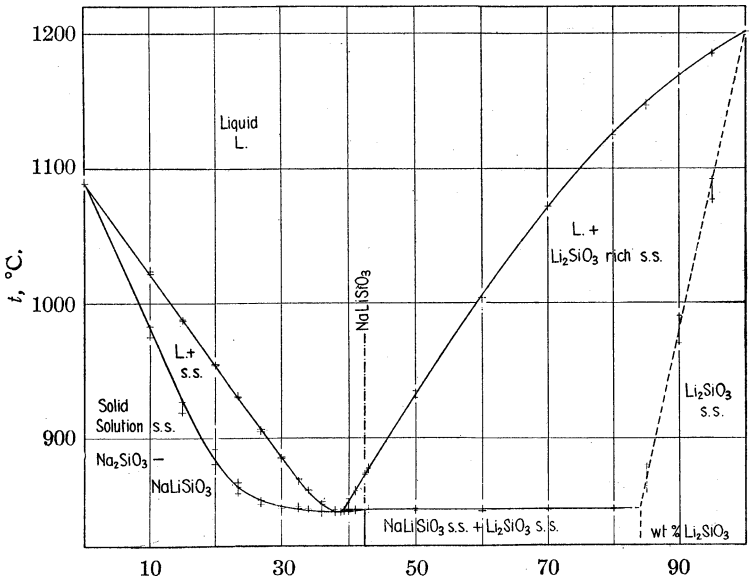


Fig. 1.—Equilibrium diagram for the system, Na_2SiO_3–Li_2SiO_3. Liquidus determinations, 60.0 to 100.0% Li_2SiO_3 by heating curve thermal analysis. All other determinations by quenching.

a continuous series of solid solutions whose composition varies from Na_2SiO_3 to $NaLiSiO_3$. Beginning at the melting point of Na_2SiO_3, 1089 ± 1°,[7] the liquidus and the solidus curves first drop, and follow their courses separately to meet again at the minimum point, 38.5 ± 0.2% Li_2SiO_3, 845 ± 1°. From the minimum point the liquidus curve rises to the end of the peritectic line, 39.3% Li_2SiO_3, 847 ± 1°. The solidus also rises to the peritectic, but meets it at the composition of the compound, $NaLiSiO_3$. The solid solution series becomes saturated at this composition, or, at the

(5) L. H. Adams, "International Critical Tables," Vol. I, 1925, p. 57.

(6) F. M. Jaeger, *J. Wash. Acad. Sci.*, **1**, 49 (1911); A. L. Day, R. B. Sosman and E. T. Allen, "High Temperature Gas Thermometry," *Carnegie Inst. Wash. Pub.*, **157**, 101 (1911).

(7) F. M. Jaeger, ref. 6; F. C. Kracek, *J. Phys. Chem.*, **34**, 1583 (1930).

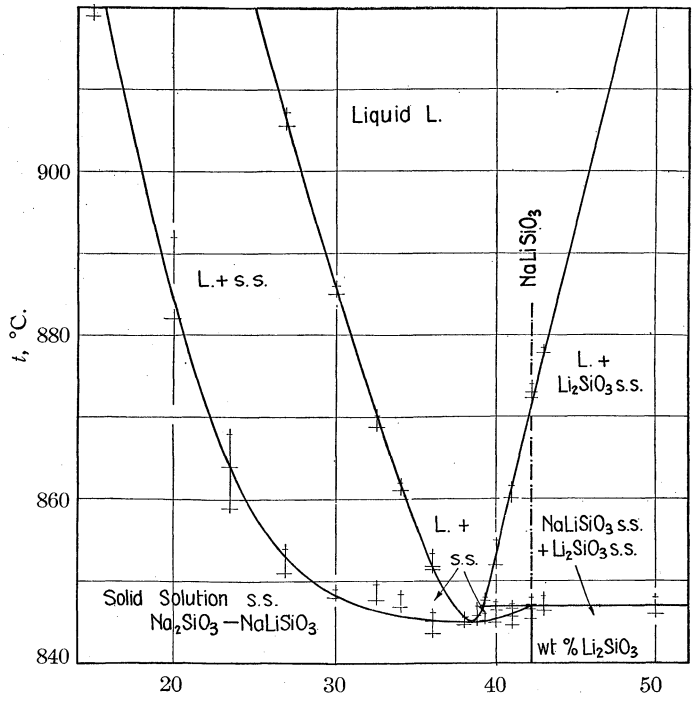


Fig. 2.—Portion of the equilibrium diagram for the system, Na_2SiO_3–Li_2SiO_3, enlarged to demonstrate the phase relations in the neighborhood of the minimum on the liquidus.

most, only a few tenths of a per cent. beyond, since quenches of this composition from below the peritectic contained only the one kind of homogeneous crystals, while those of 43.0% Li_2SiO_3 contained, in addition, a definite quantity of the Li_2SiO_3-like crystals of the other series of solid solutions.

To establish the properties of the crystalline phase (or phases) in this region, we have examined, microscopically, quenched samples of the various compositions, first completely crystallized, and then brought to equilibrium by long annealing at temperatures both above and below the solidus.[8] Only one equilibrium crystalline phase could be found. Its refractive indices were found to vary continuously with the composition, as would be expected for a continuous series of solid solutions. This is illustrated in Fig. 3. The results of these optical measurements agree with the thermal data on the liquidus and solidus, and exclude from consideration the possibility of any type of eutectic relations in the system.

Optical Properties of the Various Phases

During the course of the work we have measured the refractive indices of the glasses and the crystals in the quenched samples. The data for the glasses are listed in Table I. No measurements could be made on annealed glasses, since all the vitreous preparations within the system devitrify rapidly at annealing temperatures. The value for Na_2SiO_3 glass, 1.517, is interpolated from the data of Morey and Merwin.[9]

The refractive indices of the various phases are plotted against the composition in Fig. 3.

The optical properties of crystalline Na_2SiO_3 and Li_2SiO_3 are already known.[10]

The properties of $NaLiSiO_3$, end-member of the Na_2SiO_3–$NaLiSiO_3$ series of solid solutions, as measured by H. E. Merwin, are:

Orthorhombic prisms with two good lengthwise cleavages; elongation || to γ; near endwise sections crystals show acute bisectrix or an optic axis, 2V very large. Refractive indices for Na light: γ 1.571, β 1.557, α 1.552, all within about 0.002.

In cleavage splinters, crystals of this compound bear a superficial resemblance

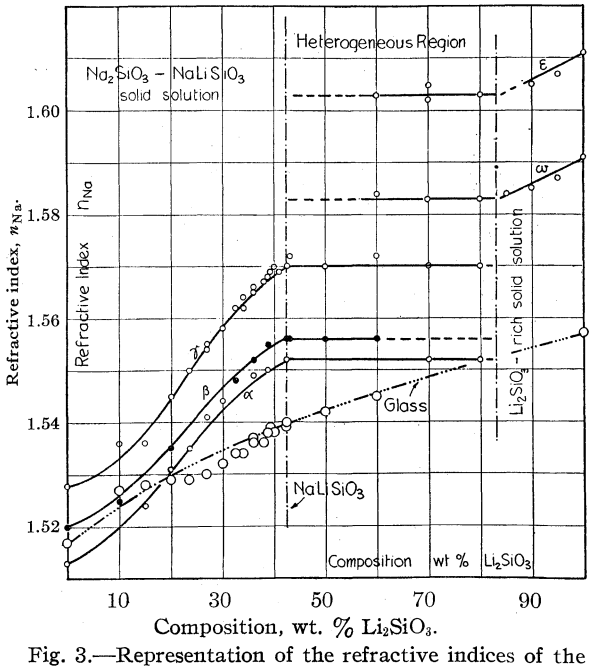


Fig. 3.—Representation of the refractive indices of the various phases in the system, Na_2SiO_3–Li_2SiO_3, as a function of the composition.

(8) I am indebted to my colleague H. E. Merwin for much valuable help on this question.

(9) G. W. Morey and H. E. Merwin, *J. Optical Soc. Am.*, **22**, 632 (1932).

(10) Na_2SiO_3: G. W. Morey and N. L. Bowen, *J. Phys. Chem.*, **28**, 1167 (1924). Li_2SiO_3: F. M. Jaeger, *Proc. K. Akad. Wet. Amsterdam*, **16**, 857 (1914); measurements by H. E. Merwin, in F. C. Kracek, *J. Phys. Chem.*, **34**, 2647 (1930).

to Li_2SiO_3, in spite of their lower indices of refraction. This resemblance is due to (1) a similarity of the cleavage habit, (2) similarity in the orientation with respect to the indices of refraction, and (3) comparable magnitudes of the birefringence, that of $NaLiSiO_3$ being somewhat smaller. It explains, at least in part, why Wallace[1] found crystals resembling Li_2SiO_3 in compositions as low as 30% Li_2SiO_3. However, crystals of the Li_2SiO_3-rich solid solutions sometimes are formed from the melt in mixtures of Li_2SiO_3 content lower than 39.3%, the equilibrium termination of the liquidus for this phase at the peritectic (see Fig. 2). Such crystals are metastable, and are formed occasionally when a melt is cooled rapidly to a temperature below the metastable extension of this liquidus. In the completely crystallized preparation they remain as inclusions within crystals of the stable Na_2SiO_3–$NaLiSiO_3$ solid solution. On reheating they redissolve before the solidus temperature is reached, and the preparation recrystallizes to the stable solid solution phase.

Acknowledgment.—I am indebted to my colleague H. E. Merwin for measurements of the optical properties of the compound, $NaLiSiO_3$, and for help in various other parts of this work.

Summary

The binary system, Na_2SiO_3–Li_2SiO_3, a binary section within the ternary system, Na_2O–Li_2O–SiO_2, contains an intermediate compound, $NaLiSiO_3$, which melts incongruently at 847 ± 1°. The liquidus consists of two branches. One of these begins at the melting point of Na_2SiO_3, 1089 ± 1°, falls to a minimum at 38.5 ± 0.2% Li_2SiO_3, 845 ± 1°, and then rises to its junction with the other branch at the peritectic point 39.3 ± 0.2% Li_2SiO_3, 847 ± 1°. The second branch of the liquidus rises from the peritectic point to the melting point of Li_2SiO_3, 1201 ± 1°. The primary phases in equilibrium with the liquid are two series of solid solutions. The first series extends from Na_2SiO_3 to $NaLiSiO_3$; the second series is a limited one, and ranges in composition from 83 ± 3 to 100% Li_2SiO_3. The optical properties of the various phases have been measured, and are reproduced graphically in a diagram giving the variation of the refractive indices with the composition.

WASHINGTON, D. C. RECEIVED MAY 29, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE NATIONAL UNIVERSITY OF CHEKIANG]

"Effective Electron Density" and Chemical Behavior[1]

BY HEOU-FEO TSEOU

In a previous exposition a theory was proposed by us for the explanation of various types of organic reactions.[2] The purpose of the present paper is to show the concordance which it bears to the chemistry of other elements than carbon.

The essential idea of the theory was that as concerned with chemical properties an element may be imagined not to occupy a fixed position in the periodic table but it changes as the position of a part of the outer electrons is affected by certain adjoined atoms or groups of atoms; an inward shift causes a displacement of the element to the right side in the periodic series, while an outward shift displaces it toward the left side. The change as stated should be most conspicuously reflected in a change of its effective atomic radius which corresponds to what we call a compact or open octet.[3] If this statement is universally true, then it would follow as a logical sequence that, in passing through a periodic series, a constant decrease in atomic radius will be observed as the atomic number of the elements increases. To testify to the validity of the statement the atomic dimensions of the first three short periods are collected in Table I.

A glance at the table will show immediately that these values arranged in the descending order fit in nicely with our postulate. Note should be taken that these are the dimensions of covalent linkages, which are what we have uniquely dealt with in organic reactions. These measurements

(1) This article has been edited, with the author's consent, by a member of the Editorial Board. Except insofar as a few examples have been retained to clarify the principles formulated, the author's applications of his theory have been omitted. It seems better to leave the applications to the reader's imagination than to attempt what must be a too limited discussion.—THE EDITOR.

(2) Tseou, "A New Electronic Theory of Organic Reactions," 1937.

(3) The change of atomic radius of the carbon atom in different organic compounds as shown to be complying with the author's postulation rules is given in a table in the chapter "Evidence of Physical Measurements."

TABLE I

Element	H^4						
r	0.375						
Element	Li^5	Be^5	B^4	C^6 aliph.	N^4	O^4	F^4
r	1.50	1.12	0.89	0.75	0.70	0.66	0.64
Element	Na^5	Mg^5	Al^5	Si^4	P^4	S^4	Cl^5
r	1.84	1.60	1.43	1.17	1.10	1.04	0.97
Element	K^5	Ca^5	Sc	Ti^5	V^5	Cr^5	Mn^5
r	2.31	1.97	..	1.45	1.30	1.25	1.18

r = effective atomic radius in Å.

offer actually a most suitable means for comparing the chemical behavior of the different elements, which, as shown in our previous article, is dependent on the compactness of the outermost electronic shell of the atoms. A closer observation shows that the compactness of an octet is concerned with two factors: (a) the effective atomic radius r and (b) the number of outermost electrons n properly allocated to the particular atom. The oxygen atom linked by a semi-polar bond to sulfur in sulfoxides or sulfones, for example, may be considered to contain seven outer electrons instead of six. We propose to use a new term "effective electron density" as a determining quantity of the chemical behavior and denote its relative magnitude by the empirical formula n/r. To state it in other words, the effect of each outer electron to be displaced toward the atomic center during the formation of a link is a linear function of its distance from the nucleus $(1/r)$, and the total relative effect of all the outermost electrons is expressed by the term n/r.

TABLE II

Element	H						
n/r	2.70						
Element	Li	Be	B	C, aliph.	N	O	F
n/r	0.66	1.78	3.37	5.19	7.14	9.09	10.9
Element	Na	Mg	Al	Si	P	S	Cl
n/r	0.54	1.25	2.09	3.41	4.54	5.76	7.07
Element	K	Ca	Sc	Ti	V	Cr	Mn
n/r	0.43	1.01	..	2.75	2.84	4.80	5.93

These are only for single bonds. In the case of multiple links, which involve a packing together of pairs of electrons toward the atomic centers, the correspondingly larger values of the effective electron density causes a displacement of the elements toward the right side in the periodic table.

TABLE III

Double Bonds

Element	C	N	O	C[a]
r	0.67	0.61	0.60	0.70
n/r	5.97	8.19	10.0	5.71

Triple Bonds

Element	C	N
r	0.60	0.55
n/r	6.66	9.09

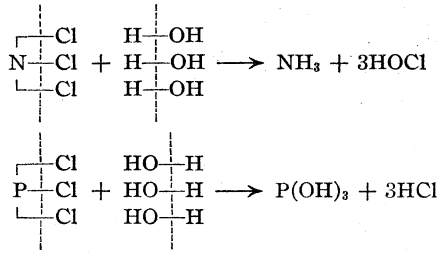
[a] Aromatic resonance between single and double bonds.

In reading over the elements listed above it will be remarked that potassium and sodium stand foremost among the electropositive elements, while trebly linked nitrogen and doubly linked oxygen are the most electronegative ones, the latter, being joined to other elements by two or three electron pairs each exercising an effect comparable with that of fluorine, possessing the greatest capacity of displacing electrons away from the multiply bonded atoms. Trebly linked carbon possesses an "effective electron density" nearly as high as the singly linked nitrogen, a fact which complies with the formation of stable metallic acetylides, the metal being joined to the carbon by a single bond. The position of hydrogen is peculiar. It has long been taken as electrodual in character; for, although univalent, it exhibits no property of the alkali metals or of the halogens. Its abased position in the electrochemical series together with its characteristic behavior revealed in organic and other non-dissociated compounds point to the conclusion that it should occupy a particular position in the periodic table. As indicated in Table II it is more electronegative than beryllium and aluminum, although somewhat more positive than boron and carbon. This estimation coincides with its behavior revealed in different types of organic reactions described in our previous treatise.

In the table the effective electron density of chlorine is shown to be remarkably low in comparison with fluorine and oxygen. This accounts for the relative electropositivity of the atom in many covalently linked compounds. One conspicuous example is the chlorine atom in hypochlorous acid and metallic and alkyl hypochlorites. Chlorine atoms in chloric and perchloric acids are really comparable with boron and carbon in boric and carbonic acids. Hypofluorous, fluoric and perfluoric acids are for example unknown (see below). The small orientation capacity of chlorine in chlorobenzene vis-à-vis the hydroxyl and amino groups in phenols and aniline and the comparative inertness of alkyl and aryl halides also point in the same direction. Indeed, numerous reactions, especially organic ones, become interpretable only when chlorine atoms in certain compounds are regarded as electropositive

(4) Pauling, *Proc. Natl. Acad. Sci. Wash.*, **18**, 293 (1932).
(5) Neuburger, "Gitterkonstanten," Leipzig, 1931.
(6) Wierl, *Ann. Physik*, **8**, 521 (1931).

in nature, although in electrovalency the element is invariably negative. As one of the most simple and convincing examples showing the electron density relationships among chlorine, nitrogen and phosphorus can be cited the hydrolysis of nitrogen and phosphorus chlorides.



It is obvious that the different courses taken by the two halides in hydrolysis are simply due to the fact that the e. e. d. (effective electron density) of chlorine is just situated intermediate between those of nitrogen and phosphorus.

It is a remarkable fact that carbon is the most prominent element capable of forming stable polyatomic compounds. The explanation formulated by us has been that its position is right in the vicinity of the equilibrium point, which condition entails little strain in its atomic linkings[2] (p. 141). The element which comes next appears to be sulfur. This can be well predicted from the data in Table II. In polysulfides, which are compounds very easily formed, many sulfur atoms are connected in series or in ring forms, and elementary sulfur itself is shown to be a very stable octa-atomic ring which can be scarcely attacked by common reagents. On the other hand, an element with an effective electron density very different from that of carbon does not form stable and inert polyatomic chains. Thus the linkages between oxygen atoms (e. e. d. = 9.09) are so unstable that peroxides and ozonides are generally explosive. The equilibrium point of effective electron density is probably nearer to that of aromatic carbon (5.71) than to that of aliphatic carbon (5.19).

Covalent linkages between atoms having very different effective electron densities degenerate to ionic linkages. Thus the stepped line dividing the electrovalent and covalent chlorides shown in Table IV is a line separating elements with effective electron densities greater than 1.7 from those with smaller values.

TABLE IV

H			
Li	Be	B	C
Na	Mg	Al	Si
K	Ca	Sc	Ti

The expansion of a valence shell should be considered as a mechanism for the increase of an effective electron density to a value that permits the formation of covalent bonds.

Summary

It is pointed out that many properties of an element depend on the density of its valence electrons in a covalent compound.

This characteristic is called the effective electron density, and is determined from the number of valence electrons and the covalent atomic radii of the metals.

In doubly and triply bonded atoms the radii are smaller and the effective electron densities are higher than in singly bonded atoms.

High effective electron densities are associated with high electronegativity. Stable polyatomic chains are associated with elements that have intermediate effective electron densities. Covalent bonds between atoms of high and low effective electron densities degenerate to ionic linkages.

CHEKIANG, CHINA RECEIVED APRIL 4, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF KANSAS]

Some Studies in the System Zinc Acetate–Hydrogen Chloride–Acetic Acid

BY ARTHUR W. DAVIDSON AND WILBERT CHAPPELL

In previous papers from this Laboratory and elsewhere, numerous similarities have been pointed out between solutions of acids, bases and salts in anhydrous acetic acid on the one hand, and familiar aqueous systems on the other. As yet, however, few acetic acid systems containing analogs of so-called acid or basic salts have been described. It is obvious that the anhydrous ternary systems zinc chloride–zinc acetate–acetic acid and zinc chloride–hydrogen chloride–acetic acid might be regarded as analogous, respectively, to zinc chloride–zinc oxide–water and zinc chloride–hydrogen chloride–water; and that in the former case basic salts might be expected to occur, in the latter case, acid salts.

The study of equilibria between solid and liquid phases in binary solutions of zinc chloride in acetic acid presents extraordinary difficulties because of the extremely high viscosity of the concentrated solutions, which, as previously noted by Reddelien,[1] form thick sirups at ordinary temperatures. The same difficulty arises also in ternary solutions containing hydrogen chloride. Hence, except for a rough determination of the solubility of zinc chloride, the quantitative data obtained for these "neutral" and "acid" systems are limited to solutions from which acetic acid separates as solid phase. It was found possible, however, to investigate the "basic" system over a considerable concentration range at 30°, and to isolate two "basic" salts in the solid state.

Method

Preparation of Materials.—Pure anhydrous acetic acid and zinc acetate were prepared as described in previous papers of this series.[2]

Because of the difficulty of preparing and handling anhydrous zinc chloride, no attempt was made to use the solid salt, except in preliminary qualitative experiments. It was found, however, that a solution of zinc chloride in acetic acid might be obtained readily by the passage of dry hydrogen chloride over dry zinc acetate; a metathetic reaction takes place, which may be regarded as a neutralization

$$Zn(C_2H_3O_2)_2 + 2HCl = 2HC_2H_3O_2 + Zn^{++} + 2Cl^-$$

Gaseous hydrogen chloride, prepared in the usual manner, was dried by passage through two towers filled with glass wool which had been moistened with anhydrous sulfuric acid. The gas was then passed into a flask containing zinc acetate (suitably protected from atmospheric moisture), and the mixture was warmed, with gentle agitation; gradual liquefaction resulted, in accordance with the above equation. After all the solid had disappeared, the solution, which contained at this stage a slight excess of hydrogen chloride, was analyzed both for chlorine and for zinc; the former was determined gravimetrically, the latter by titration against potassium ferrocyanide solution, with uranyl nitrate solution as an external indicator. From these data the amount of excess hydrogen chloride was calculated, and zinc acetate was added to the solution in quantity just sufficient to react with this excess. Thus a mixture containing 1 mole of zinc chloride to 2 of acetic acid was obtained; this was used as a stock solution, from which more dilute solutions were prepared by the addition of acetic acid.

Binary System $ZnCl_2$–$HC_2H_3O_2$.—Cryoscopic determinations were made, as described in previous papers, on samples of known composition prepared by dilution of the stock solution. The freezing points reported, except for concentrations of above 16 mole % of solute, are believed to be correct to within 0.1°. Up to a concentration of 22 mole %, only acetic acid was obtained as solid phase. Beyond this point the solutions became so viscous that they yielded no solid phase on cooling.

Reddelien[1] gave the solubility of zinc chloride in glacial acetic acid at 15° as 47.8 g. per 100 cc. of solution. While this figure, in the absence of density data, cannot be exactly interpreted, it appears to be much too low, for even our 33.33 mole % solution proved to be still unsaturated at 30°. Some of this solution was warmed with an excess of solid zinc chloride and then maintained in contact with the solid at 30°, with occasional agitation, for three months. Before the end of this period, additional crystals were observed to have separated out. Samples of the extremely viscous solution, upon analysis, showed 40.1 mole % of zinc chloride. Since the solid used may not have been absolutely anhydrous and since equilibrium was approached from supersaturation, this figure may be regarded only as a maximum value for the solubility of zinc chloride at 30°.

Ternary System $ZnCl_2$–HCl–$HC_2H_3O_2$.—Solutions containing zinc chloride in proportions up to 33.33 mole %, and saturated with hydrogen chloride, yielded, on cooling, no solid phase other than acetic acid. In many cases such solutions, even on being cooled to liquid air temperatures, showed no tendency to crystallize, but merely set to glassy solids. A few cryoscopic determinations were made, however, upon dilute solutions containing both zinc chloride and hydrogen chloride, in the following manner. Freezing point measurements were first made on solutions of hydrogen chloride, the composition of which had been determined by analysis. Then small weighed quantities of concentrated zinc chloride solution were added, and the freezing points were again determined. Because of the

(1) Reddelien, *Ann.*, **388**, 190 (1912).

(2) Davidson and McAllister, THIS JOURNAL, **52**, 512, 519 (1930).

relatively high vapor pressure of hydrogen chloride from dilute solutions in acetic acid,[3] no great accuracy is claimed for these results.

Ternary System $ZnCl_2$–$Zn(C_2H_3O_2)_2$–$HC_2H_3O_2$.—Equilibrium in this system at 30° was studied by the analytical method; because of the high viscosity of many of the solutions, seeding was necessary in order that equilibrium might be attained in a reasonable time. Portions of the stock solution referred to above were diluted to the desired extent with acetic acid, and varying quantities of zinc acetate were added. The mixtures were placed in glass-stoppered bottles, heated until all of the solid had dissolved, cooled to about 40° and seeded with the appropriate solid phase, as determined from preliminary experiments. The bottles were then sealed, placed in a thermostat maintained at 30°, and agitated mechanically for about two weeks. (Preliminary experiments had shown this time to be sufficient for the attainment of equilibrium, even in the most viscous of the solutions.) The solutions were then allowed to stand for a day in order to allow complete settling of the solid phase, portions of the liquid were withdrawn, and their zinc and chlorine contents were determined as described above. The proportions of zinc chloride and of zinc acetate were calculated from these analyses, and that of acetic acid was determined by difference. It was found possible to investigate this system up to concentrations of almost 30 mole % (48% by weight) of zinc chloride, beyond which point the solutions were too viscous to permit reliable results to be obtained.

The composition of solid phases was determined both by direct analysis of crystals which had been freed from mother liquor by means of filtration and pressure between porous tiles, and by the Schreinemakers method of analysis of wet residues.

Results

1. Freezing Point Data.—In Table I, S denotes the mole percentage of zinc chloride in the binary solution, and T is the temperature at which the solution is in equilibrium with solid acetic acid.

TABLE I

ZINC CHLORIDE–ACETIC ACID

S	T	S	T
0	16.60	12.88	8.55
1.77	15.75	14.14	7.30
3.46	14.95	16.16	4.80
4.31	14.45	17.80	2.8
7.31	12.85	18.45	2.0
9.67	11.45	22.07	−4.0
10.99	10.35		

In Table II, S_1 and S_2 denote the mole percentages of zinc chloride and of hydrogen chloride, respectively, in the mixed solution, and Δ_1 and Δ_2 are the freezing point depressions corresponding to these mole percentages of solute in the respective binary systems.[4] R is the ratio of the number of moles of zinc chloride to the number of moles of hydrogen chloride, and Δ_3 is the observed freezing point depression in the mixed solution.

TABLE II

ZINC CHLORIDE–HYDROGEN CHLORIDE–ACETIC ACID

S_1	Δ_1	S_2	Δ_2	R	$\Delta_1 + \Delta_2$	Δ
2.53	1.22	0.74	0.44	3.42	1.66	1.05
1.60	0.78	1.50	1.03	1.07	1.81	0.75
0.57	.30	1.51	1.04	0.38	1.34	.95

It will be noted that, in each case, Δ_3 is much less than the sum of Δ_1 and Δ_2.

2. System $ZnCl_2$–$Zn(C_2H_3O_2)_2$–$HC_2H_3O_2$.—In Table III, S_1 and S_2 represent the mole percentages of zinc chloride and of zinc acetate, respectively, in the ternary solution which is in equilibrium, at 30°, with the solid phase indicated. These data are also represented graphically in Fig. 1.

TABLE III

ZINC CHLORIDE–ZINC ACETATE–ACETIC ACID

S_1	S_2	S_1	S_2
Solid phase A, $Zn(C_2H_3O_2)_2$		Solid phase B	
0	0.0025[a]	7.45	1.68
0.334	.115	9.24	1.88
.431	.175	11.50	2.09
.611	.255	12.86	2.33
.834	.356	15.81	2.66
.931	.414	17.65	2.85
		Solid phase C	
Solid phase B, $Zn(C_2H_3O_2)Cl$		$Zn(C_2H_3O_2)Cl \cdot ZnCl_2$	
1.24	0.365	21.20	2.78
1.88	.426	22.83	2.45
2.18	.582	25.01	1.93
3.12	.844	27.39	1.43
4.99	1.17	28.91	1.07
6.18	1.43	29.36	0.828

[a] Ref. 2, p. 522.

The mean of four analyses on dried samples of the solid phase B, from solutions of different composition, gave Zn, 41.3%; Cl, 22.5% (calcd. for $Zn(C_2H_3O_2)Cl$: Zn, 40.9%; Cl, 22.2%). Because of the hygroscopic nature of this compound, and the difficulty of completely removing the very viscous mother liquor from it, it seemed desirable to supplement these analyses by determinations made by the Schreinemakers method. Accordingly, tie-lines through six pairs of corresponding compositions of solution and wet residue were plotted on a triangular diagram (not reproduced here), and were found to intersect the $Zn(C_2H_3O_2)_2$–$ZnCl_2$ axis at a point corresponding to 49.88 mole % $Zn(C_2H_3O_2)_2$, 50.12 mole % $ZnCl_2$. This result confirms the analysis of the dried salt, and

(3) Rodebush and Ewart, THIS JOURNAL, **54**, 419 (1932).

(4) The values for Δ_1 and Δ_2 were determined by interpolation, from plots which for space considerations are not reproduced here.

shows the solid phase to be a compound of the composition $Zn(C_2H_3O_2)_2 \cdot ZnCl_2$, or $Zn(C_2H_3O_2)Cl$, which may be regarded as a basic salt of the acetic acid system.

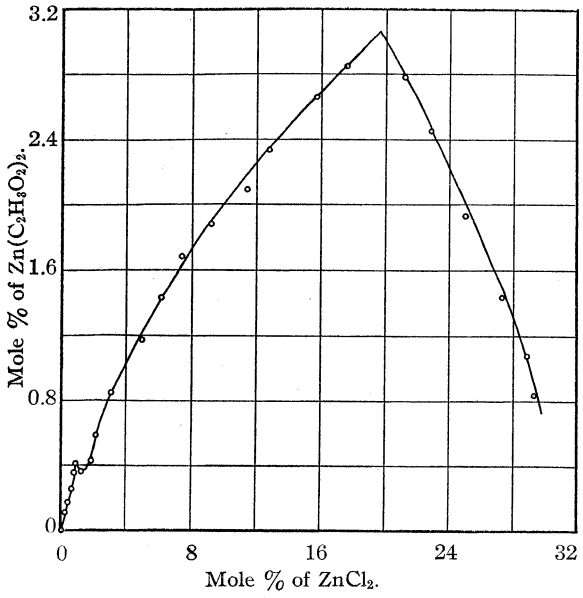


Fig. 1.—System $ZnCl_2$–$Zn(C_2H_3O_2)_2$–$HC_2H_3O_2$ at 30°.

The mean of two analyses of solid phase C (which was very sticky when moist and could be dried only with difficulty) gave Zn, 43.4%; Cl, 35.5% (calcd. for $Zn(C_2H_3O_2)Cl \cdot ZnCl_2$: Zn, 44.1%; Cl, 35.9%). Again these results were checked by the method of wet residues; tie-lines through four pairs of corresponding compositions of solution and wet solid intersected the $Zn(C_2H_3O_2)_2$–$ZnCl_2$ axis of the triangular diagram at a point corresponding to 23.72 mole % $Zn(C_2H_3O_2)_2$, 76.28 mole % $ZnCl_2$. These results prove the compound to be a second basic salt of the composition $Zn(C_2H_3O_2)_2 \cdot 3ZnCl_2$, or $Zn(C_2H_3O_2)Cl \cdot ZnCl_2$.

The composition of solid phase A was determined by means of wet residues only. Wet residues from this portion of the system contain only very small amounts of chlorine, and hence the tie-lines lie very close to the $Zn(C_2H_3O_2)_2$–$HC_2H_3O_2$ axis, and are almost parallel to it. Since it has been found in previous work[2,5] that zinc acetate forms no solvates with acetic acid, it may be safely concluded that this solid phase consists of unsolvated zinc acetate.

It may be seen from Fig. 1 that at 30° the solubility of zinc acetate increases from 0.0025 mole % in pure acetic acid to a maximum of about 0.41 mole % in a solution containing about 0.93 mole % of zinc chloride. With the appearance of a new solid phase, the proportion of zinc acetate in the saturated solution at first falls off slightly with increasing concentration of zinc chloride, then rises to a maximum of about 3% at approximately 20% of zinc chloride. Here another new phase appears, and thereafter the proportion of zinc acetate again declines sharply with increasing concentration of chloride.

(5) Davidson and Griswold, THIS JOURNAL, **57**, 423 (1935).

Discussion

Zinc chloride is found to be by far the most soluble in acetic acid of any salt so far studied, its saturated solution at 30° containing more than 11 moles per 1000 g. of solvent.

Freezing point data for this salt show that the value of j, the freezing point divergence function, remains practically constant at 0.74 for molalities from 0.3 to 1.3. Such constancy in the value of j, while quite contrary to the behavior of aqueous solutions, appears to be characteristic of most salt solutions in acetic acid.[6]

With regard to the system $ZnCl_2$–HCl–$HC_2H_3O_2$, although it would be unwarranted to attempt to draw quantitative conclusions as to the molecular complexity of ionizable solutes from cryoscopic data, yet the relatively small freezing point depressions in solutions containing both zinc chloride and hydrogen chloride point strongly toward the formation of some sort of addition compound between the two solutes. Hildebrand and Bowers[7] have presented evidence of the existence of a complex acid, of the composition $HZnCl_3$, in dilute aqueous solution, and hydrates of this acid and of HZn_2Cl_5 have been obtained in the solid state[8]; no such complex has as yet been isolated from acetic acid solutions, however.

The system $ZnCl_2$–$Zn(C_2H_3O_2)_2$–$HC_2H_3O_2$, as has been stated previously, may be regarded as analogous to the system $ZnCl_2$–ZnO–H_2O, which has been studied recently by Feitknecht[9] and by Holland.[10] It is of interest to note that both of these observers isolated the compound $ZnCl_2 \cdot ZnO \cdot H_2O$, or Zn(OH)Cl, of which the exact analog, $Zn(C_2H_3O_2)Cl$, was found to be stable over a considerable range of concentrations in the present work. The other "basic" salt found here, Zn-

(6) Davidson and Chappell, *ibid.*, **60**, 2043 (1938).
(7) Hildebrand and Bowers, *ibid.*, **38**, 785 (1916).
(8) Engel, *Compt. rend.*, **102**, 1068 (1886); Kuznetzov and Kozhukhovskiĭ, *J. Applied Chem.* (U. S. S. R.), **9**, 185 (1936).
(9) Feitknecht, *Helv. Chim. Acta*, **13**, 22 (1930).
(10) Holland, *J. Chem. Soc.*, 643 (1930).

$(C_2H_3O_2)Cl \cdot ZnCl_2$, is analogous to the compound $Zn(OH)_2 \cdot 3ZnCl_2$, or $Zn(OH)Cl \cdot ZnCl_2$, earlier described by Ephraim.[11] Neither of these aquobasic salts can be dissolved in water without decomposition, but, like their acetic acid analogs, they are stable in contact with solutions containing a large excess of zinc chloride.

Summary

1. A convenient method of preparing anhydrous zinc chloride–acetic acid solutions has been devised, and the freezing points of such solutions, over a wide concentration range, have been determined.

2. Evidence for the presence of an addition compound of zinc chloride and hydrogen chloride, even in dilute solution in acetic acid, has been obtained.

3. The system $ZnCl_2$–$Zn(C_2H_3O_2)_2$–$HC_2H_3O_2$ has been studied at 30°. Two new double salts, $Zn(C_2H_3O_2)Cl$ and $Zn(C_2H_3O_2)Cl \cdot ZnCl_2$, have been isolated and analyzed.

(11) Ephraim, *Z. anorg. Chem.*, **59**, 67 (1908).

LAWRENCE, KANSAS RECEIVED MAY 8, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, INDIANA UNIVERSITY]

Effect of Polar Groups upon Esterification Velocities of Substituted Benzoic Acids with Cyclohexanol

BY R. J. HARTMAN, L. B. STORMS[1] AND A. G. GASSMANN

The effect of substituents on the reaction velocity of various compounds has long been of interest. There have been attempts made to group the effect of substituents under a single theory. Williams[2] classifies reactions into three groups according to the effect of polar substituents on reaction rates as follows: (A) those favored by accession of electrons to the point of reaction; (B) those favored by recession of electrons from the point of reaction; and (C) those in which the data available are insufficient to classify in either group A or B. Of the three esterification studies cited by Williams, two, those by Goldschmidt[3] and Kailan[4] are in group C. The third, by Michael and Oeschlin[5] is placed in group B, *i. e.*, the esterification reaction was accelerated by a substituent such as the nitro group. Hammett[6] has expressed the effect of a substituent in the meta or para position on the benzene ring upon the rate of a side chain reaction by the equation

$$\log k = \log k_0 + \sigma\rho$$

where k is the velocity constant for the substituted reactant, k_0 the constant for the unsubstituted reactant, σ a constant depending upon the substituent, and ρ a constant depending on the reaction, medium, and temperature. Hammett found a probable error for log k of less than 0.1 in thirty-three of thirty-nine reactions, including equilibrium as well as velocity constants. The equation was applied to the esterification work of Goldschmidt.[3] The probable error found was 0.118. Hartman and Borders[7] applied the equation to the esterification of substituted benzoic acids with methanol. They found an average error of 0.058. The values of σ used in the work of Hartman and Borders as well as those used in this work were taken from Hammett[6] and were determined by him from the data of Dippy[8] for the dissociation constants in water of substituted benzoic acids.

The object of this investigation was to determine the velocity constants of hydrion-catalyzed esterification of substituted benzoic acids with cyclohexanol. Using the data thus obtained, the energies of activation are determined in order to analyze the data from the point of view of the Arrhenius equation. Hammett's equation is tested for its applicability to the esterification of the cyclic alcohol, cyclohexanol.

Experimental

Materials.—Pure cyclohexanol was first dried by the method of Bjerrum and Lund[9] and then by refluxing over calcium oxide. The acids were

(1) This paper is constructed from a dissertation presented by Lee B. Storms to the Faculty of the Graduate School of Indiana University in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Chemistry.

(2) Williams, *J. Chem. Soc.*, 37 (1930).

(3) Goldschmidt, *Ber.*, **28**, 3220 (1895).

(4) Kailan, *Ann.*, **351**, 186 (1907).

(5) Michael and Oeschlin, *Ber.*, **42**, 317 (1909).

(6) Hammett, THIS JOURNAL, **59**, 97 (1937).

(7) Hartman and Borders, *ibid.*, **59**, 2107 (1937).

(8) Dippy, *J. Chem. Soc.*, 644 (1936).

(9) Bjerrum and Lund, *Ber.*, **64B**, 210 (1931).

purchased from the Eastman Kodak Co. They were dried carefully over phosphorus pentoxide.

Procedure.—The experimental procedure was the same as that followed by Hartman and Borders.[7] The concentration of hydrogen chloride used was 0.1 normal. The thermostats were maintained at 55.00, 60.00, 70.00 and 75.00 ± 0.01°.

Calculations.—The velocity constants were calculated using the formula developed by Goldschmidt[10] which corrects for the retardation of esterification caused by the water formed in the course of the reaction

$$k = \frac{[(a + r) \ln a/a - x] - x}{rct}$$

where a is the original acid concentration, x the amount of acid esterified at time t, and c the H^+ concentration. The units are g. mole/liter/sec. The constant r allows for the retardation of the hydrion-catalyzed esterification by water. The values used in this investigation were calculated by the method of Williamson and Hinshelwood,[11] and were

t	55	60	70	75
r	0.10	0.19	0.31	0.40

The average value of k at each temperature is reported for the determination in which k varied the least. The values of the energy of activation were calculated in the usual way by means of the Arrhenius equation.

Results and Discussion

TABLE I

VELOCITY CONSTANTS AND ENERGIES OF ACTIVATION FOR HYDRION-CATALYZED ESTERIFICATION OF AROMATIC ACIDS WITH CYCLOHEXANOL

Acid	$k \times 10^5$ 55°	60°	70°	75°	Energy of activation, E
o-Nitrobenzoic	...	0.625	1.44	2.20	20,000
o-Toluic	0.889	1.34	2.52	4.26	17,800
o-Bromobenzoic	1.21	1.72	3.92	5.59	17,400
p-Toluic	1.45	2.16	5.03	7.81	19,500
o-Chlorobenzoic	1.61	2.35	5.26	7.31	17,500
m-Toluic	2.03	2.94	6.26	9.08	16,900
Benzoic	2.21	3.25	7.19	10.88	17,700
p-Chlorobenzoic	2.41	3.71	7.60	11.14	17,100
m-Bromobenzoic	2.83	4.26	8.77	12.47	17,000
m-Chlorobenzoic	2.96	4.07	8.55	12.14	15,900
m-Nitrobenzoic	3.05	4.30	10.57	15.91	18,300

Table II gives the values of log k_{55} obtained in this investigation for the esterification of the meta and para substituted benzoic acids and the corresponding values as calculated from Hammett's equation. The value of ρ adopted, 0.262, was obtained by the least squares method (see Hammett[6]).

TABLE II

COMPARISON OF LOG k_{55} OBSERVED WITH LOG k CALCULATED WITH THE EQUATION: LOG $k = -4.656 + \sigma$ (0.262)

Acid	Log k, obsd.	Log k, calcd.	Error
m-Toluic	−4.692	−4.674	0.018
p-Toluic	−4.839	−4.701	.138
p-Chlorobenzoic	−4.618	−4.596	.022
m-Bromobenzoic	−4.548	−4.554	.006
m-Chlorobenzoic	−4.529	−4.558	.029
m-Nitrobenzoic	−4.516	−4.470	.046
		Av.	.043

The average error of log k for the work of this investigation was 0.043. This compares favorably with the mean of probable errors of less than 0.1 found by Hammett[6] for a series of thirty-nine reactions, and of 0.122 for the data of Goldschmidt.[3] Hartman and Borders[7] report an average error of 0.054. The authors recalculated the value of ρ from the data of Hartman and Borders and found it to be − 0.53 instead of − 0.58 which they reported. Using this corrected value of ρ together with the values of σ given by Hammett,[6] their average error is found to be 0.049 instead of 0.054 as reported.[7] The results presented here indicate that the equation of Hammett can be applied to the esterification of cyclic alcohols.

Ortho substituted acids are not included in Hammett's theory. Since the effect of a substituent in the ortho position upon the velocity of side chain reactions is of an entirely different mechanism from that of the meta and para substituted acids, the velocity of the ortho substituted acids is not discussed here.

The outstanding difference in the order of the esterification of substituted acids with cyclohexanol and with methanol is that the order is practically reversed. Hartman and Borders[7] found that the order of decreasing speed of esterification with methyl alcohol is *m*-CH_3 > *p*-CH_3 > *m*-Br > *m*-Cl > *p*-Cl > *p*-NO_2. The order found by the authors for cyclohexanol is *m*-NO_2 > *m*-Cl > *m*-Br > *p*-Cl > *m*-CH_3 > *p*-CH_3. It should be noted that the value of ρ for methanol reported by Hartman and Borders is negative, whereas that found in this investigation for cyclohexanol is positive. This change in sign probably accounts for the reversal of the order of the esterification with cyclohexanol

(10) Goldschmidt, *Ber.*, **39**, 711 (1906).

(11) Williamson and Hinshelwood, *Trans. Faraday Soc.*, **30**, 1145 (1934).

Evans, Morgan, and Watson[12] found in the bromination of substituted acetophenones what they considered to be a significant variation in the non-exponential factor, P, of the Arrhenius equation: $k = PZe^{-E/RT}$. Nathan and Ingold[13] criticized this conclusion because the range of velocities was not sufficient for accurate separation of the factors E and P. This criticism of these factors might also apply to the present work because the ratio of the velocity of the fastest to the slowest acid is only 3.4 to 1.

The change in the various factors of the Arrhenius equation may be analyzed at least qualitatively by plotting the values of E for the various acids against log k_{55}. This relationship is shown in Fig. 1. If the change in the velocity of esterification of the acids produced by the substituents were entirely dependent upon changes in E, a straight line having a slope of $2.303RT$ would be obtained. The solid line in Fig. 1 represents an approximate graphical average obtained from plotting the data of this investigation. The broken line represents the theoretical line having a slope of $2.303RT$. If the experimental line can be considered to be approximately correct, it is apparent that the two lines have nearly identical slopes. The scattered points obtained from the data, however, indicate that such a conclusion cannot be drawn with certainty. If the line can be regarded as nearly true, it could be concluded that the steric factor, P, does not undergo an appreciable change in the Arrhenius equation. As has been pointed out already, however, the small range of velocities studied and the effect of large experimental error at high temperatures upon the values of E, precludes the possibility of a positive statement of this point.

(12) Evans, Morgan and Watson, *J. Chem. Soc.*, 1168 (1935).
(13) Nathan and Ingold, *ibid.*, 222 (1936).

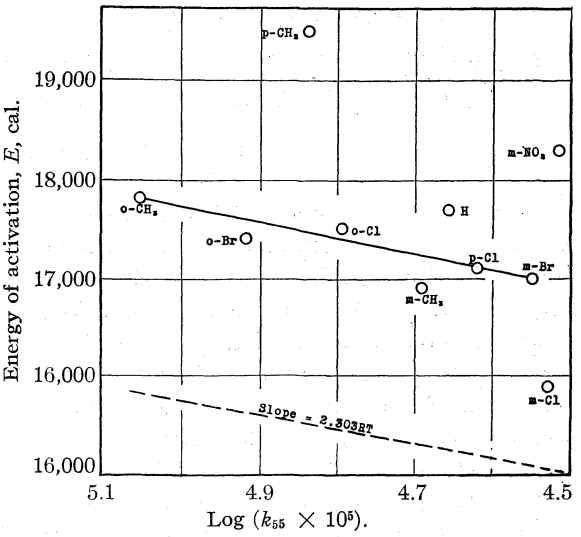


Fig. 1.—Relationship between speed of reaction and activation energy.

Summary

1. The investigation of the effect of polar substituents on the reaction velocity of hydrion-catalyzed esterification of substituted benzoic acids with cyclohexanol shows that the velocity is decreased by the displacement of electrons toward the carboxyl group.

2. Excellent agreement was found between the experimental values of log k for the esterification reactions and the values calculated from Hammett's equation. This equation is therefore applicable to the esterification of cyclohexanol.

3. It appears that the value of E in the Arrhenius equation is the chief factor in determining the velocity of esterification.

BLOOMINGTON, INDIANA RECEIVED JUNE 6, 1939

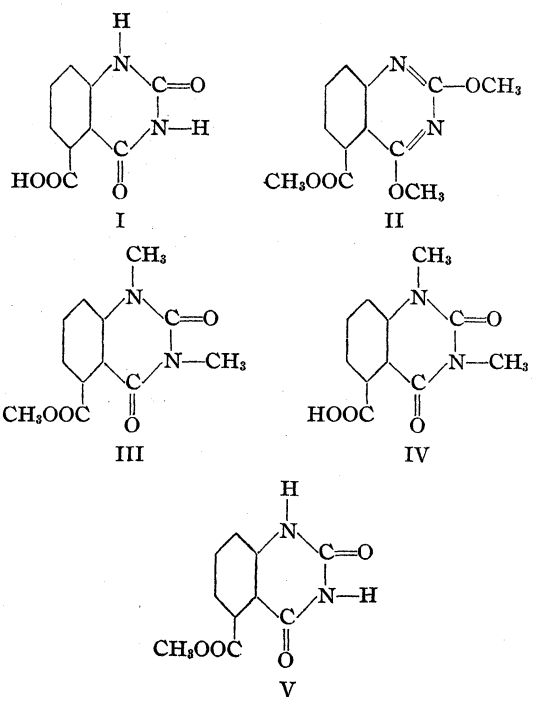
[CONTRIBUTION FROM THE MORLEY CHEMICAL LABORATORY, WESTERN RESERVE UNIVERSITY]

Quinazolines. VIII. The Methyl Esters of 1,3-Dimethylbenzoylene-urea-5-carboxylic Acid and 2,4-Dimethoxyquinazoline-5-carboxylic Acid

BY N. A. LANGE, DOUGLAS C. CHISHOLM[1] AND J. LESTER SZABO

Scott and Cohen[2] prepared benzoylene-urea-5-carboxylic acid (2,4-diketo-1,2,3,4-tetrahydroquinazoline-5-carboxylic acid) (I). In reaction with dimethyl sulfate in alkaline solution, it yielded a product to which they assigned structure II. In previous studies of this method of alkylation of compounds of type I, it has been found that —NCH_3CO— derivatives invariably are formed and not —N=$COCH_3$— derivatives.[3-5]

A reinvestigation by the authors of the work of Scott and Cohen shows conclusively that their product is actually methyl 1,3-dimethylbenzoylene-urea-5-carboxylate (III). In confirmation of this claim, methyl 2,4-dimethoxyquinazoline-5-carboxylate (II) was prepared from I by the reaction with phosphorus pentachloride to yield the chloride of 2,4-dichloroquinazoline-5-carboxylic acid, followed by replacement of the halogen with three methoxy groups through the use of sodium methoxide.



I II III IV V

As was to be expected, it has been found that the quinazoline in question reacts tautomerically to yield either O,O- or N,N-dimethyl derivatives and Zeisel determinations have shown that the Scott–Cohen product conforms to structure III and ours to structure II.

Experimental Part

Benzoylene-urea-5-carboxylic acid (2,4-diketo-1,2,3,4-tetrahydroquinazoline-5-carboxylic acid) (I) was prepared by the method of Scott and Cohen.[2] It forms colorless, shining, micro crystals, m. p. 346° (copper block, uncorr.). Scott and Cohen reported that this compound does not melt below 320° but sublimes slowly above 280°. The *p*H of a saturated aqueous solution of this acid was found to be 2.9 (quinhydrone electrode).

1,3-Dimethylbenzoylene-urea-5-carboxylic acid (1,3-dimethyl-2,4-diketo-1,2,3,4-tetrahydroquinazoline-5-carboxylic acid) (IV), prepared by the method of Scott and Cohen,[2] from I in alkaline solution and dimethyl sulfate, crystallized from dilute alcohol in minute needles, m. p. 318° (uncorr.). It is sparingly soluble in water or alcohol but dissolves in alkalies, from which it is precipitated unchanged on the addition of acids, even after prolonged boiling of the alkaline solution.

Methyl Benzoylene-urea-5-carboxylate (Methyl 2,4-diketo-1,2,3,4-tetrahydroquinazoline-5-carboxylate) (V).—Since the method described by Scott and Cohen for the preparation of III was found to proceed much slower than claimed and invariably resulted in a mixture of III and IV, experiments were made in the hope of improving their method of preparation. More satisfactory results were obtained by first esterifying the carboxyl group of I and then alkylating the two nitrogen atoms. Two grams of benzoylene-urea-5-carboxylic acid (I) was placed in a flask equipped with reflux condenser, 40 cc. of anhydrous methyl alcohol was added, and dry hydrogen chloride passed into the gently boiling mixture for four hours. The solution was allowed to cool while still passing in hydrogen chloride until it was completely saturated at room temperature; after standing overnight it was heated to boiling and more hydrogen chloride was passed in. On cooling, fine, colorless needles separated which were collected, washed with water, and dried; m. p. 318° (uncorr.). An extraction of this product with dilute sodium carbonate solution to remove any unreacted I, followed by crystallization of the undissolved residue from ethyl alcohol gave fine colorless needles of methyl benzoylene-urea-5-carboxylate (V), m. p. 307–309° (uncorr.). Scott and Cohen reported that this compound turns yellow at 180° and melts at 310–312°.

This ester (V) is best prepared by treating the acid (I)

(1) At the Chemical Laboratory of the Case School of Applied Science.

(2) Scott and Cohen, *J. Chem. Soc.*, **119**, 664 (1921).

(3) Scott and Cohen have here inadvertently applied the erroneous term "hydantoin" to quinazoline derivatives which, in fact, contain one more ring carbon than the hydantoins.

(4) Lange and Sheibley, THIS JOURNAL, **55**, 2113 (1933).

(5) Bogert and Seil, *ibid.*, **29**, 526 (1907).

with thionyl chloride to form the carboxylic acid chloride, thus avoiding the introduction of halogen into the ring at the 2,4-positions, which occurs when phosphorus pentachloride is used.[6] The acid chloride on treatment with anhydrous methyl alcohol gave the desired ester (V). To 8 g. of the quinazoline carboxylic acid (I) 100 cc. of thionyl chloride was added and the mixture refluxed for three and one-half hours, after which it was allowed to stand overnight. The excess thionyl chloride was decanted from residual solids and the latter placed in a desiccator containing calcium chloride and alkali. This crude material formed colorless clusters of thin plates and micro prisms which darkened when heated to 300° and melted at 331–332° (uncorr.) with decomposition. Attempts to recrystallize this material were not successful because of its insolubility in hot or cold chloroform, carbon tetrachloride, benzene, xylene, anisole or thionyl chloride. On titration with standard silver nitrate solution the chlorine content indicated a purity of 90% acid chloride. Refluxing this product with various anhydrous alcohols and with ammonia gave products which were purified by recrystallization but not analyzed and which are most likely the following derivatives: methyl ester, colorless, thin, micro, needle-like plates, m. p. 318°; ethyl ester, colorless, thin, micro, needle-like plates, m. p. 297–299°; benzyl ester, colorless, shining, thin, irregular plates, m. p. 257–261°; amide, colorless, cotton-like, micro needles, m. p. 359°, this last, when mixed with the carboxylic acid (I) gave a melting point of 338°. These melting points are uncorrected.

Methyl 1,3-Dimethylbenzoylene-urea-5-carboxylate (Methyl 1,3-Dimethyl-2,4-diketo-1,2,3,4-tetrahydroquinazoline-5-carboxylate) (III).—Four grams of the crude acid chloride and 150 cc. of anhydrous methyl alcohol were refluxed several hours, a part of the material remaining undissolved. The mixture was placed in a refrigerator overnight and the undissolved solids filtered off and partially dried. The 4.6 g. of crude ester (V) obtained in this way was dissolved in a solution of 4 g. of potassium hydroxide in 30 cc. of water, and 4.5 g. of dimethyl sulfate added with vigorous shaking. This mixture was allowed to stand overnight at room temperature and then placed in a refrigerator. The crystalline material which separated was filtered off, washed with water and dried; yield about 1 g. Crystallization from a small amount of methyl alcohol gave a product which is not volatile with steam and which forms very long (sometimes 3–4 cm.), colorless needles, m. p. 144.4–145.5° (corr.). Scott and Cohen[2] reported a melting point of 144° for this product. It is unaffected by boiling for a short time with hydrochloric acid; prolonged boiling, however, causes gradual hydrolysis of the ester group.

Anal. Calcd. for $C_{11}H_9O_3N_2(OCH_3)$: CH_3O, 12.50. Found: CH_3O, 12.38, 12.61.

Methyl 2,4-Dimethoxyquinazoline-5-carboxylate (II).—One gram of pure benzoylene-urea-5-carboxylic acid (I), 5 g. of phosphorus pentachloride, and 1.4 cc. of phosphorus oxychloride in an acetylating flask were refluxed in an oil-bath until all of the carboxylic acid had dissolved. The excess of phosphorus halides was removed under reduced pressure and the dark brown liquid residue became viscous on cooling. To this residue a solution of 0.4 g. of metallic sodium in 8 cc. of anhydrous methyl alcohol was added gradually with shaking and cooling in running water. The viscous material dissolved slowly and sodium chloride gradually precipitated. The undissolved material was removed by filtration, and from the filtrate small, pale yellow plates began to separate. The mixture was cooled thoroughly and the separated material collected. A single crystallization of this product from methyl alcohol gave 1 g. of colorless plates, m. p. 134.5–135.5° (corr.). The cautious addition of water to the alcoholic solution increases the amount which separates on crystallization. This compound is not volatile with steam. It is partially demethylated on boiling with dilute hydrochloric acid with the formation of the benzoylene-ureacarboxylic methyl ester (V), identified by determining the melting point of a mixture with a known sample of the ester.

Anal. Calcd. for $C_9H_3ON_2(OCH_3)_3$: C, 58.05; H, 4.87; CH_3O, 37.51. Found: C, 58.40; H, 4.97; CH_3O, 37.40.

Summary

Methyl 2,4-dimethoxyquinazoline-5-carboxylate has been synthesized and found to possess properties expected for a compound of this structure. It also has been shown that a compound previously assigned this constitution is actually the isomeric methyl 1,3-dimethylbenzoylene-urea-5-carboxylate.

CLEVELAND, OHIO RECEIVED JUNE 2, 1939

(6) Abt, *J. prakt. Chem.*, [2] **39**, 150 (1889).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

The Molecular Size of Starch by the Mercaptalation Method[1]

BY M. L. WOLFROM, D. R. MYERS AND E. N. LASSETTRE

In a previous publication from this Laboratory[2] we have reported an estimate of the molecular size of methylated cellulose (from acetone-soluble cellulose acetate) made by a mathematical extrapolation to zero time of the data obtained by subjecting the polysaccharide to hydrolysis at 0° with fuming hydrochloric acid under conditions of continuous mercaptalation and determining the amount of combined sulfur at stated time intervals. We wish now to report the extension of this procedure to a sample of high grade commercial potato starch.

Shortly after the publication of the work of Willstätter and Zechmeister[3] on the action of fuming hydrochloric acid (d. 1.20) on cellulose, Daish[4] reported a careful study of the mutarotation of a sample of "soluble" starch at 20° in the same reagent and in ordinary concentrated hydrochloric acid (d. 1.16). He showed that the mutarotation was a continuous function and that the specific rotation changed from an initial value of approximately +200° to a value very close to that of *d*-glucose in the same solvent. He found that under the same conditions maltose yielded mutarotation data from which a first order specific rate constant could be calculated but that this was not true for starch.

Our sample of commercial potato starch gave a clear solution in hydrochloric acid, showed no detectable Fehling's reduction, and gave a very low alkali number by the Schoch and Jensen[5] procedure.

For the mercaptalation work the starch was suspended in water at 0° (undercooled) and to this was added fuming hydrochloric acid (d. 1.21) so that the resultant mixture was a 5% solution of starch in hydrochloric acid containing 37.5 g. of hydrogen chloride per 100 cc. of solution. An excess of ethyl mercaptan was then added and samples were withdrawn from the hydrolysis mixture and neutralized at various time intervals during the first twenty-six hours. Since no water-insoluble products were obtained, acetylation was employed in order to effect a separation from inorganic salts. The neutralization mixtures were concentrated to dryness and the mercaptalated hydrolyzed starches converted to their acetates by acetylation with acetic anhydride in pyridine. The acetate mixtures were isolated, dried and precisely analyzed for sulfur. The average chain lengths indicated by the analytical data varied from two to seventeen glucose units. The results are recorded in Table I.

The course of the hydrolysis was followed polarimetrically at 0° by means of a separate sample of the hydrolysis mixture, withdrawn for this purpose before the addition of the ethyl mercaptan. The specific rotations for various time intervals are recorded in Table I. Figure 1 represents the change in rotation with increasing time of hydrolysis. Extrapolation of this curve to zero time (time of addition of the acid to the starch) indicates an initial specific rotation of approximately +203° for the original starch.

Figure 2 represents the degree of polymerization as calculated from the analytical data, plotted against the time of hydrolysis, initial time being taken as the time of addition of the acid. A smooth curve may be drawn through the points but the initial curvature is such that a graphic extrapolation to zero time is uncertain. The data were then subjected to a graphic analysis by application of the equation (2) previously developed for methylated cellulose

$$\frac{d-1}{d} = \frac{d_0-1}{d}e^{-kt}$$

where d is the average degree of polymerization in glucose units at time t as defined by the expression

$$d = \frac{\text{total number of glucose units}}{\text{number of polymers}}$$

d_0 is the initial degree of polymerization or the number of glucose units initially present in each polymer; k is the specific rate constant.

When the above equation is satisfied a plot of $\log_e (d-1)/d$ against t will give a straight line,

(1) The experimental data herein reported were presented before the Division of Organic Chemistry at the 96th Meeting of the American Chemical Society, Milwaukee, Wisconsin, September 8, 1938. Original manuscript received December 27, 1938.

(2) M. L. Wolfrom, J. C. Sowden and E. N. Lassettre, THIS JOURNAL, **61**, 1072 (1939).

(3) R. Willstätter and L. Zechmeister, *Ber.*, **46**, 2401 (1913).

(4) A. J. Daish, *J. Chem. Soc.*, **105**, 2065 (1914).

(5) T. J. Schoch and C. C. Jensen, paper presented before the Division of Sugar Chemistry at the 96th Meeting of the American Chemical Society, Milwaukee, Wisconsin, September 8, 1938.

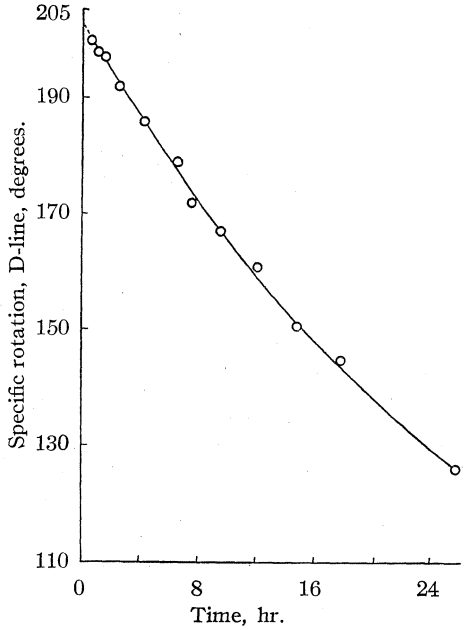


Fig. 1.—Mutarotation of potato starch (c, 4.84) in hydrochloric acid (37.5 g. HCl per 100 cc. soln.) at 0°.

the slope of which is $-k$ and from the intercept of which d_0 can be calculated. The experimental results are shown graphically in Fig. 3. A straight line is obtained and the closely approximate validity of the equation as applied to starch is accordingly confirmed. The points do show a slight tendency to oscillate about the line but this is of no significance as the polarimetric data (Fig. 1) show no discontinuities. The extrapolated points lie close to the axis. The degree of polymerization reaches such a low value that deviations from linearity might well be expected. However, the accuracy of the present experimental results is such that further refinement of the calculations is not required. The value of the specific rate constant k (hours^{-1}) at 0° is 2.66×10^{-2}. The average degree of polymerization, d_0, for the original starch is 20 ± 4, the uncertainty being estimated graphically.

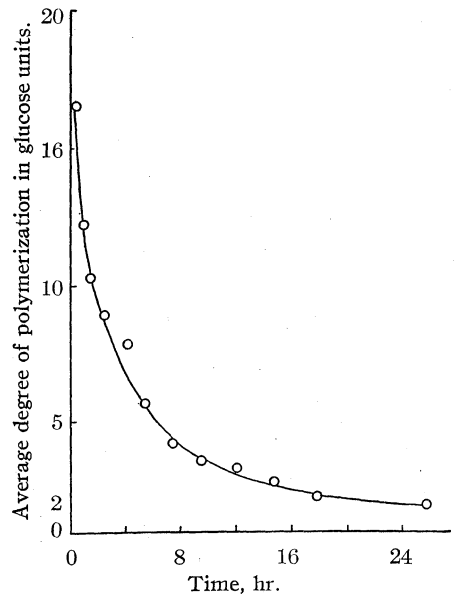


Fig. 2.—Relationship between time of hydrolysis of potato starch and average degree of polymerization as calculated from sulfur content of mercaptalated products.

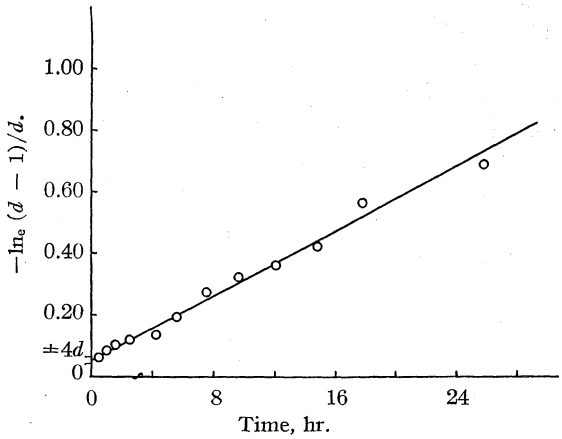


Fig. 3.—Potato starch in hydrochloric acid at 0°.

The value which we have obtained for our sample of potato starch lies within the range of the value of 23–24 glucose units (5% tetramethylglucopyranose in final hydrolysis mixture) found by Hirst, Plant and Wilkinson[6] for both the amylose and amylopectin fractions of potato starch. Hirst and co-workers employed the tetramethylglucopyranose end-group assay method developed by Haworth and Machemer.[7] Application of this end-group assay method to other samples of starch from several plant sources have all yielded values within the range of 25–30 glucose units.[8] Hassid and Dore employed an extraction technique for the tetramethylglucopyranose isolation instead of the distillation technique of Haworth and Machemer.

Neumann and Hess[9] have developed a method

(6) E. L. Hirst, M. M. T. Plant and M. D. Wilkinson, *J. Chem. Soc.*, 2375 (1932).

(7) W. N. Haworth and H. Machemer, *ibid.*, 2270 (1932).

(8) (a) W. N. Haworth, E. L. Hirst and M. D. Woolgar, *ibid.*, 177 (1935); (b) K. D. Baird, W. N. Haworth and E. L. Hirst, *ibid.*, 1201 (1935); (c) W. Z. Hassid and W. H. Dore, THIS JOURNAL, **59**, 1503 (1937).

(9) F. Neumann and K. Hess, *Ber.*, **70B**, 721 (1937).

for tetramethylglucopyranose end-group assay which is different from that of Haworth and Machemer[7] and for which a high degree of accuracy is cited. Application of this procedure to potato starch by Hess and Lung[10] yielded a value of 52.0–52.4 glucose units. It is rather surprising that a refinement in the end-group assay method should yield a higher rather than a lower value. The results of Hess and Lung are not directly comparable with other values on potato starch as these workers isolated the starch from the plant source by their own method. The end-group assay of Neumann and Hess[9] has been criticized by Hirst and Young[11] and by Averill and Peat.[12]

Evidence that the starch particle in dilute solution is a molecular aggregate rather than a single molecule has been presented frequently.[13] The ultracentrifuge results so far obtained[14] show a wide distribution of particle size ranging from an apparent molecular weight of 60,000 to 1,000,000. The Staudinger viscosity methods yield a value of more than 1000 glucose units for starch.[15]

This discrepancy between values for molecular size by the viscosity and chemical methods is explained by Staudinger by postulating a branched chain structure for the starch molecule. One of the arguments for such a structure is the isolation of dimethyl glucose from the hydrolysis products of methylated starch by Irvine.[16]

Hess[10] claims that the amount of dimethylglucose isolated corresponds to the degree to which the methylation of the original starch is incomplete.

It is interesting to point out that a branched structure would not affect the value for molecular size obtained in the present work. In order for this value from the mercaptalation technique to represent the true molecular size, it is only necessary that a reducing group be produced whenever a bond is broken by hydrolysis.

Experimental

Characterization of Starch.—The sample of starch used in this work was a high grade commercial (J. L. Hopkins Co., New York) potato starch. It showed no detectable Fehling's reduction. According to Schoch and Jensen,[5] Fehling's solution procedures are not reliable when applied to starch and they have devised a measure which they term "alkali number." This value is determined by heating the starch under controlled conditions with 0.1 *N* sodium hydroxide for one hour at the temperature of boiling water. The amount of alkali consumed is then determined and the "alkali number" is expressed as the number of cc. of 0.1 *N* alkali consumed by one gram of starch during one hour of digestion. Dr. Schoch has kindly determined the alkali number of our sample of potato starch in comparison with those of several other starches and reports as follows:

	Alkali number
Your sample	5.7
Imported potato starch	6.6
Domestic potato starch	6.9
Corn starch	9.8

Dr. Schoch states that "these results indicate that your material is of exceptionally high quality, and that manufacturing processes have produced little or no hydrolytic degradation."

Hydrolysis and Mercaptalation.—The starch (71 g., moisture content 12.22%) was placed in a 2-liter, 3-necked flask at 0°, equipped for rapid mechanical stirring and for rapid removal of samples through a delivery tube, and was treated with water (100 cc.) previously undercooled to 0°. The starch was suspended by rapid stirring and then fuming hydrochloric acid (1150 cc., d^0_4 1.212), previously cooled to 0°, was added. As soon as solution (d^0_4 1.214, 4.84 g. starch (moisture free) per 100 cc. soln. at 0°) was complete, polarimeter and density samples were withdrawn and maintained at 0°. Well-purified ethyl mercaptan (200 g.), previously cooled to 0°, was then added and the stirring continued at 0°. Samples of 50 cc. were withdrawn after the time intervals recorded in Table I, and immediately poured, with stirring, into mixtures of sodium bicarbonate (54 g.) and water (185 cc.). The neutralization mixtures were then concentrated to dryness under reduced pressure at 37–40°, and the resulting mixtures of salt and hydrolyzed starch mercaptals were dried in the vacuum oven at 40°.

Acetylation of Mercaptalated Products.—The mixtures of salt and mercaptalated products were individually acetylated for four days with acetic anhydride (20 cc.) and pyridine (40 cc.). The resulting pyridine solutions were poured into ice and water (1000 cc.) and the insoluble acetates extracted with chloroform. The chloroform extracts were washed successively with hydrochloric acid (5%), saturated sodium bicarbonate solution, and water. Concentration of the dried extracts under reduced pressure at 37–40° produced the acetates, usually as amorphous solids, but as sirups in a few instances. Several of these products were analyzed for acetyl content by the Kunz procedure. The results are tabulated in Table I.

Optical Rotation of Potato Starch in Hydrochloric Acid at 0°.—The polarimeter sample from the hydrolysis mixture was maintained at 0° and its optical rotation observed at various time intervals as the hydrolysis progressed. The concentration of starch in the solution was 4.84 g. per 100 cc. and the concentration of hydrogen chloride, 37.5 g. per 100 cc. The hydrolysis solution had a density of

(10) K. Hess and K. H. Lung, *Ber.*, **71B**, 815 (1938).
(11) E. L. Hirst and G. T. Young, *J. Chem. Soc.*, 1247 (1938).
(12) F. J. Averill and S. Peat, *ibid.*, 1244 (1938).
(13) M. Samec, B. Lavrenčič and S. Premrl, *Kolloid-Beihefte*, **37**, 91 (1933); refs. 8a and 8b.
(14) O. Lamm, *Kolloid-Z.*, **69**, 44 (1934); T. Svedberg, *Ber.*, **67A**, 117 (1934).
(15) H. Staudinger and E. Husemann, *ibid.*, **70B**, 1451 (1937); *Ann.*, **527**, 195 (1937); *Ber.*, **71B**, 1057 (1938); E. Husemann, *Papier-Fabr.*, **36**, Tech. Wiss. Th., 559 (1938).
(16) J. C. Irvine, *Nature*, **129**, 470 (1932).

1.214 at 0°. The polarimetric data are recorded in Table I and are plotted in Fig. 1.

TABLE I

DEGREE OF POLYMERIZATION OF POTATO STARCH (*c*, 4.84) AFTER HYDROLYSIS WITH HYDROCHLORIC ACID (37.5 G. HCl PER 100 CC. SOLN.) AT 0° FOR VARIOUS TIME INTERVALS

Time of hydrolysis, hrs.[a]	$[\alpha]^0D$	Acetylated mercaptalated product from 2.42 g. starch, wt., g.	%S	D. P.[c] by S content	Acetyl content (cc. 0.1 *N* NaOH) Calcd.	Found
0	+203°[b]	...	..	..	...	...
0.55	200	2.5	1.29	16.5	...	...
1.05	198	3.7	1.72	12.2	...	...
1.55	197	4.0	2.03	10.2	10.37	10.43
2.55	192	4.0	2.31	8.9	10.35	10.51
4.25	186	5.0	2.59	7.9	...	...
5.55	179	4.5	3.46	5.7	10.32	10.39
7.55	172	4.0	4.51	4.2	10.29	10.06
9.55	167	4.2	5.23	3.5	...	...
12.05	161	4.7	5.56	3.3	...	...
14.80	151	3.9	6.31	2.8	10.24	10.01
17.80	145	3.7	7.59	2.2	...	...
25.80	126	4.2	8.35	2.0	10.20	10.13

[a] Initial time taken as time of addition of the acid to the starch. [b] By extrapolation. [c] Average degree of polymerization in glucose units, assuming complete acetylation.

Sulfur Analyses of Acetylated Mercaptalated Products.—The sulfur analyses were performed by the Parr bomb method, employing total samples of approximately 1 g., on a moisture-free basis, in the manner described previously.[2] In Table I are recorded the sulfur analytical data and the corresponding average degrees of polymerization calculated from them. The degree of polymerization (D. P.) may be calculated from the sulfur content by the equation

$$\text{D. P.} = 2 + \left[\frac{6412}{\%S + C_{12}H_{16}O_8}\right] - 2\left[\frac{C_{14}H_{19}O_9 + C_2H_5S}{C_{12}H_{16}O_8}\right]$$

where $C_{14}H_{19}O_9$ is the molecular weight of the end structural units and $C_{12}H_{16}O_8$ is the molecular weight of the intervening units.

Summary

1. Potato starch has been hydrolyzed with a concentrated solution of hydrochloric acid at 0° in the presence of an excess of ethyl mercaptan. The resulting mercaptalated mixtures of hydrolyzed products were isolated as their acetates at various time intervals, during the first twenty-six hours of the hydrolysis.

2. Sulfur analytical data indicated that the average degree of polymerization of the mercaptalated products varied from 17 glucose units after one-half hour to 2 glucose units after twenty-six hours.

3. The course of the hydrolytic reaction (without mercaptalation) at 0° was followed by optical rotation measurements.

4. A graphic analysis of the data yields a value of 2.66×10^{-2} for the specific rate constant (hours^{-1}) of the rate of change of the degree of polymerization in concentrated hydrochloric acid at 0°.

5. By graphic analysis the value 20 ± 4 glucose units is obtained for the initial average degree of polymerization of the potato starch.

COLUMBUS, OHIO RECEIVED JUNE 10, 1939

[CONTRIBUTION FROM THE UNITED STATES DEPARTMENT OF AGRICULTURE, BUREAU OF ENTOMOLOGY AND PLANT QUARANTINE]

The Action of Isobutylmagnesium Bromide on 3,4,5-Trimethoxybenzonitrile

BY H. L. HALLER AND P. S. SCHAFFER[1]

A recent communication by Suter and Weston[2] describes the preparation of some 5-alkylresorcinols. As work along similar lines has been under way for some time in this Laboratory, occasion is taken to present some of the results that are closely related to the studies of Suter and Weston. This work had for its object the preparation of 5-isoamylresorcinol[3] in order that its properties might be compared with those of 4-isoamylresorcinol[4] and 2-isoamylresorcinol.[5]

4-Isoamylresorcinol was first prepared by Dohme[4] in connection with his studies on the bactericidal action of 4-alkylresorcinols, and 2-isoamylresorcinol was first synthesized by Haller[5] and shown to be identical with tetrahydrobutanol,[6] a degradation product of rotenone.[7]

The reaction of 3,5-dimethoxybenzonitrile with

(1) Present address: Bureau of Dairy Industry, U. S. Department of Agriculture, Washington, D. C.

(2) Suter and Weston, THIS JOURNAL, **61**, 232 (1939).

(3) Because the junior author has been assigned to new duties, the work was interrupted before its completion.

(4) Dohme, Cox and Miller, THIS JOURNAL, **48**, 1688 (1926).

(5) Haller, *ibid.*, **55**, 3032 (1933).

(6) Haller and LaForge, *ibid.*, **53**, 4460 (1931); **54**, 1988 (1932).

(7) LaForge, Haller and Smith, *Chem. Rev.*, **12**, 181 (1933).

isobutylmagnesium bromide according to the procedure described by Haller[5] in his work on 2,6-dimethoxyphenyl isobutyl ketone was first studied. The yield of the resulting ketone was 45 to 50% based on the nitrile.

Several methods for the reduction of the ketone were investigated, with results similar to those described by Suter and Weston[2] in the reduction of their ketones.

Reduction with sodium and alcohol, as described by Asahina[8] for the 3,4,5-trimethoxyphenyl alkyl ketone, yielded mixtures which were difficult to separate. When the ketone was shaken in an atmosphere of hydrogen with palladium charcoal as described by Hartung and Crossley,[9] no hydrogen was absorbed and the unchanged starting material was recovered. The Clemmensen method likewise failed to yield a satisfactory reduction product.

Owing to the high cost of 3,5-dimethoxybenzonitrile, a study of the reaction between 3,4,5-trimethoxybenzonitrile and isobutylmagnesium bromide was undertaken, as it has been shown[10] that the methoxyl group in the 4-position of trimethylpyrogallol derivatives can be replaced by hydrogen. The reaction of this nitrile and the Grignard reagent yielded, after hydrolysis, in addition to the expected 3,4,5-trimethoxyphenyl isobutyl ketone, two other products. One of these products is soluble in aqueous alkali and forms a semicarbazone, an oxime, and an acetyl and a benzoyl derivative. With ferric chloride in alcohol it gives a faint green color. On the basis of these reactions, analytical data, and the known reactivity of the methoxyl group in the 4-position of trimethylpyrogallol derivatives, it is suggested that the compound is 3,5-dimethoxy-4-hydroxyphenyl isobutyl ketone. The other compound forms a crystalline semicarbazone, possesses two methoxyl groups, and is insoluble in aqueous alkali. Analyses of the compound and of its semicarbazone indicate the empirical formula $C_{17}H_{26}O_3$. It is suggested that this compound possesses a butyl group in the 4-position of the benzene ring and that the compound is probably a 3,5-dimethoxybutylphenyl isobutyl ketone.

Several attempts were made to reduce the trimethoxyphenyl isobutyl ketone. In some cases a reduction was accomplished, but it could not be repeated and further studies are desirable.

(8) Asahina, *Ber.*, **69B**, 1643 (1936).

(9) Hartung and Crossley, THIS JOURNAL, **56**, 158 (1934).

(10) Houben, "Die Methoden der organischen Chemie," pt. 3, 1930, p. 179.

Experimental

3,5-Dimethoxybenzonitrile.—This compound was obtained on dehydration of the corresponding amide[11] with phosphorus pentoxide.

Five-tenths of a gram of 3,5-dimethoxybenzamide was mixed intimately with 0.4 g. of phosphorus pentoxide, and the mixture heated in a sand-bath. After the vigorous reaction had subsided, the mixture was treated with ice and water, filtered, thoroughly washed with water, and then dried. The product was recrystallized from 60% ethanol. It melted at 87–88°.

Anal. Calcd. for $C_9H_9NO_2$: N, 8.6. Found: N, 8.58.

In attempts to prepare the nitrile from the amide and phosphorus pentachloride according to the procedure of Kauffmann,[12] dehydration took place, but the product also contained chlorine.

A mixture of 0.4 g. of 3,5-dimethoxybenzamide and 0.65 g. of phosphorus pentachloride was heated in a sand-bath to initiate reaction. After the vigorous reaction had subsided and the mixture had cooled, ice and water were added. The reaction product was thoroughly washed with water and dried. After recrystallization from ethanol it melted at 124–125°.

Anal. Calcd. for $C_9H_8ClNO_2$: N, 7.1. Found: N, 7.18.

3,5-Dimethoxyphenyl Isobutyl Ketone.—A Grignard reagent was prepared in the usual manner from 2.4 g. (0.1 mole) of magnesium suspended in 40 cc. of ether and 13.0 g. (0.095 mole) of isobutyl bromide dissolved in 25 cc. of ether. To this ether solution was added, in the course of five minutes and with constant stirring, 3.2 g. (0.02 mole) of 3,5-dimethoxybenzonitrile dissolved in 50 cc. of ether. The reaction mixture was then refluxed for one hour, cooled, and poured into ice and concentrated hydrochloric acid. The aqueous solution, after separation from the ether solution, was extracted twice with ether, placed in an open beaker, and heated on the steam-bath to remove the dissolved ether. Finally the solution was boiled vigorously under reflux for one hour. The separated oil was extracted from the cooled solution with ether; the ether extract was washed with water and dried over sodium sulfate. The oil remaining after the ether had been removed was distilled. It boiled at 143–145° (2.0 mm.). The yield was 3.6 g. When treated with semicarbazide hydrochloride and sodium acetate, according to the procedure described by Shriner and Turner,[13] 3.6 g. of the oil yielded 4.0 g. of a crystalline semicarbazone. The product after recrystallization from ethanol melted at 195–196°.

Anal. Calcd. for $C_{14}H_{21}N_3O_3$: C, 60.21; H, 7.53. Found: C, 59.86; H, 7.70.

3,4,5-Trimethoxybenzonitrile.—Gallic acid was methylated with dimethyl sulfate according to the directions in "Organic Syntheses."[14] The methylated acid on treatment with thionyl chloride yielded the acid chloride, which was converted to the amide[15] by treatment with concen-

(11) Mauthner, *J. prakt. Chem.*, **87**, 403 (1913).

(12) Kauffmann, *Ann.*, **344**, 30 (1906).

(13) Shriner and Turner, THIS JOURNAL, **52**, 1267 (1930).

(14) "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, 1932, p. 522.

(15) Harding, *J. Chem. Soc.*, **99**, 1585 (1911).

trated aqueous ammonia. The amide, on being heated in benzene solution with phosphorus pentachloride, yielded the nitrile.[16]

Reaction of 3,4,5-Trimethoxybenzonitrile with Isobutylmagnesium Bromide.—To the Grignard reagent prepared from 34.2 g. (0.25 mole) of isobutyl bromide in 65 cc. of ether and 6.07 g. (0.25 mole) of magnesium turnings suspended in 200 cc. of dry ether was added, in the course of twenty minutes and with constant stirring, 19.3 g. (0.1 mole) of 3,4,5-trimethoxybenzonitrile dissolved in 200 cc. of dry toluene. The reaction mixture was then heated in an oil-bath and the ether removed by distillation, toluene being added gradually to maintain the original volume.[17] After all of the ether had been replaced with toluene, the mixture was refluxed for three hours with constant stirring. The reaction mixture was then poured onto ice containing 30 cc. of concentrated hydrochloric acid. The aqueous layer, after separation of the toluene, was washed twice with ether, placed in an open beaker, and heated on the steam-bath until all the dissolved ether was removed. It was then boiled for two hours under reflux and cooled, and the oil that separated was removed by extraction with ether. The combined ether extracts were washed with 5% sodium hydroxide and with water, and then dried over sodium sulfate. The oil (A) remaining after removal of the ether was distilled under reduced pressure. It boiled at 147–150° (1 mm.). The yield was 6.5 g. Analysis indicated the compound to be trimethoxyphenyl isobutyl ketone.

Anal. Calcd. for $C_{14}H_{20}O_4$: C, 66.66; H, 7.93; OCH_3 (3), 36.9. Found: C, 66.43; H, 7.88; OCH_3, 36.4.

A crystalline semicarbazone was obtained readily when 0.5 g. of the distilled oil (A) in 5 cc. of ethanol was treated with 2 cc. of pyridine and 0.5 g. of semicarbazide hydrochloride dissolved in a small quantity of hot water. The yield was 0.6 g. The product, after crystallization from ethanol, melted at 205°.

Anal. Calcd. for $C_{15}H_{23}N_3O_4$: C, 58.3; H, 7.44; OCH_3 (3), 30.1. Found: C, 58.45; H, 7.81; OCH_3, 30.0.

The alkali-soluble fraction (B) obtained on extraction of the ether solution was acidified with dilute sulfuric acid and the separated product removed by extraction with ether. The ethereal solution was washed with water and dried with sodium sulfate. On removal of the ether a colorless crystalline product was obtained. The yield was 6.0 g. When recrystallized from 50% ethanol, it melted at 94°. Analyses indicate it to be a dimethoxyhydroxyphenyl isobutyl ketone.

Anal. Calcd. for $C_{13}H_{18}O_4$: C, 65.54; H, 7.56; OCH_3 (2), 26.05. Found: C, 66.04; H, 7.80; OCH_3, 26.09.

A crystalline semicarbazone was obtained readily when the product (B) was treated with semicarbazide hydrochloride as described above for the trimethoxyphenyl isobutyl ketone. After recrystallization it melted at 162.5°.

Anal. Calcd. for $C_{14}H_{21}N_3O_4$: C, 56.9; H, 7.12; OCH_3(2), 21.0. Found: C, 57.75; H, 7.67; OCH_3, 21.2.

With hydroxylamine the alkali-soluble product yielded an oxime. A solution of 1.2 g. of the oil (B), 0.35 g. of hydroxylamine hydrochloride, and 0.45 g. of anhydrous sodium acetate in 10 cc. of absolute ethanol was refluxed for two hours. The solution was filtered and concentrated to a small volume, and water was added. The separated product was filtered and dried. The yield was 1.0 g. After recrystallization from dilute ethanol it melted at 110°.

Anal. Calcd. for $C_{13}H_{19}NO_4$: OCH_3(2), 24.5. Found: OCH_3, 24.4.

Fraction B with benzoyl chloride yielded a benzoyl derivative.

One gram of the oil (B), 1 g. of benzoyl chloride, and 1 cc. of pyridine in 7 cc. of benzene were heated in a boiling water-bath for one hour. To the cooled reaction mixture dilute hydrochloric acid was added and the solution was extracted with ether. The ether–benzene solution was washed with dilute sodium carbonate solution, with water, and then dried over anhydrous sodium sulfate. After removal of the solvent the remaining product crystallized readily. It was recrystallized from methanol. The yield was 1 g. It melted at 111°.

Anal. Calcd. for $C_{20}H_{22}O_5$: OCH_3(2), 18.15. Found: OCH_3, 18.0.

The toluene solution obtained after separation of the aqueous acid solution was washed with water, dried over sodium sulfate, and the toluene removed by distillation. The residue was distilled and 2.0 g. of an oil that boiled at 140–145° (1 mm.) was obtained. It yielded 0.2 g. of alkali-soluble material on treatment in ether solution with 5% sodium hydroxide. The alkali-insoluble fraction distilled at 128–130° (0.35 mm.).

Anal. Calcd. for $C_{17}H_{26}O_3$: C, 73.4; H, 9.35; OCH_3(2), 22.3. Found: C, 72.8; H, 9.14; OCH_3, 23.0.

When treated in ethanol with semicarbazide hydrochloride and pyridine, the oil yielded a crystalline semicarbazone. When recrystallized from methyl alcohol it melted at 184°.

Anal. Calcd. for $C_{18}H_{29}O_3N_3$: C, 64.5; H, 8.66; OCH_3(2), 18.5. Found: C, 64.53; H, 8.82; OCH_3 18.5.

Summary

Reaction of 3,5-dimethoxybenzonitrile and isobutylmagnesium bromide yields 3,5-dimethoxyphenyl isobutyl ketone.

Interaction of 3,4,5-trimethoxybenzonitrile and isobutylmagnesium bromide yields, in addition to the expected 3,4,5-trimethoxyphenyl isobutyl ketone, two other products. The one has the empirical formula $C_{14}H_{20}O_4$, is soluble in alkali, and forms both carbonyl and hydroxyl derivatives. It is probably 3,5-dimethoxy-4-hydroxyphenyl isobutyl ketone. The other product has the empirical formula $C_{17}H_{26}O_3$, is insoluble in alkali, and forms a semicarbazone. It is suggested that the compound is probably a 3,5-dimethoxy-4-butylphenyl isobutyl ketone.

WASHINGTON, D C. RECEIVED MAY 17, 1939

(16) Harding, *J. Chem. Soc.*, **105**, 2790 (1914).

(17) When the reaction was carried out in ether only, in which the nitrile is slightly soluble, about two-thirds of the starting material was recovered unchanged.

[CONTRIBUTION FROM THE DEPARTMENT OF COLLOID CHEMISTRY, D. J. MCCARTHY FOUNDATION, AND DEPARTMENT OF PHYSICS, TEMPLE UNIVERSITY SCHOOL OF MEDICINE]

Studies on Melanins.[1] III. X-Ray Diffraction Patterns of Photosynthetic and Genuine Melanins

BY MONA SPIEGEL-ADOLF AND GEORGE C. HENNY

Although ultra-spectrographical investigations[2] have made it possible to distinguish several groups of melanins, no clues are as yet available as to the structure of the melanin molecule. X-Ray diffraction patterns of melanins have been made in an attempt to fill this gap.

Method.—X-Rays are provided by a gas type, self-rectifying X-ray tube[3] used with a copper target and operated at 35 kv. peak at an average current of 15 m. a. Aluminum foil windows (0.013 mm.) and lead diaphragm 1 mm. in diameter and 47 mm. effective length are used. With this arrangement, a fairly monochromatic beam of X-rays of average wave length of 1.54 Å. is secured. The finely ground specimen is pressed into a hole drilled in a microscope slide.[4] The specimen is at a distance of 88 mm. from the focal spot and of 37.7 mm. from the film (Eastman X-ray); the rigid construction of the cameras and of their attachment to the tube assures a correct alignment. The necessary time of exposure was found to be one hour. The table of Katz[5] (corrected for our cameras) was used for the conversion of the diffraction rings into the plane distances in Ångström units.

Material.—The preparation and some properties of the three so-called photosynthetic melanins, *i. e.*, melanin-like products derived from phenylalanine, tryptophan, and tyrosine through the influence of ultraviolet light have been described before.[6] The chemical as well as the ultraspectrographical properties of the samples of human tumor melanins as well as of two samples of sepia and a sample of mouse melanin have been given in a former paper.[2] All the preparations have been kept in powder form at room temperature.

Experimental Results.—All melanins show an X-ray diffraction pattern consisting of either one or two diffuse rings. The diameter of these rings as well as the corresponding planar separations are summarized in Tables I and II. Table I contains besides comparable data for phenylalanine, tryptophan and tyrosines, which were used as sources of photosynthetic melanins.

TABLE I[a]

	Diameter, mm.[b]	Plan. Sep., Å.
Phenylalanine melanin	24 (6)	6.89
Tryptophan melanin	30 (5)	4.10
Tyrosine melanin	30 (4)	4.10
dl-β-Phenylalanine	16, 24, 30, 35, 38, 41, 53	
l-Tryptophan	6.5, 13, 21, 25, 32 (1.5),* 47, 55, 64	
l-Tyrosine	13, 18, 21, 25, 28, 36,* 41, 45, 50,* 54, 57, 62, 69, 76, 84	

[a] The three photosynthetic melanins show besides evidence on an inner ring less than 9 mm. in diameter.

[b] The figures in parentheses indicate the width of the ring, * indicates a band instead of a sharp line.

TABLE II[a]

Melanins	Outer ring Mm.	Outer ring Å.	Inner ring Mm.	Inner ring Å.	Log *E* Å. = 3000
Sepia gen.	32 (8)	3.86	12	9.8	2.62
Sepia digest.	31	3.98	11	10.6	2.42
Hum. tumor F_2	30	4.10	11	10.6	2.38
Hum. tumor F_1	28	4.35	12	9.8	2.34
Hum. tumor P	28	4.35	11	9.8	2.30
Hum. tumor F_3	27	4.5	11	9.8	..
Mouse melanoma	26 (4)	4.66	11	9.8	1.94

[a] Melanins P and F_1 are chemically identical; F_3 shows only slight differences; F_2 larger differences.

Conclusions

1. The three photosynthetic melanins show a similar diffraction pattern which is very different from the elaborate sharp line pattern of their mother substances. Only tryptophan contains one diffuse ring similar to the one of tryptophan and tyrosine melanin. These findings confirm former observations of Spiegel-Adolf[2] according to which only irradiated tyrosine, but not phenylalanine, solutions gave a positive Hopkins–Cole reaction.

2. The diffraction pattern of the tumor melanins and of sepia although of greater intensity are similar to the ones of the photosynthetic melanins. There exist certain differences in the diameters of the various genuine melanins. These differences seem to run parallel to differences in chemical and optical properties of the genuine melanins.

3. The planar separations of the genuine melanins vary between 9.8–10.6 Å. and 3.86–4.66 Å. These values are close to the ones found by Astbury and his co-workers in proteins. (All our melanins were free from any protein contamina-

(1) Read before the meeting of the American Chemical Society at Baltimore, Md., April 6, 1939.

(2) M. Spiegel-Adolf, *Fundamenta Radiologica*, **5**, 36 (1939).

(3) R. W. G. Wyckoff, *Rev. Sci. Instruments*, **7**, 35 (1936).

(4) W. T. Astbury and R. Lomax, *J. Chem. Soc.*, 896 (1935).

(5) J. R. Katz, "Die Roentgenspektrographie, etc.," Handbuch der biol. Arbeitsmeth. (Abderhalden) Abt. II., Physikal. Meth., Teil 3, H. 6, p. 222, 1934.

(6) M. Spiegel-Adolf, *Biochem. J.*, **31**, 1303 (1937).

tion.) The interpretation of these results ought therefore to follow lines similar to the interpretation of the protein diffraction pattern. Either melanins must be considered as "anisotropic amorphous solid substances" according to Freundlich[7] or as non-amorphous crystalline substances according to Astbury.[4]

Acknowledgments.—We are indebted to Drs. H. K. Barrenscheen (Vienna) and B. Gruskin (Philadelphia) for some of the melanin material, to Dr. R. W. G. Wyckoff for helpful suggestions facilitating the construction of the X-ray tube and to the National Research Council Committee on Radiation, whose grant to one of us (Sp.-A.) has made these investigations possible.

(7) H. Freundlich, "Kapillarchemie," Akad. Verlagsgesellschaft Leipzig, 1922, p. 999.

Summary

X-Ray diffraction patterns of photosynthetic melanins as well as of the corresponding amino acids and of various tumor melanins and sepia are described. Slight differences observed in the diffraction patterns of the genuine melanins (from 9.8–10.6 Å. and from 3.86–4.66 Å.) run parallel with observed differences in the optical absorption power of the same substances.

PHILADELPHIA, PENNA. RECEIVED APRIL 15, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

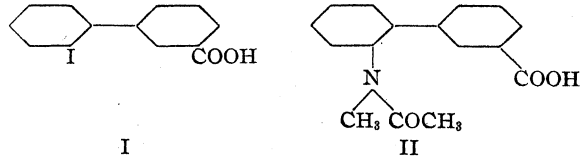
Stereochemistry of Biphenyls. XLVI.[1] 2-Substituted Biphenyls

BY ROGER ADAMS AND T. L. CAIRNS[2]

The prediction of restricted rotation in biphenyls by means of calculated interferences based on atomic radii has proved very helpful. In 2,2′-disubstituted biphenyls, however, the actual stability of the optically active forms is less than would be anticipated from the stability of closely related 2,2′,6- and 2,2′,6,6′-tri- and tetrasubstituted compounds. On these grounds, biphenyls monosubstituted in the 2-position should show even greater instability than atomic radii calculations would indicate. The published results of Meisenheimer[3] and Lesslie and Turner[4] confirm this. These latter investigators found it impossible to resolve the 3′-bromobiphenyl-2-tetramethylammonium iodide but obtained the corresponding tetramethylarsonium iodide as a mutarotating compound. In the same paper they mention that 2-iodo-3′-carboxybiphenyl was prepared and could not be resolved. However, this latter compound and its method of preparation were not described. The fact that 2,2′-diiodo-4,4′-dicarboxybiphenyl has been separated into two optically active forms[5] indicates beyond a doubt that an iodine atom is sufficiently large to interfere with a hydrogen and consequently that, unless some mobility greater than that found in 2,2′-disubstituted biphenyls is present in monosubstituted compounds, 2-iodo-3′-carboxybiphenyl should be resolvable.

The syntheses of biphenyls with a substituent in the 2-position and, in addition, a salt-forming group are difficult. 2-Amino-3′-carbethoxybiphenyl offers an attractive starting point for the preparation of such biphenyls since the amino group should be converted readily into or replaced by groups of large radii without difficulty. The details have now been determined by which this compound can be made from the condensation of *o*-bromonitrobenzene and ethyl *m*-iodobenzoate followed by reduction of the nitro group. This synthesis, which appears simple, required much experimentation before a satisfactory procedure was found.

In this communication the preparation of 2-iodo-3′-carboxybiphenyl (I) and N-acetyl-N-methyl-2-amino-3′-carboxybiphenyl (II) from 2-amino-3′-carbethoxybiphenyl is described. The



I II

work of Lesslie and Turner was confirmed in that the iodo compound could not be resolved.

In view of the success of Mills and Kelham[6] in

(1) For previous paper see Adams and Joyce, THIS JOURNAL, **60**, 1491 (1938).

(2) Solvay Process Company Fellow, 1938–1939. An abstract of a thesis submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy in chemistry.

(3) Meisenheimer and Beitswenger, *Ber.*, **65B**, 32 (1932).

(4) Lesslie and Turner, *J. Chem. Soc.*, 1588 (1933).

(5) Searle and Adams, THIS JOURNAL, **55**, 1649 (1933).

(6) Mills and Kelham, *J. Chem. Soc.*, 274 (1937).

resolving N-acetyl-N-methyl-2-amino-8-naphthalene sulfonic acid and N-acetyl-N-methyl-2-amino-4-methylbenzene sulfonic acid, the N-acetylmethylamino group was introduced into the 2-position as shown in compound II. The sphere of influence assumed by Mills for this group should result in restricted rotation in molecule II. This might occur not only between the phenyl groups but also between the nitrogen atom and the carbon atom of the ring. If in both places, two diastereoisomeric forms should result. Careful fractionation of this product from methanol indicated the presence merely of a single compound.

When resolution of II was attempted through the quinine salt by fractionation from acetone, two salt fractions were obtained. They had different specific rotations (−125 and −140°) and different solubilities. They were not interconvertible, however, and did not mutarotate. Upon hydrolysis, both gave the original acid in the inactive form. Although the explanation of the two salt fractions is not clear, the results indicate that resolution was not accomplished.

The replacement of the amino group in 2-amino-3′-carboxybiphenyl by other groups of large radius is now being studied.

Experimental

2-Nitro-3′-carboxybiphenyl.—A mixture of 25.8 g. of *o*-bromonitrobenzene and 28 g. of ethyl *m*-iodobenzoate was heated under reflux, with mechanical stirring, to a temperature of 215°. In small quantities at a time, 48 g. of activated copper-bronze[7] was added. The temperature was then raised to 235–250° and maintained for forty-five minutes. After cooling, the mixture was extracted with acetone (500–600 cc.) and the copper and copper salts removed by filtration. The acetone solution was concentrated to about 50 cc., 100 cc. of ethanol was added, and the distillation continued until all the acetone was removed. A mixture of 500 cc. of ethanol and 160 cc. of 10% aqueous sodium hydroxide was then added and the solution refluxed for one hour. The alcohol was removed by distillation and 500 cc. of water added to the residue. After filtration, the filtrate was cooled and was extracted with ether to remove alkali-insoluble products. After warming the aqueous solution to evaporate the residual ether it was cooled in an ice-bath and acidified with dilute hydrochloric acid. The brownish mass which separated became hard on standing. This was dissolved in a minimum quantity of glacial acetic acid (150–200 cc.) and on cooling a crystalline product separated. It was recrystallized from ethanol with the use of norite: yellow crystals, m. p. 207–208° (corr.); yield, 7.6 g. (31%).

Anal. Calcd. for $C_{13}H_9O_4N$: C, 64.19; H, 3.70. Found: C, 64.46; H, 3.97.

(7) Kleiderer and Adams, THIS JOURNAL, **55**, 4219 (1933).

2-Nitro-3′-carbethoxybiphenyl.—A mixture of 7.5 g. of 2-nitro-3′-carboxybiphenyl and 30 cc. of thionyl chloride was refluxed gently for twenty to thirty minutes. The excess thionyl chloride was removed under reduced pressure and 50 cc. of ethanol was added drop by drop at first and then faster after the exothermic reaction subsided. The mixture was then refluxed until all the ester was in solution, cooled and poured onto 200 cc. of cracked ice. The pale yellow oil which separated solidified on standing. It was purified by distillation *in vacuo*, b. p. 215° (11 mm.), and then recrystallization from ethanol: white crystals, m. p. 63–65° (corr.); yield, 8 g. (84%).

Anal. Calcd. for $C_{15}H_{13}O_4N$: C, 66.42; H, 4.80. Found: C, 66.90; H, 4.78.

2-Amino-3′-carbethoxybiphenyl.—A solution of 16.5 g. of 2-nitro-3′-carbethoxybiphenyl in 150 cc. of 95% ethanol was refluxed for one hour and fifteen minutes with a teaspoonful of Raney nickel. This procedure was used to remove impurities which interfered with the normal reduction of the nitro to the amino group. After filtration, 0.22 g. of platinum oxide was added and reduction was carried out at 3–3.5 atmospheres (about thirty minutes). After filtration of the platinum, the solution was concentrated to 50 cc. and then poured into 400 cc. of ice water. The pale yellow oil which separated was extracted with 300 cc. of ether and the ether solution, in turn, extracted several times with dilute hydrochloric acid. The hydrochloric acid extract was warmed to remove the ether, filtered, cooled, and neutralized with a slight excess of aqueous ammonia. The oil which separated, rapidly solidified and was recrystallized from ethanol: white crystals, m. p. 75–76° (corr.); yield, 11.5 g. (80%).

Anal. Calcd. for $C_{15}H_{15}O_2N$: N, 5.81. Found: N, 5.86.

2-Iodo-3′-carboxybiphenyl.—In the replacement of the amino group by the iodine, crude 2-amino-3′-carbethoxybiphenyl was often used. Consequently, it was desirable to add 1 g. of the amino compound to a boiling mixture of 100 cc. of concentrated hydrochloric acid and 25 cc. of water and any insoluble material removed by filtration through glass wool. The solution was then cooled to below 5° and, over a period of two hours, 6 cc. of aqueous 10% sodium nitrite solution was added drop by drop. A saturated aqueous solution of 0.5 g. of potassium iodide was added and the mixture allowed to stand overnight at room temperature. The temperature was then raised to 80–85° and sufficient sodium bisulfite added to remove the free iodine. After cooling to room temperature and filtering, the product was washed and recrystallized from dilute dioxane (3:1 water to dioxane, by volume). Very pale pink crystals were obtained, m. p. 168–170° (corr.); yield, 0.9 g. (69%).

Anal. Calcd. for $C_{13}H_9O_2I$: C, 48.14; H, 2.78. Found: C, 48.05; H, 2.80.

Attempted Resolution of 2-Iodo-3′-carboxybiphenyl.—A solution of 0.504 g. of quinine in 25 cc. of anhydrous acetone was added to a solution of 0.504 g. of 2-iodo-3′-carboxybiphenyl in 10 cc. of anhydrous acetone. About 5 cc. of acetone was used to wash out the flask. The mixture was brought to boiling, filtered and the filter paper washed with 5 cc. more of acetone. After standing

overnight, 0.64 g. of pinkish crystals separated, m. p. 184–187° (corr.).

Upon concentration of the filtrate, other fractions were obtained which gave essentially the same melting point as the first fraction. Upon recrystallization of the various fractions from dilute methanol (5:1 methanol to water, by volume), the samples of salt obtained in every instance appeared to be identical, and within experimental error to give a constant rotation and no mutarotation.

Rotation. 0.0488 g. made up to 10 cc. in methanol, $\alpha^{0-2}D$ −0.516; $l = 1$; $[\alpha]^{0-2}D$ −106.

Anal. Calcd. for $C_{33}H_{33}O_4N_2I$: N, 4.32. Found: N, 4.11.

N-Acetyl-2-amino-3′-carbethoxybiphenyl.—A solution of 6 g. of 2-amino-3′-carbethoxybiphenyl in 40 cc. of glacial acetic acid was warmed almost to boiling and 2.4 g. of acetic anhydride and one drop of concentrated sulfuric acid were added. After heating for thirty minutes, the mixture was allowed to stand at room temperature for one hour and was then poured into 500 cc. of ice water. The oil which separated rapidly solidified and was purified by crystallization from petroleum ether (b. p. 60–110°): white crystals, m. p. 111–111.5° (corr.); yield, 6.5 g. (90%).

Anal. Calcd. for $C_{17}H_{17}O_3N$: C, 72.10; H, 6.01. Found: C, 71.87; H, 6.05.

N-Acetyl-N-methyl-2-amino-3′-carboxybiphenyl.—The general procedure followed was that described by Mills and Kelham.[6] To a solution of 4.5 g. of N-acetyl-2-amino-3′-carbethoxybiphenyl in 100 cc. of dry benzene was added 0.5 g. of powdered sodium and the mixture was refluxed for five hours. A solution of 3 g. of dimethyl sulfate in 20 cc. of dry benzene was now added and refluxing was continued for one hour and thirty minutes. The remaining sodium was decomposed by the addition of a small amount of ethanol and then a solution of 5 g. of potassium hydroxide in 100 cc. of 50% ethanol was added. After steam distillation to remove all the benzene, the alkaline solution was refluxed for two hours, treated with norite, filtered and, while still hot, acidified with dilute hydrochloric acid. The yellow precipitate was filtered and purified by solution in essentially the calculated amount of 1–2% aqueous potassium hydroxide, treatment with norite, filtration and acidification. It may be recrystallized from methanol: white crystals, m. p. 228–239° (corr.); yield, 3 g. (70%).

Anal. Calcd. for $C_{16}H_{15}O_3N$: C, 71.36; H, 5.57. Found: C, 71.46; H, 5.62.

From the filtrate a small quantity of N-acetyl-2-amino-3′-carboxybiphenyl was isolated. This was purified by recrystallization from water; white crystals, m. p. 183–188° (corr.).

Anal. Calcd. for $C_{15}H_{13}O_3N$: C, 70.60; H, 5.10. Found: C, 70.52; H, 4.85.

Fractionation of N-Acetyl-N-methyl-2-amino-3′-carboxybiphenyl.—A careful fractionation of the N-acetyl-N-methyl-2-amino compound from methanol gave no indication of the presence of more than a single compound. Practically every fraction had similar melting points and solubilities.

Attempted Resolution of N-Acetyl-N-methyl-2-amino-3′-carboxybiphenyl.—A solution of 0.94 g. of quinine in 20 cc. of methanol was added to a solution of 0.83 g. of N-acetyl-N-methyl-2-amino-3′-carboxybiphenyl in 60 cc. of methanol. The mixture was boiled and filtered and the filter washed with 20 cc. of methanol. The solution thus obtained deposited no crystals after many hours at 5°. It was evaporated, therefore, to dryness at room temperature and a pale yellow oil resulted. This was dissolved in 40 cc. of boiling dilute acetone (4:1 water to acetone, by volume) and after standing for thirty-six hours at 5–7°, 1.2 g. of white crystals separated, m. p. 170.5–173.5° (corr.).

Rotation. 0.0733 g. made up to 10 cc. in chloroform. $\alpha^{26}D$ −1.031; $l = 1$; $[\alpha]^{26}D$ −140.

This product was dissolved in 120 cc. of dry boiling acetone and filtered. After standing for four hours at 5–7°, 0.77 g. of white crystals separated: (Fraction A) m. p. 173–182° (corr.).

Rotation. 0.0691 made up to 10 cc. in chloroform. $\alpha^{27}D$ −0.89; $l = 1$; $[\alpha]^{27}D$ −129.

Anal. Calcd. for $C_{36}H_{39}O_5N_3$: C, 72.85; H, 6.58; N, 7.08. Found: C, 72.46; H, 6.86; N, 6.90.

The filtrate from this material was evaporated to dryness and yielded a pale yellow oil. This was dissolved in boiling water (about 50 cc.), filtered and cooled. About 0.2 g. of white crystals (Fraction B), m. p. 172.5–173.5° (corr.).

Rotation. 0.0778 g. made up to 10 cc. in chloroform. $\alpha^{28}D$ −1.088; $l = 1$; $[\alpha]^{28}D$ −140.

Anal. Calcd. for $C_{36}H_{39}O_5N_3$: C, 72.85; H, 6.58; N, 7.08. Found: C, 73.17; H, 6.81; N, 6.90.

Fraction A was recrystallized from acetone and fraction B from water. In the case of fraction B cooling must be carried out slowly to avoid separation as an oil. The melting points and rotations of the fractions were essentially unchanged.

Upon decomposition of these two fractions with hydrochloric acid at 0°, the free acids were obtained which showed no optical activity.

The two fractions also showed no mutarotation upon heating in chloroform solution.

Summary

1. A satisfactory method for the preparation of 2-amino-3′-carbethoxybiphenyl has been developed.

2. 2-Iodo-3′-carboxybiphenyl and N-acetyl-N-methyl-2-amino-3′-carboxybiphenyl could not be resolved by fractionation of the quinine salts.

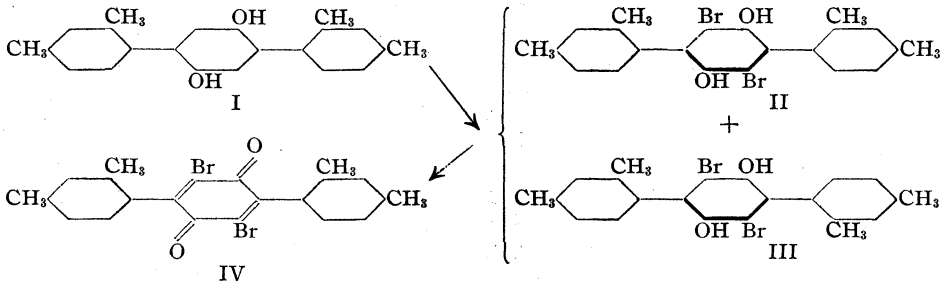
URBANA, ILLINOIS RECEIVED JUNE 5, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Stereochemistry of Biphenyls. XLVII.[1] Certain 3,6-Di-(2,4-dimethylphenyl)-hydroquinones and their Derivatives

BY ROGER ADAMS AND G. C. FINGER[2]

Browning and Adams[3] condensed *m*-xylene with *p*-benzoquinone to give 3,6-di-(2,4-dimethylphenyl)-hydroquinone (I). Upon bromination of this compound, two diastereoisomeric 3,6-di-(2,4-dimethylphenyl)-2,5-dibromohydroquinones (II and III) were readily formed and separated from each other by their different solubilities.

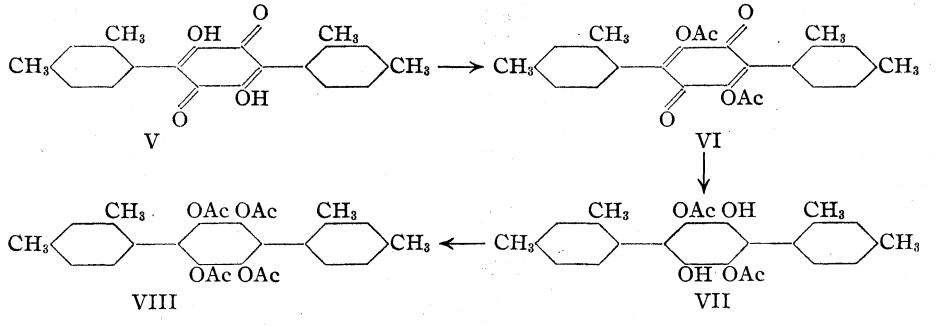


The two dibromohydroquinones (II and III) formed their own characteristic diacetates and tetranitrodiacetates. On the other hand, the oxidation of II or III gave the same 3,6-di-(2,4-dimethylphenyl)-2,5-dibromoquinone (IV). Reduction of IV gave a mixture of II and III. From this it is evident that a methyl, bromine, hydroxyl, and hydrogen in the 2,2′,6,6′-positions of a biphenyl are sufficient to cause restricted rotation. However, in a phenylquinone, a bromine, methyl and hydrogen in addition to the carbonyl will not cause restricted rotation.

The investigation has now been extended to analogous derivatives. The dibromoquinone (IV) upon treatment with alkali gave 3,6-di-(2,4-dimethylphenyl)-2,5-dihydroxyquinone (V) which formed the diacetyl derivative (VI). This in turn was reduced to the diacetoxy hydroquinone (VII) which upon acetylation gave 3,6-di-(2,4-dimethylphenyl)-1,2,4,5-tetraacetoxybenzene (VIII).

In none of these derivatives was the presence of diasteroisomeric forms observed. It may thus be deduced that in a biphenyl, two acetoxyls, a methyl and a hydrogen or one acetoxyl, a hydroxyl, a methyl and a hydrogen in the 2,2′,6,6′-positions will not cause restricted rotation.

On the basis of atomic radii, two hydroxyls, a methyl, and a hydrogen in the 2,2′,6,6′-positions of a biphenyl should result in a slightly restricted rotation, provided a rather rigid coaxial formula is assumed. Since greater mobility is always observed in 2,2′,6-trisubstituted biphenyls, to which group the products studied belong, than in 2,2′,-6,6′-tetrasubstituted compounds, it is not surprising that the substances described show absence of restricted rotation. Apparently, the acetoxy groups are not sufficiently larger than the hydroxyl to modify the results.



Experimental

3,6 - Di - (2,4 - dimethylphenyl) - hydroquinone (I) and 3,6 - Di - (2,4 - dimethylphenyl) - 2,5 - dibromo-

(1) For previous paper see Adams and Cairns, THIS JOURNAL, **61**, 2179 (1939).

(2) An abstract of a thesis submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy in chemistry.

(3) Browning and Adams, THIS JOURNAL, **52**, 4098 (1930).

hydroquinones (II and III).—The procedures used for the preparation of these compounds were those described by Browning and Adams.[3] The preparation of the former was modified in that the original reaction mixture was not allowed to stand overnight but worked up after the addition of the quinone was complete and the mixture had been stirred for two hours. The yield by these former authors was miscalculated as it should have been about 15% as obtained in this investigation.

3,6 - Di - (2,4 - dimethylphenyl) - 2,5 - dihydroxyquinone (V).—To a cold solution of 21 g. of 3,6-di-(2,4-dimethylphenyl)-2,5-dibromoquinone (m. p. 192–193°) in 1200 cc. of ethanol was added with stirring a cold solution of 180 g. of sodium hydroxide in 720 cc. of water. The rate of addition was controlled so that no appreciable rise in temperature took place. The mixture was allowed to come to room temperature and stirred continuously for twenty-four hours. It was then poured with stirring into ice and concentrated hydrochloric acid was added until the mixture was just acid to litmus. During this neutralization the temperature was maintained at 25° by the addition of ice. The dihydroxyquinone separated as a red precipitate which was coagulated by heating on a steam-bath and allowing to stand for several hours. The crude product weighed 14.5 g. (94%). No satisfactory solvent was found for this product and the sample for analysis was obtained by hydrolysis of the pure diacetate. When obtained in this manner it recrystallized from hot benzene as small red needles (m. p. 282–284°).

Anal. Calcd. for $C_{22}H_{20}O_4$: C, 75.82; H, 5.79. Found: C, 75.52; H, 5.86.

3,6 - Di - (2,4 - dimethylphenyl) - 2,5 - diacetoxyquinone (VI).—To a solution of 14.5 g. of crude 3,6-di-(2,4-dimethylphenyl)-2,5-dihydroxyquinone in 50 cc. of hot pyridine was added 50 cc. of acetic anhydride and the mixture was then refluxed for fifteen minutes. Upon cooling the diacetate precipitated. After filtering, washing with a little acetic anhydride, then with water containing a small amount of hydrochloric acid the crude product was dried and purified from ethanol or butanol. It crystallized in bright yellow needles, m. p. 186–188°.

Anal. Calcd. for $C_{26}H_{24}O_6$: C, 72.19; H, 5.59. Found: C, 72.57; H, 5.8.

The filtrate from the original reaction mixture of diacetate upon dilution with a liter of water resulted in the separation of unreacted dihydroxyquinone.

A solution of 0.52 g. of pure diacetoxyquinone in 10 cc. of hot glacial acetic acid and 2 cc. of dilute hydrochloric acid was refluxed for a few minutes. Hydrolysis took place rapidly and small red needles of the dihydroxyquinone separated which were readily purified from benzene, m. p. 282–284°.

3,6 - Di - (2,4 - dimethylphenyl) - 2,5 - diacetoxyhydroquinone (VII).—A solution of 2 g. of 3,6-di-(2,4-dimethylphenyl)-2,5-diacetoxyquinone (m. p. 186–188°) in 270 cc. of hot ethanol was heated with 1 g. of stannous chloride and the mixture refluxed for fifteen minutes. The deep color of the original solution changed to faint yellow. The mixture was poured into a liter of 4 *N* hydrochloric acid, stirred and allowed to stand until coagulation took place. The crude product weighed 1.5 g. (75%). It was purified best from hot butanol forming white crystals, m. p. 213–215°.

Anal. Calcd. for $C_{26}H_{26}O_6$: C, 71.85; H, 6.03. Found: C, 71.99; H, 5.73.

3,6 - Di - (2,4 - dimethylphenyl) - 1,2,4,5 - tetraacetoxybenzene (VIII).—Acetylation was carried out on crude diacetoxyhydroquinone, either in acetone or in pyridine; the latter proved to be the better procedure. A solution of 1.9 g. of diacetoxyhydroquinone in 20 cc. of hot acetic anhydride, 3–5 cc. of pyridine and a pinch of stannous chloride was refluxed. In the course of a few minutes a heavy precipitate of the tetraacetoxy compound formed. The reaction mixture was poured into 100 cc. of water and 20 cc. of concentrated hydrochloric acid. The crude product weighed 1.9 g. (84%). It was purified from butanol, forming large flake-like crystals, m. p .276–278°.

Anal. Calcd. for $C_{30}H_{30}O_8$: C, 69.46; H, 5.83. Found: C, 69.26; H, 6.01.

The tetraacetoxy compound just described was taken in the crude state and crystallized from four different solvents, acetic anhydride, acetone, methanol, and butanol. In no case was it possible to obtain more than a single individual compound.

Summary

3,6 - Di - (2,4 - dimethylphenyl) - 2,5 - dibromoquinone was converted by the action of alkali to 3,6 - di - (2,4 - dimethylphenyl) - 2,5 - dihydroxyquinone. This was acetylated to the diacetoxyquinone which was reduced to 3,6-di-(2,4-dimethylphenyl) - 2,5 - diacetoxyhydroquinone. Acetylation of this last product gave 3,6-di-(2,4-dimethylphenyl)-1,2,4,5-tetraacetoxybenzene.

In no case were diastereoisomeric forms obtained. It is thus concluded that two acetoxyls, a methyl, and a hydrogen or one acetoxyl, one hydroxyl, a methyl, and a hydrogen in the 2,2′,-6,6′-positions of a biphenyl will not cause restricted rotation.

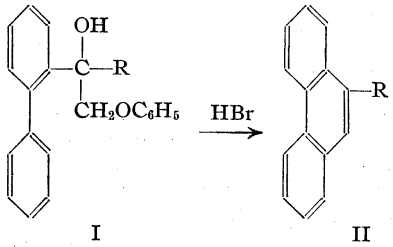
URBANA, ILLINOIS RECEIVED JUNE 5, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE UNIVERSITY OF ILLINOIS AND DUKE UNIVERSITY]

Synthesis of Phenanthrene Derivatives. III.[1] 9-Methylphenanthrene

BY CHARLES K. BRADSHER[2,3] AND ROY W. H. TESS

It has been demonstrated that 1-aryl-1-(2-biphenyl)-2-phenoxyethanols (I, R = aryl) readily undergo cyclization to give 9-arylphenanthrenes.[4]

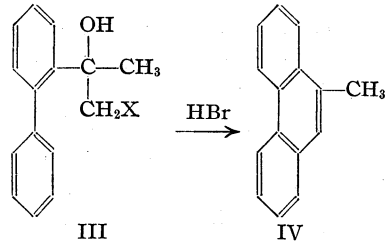


I II

In view of this, it seemed not improbable that the corresponding 1-alkylethanols (I, R = alkyl) might be made to undergo a similar reaction.

We have found that in the case of the methylethanol (I, R = CH_3) such a reaction does take place. When 2-biphenylmagnesium iodide was treated with phenoxyacetone, and the crude carbinol (I, R = CH_3) cyclized by refluxing in a mixture of hydrobromic and acetic acids, 9-methylphenanthrene was obtained in a yield of 32%.

In an effort to find a more satisfactory route to the desired hydrocarbon, the cyclization of a series of carbinols of type III was studied. The



III IV

(X = OCH_3, OC_6H_5, $OC_{10}H_7(\beta)$, $N(C_2H_5)_2$ or Cl)

methods by which the carbinols were prepared together with the over-all yields of methylphenanthrene (IV) are recorded in Table I.

Although all of the carbinols investigated afforded some methylphenanthrene, the yields varied widely. Since these are the over-all yields for both the Grignard reaction and the cyclization, they may not be interpreted as indicative of the tendency of the several carbinols to cyclize. They do, however, afford us a means for the evaluation of the methods of synthesis studied.

TABLE I

Carbinol III, X =	Method of preparing carbinol: Grignard reagent	Ketone	% yield[a] of hydrocarbon
OCH_3	CH_3MgI	o-$C_{12}H_9COCH_2OCH_3$	50
OC_6H_5	o-$C_{12}H_9MgI$	$CH_3COCH_2OC_6H_5$	32
$OC_{10}H_7(\beta)$	o-$C_{12}H_9MgI$	$CH_3COCH_2OC_{10}H_7(\beta)$	23
$N(C_2H_5)_2$	o-$C_{12}H_9MgI$	$CH_3COCH_2N(C_2H_5)_2$	10
Cl	o-$C_{12}H_9MgI$	CH_3COCH_2Cl	< 1

[a] In each case the percentage yield is calculated from the amount of ketone taken.

Calculated from the amount of *ketone* used, the route through the methoxyethanol (III, X = OCH_3) gave the highest yield of the desired hydrocarbon. This carbinol, however, was prepared from 2-(ω-methoxy)-acetobiphenyl which was itself prepared from 2-iodobiphenyl in a yield of 60%. Thus the average over-all yield from the halide was about 30% whether the route was through the methoxy- or phenoxy-ethanol (III, X = OCH_3 or OC_6H_5) although the latter is more direct. The other routes studied lack the preparative value of these two, but are of interest in illustrating the generality of the cyclization reaction.

Our methods for the synthesis of 9-methylphenanthrene, though more convenient than those of Windaus[5] and of Haworth,[6] cannot compare with the method of Bachmann[7] which involves only the action of methyl iodide on 9-phenanthrylmagnesium bromide. If our synthesis finds application, it will be in the preparation of derivatives rather than of the hydrocarbon itself.

One further observation of interest is that 1-methyl-1-(2-biphenyl)-2-phenoxyethanol-1 (III, X = OC_6H_5) can be cyclized to 9-methylphenanthrene in 10% yield by the action of aluminum chloride. This constitutes a new type of Friedel and Crafts reaction.

Experimental

Phenoxyacetone.[8]—This ketone was prepared by a modification of the general procedure of Bradsher and

(1) For the preceding paper of this series see THIS JOURNAL, **61**, 1524 (1939).

(2) Du Pont Post-doctorate Fellow, 1938.

(3) Present address: Duke University, Durham, N. C.

(4) Bradsher and Schneider, THIS JOURNAL, **60**, 2960 (1938); also in unpublished work from this Laboratory.

(5) Windaus, *Ann.*, **439**, 59 (1924).

(6) Haworth and Mavin, *J. Chem. Soc.*, 2720 (1932).

(7) Bachmann, THIS JOURNAL, **56**, 1363 (1934).

(8) Previously prepared in unstated yields by the addition of sodium to a phenol solution of chloroacetone, Stoermer, *Ber.*, **28**, 1253 (1895). Since the completion of this problem, a more satisfactory method has been reported using bromoacetone, Calaway and Henze, THIS JOURNAL, **61**, 1355 (1939).

Rosher[1] for the preparation of α-phenoxy ketones. Phenol (51.7 g.), anhydrous potassium carbonate (76 g.) and acetone (300 cc.) were placed in a 3-necked flask and mechanically stirred while a solution of chloroacetone (46.8 g.) in acetone (50 cc.) was added slowly over the period of a half hour. Sufficient heat was evolved to cause refluxing of the acetone. Stirring was continued for twenty-four hours. The inorganic salts were then filtered off, the solution concentrated, poured into water and extracted with ether. The ethereal solution was washed with dilute alkali, dried, concentrated and the residue distilled under reduced pressure. The product was a nearly colorless liquid, b. p. 117–124° (19 mm.); yield 17.7 g. (23%). If the mixture is refluxed for three hours instead of being stirred at room temperature for twenty-four hours, the yield is 21%.

1-Methyl-1-(2-biphenyl)-2-phenoxyethanol-1 (III, X = OC_6H_5).—A Grignard reagent was prepared from 20 g. of 2-iodobiphenyl. To this was added a solution of 10 g. of phenoxyacetone in dry ether. After refluxing for forty-five minutes, the mixture was decomposed with a 20% solution of ammonium chloride. Upon concentration of the ethereal extract, the carbinol was obtained as a brown oil. This was not purified further.

Cyclization of 1-Methyl-1-(2-biphenyl)-2-phenoxyethanol-1.—The crude carbinol obtained above was dissolved in 110 cc. of acetic acid, and 60 cc. of 40% hydrobromic acid added. The mixture was refluxed for twenty-four hours. It was then neutralized, steam-distilled from some tarry material and the product collected by filtration. Once recrystallized from methanol, this product gave 3.1 g. (32%) of **9-methylphenanthrene** as white needles, m. p. 91–92.5°. An analytical sample obtained by repeated crystallization melted at 91.5–92.5°.

Anal. Calcd. for $C_{15}H_{12}$: C, 93.69; H, 6.31. Found: C, 93.68; H, 6.31.

The picrate, recrystallized from alcohol, was obtained as fine orange needles, m. p. 153–154°.

1-Methyl-1-(2-biphenyl)-2-methoxyethanol-1 (III, X = OCH_3).—A Grignard reagent was prepared from 2.8 g. of methyl iodide and an ether solution of 2.1 g. of 2-(ω-methoxy)-acetobiphenyl[4] was added. The mixture was decomposed with ammonium chloride solution, and the crude carbinol obtained by evaporation of the ethereal solution.

Cyclization of 1-Methyl-1-(2-biphenyl)-2-methoxyethanol-1.—The crude carbinol obtained above was refluxed for twenty-four hours with a mixture of 20 cc. of acetic acid and 10 cc. of 40% hydrobromic acid. There was little evidence of tar formation, and upon cooling the 9-methylphenanthrene crystallized from the solution. Twice crystallized from methanol, the hydrocarbon was obtained in a yield of 1.78 g. (50%); m. p. 88–91°.

1-(2-Naphthoxy)-acetone[9] was prepared by refluxing a mixture of 46.8 g. of chloroacetone, 79.2 g. of β-naphthol, and 76 g. of anhydrous potassium carbonate in 500 cc. of acetone. The product was worked up as in the case of phenoxyacetone except that the crude material was purified by crystallization from methanol rather than by distillation. Twice crystallized, the product was obtained as small irregular white crystals, m. p. 69–72°; yield 21 g. (21%).

(9) This ketone has been prepared previously in unstated yields by Stoermer, *Ann.*, **312**, 237 (1900).

1-Methyl-1-(2-biphenyl)-2-(2-naphthoxy)-ethanol-1 (III, X = $OC_{10}H_7(\beta)$).—A Grignard reagent was prepared from 15.4 g. of 2-iodobiphenyl and to it was added a solution of 10 g. of 1-(2-naphthoxy)-acetone in 50 cc. of dry benzene. The crude carbinol was isolated as in the case of the corresponding phenoxy carbinol (III, X = OC_6H_5).

Cyclization of 1-Methyl-1-(2-biphenyl)-2-(2-naphthoxy)-ethanol-1.—The crude carbinol was cyclized by refluxing for sixteen hours in a mixture containing 50 cc. of acetic acid and 50 cc. of 34% hydrobromic acid. The product was worked up as in the cyclization of the phenoxy carbinol (III, X = OC_6H_5). The yield was 2.24 g. (32%); m. p. 91–92°.

1-Methyl-1-(2-biphenyl)-2-diethylaminoethanol-1 (III, X = $N(C_2H_5)_2$).—A Grignard reagent was prepared from 28 g. of 2-iodobiphenyl and 12.9 g. of diethylaminoacetone[10] added in ether solution. The mixture was refluxed for thirty minutes and then decomposed with ammonium chloride solution. The crude carbinol was obtained in ether solution.

Cyclization of 1-Methyl-1-(2-biphenyl)-2-diethylaminoethanol-1.—The ether solution obtained above was extracted with 2 *N* hydrochloric acid and the acid extract concentrated to a small volume under reduced pressure. To the residue was added 125 cc. of 34% hydrobromic acid and the mixture refluxed for forty-eight hours. The solution was extracted with ether, the ether evaporated and the residue crystallized from methyl alcohol; yield 2.0 g. (10%), m. p. 92–93°.

1-Methyl-1-(2-biphenyl)-2-chloroethanol-1 (III, X = Cl) was prepared in a manner analogous to that employed in the synthesis of the corresponding phenoxyethanol (III, X = OC_6H_5). A Grignard reagent was prepared from 19.9 g. of 2-iodobiphenyl and treated with 6.55 g. of chloroacetone. The crude carbinol, obtained as in the preceding cases, was a viscous brown liquid.

Cyclization of 1-Methyl-1-(2-biphenyl)-2-chloroethanol-1.—The crude carbinol obtained above was cyclized as in the case of the corresponding phenoxyethanol. The resinous product, after vacuum distillation, yielded a few crystals of 9-methylphenanthrene, m. p. 90–92°. Attempts to cyclize the carbinol with 85% sulfuric acid or aluminum chloride were unsuccessful.

Cyclization of 1-Methyl-1-(2-biphenyl)-2-phenoxyethanol-1 by the Action of Aluminum Chloride.—The crude carbinol, obtained from 10 g. of phenoxyacetone by the method previously described, was dissolved in 240 cc. of carbon bisulfide and 10 g. of aluminum chloride added. The reaction was allowed to proceed overnight. The mixture was treated in the usual way and the 9-methylphenanthrene isolated as the picrate, yield 2.8 g. (10%).

Summary

The new type of ring closure has been extended to the synthesis of 9-methylphenanthrene. Several variations of the ring closure have been studied.

DURHAM, N. C. RECEIVED JUNE 19, 1939

(10) Stoermer and Dzimski, *Ber.*, **28B**, 2220 (1895).

[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY, UNIVERSITY OF VIRGINIA, AND THE NATIONAL INSTITUTE OF HEALTH]

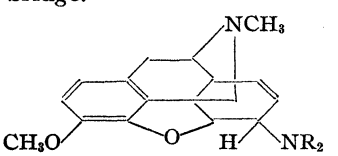
The Aminomorphides and Aminocodides[1]

BY LYNDON SMALL AND FRED S. PALMER[2]

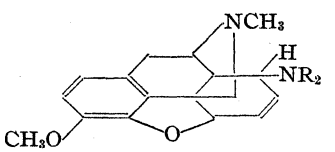
The investigation of compounds derived from the morphine series and carrying basic groups in ring III was begun in the Virginia Laboratory in 1934, with the object of determining the effect of such basic radicals upon physiological action. As early as 1903, Vongerichten and Müller[3] found that α-chlorocodide entered into reaction with piperidine to yield a dibasic compound in which the piperidino group was assumed to have taken the place of the chlorine atom of α-chlorocodide. Some years later, Wieland and Kappelmeier[4] carried out the parallel reaction between α-chloromorphide and diethylamine (diethylaminomorphide), as did von Braun and Kindler[5] with α-chlorocodide and dimethylamine and diethylamine.

As is now well known, replacement of the halogen atom in the halogenomorphides or halogenocodides by other groups may involve both configurational and positional changes, as exemplified in the hydrolysis of these halogeno compounds to α-, β- and γ-isomorphines, or to the corresponding codeine isomers. Before significant conclusions concerning structure and physiological action can be drawn, it is therefore necessary to scrutinize the structural evidence for any derivative originating from replacement of a halogen atom (or perhaps other groups) in ring III of the morphine series.

There exist, to our knowledge, no distinctive physical or chemical criteria that may be applied to the determination of the configuration of groups at C-6 or C-8 relative to any arbitrarily chosen standard. We have, in the past, classified certain derivatives as having the codeine or isocodeine, the pseudocodeine or allopseudocodeine configuration, on the basis of similarities in pharmacological action,[6] with full realization, however, of the limitations and weaknesses of such deductions. In respect to positional differences, between the unsaturated 6- and 8-substituted types, we possess, in catalytic hydrogenation, a determinative method that has been in agreement with so many compounds of proved structure that it probably may be considered reliable as far as the morphine series is concerned. Namely, for all those derivatives having the substituent (or hydrogen) in the 8-position, and a double bond at the 6,7-position, the usual course taken by hydrogenation results in opening the oxygen bridge simultaneously with, or before, saturation of the double bond. The derivatives with the 6-substituent (halogen excepted) and the 7,8-double bond undergo hydrogenation normally, without involving the oxygen bridge.



6-Aminocodides



8-Aminocodides

As would be expected from observations already reported in the thiocodide and other series, two of the examples cited, reactions of α-chlorocodide with piperidine and of α-chloromorphide with diethylamine, result, respectively, in 8-piperidocodide and 8-diethylaminomorphide. There can be little doubt that the dimethylaminocodide of von Braun and Kindler also carries the new basic group in the 8-position. The reaction product from α-chlorocodide and piperidine, 8-piperidocodide, under the ordinary conditions of hydrogenation, takes up two moles of hydrogen, to give the tetrahydro derivative, in which not only has the alicyclic double bond been saturated, but the

(1) The work reported in this paper is part of a unification of effort by a number of agencies having responsibility for the solution of the problem of drug addiction. The organizations taking part are: The Rockefeller Foundation, the National Research Council, the U. S. Public Health Service, the U. S. Bureau of Narcotics, the University of Virginia and the University of Michigan. Publication authorized by the Surgeon General, U. S. Public Health Service.

(2) Mallinckrodt Fellow in Alkaloid Chemistry 1934–1935. Present address Jackson Laboratory, E. I. du Pont de Nemours and Co., Wilmington, Del.

(3) Vongerichten and Müller, *Ber.*, **36**, 1590 (1903).

(4) Wieland and Kappelmeier, *Ann.*, **382**, 306 (1911).

(5) Von Braun and Kindler, *Ber.*, **49**, 2655 (1916).

(6) "Studies on Drug Addiction," Supplement No. 138 to the Public Health Reports, Washington, 1938, p. 15. Lutz and Small, "Reduction Studies in the Morphine Series," IX, *J. Org. Chem.*, in press.

cyclic ether group been opened reductively as well. As with other examples of 6,7-unsaturated morphine types,[7] 8-piperidocodide, under special hydrogenation conditions, can be converted in part to the non-phenolic "normal" dihydro derivative. The latter, no longer possessing the pseudocodeine type of unsaturated system, is indifferent toward further reduction.

By the reaction of α-chloromorphide with piperidine, the analogous 8-piperidomorphide is obtained, whose relationship to the known 8-piperidocodide can be shown by methylation. 8-Piperidomorphide, like its methyl ether, absorbs two moles of hydrogen readily, to yield the corresponding diphenolic tetrahydro derivative. Although reduction of the hydrochloride in glacial acetic acid resulted in diminished hydrogen absorption, the desired dihydro derivative was not isolated in pure form.

We have verified the Wieland and Kappelmeier reaction of diethylamine with α-chloromorphide, to form a diethylaminomorphide, but because of the more favorable solubility of the codides, and their greater stability toward oxidation, turned our attention to the 8-diethylaminocodide of von Braun and Kindler. As a pseudocodeine type, this undergoes reduction with additon of two moles of hydrogen, to give tetrahydro-8-diethylaminocodide, so that the 8-position for the basic group seems assured.

α-Chlorocodide also reacts with liquid ammonia at about 50°, with substitution of an amino group at the 8-position and loss of the 6-halogen atom. 8-Aminocodide, as a primary amine, undergoes acetylation readily with cold acetic anhydride to yield 8-diacetylaminocodide. 8-Aminocodide behaves in a typical way toward catalytic reduction. As hydrochloride, in glacial acetic acid, it can be reduced to a non-phenolic dihydro derivative. As base, in alcohol, on the other hand, it takes up two moles of hydrogen, giving the phenolic tetrahydro-8-aminocodide.

All of the products that we have examined derived from amination of α-chloromorphide or α-chlorocodide, appear to have resulted from an α,γ-shift, and carry the basic group in the 8-position. The halogeno compounds of the morphine series that are generally believed to carry the halogen atom at the 8-position, namely, bromocodide and bromomorphide, and β-chlorocodide and β-chloromorphide, seem to react with amino compounds with the reverse α,γ-shift, to yield the 6-amino derivatives. Bromomorphide and piperidine, at 100°, give 6-piperidomorphide. We believe the assignment of the 6-position to the substituent to be justified from the fact that the compound cannot be induced to take up more than one mole of hydrogen, and yields only a dihydro derivative. 6-Piperidomorphide undergoes methylation to give 6-piperidocodide, a compound that also results from the action of piperidine with either bromocodide or β-chlorocodide. 6-Piperidocodide likewise is saturated by addition of one mole of hydrogen, although the reduction product was so difficult to purify that analytical data cannot be advanced.

The identity of the amination products from bromocodide and β-chlorocodide lends additional support to the conception that both of these compounds carry the halogen atom in the 8-position. It is remarkable that while the reactions of the α-halogeno types, and of β-chlorocodide and bromocodide, with piperidine seemed to proceed with equal facility, bromocodide was regained quite unchanged from attempted reaction with liquid ammonia. 6-Aminocodide will perhaps be obtained when facilities for working at higher temperatures and pressures are available. The failure with bromocodide is the more unexpected in view of the fact that the bromo base seems to enter into replacement reactions with hydriodic acid and with mercaptans as readily as does α-chlorocodide, in contrast to the inactive β-chloro series.

The aminocodides and aminomorphides are outstanding exceptions to the general rule that replacement of the alcoholic hydroxyl of the morphine types by other groups leads to increased physiological activity. Introduction of the basic group usually reduced toxicity, and greatly decreased analgesic action.[8] We have observed that the substitution of a basic group in the aromatic ring of morphine (2-aminomorphine[4,9]) also results in a great diminution of physiological action. The intramolecular acidic and basic relationship in the morphine types appears to be intimately associated with biological effect.

Experimental

8-Diethylaminomorphide.—This base was prepared essentially according to the procedure of Wieland and Kap-

(7) Small and co-workers, THIS JOURNAL, **54**, 4715 (1932); **56**, 2466 (1934); **57**, 364 (1935); **56**, 1928 (1934); **57**, 361 (1935); *J. Org. Chem.*, **1**, 194 (1936); THIS JOURNAL, **57**, 2651 (1935); **55**, 2874 (1933).

(8) "Studies on Drug Addiction," pp. 21, 24.

(9) Ochiai and Nakamura, *Ber.*, **72**, 684 (1939).

pelmeier. After three sublimations in a high vacuum, it had the melting point 201–204° (evac. tube) and $(\alpha)^{21}D$ +49.1° (methanol, *c*, 0.87) (W. and K. observed the melting point 203°).

Anal. Calcd. for $C_{21}H_{28}N_2O_2$: N, 8.2. Found: N, 8.1.

On treatment with diazomethane it yielded 8-diethylaminocodide. 8-Diethylaminomorphide dihydriodide was prepared in the usual way and purified from water; m. p. 87–93° (evac. tube), $(\alpha)^{25}D$ +2.6° (water, *c*, 0.38). The salt appears to be a sesquihydrate.

Anal. Calcd. for $C_{21}H_{30}I_2N_2O_2 + 1.5H_2O$: I, 40.8; H_2O, 4.3. Found: I, 41.1; H_2O, 4.6.

The diperchlorate was crystallized from water, m. p. 114–116° (evac. tube), $(\alpha)^{19}D$ +4.4° (water, *c*, 0.91).

Anal. Calcd. for $C_{21}H_{30}Cl_2N_2O_{10}$: Cl, 13.1. Found: Cl, 13.5.

8-Piperidomorphide.—Ten grams of α-chloromorphide with 10 g. of piperidine was heated in an evacuated sealed tube at 100° for thirty minutes. The product was dissolved in 3 *N* hydrochloric acid, precipitated with excess of sodium carbonate and the precipitate extracted into ether. The yield of crystalline product was 9.2 g. It was purified from alcohol and sublimed in a high vacuum at 200°; m. p. 222–224° (evac. tube), $(\alpha)^{24}D$ +28.7° (methanol, *c*, 1.15).

Anal. Calcd. for $C_{22}H_{28}N_2O_2$: C, 74.9; H, 8.0; N, 7.9. Found: C, 74.9; H, 7.8; N, 8.2.

The dihydriodide was prepared in 10% acetic acid with potassium iodide, redissolved in dilute acetic acid and again precipitated with potassium iodide. It was purified from water and had $(\alpha)^{23}D$ +14.9° (water, *c*, 0.37), m. p. 208–214° (evac. tube).

Anal. Calcd. for $C_{22}H_{30}I_2N_2O_2$: I, 41.7. Found: I, 42.3.

The monomethiodide was prepared in methanol solution, and purified from water; m. p. 243–245° (evac. tube), $(\alpha)^{23}D$ +23.7° (50 vol. % alcohol, *c*, 1.14).

Anal. Calcd. for $C_{23}H_{31}IN_2O_2$: I, 26.4. Found: I, 25.8.

Tetrahydro-8-piperidomorphide.—Two grams of 8-piperidomorphide in 30 cc. of 5% acetic acid with 50 mg. of platinum oxide absorbed two moles of hydrogen rapidly. The new base was isolated with sodium carbonate and ether and was sublimed three times in a high vacuum. It had the m. p. 270–280° (evac. tube, dec.) and $(\alpha)^{26}D$ +45.1° (10% acetic acid, *c*, 0.63). The ferric chloride test was moss-green. No crystalline salts could be obtained.

Anal. Calcd. for $C_{22}H_{32}N_2O_2$: C, 74.1; H, 9.0; N, 7.9. Found: C, 73.8; H, 8.9; N, 8.1.

Acetylation with acetic anhydride resulted in a base of m. p. 172–178°.

8-Diethylaminocodide.—This compound, prepared according to von Braun and Kindler and sublimed three times in a high vacuum, had the m. p. 101–103° (von B. and K., 102°) and $(\alpha)^{23}D$ +42.6° (methanol, *c*, 1.0). The same compound was obtained from the methylation of the 8-diethylaminomorphide described above.

The diperchlorate was prepared in dilute perchloric acid in the presence of a little alcohol, and purified from water or alcohol; $(\alpha)^{19}D$ +3.3° (water, *c*, 0.92), m. p. 180.5–183°.

Anal. Calcd. for $C_{22}H_{32}Cl_2N_2O_{10}$: Cl, 12.8. Found: Cl, 12.7.

The dihydriodide was prepared in the usual way and recrystallized from water or alcohol to constant rotation, $(\alpha)^{26}D$ +22.9° (absolute alcohol, *c*, 0.39); m. p. 179–182°.

Anal. Calcd. for $C_{22}H_{32}I_2N_2O_2$: I, 41.6. Found: 1, 41.0, 42.3.

Tetrahydro-8-diethylaminocodide.—Two grams of 8-diethylaminocodide in 50 cc. of ethanol with 80 mg. of platinum oxide absorbed two moles of hydrogen in five hours. The residue from evaporation of the alcohol was washed with a little cold ether. This material melted at 116–119° with gas evolution and was probably hydrated. It was sublimed four times in a high vacuum at 130°; m. p. 154–157°, rotation constant at $(\alpha)^{25}D$ +31.5° (methanol, *c*, 0.75).

Anal. Calcd. for $C_{22}H_{34}N_2O_2$: C, 73.7; H, 9.6. Found: C, 73.6; H, 9.5.

The monoperchlorate was prepared in dilute perchloric acid and crystallized by cooling the solution after addition of a drop of alcohol. It was purified from water, $(\alpha)^{26}D$ +18.3° (water, *c*, 0.30); m. p. 234–238° (evac. tube).

Anal. Calcd. for $C_{22}H_{35}ClN_2O_6$: Cl, 7.7. Found: Cl, 8.0.

8-Piperidocodide.—This base, prepared according to Vongerichten and Müller, was purified from methanol and had the m. p. 116–117° (V. and M. observed m. p. 118°). After four sublimations in a high vacuum, the rotation was constant, $(\alpha)^{22}D$ +25.8° (methanol, *c*, 0.89). The same base was obtained by methylation of 8-piperidomorphide with diazomethane.

Anal. Calcd. for $C_{23}H_{30}N_2O_2$: N, 7.7. Found: N, 7.7.

The di-acid sulfate dihydrate was prepared by dissolving the base in 10% sulfuric acid, from which the salt crystallized immediately. It was crystallized twice from 10% sulfuric acid and twice from alcohol, $(\alpha)^{26}D$ +19.8° (water, *c*, 1.46); m. p. 161–163.5° (evac. tube).

Anal. Calcd. for $C_{23}H_{38}N_2O_2S_2 = C_{23}H_{30}O_2N_2 \cdot 2H_2SO_4 \cdot 2H_2O$: SO_4, 32.1; H_2O, 6.0. Found: SO_4, 32.5; H_2O, 5.4.

The monohydriodide was prepared in the usual way and purified from water. It has $(\alpha)^{24}D$ +13.3° (water, *c*, 0.337); m. p. 234–237° (corr., evac. tube).

Anal. Calcd. for $C_{23}H_{31}IN_2O_2$: I, 25.7. Found: I, 27.3.

A homogeneous salt is very difficult to obtain. Other preparations consisted mostly of the dihydriodide (Calcd.: I, 40.8. Found: I, 38.4, 38.6).

For the monomethiodide of V. and M. we observed the value $(\alpha)^{25}D$ +22.0° (water, *c*, 0.86).

The diperchlorate, purified from water, has the m. p. 181–183° and $(\alpha)^{23}D$ +13.2° (50 vol. % alcohol, *c*, 1.02).

Anal. Calcd. for $C_{23}H_{32}Cl_2N_2O_{10}$: Cl, 12.5. Found: Cl, 12.3.

Tetrahydro-8-piperidocodide.—A solution of 2 g. of 8-piperidocodide in 60 cc. of ethanol with 50 mg. of platinum oxide absorbed 2 moles of hydrogen rapidly. The residue from evaporation of the alcohol was washed with

a little cold ether, and the crystals sublimed twice in a high vacuum; m. p. unsharp at about 125°, rotation constant at $(\alpha)^{25}D$ +36.7° (methanol, *c*, 1.07); ferric chloride test, deep emerald-green.

Anal. Calcd. for $C_{23}H_{34}N_2O_2$: C, 74.5; H, 9.3; N, 7.6. Found: C, 74.7; H, 9.1; N, 7.5.

Dihydro-8-piperidocodide.—Three grams of the amorphous powdery hydrochloride, obtained by treating an ethereal solution of 8-piperidocodide with ethereal hydrogen chloride, was dissolved in 50 cc. of glacial acetic acid and hydrogenated in the presence of 150 mg. of platinum oxide. The absorption of hydrogen stopped at 1.6 moles. The filtered solution was diluted with an equal volume of water, made alkaline with ammonia, and the precipitate extracted into ether. The crystalline residue from evaporation of the ether was recrystallized from alcohol, yield 0.95 g., m. p. 164–167°. Two crystallizations from alcohol and two sublimations in a high vacuum yielded a product of melting point 167–169°, $(\alpha)^{23}D$ −1.2° (methanol, *c* 1.68). The ferric chloride test was negative.

Anal. Calcd. for $C_{23}H_{32}N_2O_2$: C, 74.9; H, 8.8; N, 7.6. Found: C, 75.0; H, 9.1; N, 8.0.

From the alcohol mother liquors, 0.46 g. of pure tetrahydro-8-piperidocodide could be isolated.

8-Aminocodide.—Ten grams of α-chlorocodide in 180 g. of liquid ammonia was held at 50° for twenty-four hours. After excess ammonia had evaporated, the residue was dissolved in dilute hydrochloric acid, and the base was precipitated with sodium hydroxide and brought into ether. The amorphous product was dissolved in warm alcohol and the crystalline base precipitated by slow addition of ether. It was converted to the hydrochloride with alcoholic hydrogen chloride, yield 11 g.[10] A solution of the hydrochloride was treated with alkali and extracted rapidly with a large volume of ether. The ether solution quickly deposited star-shaped crystalline aggregates of the base. It was recrystallized from ether and sublimed in a high vacuum at 130°. It has the melting point 128.5–129°, $(\alpha)^{21}D$ −79.2° (alcohol, *c*, 0.48).

Anal. Calcd. for $C_{18}H_{22}N_2O_2$: C, 72.4; H, 7.4; N, 9.4. Found: C, 72.3; H, 7.4; N, 9.8.

The dihydrochloride, purified from 95% alcohol, has the melting point 300–305° (corr., evac. tube) and $(\alpha)^{24}D$ −40.7° (water, *c*, 0.88).

Anal. Calcd. for $C_{18}H_{24}Cl_2N_2O_2 + H_2O$: Cl, 18.2; H_2O, 4.6. Found: Cl, 18.2; H_2O, 3.6.

8-Diacetylaminocodide was prepared by allowing 0.5 g. of 8-aminocodide in 5 cc. of acetic anhydride to react for eighteen hours at room temperature. Neutralization with sodium carbonate yielded 0.6 g. of crystalline base, which was purified from ethyl acetate. It crystallizes with a molecule of ethyl acetate, which could not be determined directly because of the tendency of the base to sublime; the m. p. is 218–220° (decomp.); in an evacuated tube, 165–175°, solidifying and remelting at 205°; $(\alpha)^{24}D$ −83.1° (alcohol, *c*, 1.04).

Anal. Calcd. for $C_{26}H_{34}N_2O_6$: C, 66.4; H, 7.3. Found: C, 66.5, 66.4; H, 7.0, 7.1.

(10) We are indebted to Dr. B. F. Faris, Experimental Station of E. I. du Pont de Nemours and Co., for this preparation.

Tetrahydro-8-aminocodide.—A solution of 8-aminocodide in methanol, with platinum oxide, absorbed two moles of hydrogen in fifteen minutes. The base could not be obtained crystalline from solvents, but sublimed onto a cold finger in a high vacuum at 130° in large white crystals; m. p. 138.5–140°, $(\alpha)^{24}D$ −9.7° (alcohol, *c*, 1.13). It is soluble in alkali; ferric chloride test, intense blue-green.

Anal. Calcd. for $C_{18}H_{26}N_2O_2$: C, 71.5; H, 8.7. Found: C, 71.7; H, 8.6.

The dihydrochloride was prepared with alcoholic hydrogen chloride and purified from absolute alcohol; $(\alpha)^{24}D$ +6.6° (water, *c*, 0.91).

Anal. Calcd. for $C_{18}H_{28}Cl_2N_2O_2$: Cl, 18.9. Found: Cl, 18.2.

Dihydro-8-aminocodide.—A suspension of 2.3 g. of 8-aminocodide dihydrochloride in 20 cc. of glacial acetic acid with 50 mg. of platinum oxide absorbed about 1.7 moles of hydrogen in thirty minutes. The product was precipitated with excess dilute sodium hydroxide, brought into ether, and the ethereal solution was extracted several times with dilute alkali. The dihydro compound could not be obtained crystalline, and was distilled twice in a high vacuum at 170°. It consisted of a colorless, glassy solid having $(\alpha)^{21}D$ −28.7° (alcohol, *c*, 1.08). The base is so soluble in water (like 8-aminocodide itself) that the absence of a phenolic group cannot be demonstrated with alkali. It gives a faint green ferric chloride test, and may contain a little of the tetrahydro derivative.

Anal. Calcd. for $C_{18}H_{24}N_2O_2$: C, 71.9; H, 8.0. Found: C, 71.7; H, 8.0.

The dihydrochloride, prepared with alcoholic hydrogen chloride and purified from a mixture of 1 part of absolute alcohol with 2 parts of 95% alcohol, has the m. p. 274–277° (evac. tube) and $(\alpha)^{24}D$ −14.7° (water, *c*, 1.08).

Anal. Calcd. for $C_{18}H_{26}Cl_2N_2O_2 + H_2O$: Cl, 18.1; H_2O, 4.6. Found: Cl, 17.8; H_2O, 4.6.

6-Piperidomorphide.—A mixture of 20 g. of bromomorphide and 20 g. of piperidine in a sealed evacuated tube was heated for thirty minutes in the boiling water-bath. The product was dissolved in 3 *N* hydrochloric acid, from which the base was precipitated with sodium carbonate and extracted into ether. The crystalline residue from the ether had the melting point 213–215°, yield 14.6 g. It was crystallized from ethyl acetate and sublimed four times in a high vacuum at 200°; m. p. 216–217° (evac. tube), $(\alpha)^{23}D$ −234.8° (methanol, *c*, 0.871). No other crystalline product could be isolated from the reaction.

Anal. Calcd. for $C_{22}H_{28}N_2O_2$: C, 74.9; H, 8.0; N, 7.9. Found: C, 75.2; H, 8.0; N, 8.2.

By methylation with diazomethane, 6-piperidomorphide was converted to 6-piperidocodide.

The methiodide was prepared in methanol, and separated crystalline when absolute ether was added cautiously. It crystallized as long needles from water; m. p. 236–241° (corr., evac. tube), $(\alpha)^{23}D$ −145.8° (50 vol. % alcohol, *c*, 1.05).

Anal. Calcd. for $C_{21}H_{31}IN_2O_2$: C, 53.6; H, 6.6. Found: C, 54.8, 54.3; H, 6.3, 6.2.

Dihydro-6-piperidomorphide.—A solution of 5 g. of 6-piperidomorphide in 80 cc. of ethanol with 0.2 g. of plat-

inum oxide absorbed 1 mole of hydrogen in twenty-two hours. After removal of the alcohol under diminished pressure, the oily residue was crystallized by addition of ether; yield 3.6 g., m. p. 203–210°. After four crystallizations from ethyl acetate it had the m. p. 215–217° and $(\alpha)^{24}D$ −155.9° (methanol, *c*, 0.76).

Anal. Calcd. for $C_{22}H_{36}N_2O_2$: C, 74.6; H, 8.5; N, 7.9. Found: C, 74.2; H, 8.8; N, 7.8.

6-Piperidocodide.—A mixture of 10 g. of bromocodide and 10 g. of piperidine in an evacuated sealed tube was heated in the boiling water-bath for forty-five minutes. The product was dissolved in acid, precipitated with sodium carbonate, and extracted into ether. The residue from the ether was again put through this procedure to remove piperidine. The oily product (10 g.) was treated with 6 cc. of 60% perchloric acid and diluted with 75 cc. of water, warming into solution. When the solution cooled, oily material began to separate, and was brought just into solution with alcohol. After twelve hours, the solution had deposited 6.5 g. of crystalline diperchlorate, which was purified from water to constant rotation $(\alpha)^{23}D$ −113.4° (water, *c*, 0.44); m. p. 172–175°.

Anal. Calcd. for $C_{23}H_{52}Cl_2N_2O_{10}$: Cl, 12.5. Found: Cl, 12.1.

The perchlorate was converted to the base, extracted with ether, and the residue from the ether was washed with cold 30–60° ligroin. The base was sublimed four times in a high vacuum at 130° (to constant rotation); melting point, 75–80°, $(\alpha)^{25}D$ −233.9° (methanol, *c*, 0.87).

Anal. Calcd. for $C_{23}H_{30}N_2O_2$: C, 75.4; H, 8.2; N, 7.6. Found: C, 75.1; H, 8.2; N, 7.6.

The same base and perchlorate were obtained by treatment of 6-piperidomorphide with diazomethane, likewise by heating β-chlorocodide with piperidine for six hours at 130°. Hydrogenation of 6-piperidocodide resulted in absorption of 1 mole of hydrogen, but the product was a viscous liquid from which no crystalline derivatives could be prepared. A similar substance was obtained when dihydro-6-piperidomorphide was methylated with diazomethane.

Treatment of 50 g. of bromocodide with liquid ammonia at 50° for twenty-four hours resulted in recovery of 40 g. of unchanged material. No halogen-free product could be isolated.

Summary

The reaction of α-chloromorphide and α-chlorocodide with secondary amines or ammonia proceeds with a rearrangement such that the new basic groups appear at the 8-position. The morphine derivatives that are believed to have the halogen atom in the 8-position, as bromomorphide, bromocodide, and β-chlorocodide, react with a rearrangement in the reverse sense, to give 6-aminomorphide and 6-aminocodide derivatives. The introduction of basic groups into the morphine or codeine molecule results in a considerable diminution of physiological action, especially analgesic effect.

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[CONTRIBUTION FROM THE DIVISION OF INDUSTRIAL AND CELLULOSE CHEMISTRY, MCGILL UNIVERSITY]

Studies on Lignin and Related Compounds. XLI. The Detection, Isolation and Estimation of the Syringyl Radical in Plant Products[1]

BY M. J. HUNTER AND HAROLD HIBBERT

The syringyl group was first identified in natural products as a unit in the glucoside, syringin,[2] and later in the anthocyanidin, malvin chloride.[3] Although its presence in hard wood lignin occasionally had been inferred from indirect evidence of various kinds,[4] the first isolation of syringyl components from this source was accomplished in these Laboratories.[5] More recently, it was shown that the ethanolysis of hard woods gave much higher yields[6a] than previous methods, and α-ethoxypropiovanillone and α-ethoxypropiosyringone were successfully isolated in almost equal amounts.[6b] The far-reaching implications which the corresponding hydroxy compounds (I) and (II) have for the theory of lignin structure have already been discussed exhaustively,[6,7] and it will suffice to emphasize our view that hard wood lignin is a condensation product of the unit structures (I) and (II) in equal

(1) From a thesis submitted to the Faculty of Graduate Studies and Research, McGill University, by Melvin J. Hunter in partial fulfilment of the requirements for the Degree of Doctor of Philosophy, May, 1939.

(2) Vintilesco, *J. pharm. chim.*, [6] **24**, 529 (1906).

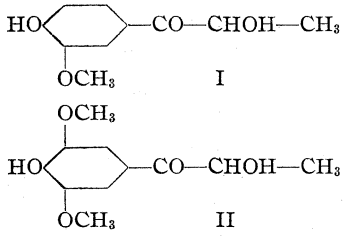
(3) (a) Karrer, *Helv. Chim. Acta*, **10**, 67, 79 (1927); **12**, 292 (1929); **15**, 507 (1932); (b) Robinson, *J. Chem. Soc.*, 25, 1687 (1931); 1647 (1932); 206 (1933).

(4) (a) Wacek, *Ber.*, **63**, 282, 2984 (1930); *Oesterr. Chemiker-Zeitung*, **36**, 84 (1933); (b) Freudenberg, Zocher and Dürr, *Ber.*, **62**, 1821 (1929); (c) Schorger, "The Chemistry of Cellulose and Wood," McGraw-Hill, London, 1926, p. 111; (d) Brauns and Hibbert, *Can. J. Research*, **13**, 28 (1935); (e) Freudenberg, Knopf and Haag, *Ber.*, **69**, 1415 (1936).

(5) (a) Hawkins, Wright and Hibbert, THIS JOURNAL, **59**, 2447 (1937); (b) Leger and Hibbert, *Can. J. Research*, **B16**, 151 (1938); THIS JOURNAL, **60**, 565 (1938); (c) Brickman, Pyle, McCarthy and Hibbert, *ibid.*, **61**, 868 (1939).

(6) (a) Cramer, Hunter and Hibbert, *ibid.*, **61**, 509 (1939); (b) Hunter, Cramer and Hibbert, *ibid.*, **61**, 516 (1939).

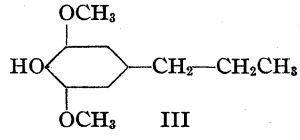
(7) Hibbert, *ibid.*, **61**, 725 (1939).



amounts, while in soft wood lignin the syringyl nucleus is lacking. Unpublished results[8] indicate that both the extracted lignins and the individual units give C_6–C–C–C derivatives, in practically quantitative yield, on hydrogenation at high pressure. The methoxyl content of spruce lignin, 15–17%, is in accord with that of α-hydroxypropiovanillone (I), 15.8%. An equimolecular mixture of (I) and (II) has a calculated value of 21.6%, in comparison with an observed methoxyl content of 20–21.5% for maple and other hard wood lignins.[4a,9] Ethanol lignin from maple wood[6b] contains 27–28% alkoxyl calculated as methoxyl. Of this, 10% is ethoxyl, equivalent to one ethoxyl group per molecular weight of 450 and identical with that of an equimolecular mixture of the ethoxy derivatives from (I) and (II). As a result of improvements in the separation of syringyl from guaiacyl derivatives, we are now able to show that 53% of the phenol fraction from ethanol maple lignin consists of α-ethoxypropiosyringone. All these observations support our view as to the nature of hard wood lignins. On the other hand, the presence of the very small amounts (a fraction of 1%) of syringyl derivatives reported in a soft wood lignin[10] (spruce) could not be confirmed, due possibly to the fact that less than 3–5% of syringyl in presence of 95–97% of guaiacyl derivatives cannot be detected by our method.

Separation of Syringyl and Guaiacyl Derivatives.—The recent discovery[6b] of the presence of both of these type substances in hard woods has necessitated the development of practical methods for their isolation and quantitative separation. In this communication[6b] a separation of syringyl from guaiacyl derivatives by formation of their *p*-nitrobenzoates was given, and, while this procedure served for the characterization of the former, the method was unsuitable, quantitatively, and the original compounds were difficult to reclaim. The following new method does away with these disadvantages. It rests on the discovery that addition of an anhydrous ethanol solution of potassium acetate to an ethanol solution of a mixture of guaiacyl and syringyl derivatives brings about precipitation of the latter in the form of a crystalline potassium salt, usually in high yield; the potassium salt of the guaiacyl-containing product is more soluble and remains in solution. The efficiency of the method when applied to a number of different syringyl compounds is shown in Table I.

The fact that 3,5-dimethoxy-4-hydroxyphenylpropane-1 (III) is not precipitated by potassium



acetate would seem to indicate that precipitability with this reagent apparently is limited to syringyl compounds having a carbonyl group in the para position. This is in harmony with the evidence presented by Lock,[11] indicating a direct relationship between the 1,4-hydroxycarbonyl groups in the benzene nucleus. The much lower value obtained with α-acetoxypropiosyringone (Table I, no. 5) is possibly the result of an intramolecular effect exerted between the acetate and the carbonyl groups.

The reaction appears to be a general one, although trinitrophenol, which contains a strongly acidic hydroxyl group, is also precipitated readily with potassium acetate under the same conditions. Apparently phenols with both ortho hydrogen atoms substituted, and also having a strongly negative group in the para position, are precipitated by potassium acetate in absolute ethanol.

The quantitative efficiency of the method is shown in Table II.

The actual process of separation may be varied greatly, depending on the nature of the products under investigation. Addition of one to three volumes of dry ether to the potassium acetate solution, in the case of the more difficultly precipitable syringyl derivatives, was found greatly to increase the yield of potassium salts. Other reagents such as dry ammonia, and potassium and sodium hydroxides in ethanol, were found effective in bringing about a practical separation

(8) Cooke, McCarthy and Hibbert, unpublished results.

(9) (a) Harris, THIS JOURNAL, **58**, 894 (1936); (b) Hibbert and Steeves, *ibid.*, **59**, 1768 (1937); (c) Freudenberg and Müller, *Ber.*, **71**, 1821 (1938).

(10) Freudenberg, Engler, Flickinger, Sobeck and Klinck, *ibid.*, **71** 1817 (1938).

(11) Lock, *ibid.*, **61**, 2245 (1928); *ibid.*, **62**, 1177 (1929).

TABLE I

PRECIPITATION OF SYRINGYL DERIVATIVE WITH POTASSIUM ACETATE IN ABSOLUTE ETHANOL SOLUTIONS

	Syringyl derivative	Weight used, g.	Potassium salt precipitated G.	%	OCH_3 (calcd. on wt. of potassium salt) Found, %	Calcd., %	Color of ppt.
1	α-Bromopropiosyringone	0.1000	0.1057	93.5	18.1	18.9	Lemon-yellow
2	Propiosyringone	.1000	.1042	91.8	24.4	25.0	Cream
3	α-Hydroxypropiosyringone	.1000	(a) .1250	107.4	23.7	23.6	Pale yellow
			(b) .1242				
4	Syringaldehyde	.1000	.0877	72.3	27.7	28.2	Peach
5	α-Acetoxypropiosyringone	.1000	.0480	42.7	21.6	20.3	Pale yellow
6	3,5-Dimethoxy-4-hydroxy-phenylpropane	.1000	.000	0.00	..	..	.....

TABLE II

QUANTITATIVE SEPARATION OF α-BROMOPROPIOSYRINGONE AND α-HYDROXYPROPIOVANILLONE BY USE OF POTASSIUM ACETATE IN ETHANOL SOLUTIONS

	Amounts in mixture α-Bromopropio-syringone, g.	α-Hydroxypro-piovanillone, g.	Precipitated potassium syringyl derivative G.	%
1	0.1000	0.1000	0.1058	93.5
2	.0500	.1000	.0525	92.2
3	.0250	.1000	.0214	73.3
4	.0000	.1000	.0000	0.0

in dilute solution in many cases, although they are not entirely specific, since most of the guaiacyl analogs are precipitated, to some extent, when *concentrated* ethanol solutions are used.

Sodium acetate, apparently because of its low solubility in ethanol, does not precipitate syringyl compounds, while ammonia, *in anhydrous ether*, precipitates both guaiacyl and syringyl compounds containing a carbonyl group in the para position to the hydroxyl group.

In Table III a survey of the conditions necessary for the qualitative precipitation of syringyl and guaiacyl derivatives is given.

The progressive order (1 to 5) in which the reagents are tabulated is that of their increasing relative value as precipitating media for phenolic derivatives. Thus compounds precipitated by reagent no. 1 will be precipitated more readily by each subsequent reagent, nos. 2, 3, 4 and 5, in the order named, and the conditions for separating a given mixture of syringyl and guaiacyl components will be determined by the relative ease with which they are precipitated in the form of their potassium or ammonium salts. Both potassium and ammonium derivatives of syringyl compounds separate in a microcrystalline form; the former on heating do not melt, while the latter do, with evolution of ammonia, over a wide range depending on the rate of temperature increase.

Application of the above methods to the distilled phenol fraction obtained in the ethanolysis of maple wood[6b] showed that 53% consisted of α-ethoxypropiosyringone.

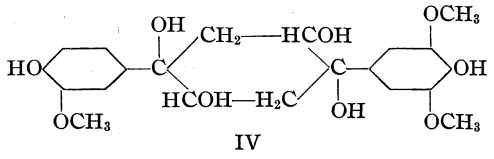
While these results are in harmony with the assumption of the presence of a mixed dimeric

TABLE III

QUALITATIVE PRECIPITATION OF SYRINGYL AND GUAIACYL DERIVATIVES

Derivative	(1) AcOK (ethanol soln.)	(2) AcOK (ethanol + ether soln.)	(3) NH_3 (ethanol soln.)	(4) NH_3 (ether soln.)	(5) KOH (ethanol soln.)
α-Hydroxypropiosyringone	Pptn. is approx.	.....	.....	.....	.....
α-Bromopropiosyringone	complete	.....	.....	.....	.....
Syringoylacetaldehyde	Pptn. is approx.	.....	.....	.....	.....
Propiosyringone	complete	.....	.....	.....	.....
Syringaldehyde	Partial pptn.	Pptn. is approximately complete		.....	.....
α-Acetoxypropiosyringone	Partial pptn. (45%)	Pptn. is approx. complete	Pptn. is approx. complete	.....	.....
α-Ethoxypropiosyringone	Partial pptn.	Pptn. 80% complete	Pptn. is approx. complete	.....	.....
3,5-Dimethoxy-4-hydroxy-phenyl propane	No pptn.	No pptn.	No pptn.	Partial pptn.	Pptn. is approx. complete
Pyrogallol 1,3-dimethyl ether	No pptn.	No pptn.	No pptn.	No pptn.	Pptn. is approx. complete
α-Hydroxypropiovanillone	No pptn.	No pptn.	Partial pptn.	Pptn. is approx. complete	
α-Bromopropiovanillone	No pptn.	No pptn.	No pptn.	Pptn. is approx. complete	
Vanillin	No pptn.	No pptn.	Partial pptn.	Pptn. is approx. complete	Partial pptn.

lignin building unit in hard woods of type IV derived from one mole each of α-hydroxypropiovanillone and α-hydroxypropiosyringone, it should be emphasized that up to the present no experimental evidence has been obtained of its actual existence.



IV

Experimental

Quantitative Precipitation of Syringyl Derivatives.—The syringyl compound (0.1000 g.) is dissolved in 2 cc. of absolute ethanol and then a saturated solution (3 cc.) of anhydrous potassium acetate in absolute ethanol (3 cc.) added. The potassium salt generally separates out very rapidly as a microcrystalline product, the color varying in shade from colorless to deep orange. After standing at room temperature (25°) for thirty minutes, the mixture is filtered, washed with absolute ethanol (5 cc.) and dry ether (5 cc.) and dried for one hour at 100° (760 mm.) before weighing. Prior to analysis the precipitate is dried over phosphorus pentoxide at 56° (14 mm.). The results are given in Table I.

Quantitative Separation of Guaiacyl and Syringyl Derivatives.—To the mixture in anhydrous ethanol (2 cc.) of 0.1000 g. of the guaiacyl derivative and varying quantities of the syringyl product, as indicated, was added a saturated anhydrous ethanol solution of potassium acetate (3 cc.), and the precipitated potassium salt of the syringyl derivative filtered, washed and weighed. The results are shown in Table II.

Separation of the Syringyl and Guaiacyl Components in the Phenol Fraction Obtained in the Ethanolysis of Maple Wood.[6b]—The distilled phenol fraction (9.6 g.) was added to a solution of anhydrous potassium acetate (10 g.) dissolved in absolute ethanol (75 cc.) and the mixture well shaken. To this was added dry ether (175 cc.) and the yellow precipitate filtered, washed with ethanol, then with ether and dried (wt. 4.7 g.). The filtrate was shaken with 500 cc. of water and the aqueous layer then extracted thoroughly with benzene. The combined ether and benzene solutions were then concentrated and the residual oil distilled as usual under reduced pressure. The total distillate (4.96 g.) was dissolved in 40 cc. of *anhydrous ethanol* and dry ammonia gas passed into the solution for a few minutes. The yellow crystalline ammonium salt (1.1 g.) was filtered off, washed with ethanol and ether and dried under reduced pressure at room temperature. Both the ammonium and potassium salts when treated with an equivalent of *p*-nitrobenzoyl chloride in dry pyridine yielded the *p*-nitrobenzoate of α-ethoxypropiosyringone.[6b] The combined weights of the two crystalline fractions are equivalent to 5.07 g. of α-ethoxypropiosyringone or 53% of the original mixed phenol fraction.

Synthesis of 3,5-Dimethoxy-4-hydroxyphenylpropane-1.—This derivative was prepared by Mauthner[12] by a molecular rearrangement of the allyl ether of pyrogallol 1,3-dimethyl ether followed by hydrogenation of the acetate of the resulting phenol with a palladium catalyst. The material used in these experiments was prepared by a Clemmensen[13] reduction of propiosyringone[6b] obtained by demethylating 3,4,5-trimethoxypropiophenone with concentrated sulfuric acid.

From 2.0 g. of propiosyringone there was obtained 0.9 g. of product. Distillation of this gave a colorless, mobile oil (0.50 g., 26.6%) which solidified at −5 to 0°; b. p. 123–126° (0.004 mm.), 279–281° (749 mm.); reported by Mauthner[12] 285° (760 mm.). The product could not be purified further.

Anal. Calcd. for $C_9H_{10}O(OCH_3)_2$: OCH_3, 31.6. Found: OCH_3, 30.3.

Synthesis of α-Hydroxypropiosyringone.—The method used was similar to that developed by Robinson[14] for an analogous compound.

α-Acetoxypropiosyringone[6b] (12.5 g.) was dissolved in boiling anhydrous methanol (120 cc.) and mixed with a warm methanol solution of potassium hydroxide (12.0 g.). There was a vigorous reaction, the solution darkened and in a few seconds a yellow crystalline material was precipitated. After filtration, washing first with methanol, then with ether, it was dried in a vacuum desiccator; yield, 12.0 g. (98% calculated as potassium salt of α-hydroxypropiosyringone).

This potassium salt (11.1 g.) was dissolved in a dilute acetic acid solution (50 cc. of water and 7.2 cc. of glacial acetic acid), the solution inoculated with crystals of α-hydroxypropiosyringone and allowed to stand at room temperature for twenty-four hours, the crystalline product removed by filtration, the filtrate carefully extracted with chloroform and the chloroform solution dried with anhydrous sodium sulfate and concentrated, under reduced pressure, to a thick sirup. To this was added the previous crystalline material and the combined product dissolved in a minimum amount of hot benzene. After filtration and cooling, 8.6 g. of crystalline precipitate (90%) was obtained. Three recrystallizations from benzene gave a pure white product in the form of square-shaped crystals, m. p. 126–127°.

Anal. Calcd. for $C_9H_8O_3(OCH_3)_2$: C, 58.4; H, 6.20; OCH_3, 27.4. Found: C, 58.3; H, 6.38; OCH_3, 27.1.

The authors desire to express to the Dow Chemical Company their best thanks for the assistance rendered in the form of a Scholarship granted to one of them (M. J. H.).

Summary

1. A simple method for the quantitative separation of syringyl from guaiacyl derivatives is given.

2. A characteristic difference between hard and soft woods is shown to consist in the presence in the lignin derived from the former of an equal amount of guaiacyl and syringyl analogs;

(12) Mauthner, *J. prakt. Chem.*, **102**, 36 (1921).

(13) (a) Clemmensen, *Ber.*, **46**, 1837 (1913); (b) Hurd and Fowler, THIS JOURNAL, **61**, 252 (1939).

(14) Robinson, *J. Chem. Soc.*, 2701 (1931).

in the latter only the corresponding guaiacyl components are present.

3. It is suggested that in hard woods the lignin building unit may be a mixed dimer, derived, for example, from one mole each of α-hydroxypropiovanillone and α-hydroxypropiosyringone.

4. A method for the synthesis of α-hydroxypropiosyringone (possibly a building unit of hard wood lignins) is described.

MONTREAL, CANADA RECEIVED MAY 18, 1939

[CONTRIBUTION FROM THE DIVISION OF INDUSTRIAL AND CELLULOSE CHEMISTRY, MCGILL UNIVERSITY]

Studies on Lignin and Related Compounds. XLII. The Isolation of a Bisulfite Soluble "Extracted Lignin"

BY WILLIAM H. STEEVES[1] AND HAROLD HIBBERT

The fact that "extracted lignins," isolated for example by the use of acids and of organic solvents in presence of a catalyst (hydrochloric acid, etc.), are insoluble on heating with bisulfite solution points to their having undergone deep-seated changes in structure during their isolation, since "protolignin" as present in the wood is readily bisulfite soluble.

In a recent investigation[2] it was shown that an acetylated oak lignin isolated by the acetylation procedure developed by Suida and Titsch[3] (use of a mixture of acetic anhydride, glacial acetic acid and a small amount of concentrated sulfuric acid) gave, on deacetylation, and for the first time, an extracted lignin completely soluble in hot bisulfite solution at 110°. As shown in another communication[4] the oak lignin sulfonic acid thus formed, on heating with alkali, gave a mixture of vanillin and syringaldehyde in approximately equal amounts.

Under the same conditions of acetylation, the reactive sugar, fructose,[5] and its dehydration product, hydroxymethylfurfural,[6] yield crystalline acetates and no appreciable amounts of acetylated lignin-like materials.

These results thus serve to indicate that lignin is not formed during isolation from carbohydrate material as postulated by Hilpert.[7]

This method of lignin isolation, through acetylation, evidently gives a relatively unchanged, and only slightly polymerized, form of "protolignin." This recently has been confirmed by the partial reconversion of an acetylated lignin, isolated in this manner, to simple lignin building units by treatment with hydrogen chloride and ethanol.[8]

More recently it has been shown that after deacetylation the recovered oak lignin can also be depolymerized in the same manner.[9]

Experimental

Extraction with Alkali.—The procedure followed was that used by Suida and Titsch.[3] Alcohol–benzene and hot water extracted red oak meal (600 g.) was stirred for forty-eight hours at room temperature with 12 liters of 5% sodium hydroxide solution. The wood meal was then removed by filtration, washed with water at 60°, and the extraction repeated in an identical manner three times to ensure complete removal of soluble hemicelluloses. An atmosphere of nitrogen was maintained during the alkali treatments. The extracted wood meal was finally washed with distilled water, 1% acetic acid, water and methyl alcohol, in the order named, and dried (50° at 15 mm.). The pale yellow residual wood meal represented about 80% of the original wood.

Anal. Found: methoxyl, 6.8; lignin, 31.0; cellulose, 66.6; pentosan, 13.3.

Acetylation of the Extracted Wood Meal and Isolation of Acetylated Oak Lignin.—The dried, alkali-extracted oak wood meal (50 g.) was acetylated with a mixture of acetic anhydride (450 g.), glacial acetic acid (250 g.), and concentrated sulfuric acid (3.5 g.), the reaction being carried out in a bronze Werner–Pfleiderer mixer provided with a water cooling system. The temperature was allowed to rise gradually from 15 to 30°, as follows: two and one-half hours at 15°, one-half hour at 15–20°, two hours at 20–25°, and two hours at 25–30°. The highly viscous, dark brown solution was allowed to stand overnight in an atmosphere of nitrogen without stirring. It was then poured into 2 liters of a vigorously stirred 20% sodium acetate solution. The resulting solid, acetylated product

(1) From the thesis of William H. Steeves submitted to McGill University in partial fulfilment of the requirements for the Degree of Doctor of Philosophy, May, 1936. (Previous paper, THIS JOURNAL, **59**, 1768 (1937).)

(2) Steeves, Ph.D. Thesis, McGill University, 1936; Hibbert and Steeves, THIS JOURNAL, **59**, 1768 (1937).

(3) Suida, Hermann and Titsch, *Monatsh.*, **54**, 700 (1929).

(4) Hawkins, Wright and Hibbert, THIS JOURNAL, **59**, 2447 (1937).

(5) Hudson and Brauns, *ibid.*, **37**, 1283 (1915).

(6) Blanksma, *Chem.-Ztg.*, **2**, 1220 (1909).

(7) Hilpert and Hellwage, *Cellulosechemie*, **17**, 25 (1936).

(8) Peniston, McCarthy and Hibbert, THIS JOURNAL, **61**, 530 (1939).

(9) Peniston, McCarthy and Hibbert, unpublished results.

was collected in a cotton sack and washed for forty-eight hours with running water and dried; yield approximately 80 g.

The dried acetylated wood meal was then mixed with a liter of chloroform, stirred for two hours, and allowed to stand for twelve hours at room temperature. The viscous solution was then filtered through finely powdered, anhydrous sodium sulfate, leaving an insoluble residue amounting to about 10 g. The clear chloroform solution was concentrated under reduced pressure and the residual solvent allowed to evaporate in air at room temperature. The resulting hard, glassy solid was crushed, pulverized, and extracted with acetone for five days in a Soxhlet apparatus. The acetone extract was concentrated to 200 cc., filtered, and poured into two liters of water. The acetylated lignin product was collected on a filter, washed with water, and dried; yield 27 g.

Purification of the Fully Acetylated Crude Oak Lignin.—The dry, acetylated product (10 g.) was dissolved in acetone (50 cc.), filtered, and precipitated by pouring in a fine stream into anhydrous ether (500 cc.). A very light-colored precipitate was obtained which was collected on a filter, washed with ether, then with petroleum ether, and dried.

Anal. Found: OCH_3, 11.0; $COCH_3$, 35.4; Klason lignin, 75.2.

The acetylated oak lignin was fractionated further by precipitating from dioxane solution into anhydrous ether. After three such precipitations, the methoxyl content remained unchanged (11.1%). Apparently, either the non-ligneous materials present are chemically bound to the acetylated lignin or the acetylated carbohydrates have solubility characteristics very similar to those of the acetylated lignin. The purified product contained about 10% pentosan which could be completely removed by deacetylation of the material with dilute alkali.

Deacetylation and Isolation of Native Oak Lignin.—Thirty grams of crude acetylated oak lignin (OCH_3, 11.1%) was dissolved in 1 liter of acetone, and 1 liter of 20% sodium hydroxide was slowly added with stirring. The mixture was allowed to stand for twenty-four hours at room temperature, the acetone removed under reduced pressure, and water added to maintain the volume at 2 liters. After two weeks' standing, the mixture was filtered to remove the alkali insoluble material (about 5 g.). After washing with water and drying, this was found to contain 4.1% methoxyl. The alkaline filtrate was acidified with 5% sulfuric acid and the resulting buff-colored precipitate collected, washed free from sulfate and dried; yield 15 g. The product was purified by dissolving in 50 cc. of dioxane and precipitating into anhydrous ether. The precipitate was collected in a centrifuge, washed with ether followed by petroleum ether, and dried. Found: OCH_3, 20.8.

The alkali insoluble material apparently is composed of methoxyl-containing substances still chemically bound to polysaccharides. It was found to be insoluble in all common organic solvents.

The alkali soluble, deacetylated native oak lignin, after purification by precipitation from dioxane solution into ether, could be fractionated into a chloroform soluble and a chloroform insoluble fraction. Chloroform soluble fraction: OCH_3, 23.4. Chloroform insoluble fraction: OCH_3, 20.6; C, 64.0; H, 6.2.

On methylation with diazomethane in dioxane solution both of the above fractions gave, after three treatments, products having the same constant methoxyl value of 26.6%.

Acetylation of the Native Oak Lignin.—Ten grams of the unfractionated native oak lignin (OCH_3, 20.6%) was acetylated at room temperature with a mixture of 50 cc. of acetic anhydride and 100 cc. of pyridine. After standing for twelve hours, the solution was poured into a liter of ice water and the precipitate removed by filtration, washed, dried, and reprecipitated from acetone into ether. Found: OCH_3, 18.2. Ten grams of the acetylated product was reacetylated by dissolving in a mixture of acetic anhydride (100 g.), glacial acetic acid (50.0 g.) and concentrated sulfuric acid (0.7 g.). The mixture was held at 20–25° for twenty-four hours and then poured into a liter of 20% sodium acetate. The product was filtered, washed, dried, and purified by precipitation from acetone into ether followed by a reprecipitation from dioxane into ether. Found: C, 62.3; H, 5.9; OCH_3, 16.8; $COCH_3$, 22.9.

Solubility of Native Oak Lignin in Bisulfite Solution.—A sample of the chloroform soluble fraction of native oak lignin (OCH_3, 23.4%) was heated in a sealed tube with a bisulfite solution containing 6.0% "total" and 1.4% "combined" sulfur dioxide. Solution was complete on heating for twelve hours at 110°.

Preparation of 5-Acetoxymethylfurfurylidene Diacetate.—The method of Blanksma[6] was used. A higher yield (75%) was obtained by adding the sulfuric acid to the acetic anhydride and keeping the temperature below 0°. This mixture was added slowly to the hydroxymethylfurfural. The acetate was isolated in the manner outlined by Blanksma; m. p. 73°.

Acknowledgment.—The authors are indebted to Dr. Saul M. Trister for the preparation of the 5-acetoxymethylfurfurylidene diacetate.

Summary

1. A description is given of a simple method for the isolation of a lignin from oak wood which retains the reactive character of "protolignin," namely, solubility in hot bisulfite solution.

2. Under the same conditions of acetylation used in the isolation of the above "native oak lignin," fructose and hydroxymethylfurfural yield crystalline acetylated products with practically no formation of material resembling lignin. This is considered an argument against Hilpert's theory[7] of lignin formation as a change arising during the extraction process from the action of the extractant on a sensitive carbohydrate.

3. It has been found possible to reacetylate "native oak lignin" to give a product soluble in acetone or dioxane and containing 22.9% acetyl.

MONTREAL, CANADA RECEIVED MAY 18, 1939

[CONTRIBUTION FROM THE DIVISION OF INDUSTRIAL AND CELLULOSE CHEMISTRY, MCGILL UNIVERSITY]

Studies on Lignin and Related Compounds. XLIII. The Absence of the Piperonyl Group in the Lignin Structure

BY M. J. HUNTER[1] AND HAROLD HIBBERT

Formaldehyde was first isolated from lignin materials by Freudenberg and Harder,[2] a discovery confirmed by Sarkar,[3] the yields amounting to 0.5–2.0% calculated on the weight of (Klason) lignin present. Freudenberg[4] as well as Sarkar[3] regards the isolation of formaldehyde as direct proof of a piperonyl radical in the lignin complex and the former uses the formaldehyde values to calculate the size of the lignin building unit.[4] Phillips and Goss[5] have objected to this interpretation. Formaldehyde yields from various lignins were given recently[6] and it was shown that these are dependent on the method of extraction of the lignin from the wood. The improbability of the existence of the dioxymethylene group in lignin as part of a piperonyl radical was indicated.

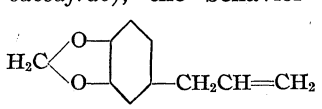
Recently, Freudenberg[7] has found additional support for the presence of the piperonyl group in new experimental technique involving acridane formation by the action on lignin and related products of a mixture of aniline and concentrated hydrochloric acid at a high temperature and pressure. The use of such a drastic procedure with a highly sensitive complex such as lignin would seem open to serious objection as a criterion for distinguishing between formaldehyde formation from piperonyl groups and other sources, respectively.

It was shown recently[6] that the dioxymethylene group in the piperonyl radical, when subjected to various reagents and procedures used in lignin extraction, is decomposed to the extent of only 25%, so that if present in "protolignin" it also should be found to a correspondingly large extent in the extracted lignin. However, the wide variation in formaldehyde yields from various lignins[6b] may be considered as indirect evidence against the view of the piperonyl group as the formaldehyde precursor. The approximate relationship found in certain acetic acid lignins between the amounts of furfural and formaldehyde cleavage products indicated the possibility of both being formed simultaneously from certain hexoses, adsorbed by, or combined with, the extracted lignins. Hexoses[6] gave traces of formaldehyde and furfural in most cases on treatment with mineral acids, but the yields were much too low to account for the amounts obtained from isolated lignins; also certain lignins which gave the highest amounts of formaldehyde yielded only traces of furfural.

The outstanding relationship noted[6] was that extracted lignins when refluxed with 95% formic acid gave a very low yield of formaldehyde. The stability of the piperonyl group to formic acid and the action of the latter reagent on ethanol lignin, both with respect to removal of this group and to the suppression of the formaldehyde-yielding constituent, have now been investigated.

Piperonal on refluxing with formic acid (95%) for sixteen hours was decomposed to the extent of only 15%, while treatment of ethanol lignins removed 90–95% of the formaldehyde-producing component.

Klason[8] regarded lignin as related to coniferyl alcohol, present as a glucoside in coniferin, the latter being found in the cambium sap of a wide variety of woods. Since safrole (I) is found in the cambium sap of the roots of the sassafras tree (*Sassafras sassafras*), the behavior of ethanol



I

sassafras lignin toward hot dilute acids was investigated. This lignin was prepared by the usual procedure[9] and the yields of formaldehyde obtained from it and maple and spruce ethanol lignins are shown in Table I.

(1) From a thesis submitted to McGill University by Melvin J. Hunter in partial fulfilment of the requirements for the Degree of Doctor of Philosophy, May, 1939.

(2) Freudenberg and Harder, *Ber.*, **60**, 581 (1927); Freudenberg and Sohns, *ibid.*, **66**, 282 (1933).

(3) Sarkar, *J. Indian Chem. Soc.*, **11**, 691 (1934).

(4) Freudenberg, "Tannin, Cellulose, Lignin," Verlag von Julius Springer, Berlin, 1933, p. 134.

(5) Phillips and Goss, THIS JOURNAL, **54**, 3374 (1932).

(6) (a) Hunter, Wright and Hibbert, *Ber.*, **71**, 734 (1938); (b) *ibid.*, Table 3.

(7) Freudenberg, Klinck, Flickinger and Sobek, *ibid.*, **72**, 217 (1939).

(8) Klason, *Arkiv. Kemi. Mineral. Geol.*, **3**, No. 5, 17 (1908).

(9) Cramer, Hunter and Hibbert, THIS JOURNAL, **61**, 509 (1939); Hunter, Cramer and Hibbert, *ibid.*, **61**, 516 (1939); Brickman, Pyle, McCarthy and Hibbert, *ibid.*, **61**, 868 (1939).

TABLE I

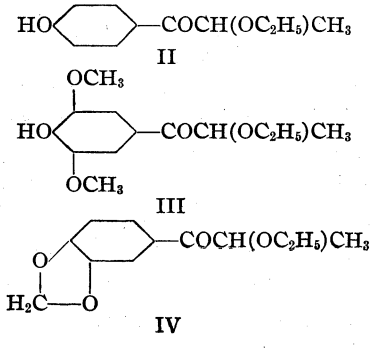
YIELDS OF FORMALDEHYDE FROM SASSAFRAS, MAPLE AND SPRUCE ETHANOL LIGNINS

	Wood species	Method of isolation	Hrs.	Secondary treatment, refluxed with	Alkoxyl content calcd. as methoxyl, %	Formaldehyde analyses: Sample, g.	Dimedone deriv., g.	Formaldehyde, %
1	Maple	Ethanol–2% HCl	20	.....	27.1	1.000	0.0490	0.50
2	Maple	Ethanol–0.3% HCl	100	.....	28.4	1.000	.1229	1.26
3	Maple	Ethanol–0.3% HCl	100	95% formic acid for 16 hrs.	23.6	1.000	.0064	0.066
4	Sassafras	Ethanol–2.0% HCl	24	.....	26.4	1.000	.0392	.40
5	Sassafras	Ethanol–2.0% HCl	24	95% formic acid for 16 hrs.	23.2	1.000	.0032	.033
6	Spruce	Ethanol–3.0% HCl	40	.....	19.2	1.000	.0244	.25

The analyses show that boiling 95% formic acid removes the component responsible for formaldehyde formation from maple and sassafras ethanol lignins with equal ease, and, since the piperonyl group in various derivatives is decomposed to the extent of only 15% under identical conditions, the results provide conclusive evidence against the existence of the piperonyl group in lignin.

Also piperonal when refluxed for twenty-four hours with absolute ethanol containing 3% hydrogen chloride can be recovered in 90% yield, while, from the data given in Table I, it would appear that a large percentage of the original formaldehyde-producing constituent is removed, or transformed, even by the action of the (2%) ethanol–hydrochloric acid during the lignin extraction, since an extracted lignin prepared from maple wood meal by heating with ethanol, containing only 0.3% hydrogen chloride, for one hundred hours, showed a much higher formaldehyde content.

The water-soluble oils obtained in the ethanolysis of sassafras wood[9] gave no formaldehyde on treatment with hot dilute acids by the customary procedure. If sassafras lignin contained a piperonyl group, this should be present as α-ethoxypropiopiperonylone (IV) in the neutral water-soluble ethanolysis fraction[9] as an analog of the guaiacyl (II) and syringyl (III) compounds[9] obtained from the ethanolysis of spruce and maple woods, respectively, but not the slightest trace of formaldehyde could be obtained.



Regarding the origin of the formaldehyde from extracted lignins, Freudenberg[10] has shown recently that cinnamyl alcohol when distilled with 28% sulfuric acid gives about 2% formaldehyde. He concludes[10] that this configuration, if present in lignin, is not responsible for the formaldehyde formation since no acridane formation[7] takes place with cinnamyl alcohol under conditions whereby it is formed both from lignins and piperonyl derivatives. The drastic conditions employed, namely, heating with aniline and concentrated hydrochloric acid under pressure at 270–290° for thirty-four hours, would seem to preclude application of this method to such a highly reactive substance as the lignin aggregate.

Whilst the more unstable methylals and cyclic acetals[11] would yield formaldehyde readily under the conditions employed, no evidence has been found, as yet, indicating the presence of such groupings in wood.

According to Kohler[12] vinyl phenyl ketone loses formaldehyde spontaneously at room temperature and the possible relation of this type of structure to that of α-hydroxypropiosyringone and α-hydroxypropiovanillone should not be overlooked.

The amount, if any, of piperonyl-containing constituent present in lignin would seem to be so small that it cannot be regarded as an essential part of the lignin structure, and the evidence obtained thus far appears to indicate that the formaldehyde (1–4%) is formed from an aromatic side-chain, possibly one existing as part of a complex present in lignin condensation polymers[13] and similar to cinnamyl alcohol.

(10) Freudenberg, Engler, Flickinger, Sobek and Klinck, *Ber.*, **71**, 1810 (1938).

(11) Hibbert and Carter, THIS JOURNAL, **50**, 3120 (1928).

(12) Kohler, *Am. Chem. J.*, **42**, 380 (1909).

(13) Hibbert, THIS JOURNAL, **61**, 730 (Structure XXXVI) (1939).

Experimental

Determination of the Formaldehyde Liberated by the Action of Acids on Extracted Lignins and Related Substances.—This was carried out as described in the previous communication.[6]

Stability of Piperonal toward Boiling Formic Acid (95%).—Piperonal (2.000 g.) was refluxed with 95% formic acid (20 cc.) for sixteen hours following the method of Wright and Hibbert.[14] After removing the formic acid under reduced pressure, the residue was dissolved in ether and the ether solution extracted with cold 1% sodium hydroxide solution. The ether extract was dried over anhydrous calcium chloride, concentrated, and the residue distilled under reduced pressure. The distillate (1.696 g., equivalent to 84.8%) crystallized at room temperature, m. p. 36–38°. A mixed melting point with the original product showed no depression.

Stability of Piperonal to Hot Ethanol Containing 3% Hydrogen Chloride.—Piperonal (2.000 g.) was refluxed for twenty-four hours with absolute ethanol containing 3% hydrogen chloride. These conditions were somewhat more drastic than those used for the ethanolysis of maple and sassafras woods. The ethanol was removed under reduced pressure, the residue dissolved in ether, and the piperonal isolated as above: weight of recovered piperonal, 1.827 g. (91.3%).

Behavior of Lignins toward Boiling Formic Acid (95%).—The various ethanol lignins (3.0 g.) were each refluxed with 95% formic acid (30 cc.) for sixteen hours. The solution was then poured with stirring into 300 cc. of distilled water and the precipitated lignins washed free from acid. The precipitates were vacuum dried over calcium chloride at room temperature and then over phosphorus pentoxide at 56° (14 mm.). The products were analyzed for methoxyl and the formaldehyde yield determined. The results are shown in Table I.

Preparation of Sassafras Ethanol Lignin.—Sassafras woodmeal (450 g.) previously extracted with (i) alcohol–benzene, (ii) benzene and (iii) water, after drying was refluxed for twenty-four hours with 3 liters of absolute ethanol containing 2% hydrogen chloride, as previously described.[9] This gave 52.0 g. of sassafras ethanol lignin and 36.3 g. of crude ether soluble oils, as compared with 44.6 g. of lignin and 36.7 g. of crude oils from a similar run with maple wood. From the sassafras crude oils there was obtained a neutral fraction of 2.2 g. Distillation of this latter with 28% sulfuric acid gave no formaldehyde.

(14) Wright and Hibbert, THIS JOURNAL, **59**, 125 (1937).

Acknowledgment.—The authors wish to thank the Dow Chemical Company for kind financial assistance, in the form of a Scholarship (to M. J. H.).

Summary

The absence of the piperonyl group in the structure of lignin is indicated by (a) the inability of workers in this field to isolate from an extracted lignin a piperonyl-containing derivative; (b) the pronounced instability toward formic acid of the formaldehyde-producing constituent in lignin as compared with the very much greater stability of the piperonyl radical present in known compounds; (c) the liberation of formaldehyde from such derivatives as cinnamyl alcohol, and the probability of the presence of this type of grouping in extracted lignins; (d) the behavior of ethanol sassafras lignin and the water-soluble ethanolysis products from sassafras wood toward hot dilute acids, whereby yields of formaldehyde similar in amount to those found with other woods are obtained from the former, and none from the latter.

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[CONTRIBUTION FROM THE DIVISION OF INDUSTRIAL AND CELLULOSE CHEMISTRY, MCGILL UNIVERSITY]

Studies on Lignin and Related Compounds. XLIV. The Ethanolysis of Maple Wood; Separation and Identification of the Water-Soluble Aldehyde Constituents[1]

BY JAMES J. PYLE, LEO BRICKMAN AND HAROLD HIBBERT

In two recent communications[2] of this series, a description was given of the isolation, in considerable amount, of water-soluble aromatic constituents formed in the ethanolysis of spruce and maple woods. The crude oils were shown to consist of a phenolic, aldehydic, acidic and neutral fraction. In a later paper,[3] a revised method for their isolation was given by which much improved yields were obtained. The phenol fraction from spruce wood[2a] has been shown to consist in large part of α-ethoxypropiovanillone and that from maple wood[2b] of a mixture, in approximately equal amounts, of this and α-ethoxypropiosyringone.

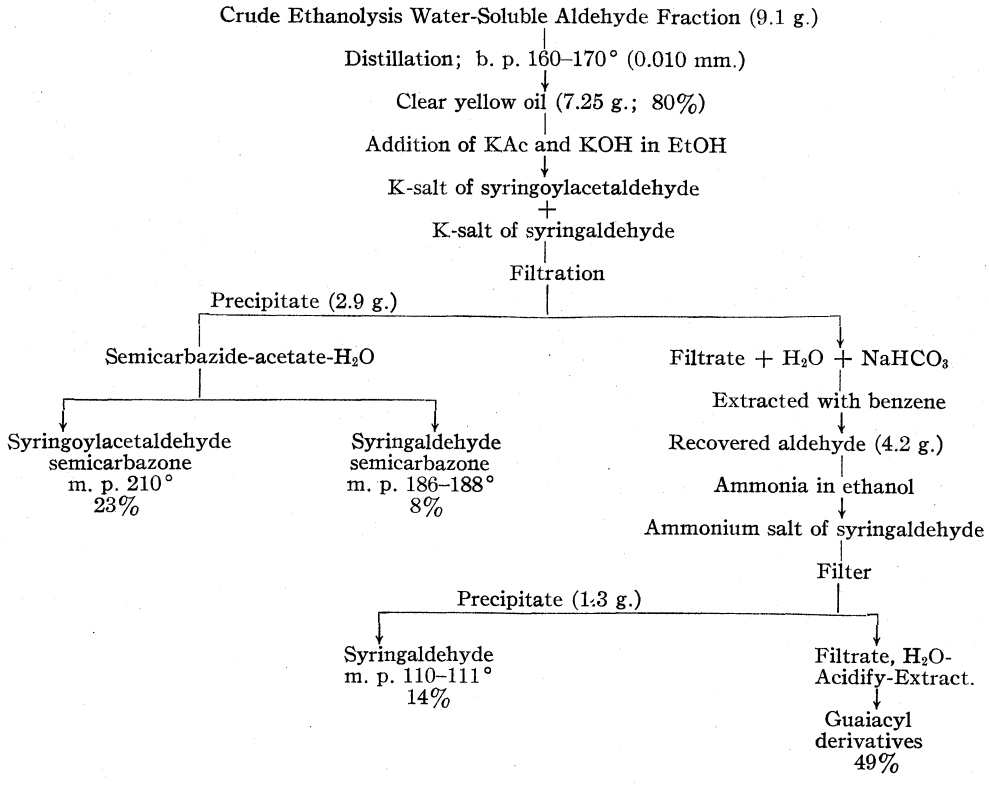
In the present communication an account is given of the separation and identification of the

(1) From a thesis submitted to the Faculty of Graduate Studies and Research, McGill University, by James J. Pyle in partial fulfilment of the requirements for the degree of Doctor of Philosophy, May, 1939.

(2) (a) Cramer, Hunter and Hibbert, THIS JOURNAL, **61**, 509 (1939); (b) Hunter, Cramer and Hibbert, *ibid.*, **61**, 516 (1939).

(3) Brickman, Pyle, McCarthy and Hibbert, *ibid.*, **61**, 868 (1939).

METHODS OF SEPARATION OF SYRINGYL AND GUAIACYL COMPONENTS IN THE WATER-SOLUBLE ALDEHYDE FRACTION FROM MAPLE WOOD



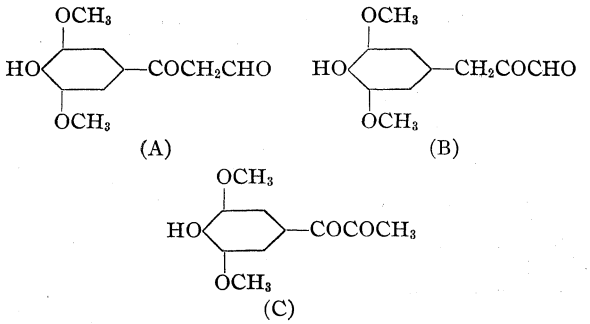
aldehydic constituents present in the ethanolysis fraction from maple wood. It has been found that this consists of a mixture of syringoylacetaldehyde, syringaldehyde, vanilloylacetaldehyde and vanillin in approximately equal amounts, thus providing a further significant proof of this characteristic difference between soft and hard woods emphasized repeatedly by Hibbert and co-workers.[4] The total syringyl and guaiacyl fractions amount to 8.2% calculated on the weight of (Klason) lignin present in the wood.

The method used in separating these two types was that outlined in a previous communication,[4d] namely, precipitation of the syringyl, but not the guaiacyl, components by the addition of potassium acetate in anhydrous ethanol. Advantage was taken of an improvement on this method, found in the use of a solution of anhydrous ammonia in ethanol, whereby a quantitative precipitation of the syringyl derivatives is effected. Use of both reagents with the corresponding aldehydic fraction from spruce, and in which only the guaiacyl derivatives (vanilloylacetaldehyde and vanillin in equal amounts) are present, gave no precipitate. The use of potassium acetate in ethanol brought about a practically complete precipitation of the syringoylacetaldehyde and a partial precipitation of the syringaldehyde. The remaining portion was recovered by treatment with anhydrous ammonia in ethanol as a yellow, crystalline precipitate. The filtrate from this latter treatment contained the whole of the guaiacyl components (vanilloylacetaldehyde and vanillin) the details of the separation and identification of which are to appear in a later communication.

The method of separation is outlined in the flow-sheet.

The analysis of the syringoylacetaldehyde and the preparation and analysis of its mono- and disemicarbazones established its empirical formula as $C_{11}H_{12}O_5$, and showed the presence of two carbonyl groups. Oxidation with hydrogen peroxide yielded syringic acid, thus establishing definitely the presence of the syringyl nucleus. Its structure must, therefore, correspond to one of three products

(4) (a) Hawkins, Wright and Hibbert, THIS JOURNAL, **59**, 2447 (1937); (b) Leger and Hibbert, *Can. J. Research*, **B16**, 151 (1938); (c) Leger and Hibbert, THIS JOURNAL, **60**, 565 (1938); (d) Hunter and Hibbert, *ibid.*, **61**, 2190 (1939).



Formula C may be eliminated on the basis of the following results:

(a) Syringoylacetaldehyde gave a negative iodoform test, indicating the absence of the (—CO—CH_3) group; (b) it reduces ammoniacal silver nitrate indicating presence of an aldehydic group; and (c) it reacts *almost immediately* with semicarbazide hydrochloride in 3 *N* hydrochloric acid. Michael[5] has shown that ketones do not react under these acidic conditions.

In view of these facts structure (C) was eliminated and a decision between (A) and (B) was reached on the basis of the following experimental facts.

(a) Syringoylacetaldehyde gave a negative test with *o*-phenylenediamine, indicating absence of a 1,2-diketone.

(b) On oxidation with hydrogen peroxide a 65% yield of syringic acid was obtained, insufficient hydrogen peroxide being added to effect complete degradative oxidation of the side-chain.

Mechanism of Formation of Syringic Acid.—This will vary in the case of structures (A) and (B) as shown

$$\text{R—COCH}_2\text{CHO} \longrightarrow \text{R—C(OH)=CHCHO} \xrightarrow{H_2O_2} \text{R—COOH}$$

$$\text{R—CH}_2\text{COCHO} \longrightarrow \text{R—CH=C(OH)CHO} \xrightarrow{H_2O_2}$$

$$\text{R—CHO} \xrightarrow{H_2O_2} \text{R—COOH}$$

where R = syringyl

It is evident that with formula (B) oxidation to the acid proceeds through the intermediate compound, syringaldehyde. Syringaldehyde was therefore treated with hydrogen peroxide under the same experimental conditions and was *recovered unchanged*, indicating that it could not be an intermediate in the formation of the syringic acid.

(c) The similarity between formula (A) and compounds of the acetoacetic ester type, that is, with an active methylene group between two carbonyls, is evident. Thus under the influence of strong alkali, syringoylacetaldehyde would be expected to cleave to give syringic acid in the same manner that acetoacetic ester yields acetic acid. Karrer and Widmer[6] heated syringidin with 20% sodium hydroxide in a stream of hydrogen, and obtained a 30% yield of syringic acid. Isolation of syringic acid from syringoylacetaldehyde, also in yields of approximately 30% of the theoretical, under conditions in which no oxidizing medium is present, definitely establishes the position of the second carbonyl as adjacent to the nucleus.

On the basis of these results, this new aldehyde isolated from the ethanolysis products of maple wood must have formula (A).

Further evidence in support of this conclusion was obtained when the syringoylacetaldehyde was subjected to the action of aqueous bisulfite followed by alkaline cleavage. This experiment was one of a series[7] on the mechanism of sulfite pulp manufacture to determine whether any of the products isolated by ethanolysis would give rise to vanillin or syringaldehyde when heated with aqueous bisulfite followed by alkaline cleavage.

Instead of syringaldehyde the products isolated were acetosyringone and syringic acid. This result apparently is due to the incomplete removal of oxygen from the nitrogen used during the experiment to provide an inert atmosphere. Some of the syringoylacetaldehyde evidently was oxidized to syringoylacetic acid which latter, being a β-keto acid, underwent decarboxylation in the presence of the alkali, to give acetosyringone.

$$\text{RCOCH}_2\text{CHO} \xrightarrow{[O]} \text{RCOCH}_2\text{COOH} \xrightarrow{[-CO_2]} \text{RCOCH}_3$$

R = syringyl

The accompanying syringic acid probably is formed from some unoxidized syringoylacetaldehyde. Unfortunately it was not found possible to duplicate this experiment.

Recovery of Syringaldehyde.—As indicated in the flow-sheet, the monosemicarbazone of syringoylacetaldehyde was obtained directly from the potassium salt of the mixture of the two aldehydes. The filtrate from this contained the semicarbazone of syringaldehyde, which precipitated out from the solution on boiling and was identified as such.

The crystalline ammonium salt of the syringal-

(5) Michael, THIS JOURNAL, **41**, 393 (1919).

(6) Karrer and Widmer, *Helv. Chim. Acta*, **10**, 5 (1927).

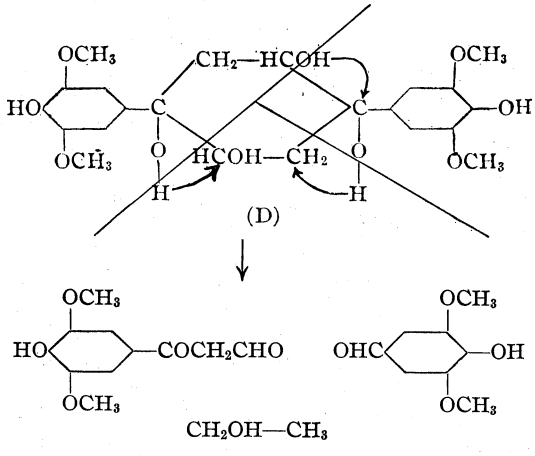
(7) Under investigation in these Laboratories by Dr. Rodger Dorland.

dehyde (see flow-sheet) gave with 2,4-dinitrophenylhydrazine the hydrazone of syringaldehyde, the yield indicating that the ammonium salt was practically pure syringaldehyde.

On the basis of the yields of the semicarbazones and 2,4-dinitrophenylhydrazone and those obtained using known quantities of the pure aldehydes under the same experimental conditions, the syringoylacetaldehyde and syringaldehyde amount to 23 and 22%, respectively, of the total aldehyde fraction. Analysis of the guaiacyl fraction indicates that approximately the same ratio holds for the vanilloylacetaldehyde and vanillin.

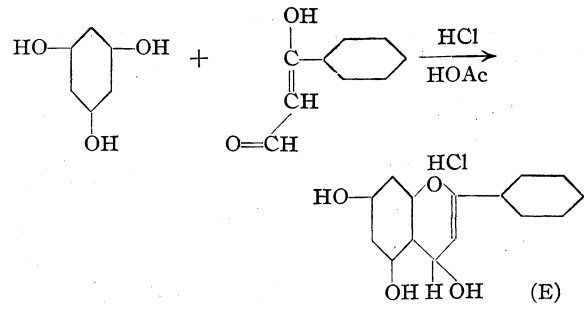
The relationship of the various ethanolysis products to the structure of "protolignin" has been discussed by Hibbert[8] in a previous communication. He suggests that lignin is probably derived from the condensation of an aldehyde (methyl glyoxal) with a phenol (guaiacol or 1,3-pyrogallol dimethyl ether). Such a dimeric building unit (D) can, theoretically, undergo ring fission by hydrogen migration in a number of ways. Cleavage may thus give rise, as pointed out by him, to (a) two moles of a hydroxy ketone (α-hydroxypropiovanillone and α-hydroxypropiosyringone), or (b) to aldehydic constituents.

It is thus of considerable interest that the aldehydes obtained in the present investigation can be visualized as cleavage products formed by a specialized type of reversed aldol formation, from Hibbert's hypothetical dimer (D).

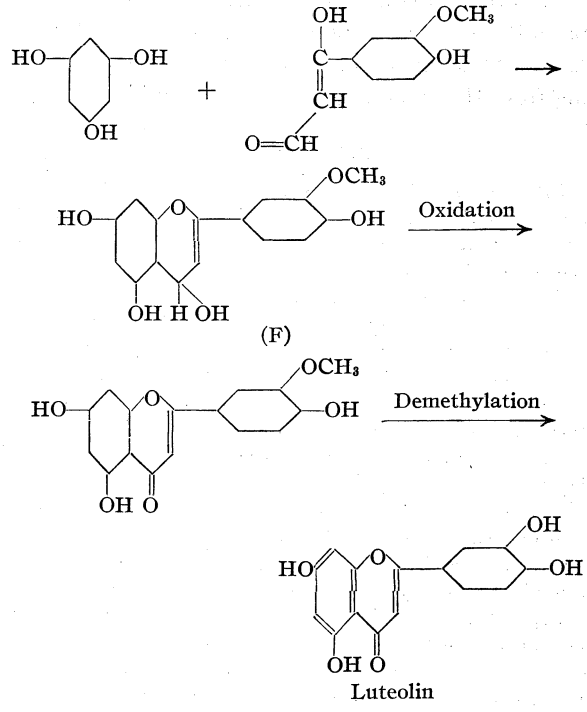


to give products of the type (E) shown

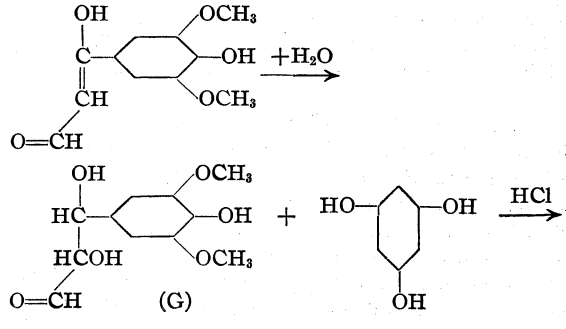
(8) Hibbert, THIS JOURNAL, **61**, 725 (1939). Due to a printer's error, p. 729, the structure of the aldehyde isolated from maple wood was incorrectly given as corresponding to Formula IV instead of Formula VI.

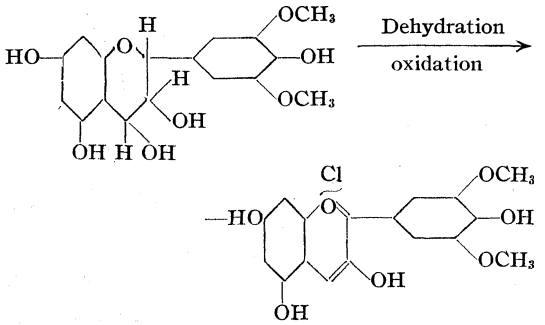


It is to be anticipated that vanillylacetaldehyde would undergo a similar condensation to give (F). The latter on oxidation and loss of methoxyl would yield a typical flavone, namely, luteolin.



On the other hand, hydration of syringoylacetaldehyde could give rise to formation of (G) which on condensation with phloroglucinol followed by loss of water and accompanying oxidation would give a typical anthocyanidin, namely, syringidin





Experiments with a view to effecting such typical syntheses are to be carried out.

It is thus of considerable interest that such apparently unrelated plant constituents as lignin and plant pigments may be visualized as originating from the same type of building unit.

Experimental

Ethanolysis of Maple Wood.—A complete and detailed account of the ethanolysis procedure and fractionation of water soluble oils is given in a recent communication,[3] so that only a brief summary is necessary.

A solvent-extracted maple wood meal was refluxed with ethanol containing anhydrous hydrogen chloride in an inert atmosphere (carbon dioxide) and the reaction mixture filtered. The ethanol filtrate was brought almost to neutrality by addition of a solution of sodium ethylate in ethanol, then concentrated, and precipitated into water. The filtrate was concentrated, and continuously extracted with benzene.

The benzene extract was shaken with aqueous bisulfite solution, the solution acidified and back-extracted with benzene. The benzene solution of the crude aldehyde fraction was used for the following investigation.

Separation of Guaiacyl and Syringyl Components.—A portion of the benzene solution was concentrated under reduced pressure, leaving 9.1 g. of a brownish-colored, very viscous residue. This on distillation gave two fractions (88% yield): (1) b. p. 160–170° (0.010 mm.), 7.25 g., clear yellow oil; (2) b. p. 250–350° (0.025 mm.), 0.73 g., red resin.

To a solution of the distilled aldehyde (Fraction 1, 7.25 g.) dissolved in ethanol (60 cc.) was added a saturated ethanolic solution of potassium acetate (60 cc.) followed by 18 cc. of 2% potassium hydroxide in ethanol to neutralize the acetic acid formed, and the mixture shaken well. The red crystalline precipitate was filtered, washed with ethanol and dried; yield, 2.9 g., or 34.6% on the basis of free aldehyde.

The filtrate was diluted with 2–3 volumes of water, made slightly alkaline with sodium bicarbonate, and continuously extracted with benzene in an atmosphere of carbon dioxide. The amount of recovered aldehyde was 4.2 g. or 90% of the theoretical. This recovered aldehyde gave no precipitate with potassium acetate in ethanol solution.

The recovered aldehyde mixture (4.2 g.) was now dissolved in 25 cc. of anhydrous ethanol and 0.7 g. of anhydrous ammonia dissolved in 10 cc. of ethanol added. A yellow crystalline precipitate formed immediately. This was filtered and dried; wt. 1.3 g., or 16.8% calculated as the free aldehyde.

The guaiacyl derivatives were recovered from the filtrate by diluting again with several volumes of water, acidifying with sulfuric acid and continuously extracting with benzene in an atmosphere of carbon dioxide.

Isolation of Syringoylacetaldehyde.—The red crystalline potassium salt (11.3 g.) obtained above was dissolved in 100 cc. of water and 1 cc. of concentrated sulfuric acid added. The solution was extracted with benzene leaving after removal of the solvent 9.3 g. of a yellow oil, which crystallized almost completely on standing. Recrystallization first from low-boiling (60–70°), and then from high-boiling petroleum ether (100–110°) gave 4.0 g. of crude syringoylacetaldehyde, m. p. 64–68°. After several recrystallizations a constant melting point, 74.0–74.5°, was reached.

Concentration of the mother liquors yielded an oil which on treatment with semicarbazide acetate gave, as shown later, a mixture of the semicarbazones of syringoylacetaldehyde and syringaldehyde.

Analysis of Syringoylacetaldehyde.—Calcd. for $C_{11}H_{12}O_5$: C, 58.9; H, 5.4: OCH_3, 27.9. Found: C, 58.8; H, 5.6; OCH_3, 27.9.

Syringoylacetaldehyde is soluble in almost all organic solvents and also relatively soluble in water. When crystallized very slowly from petroleum ether (b. p. 100–110°), it separates in the form of colorless, hexagonal crystals.

Proof of Presence of the Syringyl Nucleus.—The aldehyde (0.050 g.) was dissolved in 5 cc. of water and 0.2 cc. of 3% hydrogen peroxide added. The reaction mixture was allowed to stand at room temperature for four hours, and then at 0° for a further two hours. Long colorless needles crystallized from the aqueous solution, m. p. (crude) 198–200°. After recrystallization from water the melting point rose to 204–205° and a mixed melting point with an authentic sample of syringic acid showed no depression.

Proof of the Dicarbonyl Structure by Preparation of a Mono- and Disemicarbazone. (a) Monosemicarbazone.—The isolated syringoylacetaldehyde (0.050 g.), semicarbazide hydrochloride (0.030 g.) and potassium acetate (0.035 g.) were dissolved in 5 cc. of water. Long, colorless needles crystallized from the solution on standing for several hours and were recrystallized from hot water; yield, 0.045 g., 71.5%; m. p. 210–210.5°.

This derivative was also prepared in 1 and 3 *N* hydrochloric acid solution. It could be obtained directly from the crystalline mixture of the potassium salt of syringoylacetaldehyde and syringaldehyde (see flow-sheet) by dissolving the mixture in an aqueous solution of semicarbazide acetate and removing the crystalline monosemicarbazone after a period of two hours in order to avoid admixture with the semicarbazone of syringaldehyde.

Analysis of Monosemicarbazone of Syringoylacetaldehyde.—Calcd. for $C_{12}H_{15}O_5N_3$: C, 51.2; H, 5.59; N, 14.9; OCH_3, 22.0. Found: C, 51.6; H, 5.61; N, 14.8; OCH_3, 22.0.

(b) Preparation of the Disemicarbazone.—The monosemicarbazone (0.090 g.) was mixed with a solution of 0.050 g. of freshly-prepared, free semicarbazide in 10 cc. of eth-

anol and refluxed for five hours. The hot ethanol solution containing the insoluble disemicarbazone was filtered and the product recrystallized from hot water; short, colorless needles, insoluble in all common organic solvents; yield, 0.080 g., 75%; m. p. 239.0°.

Anal. Calcd. for $C_{13}H_{18}O_5N_6$: C, 46.2; H, 5.3; N, 24.9; OCH_3, 18.4. Found: C, 46.5; H, 5.6; N, 24.9; OCH_3, 18.4.

Alkaline Cleavage of Syringoylacetaldehyde.—Syringoylacetaldehyde (0.100 g.) dissolved in 5 cc. of water was placed in a small distilling flask, fitted with a reflux condenser ("cold finger") and then a stream of nitrogen, from which all traces of oxygen had been removed, was passed into the flask through the side-arm. When all of the oxygen had been removed, 1.2 g. of sodium hydroxide was added and the reaction mixture heated to 130–140° for twelve hours, a nitrogen atmosphere being maintained throughout. The solution was cooled, acidified with dilute sulfuric acid and extracted continuously with benzene. The benzene was removed and the residue sublimed at 117–125° (2 mm.). The white, crystalline sublimate was recrystallized from water; melting point 203–205°, a mixed melting point with authentic syringic acid showed no depression; yield, 0.026 g., 30%.

Action of Bisulfite Followed by Alkaline Cleavage.—A solution of 0.050 g. of syringoylacetaldehyde in 2 cc. of "sulfite cooking liquor" (containing 6% free sulfur dioxide and 1.1% combined sulfur dioxide) was placed in a small sealed tube and heated to 110° for twelve hours.

The sealed tube was cooled, opened, and the contents transferred by use of 3 cc. of water into a small distilling flask, fitted as in the preceding experiment. Sodium hydroxide (1.2 g.) was added as before, but inadvertently the oxygen was incompletely removed from the stream of nitrogen. The alkaline solution was heated to 135° for twelve hours, cooled, acidified and continuously extracted with benzene. The benzene solution was shaken with aqueous bisulfite (5%) and the bisulfite solution acidified and extracted with ether. The benzene solution left after the bisulfite treatment was evaporated to dryness and the residual dark brown solid sublimed at 115–120° (2 mm.). The sublimate was washed with cold petroleum ether (30–50°) and resublimed, m. p. 117–118°; a mixed melting point with authentic acetosyringone showed no depression; yield, 0.015 g., 34%.

The ether solution was treated in the same manner and yielded 0.008 g. of a white, crystalline sublimate which was shown by melting point (202–204°) and mixed melting point to be syringic acid.

Isolation and Identification of Syringaldehyde

(1) From the Crystalline Potassium Salt.—The mixture of the reddish-colored crystalline potassium salts (0.45 g.) was dissolved in 15 cc. of water and semicarbazide hydrochloride (0.30 g.) and potassium acetate (0.40 g.) added. The homogeneous reaction mixture was allowed to stand at room temperature for an hour, cooled to 0° and filtered. The crystalline precipitate was the monosemicarbazone of syringoylacetaldehyde obtained above; yield 0.22 g.

The filtrate was heated to 100° and then kept at 0° for several days. Clusters of short, colorless needles slowly formed throughout the solution. These were filtered off and dried. Recrystallization from water and methanol raised the melting point to 186–188° and a mixed melting point with an authentic sample of syringaldehyde semicarbazone showed no depression.

Anal. Calcd. for $C_{10}H_{13}O_4N_3$: OCH_3, 25.9. Found: OCH_3, 26.1.

(2) From the Crystalline Ammonium Salt.—To a solution of 0.10 g. of the ammonium salt, dissolved in 7 cc. of ethanol containing a few drops of concentrated hydrochloric acid, was added 0.085 g. of 2,4-dinitrophenylhydrazine, also dissolved in 5 cc. of ethanol–hydrochloric acid. The solution was allowed to stand at room temperature for four to six hours, during which period a voluminous red crystalline precipitate formed. The product was filtered off and recrystallized from ethyl acetate; yield, 0.165 g., 82%; m. p. 235–235.5°.

The 2,4-dinitrophenylhydrazone of an authentic sample of syringaldehyde was prepared in the same manner, m. p. 235.5–236.5°. A mixed melting point showed no depression.

Anal. Calcd. for $C_{15}H_{15}O_7N_4$: OCH_3, 17.2. Found: OCH_3, 17.3.

Acknowledgment.—The authors wish to thank the Carnegie Corporation of New York, the Canadian Pulp and Paper Association and the Spruce Falls Power and Paper Company for their kind financial assistance.

Summary

1. The water soluble "aldehyde fraction" obtained in the ethanolysis of maple wood has been shown to consist of a mixture of syringyl and guaiacyl derivatives, present in approximately equal amounts.

2. A method has been devised for the complete separation of syringyl constituents by precipitation of their insoluble potassium and ammonium salts.

3. The syringyl fraction has been shown to consist of syringoylacetaldehyde and syringaldehyde, present in approximately equal amounts.

4. Syringoylacetaldehyde has been isolated and completely characterized by analysis, preparation of derivatives, and degradation to known compounds.

5. The significance of the presence of syringaldehyde and syringoylacetaldehyde among the ethanolysis products from maple wood with regard to the structure of "protolignin" and their relation to the synthesis of plant pigments has been pointed out.

MONTREAL, CANADA RECEIVED JUNE 2, 1939

[CONTRIBUTION FROM THE DIVISION OF INDUSTRIAL AND CELLULOSE CHEMISTRY, MCGILL UNIVERSITY]

Studies on Lignin and Related Compounds. XLV. Synthesis and Properties of α-Hydroxypropiovanillone

BY A. B. CRAMER[1] AND HAROLD HIBBERT

In a previous communication the isolation of α-ethoxypropiovanillone from the ethanolysis products of spruce[2] and of maple woods[3] was described. The relation of these to the corresponding hydroxy derivatives in connection with the role of the latter as the possible precursors of lignin has been discussed in a comprehensive manner by Hibbert[4] in a recent paper.

The present communication deals with the synthesis and properties of α-hydroxypropiovanillone.

This synthesis was carried out by the following series of reactions

(1) Veratrole + α-bromopropionyl bromide $\xrightarrow{AlCl_3}$ α-bromopropiovanillone

α-bromopropiovanillone $\xrightarrow[\text{acetic anhydride}]{\text{sodium acetate}}$ α-acetoxypropiovanillone acetate

α-acetoxypropiovanillone acetate $\xrightarrow{\text{alcoholic potash}}$ α-hydroxypropiovanillone

Reaction (1), which is based on the synthesis of α-bromoacetovanillone,[5] is of interest in that condensation and demethylation occur simultaneously.

α-Bromopropiovanillone is a colorless, crystalline product (m. p. 105–106°), which on prolonged heating with organic solvents (such as petroleum ether), in which it is only slightly soluble, undergoes conversion to tarry materials. This did not occur with solvents such as ethanol in which it is readily soluble, so that its purification entailed considerable experimentation; yield 35%. Its conversion into the crystalline diacetate (m. p. 122–123°) in yield of 84% takes place quite smoothly. This acetate, on treatment with alcoholic potassium hydroxide, gives almost the theoretical yield (92%) of crystalline α-hydroxypropiovanillone, m. p. 109–110°.

Properties of α-Hydroxypropiovanillone.—The secondary hydroxyl group present in the side chain has certain rather remarkable properties. Thus it is etherified, as in the case of benzoin,[6] by ethanol–hydrogen chloride, but does not react with diazomethane. The carbonyl group, due to its location *para* to the phenol group, shows similar abnormal properties to those possessed by related substances,[7] such as *p*-oxybenzaldehyde, vanillin and certain syringyl derivatives. Thus in the Grignard machine[8] the amounts of active hydrogen and carbonyl addition, 1.75 and 0.75 moles, respectively (based on a molecular weight of 196), are much smaller than the theoretical values 2.0 and 1.0, respectively.

Action of Acids.—α-Hydroxypropiovanillone exhibits a similar, reactive behavior, on treatment with acids, to that shown by various benzoins.[9] When it is refluxed with dilute sulfuric acid (5%), methanol–hydrochloric acid or formic acid, amorphous lignin-like products are formed. The carbon content of these derivatives is high, namely, 70–70.3% as compared with values of 63.6–67% found for "extracted lignins."[10] Whether this is due to the presence of carbohydrate condensation products in the customarily "extracted" lignins or to a different type of polymerization–condensation reaction taking place in the plant, as compared with that brought about by acids,[10] can only be decided after considerable further experimentation.

It is of interest, however, that the analytical values for a condensation, furan trimer (A) of α-hydroxypropiovanillone, of the type shown below, are in agreement with the theoretical figures for the formic acid polymer. No great significance can, however, be attached to this until a more complete investigation (now in progress) has been completed.

The similarity, however, between (A) and the furan trimer (B) obtained by Japp and Meldrum[11]

(1) Postgraduate Student and holder of a Hibbert–Cole Scholarship.

(2) (a) Cramer, Hunter and Hibbert, THIS JOURNAL, **61**, 509 (1939); (b) Brickman, Pyle, McCarthy and Hibbert, *ibid.*, **61**, 868 (1939).

(3) Hunter, Cramer and Hibbert, *ibid.*, **61**, 516 (1939).

(4) Hibbert, *ibid.*, **61**, 725 (1939).

(5) Doig and Robertson, *J. Chem. Soc.*, **123**, 750 (1923).

(6) E. Fischer, *Ber.*, **26**, 2413 (1893).

(7) (a) Lock, *ibid.*, **61**, 2234 (1928); **62**, 1177 (1929); (b) Lieff, Wright and Hibbert, THIS JOURNAL, **61**, 865 (1939); (c) Hunter and Hibbert, *ibid.*, **61**, 2190 (1939).

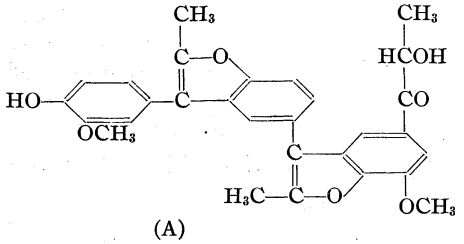
(8) Kohler, Fuson and Stone, *ibid.*, **49**, 3181 (1927); Kohler and Richtmyer, *ibid.*, **52**, 3736 (1930).

(9) Irvine and McNicol, *J. Chem. Soc.*, **93**, 950, 1609 (1908).

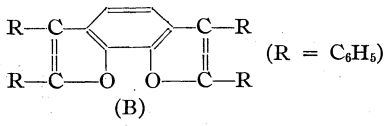
(10) Freudenberg, "Tannin, Cellulose, Lignin," Verlag von Julius Springer, Berlin, 1933, p. 118; Freudenberg, Zocher and Dürr, *Ber.*, **62**, 1816 (1929).

(11) Japp and Meldrum, *J. Chem. Soc.*, **75**, 1037 (1890).

by heating a mixture of benzoin and pyrocatechol with sulfuric acid (73%) is noteworthy.



(A)



(B)

Experimental Part

I. Synthesis of α-Hydroxypropiovanillone

Step I. Preparation of α-Bromopropiovanillone.—Aluminum chloride (Merck) (40 g.) was added to carbon disulfide (150 cc.) in a 3-necked flask fitted with stirrer, dropping funnel and condenser. Veratrole (40 g.) was added rapidly at room temperature through the dropping funnel over a period of twenty-five minutes, the solution being stirred vigorously. When the reaction had subsided, α-bromopropionyl bromide (66 g.) was added slowly (during sixty minutes) to the mixture, and a further 40 g. of aluminum chloride then added in small portions (during sixty minutes). After stirring vigorously for a further thirty minutes the mixture was allowed to stand overnight. The carbon disulfide was decanted, and the product decomposed with ice and concentrated hydrochloric acid. The crude, oily bromo compound was washed by stirring repeatedly with dilute hydrochloric acid followed by water, dilute sodium bicarbonate, and finally water. This crude moist product was dissolved in ether, and the solvent removed slowly from the solution, in an open dish, by drawing a stream of air over the surface. Crystals formed around the edges of the dish and were stirred into the main body of the product. The thick sirup on standing for a short time changed to a sticky granular mass. This was filtered and washed with a small amount of petroleum ether, leaving a comparatively pure bromo derivative. The filtrate was concentrated similarly by slow evaporation and again filtered, giving a second crop of crude α-bromopropiovanillone; yield of relatively pure α-bromopropiovanillone obtained from three crops of crystals was 35%.

A small amount was purified for analysis by recrystallization from a chloroform–petroleum ether mixture (1:3); m. p. 105–106°.

Anal. Calcd. for $C_9H_8O_2Br(OCH_3)$: C, 46.4; H, 4.24; Br, 30.9; OCH_3, 11.9. Found: C, 46.3; H, 4.40; Br, 31.2; OCH_3, 12.1.

Step 2. Preparation of α-Acetoxypropiovanillone Acetate.—Crude α-bromopropiovanillone (70 g.), anhydrous sodium acetate (140 g.) and acetic anhydride (490 cc.) were mixed in a one-liter flask and heated on the steam-bath for four hours. The mixture was then poured into five liters of water and stirred vigorously for four hours. The resulting oil crystallized rapidly and was filtered off, washed thoroughly with water, pressed dry on the Büchner funnel, and recrystallized from alcohol; yield 60 g. (84%); m. p. 122–123°.

Anal. Calcd. for $C_{12}H_{13}O_5(OCH_3)$: C, 60.0; H, 5.72; OCH_3, 11.05. Found: C, 59.8; H, 5.90; OCH_3, 11.08.

Step 3. Hydrolysis of α-Hydroxypropiovanillone Acetate.—The diacetate (54 g.) was dissolved in hot methanol (500 cc.) and a solution of potassium hydroxide (54 g.) in hot methanol (540 cc.) added. The mixture was warmed on the steam-bath for fifteen minutes and then cooled. On allowing to stand several hours the crystalline potassium salt of α-hydroxypropiovanillone settled out and was filtered off. Concentration of the filtrate gave a further crop of crystals.

The combined potassium salts were dissolved in 125 cc. of warm water and a slight excess of sulfuric acid (30–40%) added. The heavy oil which separated from the warm solution crystallized completely on scratching the sides of the flask. The reaction mixture was cooled to about 0° and filtered. The crystalline mass was washed several times with ice water, filtered, and dried in a vacuum desiccator; yield 34 g. (92%); m. p. 101°; recrystallized from benzene, m. p. 109–110°.

Anal. Calcd. for $C_9H_9O_3(OCH_3)$: C, 61.2; H, 6.12; OCH_3, 15.8. Found: C, 61.0; H, 6.21; OCH_3, 15.7.

II. Properties of α-Hydroxypropiovanillone

(1) **Etherification.**—α-Hydroxypropiovanillone (2 g.) was dissolved in absolute ethanol (50 cc.) containing 0.5% dry hydrogen chloride. The solution was allowed to stand at room temperature for seventy-two hours during which time it became dark brown in color. It was then refluxed for six hours and the solvent removed, leaving a black tarry residue. An attempt to isolate a pure ethoxy derivative from this by solvent extraction with boiling petroleum ether (60–70°) was unsuccessful. The product was therefore freed from the last traces of solvent at 100° (30 mm.) and distilled at 125–140° (0.005 mm.). There were obtained a clear, yellow, non-crystallizable sirup (0.6 g.) and a black tarry undistillable residue. Analysis indicated the former product to be α-ethoxypropiovanillone. The slightly lower alkoxyl, carbon and hydrogen values are due presumably to the presence of a small amount of unetherified product which it was not found possible to remove by a subsequent distillation or crystallization.

Anal. Calcd. for $C_{12}H_{16}O_4$: C, 69.3; H, 7.79; alkoxyl calculated as methoxyl, 29.8. Found: C, 68.5; H, 7.20; alkoxyl calculated as methoxyl, 28.9.

(2) **Methylation with Diazomethane.**—α-Hydroxypropiovanillone (1 g.) was dissolved in ether (100 cc.) and to this an ethereal solution containing two equivalents of diazomethane was then added. The mixture was allowed to stand overnight, filtered from the diazomethane polymer and the ether removed. The product on distillation (130–150° (0.010 mm.)) yielded a clear yellowish-colored, highly viscous sirup which could not be caused to crystallize. Calcd. for $C_9H_8O_2(OCH_3)_2$: OCH_3, 28.5. Found: OCH_3, 28.1.

(3) **Grignard Analysis.**—Calcd. for α-hydroxypropiovanillone: active hydrogen 2.0 moles; carbonyl addition

1.0 moles, per molecular weight of 196. Found: 1.75 and 0.75, respectively.

(4) Action of Acids on α-Hydroxypropiovanillone

(a) Sulfuric Acid (5%).—α-Hydroxypropiovanillone (1 g.) was refluxed with 50 cc. of sulfuric acid (5%) for twenty-four hours. The resulting dark brown insoluble material was filtered, washed with water, dissolved in acetone (10 cc.) and precipitated into water (200 cc.). The flocculent precipitate was centrifuged, the liquors discarded and the product dried in the vacuum desiccator. It was redissolved in chloroform (10 cc.) and reprecipitated into petroleum ether (b. p. 60–70°) (200 cc.). The centrifuged material was stirred with petroleum ether (b. p. 30–50°), centrifuged and dried in the vacuum desiccator; yield 0.25 g. (25%). The light brown amorphous product was soluble in alkali. *Anal.* Found: C, 70.0; H, 4.94; OCH_3, 17.1.

(b) Methanolic Hydrogen Chloride.—α-Hydroxypropiovanillone (1 g.) treated similarly with a 5% solution of anhydrous hydrogen chloride in methanol (20 cc.) gave a similar dark colored, alkali-soluble, amorphous product; yield, 31%. *Anal.* Found: C, 70.3; H, 4.96; OCH_3, 20.6.

(c) Formic Acid (95%).—α-Hydroxypropiovanillone (1 g.) was treated in the same manner with 95% formic acid (20 cc.). The dark colored, alkali-soluble reaction product was purified similarly. *Anal.* Found: C, 70.0; H, 5.86; OCH_3, 17.3. A condensation trimer of type (A), $C_{27}H_{21}O_5(OCH_3)_3$ (mol. wt. 518) requires C, 69.5; H, 5.8; OCH_3, 17.9.

Acknowledgment.—The authors wish to thank the Carnegie Corporation of New York for kind financial assistance.

Summary

1. A description is given of the synthesis of α-hydroxypropiovanillone, a possible precursor of lignin, and of its behavior toward diazomethane and the Grignard reagent.

2. Hot dilute sulfuric acid, methanol–hydrochloric acid and formic acid (95%) convert it into alkali-soluble, lignin-like products.

MONTREAL, CANADA RECEIVED JUNE 20, 1939

[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY, HARVARD UNIVERSITY]

Synthesis of Quinones Related to Vitamins K_1 and K_2

BY LOUIS F. FIESER, WILLIAM P. CAMPBELL[1] AND EDWARD M. FRY[2,3]

In a recent Communication[4] we advanced structural formulas for the antihemorrhagic vitamins which Doisy and co-workers[5] isolated in a condition of demonstrated purity, and there are now further indications that our conception of the structures is essentially correct. Of particular importance is the degradative work on vitamin K_1 by the Doisy group,[6] reported in a Communication submitted about the same time as ours.

Since the evidence from the degradations is still incomplete and in some points uncertain, we shall include in the present paper a fuller account of the previous deductions and report certain observations of significance made in a study of synthetic model substances.

Following Doisy's report of the quinonoid character of vitamins K_1 and K_2, Dr. R. N. Jones pointed out to us that in absorption spectra[5,7] the substances resemble 1,4-naphthoquinones more closely than quinones of other series. Such a structure would account for the known lability to light,[8,9] heat,[5a] and alkali,[7] for the yellow color and for the sensitivity of the hydroquinones to air oxidation.[5b] Anthraquinones possess the last-named property but are far more stable substances. The next clue was the resistance of the dihydro vitamin diacetates to alkaline hydrolysis,[5b] which suggested the presence of hindering substituents in the 2 and 3 positions adjacent to the acetoxyl groups, and an entirely analogous behavior has been encountered in 2,3-diallyl-1,4-naphthohydroquinone diacetate. Hindering substituents are also indicated by the failure of vitamin K_1 concentrates to react with carbonyl reagents.[10,11] From these considerations it seemed

(1) Squibb Research Fellow.

(2) Du Pont Research Fellow.

(3) We are indebted to Mary Fieser and Marshall D. Gates, Jr., for the participation in the synthetic work indicated in the Experimental Part and to Dr. R. Norman Jones and Douglas M. Bowen for the determination of the absorption spectra.

(4) Fieser, Bowen, Campbell, M. Fieser, Fry, Jones, Riegel, Schweitzer and Smith, THIS JOURNAL, **61**, 1925 (1939).

(5) (a) McKee, Binkley, MacCorquodale, Thayer and Doisy, *ibid.*, **61**, 1295 (1939); (b) Binkley, MacCorquodale, Cheney, Thayer, McKee and Doisy, *ibid.*, **61**, 1613 (1939).

(6) MacCorquodale, Binkley, Thayer and Doisy, *ibid.*, **61**, 1928 (1939).

(7) Dam, Geiger, Glavind, P. Karrer, W. Karrer, Rothschild and Solomon, *Helv. Chim. Acta*, **22**, 310 (1939).

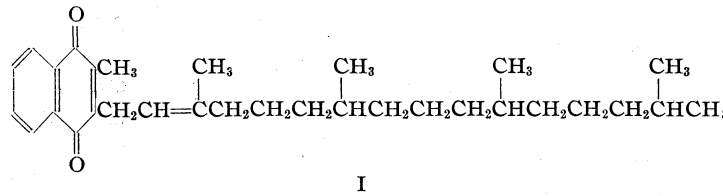
(8) Almquist, *J. Biol. Chem.*, **117**, 517 (1937); **120**, 635 (1937).

(9) MacCorquodale, Binkley, McKee, Thayer and Doisy, *Proc. Soc. Expil. Biol. Med.*, **40**, 482 (1939).

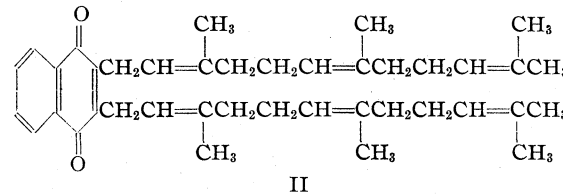
(10) Klose, Almquist and Mecchi, *J. Biol. Chem.*, **125**, 681 (1938). These investigators observed that the antihemorrhagic activity is not destroyed by reduction and concluded that the vitamin is inert to reducing agents, but it is now evident that reoxidation could have occurred before the test was made.

(11) Riegel, Schweitzer and Smith, in press (personal communication from Dr. Riegel).

likely that both vitamins are 2,3-dialkyl-1,4-naphthoquinones, and this was further supported by preliminary data on the oxidation–reduction potential of alfalfa concentrates of which Dr. Byron Riegel kindly informed us.[4]



I



II

If the vitamins are 1,4-naphthoquinones they must, according to Doisy's analyses,[5] have one or more long side chains containing a certain number of double bonds. If the values for the hydrogen absorption observed by Doisy[5a] in microhydrogenation experiments were due entirely to saturation of such linkages, vitamin K_1 would have three side chain double bonds and vitamin K_2 would have eight, but in the naphthoquinone series such a formulation would not be compatible with the analytical figures. We therefore assumed that under the as yet unreported conditions of the hydrogenation the reaction proceeded beyond the first possible stopping point and resulted in saturation of the oxygen-free ring of the naphthalene nucleus, giving a 5,6,7,8-tetrahydro-1,4-naphthohydroquinone which could revert to a quinone on air oxidation,[5a] an interpretation also reached by Doisy.[6] This would mean that vitamins K_1 and K_2 have 1 and 6 lateral double bonds, respectively.

It then occurred to us that the presence of a phytyl group in vitamin K_1 and of two farnesyl groups in vitamin K_2 not only would satisfy these unsaturation requirements but also would give structures of the observed carbon content, interpreted by Doisy[5a] in terms of C_{32} and C_{40} formulas, respectively. It was postulated that vitamin K_1 has the basic structure of 2-methyl-3-phytyl-1,4-naphthoquinone (I), with or without a second methyl group in the benzenoid ring, and that vitamin K_2 is 2,3-difarnesyl-1,4-naphthoquinone (II). There is a certain amount of coincidental circumstance to lend appeal to the hypothesis, considered as a whole. It is striking that among the radicals of the known naturally occurring alcohols those two which give the correct degree of unsaturation are also those which provide the proper number of carbon atoms in the side chains. Naphthoquinone and methylnaphthoquinone derivatives are widely distributed in nature, and it is perhaps significant that the vitamin regarded as a phytyl derivative occurs along with the phytol-containing chlorophyll in green leaves.[12]

According to formula I an interesting relationship exists to another type of vitamin (E). α-Tocopherol apparently arises in nature by the nuclear substitution of a phytyl group into trimethylhydroquinone, followed by ring closure between a hydroxyl group and the double bond in the side chain; vitamin K may arise by a similar condensation of phytol with a 2-alkyl-1,4-naphthohydroquinone, followed by oxidation. The occurrence of vitamin K_2 in putrefied fish meal (Doisy[5a]) is also suggestive of a significant relationship, for the farnesyl group postulated to be present in this substance is associated structually with squalene, a known constituent of fish liver oils, which has the structure di-farnesyl.

According to the suggested structures the vitamins are further related to the natural products lapachol and lomatiol, for these substances are 1,4-naphthoquinones having β-unsaturated, isoprenoid side chains. It is to be noted that the yellow color of the vitamins rules out alternate formulas with double bonds adjacent to the quinonoid nucleus, for such substances are all red or orange.[13] Also of significance is the fact that the spectrum of the highly unsaturated vitamin K_2 is very similar to that of vitamin K_1 and gives no indication of conjugation in the side chains. The distribution of the six double bonds according to the farnesyl pattern is one of a very limited number of ways possible which avoid both conjugation and α-unsaturation.

As mentioned above, Doisy[5] interpreted the analytical results with carefully purified vitamin K_1 in terms of the empirical formula $C_{32}H_{48}O_2$ or $C_{32}H_{50}O_2$. In accordance with the first formula we originally considered the possibility that the substance has a structure similar to I but with a second methyl group in the benzenoid nucleus,

(12) Dam, *Z. Vitaminforsch.*, **8**, 248 (1939).

(13) Hooker, THIS JOURNAL, **58**, 1163, 1174 (1936).

for example at position 6. Our observation[14] that the model substance 2,6-dimethyl-3-allyl-1,4-naphthoquinone has an absorption curve very similar to that of vitamin K_1 but shifted to a considerable extent in the direction of longer wave length led us recently to question the presence of this second nuclear substituent, and Doisy's isolation of phthalic acid as an oxidation product of the vitamin[6] now proves definitely that the benzenoid ring is not substituted. Doisy also has obtained evidence from ozonization experiments which already provides a strong indication of the presence of the phytyl group. In accordance with the C_{32}-formulation, and on the basis of the isolation of an as yet unidentified oxidation product having the composition of 2-ethyl-1,4-naphthoquinone-3-acetic acid, Doisy has suggested the structure of 2-ethyl-3-phytyl-1,4-naphthoquinone. Until the evidence is complete there is little choice between this structure and that of the lower homolog I. We may point out that the C_{31}-formulation is entirely admissible on the basis of the available analytical data, as shown in the table, and that the occurrence of methylnaphthoquinones is common while ethyl derivatives have not previously been encountered.

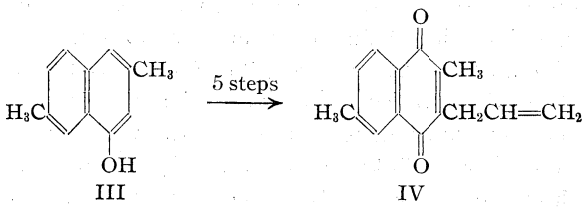
TABLE I

ANALYSES BY DOISY AND CO-WORKERS

	C, %		H, %	
Calcd. for $C_{31}H_{46}O_2$	82.61		10.29	
Vitamin K_1, purified[5a]	82.76	82.54	10.65	10.66
Regenerated from derivative[5b]	82.34		10.13	
Calcd. for $C_{35}H_{52}O_4$	78.31		9.77	
Dihydro K_1 Diacetate[5b]	78.21	78.01	10.07	10.03

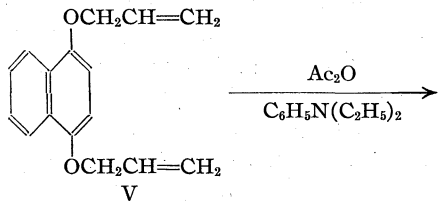
Methods of Synthesis.—In undertaking synthetic work on the problem we thought it of importance first of all to investigate the properties of reasonably accessible allyl derivatives of α-naphthoquinone even though the methods of preparation might not be directly applicable to the synthesis of the vitamins. Thus the allyl group is introduced into phenols more conveniently by the Claisen rearrangement than by direct allylation of the sodium salt, while the introduction of higher β-unsaturated groups of the desired structure from the available primary halides would require the use of the second method (which is now under investigation).

2-Allyl-1,4-naphthoquinone was obtained from the known 2-allyl-1-naphthol by the standard procedure of coupling with diazotized sulfanilic acid, reduction with hydrosulfite, and oxidation employed previously on numerous occasions in this Laboratory. Hydrogenation, followed by reoxidation of the hydroquinone, gave the 2-*n*-propyl derivative, which was obtained as well from the intermediate allylaminonaphthol. In the same way 2,6-dimethyl-8-naphthol (III) was



III IV

converted through the allyl ether to the 3-allyl derivative and thence to 2,6-dimethyl-3-allyl-1,4-naphthoquinone, IV, which presents an interesting analogy to the structure I. In one of two routes developed for the synthesis of a simple model for structure II, α-naphthohydroquinone was first allylated by Claisen's allyl bromide–potassium carbonate–acetone procedure. The yield was poor, possibly because of appreciable C-allylation,



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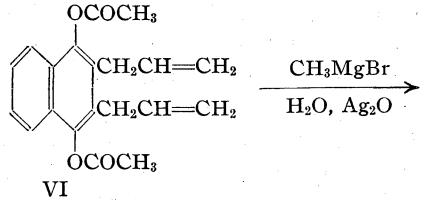

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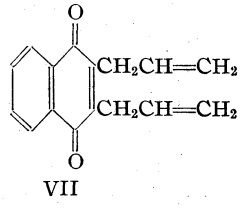


VII

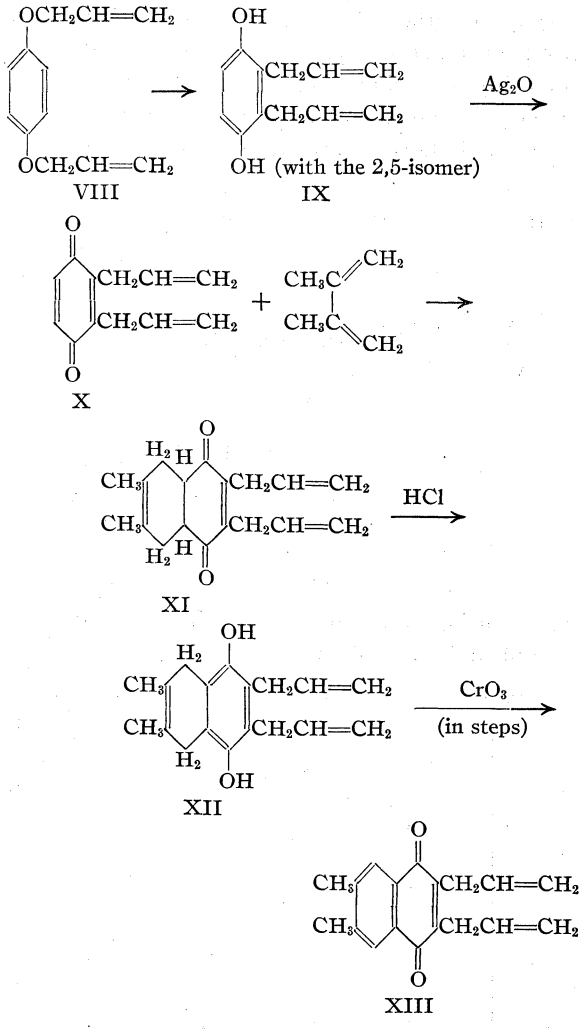
and the crystalline ether V could not be rearranged satisfactorily by the usual methods because of the sensitivity of the product. Good use was made, however, of the device employed on a previous occasion[15] of heating the allyl ether with acetic anhydride in diethylaniline solution. The sensitive hydroquinone is protected as formed by

(14) Fieser, Bowen, Campbell, Fry and Gates, THIS JOURNAL, **61**, 1926 (1939).

(15) Fieser and Lothrop, *ibid.*, **58**, 749 (1936).

acetylation and the diacetate VI is obtained in excellent yield. The hindered character of the acetoxyl groups of this compound and its analogy to the corresponding vitamin derivatives already has been mentioned. The best method found for effecting hydrolysis is exactly that employed in the vitamin series by Doisy,[5b] namely, interaction with a methyl Grignard reagent and oxidation in ethereal solution with either air or silver oxide. The resulting 2,3-diallyl-1,4-naphthoquinone (VII) is a low melting yellow solid (m. p. 29–30°) resembling the vitamins in general properties. When the diacetate VI was refluxed for prolonged periods with ethyl or *n*-butylmagnesium bromide the reagent apparently exerted a reducing action, for there was isolated a small amount of a quinone having two hydrogen atoms more than the normal product VII. The spectrum[4] is very similar to that of 2,3-dimethyl-1,4-naphthoquinone, showing that the naphthoquinone nucleus is intact and that the reduction occurs in the side chain or chains, possibly with condensation to give a third ring.

Another route to 2,3-diallyl derivatives of 1,4-naphthoquinones was found starting with hydroquinone diallyl ether. This method was based upon preliminary observations of H. B. Dunkle.[16] The diallyl ether VIII rearranges smoothly when heated in kerosene solution, from which the phenolic product crystallizes, giving a mixture of two isomers. The higher melting substance presumably is 2,5-diallylhydroquinone, but the structure was not established; the other compound is identified as the 2,3-isomer IX by the successful outcome of the following synthesis. The corresponding quinone X, employed as an unpurified oil, was condensed with 2,3-dimethylbutadiene and the product (XI) isomerized with acid to the dihydronaphthohydroquinone XII. As with simpler examples reported in the patent literature,[17] it was found that treatment of this with chromic acid under rather mild conditions gives a yellow crystalline complex intermediate in composition between the desired naphthoquinone and its dihydride. Further oxidation with excess reagent at 90–100° gave the unsaturated naphthoquinone derivative XIII in a pure condition and in reasonably good yield; probably a portion of the quinone is exhaustively oxidized to easily



eliminated products. Similar intermediate complexes were isolated in syntheses of 6,7-dimethyl-1,4-naphthoquinone and 2,3-diallyl-1,4-naphthoquinone involving the same type of oxidation. The substances do not have the deep color characteristic of quinhydrones and their nature is still obscure.

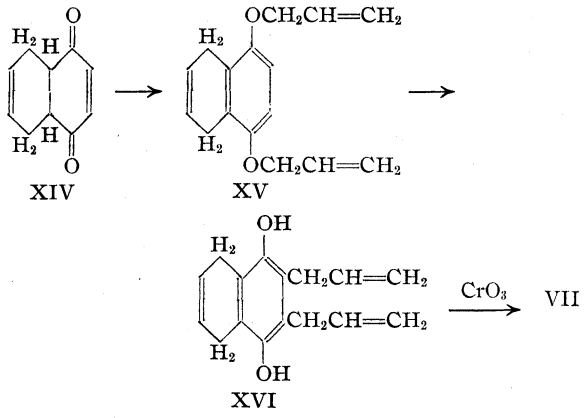
The above diene synthesis makes possible the introduction of substituents in the benzenoid nucleus of the naphthoquinone. By reversing the sequence of the Claisen rearrangement and the diene addition a practical method was found which permits variation in the nature of the unsaturated side chain. The product XIV of the addition of butadiene to quinone is known to be isomerized easily by acids or bases to 5,8-dihydro-1,4-naphthohydroquinone,[18] and it was found that the change occurs in the presence of potassium carbonate, allyl bromide, and acetone, for the

(16) H. B. Dunkle, Dissertation, Harvard University, 1937.

(17) I. G. Farbenindustrie A.-G., English Patent 324,661 (1930); German Patent 521,621 (1931) [*Chem. Zentr.*, **101**, 2, 809 (1930); **102**, 2, 1758 (1931)].

(18) Diels and Alder, *Ber.*, **62**, 2337 (1929).

crystalline ether XV was obtained satisfactorily from this reaction mixture. The ether rearranged smoothly in boiling kerosene to XVI, and the latter on stepwise oxidation with chromic acid gave 2,3-diallyl-1,4-naphthoquinone, identical



with the material obtained by the synthesis from α-naphthohydroquinone.

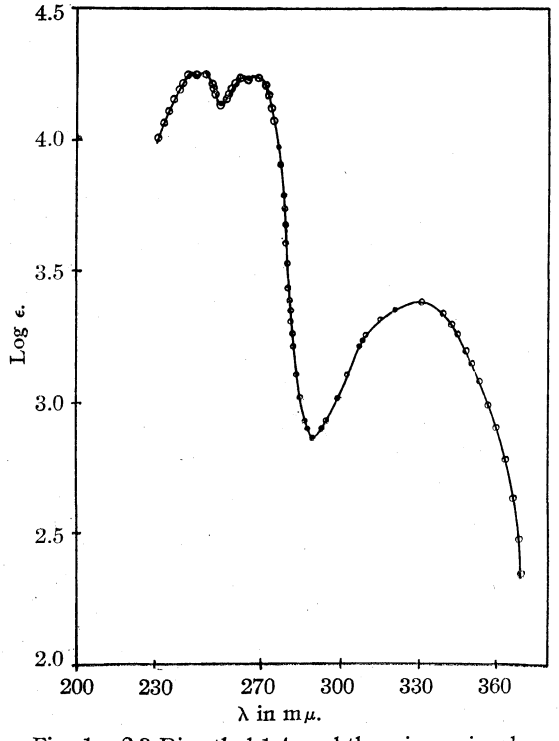


Fig. 1.—2,3-Dimethyl-1,4-naphthoquinone in absolute alcohol. Maxima in mμ (with log ε values in parentheses): 243, 249 (4.26); 262, 267 (4.24); 330 (3.38).

Absorption Spectra.—Table II of our second Communication[14] summarizes the spectrographic data on most of the above synthetic naphthoquinones except the 2,3-diallyl derivative, and the

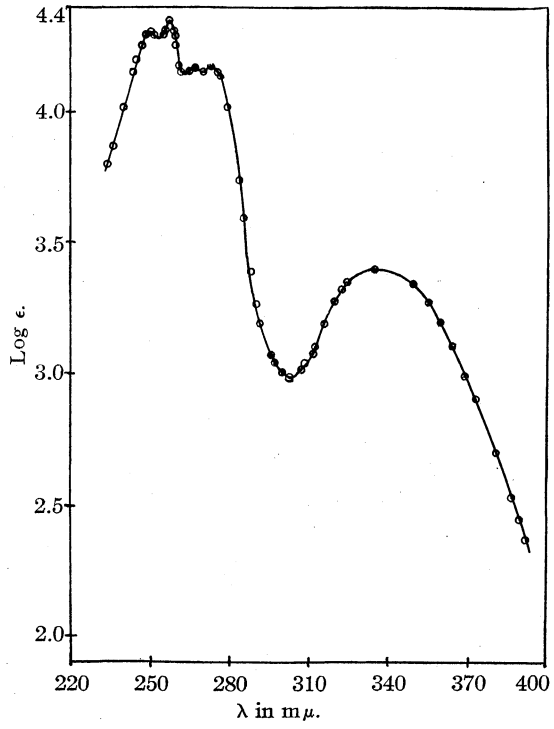


Fig. 2.—2,6-Dimethyl-3-allyl-1,4-naphthoquinone in absolute alcohol. Maxima in mμ: 249 (4.30), 256 (4.35); 265, 272 (4.17); 335 (3.39).

absorption curves for this and other compounds of interest are given in Figs. 1–4. The only set of complete data for comparison consists in the curve published by Dam, Karrer, *et al.*,[7] for a purified preparation from alfalfa consisting largely of vitamin K_1, but the positions of the maxima are very close to those reported by Doisy[5] for pure K_1. According to Doisy vitamins K_1 and K_2 are spectrographically almost identical. As the chief characteristics the spectra show two intense bands, centering in the neighborhood of 245 and 265 mμ, and a broader band of low intensity at about 324 mμ. The first intense band shows some evidence of resolution, with maxima at 243 and 248 mμ (Doisy, K_1) while the second one has definite fine structure with peaks at 261 and 270 mμ (K_1 and K_2). In comparing the synthetic compounds with the vitamins it is significant that naphthoquinones which depart appreciably from the suggested structures I and II of 2,3-dialkyl derivatives diverge considerably in spectrographic characteristics. Thus the 2,6-dimethyl compound has only one intense absorption band and the 2-methyl derivative has two such bands but both are lacking in fine structure. 2,3-Dimethyl-1,4-naphthoquinone, however, gives

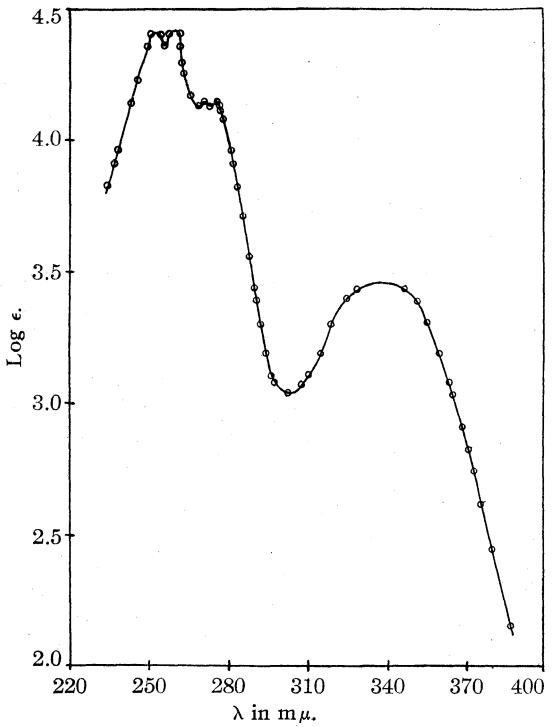


Fig. 3.—6,7-Dimethyl-2,3-diallyl-1,4-naphthoquinone in hexane. Maxima in mμ: 253, 260 (4.41); 271, 276 (4.14); 338 (3.46).

indications of resolution in the first intense band and the second one is definitely resolvable. This fine structure was first pointed out to us by Dr. T. J. Webb of the Merck Research Laboratories, and decisive evidence on the question has been obtained through the kind coöperation of Dr. H. H. Darby, Columbia University. Dr. Darby examined the plates prepared by D. M. Bowen using the Krüss densitometer at the Bartol Institute and found unquestioned resolution of the second band, as shown in Fig. 1, and probable resolution of the first band. In both the positions and the special characteristics of all three principal absorption bands this 2,3-dialkyl-1,4-naphthoquinone corresponds very closely with the natural vitamins, and the only difference is that in the Dam–Karrer curve the second intense band is somewhat less intense than the first. This same characteristic is met with in 2,6-dimethyl-3-allyl-1,4-naphthoquinone (Fig. 2), and indeed the form of the curve throughout almost duplicates that given by Dam, Karrer, *et al.* The reading of the plates in this case was verified by Dr. Darby with the densitometer and the more accurate values for the maxima are recorded in the legend of Fig. 2. The whole curve for the 2,6-dimethyl-3-allyl compound, however, is shifted about 5 mμ toward the red end of the spectrum, and we interpret this difference as due to the presence of a 6-methyl group in the model substance and not in the vitamins. A smilar and even more pronounced shift (av. 11 mμ) is observable in the 6,7-dimethyl-2,3-diallyl compound (Fig. 3) as compared with 2,3-diallyl-1,4-naphthoquinone (Fig. 4). Examination of the previously reported[14] data for 2-allyl-1,4-naphthoquinone will show that a second band of high intensity is clearly resolvable only when hexane is used as the solvent and that this is relatively closer to the first band than in the case of the synthetic 2,3-dialkyl derivatives and the natural vitamins; the 2-allyl compound indeed seems related more closely to the 2-methyl quinone than to these substances.

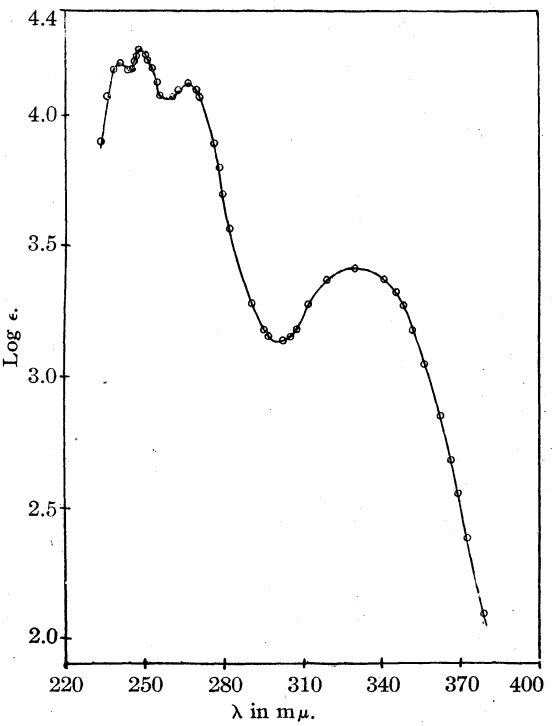


Fig. 4.—2,3-Diallyl-1,4-naphthoquinone in absolute alcohol. Maxima in mμ: 240 (4.20); 249 (4.24); 267 (4.12); 330 (3.42).

The spectrographic evidence as a whole provides convincing evidence for the proposed formulations I and II. From the form of the curves and the positions of the maxima it is evident that 2,3-dimethyl and 2,3-diallyl-1,4-naphthoquinone constitute very close optical models for the vitamins, whereas nuclear homologs and compounds lacking the feature of 2,3-disubstitution depart signifi-

cantly from the natural pattern. An alteration in the size of the alkyl substituents in the quinonoid ring clearly does not influence the spectrum, and 2-methyl and 2-ethyl-3-phytyl-1,4-naphthoquinone would of course be spectrographically equivalent.

Bio-assays.—We had hoped to gain an insight into the nature of the antihemorrhagic vitamins from a knowledge of the biological properties of synthetic models, and we are of course also interested in producing synthetic vitamins or synthetic substitutes. Indeed Doisy's isolation[5a] of two antihemorrhagically active substances differing by as much as eight or nine carbon atoms and containing from one to six lateral double bonds adequately demonstrates that vitamin K activity is not specific to a single structure. Our new compounds, as well as various known substances, have been examined in exploratory assays by Dr. W. L. Sampson of the Merck Institute, through the courtesy of Dr. R. T. Major, and most of the results have been reported in our two Communications.[4,14] These assays by the rapid Ansbacher procedure[19] were recognized as preliminary and now seem rather uncertain. Thus 2-allyl-1,4-naphthoquinone gave evidence of high vitamin K potency in an assay with one series of chicks[14] but in a subsequent test it appeared to be inactive even at a higher dosage level. A similar inconsistency appears in recent reports concerning 2-methyl-1,4-naphthoquinone. The Doisy group[20] find the 2-methyl compound to be only slightly more potent than phthiocol, which various workers have described as greatly inferior to the natural vitamins in activity.[20,21,22] Ansbacher and Fernholz,[22] on the other hand, state that 2-methyl-1,4-naphthoquinone is practically as active as vitamin K. Evidently the rapid assay procedures require considerable further investigation for application to the testing of pure compounds, and for the present it is necessary to reserve judgment on the preliminary results.

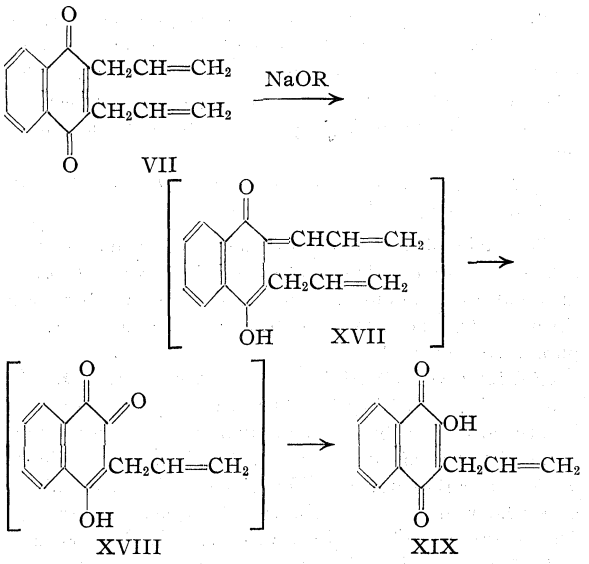
Dr. Sampson has tested three compounds from our Laboratory by the Almquist procedure.[23] Lapachol, tested at a level of 8 mg. and 15 mg. per kilogram of diet was entirely inactive, as was lomatiol at the 5-mg. and 10-mg. levels. Almquist and Klose obtained similar results at still higher levels. 2,3-Dimethyl-1,4-naphthoquinone was dosed at 8 mg., 3 mg., and 0.5 mg. The 8 mg. level was about as effective as 2 g. of the Walker–Gordon standard, giving an average blood clotting time of 7.5 minutes for 8 birds (two prolonged). The birds on the two lower doses were but slightly different from the controls.

Color Reaction with Sodium Ethylate.—Dam, Karrer, *et al.*,[7] reported that their highly purified vitamin K_1 preparation gave with sodium ethylate in alcohol a transient purple color changing to reddish-brown, and Almquist and Klose[24] have published an extensive comparison of the color reactions and bio-assays of concentrates which strongly indicates that the color is due to the vitamin. Fernholz, Ansbacher and Moore,[25] however, question this conclusion and the matter is still unsettled; unfortunately the behavior of pure vitamins K_1 and K_2 in the color reaction has not been reported.

The response of our synthetic models to treatment with alcoholic alkalies presents certain points of special interest. All of the above 1,4-naphthoquinones containing at least one allyl group in the quinonoid ring give strikingly beautiful purple or blue solutions changing in a minute or two to dull brown-red, whereas naphthoquinones containing saturated alkyl groups show no purple or blue phase. The contrast between 2-allyl and 2-*n*-propyl-1,4-naphthoquinone is so marked that the color test was used to determine when traces of the former substance had been removed completely from a preparation of the latter.

Speculating on the nature of the changes involved, we were impressed by a similarity to observations on the behavior of 2-hydroxy-3-alkenyl-1,4-naphthoquinones on treatment with sodium acetate and acetic anhydride. Lapachol gives an unusual reaction product referred to in the early literature as Paternò's isolapachone, and the structure of this substance was fully established in the later researches of Hooker.[26] In connection with a recent study of the tautomerism of certain alkylated β-naphthoquinones in this Laboratory,[27] the abnormal reaction was interpreted as involving in the essential step a tautomeric shift of hydrogen from the activated methylene group between the unsaturated quinone ring and the external double bond and it was noted that similar

(19) Ansbacher, *J. Nutrition*, **17**, 303 (1939).
(20) Thayer, Cheney, Binkley, MacCorquodale and Doisy, THIS JOURNAL, **61**, 1932 (1939).
(21) Almquist and Klose, *ibid.*, **61**, 1923 (1939).
(22) Ansbacher and Fernholz, *ibid.*, **61**, 1925 (1939).
(23) Almquist, Mecchi and Klose, *Biochem. J.*, **32**, 1897 (1938).
(24) Almquist and Klose, THIS JOURNAL, **61**, 1610 (1939).
(25) Fernholz, Ansbacher and Moore, *ibid.*, **61**, 1613 (1939).
(26) Hooker, *ibid.*, **58**, 1190 (1936).
(27) Fieser and Fieser, *ibid.*, **61**, 596 (1939).



abnormal acylations occur with the 3-allyl[28] and 3-benzyl derivatives of 2-hydroxy-1,4-naphthoquinone, but not with substances having no activating double bond or phenyl group attached to the α-carbon atom of the side chain.

Applied to the case at hand, these inferences suggested that the color reaction of 2,3-diallyl-1,4-naphthoquinone, for example, may be due to a similar tautomeric shift to the hydroxyquinonemethane XVII, the intense color being due to the orthoquinonoid group and salt formation with the acidic hydroxyl substituent. Such an intermediate might well be subject to fission by hydrolysis, or by some process involving disproportionation and cleavage, and we consequently sought to isolate the pigment from the dull red end solution by a procedure adapted to the properties of a 2-hydroxy-3-alkyl-1,4-naphthoquinone. These substances are strongly acidic and give cherry-red or orange-red solutions in aqueous sodium carbonate, and indeed soda extraction of the pigment from the 2,3-diallyl compound gave an easily purified yellow substance identified as 2-hydroxy-3-allyl-1,4-naphthoquinone by analysis and by direct comparison with a sample available from a previous synthesis.[28] The color reaction with alcoholic alkali, which in the above case goes to completion at room temperature in less than ten minutes, thus involves the cleavage of one allyl group and its replacement by hydroxyl. 2-Allyl-1,4-naphthoquinone similarly gives a substance very probably identical with 2-hydroxy-1,4-naphthoquinone.

(28) Fieser, THIS JOURNAL, **48**, 3201 (1926).

This observation probably is of considerable significance to the vitamin K problem although application of the information must remain somewhat uncertain until more is known of the behavior of the vitamins. If the pure substances K_1 and K_2 are found to give the color test, the present experiments will afford a good indication of the presence of a β-unsaturated side chain. Furthermore, it should be possible to degrade vitamin K_1 to phthiocol or to the ethyl homolog, and to convert K_2 to a 2-hydroxy-3-alkyl(farnesyl ?)-1,4-naphthoquinone which should be obtainable by a known process of synthesis.[28,29]

Of considerable interest is the observation of Almquist and Klose[21] that the pigment resulting as the end-product of the action of sodium methylate on vitamin K concentrates gives color changes and tests very similar to those exhibited by phthiocol and its homologs. This provides at least a preliminary confirmation of the above prediction and encourages us to mention tentatively a further speculation. Almquist and co-workers[30] have demonstrated that various bacteria are capable of producing vitamin K, including *Mycobacterium tuberculosis*, from which Anderson and Newman[31] isolated phthiocol. Since their isolation procedure involved saponification with alcoholic potassium hydroxide, it is conceivable that the phthiocol was not a true natural constituent of the organism but arose as a product of the alkaline cleavage of vitamin K_1 or a homolog.

Experimental Part[32]

2-Allyl- and 2-*n*-Propyl-1,4-naphthoquinone (W. P. C.).—2-Allyl-1-naphthol was prepared from α-naphthol by allylation in acetone and rearrangement of the ether according to Claisen and Eisleb[33]; over-all yield 67%, b. p. 144° at 4 mm. The coupling of this substance (2.02 g.) with diazotized sulfanilic acid and reduction of the dye was conducted by exactly the procedure given for α-naphthol[34] except that more water was required in dissolving the amine hydrochloride, which is rather sparingly soluble. After one recrystallization from a solution containing excess hydrochloric acid and a trace of stannous chloride, **2-allyl-4-amino-1-naphthol hydrochloride** was obtained as colorless needles; yield 1.60 g. (62%). The sample for analysis was dried at 110° and 15 mm.

Anal. Calcd. for $C_{13}H_{14}ONCl$: N, 5.94. Found: N, 5.90 (Kjeldahl).

(29) Synthesis of lapachol, Fieser, *ibid.*, **49**, 857 (1927).

(30) Almquist, Pentler and Mecchi, *Proc. Soc. Exptl. Biol. Med.*, **38**, 336 (1938).

(31) Anderson and Newman, *J. Biol. Chem.*, **101**, 773 (1933).

(32) All melting points are corrected. Microanalyses by Lyon Southworth and Herbert S. Wight.

(33) Claisen and Eisleb, *Ann.*, **401**, 21 (1913).

(34) Fieser and Fieser, THIS JOURNAL, **57**, 491 (1935); Fieser, *Org. Syn.*, **17**, 9 (1937).

2-Allyl-1,4-naphthoquinone.—On adding a solution of 2.7 g. of ferric chloride crystals and 1 cc. of concentrated hydrochloric acid in 5 cc. of water to a solution of 1 g. of the above hydrochloride and 0.5 cc. of concentrated hydrochloric acid in 90 cc. of warm water the solution turned deep orange and deposited a greenish-black solid. After cooling, this was collected and extracted while moist with ether and the solution was clarified with Norite and evaporated. The yellow residue was obtained crystalline from ether–petroleum ether and afforded 0.65 g. (76%) of product in the form of yellow needles melting constantly at 36–36.5°.

Anal. Calcd. for $C_{13}H_{10}O_2$: C, 78.77; H, 5.09. Found: C, 78.82; H, 5.14.

The quinone darkens rapidly in direct sunlight. It reacts with acetic anhydride–sulfuric acid in the cold to give an apparently colorless substance very soluble in organic solvents. It is very readily soluble in ether or alcohol, less so in petroleum ether, and sparingly soluble in water. On adding 0.5 cc. of a solution prepared from 0.5 g. of sodium and 25 cc. of alcohol (95%) to a solution of 1–2 mg. of the quinone in 1 cc. of alcohol the solution at once acquires an intense, vivid purple color, and after about one minute this changes to dull red. The color changes were similar when 2 cc. of 10% aqueous potassium hydroxide was added to 0.2 g. of the quinone in 5 cc. of alcohol (L. F. F.); on diluting and acidifying the red solution a gelatinous precipitate separated which yielded only a trace of a yellow hydroxyquinone on extraction with ether or hot water. In repeating the experiment two drops of 30% hydrogen peroxide was added to the alcoholic solution and after dilution of the final red solution this was extracted with ether and the acidic material separated with soda solution, taken into ether, crystallized from dilute alcohol, and sublimed. There was obtained 5 mg. of yellow material giving the color reactions of hydroxynaphthoquinone and melting at 178–180°, dec. Mixed with an authentic sample, m. p. 186–188°, dec., the m. p. was 180–181°. The purple phase in the color test is seen best in a dilute solution with a very small amount of alkali. With one drop of 10% methyl alcoholic potassium hydroxide added to 1–2 mg. of the quinone in 25 cc. of alcohol the solution becomes so strongly purple that it is not transparent when viewed lengthwise in a 2 × 15-cm. test-tube and the purple phase persists for about thirty minutes before fading.

2-*n*-Propyl-1,4-naphthoquinone.—On shaking a solution of 2 g. of the allylaminonaphthol hydrochloride in 200 cc. of water with 0.1 g. of Adams catalyst and hydrogen, one mole of gas was absorbed in about twenty-four hours. After removing the catalyst, hydrochloric acid was added to turbidity at the boiling point and the reduction product was obtained as nearly colorless needles. The material was dissolved while still moist in 175 cc. of hot water and a solution of 6 g. of ferric chloride crystals and 2 cc. of concentrated hydrochloric acid in 15 cc. of water added. The quinone separating as a red oil was extracted with ether and the solution was washed, dried, clarified with Norite, and concentrated. Crystallization from ether–petroleum ether gave 1 g. (59%) of crude product sintering at 36° and melting at 38–39.5°. This gave a purple color in the test with alcoholic potassium hydroxide, indicating contamination with allylnaphthoquinone. Several recrystallizations from petroleum ether gave pure material crystallizing in clusters of pale yellow needles, m. p. 39–39.5° (no previous sintering). This gave an immediate red color with alcoholic alkali, with no blue or purple phase.

Anal. Calcd. for $C_{13}H_{12}O_2$: C, 77.97; H, 6.07. Found: C, 78.06; H, 6.21.

The allylnaphthoquinone was also hydrogenated (1 g. in 25 cc. of absolute alcohol), 2 moles of gas being absorbed in about three minutes. After oxidation in ether with silver oxide, the propylnaphthoquinone was obtained pure in 70% yield.

2,6-Dimethyl-3-allyl-1,4-naphthoquinone (M. D. G., W. P. C.).—2,6-Dimethyl-8-naphthol[35] was converted into the allyl ether by heating a mixture of 5 g. of the material with 3 g. of allyl bromide, 8 g. of finely powdered potassium carbonate, and 75 cc. of purified acetone for fifteen hours on the steam-bath with mechanical stirring. The mixture was diluted with water, extracted with ether, and, after extraction of a trace of phenolic material with 10% potassium hydroxide containing sodium hydrosulfite, the ethereal solution was dried and evaporated. The oily residue of the crude ether was heated with 30 cc. of freshly distilled dimethylaniline in an atmosphere of nitrogen for two and three-quarters hours in a salt-bath maintained at 240°, and the cooled solution taken up in ether and extracted with dilute hydrochloric acid. For separation of the **2,6-dimethyl-3-allyl-8-naphthol** the ethereal solution was extracted several times with 10% potassium hydroxide, which removed successive small amounts, and then with Claisen's aqueous alkali–methanol mixture. The combined extracts were acidified and extracted with ether. The product distilled at 152–157° (2 mm.) as a rather dark oil (3 g., 49%) which was used directly without further purification.

Anal. Calcd. for $C_{15}H_{16}O$: C, 84.86; H, 7.60. Found: C, 84.20; H, 7.74.

In an early experiment using crude starting material containing 2,6-dimethyl-3-naphthol the rearrangement gave a small amount of a crystalline product which forms long fibrous needles, m. p. 109–110°, from ligroin (b. p. 70–90°). The substance fails to couple with diazotized amines and evidently is **2,6-dimethyl-4-allyl-3-naphthol.**

Anal. Calcd. for $C_{15}H_{16}O$: C, 84.86; H, 7.60. Found: C, 84.69; H, 7.67.

The introduction of an amino group into the liquid isomer was conducted as above and the crude **2,6-dimethyl-7-allyl-5-amino-8-naphthol** collected as a nearly colorless precipitate; yield 2.3 g. (72%). The substance is very sparingly soluble in the usual solvents and dissolves to only a slight extent in a large volume of boiling, dilute hydrochloric acid. The filtered solution on cooling deposits very fine, colorless needles of the **hydrochloride,** which apparently forms a stable trihydrate.

Anal. Calcd. for $C_{15}H_{18}ONCl\cdot 3H_2O$: N, 4.41. Found: N, 4.32 (Kjeldahl), 4.39 (Dumas).

Conversion to the Quinone.—For oxidation, 1.3 g. of the free amine was suspended in 50 cc. of acetone and treated

(35) Weissgerber and Kruber, *Ber.*, **52**, 360 (1919).

with 30 cc. of a solution of 27 g. of ferric chloride crystals and 10 cc. of concentrated hydrochloric acid diluted to 245 cc. On warming and stirring the solid dissolved (ten minutes) and the cooled solution was diluted and extracted with ether. After clarification and drying the solvent was removed in vacuum and the residual oil taken up in petroleum ether. On cooling, the quinone separated as yellow needles, m. p. 42–42.5°, and the melting point was not raised on recrystallization; yield 0.75 g. (57%).

Anal. Calcd. for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 79.82; H, 6.36.

In the color test with sodium ethylate in alcohol the quinone gives first a deep blue solution, changing to purple and then brown. Treated with 5% methyl alcoholic potassium hydroxide, the quinone gives a deep blue solution which changes in one to two minutes to a dull greenish-brown and then to a dull red; the diluted solution gives a gelatinous precipitate on acidification. Intense coloration does not develop if much water is present; the addition of 10% aqueous potassium hydroxide to a solution in alcohol gave a faint dull green color changing to weak purplish-red and then to a dull, weak red.

2,3-Diallyl-1,4-naphthoquinone from α-Naphthoquinone (M. F.)

α-Naphthohydroquinone Diallyl Ether.—The α-naphthohydroquinone required as starting material was prepared by dissolving 10 g. of the quinone in 50–75 cc. of hot alcohol and adding gradually a solution of 20 g. of stannous chloride crystals and 20 cc. of concentrated hydrochloric acid in 50 cc. of water. After heating gently until the color faded to pale yellow, and filtering if necessary, the solution was diluted with water and cooled in an ice-bath. The product separated as colorless or gray needles; yield 8.2–8.8 g.

For allylation, 6.1 g. of α-naphthohydroquinone was refluxed for ten to fifteen hours with 6.5 cc. of allyl bromide, 10.4 g. of potassium carbonate, and 20 cc. of acetone. The mixture usually became very dark, even in an atmosphere of nitrogen, and when the ether extract was shaken with alkali containing hydrosulfite considerable phenolic material was removed. After drying with magnesium sulfate the ethereal solution was cooled in a solid carbon dioxide bath, when the diallyl ether separated as a pasty solid. After adding petroleum ether, the crystalline material was collected, and an additional quantity was obtained by diluting the mother liquor with petroleum ether, filtering the solution through a tower of activated alumina, concentrating, and cooling as before. The yield of satisfactory material was 2–3.5 g. (22–38%). Repeated crystallization from petroleum ether containing a trace of ether gave colorless plates, m. p. 49.5–50°.

Anal. Calcd. for $C_{16}H_{16}O_2$: C, 79.96; H, 6.72. Found: C, 80.09; H, 6.74.

2,3-Diallyl-1,4-naphthohydroquinone Diacetate.—Attempted rearrangement of the ether in kerosene in an atmosphere of nitrogen gave only dark tars, but the expedient of acetylating the reaction product as produced[15] gave satisfactory results. A mixture of 3 g. of the diallyl ether, 3 cc. of acetic anhydride, and 3 cc. of diethylaniline was heated under reflux in a stream of hydrogen at 200–210° for five hours. The cooled mixture was taken into ether and the solution extracted with dilute hydrochloric acid, dried, and evaporated to a small volume. On slow cooling the diacetate separated as large hexagonal prisms; yield 3.2 g. (79%). The substance is very readily soluble in benzene or alcohol and moderately soluble in ligroin. Recrystallized from ether–petroleum ether or from ligroin (b. p. 70–90°) it formed large, colorless prisms, m. p. 92.5–93°.

Anal. Calcd. for $C_{20}H_{20}O_4$: C, 74.05; H, 6.22. Found: C, 74.18; H, 6.33.

2,3-Diallyl-1,4-naphthoquinone (M. D. G.).—The diacetate is resistant to hydrolysis by alkalies, and considerable material was recovered unchanged after boiling for two hours with 12% sodium hydroxide solution. Hydrolysis occurs with mixtures of alcohol and 25% alkali on warming, but the isolation of a satisfactory reaction product is not easily accomplished. For best results the diacetate is cleaved with a Grignard reagent having little reducing action.

To the Grignard solution prepared under nitrogen from 3 g. of magnesium, 100 cc. of absolute ether and sufficient methyl bromide to give complete reaction, was added 2.86 g. of 2,3-diallyl-1,4-naphthohydroquinone diacetate. The solution was refluxed for forty-five minutes, the ether was largely replaced with dry benzene, and after refluxing for one-half hour longer the mixture was decomposed with 25% ammonium chloride solution and a little acid. The organic layer was washed and dried and stirred mechanically with 2.05 g. of silver oxide and 10 g. of Drierite for fifteen minutes (oxidation can be accomplished also by shaking with air). The filtered, yellow solution was concentrated, eventually under vacuum, and the residual, dark yellow oil was cooled well and caused to solidify. After two crystallizations from alcohol (collecting the crystals in the cold room) the substance formed glistening yellow blades, m. p. 29–30°. It gave no depression when mixed with the analyzed sample prepared by the synthesis described below. The total yield of pure material was 1.05 g. (50%). The quinone is very readily soluble in ether or petroleum ether, sparingly soluble in water. It gives a yellow or brown solution in concentrated sulfuric acid.

Alkaline Cleavage of the Quinone (L. F. F.).—2,3-Diallyl-1,4-naphthoquinone gives a characteristic, intense color reaction with alcoholic alkali. When one drop of 10% aqueous alkali is added to a dilute solution of the substance in 1–2 cc. of alcohol, the solution becomes pale greenish-blue, then deep blue, slowly fading to a dull, weak green. With a larger amount of aqueous or alcoholic alkali the green phase is not observed and at the end the solution is red. In one experiment a solution of 0.1 g. of the quinone in 5 cc. of alcohol was treated with 1 cc. of 10% aqueous potassium hydroxide. The solution became deep indigo blue (ten seconds), purplish blue (forty seconds), intense purple (about one minute); a small amount of a cloudy gray precipitate then separated (two minutes) and the solution soon became dull red (two to three minutes) and underwent no further change on standing or heating. After dilution with water, which caused more of the gray material to separate, the mixture was acidified and shaken with ether, when all of the precipitated ma-

terial dissolved. Extraction of the ether solution with sodium carbonate gave a cherry-red aqueous layer and left a dark brown ether layer which gave on evaporation a resin showing no blue color with alcoholic alkali. After washing the red aqueous extract once with ether it gave on acidification a yellow emulsion of crude **2-hydroxy-3-allyl-1,4-naphthoquinone.** This was taken into ether and the solution dried and evaporated. The glassy residue largely dissolved in boiling ligroin (b. p. 70–90°) and after clarification and cooling the hydroxyquinone separated as bright yellow prism clusters, m. p. 115–116°; yield 5 mg. This was combined with material from two other experiments and recrystallized from dilute alcohol–acetic acid, giving fine yellow needles, m. p. 115.5–116°.

Anal. Calcd. for $C_{13}H_{10}O_3$: C, 72.88; H, 4.71. Found: C, 73.19; H, 5.02.

Mixed with synthetic 2-hydroxy-3-allyl-1,4-naphthoquinone,[28] m. p. 115.5–116°, the above sample gave no depression; other preparations were compared with similar results. In a further experiment the hydroxyquinone was purified by sublimation at 2 mm. pressure and the product dissolved in concentrated sulfuric acid. The red solution was poured into water and the product extracted and dried in ether and crystallized from ligroin (b. p. 70–90°), giving ball-like clusters of red microcrystals, m. p. 130–131.5°. A mixture with a synthetic sample of 1-methyl-3,4-benzo-5,6-coumaranequinone[28] (m. p. 134.5–135°, purified with bisulfite) melted at 131–132°.

Reducing Action of the Grignard Reagent (L. F. F.).—On cleavage of 2,3-diallyl-1,4-naphthohydroquinone diacetate by refluxing overnight with excess ethyl or *n*-butylmagnesium bromide in ether and working up the reaction mixture as before, small amounts of a quinone much less soluble than the main reaction product separated in a crystalline condition on concentrating the final ethereal solution to a small volume. Washed free of adhering oil with ether, the substance was obtained as bright yellow prisms, m. p. 127–128°. It was purified by crystallization from dilute alcohol and sublimation at 1 mm. pressure (about 125°), giving bright yellow needles, m. p. 129–130°.

Anal. Calcd. for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 79.93, 80.32, 80.06; H, 6.76, 6.91, 6.78.

The absorption spectrum is very similar to that of 2,3-dimethyl-1,4-naphthoquinone. The addition of dilute alkali to an alcoholic solution of the quinone gives a weak purplish-pink color which develops rather slowly and gradually changes to red.

Preparation of the Diallylbenzoquinones (E. M. F.)

Hydroquinone diallyl ether was prepared more satisfactorily by the following method than by that described by Hahn and Stenner.[36] A mixture of 44 g. of hydroquinone, 200 cc. of acetone, 96.8 g. of allyl bromide, and 112 g. of potassium carbonate was refluxed for nine hours, water was added to dissolve the inorganic salts, and the reaction product was extracted with ether. Phenolic material was removed by extraction with 1 *N* sodium hydroxide and the solution was washed well with water, dried and evaporated. The orange-yellow residue was induced to crystallize from a cooled solution in dilute alcohol, giving 52 g. of colorless, lustrous plates, m. p. 33–34°; 5 g. of yellowish material was obtained in a second crop, making the total yield 75%.

Rearrangement.—A solution of 53 g. of hydroquinone diallyl ether in 330 cc. of kerosene (b. p. 210–215°) was refluxed vigorously under a stream of nitrogen for two and one-quarter hours. The phenolic reaction product largely crystallized on cooling, and a small additional quantity was obtained on concentrating the mother liquor. The combined, almost colorless material was washed with petroleum ether to remove most of the kerosene and dried at 50°; yield 57.5 g.

2,5-Diallylhydroquinone was separated from this mixture by crystallization from water and the 2,3-isomer subsequently was isolated from the aqueous liquors. The crude rearrangement product was heated to boiling with 2 l. of water containing a little sodium hydrosulfite and steam distilled to remove kerosene still present. A considerable amount of material remained undissolved as an oily solid and the hot solution was decanted from this and filtered. On cooling the colorless filtrate a large crop of 2,5-diallylhydroquinone crystallized, and after collecting this the mother liquor was used to extract a further quantity of material from the semi-solid residue. After heating to boiling, the solution was filtered from a small amount of dark brown oil and cooled, giving another crop of colorless crystals. The total yield of crude 2,5-isomer was 25 g.; recrystallization from 2 l. of water gave 15.2 g. (29%) of pure product in the form of broad, flat needles, m. p. 129.5–131°.

Anal. Calcd. for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found (H. B. Dunkle): C, 75.80; H, 7.40.

The **diacetate** was prepared by adding 1.5 cc. of pyridine to a supension of 1.5 g. of the hydroquinone in 3 cc. of acetic anhydride. The mixture became warm, the solid dissolved, and on cooling the product crystallized. It separated from dilute alcohol as colorless needles, m. p. 111–112° (1.8 g.).

Anal. Calcd. for $C_{16}H_{18}O_4$: C, 70.05; H, 6.62. Found: C, 70.25; H, 6.70.

The dimethyl ether was prepared by the action of dimethyl sulfate in alkali containing hydrosulfite and the chief fraction boiled at 132–135° (1.5 mm.) and melted at about 40°. On oxidation with alkaline permanganate at 30–40° the ether gave a high yield of oxalic acid as the only observed product.

2,3-Diallylhydroquinone.—The combined aqueous mother liquors remaining from the above experiment after removal of the 2,5-isomer on extraction with ether gave 22.2 g. of colorless, crystalline material consisting largely of 2,3-diallylhydroquinone. This is very soluble in hot water but crystallizes satisfactorily from this solvent in fine, colorless needles, m. p. 87–90°.

Anal. Calcd. for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 76.17; H, 7.60.

2,5-Diallyl-1,4-benzoquinone.—A solution of 2.5 g. of the hydroquinone in 150 cc. of dry ether was stirred mechanically for two hours with 6.3 g. of silver oxide and 6.5 g. of anhydrous sodium sulfate with exclusion of air. The course of the oxidation can be followed by transfer-

(36) Hahn and Stenner, *Z. physiol. Chem.*, **181**, 88 (1929).

ring a drop of the solution to a watch glass; a violet color appears if hydroquinone is still present, otherwise the spot is completely yellow. The yellow solution was filtered and evaporated, leaving the quinone as a dark orange-yellow oil. It was purified by careful distillation from a salt-bath, b. p. 105–106° (1 mm.), which gave 1.6 g. of a clear yellow oil. Local overheating or distillation at a higher pressure results in decomposition, as evidenced by darkening or by the appearance of a green coloration. The yellow distillate crystallized on cooling in rectangular tablets, m. p. 16°.

Anal. Calcd. for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found: C, 76.71; H, 6.75.

2,3-Diallyl-1,4-benzoquinone was prepared from the corresponding hydroquinone (2.5 g.) in an analogous manner and the dark reddish-yellow oil (2.4 g.) remaining after evaporation of the ether was used directly in the synthesis and not purified further.

Diene Synthesis of Naphthoquinones (E. M. F.)

6,7-Dimethyl-1,4-naphthoquinone was prepared essentially as described in the patent literature.[17] A solution of 1 g. each of benzoquinone and 2,3-dimethylbutadiene in 2 cc. of benzene was refluxed for five hours and the addition product which crystallized on cooling (1.9 g.) was purified from dilute alcohol and thus separated from a little high melting material. The substance (m. p. 113–115°) was isomerized with 1 *N* alkali under nitrogen and acidification, or by adding dilute hydrochloric acid to a warm solution of the addition product in alcohol (nearly quantitative). The once crystallized (alcohol) dihydronaphthohydroquinone derivative (0.4 g.), m. p. 232–238°, was dissolved in glacial acetic acid (2 cc.) and treated with 0.3 g. of chromic anhydride, when a sharp temperature rise was noted. After a short period water was added and the yellow precipitate purified from alcohol (0.37 g.). It formed somewhat dull yellow crystals, m. p. 120–126°, dec. (blackening). The substance is intermediate in composition between the naphthoquinone and its dihydride and appears to be a complex.

Anal. Calcd. for $(C_{12}H_{11}O_2)_x$: C, 76.98; H, 5.92. Found: C, 77.19, 76.98; H, 6.14, 6.08.

Further treatment of the intermediate with chromic anhydride gave 6,7-dimethyl-1,4-naphthoquinone, which crystallized from alcohol in bright yellow needles of constant m. p. 118–119°.

Anal. Calcd. for $C_{12}H_{10}O_2$: C, 77.40; H, 5.41. Found: C, 77.43; H, 5.61.

6,7-Dimethyl-2,3-diallyl-1,4-naphthoquinone.—The addition product which separated after refluxing 2.4 g. of 2,3-diallyl-1,4-benzoquinone and 3.4 cc. of 2,3-dimethylbutadiene in 3 cc. of benzene for twenty hours was isomerized by short boiling with dilute alcoholic hydrochloric acid to **6,7-dimethyl-2,3-diallyl-5,8-dihydro-1,4-naphthohydroquinone,** which formed somewhat brownish crystals from alcohol, m. p. 156.5–159° (2.3 g.).

Anal. Calcd. for $C_{18}H_{22}O_2$: C, 79.96; H, 8.20. Found: C, 80.27; H, 8.15.

A solution of 0.5 g. of this material in acetic acid was treated at room temperature with 0.25 g. of chromic anhydride in glacial acetic acid. A rapid reaction ensued with rise in temperature (40°). After heating to 60° the solution was cooled and a dull yellow intermediate precipitated with water. This formed rectangular plates from alcohol, m. p. 54–56° with previous sintering; yield 0.4 g.

Anal. Calcd. for $(C_{18}H_{19}O_2)_x$: C, 80.87; H, 7.16. Found: C, 80.80; H, 7.17.

For further oxidation to the naphthoquinone 1 g. of the intermediate in 20 cc. of solvent was heated with 0.3 g. of chromic anhydride to 80°, when the solution warmed spontaneously to 90°, and then to 100°. The product then crystallized from alcohol in long flat needles or rectangular plates; both forms are bright yellow and melt at 69.5–70.7°.

Anal. Calcd. for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.46; H, 6.96.

The color changes in the reaction with sodium ethylate are similar to those of 2,3-diallyl-1,4-naphthoquinone.

2,3-Diallyl-1,4-naphthoquinone from Butadiene-benzoquinone (L. F. F.)

5,8-Dihydro-1,4-naphthohydroquinone Diallyl Ether.—A mixture of 7 g. of monobutadiene-*p*-benzoquinone,[18] 10 cc. of allyl bromide, 23.8 g. of finely powdered potassium carbonate, and 150 cc. of purified acetone was refluxed overnight, diluted with water and extracted with ether. After washing with alkali–hydrosulfite and water the light yellow ethereal solution was dried and evaporated, eventually with suction. The residue was taken up in warm methanol and on cooling the ether crystallized in colorless, pearly plates, m. p. 63–64°; yield 5.6 g. (54%). Recrystallized twice from methanol it melted at 64–65°.

Anal. Calcd. for $C_{16}H_{18}O_2$: C, 79.30; H, 7.49. Found: C, 79.51; H, 7.55.

2,3-Diallyl-5,8-dihydro-1,4-naphthohydroquinone.—A solution of 5.6 g. of the diallyl ether in 34 cc. of kerosene was heated under nitrogen in a bath maintained at 240–250° for two hours, and on cooling (under nitrogen) the rearrangement product separated as a crystalline paste. It was collected, washed well with petroleum ether in which it is sparingly soluble, and obtained as completely colorless plates, m. p. 107–108.5°; yield 4.9 g. (88%). The substance is moderately soluble in ligroin (b. p. 70–90°) and crystallizes from this solvent in clusters of microcrystals, m. p. 108–109°. The solution turns slightly yellow in the air and the crystals acquire a pale tan color.

Anal. Calcd. for $C_{16}H_{18}O_2$: C, 79.30; H, 7.49. Found: C, 79.36; H, 7.78.

Oxidation (E. M. F.).—This was conducted in stages as above, first using 4.35 g. of the dihydronaphthohydroquinone in 25 cc. of acetic acid and 4.3 g. of chromic anhydride and warming to 50° to start the reaction. The initial reaction was controlled to 70° and after heating to 100°, cooling and diluting, the oily intermediate product was extracted with ether. Seed was obtained by cooling in alcohol to −78° and the product then crystallized from alcohol in bright yellow, rectangular tablets, m. p. 19.5–21° (previous sintering).

Anal. Calcd. for $(C_{16}H_{15}O_2)_x$: C, 80.31; H, 6.32. Found: C, 80.11; H, 6.30.

Further oxidation of 3.2 g. of the intermediate in 10 cc. of solvent was conducted with 1 g. of chromic anhydride at 60–90°, and the collected product (2 g.), being part liquid and part solid, was oxidized again as before, when an exothermic reaction was noted at 80–90°. The material recovered by ether extraction as a yellow oil crystallized readily from alcohol after obtaining seed and formed long, rectangular, bright yellow plates, m. p. 28–29.5°, identical with the sample described above.

Anal. Calcd. for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.53; H, 6.02.

Summary

Details are given of observations summarized in two recent Communications. The chemical properties and absorption spectra of synthetic model compounds and the marked antihemorrhagic activity of at least one of these substances (2,3-dimethyl-1,4-naphthoquinone, assayed by the Almquist procedure) lends support to the formulation of vitamin K_1 as 2-methyl- (or ethyl)-3-phytyl-1,4-naphthoquinone and of vitamin K_2 as 2,3-difarnesyl-1,4-naphthoquinone.

A theoretical interpretation is given of the purple-blue color reaction of β-unsaturated alkyl naphthoquinones with sodium ethylate and it is shown that the reaction involves the replacement of the unsaturated side chain by hydroxyl. This accounts for the formation of a phthiocol-like pigment as the end-product of the color reaction with vitamin K concentrates, and the pigment probably is phthiocol or the ethyl homolog. The phthiocol isolated from human tubercle bacilli may have arisen from the alkaline cleavage of a K-type vitamin.

CONVERSE MEMORIAL LABORATORY
CAMBRIDGE, MASSACHUSETTS RECEIVED JULY 8, 1939

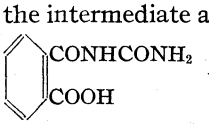
[CONTRIBUTION FROM THE DEPARTMENT OF PHYSIOLOGICAL CHEMISTRY, COLLEGE OF MEDICINE THE OHIO STATE UNIVERSITY]

A Study of Some Derivatives of Phthalyl Urea

BY CLAYTON S. SMITH AND CHESTER J. CAVALLITO

Many types of derivatives of urea have been prepared, most of them in the search for compounds possessing hypnotic activity. A large number of substituted ureas possess some degree of hypnotic activity.[1] The most active hypnotics are found among the cyclic ureas, especially the ureides of substituted malonic acid.

The object of the present work was to synthesize derivatives of phthalyl urea, the cyclic ureide of phthalic acid, and to study them for hypnotic activity.

Phthalyl urea was first described by A. Piutti.[2] He prepared the compound by heating equimolecular quantities of phthalic anhydride and urea to 120–125°, forming first the intermediate acyclic ureide of phthalic acid, 

which when treated with phosphorus oxychloride yielded the closed ring structure.

In the present work, the general method of Piutti was used for the synthesis.

(1) A. Hjort, E. J. de Beer and co-workers, *J. Pharmacol.*, **52**, 211 (1934), to *ibid.*, **61**, 175 (1937).

(2) A. Piutti, *Ann.*, **214**, 17 (1882); *Gazz. chim. ital.*, **12**, 169 (1882).

Experimental Procedure

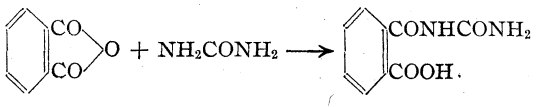
Preparation of Phthalyl Urea and Phthalyl Thiourea.—Equimolecular quantities of phthalic anhydride and urea were ground together in a mortar, then transferred to a round-bottomed flask. The mixture was heated at about 124° on a sulfuric acid bath until the reaction mixture became pasty and finally solidified to a hard mass. The melt should not be heated to such a temperature as to cause the evolution of gas bubbles. The product was pulverized, washed several times with cold water and ether, then recrystallized from hot water (about 35% yield).

Ring closure was brought about by treating the acyclic ureide with enough phosphorus oxychloride to form a thin paste and warming slowly on a water-bath. The reaction was considered complete when hydrogen chloride fumes were no longer liberated. Ether was then added to the reaction mixture, and the product filtered, washed with ether, and recrystallized from hot water.

Phthalyl urea decomposes at 185 to 190° leaving a residue which melts partly at about 230°, and completely above 300° with decomposition. Phthalimide and cyanuric acid $(CONH)_3$ are present as decomposition products.[2]

Phthalyl thiourea was prepared by the same general procedure as described above. The intermediate acyclic ureide did not form as rapidly in the case of thiourea as with urea.

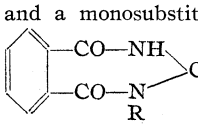
Attempts to prepare the cyclic ureides by treating phthalic anhydride and urea directly with phosphorus oxychloride were unsuccessful. It appears necessary first to bring about the combination



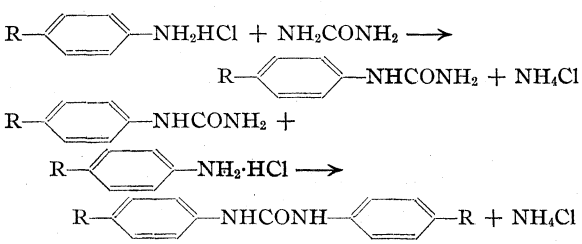
by fusing the two components.

Δ^2-Tetrahydrophthalyl Urea.—This compound was prepared from urea and Δ^2-tetrahydrophthalic anhydride. Tetrahydrophthalic acid was prepared by reducing phthalic acid with sodium amalgam in a strongly alkaline solution.[3] The acid was purified and treated with acetyl chloride to form the anhydride. Δ^2-Tetrahydrophthalic anhydride combined with the urea less readily than did phthalic anhydride, as measured by the time necessary for the fused mixture to solidify. Ring closure was brought about by treatment with phosphorus oxychloride as described above.

N-Substituted Phthalyl Ureas.—This type of derivative was prepared by starting with phthalic anhydride and a monosubstituted urea. Compounds of the type



were prepared, where R consisted of the following groups: methyl, allyl, phenyl, *o*-tolyl, *m*-tolyl, *p*-tolyl, *o*-phenetyl, *p*-phenetyl, *o*-anisyl, and *p*-anisyl. The aromatic substituted ureas used were prepared by heating an aqueous solution of urea with the corresponding aromatic amine hydrochloride.[4]

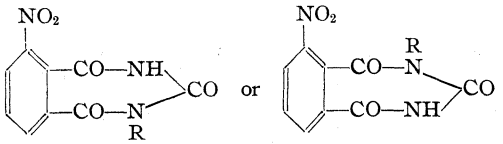


The monosubstituted urea formed by the above reaction in about 50% yield was separated from the disubstituted urea by solution of the former in hot water. The alkyl substituted ureas were purchased from the Eastman Kodak Company.

The monosubstituted ureas combined with phthalic anhydride more slowly than did urea. Attempts to combine phthalic anhydride with N,N^1-disubstituted ureas by the fusion method were unsuccessful. It may be that the high temperature necessary to fuse this mixture is above the decomposition temperature of the expected product.

Nitrophthalyl Ureas.—3-Nitrophthalyl urea and 4-nitrophthalyl urea were prepared from urea and the corresponding 3- and 4-nitrophthalic anhydrides. The nitro acids were prepared by direct nitration of phthalic anhydride[4] (p. 399),[3] (p. 828). The nitro anhydrides were prepared by treating the acids with acetic anhydride. 3-Nitrophthalyl derivatives of *p*-tolyl urea and of *p*-phenetyl urea were also prepared. The nitro anhydrides reacted with the ureas more rapidly upon fusion than did phthalic anhydride.

These last two compounds may possess either of two structures



It has not yet been determined whether both or just one of the above types are formed.

The compounds prepared are listed in Table I, together with some of their physical constants and properties. These compounds generally decompose before melting, and the decomposition points are not sharp. Phthalyl urea when heated slowly decomposes between 185–190° into phthalimide and cyanuric acid, and this mixture softens again at about 230°. If, however, the melting point is determined by lowering the temperature of the melting point apparatus from some high point, to the lowest point which will produce complete liquefaction of freshly added phthalyl urea, it will be found to melt at 207°. The melting points of the compounds were determined in this manner.

The derivatives of phthalyl urea are all relatively insoluble in cold water, but are more soluble in hot water or in hot alcohol. The solubility in hot water is greatly diminished with increase in the molecular weight of the compounds. The above phthalyl ureas are fairly soluble in alkali. This can be explained on the basis of enol formation. The alkali solubility of the nitro phthalyl ureas is greater than that of the phthalyl ureas without a nitro group.

With the exception of phthalyl allyl urea, the compounds prepared appear quite stable. The allyl derivative was observed to liberate formaldehyde in the presence of air and moisture at room temperatures, and its melting point also dropped about 10° in a few months. It is fairly stable in the absence of moisture.

The yields in the synthesis of these compounds are rather low. Practically all the loss of material takes place in the first step of the reaction. The ring closure takes place with little loss.

In order to purify some of the more insoluble substituted phthalyl ureas, several washings were made with water containing a few drops of ammonium hydroxide, and then with several portions of warm water. This procedure, when carried out after the ether washings, removed any phthalimide or non-cyclic acid ureide present.

Pharmacological Procedure

Preliminary tests for pharmacological activity of the phthalyl ureas were conducted on rats.

(3) Beilstein, 4th ed., Vol. IX, p. 770.
(4) "Organic Syntheses," Coll. Vol. I, p. 442.

TABLE I

Most of these compounds crystallize from hot water as small white needles or rods. Those indicated with an asterisk* appear as plates. The colored derivatives are: [1] light yellow, [2] orange-yellow, [3] light greenish-yellow.

Phthalyl urea deriv.	Mol. wt.	% yield	M. p., °C.	Analyses, % Calcd.	Found	Calcd.	Found
Phthalyl urea	190.06	35	207–207.5	C, 56.9	57.1	H, 3.18	3.38
Phthalyl thiourea*	206.12	49	181–181.5	S, 15.55	15.35		
Δ^2-Tetrahydro	194.10	19	270	C, 55.7	56.0	H, 5.20	5.12
3-Nitro[1]	235.10	57	190 (dec.)	C, 45.9	46.1	H, 2.14	2.30
4-Nitro[1]	235.10	61	206–207	C, 45.9	46.2	H, 2.14	2.25
N-Methyl	204.08	40	190–192	C, 58.5	58.8	H, 3.95	4.11
N-Allyl	230.09	30	135–?	C, 62.6	62.9	H, 4.38	4.53
N-Phenyl*	266.09	48	164–165 residue—194	C, 67.6	67.7	H, 3.79	3.78
N-*o*-Tolyl	280.11	18	190 (dec.) heat slow 200.5	C, 68.5	68.7	H, 4.32	4.45
N-*m*-Tolyl	280.11	38	139	C, 68.5	68.9	H, 4.32	4.51
N-*p*-Tolyl	280.11	21	155–160	C, 68.5	68.5	H, 4.32	4.47
3-Nitro, N-*p*-tolyl[1]	325.11	38	189–190	C, 59.1	59.3	H, 3.41	3.48
3-Nitro, N-*p*-phenetyl[1]	355.13	35	191–195	C, 57.5	57.5	H, 3.66	3.78
N-*o*-Phenetyl	310.13	17	220	C, 65.8	66.0	H, 4.55	4.50
N-*p*-Phenetyl[2]	310.13	42	196–198	C, 65.8	65.7	H, 4.55	4.75
N-*o*-Anisyl	296.11	20	218	C, 64.8	65.0	H, 4.08	3.94
N-*p*-Anisyl[3]	296.11	12 (low)	199	C, 64.8	64.8	H, 4.08	4.00

In order to facilitate rapid absorption of the compounds, it was decided to inject them by the intraperitoneal route. Since the *p*H necessary to dissolve the compounds in the concentrations desired was too high for animal administration, the compounds were pulverized to pass through a 100-mesh sieve, then suspended in an aqueous solution of glycerol and glucose (20 g. glucose, 20 g. glycerol per 100 cc. solution). About 2 cc. of fluid was injected into each rat, with the amount of compound to be tested in suspension. The glycerol–glucose solution alone produced a little irritation for about five minutes as evidenced by the behavior of the rat, but if the rat were killed the next day and examined, the internal organs appeared normal.

The pharmacological tests were made to determine whether the compounds possessed hypnotic activity, and to study the effect of various chemical groups upon the activity. For the sake of comparison, all the compounds were tested in doses of 500 mg. per kilogram body weight. It was observed that if the compounds possessed any activity it would be evident with this dose. Larger doses did not produce greater degrees of depression, and the absorption of larger quantities was not always complete. This was probably due to the limited solubility of these compounds. Most of the compounds did not produce complete anesthesia; therefore, some criterion for judging the degree of depression was necessary. It was observed that a rat deeply depressed but not completely anesthetized would remain on his back when so placed, and would not turn over ($^{++++}$ in Table II). A rat showing somewhat less depression would turn over if placed on his back but would remain lying on his side if so placed ($^{+++}$ in Table II). One still less depressed would not remain lying on his side but would not struggle if held in the hand in the inverted position ($^{++}$ in Table II). A normal rat (0 in Table II) or one but very slightly depressed ($^{+}$ in Table II) would struggle if held in this fashion. The above criteria merely served to compare the hypnotic activities of the compounds with one another. Table II shows the results obtained.

TABLE II

Phthalyl urea deriv.	Relative order of hypnotic activity
3-Nitro	+ + + +
N-*p*-Tolyl	+ + +
3-Nitro-, N-*p*-Tolyl	+ + +
N-*p*-Anisyl	+ +
N-*p*-Phenetyl	+ +
N-*m*-Tolyl	+
N-*o*-Anisyl	+
N-Phenyl	+
N-*o*-Tolyl	+
N-*o*-Phenetyl	+
N-Methyl	0
Δ^2-Tetrahydro	0
Phthalyl urea	0

The induction period for depression ranged from five to fifteen minutes, after which the effects of the more active compounds lasted for three to four hours.

Degrees of depression simulating natural sleep are very often observed in rats under the influence

of these compounds. Doses of 150–200 mg./kg. of the more active compounds induce sleep, from which, however, the animals may be aroused rather easily.

The compounds 4-nitrophthalyl urea, phthalyl allyl urea, and phthalyl thiourea are not included in the above table, as they are toxic with the doses required to produce depression. The minimum fatal dose for the 4-nitrophthalyl urea is between 100 and 250 mg./kg.; phthalyl allyl urea and phthalyl thiourea are fatal with a dose of about 500 mg./kg. The 3-nitrophthalyl urea is toxic with a dose of about 1000 mg./kg.

It may be observed from the above table that phthalyl urea itself is practically inactive as a hypnotic. The introduction of a nitro group in the 3-position of the aromatic nucleus increases the activity without increasing the toxicity, while a 4-nitro group increases the toxicity considerably. The introduction of a thio group in the urea molecule also increases toxicity. The partial hydrogenation of the aromatic nucleus has practically no effect in increasing hypnotic activity of phthalyl urea. The introduction of a methyl group on a nitrogen does not enhance the activity. However, if an allyl group is substituted, the activity increases. A phenyl group on the nitrogen produces greater activity than does a methyl, but less than does the allyl. A *p*-tolyl group on a nitrogen increases the activity almost as much as does the allyl group, and the former is much less toxic. If a *p*-phenetyl or *p*-anisyl group is introduced on a nitrogen, the activity is increased but not as much as by the *p*-tolyl group. The ortho compounds and the meta tolyl derivative are relatively inert.

Since 3-nitrophthalyl urea and phthalyl *p*-tolyl urea were found to produce the greatest depression, together with the least toxicity, the compound 3-nitro phthalyl *p*-tolyl urea was prepared. It proved to be, if anything, slightly less active than the phthalyl *p*-tolyl urea. 3-Nitrophthalyl *p*-phenetyl urea was also prepared and found to differ little in activity from phthalyl *p*-phenetyl urea. If chemical structure were the only deciding factor in hypnotic activity, the nitro substituted phthalyl *p*-tolyl and *p*-phenetyl ureas should be very much more active. This apparently is not the case.

Summary and Conclusions

The synthesis and properties of a series of seventeen phthalyl urea derivatives have been described.

The hypnotic activity of the compounds was tested on rats by intraperitoneal injections of suspensions of the compounds in an aqueous solution of glucose and glycerol. The derivatives of phthalyl urea prepared do not appear to be very active as hypnotics. This is of theoretical interest, since several other types of cyclic ureides such as the barbiturates are quite active as hypnotics. The low solubility of the phthalyl ureas may be a limiting factor preventing the compounds from reaching their site of action in effective concentrations.

The combination in a molecule of two groups, each of which separately increases activity, does not necessarily lead to a compound more potent than one with either of the active groups alone, as in the case of 3-nitrophthalyl urea, phthalyl *p*-tolyl urea, and 3-nitrophthalyl *p*-tolyl urea.

COLUMBUS, OHIO RECEIVED MAY 8, 1939

[CONTRIBUTION FROM THE HERCULES EXPERIMENT STATION, HERCULES POWDER COMPANY]

Arrangement of Substituents in Cellulose Derivatives[1]

BY H. M. SPURLIN

In the course of our consideration of published work and our own results on cellulose derivatives, members of our organization frequently have had occasion to take account of the method of arrangement of the substituents on partially substituted cellulose derivatives. In order to visualize as well as possible the differences that might exist between cellulose derivatives in which the manner of arrangement of the substituents is determined by different influences, several series of calculations have been carried out and the results plotted. While there is nothing original in the considerations on which these calculations were made, they are contributed in order to save others working on the same subject the labor involved, and possibly to bring to the attention of those who have not given the matter much thought the rather interesting conclusions that may be drawn from this study.

The necessity for considering cellulose as having large units of structure in which the substituents are distributed among the available positions according to the laws of chance seems to have been brought out first by Cross and Bevan.[2] Since that time, this conception of a statistical distribution seems to have been before most cellulose investigators at all times. However, a quantitative treatment of the subject was not possible until Denham and Woodhouse's[3] demonstration that substitution on cellulose occurs only on the 2,3- and 6-positions of the glucose units of which cellulose is composed (Fig. 1). This treatment does not seem to have been made, although Thiersch[4] has shown the behavior of the somewhat similar case of coupled reactions.

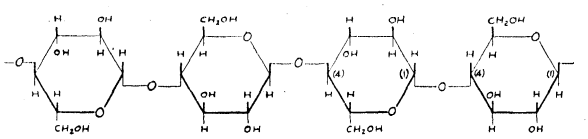


Fig. 1.—Theoretical configuration of a portion of a cellulose molecule.

(1) Delivered at the Baltimore meeting of the American Chemical Society, Cellulose Section, April, 1939.

(2) C. F. Cross and E. J. Bevan, "Researches on Cellulose," Longmans, Green and Co., London, 1913, p. 47. Vol. II, 1900–1905, 2nd ed.

(3) W. S. Denham and H. Woodhouse, *J. Chem. Soc.*, **111**, 244 (1917); see also W. N. Haworth, "The Constitution of Sugars," Edward Arnold and Co., London, 1929, p. 56.

(4) Fr. Thiersch, *Z. physik. Chem.*, **111**, 175 (1924).

Basis of the Calculations.—Before beginning the calculations, it is necessary to decide what simplifying assumptions may be made. To begin with, cellulose is considered as a chain of glucose units sufficiently long for the end-groups to be neglected. Other disturbances in the structure, such as partial oxidation of some of the glucose units, may be neglected or may be considered as a form of substitution.

The most important assumption that we make is that the ratio of the reactivities of the three sorts of hydroxyl groups is independent of the degree of substitution of the cellulose chain as a whole or of the state of substitution of neighbor hydroxyls. Of these two influences, we may surmise that the degree of substitution of the chain as a whole will influence more the solubility of the chain, and thereby its rate of reaction, than it will influence the ratios of the reactivities of its hydroxyls. Of course, we know that the influence of substitution on the absolute value of the rate of reaction may be very large. Lorand[5] has shown that this is the case with etherification in the presence of dilute alkali. It must, therefore, be emphasized that all that is assumed in the present work is that the rates of reaction of the three sorts of hydroxyls maintain the same ratios of reactivity constants (*i. e.*, equilibrium constants and reaction rate constants) to one another throughout the course of the reaction, however much the reactivity as a whole may vary.

It is not possible to justify on the basis of any quantitative data the assumption that the substitution of one hydroxyl, in, say, the 2-position, will not influence the reactivity of its neighbor, in the 3-position. However, from what is known of action at a distance in a molecule, it appears that so long as neither group bears an electric charge there will be little influence of the 2- and 3-hydroxyls on one another (they are *trans* to one another). There should be no interaction between the secondary and the primary hydroxyls.

Briefly, then, what has been done is as follows. A certain reactivity has been assigned to each sort of hydroxyl, the fraction of each sort that has reacted calculated for a given degree of substitution,

(5) E. J. Lorand, *Ind. Eng. Chem.*, **31**, 891 (1939).

and the probability that two hydroxyls on the same glucose unit are substituted is set equal to the product of the reacted fractions of those two hydroxyls. In the same manner, the fraction of the glucose units that contains all three hydroxyls in the substituted state is equal to the product of the fractions reacted of the three individual hydroxyls. Obviously, the fraction reacted in the 2- and 3-positions only is equal to the total fraction with substituents on the 2- and 3-positions minus the 2,3,6-trisubstituted fraction. In the same manner, the fraction substituted only in the 2-position is obtained by subtracting the 2,3-, the 2,6- and the 2,3,6-portions from the fraction that contains substituents in the 2-position. Analogous methods are used for the other possible manners of reaction.

Extent of Reaction Governed by an Equilibrium.—The following symbols will be employed in the general discussion: x_2, x_3, x_6 are the fractions of the glucose units that contain substituents in the 2, 3 and 6 positions, respectively; s_2, s_3 and s_6, the fractions with substituents *only* in the positions named. In the same manner, $s_{2,6}$ indicates the fraction of the glucose units containing substituents only in the two and six positions. To indicate the fraction of the glucose units that are unsubstituted, c_0 is employed; monosubstituted, c_1; disubstituted, c_2; trisubstituted, c_3. The average number of substituents per glucose unit, S, is obviously equal to the sum of x_2, x_3 and x_6.

If the extent of the reaction is determined by an equilibrium between some substituting medium and the hydroxyl groups, as in nitration, we may write (considering only reaction of one of the hydroxyls, say that in the 2-position, while those in the 3- and 6-position may or may not be reacting at the same time)

$$C_6H_{10}O_5 + RX \rightleftarrows C_6H_9O_5R + HX$$

$$\frac{(C_6H_9O_5R)}{(C_6H_{10}O_5)} = \frac{(RX)}{(HX)} K$$

or

$$x_2/(1 - x_2) = AK_2;\ x_2 = AK_2/(1 + AK_2)$$

Similarly

$$x_3 = AK_3/(1 + AK_3) \qquad (1)$$
$$x_6 = AK_6/(1 + AK_6)$$

A is a constant denoting the substituting power of the reaction mixture, while K_2, K_3 and K_6 are the equilibrium constants for the substitution reactions of the three sorts of hydroxyls

$$c_3 = s_{2,3,6} = x_2x_3x_6 = \frac{A^3K_2K_3K_6}{(1 + AK_2)(1 + AK_3)(1 + AK_6)} = \frac{A^3K_2K_3K_6}{D} \qquad (2)$$

setting D equal to the denominator of the above expression. Also

$$s_{2,3} = x_2 \cdot x_3 - s_{2,3,6} = A^2K_2K_3/D$$
$$s_{2,6} = A^2K_2K_6/D \qquad (3)$$
$$s_{3,6} = A^2K_3K_6/D$$

$$s_2 = x_2 - s_{2,3} - s_{2,6} - s_{2,3,6} = AK_2/D$$
$$s_3 = AK_3/D \qquad (4)$$
$$s_6 = AK_6/D$$

Collecting the equations for the fractions of unsubstituted, mono-, di- and trisubstituted glucose, we have

$$c_0 = 1 - s_2 - s_3 - s_6 - s_{2,3} - s_{2,6} - s_{3,6} - s_{2,3,6} = 1/D \qquad (5)$$

$$c_1 = A(K_2 + K_3 + K_6)/D \qquad (6)$$

$$c_2 = A^2(K_2K_3 + K_2K_6 + K_3K_6)/D \qquad (7)$$

$$c_3 = A^3K_2K_3K_6/D \qquad (2)$$

The substitution S, equal to $x_2 + x_3 + x_6$, is calculated most easily from the relationship

$$S = 3 - 3c_0 - 2c_1 - c_2 \qquad (8)$$

Extent of Substitution Governed by Rates of Reaction.—Many reactions of cellulose, and in particular acylation with an acid anhydride and etherification, are characterized by the fact that they do not stop until complete substitution is reached, the reagent is exhausted, or the reaction is interrupted; there is no back reaction.

For these types of reactions, if the concentration of reagents in the reaction medium were kept constant, the rate of disappearance of the three hydroxyls would be given by an equation of the type

$$dx_2/dt = k_2'(1 - x_2)$$
$$x_2 = 1 - e^{-k_2't} \qquad (9)$$

We are not restricting ourselves to the case where the rates remain constant. However, if the rates of the three reactions retain a constant ratio to one another at all times, the ratios of the substituted fractions will bear the same ratio to one another as if the above equation had been followed. In order to avoid confusion, the exponent in equation (9) has been changed from $-k_2't$ to $-Bk_2$, and we have (k_2 and k_2' are reaction rate constants

$$x_2 = 1 - e^{-Bk_2},\ x_3 = 1 - e^{-Bk_3},\ x_6 = 1 - e^{-Bk_6} \qquad (10)$$

$$c_3 = s_{2,3,6} = (1 - e^{-Bk_2})(1 - e^{-Bk_3})(1 - e^{-Bk_6}) \qquad (11A)$$

$$s_{2,3} = (1 - e^{-Bk_2})(1 - e^{-Bk_3})\, e^{-Bk_6}$$
$$s_{2,6} = (1 - e^{-Bk_2})(1 - e^{-Bk_6})\, e^{-Bk_3}$$
$$s_{3,6} = (1 - e^{-Bk_3})(1 - e^{-Bk_6})\, e^{-Bk_2} \qquad (12)$$

$$s_2 = (1 - e^{-Bk_2})e^{-B(k_3 + k_6)}$$
$$s_3 = (1 - e^{-Bk_3})e^{-B(k_2 + k_6)}$$
$$s_6 = (1 - e^{-Bk_6})e^{-B(k_2 + k_3)} \qquad (13)$$

$$c_0 = e^{-B(k_2 + k_3 + k_6)} \qquad (14)$$

$$S = 3 - e^{-Bk_2} - e^{-Bk_3} - e^{-Bk_6} \qquad (15)$$

Grouping the equations for the fraction of the glucose units that are unsubstituted, mono-, di- and trisubstituted, and putting in a form suitable for easy calculation from a table of exponentials, we have

$$c_0 = e^{-B(k_2+k_3+k_6)} \quad (14)$$

$$c_1 = e^{-B(k_2+k_3)} + e^{-B(k_2+k_6)} + e^{-B(k_3+k_6)} - 3e^{-B(k_2+k_3+k_6)} \quad (16)$$

$$c_2 = e^{-Bk_2} + e^{-Bk_3} + e^{-Bk_6} - 2e^{-B(k_2+k_3)} - 2e^{-B(k_2+k_6)} - 2e^{-B(k_3+k_6)} + 3e^{-B(k_2+k_3+k_6)} + e^{-B(k_2+k_6)} \quad (17)$$

$$c_3 = 1 - e^{Bk_2} - e^{Bk_3} - e^{-Bk_6} + e^{-B(k_2+k_3)} + e^{-B(k_3+k_6)} - e^{-B(k_2+k_3+k_6)} \quad (11B)$$

Choice of Constants in the Equations.—In order to plot the above equations, it is necessary to assume ratios of $k_2:k_3:k_6$ or $K_2:K_3:K_6$, and calculate corresponding values of S and the other quantities for a sufficient number of values of A or B to determine the course of the curves. An explicit solution of the c's and s's in terms of S is very difficult in the general case. It will be noted that these curves will not depend on the absolute value of the K's and k's but only on their ratios.

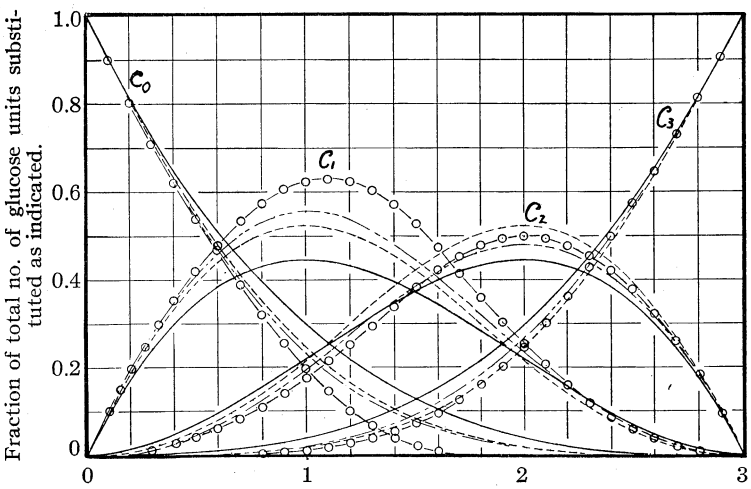


Fig. 2.

The equilibrium controlled condition will be realized only in the case of addition compounds and esters of cellulose. The data of Hatch and Adkins[6] indicate that there is little difference in the esterification equilibria for primary and secondary hydroxyls. Lieser[7] has abandoned his contention[8] that cellulose xanthogenate is exclusively substituted in the 2-position. From all that we know, it appears likely that the primary hydroxyl has an esterification equilibrium constant less than twice that of the secondary hydroxyls, and we might assume $K_2:K_3:K_6 = 1:1:2$. However, the curves so obtained would not depart noticeably from those with a ratio of 1:1:1, if the content of unsubstituted, mono-, di- and trisubstituted glucose units were plotted against the average substitution, in the manner of Fig. 2. Therefore, curves have been plotted with ratios of the constants of 1:1:1, 1:4:16 and 1:1:10 (Fig. 2). Curves for s_2, $s_{2,3}$, etc., have not been plotted, as these quantities always bear a constant ratio to c_1 and c_2, easily derivable from Equations (3) and (4). For example

$$\frac{s_2}{c_1} = \frac{K_2}{K_2 + K_3 + K_6} \quad (18)$$

$$\frac{s_{2,3}}{c_2} = \frac{K_2K_3}{K_2K_3 + K_2K_6 + K_3K_6} \quad (19)$$

While this relationship shows that the disubstituted glucose unit derived from the two hydroxyls with the smallest constants is present in relatively small quantity, it will always hold its own. This is not the case with the rate controlled distribution, as will be shown later.

Curves.—The curves of Fig. 2 show that, within the usual limits of error in working with such substances, the amounts of unsubstituted, mono-, di- and trisubstituted glucose units will be the same for the three sets of ratios of constants for the equilibrium controlled case. Detection of differences of reactivity of the three hydroxyls will always be possible if it is possible to determine the ratios of the three possible mono- or disubstituted glucose units to one another. For this purpose, it is recommended that attention be directed to products of either very low or very high substitution in order to avoid the difficulties of separating mono- and disubstituted glucoses from one another.

In the case of the rate controlled substitution, we have even fewer data for estimating the ratios of the constants. A survey of the data in Landolt–Börnstein leads to the conclusion that esterification reactions of primary alcohols proceed at about ten times the rate of esterification of sec-

(6) G. B. Hatch and H. Adkins, THIS JOURNAL, **59**, 1694 (1937).
(7) Th. Lieser, *Papier-Fabrikant*, **36**, 272 (1938).
(8) Th. Lieser, *Ann.*, **470**, 104 (1929).

ondary alcohols. Some old data on etherification[9] indicate even slighter differences. Not too much confidence can be given the application of these results to carbohydrates, but a rate ratio of 1:1:10 has been selected as a probable limit, with a ratio of 1:1:1 as the other limit. The curves in the latter case are identical with the similar curves for the equilibrium controlled substitution. The fourth set of curves of Fig. 2 gives the distribution of mono-, di-, tri-, and unsubstituted glucose units for the ratio of rate constants 1:1:10. These curves are much less symmetrical than in the case of the equilibrium curves. However, all four sets of curves are so close together that careful experimental work would be required to distinguish between actual cases with the constants used for these curves.

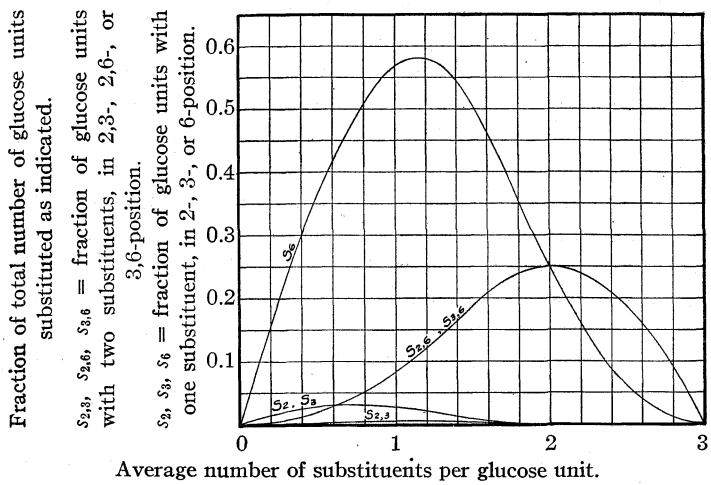


Fig. 3.—Proportions of the six different mono- or disubstituted glucoses, if the nature of substitution is determined by rates of reaction of the three hydroxyls in the ratio 1:1:10.

Again, as in the case of the equilibrium curves, an examination of the proportions of the individual monosubstituted or disubstituted glucose units gives us much more information. As no simple ratio exists between these, they have been plotted for the case $k_2:k_3:k_6$ = 1:1:10 in Fig. 3. It is evident that with this ratio of constants, practically all of the groups that are substituted at all are substituted in the 6-position after the early stages of the reaction. Conversely, if examination of a cellulose derivative of substitution above 2, whose degree of substitution is governed by the reaction time, shows that more than one sort of monosubstituted glucose is present, it is obvious that the two highest reaction rate constants must be close to one another. In order to form an idea of the relative size of the two smallest constants, the relative amounts of the three monosubstituted glucoses at the beginning of the reaction or of the two disubstituted glucoses chiefly present at some intermediate stage would have to be determined.

As the recent data of Heddle and Percival[9a] on the monomethyl glucoses from a methyl cellulose of substitution 0.5–0.6 indicate that the 2- and 3-positions are much more readily methylated than position 6, and are approximately equal in reactivity, the curves for a ratio of reaction rate constants of 1:10:10 were plotted (Fig. 4). It is evident that the proportions of mono-, di- and unsubstituted glucose for substitutions less than 1.2 are similar to those for the types of reaction plotted in Fig. 2. In this case, as well as in those previously considered, mere determination of the amount of unsubsti-

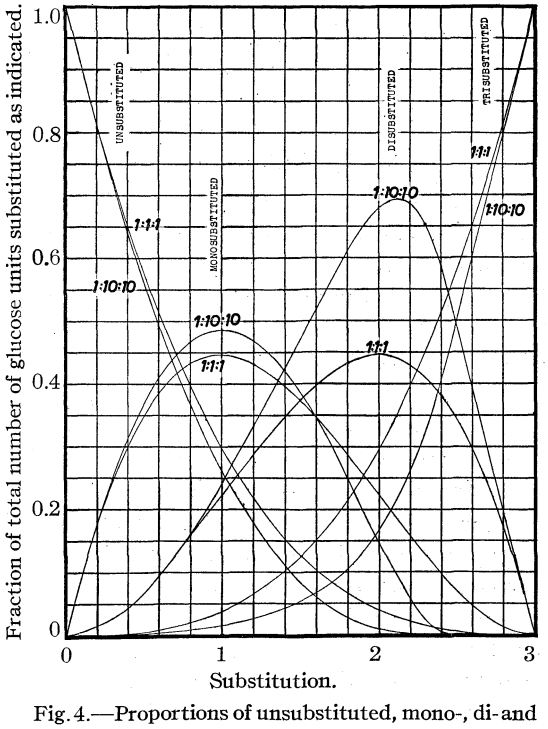


Fig. 4.—Proportions of unsubstituted, mono-, di-and tri-substituted glucose units if the nature of substitution is determined by rates of reaction of the three hydroxyls in the ratio 1:10:10 or 1:1:1.

(9) W. Sagrebin, *Z. physik. Chem.*, **34**, 149 (1900).

(9a) W. J. Heddle and E. G. V. Percival, *J. Chem. Soc.*, 1690 (1938).

tuted and mono- and disubstituted glucose in a derivative of substitution less than one will not give any information about the relative reactivity of the three hydroxyls. Only determination of the relative percentages of the three monosubstituted glucoses, as attempted by Heddle and Percival, will give this information.[10]

It may be a surprise to some to note that a monosubstituted cellulose derivative may contain less than 45% of monosubstituted glucose units and still be perfectly uniform, in the sense that each cellulose molecule has the same degree of substitution.

Variation of Substitution with Time.—As pointed out above, the constant B in the equations for the rate controlled substitution is of the nature of a time. In order to enable a picture of the relative times required for a given degree of reaction when the constants have differing ratios, Table I is given.

TABLE I

Substitution, S	Relative time, B: $k_2:k_3:k_6$ = 1:1:1	$k_2:k_3:k_6$ = 1:1:10	$k_2:k_3:k_6$ = 1:10:10
0.1	0.034	0.010	...
.5	.18	.050	0.027
1.0	.40	.14	.064
1.5	.69	.34	.12
2.0	1.1	.69	.23
2.5	1.8	1.4	.70
2.7	2.3	1.9	1.25
2.8	2.7	2.3	1.7
2.9	3.4	3.0	2.4

The time for reaching a high degree of substitution depends mainly on the rate of reaction of the slowest hydroxyl. It will be noted from Table I that the time required to reach a substitution of 2.5 is from four to ten times the time required to reach a substitution of 1.0, even if the concentration of reagents remains constant. The rate of etherification of cellulose seems to be some high power of the concentration of alkali, which of course drops during the reaction if it is not replenished. It is evident from this why so many investigators have had difficulty in reaching a high degree of substitution on etherification. Actually this is not difficult if the alkali concentration is kept high.

Comparison with the Literature.—A few papers have appeared bearing on the distribution of substituents in cellulose. Of these, the most informative are those of Compton,[11] Traube, Piwonka and Funk[12] and Schenck.[13] In Compton's paper, the yield of unsubstituted glucose from an apparently very uniform methyl cellulose with an average substitution of about 0.9 was given as 30–35%. The highest curve of Fig. 2 indicates 34%, the lowest 25%, for this substitution. From the other data in Compton's article, it would appear that the contents of mono-, di- and trisubstituted glucose were substantially as indicated in Fig. 2 or 4. It is evident that these data are in agreement with the calculations for a statistical grouping of the substituents and a low ratio of the reactivities of the most and the least reactive hydroxyl group.

Traube and his co-workers[12,13] have attempted to calculate the content of mono-, di- and trisubstituted glucose from the alkoxyl content of fractions obtained on distilling the hydrolysis products of partially alkylated cellulose. This is, of course, only justified if very good fractionation is obtained. As there is no evidence that any sort of a column was used, it appears doubtful that this separation was very good. The results reported therefore possess only qualitative value. They are sufficiently extensive, however, to justify discussion of the point whether the copper present in the reaction mixtures exerted a directive influence on the position of substitution.

The first section of Table II gives the results of Traube, Piwonka and Funk on methyl celluloses. The first four samples represent materials obtained by methylating alkaline copper complexes of cellulose, the fifth sample is a commercial methyl cellulose, and the sixth is a remethylated sample. The second section of the table gives calculated results for equal reactivities of the hydroxyls, while the third section gives the calculated results if one hydroxyl has ten times the reactivity of the other two. Table III is arranged similarly and based on Schenck's values for ethyl cellulose.[13]

It is apparent that the experimental results in Table II, third, fourth and sixth columns, are close checks of the calculated values for ratios of 1:1:10 for the reactivities of the hydroxyls. The values in the first two columns show a higher content of monosubstituted glucose than calculated. This indicates that under the conditions of these

(10) Destruction of the 6-monosubstituted glucose units of the cellulose by selective oxidation at the 2,3-position with periodic acid or lead tetraacetate should be a powerful tool for detecting the presence of other modes of monosubstitution in a highly substituted product.

(11) J. Compton, THIS JOURNAL, **60**, 2823 (1938).

(12) W. Traube, R. Piwonka and A. Funk, *Ber.*, **69**, 1483 (1936).

(13) H.-J. Schenck, "Zur Kenntniss der Alkylcellulosen," Dissertation, Berlin, 1936.

TABLE II

CONTENT OF MONO-, DI-, TRI- AND UNSUBSTITUTED GLUCOSE IN METHYL CELLULOSE (FROM TRAUBE, PIWONKA AND FUNK[12])

Sample	1	2	3	4	5	6
	Experimental Results					
S	0.73	0.79	0.91	0.94	1.44	2.15
c_0	30.2	25.6	23.1	23.9	14.7	0
c_1	61.8	63.2	62.3	57.3	34.7	21
c_2	8.0	11.1	14.6	18.8	41.2	52.5
c_3	0	0	0	0	9.3	26.5
	Calculated, $k_2:k_3:k_6 = 1:1:1$					
c_0	44	40	34	33	14	2
c_1	42	43	44	44	39	18
c_2	13	15	19	20	36	44
c_3	1	2	3	3	11	36
	Calculated, $k_2:k_3:k_6 = 1:1:10$					
c_0	37	32	25	23	3	0
c_1	54	57	61	61	56	18
c_2	9	10.5	14	15	36	49
c_3	0	0.5	1	1	6	33

TABLE III

CONTENT OF MONO-, DI-, TRI- AND UNSUBSTITUTED GLUCOSE IN ETHYL CELLULOSE (SCHENCK, DISSERTATION[13])

Sample	1	2	3
	Experimental Results		
S	0.52	1.01	1.17
c_0	53.8	32	27.4
c_1	38.9	38	36.6
c_2	7.3	27	29.8
c_3	0	3.1	6.2
	Calculated, $k_2:k_3:k_6 = 1:1:1$		
c_0	57	29	22.5
c_1	35	45	43.5
c_2	7.5	22	27.5
c_3	0.5	4	6.5
	Calculated, $k_2:k_3:k_6 = 1:1:10$		
c_0	54	19	11
c_1	42	62	62
c_2	5	17	24
c_3	0	2	3

experiments, the reactivity of one of the hydroxyls was more than ten times that of the next most reactive hydroxyl. These five samples were all made in the presence of copper oxide. The sample in column five, with 1.44 substitution, had a manner of substitution closer to the calculated values for reactivity ratios 1:1:1. This sample, therefore, does not show the same tendency for one hydroxyl to be more reactive than the others. This is undoubtedly connected with the fact that a sodium–copper derivative was not used in the preparation of Sample 5. It appears from the data of Table II that Traube and his co-workers are justified in their belief that the sodium–copper complex of cellulose is especially reactive in one of the three positions. However, examination of the data of Table III throws doubt on this conclusion, as all three of the reported results fall fairly near the calculated values for equal reactivities of the three hydroxyls.

There is no evidence to indicate that any of the products made from sodium–copper cellulose is composed of a mixture of higher and lower substitution products. However, it is interesting to observe that the composition of the product of substitution 1.44 (Table II) may be calculated fairly exactly if a mixture of products of substitution 1.2 to 1.6 is assumed, with the 2- and 3-positions about twice as reactive as position 6.

Sakurada[14] and Shorygin[15] have attempted to determine the ratio of primary to total free hydroxyls in cellulose acetates of substitution 2.3, with substantial agreement that this ratio is about 0.3. Secondary cellulose acetate probably occupies an intermediate position between the rate controlled and the equilibrium controlled distributions considered in this paper. This would lead us to believe that in the hydrolysis reaction leading to secondary acetate, the three hydroxyls are losing their acetate at very nearly the same rates.

The work of Piwonka[16] would tend to indicate that in his special conditions the 3-hydroxyl reacts preferentially. The work of Heddle and Percival[9a] indicates that both 2 and 3 hydroxyls react under these conditions, but that the 6 position does not react.

Conclusions

The available experimental evidence is entirely in harmony with the viewpoint developed in this paper: namely, that the substituents in a cellulose derivative are distributed among the hydroxyls according to the laws of chance, and the three sorts of hydroxyls are substituted to an extent relative to one another that is determined by the relative reactivities of the hydroxyls (determined by their inherent properties as well as by the reaction medium) and the nature of the reaction (proceeding to an equilibrium at a partially substituted state, or with a tendency to proceed to complete substitution, but stopped at a partially substituted state).

WILMINGTON, DELAWARE RECEIVED JUNE 13, 1939

(14) I. Sakurada and T. Kitabatake, *J. Soc. Chem. Ind. Japan*, **37**, 604B (1934).

(15) P. P. Shorygin, A. E. Veitsman and N. N. Makarova-Zemlyanskaya, *J. Gen. Chem. U. S. S. R.*, **7**, 430 (1937).

(16) R. Piwonka, *Ber.*, **69**, 1965 (1936).

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, UNIVERSITY OF MINNESOTA]

The Adsorption of *cis*- and *trans*-Azobenzene

BY HERBERT FREUNDLICH AND WILFRIED HELLER

G. Spencer Hartley[1] has shown that commercial azobenzene mainly consisting of the *trans* isomer can be converted partly into the *cis* isomer, when exposed to daylight in dilute solution. He succeeded in separating the two isomers and in preparing them in a pure form. A. H. Cook[2] and L. Zechmeister[3] found that separation could be effected by adsorption, using the chromatographic method (aluminum oxide as adsorbent, petroleum ether as solvent); *cis*-azobenzene was adsorbed more strongly than the *trans* isomer.

The stronger adsorption of the *cis* compound on aluminum oxide as it is emphasized in the latter papers might lead to the presumption that *cis* isomers generally are adsorbed more strongly than *trans* isomers. Freundlich and Schikorr[4] have found, however, that maleic acid, a *cis* compound, is adsorbed far less than the *trans* isomer, fumaric acid, in aqueous solution on charcoal. This seems to indicate that it depends on the affinity of the solute to the adsorbent and to the molecules of the solvent, whether the *cis* or the *trans* isomer is adsorbed more strongly. Taking water as a standard, as it were, one could say that the more hydrophilic or more hydrophobic nature of the adsorbent (case 1) and of the solvent (case 2) are decisive for the difference in adsorbabilities of the solutes in question. That influences of this kind have to be taken into account is shown most clearly by the adsorption of methyl violet by charcoal or silica gel in water and tetralin, respectively, investigated by E. Berl and E. Wachendorff.[5] Dissolved in "hydrophobic" tetralin, methyl violet is adsorbed more strongly by the hydrophilic silica gel; in an aqueous solution, on the contrary, by the hydrophobic charcoal. Here we are dealing with case 2. From the outset, case 1 appears to be just as likely. In any case, the strongest contrast to the behavior of aluminum oxide in petroleum ether was to be expected with a hydrophobic adsorbent like charcoal and a hydrophilic solvent.

(1) G. Spencer Hartley, *Nature*, **140**, 281 (1937); *J. Chem. Soc.*, 633 (1938).

(2) A. H. Cook, *ibid.*, 876 (1938).

(3) L. Zechmeister, O. Frehden and P. Fischer Jörgens, *Naturwissenschaften*, **26**, 495 (1938).

(4) H. Freundlich and G. Schikorr, *Kolloid-Beihefte*, **22**, 1 (1926).

(5) E. Berl and E. Wachendorff, "Zsigmondy-Festschrift," 36 (1925), Spec. No. of *Kolloid-Z.*, **36** (1925).

We prepared *cis*-azobenzene by somewhat modifying Hartley's method. We avoided vacuum distillation and the tedious fractionating by crystallization; instead of that, we separated the two isomers by the differences in their solubilities in water and purified the *cis* compound by crystallization from petroleum ether at low temperatures (−15 to −35°). The m. p. of our crystals was 71.7°, determined by quick plunging; Hartley's value is 71.4°, Cook's 71°.

trans-Azobenzene was prepared following Hartley's method.

Methyl alcohol was chosen as hydrophilic medium, petroleum ether as the hydrophobic one; aluminum oxide was the hydrophilic adsorbent, charcoal (Norit) the hydrophobic one. The adsorption experiments were done at 20°. Five cc. of solution was shaken with different amounts of adsorbent for a few minutes, until the final state of adsorption was reached. The adsorbent was then separated from the solution by centrifuging; this lasted five to ten minutes in solutions of petroleum ether (b. p. 55 to 65°), fifteen to twenty minutes with methyl alcohol. We started with a 0.5% solution and reached different final concentrations by varying the amount of adsorbent. This procedure may lead to irregularities in adsorption, when small amounts of adsorbent (below 0.1 g.) are used (this refers to two measurements at higher concentrations of the *trans* isomer not taken into account in Fig. 2; *cf.* also H. Morawitz[6]).

The concentration after adsorption was determined with a colorimeter, using standard solutions of the same isomer as comparison. In the experiments with the *cis* isomer both standard solutions and those used for adsorption were freshly prepared every thirty minutes. Light-filters were used. A small amount of adsorbent, remaining in suspension, then became noticeable by a change in absorption, when passing from blue to red, namely, by requiring different values of the layer thickness for which equality of the half-shades was observed. Samples behaving in this way were rejected.

All operations were carried out in the dark or in indirect red light. The light intensity of the

(6) H. Morawitz, *Kolloid-Beihefte*, **1**, 301 (1910).

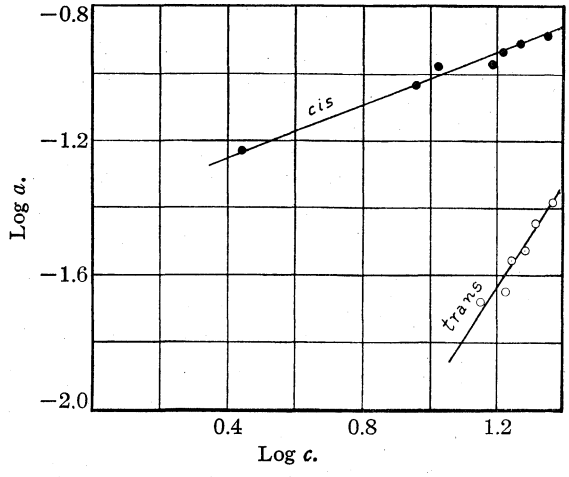


Fig. 1.—Adsorption of *cis*- and *trans*-azobenzene by aluminum oxide in petroleum ether: c in millimoles per liter, a in millimoles per 1 g. of adsorbent.

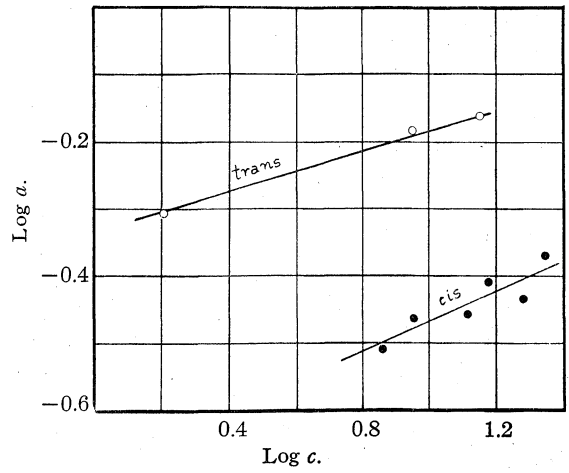


Fig. 2.—Adsorption of *cis*- and *trans*-azobenzene by charcoal in methyl alcohol: c in millimoles per liter, a in millimoles per 1 g. of adsorbent.

colorimeter was kept weak enough to prevent a noticeable *cis–trans* transformation during two minutes of illumination; the actual illumination lasted 8 times five seconds during one experiment.

The results obtained with aluminum oxide in petroleum ether and with charcoal in methyl alcohol are given in Figs. 1 and 2. c is the equilibrium concentration in millimoles per liter, a is the amount adsorbed in millimoles per 1 g. of adsorbent. The adsorption isotherms are represented in a logarithmic diagram showing that the empirical equation $a = \alpha c^{1/n}$ holds fairly well. In the case of the weak adsorption of the *trans* isomer by aluminum oxide in petroleum ether $1/n$ is practically about 1; in the other cases it lies between 0.30 and 0.45, *i. e.*, it agrees with the values generally found.

In agreement with Cook's chromatographic experiments, Fig. 1 proves that the *cis* isomer is adsorbed much more strongly than the *trans* isomer by aluminum oxide in petroleum ether. In agreement with our expectations, the behavior is reversed with charcoal as adsorbent in methyl alcohol (*cf.* Fig. 2). On comparing the values of a for an equilibrium concentration of 10 millimoles per liter, we find

a (*cis;* aluminum oxide, petroleum ether) = 0.093
a (*trans;* aluminum oxide, petroleum ether) = 0.012
a (*cis;* charcoal, methyl alcohol) = 0.34
a (*trans;* charcoal, methyl alcohol) = 0.65

Some adsorption experiments were done with aluminum oxide in methyl alcohol and with charcoal in petroleum ether. As was to be expected, the difference in the behavior of the azobenzene isomers was somewhat less pronounced. Again comparing the a-values for an equilibrium concentration of 10 millimoles per liter, we found

a (*cis;* aluminum oxide, methyl alcohol) about 0.004
a (*trans;* aluminum oxide, methyl alcohol) about 0.002
a (*cis;* charcoal, petroleum ether) = 0.43
a (*trans;* charcoal, petroleum ether) = 0.58

It was always observed that $1/n$ was larger for the solute which is adsorbed less, independent of the nature of the solvent; this is seen from the two figures and it was also very marked in the adsorption by charcoal in petroleum ether. At higher concentrations the lines of the adsorption isotherms (in the logarithmic diagram) would intersect, provided that the whole behavior is not changed by the occurrence of saturation.

In our experiments the influence of the more hydrophilic or more hydrophobic nature of the adsorbent prevails (case 1), the succession of the adsorbents is the same in both media, in contrast to the experiments with methyl violet, mentioned above. But there is also in our case an influence of the solvents in the same direction, as is shown when the differences in the amounts adsorbed are compared.

Adsorption experiments with another hydrophilic adsorbent, namely, powdered silica gel, again showed that *cis*-azobenzene is more strongly adsorbed in petroleum ether than the *trans* isomer. The difference is markedly smaller than with aluminum oxide.

Our results agree with the fact, mentioned above, that fumaric acid, the *trans* isomer, is adsorbed more strongly than maleic acid by char-

coal in water; for an equilibrium concentration of 10 millimoles per liter we have (Freundlich and Schikorr): a (maleic acid) = 0.992; a (fumaric acid) = 1.56.

The more hydrophilic nature of *cis*-azobenzene compared with the *trans* compound also is indicated in the differences of solubilities. According to Hartley the solubility (at 25°) of the *cis* isomer in water is 0.65 millimole per liter, that of the *trans* isomer 0.02 millimole per liter in petroleum ether (b. p. 40 to 60°); on the other hand, the *cis* isomer is less soluble (at 0°), 49.4 millimoles per liter, compared to a value of 192 for the *trans* isomer. We determined colorimetrically the solubilities in methyl alcohol at 0° and found a succession as in water: 410 millimoles per liter for *cis*-azobenzene, 164 for the *trans* isomer.

It is quite probable that the *cis* isomers are generally more hydrophilic than the *trans* isomers. Perhaps it is due to a *cis–trans* difference in structure that maltose is more hydrophilic than cellobiose—as it appears to be—and accordingly starch so much more hydrophilic than cellulose.

Summary

The adsorptions of pure *cis*- and *trans*-azobenzene by aluminum oxide and by charcoal in solutions of petroleum ether and of methyl alcohol were measured and compared. The *cis* isomer is adsorbed more strongly by aluminum oxide, particularly in petroleum ether, less in methyl alcohol; the *trans* isomer is adsorbed more strongly by charcoal, particularly in methyl alcohol, less in petroleum ether. This is in agreement with other experimental results, according to which the more hydrophilic solute, here the *cis* isomer, is adsorbed more strongly by a hydrophilic adsorbent, here aluminum oxide, in a more hydrophobic medium, here petroleum ether, than by a more hydrophobic adsorbent, here charcoal, in a more hydrophilic medium, here methyl alcohol.

That *cis*-azobenzene is more hydrophilic than *trans*-azobenzene is also shown by the *cis* isomer being more strongly soluble in water and methyl alcohol and less soluble in petroleum ether than the *trans* isomer.

MINNEAPOLIS, MINNESOTA RECEIVED MAY 23, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

Homogeneous Catalytic Hydrogenation

BY M. CALVIN

Last year it was announced[1] that quinone in quinoline solution could be hydrogenated using dissolved cuprous acetate as homogeneous catalyst. This is a report of further study of the kinetics of this reaction in the attempt to discover precisely what structure has this important property of bringing the highly inert hydrogen molecule into reaction.

Experimental

The apparatus was essentially the same as already has been mentioned,[1] and the experiments consisted of following the rate at which hydrogen was absorbed by a given solution varying the conditions of concentration, solvent, temperature, and reactants. The detail of the reaction vessel is shown in Fig. 1. The internal condenser was removed and weighed amounts of the catalyst and substrate introduced. The vessel was then mounted in the shaker and connected to the vacuum system through the ground joint J. The solvent was run in from a pipet and the condenser quickly replaced and the tap to the vacuum system opened. But before the air could be removed some oxidation had taken place, so that blank runs without substrate were made on a given catalyst to determine the correction to be applied to the amount of hydrogen absorbed. The heating was then commenced and pumping was continued until the McLeod gage at the other end of the system showed a pressure of 10^{-4} mm. or less. This degassing sometimes took as long as thirty minutes after the thermostating liquid had reached its boiling point. For runs at 100° water was used and for 117.7° *n*-butyl alcohol was used as thermostating liquid. In all the runs the shaker speed was about 325 vibrations per minute. In the course of one run the shaker speed was increased to 530 vibrations per minute for a time and then decreased to 325 again and no appreciable break in the rate curve was observed, showing that the rate of solution of the gas was sufficiently fast not to be a disturbing factor.

Materials

Quinoline.—Eastman Kodak Co. synthetic quinoline was purified by (1) initial fractionation at atmospheric pressure to within 1°, (2) treatment with benzoyl chloride for several days and then washed with sodium hydroxide solutions followed by distilled water, (3) fractionation at atmospheric pressure to remove water, (4) final fractionation in a 1-foot (30-cm.) Widmer column at 50–60 mm. pressure. The quinoline so obtained remains water white for months when kept in a glass-stoppered uncolored glass bottle.

(1) M. Calvin, *Trans. Faraday Soc.*, **34**, 1181 (1938).

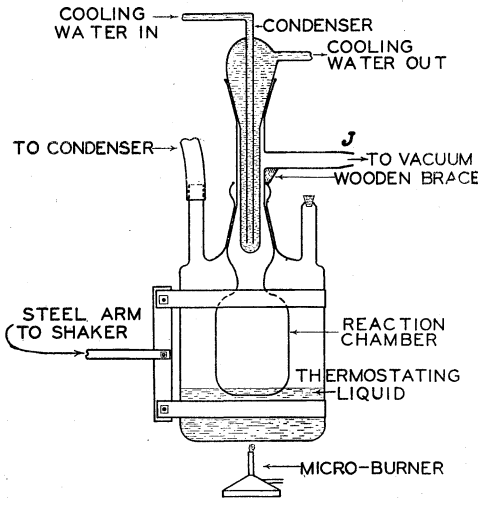


Fig. 1.

Quinone.—Eastman Kodak Co. quinone was purified by high vacuum sublimation and alternatively by recrystallization from alcohol. The two products gave the same results.

Cuprous Acetate.—Cuprous oxide (Baker) was extracted with glacial acetic acid containing 2–5% acetic anhydride, in a stream of hydrogen. The white cuprous acetate crystallized out and was filtered rapidly and washed with dry ether. The white cuprous acetate must be kept in a vacuum desiccator since moisture will hydrolyze it and oxygen oxidize it appreciably in as short a time as twenty-four hours. It was very difficult to prepare large quantities (10 g.) of absolutely pure cuprous acetate. It always contained some cupric salt. But since the method of starting the hydrogenation reaction involved some oxidation a large sample containing traces of cupric salt (pale greenish color) was standardized with respect to its catalytic power and this remained constant throughout a comparable series of experiments. The differences in individual samples were small in any case. The different samples of cuprous acetate are indicated by different letters in the tables.

α-Chloronaphthalene was fractionated in the Widmer column at 50–60 mm. pressure. The identified impurity was only naphthalene.

Hydrogen.—Normal hydrogen was prepared by collecting the gas as it evaporated from liquid hydrogen. Parahydrogen was prepared by passing *n*-hydrogen through charcoal immersed in liquid hydrogen. Deuterium was obtained from the Stuart Oxygen Company. The thermal conductivity measurements indicated that all three hydrogens were sufficiently pure.

Results

A typical run is shown in Fig. 2. All the others are identical in form and differ only in the slope of the straight line, *i. e.*, the rate of the hydrogenation. The effect in pure quinoline solution, of variation of concentration of catalyst, substrate, and hydrogen are shown in Table I. This is for one catalyst preparation. Identical results have been obtained on other preparations.

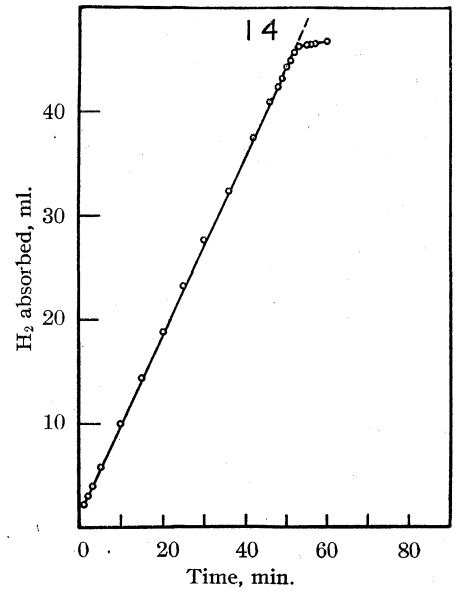


Fig. 2.—Expt. 2 in Table I.

TABLE I

Temperature, 100°; 50 cc. quinoline; catalyst preparation G.

Expt.	Catalyst, mmol.	Substrate, mmol.	Press. H_2, mm.	Rate, cc./min.	Rate per mmol. Cu^I	H_2 abs. mmol.
1	1.02	0.51	395	0.325	0.32	0.28
2	2.04	1.02	395	0.775	.39	0.57
3	4.08	2.04	395	1.81	.45	1.02
4	2.04	2.04	395	0.718	.36	1.05
5	2.04	1.02	595	.776	.39	0.60

The four points which emerge from this tabulation are: (1) the rate is strictly proportional to the concentration of hydrogen in solution (compare expts. 2 and 5; in expt. 5 the concentration of hydrogen in the gas phase and in solution has been increased by the ratio 595/395, so that when the rate in cc./min. remains the same, the rate in moles/min. has increased in precisely the same ratio); (2) the rate is somewhat more than proportional to the amount of cuprous acetate in solution, *i. e.*, when the concentration of cuprous acetate is doubled the rate is somewhat more than doubled; (3) the quinone has a small depressing effect on the rate (expts. 2 and 4); (4) the amount of hydrogen absorbed corresponds rather closely to half reduction of the quinone, *i. e.*, reduction to quinhydrone.

In Table II are shown the rates for the different kinds of hydrogen and the temperature coefficient for normal hydrogen all in quinoline solution.

It should be noted in connection with the at-

TABLE II

Expt.	Temp., °C.	Catalyst, mmol.	Substrate, mmol.	Press. H_2, mm.	Rate, ml./min.
6	100	2.04(C)	1.0 chloranil	387 *n*-H_2	0.0
8	100	2.04(C)	1.02 quinone	387 *n*-H_2	.86
9	100	2.04(C)	1.02 quinone	387 *p*-H_2(95%*p*)	.86
10	100	2.04(C)	1.02 quinone	387 D_2(100%D)	.80
14	100	2.04(F)	1.02 quinone	387 *n*-H_2	.87
15	117.7	2.04(F)	1.02 quinone	387 *n*-H_2	2.07

50 ml. quinoline

tempted reduction of chloranil that not only was the hydrogenation completely stopped but the subsequent oxidation of the cuprous complex by oxygen was very markedly slower in the presence of the chloranil than in its absence or with quinone present. The difference between hydrogen and deuterium is surprisingly small though quite real, and whether this difference is a variation in activation energy or temperature independent factor still remains to be seen. Para hydrogen reacts at the same rate as *n*-hydrogen (expts. 8, 9 and 10). The apparent activation energy for the normal hydrogen reaction is 14,300 cal. and if the temperature coefficient of the solubility of hydrogen (given in Table III) is taken into account this activation energy is reduced to 13,000 cal.

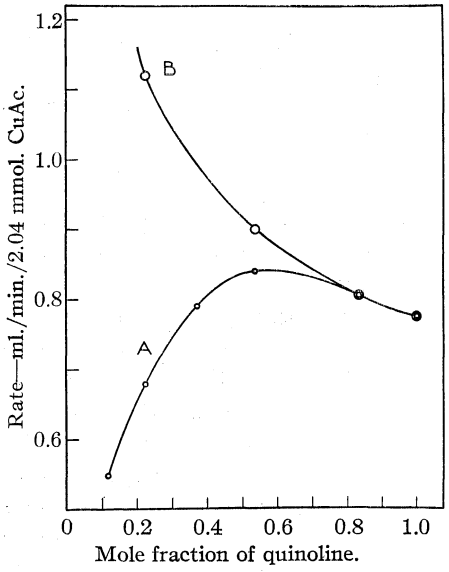


Fig. 3.—2.04 millimoles CuAc; 1.02 millimoles quinone; run at 100°; 50 ml. solvent measured at 20°; press. H_2, 395 mm. at 20°. Curve A, experimentally observed rate; Curve B, rate corrected for the solubility of CuAc.

The accuracy of these solubility measurements did not disclose any difference in the solubilities of deuterium and para hydrogen from that of normal hydrogen.

TABLE III

SOLUBILITY OF HYDROGEN

Temp., °C.	Solvent	Ml. H_2 (press. 380 mm.; temp. 20°)
100	54.5 g. quinoline,	2.1
20	(50 cc. at 20°)	1.35
117.7		2.30
100	54.5 g. quinoline + 1	2.05
20	mmol. quinone	1.4
100	54.5 g. quinoline + 2	2.2
20	mmols. CuAc	1.4
100	59.5 g. α-chloronaphthalene	
	(50 ml. at 20°)	2.15

A series of runs in quinoline–α-chloronaphthalene mixtures was made and the results are given in curve A, Fig. 3. Since the solubility of the cuprous acetate decreased as the mole fraction of the quinoline decreased, all the cuprous acetate which was added to the reaction mixture did not dissolve when the mole fraction of the quinoline dropped below about 0.55. Curve B, Fig. 3, gives the rate, calculated from the observed rate (curve A) and an independently measured solubility (Table IV), corresponding to the condition that all of the cuprous acetate added was completely dissolved.

TABLE IV

SOLUBILITY OF CUPROUS ACETATE IN QUINOLINE–α-CHLORONAPHTHALENE MIXTURES AT 100°[a]

N_Q (mole fraction quinoline)	Soly. (g. CuAc in 50 ml. solvent measured at 20°)
1	0.53
0.537	.23
.223	.14

[a] Since the solid phase was apparently different in the different solvents and in the absence of quinone, these solubilities can only be taken as an indication of what the concentration of cuprous acetate in the solution is.

Discussion

The mechanism that has been proposed previously,[1] namely, that the rate-determining step in the reduction of cupric copper or quinone is an activation of molecular hydrogen by a cuprous quinoline complex followed by a rapid reduction of the substrate, still holds. The succeeding slow absorption of hydrogen after the reduction of substrate is complete is the reduction of cuprous to free copper. There is at least one important addition to be made to this mechanism, which is that the catalytically active species is a dimer of cuprous acetate. This is based primarily on the fact that the rate increases more than linearly with the concentration of cuprous acetate, taken

together with the following line of argument. There exist no data on the molecular weight of cuprous acetate in quinoline solution but the work of Beckmann[2] on other cuprous salts, especially the chloride, indicate just such a polymerization. From the data of Beckmann one can calculate an association constant for the reaction

$$2CuCl(solution) \rightleftarrows Cu_2Cl_2(solution)$$

in quinoline solution in the neighborhood of 238° to be about 5 to 10, expressing the concentrations in moles per liter. If it is assumed that the rate of hydrogenation is proportional to the concentration of dimeric cuprous acetate one can calculate a similar constant of about 700 to 800 for the cuprous acetate in quinoline at 100°. This is entirely reasonable considering the lower temperature and the more favorable conditions afforded by the carboxyl group for polymerization. The heat of dissociation of these dimers in solution can be estimated by assuming an entropy decrease on association of about 15 cal./deg. and using the above equilibrium constants. The dissociation heat for the acetate is then about 10 kcal. and that of the chloride about 8 kcal., both not unreasonable values. Although the molecular structure of a solute as derived from its crystal structure is no proof of the state of the solute in solution, it is a good indication of the tendency of the solute as the solution approaches saturation. Just such binuclear bridged structures as the one here proposed for cuprous acetate–quinoline have been found in crystals of other cuprous and palladous compounds.[3] The function of the quinoline is first of all to bring the cuprous salt into solution by virtue of its coördinating property and second to furnish in this coördinated compound the electrons which seem to be necessary for the catalytic activity. A correlation with the basic strength or aromatic character of the coördinated molecule awaits further investigation. Whether one or two quinoline molecules per copper atom are required is still not known and in the structures written here Q will be used to represent the quinoline in the complex without implying any number. An analysis of the corresponding chloride gave (CuCl–quinoline) although from the work of Mann[3a] it would seem that two quinolines per copper atom would be more likely. In any case the considerations as far as they go at present are unaffected by whether there are one or two quinolines per copper atom or whether, if the cuprous center is four-covalent, these four covalences are planar or tetrahedral. The fact that the rate increases as the mole fraction of the quinoline decreases in the quinoline–chloronaphthalene mixtures can be attributed to the shifting of the polymerization equilibrium toward the side of the dimer and thus increasing the amount of the catalyst, specified for the same concentration of cuprous acetate. However, it seems that the actual increase in going only to solutions which are 10 mole per cent. quinoline is too large to be accounted for on this basis alone since the association constant in pure quinoline is already 700. Any attempt at a quantitative correlation between the solubility (activity) and the rates has so far been futile and should so be, since the solid phase (standard state) does not remain constant (see footnote to Table IV).

The precise path by which the quinone is reduced is still very much in the dark. In any given run the rate is independent of the state of reduction of the quinone but the total amount of quinone present does have an effect on the rate (Table I). The only plausible explanation at the moment is that the quinone forms a complex with the cuprous acetate in competition with the hydrogen and that the reduction product (quinhydrone) is about equally effective in occupying the cuprous acetate and diminishing its availability in the hydrogen activating process. That such a complex is possible is evidenced by the fact that when quinone and white cuprous acetate are kept in the same vacuum desiccator the quinone sublimes over onto the cuprous acetate and forms a very dark blue-black compound. The case of the tetrachloroquinone also is illuminating. Here it seems that the complex formation with the cuprous acetate is so strong and so complete that not only is the hydrogenation prevented but the oxidation by oxygen of the cuprous acetate is inhibited very markedly. In writing out the following mechanism the condition of the quinone is left unspecified. All that can be said is that it is not involved in the rate determining step.

The previously proposed mechanism is essentially correct and is here rewritten with the aforementioned revisions. The notation is identical with that previously used.

(2) Beckmann, *Z. anorg. Chem.*, **51**, 240 (1906).

(3) (a) Mann, *et al.*, *J. Chem. Soc.*, 873, 1503 (1936). (b) Burawoy, *et al.*, *ibid.*, 1690 (1937). (c) A. F. Wells, *Proc. Roy. Soc.* (London), **167**, 169 (1938).

$$Cu^{I} + Q \rightleftarrows Cu^{I}Q \quad (a)$$

$$2Cu^{I}Q \rightleftarrows (Cu^{I}Q)_2 \quad (a_2)$$

$$(Cu^{I}Q)_2 + H_2 \underset{k_1'}{\overset{k_1}{\rightleftarrows}} (Cu^{I}Q)_2H_2 \quad (b)$$

$$(Cu^{I}Q)_2H_2 + 2Su \xrightarrow{k_2} (Cu^{I}Q)_2 + 2HSu \quad (c)$$

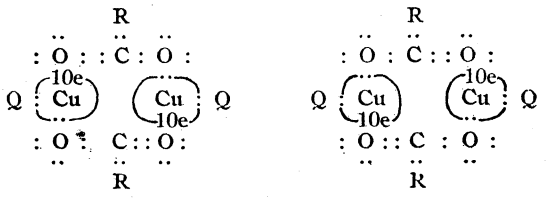
$$(Cu^{I}Q)_2H_2 \xrightarrow{k_3} 2Cu^{\circ} + 2Q + 2HAc \quad (d)$$

with $k_2 > k_1' > k_1 > k_3$

k_1' is set larger than k_1 since the equilibrium of (b) must be far to the left as evidenced by the only very small effect of cuprous acetate on the solubility of hydrogen in quinoline.

The temperature coefficient of the hydrogenation includes the shift of the equilibrium (a_2) as well as the change of the rate k_1. This shift of equilibrium affects the rate in the opposite direction from the change in k_1. If one makes a correction for this shift in equilibrium using the heat of dissociation of 10 kcal. previously calculated, one finds that the activation energy of k_1 is increased only slightly and probably is very close to 14,000 cal.

Thus it seems quite reasonable that the cuprous acetate is at least partially dimeric in solution, although the possibility of a higher polymer is not eliminated. The structure of this dimer analogous to that of other carboxylate dimers can be represented by a number of valence formulas containing chelated copper.



Any further speculation concerning the properties of such a dimer awaits an independent demonstration of its existence.

Summary

It has been shown that probably a dimer of a cuprous acetate–quinoline complex is responsible for the activation of molecular hydrogen in the homogeneous catalytic hydrogenation of quinone in solution.

BERKELEY, CALIF. RECEIVED FEBRUARY 6, 1939

[CONTRIBUTION FROM THE JOHNSON CHEMICAL LABORATORIES, UNIVERSITY OF ADELAIDE, SOUTH AUSTRALIA]

The Composition of the Colloidal Platinum Micelle

BY S. W. PENNYCUICK

Evidence brought forward by the author[1,2] has shown that the particles of colloidal platinum are composite in nature, containing platinum, platinic oxide and hexahydroxyplatinic acid.

This has now been confirmed by the microchemical analysis of the coagulated particles; and the relative amounts of the three constituents have been determined. The composition of the micelle in an average Bredig preparation is given by the formula $[3.9\ Pt, 1.16\ PtO_2, 1.0\ H_2Pt(OH)_6]_n$.

Isolation of the Micelle.—The sols were prepared from conductivity water by the Bredig method,[3] and the particles were isolated by coagulating the sol by freezing and then thawing the mixture.[4] In the preparation of the sol and in the isolation of the micelle no foreign electrolyte was added, nor was any foreign matter allowed to enter. The micelle was thus obtained in as pure a form as possible.

The particles in the frozen coagulum were sufficiently compact to settle readily; they were therefore washed free from the mother liquor by decantation, and allowed to drain and dry. Filtering was avoided.

Preliminary Observations.—In the previous work[1,2] it was not possible to decide whether the self-formed acid which acted as stabilizing electrolyte was hexahydroxyplatinic acid or one of its dehydration products. Now, however, the indications are fairly clear that the acid in the micelle is in its most highly hydrated form, namely, $PtO_2 \cdot 4H_2O$ or $H_2Pt(OH)_6$. This is based on the following observations.

First, the weight of any one sample of the air-dried micelle varies slightly from day to day. The changes are not in one direction, but appear to follow variations in the atmospheric vapor pres-

(1) Pennycuick, THIS JOURNAL, **52**, 4621 (1930).
(2) Pennycuick, *J. Chem. Soc.*, 1447 (1930), and previous papers.
(3) Pennycuick, *Aus. J. Exptl. Biol.*, **4**, 99 (1927).
(4) Pennycuick, *J. Chem. Soc.*, 2108 (1928).

sure. This is in keeping with the behavior of the highest hydrate, $PtO_2 \cdot 4H_2O$; for Wöhler[5] and Bellucci[6] have shown that it is the only hydrate of PtO_2 which suffers partial dehydration at low temperatures.

Second, when a sample of the micelle is placed in a desiccator over sulfuric acid there is a steady loss in weight, which after some weeks attains a maximum of 2.6% (see Table IA). Analysis (detailed later) shows that this loss is equal to approximately one-half the total water content. This again indicates that the highest hydrate is present in the micelle; for Wöhler[5] has shown that $PtO_2 \cdot 4H_2O$, when dehydrated by sulfuric acid, yields $PtO_2 \cdot 2H_2O$, thereby losing half its water.

TABLE I

Loss in weight of the platinum micelle, (A) on standing in desiccator, (B) on heating.

(A) In desiccator			(B) On heating Treatment			
Time	Wt., mg.	% loss	°C.	Time	Wt., mg.	% loss
....	34,445	..	...	...	34,194	..
4 hours	33,890	1.61	100	10 min.	33,714	1.40
2 days	33,700	2.17	110	4 hrs.	33,291	2.60
6 days	33,625	2.38	160	4 hrs.	33,033	3.40
20 days	33,570	2.54	400	1 hr.	32,538	4.84
23 days	33,550	2.60	Ignited		31,130	8.96

Third, when the micelle is strongly heated, all the water is driven out. Actually it appears to come out in fractions (see Table IB). Approximately one quarter comes out readily at 100°; the next quarter less readily after heating at 110° for four hours; the third quarter requires a temperature of 160° for four hours; whilst the final quarter is difficult to remove, requiring to be kept for an hour at a temperature of 400°. (Analysis, details of which are given later, shows that the further loss on ignition which appears in the last line of the table is due to the decomposition of the oxide. All the water is given up at 400°.)

This fractional decomposition is in agreement with the behavior of $PtO_2 \cdot 4H_2O$ as recorded by Wöhler, who has shown that under the action of heat the dehydration becomes progressively more difficult as the hydrate moves from $4H_2O$ to $3H_2O$ to $2H_2O$ to $1H_2O$, the last hydrate being very resistant to heat.

These three results taken together indicate that all the water in the micelle is in the form of the hydrate $PtO_2 \cdot 4H_2O$.

Analysis of the Micelle.—The air-dried micelle was used in all cases. The slight variations in initial weight were smoothed out by taking a series of analyses over several days. Constancy in weight could not be secured except at the cost of dehydrating the particles.

It proved desirable to separate the water estimation from that of the oxygen, since a quick heating was necessary to determine the former, and a slow ignition to obtain the latter.

In the water estimation, about 30 mg. of the air-dried micelle was heated rapidly to a temperature well over 400°, and the water quickly and completely expelled. The heating was carried out in a platinum boat in a shortened combustion tube using an adaptation of the microchemical combustion chain. A stream of purified nitrogen was passed continuously through the apparatus at the rate of one bubble every two seconds, and the expelled water was collected and weighed in a calcium chloride tube with the usual microchemical precautions. Two blank tests preceded each estimate, followed by a final blank.

In the oxygen estimation, on the other hand, a fresh sample of the micelle, from 10 to 15 mg., was heated very slowly to 600°, at which temperature, apart from the water being driven out, all the platinic oxide was completely decomposed into platinum and oxygen. The sudden decomposition of the oxide at about 550° was characteristic and rather striking. The micelle, with or without the water, was brown-black in color, but as the oxygen was expelled it changed almost instantaneously to light gray.

The heating was carried out slowly in order to avoid loss of weight by spluttering. The sample was then reweighed, the total loss in weight being made up of the water expelled together with that of the oxygen. As the former already had been determined, the oxygen content was at once obtained by difference. The micelle was finally ignited, but it seldom showed any further loss in weight.

A preliminary method in which the oxygen was determined as water after reduction with a stream of hydrogen was abandoned as it proved to be unreliable. The present method, however, has proved satisfactory and accurate.

The analyses of a number of different preparations are set out in Table II (i). From these it is seen that the micelle suffers a total loss in weight (at 600° or on ignition) of from 10.2 to 12.1%. Approximately one-half of this is due to the water given up by the complete dehydration of the hexahydroxy acid, and the remainder to the oxygen expelled by the decomposition of the platinic oxide.

Numerous freshly made sols (all prepared by the Bredig method) were analyzed. Four characteristic analyses (A, B, C and D in Table II (i)) are set out. Two very old samples of micelles that had been isolated ten years previously were also analyzed. One of these (F) had been kept under water, and the other (G) had been stored in the dry state. The analysis shows that over the ten-year period, although each suffered some slight variation, neither showed any abnormal change.

Calculation of the Formula.—A representative formula is quite sufficient. This can be obtained by using the average results for the micelles from the four freshly made sols, all of which were made under exactly the same conditions. These four sols (A, B, C and D in Table II) show an average water content of 5.4%, and an oxygen content of

(5) Wöhler, *Z. anorg. Chem.*, **40**, 423 (1904).
(6) Bellucci, *ibid.*, **44**, 168 (1905).

TABLE II

All sols made under the same set of conditions: 220 volts, 5 amps., 15 mins. arcing time.

Description	Loss at 600° (or on ignition) Weight, mg.	Loss	% loss	H_2O expelled H_2O	% H_2O	O_2 expelled (by dif.) O_2	% O_2
(i) Analysis of the colloid micelle							
A Freshly made	27,680	2853	10.3	1440	5.20	1413	5.10
B Freshly made	29,536	3013	10.20	1500	5.09	1513	5.11
C Freshly made	24,056	2644	10.99	1364	5.66	1280	5.32
D Freshly made	25,449	2779	10.92	1433	5.63	1346	5.29
E Three months old	31,872	3870	12.14	1958	6.14	1912	6.00
F Ten years old (wet)	30,486	3199	10.50	1707	5.60	1492	4.89
G Ten years old (dry)	23,157	2452	10.58	1401	6.05	1051	4.53
(ii) Analysis of the precipitate formed on boiling or aging							
Fresh sol (unboiled)	25,980	1557	6.00	870	3.34	687	2.66
Fresh sol (boiled)	30,074	1224	4.15	627	2.09	617	2.06
(iii) Analysis of the residue in the Bredig vessel							
Gray residue	34,783	72	0.21	20	0.06	52	0.15

5.2%. One thousand parts by weight of the colloid micelles thus contain 894 parts of platinum, 52 of oxygen and 54 of water.

Writing the constitution of the micelle as $[x\text{Pt}, y\text{PtO}_2, z\text{H}_2\text{Pt(OH)}_6]_n$, a simple calculation gives the values of x, y and z as 576, 199 and 225 g., respectively. Converting the values into gram molecules, the formula becomes $[3.9\ \text{Pt}, 1.16\ \text{PtO}_2, 1.0\ \text{H}_2\text{Pt(OH)}_6]_n$.

The Free Hexahydroxyplatinic Acid.—Quite apart from the hexahydroxy acid in the micelle, there is a further quantity which exists in solution as free electrolyte and which is responsible for practically the whole of the conductivity of the sol. The amount so present can be calculated directly from the specific conductivity.

For example, the freshly prepared sols (A, B, C and D in Table II) have an average specific conductivity (after boiling) of 12.2 gemmhos measured at 25°. Using 349 and 43 as the respective mobilities of the hydrogen ion and the hexa acid anion (and assuming complete ionization), the concentration of the hexa acid is calculated as 0.0046 g. per liter.

One liter of the above sol is found (by analysis) to contain 97 mg. of the micelle. The free hexa acid is thus 4.7% of the weight of the micelle, whereas the combined acid (from the figures already given) is 22.5% of the micelle weight. There is thus five times as much hexahydroxyplatinic acid bound up in the micelle as there is in the free state.

On continued boiling, or even on aging, some of the combined acid passes into solution. The relative amounts can be calculated at any time from the conductivity figures and from the micelle analysis. These have been determined in various cases and are set out in Table III.

TABLE III

DISTRIBUTION OF THE HEXAHYDROXYPLATINIC ACID BETWEEN THE PARTICLES AND SOLUTION

Total acid present is 27.2% of the weight of the particles.

Treatment	Acid combined in micelle, %	Acid free in solution, %	Spec. conduc. in gemmhos.
Freshly made	25.4	1.8	4.7
Boiled 0.5 hour	22.5	4.7	12.0
Boiled 30 hours	20.2	7.0	17.8 (max.)
Boiled 45 hours	(Unstable)		13.2

The results show that in the freshly made sol (before boiling) 1.8% of the acid is in solution, while 25.4% is in the micelle. After thirty minutes of boiling, the free acid content increases to 4.7%, leaving 22.4% in the micelle. After boiling for thirty hours in a reflux condenser, the free acid rises to a maximum of 7.0%, leaving 20.2% in the micelle. On further boiling, the sol becomes unstable. The fact that the greater part of the acid remains always in the micelle seems to indicate that some at least of the acid is in the interior of the particles from whence it is incapable of passing into solution.

Analysis of the Precipitate Formed on Boiling or on Aging.—When the sol is boiled or allowed to stand for some time a soft flocculate is thrown down. This can be isolated by drawing off most of the sol, then freezing and thawing the residue.

The analysis of this early precipitate is shown in Table II (ii), whence it is seen that both the oxygen and water content are low, being roughly one-half of the corresponding figures for the stable micelle. These low values are not unexpected seeing that the early precipitate would consist of the less stable particles, that is, those which contain less of the stabilizing material.

Analysis of the Residue in the Bredig Vessel.—During the arcing process there is a moderate amount of wastage which collects in the bottom of the Bredig vessel. Part of this is light gray in color, and has the appearance of the ignited micelle. Analysis of this gray matter (Table II (iii)) shows that it is practically pure platinum. Evidently it consists of the metallic particles which for some reason have failed to collect any appreciable amount of stabilizing material during the arcing process.

The author is indebted to the Trustees of the Endowment Fund of the Council for Scientific and Industrial Research of the Commonwealth of Australia for grants toward the purchase of platinum used in this work.

Summary

The colloidal platinum micelle, after isolation by freezing from Bredig preparations, has been analyzed by microchemical methods. The composition of the micelle of an average preparation can be given by the formula $[3.9Pt, 1.16PtO_2, 1.0H_2Pt(OH)_6]_n$.

There is evidence that the whole of the water in the micelle is present in the form of the highest hydrate, $PtO_2 \cdot 4H_2O$, which is hexahydroxyplatinic acid.

The total amount of this acid (in the micelle and in solution) is 27.2% of the gross weight of the particles. On continued boiling the greater part of this remains in the micelle, where some appears to be in the interior.

The precipitate formed on aging is less rich in stabilizing material than is the ordinary micelle.

The light-gray wastage in the Bredig vessel is practically pure platinum.

ADELAIDE, SOUTH AUSTRALIA RECEIVED MAY 22, 1939

[CONTRIBUTION FROM MOORE LABORATORY OF CHEMISTRY, AMHERST COLLEGE]

The Use of the Concentration Cell in Quantitative Analysis. II. The Determination of Fluoride[1]

BY GEORGE W. LOW, JR.,[2] AND EVERETT H. PRYDE

The first paper in this series[3] described in detail the procedure which may be used for the determination of traces of chloride by employing a simple concentration cell. It was pointed out that the technique involved should be perfectly general and should be applicable to the determination of any substance for which a suitable reversible electrode could be found. In the present paper is given a discussion of the application of this technique to the determination of fluoride. Detailed reviews of the literature on the subject of fluoride determination recently have been given[4] and therefore need not be considered here.

Preliminary Measurements

Our first concern was to find an electrode which would behave reversibly toward fluoride ions. Allen and Furman[5] have reviewed this subject in developing a potentiometric titration method for fluorine. Treadwell and Köhl[6] showed that the system Fe^{+++}/Fe^{++}–Pt functions as a good fluoride electrode because of the formation of the complex iron cryolite, Na_3FeF_6. This system seemed to offer the best possibilities for use in the concentration cell. Accordingly preliminary titrations were performed using the electrode pair, Pt–satd. calomel, in order to determine, if possible, the conditions of acidity and salt concentration which would be most suitable for the final concentration cell measurements and for what range of fluoride concentration the electrode would be expected to function. These titrations, the results of which are shown in Figs. 1, 2 and 3, give information, of a qualitative nature, which is of particular value to anyone who wishes to carry out concentration cell measurements under different conditions from those described in this paper.

Figure 1 shows typical curves for the titration of pure ferric chloride solutions of different concentrations with solutions of sodium fluoride, in the presence of a small amount of ferrous iron, potassium chloride of concentration 0.5 *M*, and hydrochloric acid 0.01 *M*. Under these condi-

(1) Presented at the 97th meeting of the American Chemical Society held at Baltimore, Md., April 3 to 7, 1939.

(2) Present address: American Viscose Corporation, Front Royal, Virginia.

(3) Furman and Low, THIS JOURNAL, **57**, 1585, 1588 (1935).

(4) (a) Reynolds and Hill, *Ind. Eng. Chem., Anal. Ed.*, **11**, 21 (1939); (b) McClure, *ibid.*, **11**, 171 (1939).

(5) Allen and Furman, THIS JOURNAL, **55**, 90 (1933).

(6) Treadwell and Köhl, *Helv. Chim. Acta*, **9**, 470 (1926).

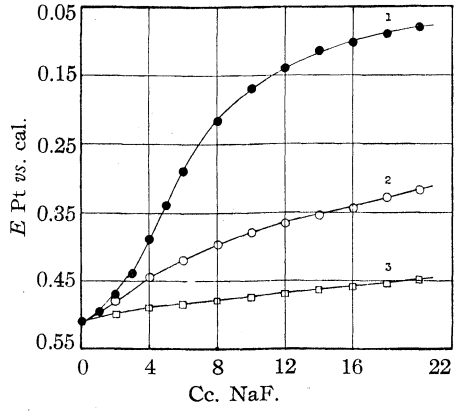


Fig. 1.—Effect of Fe^{+++} and F^- concentrations: volume at start of titration, 20 cc.

Curve	Fe^{+++}	NaF	Fe^{+++}/Fe^{++}	KCl	HCl
1	0.01	0.1	2/1	0.5	0.01
2	.001	.01	2/1	.5	.01
3	.0001	.001	2/1	.5	.01

tions, 1 cc. of 0.001 *M* sodium fluoride solution added to 20 cc. of 0.0001 *M* ferric chloride causes a measurable change in the e. m. f. of the electrode system. In Fig. 2 are presented a number of curves showing the effects of acidity and of potassium chloride concentration on the shape of the curves given in Fig. 1. The potassium chloride concentration is relatively unimportant, whereas if the solution is too acidic the sensitivity of the

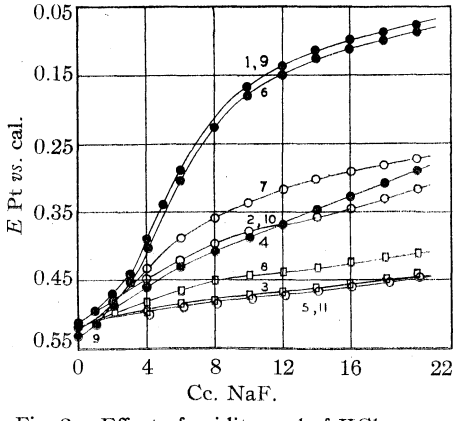


Fig. 2.—Effect of acidity and of KCl concn.

Curve	Fe^{+++}	NaF	Fe^{+++}/Fe^{++}	KCl	HCl
1	0.01	0.1	2/1	0.5	0.01
2	.001	.01	2/1	.5	.01
3	.0001	.001	2/1	.5	.01
4	.01	.1	2/1	.5	.10
5	.001	.01	2/1	.5	.10
6	.01	.1	2/1	.5	.0015
7	.001	.01	2/1	.5	.0015
8	.0001	.001	2/1	.5	.0015
9	.01	.1	2/1	0	.01
10	.001	.01	2/1	0	.01
11	.0001	.001	2/1	0	.01

electrode to fluoride ions is markedly decreased. On the other hand, the acidity should not be too low, because even in 0.001 *M* hydrochloric acid solutions hydrolysis of ferric chloride is quite rapid.[7]

Preliminary titrations of this type also give important information of a qualitative nature, with regard to the effect of impurities on the e. m. f. of the system. Anything which reacts with ferric ion, ferrous ion, or fluoride ion, would be expected to interfere with a determination of this sort.

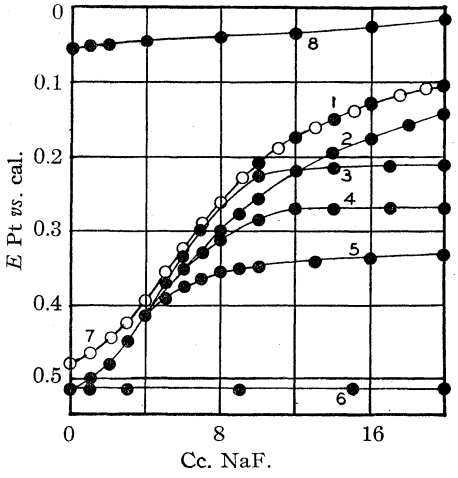


Fig. 3.—Effect of foreign salts: Fe^{+++}, 0.01; NaF, 0.1; Fe^{+++}/Fe^{++}, 2/1; KCl, 0.5; HCl, 0.01; foreign salt, 0.1: 1, none, KNO_3, NaCl, NH_4Cl, KBr, $ZnCl_2$; 2, $MgCl_2$; 3, $HgCl_2$; 4, $CuCl_2$; 5, $CaCl_2$; 6, $AlCl_3$; 7, K_2SO_4; 8, tartrate.

Figure 3 shows the effects of a number of foreign salts on curve 1 of Fig. 1. The fact that aluminum ions interfere so completely can be interpreted as evidence that the Al–F complex is more stable than the Fe–F complex. A number of bivalent metals also affect the curve (but only after about 4 cc. of the sodium fluoride solution is added) owing, presumably, to the formation of the insoluble MF_2. It is interesting to note that these curves give a measure of the relative insolubilities of the several fluorides involved. Interference by these ions is not encountered at the start of the titration, when the ferric ion concentration is relatively high; *i. e.*, we would expect calcium fluoride to dissolve in ferric chloride if the latter is present in great excess. Sulfate, citrate and tartrate interfere because of reaction with the ferric ion, and special means must be taken to eliminate this effect, as well as those mentioned

(7) Lamb and Jacques, THIS JOURNAL, **60**, 973, 1215 (1938).

above, when determining fluoride with the concentration cell.

All of the above qualitative information is valuable in considering the best conditions for determining fluoride with the concentration cell. Consideration of these curves showed that the following cell would serve as a suitable test of the concentration cell technique over the range of fluoride concentration, a, from 1–20 mg. per liter.

Cell 1

(1)		(2)	
Fe^{+++}	= 0.0005	Fe^{+++}	= 0.0005
Fe^{++}	= .0002	Fe^{++}	= .0002
Pt, KCl	= .5	KCl	= .5, Pt
HCl	= .01	HCl	= .01
F^-	=	F^-	= a

All concentrations are expressed in moles per liter.

It is a simple matter to calculate what the e. m. f. of cell 1 should be if we know the reaction which takes place between ferric and fluoride ions. The following relationship would be valid at 30°

$$E = 0.0601 \log \frac{f_1' Fe_1^{+++}}{f_1 Fe_1^{++}} \Big/ \frac{f_2' Fe_2^{+++}}{f_2 Fe_2^{++}} \qquad (1)$$

where the subscripts refer to sides 1 and 2 of cell 1, f is the activity coefficient, Fe^{+++} and Fe^{++} refer to the molar concentrations of the two ions, and E is the difference of potential between the two platinum wires. Since Fe^{++} does not enter into the reaction with fluoride, and since $f_1' = f_2'$ and $f_1 = f_2$ because of the high and essentially uniform ionic strength throughout, the equation may be simplified to

$$E = 0.0601 \log \frac{Fe_1^{+++}}{Fe_2^{+++}} \qquad (2)$$

If the reaction between ferric and fluoride ions is:

$$xF^- + Fe^{+++} = (FeF_x)^{-(x-3)}$$

then

$$Fe_2^{+++} = 0.0005 - \frac{1}{x} a$$

and

$$Fe_1^{+++} = 0.0005$$

where a is the molar concentration of fluoride and $x - 3$ represents the number of charges on the complex ion. Thus it is possible to calculate x from the e. m. f. of the cell if we work with known concentrations of fluoride. In Table I is given a summary of measurements made using cell 1. It is seen that x is not 6, as we might reasonably expect it to be, nor is it a constant. If a constant value for x is used in the Nernst equation, a curve (curve 1, Fig. 4) is obtained, whereas the experimental data fit a straight line

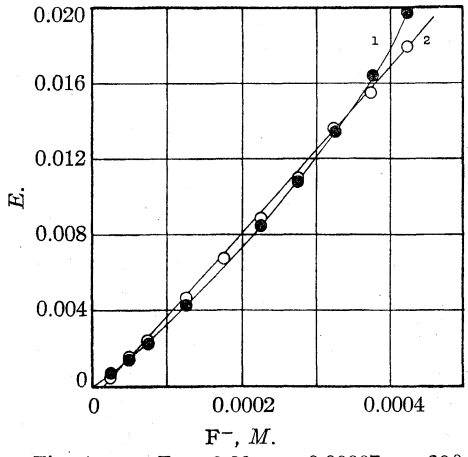


Fig. 4.—○, $E = 2.29a_2 - 0.00067$, at 30°; ●, $E = 0.0601 \log (0.0005/(0.0005 - 0.61a_1))$.

(curve 2, Fig. 4) which is described by the following empirical equation

$$E = 2.29\ a_2 - 0.00067 \text{ at } 30°$$

where E is the observed e. m. f. of the cell when the fluoride concentration, a_2, is expressed as mg. of fluoride per liter.

TABLE I

RESULTS WITH CELL 1

Fluoride concn. mol., a_1	Fluoride concn. mg./l., a_2	E	Fe_2^{+++} calcd. equation 2	x
0.000025	0.48	0.00045	0.000488	2.94
.000050	.95	.0016	.000467	1.69
.000075	1.43	.0026	.000450	1.58
.000125	2.38	.0050	.000410	1.44
.000175	3.33	.0069	.000381	1.51
.000225	4.28	.0090	.000351	1.53
.000275	5.22	.0112	.000323	1.58
.000325	6.18	.0134	.000297	1.63
.000375	7.12	.0156	.000273	1.66
.000425	8.07	.0180	.000249	1.72
.000500	9.5	.0213	.000220	1.81

The preliminary measurements described above lead us to the conclusion that an empirical but reproducible relationship, suitable for analytical determinations, exists between the e. m. f. of a given cell and the fluoride concentration. Thus if it is desired to use a concentration cell for measurements of unknown fluoride concentrations it is necessary to determine experimentally the empirical curve for the particular ferric reagent being used.

Results with the Concentration Cell

Apparatus.—The glass concentration cell has been described in detail by Furman and Low.[3] All e. m. f. measurements were made by means of a Leeds and Northrup type K2 potentiometer in conjunction with a Leeds and Northrup lamp and scale galvanometer No. 2420c. For most measurements the ordinary Students type potentiometer with a sensitive galvanometer should be satisfactory.

Platinum wires sealed into soft glass tubing were used as electrodes, and it is very important that they be cleaned frequently by dipping into chromic acid cleaning solution. All measurements were made after the cell had reached constant temperature in a water-bath designed to maintain the temperature constant within ±0.02°.

Cell Used.—Since sulfate is likely to be encountered with fluoride in waters or in distillates resulting from the separation of fluoride from other materials, it was decided to modify cell 1 for our final series of measurements by adding sulfate to each side. In this way, the effect of small amounts of sulfate on the e. m. f. of the system is masked. This addition of sulfate merely changes the slope of the straight line of Fig. 4, and offers no inconvenience, since the empirical relationship must be determined anyway. The following cell was used for all measurements described in this paper, with the exception of a few which will be indicated specifically:

Cell 2

	$FeCl_3$ = 0.000497 ± 0.000002		$FeCl_3$ = 0.000497 ± 0.000002
	Fe^{++} = any value (0.0002)		Fe^{++} = any value (0.0002)
Pt,	KCl = 0.5 ± 0.1		KCl = 0.5 ± 0.1
	Na_2SO_4 = 0.15 ± 0.01		Na_2SO_4 = 0.15 ± 0.01, Pt
	HCl = 0.0094 ± 0.0001		HCl = 0.0094 ± 0.0001
	F^- = 0		F^- = 0.000025 to 0.0016 (0.5 to 30 mg./l.)

Measurements showed that the concentrations (all expressed as molarities) must be within the limits indicated in order that the e. m. f. values fit the data presented in this paper. However, it is an easy matter for any worker to determine his own empirical curve (with known amounts of fluoride) for any given ferric ion concentration. Variation of any of the concentrations outside of the above limits results in a change of the slope of the straight line. A careful study of the preliminary titrations, shown in Figs. 1, 2, and 3, was necessary in order to decide upon the various concentrations shown in cell 2, for the determination of fluoride concentrations of from 0.5 to 30 mg. per liter. For much higher concentrations of fluoride, or lower, a different concentration of ferric ion in the cell would be necessary.

Reagents and Chemicals.—It was found convenient to prepare the following reagents. All concentrations indicated need be only approximate, standardization of solutions being unnecessary since an empirical curve must be determined. Our ferric reagents were standardized, and the final ferric ion concentration is indicated in cell 2, but only because we had hoped to find that our data would fit the Nernst equation in some way.

Hydrochloric acid: one liter of 3 *M* stock solution.

Reagent 1: one liter of ferric stock solution containing 0.16 *M* $FeCl_3$ and 0.3 *M* HCl.

Reagent 2: ferric solution containing 0.0016 *M* $FeCl_3$, 0.03 *M* HCl, 1.67 *M* KCl and 0.50 *M* Na_2SO_4. One liter of this reagent can be prepared conveniently by pipetting exactly, 10 ml. of Reagent 1 and 10 ml. of hydrochloric acid stock solution (3 *M*) into a liter volumetric flask, adding the proper amounts of C. P. potassium chloride and sodium sulfate decahydrate (weighed roughly) and diluting to one liter. It is best to dissolve the potassium chloride and sodium sulfate in boiling water before adding to the volumetric flask.

$(NH_4)_2SO_4 \cdot FeSO_4 \cdot 6H_2O$, C. P.: a stock solution of this is not prepared because of the ease of oxidation by air. Solutions are made freshly as needed.

NaF, C. P., or other material containing a known amount of fluoride: a stock solution of this is convenient, but should be kept in a paraffin lined bottle.

Procedure.—In order to make a measurement of the amount of fluoride in a given solution, the following procedure is used. Two solutions are prepared:

Solution 1		Solution 2	
Reagent 2	3 cc.	Reagent 2	3 cc.
Fe^{++} soln.	2 cc.	Fe^{++} soln.	2 cc.
Water	5 cc.	F^- soln.	5 cc.

(The ferrous ion solution is made freshly from C. P. Mohr salt and should be roughly 0.001 *M* in Fe^{++} and 0.001 *M* in hydrochloric acid. The actual concentration of Fe^{++} may vary a hundred-fold, as shown below, provided the same solution is used for both solutions 1 and 2.)

Pipets are used to measure out the quantities of solutions needed above. Solution 1 is then transferred to one side of the concentration cell, solution 2 to the other, care being taken not to make the junction between the two sides, in order to avoid mixing. A platinum electrode is inserted in each side of the cell and it is then placed in the thermostat. After five minutes have elapsed, in order for the solutions to reach temperature equilibrium, the junction is made between the sides of the cell (as described by Furman and Low[3]) and the e. m. f. measured. The e. m. f. remains constant for at least a half hour under ordinary circumstances. Drifting of the potentials indicates that the solutions are mixing or that the electrodes are not clean and the measurement is of no value. From the e. m. f. can be calculated the amount of fluoride present by means of the empirical equation obtained below from measurements of known fluoride solutions.

Results with Pure Fluoride Solutions.—In order to determine the empirical relationship between e. m. f. of the cell and amount of fluoride present, a series of measurements was made using solutions of fluoride made from C. P. sodium fluoride. Table II shows the results obtained. In the two columns at the right the data are expressed as gamma in the 5-cc. sample taken for analysis, which is diluted to 10 cc. (see procedure) to become the "final concentration" shown in the two left columns and expressed as mg. per liter. It can be seen that the method is satisfactory for amounts of fluoride, in the 5-cc. sample taken for analysis, as small as 1

gamma. That these data fit a straight line is shown in Fig. 5. The equation for the straight line was found from a series of measurements made at different temperatures, as described below, under *effect of temperature*. If more than 30 mg. per liter of fluoride is present in the final solution, the relationship is no longer linear, and therefore the fluoride sample should be adjusted so that the amount of fluoride in the final solution falls within the range indicated. As shown below larger amounts of fluoride could also be determined using a reagent in which the ferric ion concentration is higher.

TABLE II

MEASUREMENTS OF SOLUTIONS OF PURE SODIUM FLUORIDE

Final concentrations of fluoride, mg./l. or p. p. m.[a]		Fluoride in 5-cc. sample taken for analysis, γ	
Added	Found[a]	Added	Found[a]
0.10	0.07	1.0	0.7
.20	.22	2.0	2.2
.30	.25	3.0	2.5
.40	.41	4.0	4.1
.48	.47	4.8	4.7
.95	.97	9.5	9.7
1.90	1.86	19.0	18.6
2.37	2.32	23.7	23.2
2.72	2.65	27.2	26.5
3.33	3.21	33.3	32.1
4.75	4.50	47.5	45.0
4.79	4.75	47.9	47.5
7.12	6.90	71.2	69.0
9.50	9.32	95.0	93.2
11.4	11.4	114	114
15.2	15.1	152	151
24.7	24.4	247	244
30.4	29.0	304	290

[a] Calculated from the following equation, g. F^-/l. = (0.490 + 0.002t) E + 0.0001 in which E is the observed e. m. f. of the cell and t is the centigrade temperature.

Results with Known Fluoride Samples.—A series of measurements was also made using other sources of fluoride than C. P. sodium fluoride, specifically synthetic sodium fluoride made by the method suggested by Allen and Furman[8] from C. P. sodium carbonate and hydrofluoric acid, C. P. calcium fluoride, C. P. sodium fluosilicate, and Bureau of Standards fluorspar of known purity. The sodium fluoride was dissolved in water, but the others, being insoluble in water, were treated by a special procedure which was predicted on the basis of the preliminary titrations. To an accurately weighed sample, not over 0.1 g., was added 30 cc. of water and 30 cc. of Reagent 1 (measured by pipet). The mixture was stirred on the hot-plate (80–90°) for one hour, cooled and diluted to 100 cc. in a volumetric flask. This solution was then diluted to the proper concentration for measurement in the concentration cell, with a solution of potassium chloride, hydrochloric acid and sodium sulfate. The reference side of the cell was made in exactly the same way except that no fluoride was put into it. Prolonged heating on the hot-plate was found to be necessary only for the fluorspar; the calcium fluoride and sodium fluosilicate dissolved readily in fifteen minutes of stirring at room temperature. The results obtained using a number of samples of these materials are given in Table III.

(8) Allen and Furman, THIS JOURNAL, **54**, 4625 (1932).

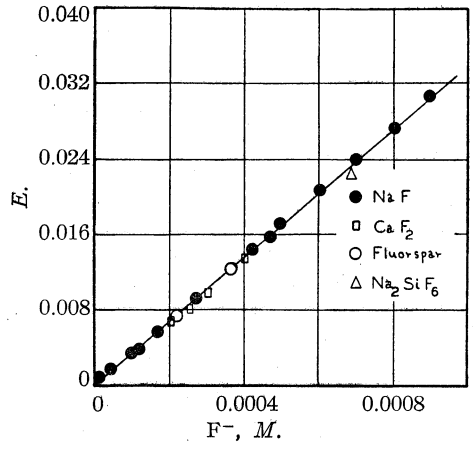


Fig. 5.

TABLE III

MEASUREMENTS OF FLUORIDE IN KNOWN SAMPLES

Substance	Final concentrations of fluoride, mg./l. or p. p. m.		Fluoride in 5-cc. sample taken for analysis, γ	
	Added	Found[a]	Added	Found[a]
NaF synthetic	2.72	2.65	27.2	26.5
CaF_2, C. P.	2.43	2.37	24.3	23.7
CaF_2, C. P.	3.82	3.65	38.2	36.5
CaF_2, C. P.	4.73	4.50	47.3	45.0
CaF_2, C. P.	5.02	4.77	50.2	47.7
CaF_2, C. P.	5.70	5.54	57.0	55.4
CaF_2, C. P.	7.60	7.41	76.0	74.1
Fluorspar, B. S.	4.07	4.03	40.7	40.3
Fluorspar, B. S.	6.96	6.78	69.6	67.8
Fluorspar, B. S.	7.04	6.42	70.4	64.2
Na_2SiF_6, C. P.	13.1	12.5	131	125

[a] Calculated from the equation: g. F^-/l. = (0.490 + 0.002t) E + 0.0001.

Effect of Ferric Ion Concentration.—It was pointed out above that the ferric ion concentration determines the slope of the straight line of Fig. 5. Quantitative data concerning the magnitude of this effect are shown in Fig. 6 and Table IV.

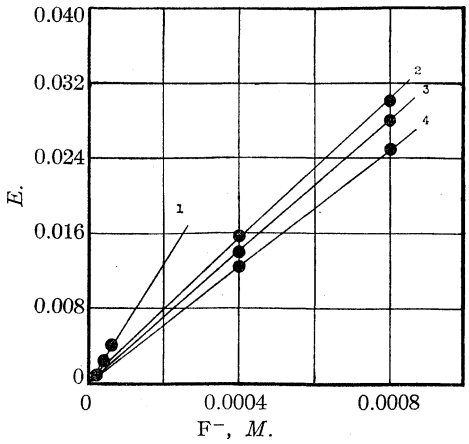


Fig. 6.—Curve 1, Fe^{+++} = 0.0000993 *M*; 2, Fe^{+++} = 0.000398; 3, Fe^{+++} = 0.000497; 4, Fe^{+++} = 0.000597.

TABLE IV

EFFECT OF CHANGE IN FERRIC ION CONCENTRATION

Fe^{+++} = 0.0000993, Reagent 3. Fe^{+++} = 0.000497, Reagent 2.

F^- present, mg./l.	E. m. f., reagent 3	E. m. f., reagent 2
0.19	0.0003	0.00017
.38	.0009	.00052
.76	.0026	.00122
1.14	.0040	.00194

In each case the reagent differs from Reagent 2 only with respect to the ferric ion concentration; all other concentrations are the same. Thus it can be seen that if we were working with very small amounts of fluoride (under 1 mg. per liter), it would be to our advantage to use a reagent whose ferric ion concentration is lower than that of Reagent 2. This reasoning cannot be carried too far, however, because if the concentration is much lower than that indicated for Reagent 3 there is so little iron present that the e. m. f. cannot be read to as many decimal places; the system is then insensitive. On the other hand, if it is desired to measure amounts of fluoride greater than 30 mg. per liter, a reagent whose ferric ion concentration is greater than that of Reagent 2 can be used, which will again cause a different slope to the line.

Effect of Ferrous Ion Concentration.—It was assumed in the preliminary discussion that the concentration of ferrous ion in the cell should not be critical since it does not enter into the reaction with fluoride. It seemed advisable, however, to obtain quantitative data showing this assumption to be valid. Table V gives the results obtained using cell 2, with the exception that the ferrous ion concentration was varied a hundredfold. This table shows definitely that the ferrous ion concentration may be any value within reasonable limits. It is important to note, however, that the concentration must be the same on each side of the cell in any given measurement. One other factor also must be considered: namely, that the ferrous ion concentration must be kept fairly low in order to make sure that no appreciable amount of ferric ion, which is always present as an impurity, is added to the cell.

TABLE V

EFFECT OF CHANGE IN FERROUS ION CONCENTRATION

Ferrous concn. in each side, *M*	E. m. f., v.	F^- found mg./l.
0.00002	0.0047	2.64
.0002	.00470	2.64
.002	.00475	2.67

Effect of Temperature.—It was expected that the e. m. f. value would, of course, be higher if the temperature were higher, for any particular cell. Accordingly, it was somewhat surprising to find exactly the opposite effect; *i. e.*, the e. m. f. of a given cell was lower at 30° than at 25°. Measurements were made, using cell 2, at a series of temperatures, allowing time for temperature equilibrium to be reached between readings. The temperature in the thermostat in which the cell was placed was raised from 15 to 35° and then lowered again to 15°. The same e. m. f. value, at any temperature, was obtained when approached from above or below the given temperature. In Table VI is given a summary of data showing this unexpected effect.

TABLE VI

EFFECT OF TEMPERATURE

Temp., °C.	F^-, 0.0004 *M* Obsd. e. m. f.	F^-, 0.0004 *M* Calcd. e. m. f.[a]	F^-, 0.0008 *M* Obsd. e. m. f.	F^-, 0.0008 *M* Calcd. e. m. f.[a]
15	0.0143	0.0143	0.0289	0.0289
20	.0141	.0145	.0284	.0294
25	.0139	.0148	.0280	.0299
30	.0137	.0150	.0275	.0304
35	.0134	.0153	.0269	.0309

[a] Calculated assuming the value at 15° to be correct; *i. e.*, the e. m. f. at 20° should be 293/288 × the value at 15°.

These results are shown graphically in Fig. 7.

This unexpected phenomenon can be explained on the basis that the degree of hydrolysis of the ferric chloride is greater at the higher temperatures. A measurement carried out at 100° supports this view, inasmuch as at this temperature a precipitate was formed, presumably of ferric hy-

droxide. That the effect is due to hydrolysis rather than to a change of the extent of dissociation of the Fe–F complex was shown by a measurement made on a similar cell put together without any fluoride present in either side. The same anomalous effect was observed with this latter cell.

If consideration is taken of this observed effect of temperature on the slope of the line of Fig. 5, equation 3 is found to be the empirical equation which fits our data at any temperature between 15 and 35°. E is the observed e. m. f. of the cell, and t the centigrade temperature.

$$\text{g. } F^-/\text{l.} = (0.490 + 0.002t)\,E + 0.0001 \quad (3)$$

This hydrolysis in no way affects the usefulness of the method, since the fact that our reagents remained perfectly stable over a period of many months shows that this partial hydrolysis of the ferric chloride is completely reversible and not progressive. It is interesting to note that a means here suggests itself for measuring the degree of hydrolysis of salts of this type by e. m. f. measurements.

TABLE VII

EFFECT OF IMPURITIES

Impurity	Impurity molarity	Final solution impurity concn. mg./l.	Concn. in final solution, mg./l. F^- added	F^- found
....	....	.....	7.6	7.6
KCl	0.1	K, 3900 Cl, 3500	7.6	6.7
KCl	.01	K, 390 Cl, 350	15.2	15.3
NaCl	.01	Na, 230	15.2	15.1
K_2SO_4	.01	SO_4, 960	15.2	15.7
Na_2SO_4	.005	SO_4, 480	15.2	15.6
K_2SO_4	.001	SO_4, 96	15.2	15.3
$CaCl_2$	.01	Ca, 400	15.2	15.8
$CaCl_2$	.001	Ca, 40	15.2	15.1
K_2HPO_4	.01	PO_4, 950	15.2	70.1
K_2HPO_4	.0001	PO_4, 10	7.6	8.6
H_3BO_3	.01	H_3BO_3, 600	7.6	7.4
$MgCl_2$	.01	Mg, 240	15.2	14.6
$MgCl_2$	.001	Mg, 24	15.2	15.3
$MnCl_2$	.01	Mn, 550	15.2	14.5
$MnCl_2$	.001	Mn, 55	15.2	15.2
$HgCl_2$	.01	Hg, 2000	15.2	14.8
$HgCl_2$	.001	Hg, 200	15.2	15.1
KBr	.01	Br, 800	15.2	15.1
Tartrate	.0001		15.2	16.0
Citrate	.0001		15.2	20.7
$CuCl_2$	.001	Cu, 64	15.2	15.1
NH_4Cl	.01	NH_4, 180	15.2	15.2
$AlCl_3$	.0001	Al, 2.7	15.2	8.5
KNO_3	.01	NO_3, 620	7.6	7.4
Na_2SiO_3	.001	SiO_3, 75	7.6	8.1
$Th(NO_3)_4$	.001	Th, 230	7.6	0.2
$NaClO_4$	.01	ClO_4, 1000	2.7	2.6

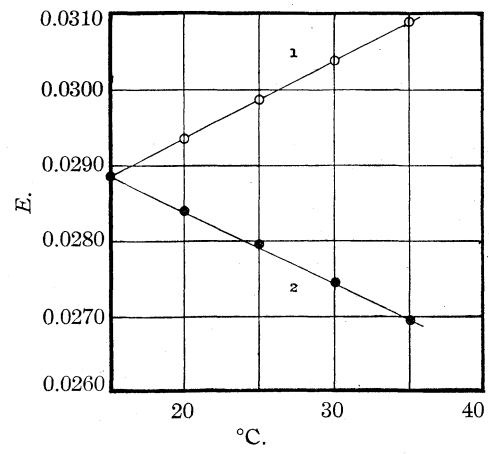


Fig. 7.—Effect of temperature: curve 1, theoretical; curve 2, experimental.

Cell

	Fe^{+++} = 0.0005		Fe^{+++} = 0.0005	
	Fe^{++} = .0002		Fe^{++} = .0002	
Pt,	KCl = .5		KCl = .5,	Pt
	Na_2SO_4 = .15		Na_2SO_4 = .15	
	HCl = .01		HCl = .01	
	F^- = 0		F^- = .0008	

Effect of Impurities.—In order that the method may be of value for the determination of fluoride, it must function, of course, in the presence of certain impurities. Consequently, a series of measurements was performed which was designed to study this effect. Different foreign salts were added with the fluoride to the concentration cell, and the effect of these salts, if any, on the e. m. f. was determined. Table VII summarizes the data obtained in this series. A study of this table shows that most of the common ions cause no trouble, but that high results are obtained if phosphate, citrate or tartrate is present (because of reaction with ferric ion), and low results if aluminum or thorium is present (because of reaction with fluoride). As was predicted on the basis of the preliminary titrations, calcium and other bivalent metal ions do not interfere if present in moderate amounts. It can be seen that appreciable amounts of sulfate, perchlorate or silicate, cause no trouble. This is very important, inasmuch as it means that the distillate obtained by separation of fluoride by the usual methods contains no ions which would interfere with the determination of the fluoride. It also should be noted that if the total concentration of impurity is greater than 0.01 M, fictitious e. m. f. values will be encountered because of a liquid junction potential.

Means of eliminating trouble due to impurities will be given below.

Distillation of Fluoride.—A very satisfactory method for the separation of fluoride from other substances has been developed by Willard and Winter.[8a] They recommend the separation of fluoride by distillation from a perchloric acid solution. The determination of fluoride in the distillate can then be made by a number of standard methods. That our concentration cell method is satisfactory for the determination of fluoride in this distillate is shown in Table VIII. A 30-cc. sample of pure sodium fluoride solution, of the concentration shown in the table, was distilled according to the Willard and Winter procedure and the amount of fluoride in the distillate measured by the technique described here.

TABLE VIII

DISTILLATION OF FLUORIDE BY WILLARD–WINTER PROCEDURE

75 cc. of distillate

Concn. of 30-cc. sample, mg./l.		Mg. of fluoride	
Added	Found	Added	Found
4.7	4.7	1.4	1.4
16.7	15.3	5.0	4.6
30	29	9.0	8.7
62	61	18.6	18.3

Another procedure commonly employed is distillation from sulfuric acid solution. This offers the advantage that the temperature can be taken much higher without the danger of explosion which is attendant upon the use of perchloric acid. It is often quite difficult to separate fluoride from a sample by a single perchloric acid distillation, and it is frequently the practice to distil twice, first from sulfuric acid and then from perchloric acid.[9] This second distillation is for the purpose of removing small amounts of sulfate which interfere with some methods of determining the fluoride. Distillation from sulfuric acid has been described in detail by Hoffman and Lundell[10] and is used by them in the determination of fluoride in phosphate rock. Their determination of fluoride in the distillate is then done by a gravimetric process, precipitation as lead chlorofluoride. The concentration cell technique is applicable to the determination of fluoride in such rocks, where the percentage of fluoride is low. Table IX shows the results obtained in determining the fluoride in Bureau of Standards sample No. 56a, by means of our technique. The distillation was carried out as described by Hoffman and Lundell, with the exception that we employed no preliminary fusion and collected the distillate in air rather than under sodium hydroxide solution. Three hundred cc. of distillate was collected, the solution made faintly alkaline to phenolphthalein, then very slightly acidic with 0.01 *M* hydrochloric acid, and diluted to 500 cc. in a volumetric flask. Five cc. of this was then taken for analysis in the concentration cell according to the procedure already described. The whole procedure, after the distillation, takes about fifteen minutes, whereas the gravimetric procedure usually employed takes much longer.

TABLE IX

ANALYSIS OF PHOSPHATE ROCK

Bureau of Standards Sample No. 56a

Sample, g.	% F^- present (certificate)	% F^- found			
0.3650	3.56		3.56		
.1988	3.56	3.61	3.57[a]	3.57[b]	

[a] A 50-cc. sample of the distillate from sample 2 was evaporated to dryness after making slightly alkaline with sodium hydroxide. It was then taken up with water, made slightly acidic with hydrochloric acid and diluted to 25 cc. Five cc. of this solution was then taken for analysis. The evaporation was carried out in Pyrex glass. [b] Same as [a] except that the evaporation was carried out in platinum.

These results show that distillates may be concentrated, if desired, by evaporation in either glass or platinum. Since our experiments concerning the effect of impurities showed that small amounts of silicate do not interfere, this was to be expected.

Elimination of Error Due to Phosphate.—The preceding section described the procedure which may be used for the separation of fluoride from any or all impurities, by distillation. It is possible to determine fluoride in the presence of phosphate by means of a procedure which involves no distillation. If phosphate is present with the fluoride, fictitiously high values for fluoride would be found by the usual concentration cell technique, because of the fact that phosphate reacts with ferric ions in much the same way as does fluoride. This difficulty can be eliminated in the following manner. First the "apparent fluoride" is measured in the usual way by the direct procedure. The measurement is then repeated on a different sample, with a small amount of aluminum ion in each side of the concentration cell. Thus the two solutions would be made as follows.

(8a) Willard and Winter, *Ind. Eng. Chem., Anal. Ed.*, **5**, 7 (1933).
(9) Churchill, Bridges and Rowley, *ibid.*, **9**, 222 (1937).
(10) Hoffman and Lundell, *J. Research Natl. Bur. Standards*, **20**, 607 (1938).

Solution 1	Solution 2
3 cc. reagent 2	3 cc. reagent 2
1 cc. Fe^{++} solution	1 cc. Fe^{++} solution
1 cc. Al^{+++} sol. (0.015 *M*)	1 cc. Al^{+++} sol. (0.015 *M*)
5 cc. H_2O	5 cc. F^- ($+PO_4$) solution

In this second cell the aluminum ions tie up the fluoride so that it cannot react with the ferric ions, whereas the phosphate does not react with aluminum ions if ferric ions are also present. The e. m. f., therefore, is due to the phosphate alone, whereas the e. m. f. of the first cell is due to both the phosphate and the fluoride. The difference between the two values gives the e. m. f. due to the fluoride. Table X shows results obtained by this procedure. The results show that the method yields only approximate values and that distillation should be resorted to if accurate values are required.

TABLE X

DETERMINATION OF FLUORIDE IN THE PRESENCE OF PHOSPHATE

		Direct procedure		Aluminum procedure		
			Apparent		E. m. f. due	
PO_4 present mg./l.	F^- present mg./l.	E. m. f.	F^- found mg./l.	E. m. f. due to phosphate	to F^- (by diff.)	F^- found mg./l.
10	1.6	0.0054	3.0	0.0024	0.0030	1.7
20	1.6	.0092	5.1	.0054	.0038	2.2
30	1.6	.0124	6.8	.0087	.0037	2.1

Analysis of Water Samples.—The technique was tested on Arizona water samples, which were kindly furnished by Professor H. V. Smith of the University of Arizona, who recently has compared[11] a number of standard methods used for the determination of fluoride in water. These samples had been analyzed in his laboratories, and his results are given with ours in Table XI as a means of comparison. Samples 4 and 5 had been passed through a bone filter devised by Smith and Smith[12] to remove fluoride from water; the original content of these samples was quite high in fluoride.

TABLE XI

ARIZONA WATER SAMPLES

	Fluoride found, mg./l.		
Sample no.	Direct proc.	Aluminum proc.	H. V. Smith Sanchis method
1	3.5	3.5	4.0
2	6.8	6.3	6.0
3	0.7	0.2	0.3
4	.9	.6	.3
5	.4	.1	.0
6	4.1	3.8	3.5

The table indicates that there was a small amount of phosphate in the water also, the effect of which was removed by means of the "aluminum procedure" already described.

(11) Smith, *Ind. Eng. Chem., Anal. Ed.*, **7**, 23 (1935).
(12) Smith and Smith, *Water Works Eng.*, Nov. 10, 1937.

Discussion of Results

Advantages of the Technique

1. *Wide range of applicability.*—The procedure should be applicable to the determination of fluoride in any substance, since it may be applied to the filtrate obtained by distilling fluoride from impurities, from either a perchloric or sulfuric acid medium.

2. *Rapidity.*—A single measurement takes about fifteen minutes, if the fluoride is present in solution. If a solid material is being analyzed, or if many impurities are present, the time to carry out the distillation to separate the fluoride must be added to this. It is very convenient to make a number of measurements at the same time, using three or four concentration cells.

3. *Simplicity.*—Since the procedure involves only the use of a pipet and the ability to read a potentiometer, it is extremely simple. In addition, no personal error enters, as it does in certain titration methods where the end-point is difficult to distinguish.

4. *Accuracy.*—For small amounts of fluoride the accuracy of the method is satisfactory, particularly if the size of sample can be so regulated that the amount of fluoride in the final cell is above 10 mg. per liter.

5. *Application to micro determination.*—As indicated in the tables, the method is suitable for quantitative determination of as little as 1 gamma of fluoride in 5 cc. of solution taken for analysis.

Disadvantages of the Technique

1. *Necessity for an empirical curve.*—Unfortunately it is impossible to relate the e. m. f. of the concentration cell to the amount of fluoride in any way except by an empirical equation. Fortunately, however, it is a straight line relationship in the range studied. Thus for all practical purposes this is no serious disadvantage. All of the measurements given in this paper, using cell 2, were made using the same empirical curve. Since the reagents are perfectly stable, a curve once determined is satisfactory for a year or more if sufficient reagent is made. The amounts suggested in this paper are sufficient for about 15,000 determinations.

2. *Limited to small amounts.*—Because of the very nature of the technique, our procedure is

limited to the determination of small amounts of fluoride. A detailed study has not been made of the application of this technique to larger amounts using a much higher concentration of ferric ion in the reagent. The preliminary titrations indicate that such an application could be made, but the range we have chosen to study should be satisfactory for most of the fluoride determinations necessary.

3. *Accuracy.*—Although, as pointed out above, the accuracy is very good for the small amounts of fluoride determined, it should also be mentioned that the method would not be satisfactory for the accurate determination of fluoride in a substance whose fluoride content is greater than 10%, because in that case a 1% error would be appreciable, whereas for very small amounts of fluoride a 1% error is not important.

4. *Liquid junction.*—It is important to keep the total impurity molarity of the unknown fluoride solution below 0.01 *M*, else an appreciable liquid junction potential will cause fictitious results. In practice this is very easily done, by distilling the sample from impurities if in no other way. The distillate is much lower than 0.01 *M* in foreign ions.

It should be pointed out that the size of sample of an unknown should be adjusted so that the amount of fluoride in the final concentration cell is between 0.1 and 30 mg. per liter, preferably greater than 10 mg. per liter, since the percentage error is smaller for larger amounts of fluoride.

The procedure we have described corresponds to the "Standard Solution" method for chloride used by Furman and Low.[3] An attempt was made to apply the "small excess" method[3] to the determination of fluoride, but with no success. The e. m. f. of the cell, with fluoride in both sides, seemed to be dependent upon the difference in fluoride concentration between the two sides rather than the ratio of the two concentrations. Because this "small excess" method offered no promising results, we abandoned a further study of it in favor of the procedure we have given.

The material presented in this paper gives indication that the technique described should be applicable to the determination of a number of other substances, such as aluminum, phosphate, sulfate, citrate or tartrate, by slight modifications of the procedure. It is hoped that further study will confirm this prediction.

Summary

A technique has been described for the determination of fluoride rapidly and accurately by means of a simple concentration cell. Interference of other ions can be eliminated entirely, since the procedure is applicable to the determination of fluoride in the distillate obtained in separating fluoride from all impurities. The range over which the method has been applied is 0.2 to 60 mg. per liter in a 5-cc. sample which is taken for analysis. Results are given showing the method's applicability to water analysis and to the determination of fluoride in phosphate rock.

AMHERST, MASS. RECEIVED JUNE 13, 1939

NOTES

Dibenzyl Sebacate

BY R. E. BURNETT AND J. J. RUSSELL

The new compound dibenzyl sebacate was synthesized recently in this Laboratory for use in another investigation.[1] Sebacic acid was esterified with benzyl alcohol, the crude ester then distilled at 0.5 mm. pressure, and the middle fraction recrystallized several times from its melt. The following are properties of the pure dibenzyl sebacate.

Temp., °C.	Refractive index n_D (Abbe)	Density d_4^t
30.0	1.5171	1.055(6)
35.0	1.5152	1.051(9)
40.0	1.5133	1.048(1)

Colorless plates, practically odorless; melting point (from cooling curve), 28.3°; boiling point (in Claisen flask), 257° (uncorr.) at 4 mm.

(1) Verhoek and Marshall, unpublished results.

RESEARCH LABORATORY
GENERAL ELECTRIC CO.
SCHENECTADY, N. Y.

RECEIVED FEBRUARY 21, 1939

On the Conversion of *l*-Abietic Acid into a *d*-Abietic Acid

BY TORSTEN HASSELSTROM AND JOHN D. MCPHERSON

The addition of hydrogen chloride to abietic acid produces dichlorodihydroabietic acid which is crystalline and easily purified.[1] We have found that dichlorodihydroabietic acid may be obtained directly from rosin and in apparently equal purity as when Steele's abietic acid[2] is used as a starting material. On splitting off of hydrogen chloride from dichlorodihydroabietic acid with sodium ethoxide, we have been able to obtain an abietic acid with the positive sign of rotation. This seemingly new abietic acid was characterized through its di-*n*-amylamine salt. According to Levy,[1] the dichlorodihydroabietic acid produces an abietic acid with the negative sign of rotation when heated at its melting point, and when treated with quinoline.

Experimental

Dichlorodihydroabietic Acid.—This compound was prepared substantially according to the directions given by Levy.[1] Ninety-five grams of "X" grade gum rosin was dissolved in 70 cc. of glacial acetic acid and boiled for four hours. The solution was then cooled to about 0°. The semi-solid mixture was saturated with dry hydrogen chloride, the bottle sealed and the mixture left standing at room temperature for two weeks. It was then filtered and the solid collected; yield 26 g. It was recrystallized from acetone and then from ethyl acetate, m. p. 190.5° dec. (corr.); $(\alpha)_D$ −10° (in ethanol).

Anal. Calcd. for $C_{20}H_{32}O_2Cl_2$: C, 63.97; H, 8.59. Found: C, 63.76; H, 8.60.

The dichlorodihydroabietic acid prepared from Steele's abietic acid,[2] m. p. 163.5–165° (corr.); $(\alpha)_D$ −76° (in ethanol) showed the following constants: m. p. 190.5° dec. (corr.); $(\alpha)_D$ −8.1 (in ethanol). Found: C, 63.96; H, 9.16.

***d*-Abietic Acid.**—Ten grams of dichlorodihydroabietic acid (m. p. 190.5° dec. (corr.); $(\alpha)_D$ −10°), was added in portions over a period of five to ten minutes to a boiling solution of sodium ethoxide (17.5 g. of sodium and 175 cc. of absolute ethanol). The mixture was refluxed for one hour. Water was then added and the excess of alcohol was distilled off. As much of the liquid as possible was poured off the remaining solid. The soapy residue was then dissolved in 3 liters of water. The solution was filtered and the filtrate acidified with dilute hydrochloric acid. The white precipitate was filtered off and crystallized from methanol, yield 3.5 g. (40%), m. p. 137–139°; $(\alpha)_D$ +27° (in ethanol), which on successive crystallization yielded an abietic acid melting at 142–143° (corr.); $(\alpha)_D$ +20° (in ethanol). Calcd. for $C_{20}H_{30}O_2$: C, 79.40; H, 10.05. Found: C, 79.33; H, 10.08; C, 79.57; H, 10.32.

(1) Rây and Simonsen, *Indian Forest Records*, **11**, 211 (1924); Levy, *Ber.*, **64**, 2441 (1931).

(2) Steele, THIS JOURNAL, **44**, 1333 (1922).

The mother liquor from this separation yielded small quantities of an acid melting at 207–212° (corr.), probably identical with the dihydroabietic acid of melting point 217.5–218.5° (corr.), previously described by us.[3]

A solution of 6 g. of *d*-abietic acid of m. p. 139–143° (corr.) was treated with 4 g. of di-*n*-amylamine (Eastman Kodak Company) in acetone. The solution was boiled for about ten minutes and filtered. On standing 10.6 g. of crude di-*n*-amylamine salt was obtained, m. p. 117.5–119° (corr.). The compound was recrystallized four times, the melting point remaining constant after the third crystallization, being 119–119.5° (corr.), $(\alpha)_D$ +3.3° (in ethanol). The amounts of recovered di-*n*-amylamine salt were too small to be converted into the original acid.

Anal. Calcd. for $C_{30}H_{53}O_2N$: C, 78.35; H, 11.62. Found: C, 78.61; H, 11.76.

The di-*n*-amylamine salt of *l*-abietic acid shows the following constants: m. p. 141–142°; $(\alpha)_D$ −74.5°.[4]

This investigation is being continued.

(3) Hasselstrom and McPherson, *ibid.*, **61**, 1228 (1939).

(4) Palkin and Harris, *ibid.*, **56**, 1935 (1934).

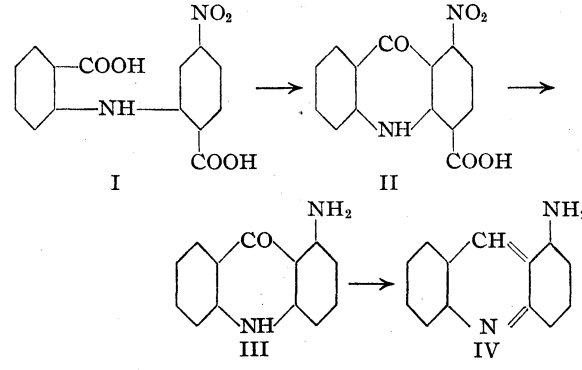
G & A LABORATORIES, INC.
SAVANNAH, GEORGIA

RECEIVED MAY 29, 1939

The Identification of 1-Nitroacridone-4-carboxylic Acid as 1-Aminoacridine

BY KONOMU MATSUMURA

In a previous paper,[1] it was stated that the nitroacridone-carboxylic acid (m. p. 333° dec.) which was obtained from 5-nitrodiphenylamine-2,2′-dicarboxylic acid (I) by ring closure should have the constitution of 1-nitroacridone-4-carboxylic acid (II) in consideration of the observations that the fluorescence and solubility of the aminoacridone (III), which was converted from the nitroacridonecarboxylic acid in question, exactly coincided with those of 1-aminoacridone but were widely different from those of the 3-isomer.



The present paper indicates the previous interpretation to be altogether correct, but not in harmony with the Lehmstedt conclusion,[2] on

(1) Matsumura, THIS JOURNAL, **60**, 591 (1938).

(2) Lehmstedt and Schlader, *Ber.*, **70**, 1526 (1937): Lehmstedt, *ibid.*, **71**, 1609 (1938).

TABLE I

COMPARISON OF THE PROPERTIES OF SUBSTITUTED ACRIDINES

Substituent		1-Amino-	3-Amino-
Fluorescence in alc. soln.		None	Intense green
M. p., °C.		178 (uncorr.) 182.3 (corr.)[a]	218 (uncorr.)[b] 223.5 (corr.)
Hydrochloride	Cryst. color	Blue-black	Orange-red
	Aq. soln.	Violet-red color with no fluores.	Orange-yellow color with green fluores.
	M. p., °C. (uncorr.)	285 (dec.)[c]	328–329 (dec.)

[a] Albert and Linnell [*J. Chem. Soc.*, 22 (1938)] give m. p. 181° (corr.), and Lehmstedt [*Ber.*, **71**, 808 (1938)] gives m. p. 165–170°. [b] Albert and Linnell [*J. Chem. Soc.*, 1618 (1936)] give m. p. 219° (corr.) and Scherlin [*Ann.*, **516**, 218 (1935)] m. p. 221–222° for their products, respectively. [c] Lehmstedt (*loc. cit.*) gives m. p. 286° (dec.) for his product.

the basis of further investigations as follows. The aminoacridine (IV) which was obtained from the aminoacridone in question (III), on admixture with synthesized 3-aminoacridine, showed a great depression of the melting point, while with synthetic 1-aminoacridine it showed no depression; moreover, its other properties were in good agreement with those of 1-aminoacridine shown in Table I.

The nitroacridone-carboxylic acid must, therefore, be 1-nitroacridone-4-carboxylic acid.

Experimental

1-Aminoacridine.—Four-tenths gram of the aminoacridone in question (m. p. 289–290°) and 5 g. of sodium amalgam (5%) in 30 cc. of dilute alcohol (33%) were heated on a water-bath for three hours with frequent shaking. The solution was decanted from mercury, acidified with hydrochloric acid and oxidized with 2 g. of ferric chloride. The base (yield, 0.25 g.) which was set free from the hydrochloride, crystallized from alcohol (33%) into gold-yellow prismatic needles, melting at 178° alone or on admixture with a sample of 1-aminoacridine (m. p. 178°), whereas a mixture (7:3) of this compound with an authentic specimen of 3-aminoacridine (m. p. 218°) melted at 135–140°.

Anal. Calcd. for $C_{13}H_{10}N_2$: C, 80.41; H, 5.15. Found: C, 80.22; H, 5.28.

The hydrochloride gives blue-black prismatic needles from dilute hydrochloric acid (5%), m. p. 285° (dec.). The aqueous solution assumes a violet-red color, while an alcoholic solution has a violet-blue color, both showing no fluorescence in any dilution.

CHEMICAL LABORATORY OF
KITASATO INSTITUTE
TOKYO, JAPAN

RECEIVED MAY 13, 1939

Synthesis of Aldehydes by Stephen's Method[1]

BY JONATHAN W. WILLIAMS

The application of Stephen's[2] procedure to the preparation of several aldehydes has led to the conclusion that the method is not as general as claimed. Stephen states, "the method is applicable to aliphatic and aromatic nitriles, and the yields are usually almost quantitative." Exceptions are made by Stephen only in the cases of *o*-tolualdehyde and α-naphthaldehyde, where "steric hindrance" is offered as an explanation for poor yields.

The method has been tried in this Laboratory with good results in the preparation of benzaldehyde, *p*-tolualdehyde and β-naphthaldehyde, and with only fair results in the preparation of phenylacetaldehyde and isocapraldehyde. Stephen's poor yields with α-naphthaldehyde and *o*-tolualdehyde have been verified, and the method has been found completely unsatisfactory for the preparation of β-hydroxypropionaldehyde.

Experimental

Preparation of Phenylacetaldehyde.—Eleven runs were made, each different, and the following was found to give the highest yield.

A mixture of anhydrous stannous chloride (57 g., 0.3 mole, prepared by heating the hydrated salt for one hour in a 200° bath, cooling and pulverizing the resulting solid mass) and dry ether (400 ml., twice distilled from sodium) was placed in a 2-liter three-necked round-bottomed flask, provided with a mechanical stirrer and a reflux condenser fitted with a calcium chloride drying tube. The mixture was saturated with dry hydrogen chloride,[3] using slow stirring to agitate the stannous chloride. Within two hours all of the solid stannous chloride had dissolved, forming a separate lower viscous layer.

The source of hydrogen chloride was then disconnected and phenylacetonitrile (16 g., 0.136 mole, freshly distilled) was added rapidly by means of a dropping funnel. The mixture was stirred vigorously for one hour and then allowed to stand for eighteen hours. The aldimine hydrochloride–stannic chloride complex began to separate after five hours.

The ethereal hydrogen chloride was removed by decantation and the residue washed twice with 100-ml. portions of dry ether to remove hydrogen chloride. To the residue were added 800 ml. of water and sufficient solid sodium bicarbonate to render the solution neutral to congo red.

(1) Presented before the Division of Organic Chemistry at the Baltimore meeting of the American Chemical Society, April, 1939.

(2) Stephen, *J. Chem. Soc.*, **127**, 1874 (1925).

(3) "Organic Syntheses," Coll. Vol. I, p. 287 (1932).

The mixture was then brought to boiling and live steam passed through it until the total volume of distillate was 250 ml.

The steam distillate was extracted with two 75-ml. portions of ether and the ethereal extract dried over sodium sulfate. The ether was removed on the steam-bath and the residue vacuum-distilled: yield of phenylacetaldehyde, b. p. 87–88° (18 mm.), 5.4 g., 0.045 mole, 33%.

The other aldehydes studied were prepared by much the same procedure. The results are summarized in the table.

Aldehyde prepared	Time allowed for pptn. of addn. complex	Yield, %
Benzaldehyde[4]	5 hours	97
β-Naphthaldehyde[5]	12 hours	91
p-Tolualdehyde[4]	12 hours	77
Phenylacetaldehyde[4]	18 hours	33
Isocapraldehyde	7 days	31
o-Tolualdehyde[7,8]	8 days	9
α-Naphthaldehyde[7]	7 days	7
β-Hydroxypropionaldehyde[6]	7 days	0

(4) Reported by Stephen[2] in almost quantitative yields.

(5) One liter of hot water was added to the residue and live steam passed through the mixture as long as any solid came over in the steam distillate. The solid was recrystallized from 50% aqueous alcohol. Fulton and Robinson, *J. Chem. Soc.*, **152**, 200 (1939), reported the preparation of β-naphthaldehyde by the Stephen technique in 75% yield. Their work was published after the preparation had been completed at the University of Maryland.

(6) Removal of the aldehyde by steam distillation was not attempted; 500 ml. of water was added to the addition complex, the mixture warmed on the steam-bath for one hour, allowed to cool and extracted with ether. The product was a thick, tarry liquid which gave negative tests with Schiff and Tollens reagents.

(7) Reported by Stephen[2] in poor yield.

(8) There was no precipitate after seven days so one-half of the ether was removed and the reaction mixture allowed to stand another twenty-four hours.

CHEMISTRY LABORATORY
UNIVERSITY OF MARYLAND
COLLEGE PARK, MD.

RECEIVED APRIL 14, 1939

Crystalline Lead Orthophosphate

BY EDWARD J. ROEHL

In the preparation of crystalline metathetical reaction products where the solubility of the reaction product is very low, it is often difficult to obtain crystals large enough for microscopic examination, and a number of methods have been employed for maintaining the necessary slight supersaturation. The writer has successfully employed a cellophane membrane for a number of such cases.

By treating a solution of lead acetate with sodium hydrophosphate, Aiders and Stähler[1] succeeded in preparing lead orthophosphate, but without any signs of microscopically recognizable crystals. In fact, it appears from the literature that the only method of preparing this salt is the rather cumbersome one of Zambonini,[2] who fused and slowly cooled the white powder. In our experiments, a cellophane membrane was tied over the mouth of a test-tube (an open tube could of course be used) containing a 1% solution of Na_2HPO_4 and the tube inverted in a slightly acidified 0.2% solution of $Pb(C_2H_3O_2)\cdot 3H_2O$. At once an almost amorphous precipitate of lead orthophosphate appeared on the under side of the membrane and in about a minute crystals of the white salt started to fall.

The crystals (some of which were 2 mm. in length) were uniaxial hexagonal prisms exhibiting strong birefringence and showing an optically negative character. The values of $\omega = 1.970$ and $\epsilon = 1.936$ check the data in the literature for the refractive indices of lead orthophosphate. Analysis of the crystals gave a value of 17.4% as compared with the calculated value of 17.5% for $Pb_3(PO_4)_2$.

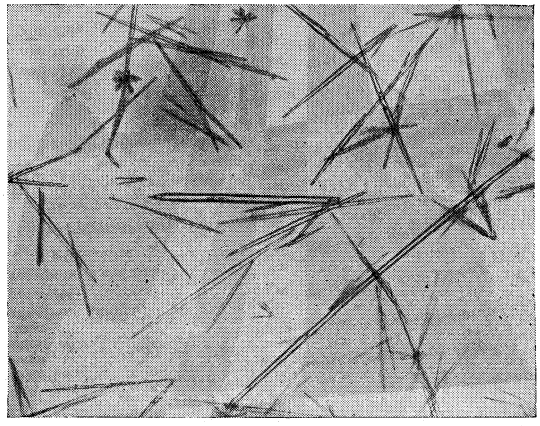


Fig. 1.

The accompanying photomicrograph at (50 ×) shows some of the crystals obtained.

RESEARCH LABORATORY
INTERNATIONAL NICKEL CO.
BAYONNE, NEW JERSEY

RECEIVED APRIL 14, 1939

(1) Aiders and Stähler, *Ber.*, **42**, 2263 (1909).

(2) Zambonini, *Z. Kryst.*, **58**, 226 (1923).

α-Furfuryl Bromide (2-Bromomethylfuran)

BY J. E. ZANETTI AND J. T. BASHOUR

In 1927 one of us[1] prepared an ether solution of α-furfuryl bromide by acting on furfuryl alcohol with phosphorus tribromide. The solution proved satisfactory in the synthesis of various furfuryl ethers but the pure bromide was not separated as its decomposition was rapid once the solvent was evaporated. Von Braun and Kohler[2] had

(1) Zanetti, THIS JOURNAL, **49**, 1065 (1927).

(2) Von Braun and Kohler, *Ber.*, **51B**, 86 (1918).

had a similar experience when they synthesized the bromide by acting on α-furfurylmethylethylamine with cyanogen bromide in ether solutions; they were unable to obtain the pure compound from the ether solution. Recently the ether solution of the bromide has been used by Paul[3] in the synthesis of alkyl furans with the Grignard reagent and by Paul and Normant[4] in a study of the preparation of phenyl-α-furfuryl ether and its rearrangement.

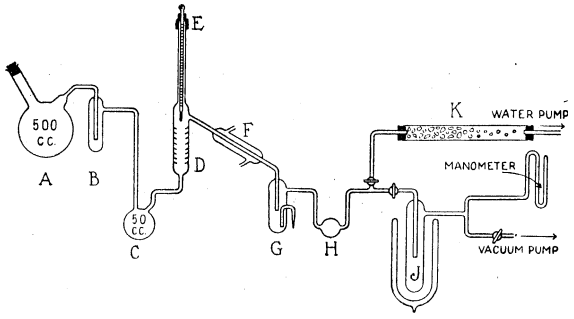


Fig. 1.

The work herein presented was undertaken with the object of obtaining the pure bromide and in this we have succeeded as far as the very unstable nature of the compound would permit. By distilling the dry ether solution under the reduced pressure of a water pump, then lowering the pressure to 2 mm. with a vacuum pump and distilling rapidly, we succeeded in obtaining a colorless product boiling at 32.5 to 34.5°. The apparatus employed is described in the Experimental Part. Though the bromide distils over as a colorless liquid, in a few minutes it begins to color yellow and then brown. Its rate of decomposition seems to be a function of the concentration of hydrobromic acid, which is one of the decomposition products. Hence it must never be kept long in a confined space as the rapidity of the decomposition reaches explosive violence. During a specific gravity determination a pycnometer containing 3 cc. of the bromide exploded a few minutes after being taken out of the balance case. The operator fortunately had moved far enough away so that he was not injured, but no trace of the pycnometer could be found except one of the caps closing the capillaries. Even when kept in loosely stoppered containers the decomposition is rapid the vessels becoming coated with tough graphitic films similar to those described in the preparation of the α-furfuryl iodide.[5]

The bromide is slightly lachrymatory and a distinct lung irritant, the irritation not appearing for some hours after inhaling the vapor.

Density determinations gave d^{20}_{20} 1.560 and the index of refraction with the Abbe refractometer was n^{20} 1.5380. Chemically the compound was identified by condensing it with furfuryl alcohol to di-α-furfuryl ether, b. p. 100–102° at 2 mm.

Because of the short life and dangerous nature of this compound and the fact that the ether solution in which it is prepared is satisfactory for synthetic work, it did not appear of importance to carry this investigation any further.

Experimental

Preparation of the α-Furfuryl Bromide.—This was carried out as described by Zanetti[1] using smaller quantities (20 g. of furfuryl alcohol and 20 g. of phosphorus tribromide). The solutions stood from twenty to forty hours over granulated sodium hydroxide. The solutions were then rapidly filtered and distilled in the apparatus shown in Fig. 1.

Apparatus.—The apparatus consisted of a 500-cc. bulb (A) connected through a trap (B) with a smaller bulb (50 cc.) C. This was connected through a 5-cm. reflux column (D) with thermometer attachment (E) and a condenser (F) with another trap (G) provided with a siphon side-tube ending in a capillary. A small bulb (H) of 50-cc. capacity was inserted before trap (J) which was immersed in "dry-ice"–ethylene trichloride mixture and used to protect the vacuum pump. (K) was a drying tube to prevent water vapor from entering the apparatus. The entire apparatus was made of Pyrex glass. The only points where the compound might come in contact with organic material were at the side tube of (A) and at the thermometer holder (E) where a piece of rubber vacuum tube was used to hold the thermometer in place. The side-tube of (A) and the thermometer holder were made of 8-mm. tubing, the stoppered ends far removed from the warm vapors so that contamination from these sources was unappreciable.

Operation of the Apparatus.—The apparatus was first exhausted to 2 mm. and warmed to take out all moisture. Air was slowly let in through (J) till atmospheric pressure was reached. The filtered ether solution was then placed in (A) and the side-tube closed with a small cork thoroughly covered with collodion. The connection leading to the vacuum pump was closed and that leading to the water pump opened. When the water pump was started the boiling of the ether solution was rapid and the temperature dropped fast. In order to keep the ether boiling it was necessary to immerse (A) in water kept at about 30°. When no more ether came over, the vacuum pump was started and the pressure in the apparatus brought down to 2 mm. A small amount of ether col-

(3) Paul, *Bull. soc. chim.*, [5] **2**, 2227 (1935).
(4) Paul and Normant, *ibid.*, [5] **5**, 1148 (1938).
(5) Zanetti, THIS JOURNAL, **49**, 1061 (1927).

lected in (J). Ice water-baths were then placed around (B) and (C) and a hot water-bath around (A). Distillation of the bromide began accompanied by darkening and film formation in (A). The distillate collected mostly in (B). When distillation was finished, the bath around (B) was heated almost to boiling and an ice water-bath placed around (G). When this distillation was over, the bath around (C) was raised to boiling and an ice-bath placed under (H). This was the final distillation, the colorless bromide distilling into (G) while the temperature remained at 32.5 to 34.5°. A very small amount of distillate passed into the bulb (H). When the distillation was complete, the apparatus was brought back to atmospheric pressure by slowly letting air through (J). The side-tube capillary was then broken and the liquid siphoned off into a small flask by gently sucking out the air from the flask.

The residues in (A), (B) and (C) were black and tarry but the distillate in (G) was colorless throughout the distillation, though shortly after it began to color. Five runs were made, each with a new apparatus as it was found easier to discard the one used than to attempt to remove the graphitic films formed in it from the bromide decomposition.

The yields were about 50% of the theoretical.

Properties of the Compound.—As mentioned, the compound is a colorless liquid which decomposes rapidly, turning yellow then brown and ending in a tarry mass which adheres tightly to the container. Attempts to keep the compound for more than a few hours proved futile. Moisture doubtless plays an important role in initiating the decomposition. Phosphorus pentoxide or anhydrous sodium sulfate, however, proved useless in stabilizing the compound. Solid potassium hydroxide, though unable to prevent blackening, delays total decomposition for a much longer time. This points to the possibility that the hydrobromic acid formed by the decomposition may act as an accelerator. The compound thus prepared and dissolved in ether remains undecomposed for days.

Identification.—Analyses gave for bromine 50.3 and 49.0%, calculated, 49.66%.

Four and one-half grams of the bromide was condensed with excess of furfuryl alcohol and potassium hydroxide and the product distilled at 2 mm. The di-α-furfuryl ether came over at 100–102°; yield 85%.

HAVEMEYER CHEMICAL LABORATORY
COLUMBIA UNIVERSITY
NEW YORK, N. Y.

RECEIVED MAY 5, 1939

COMMUNICATIONS TO THE EDITOR

HOMOGENEITY OF GONADOTROPIC HORMONE PREPARATIONS ISOLATED FROM PREGNANCY URINE

Sir:

We have reported the preparation from pregnancy urine of gonadotropic fractions containing 4000 minimal ovulating doses per milligram when assayed in the post-partum rabbit [*J. Biol. Chem.*, **128**, 525 (1939)]. Two such samples have recently been examined on the ultracentrifuge,[1] and appear to be homogeneous with respect to sedimentation. In each case, in the concentrations employed, a single sharply defined band was observed at approximately 250,000 times gravity.

In addition, electrochemical homogeneity of one of these preparations was demonstrated as a result of studies with the electrophoresis apparatus of Tiselius.[2] Evidence for the presence of only a single component (which previous analysis had shown to be a polypeptide-polysaccharide complex), was indicated by the appearance of a single migrating band having sharp boundaries in a phosphate buffer of ionic strength 0.1 (*p*H 7.0). The mobility was 4.85×10^{-5} cm.^{2}, sec.$^{-1}$, volt^{-1}.

Isoelectric point determinations, made by adsorbing the hormone upon collodion particles, and determining migration in a microelectrophoresis cell, showed an isoelectric point of *p*H 3.2–3.3.

Since such preparations appear to be identical with regard to biological activity and chemical composition, we feel that the evidence obtained with the ultracentrifuge and Tiselius apparatus demonstrates the homogeneity of our preparations.

Further detailed data bearing upon the physical and chemical properties of these and similar preparations of the hormone will be reported shortly.

DEPARTMENTS OF PHYSIOLOGICAL CHEMISTRY
AND OBSTETRICS AND GYNECOLOGY — SAMUEL GURIN
UNIVERSITY OF PENNSYLVANIA — CARL BACHMAN
PHILADELPHIA, PA. — D. WRIGHT WILSON

RECEIVED JULY 20, 1939

(1) Through the courtesy of Drs. A. E. Severinghaus and J. A. Chiles, Jr.

(2) Through the courtesy of Dr. Florence B. Seibert.

THE STABILITY OF THE KETO ACID FROM METHIONINE[1]

Sir:

The metabolic path of most amino acids seems to be preponderantly through the corresponding keto acids. Hence a thorough knowledge of the behavior of these keto acids is essential for the understanding of amino acid metabolism. In a study of the mechanism of methylation processes in the animal organism we were interested, therefore, in the behavior of the keto acid from methionine. This amino acid is one of the few physiological substances which may yield methyl groups. According to the prevailing view methionine is demethylated to homocysteine during metabolism. We have obtained evidence by studying the behavior of the corresponding keto acid that a second reaction—splitting off of the —SCH_3 group—is also possible.

Since the keto acid from methionine has as yet not been synthesized, we prepared it biologically by the deamination of methionine in the presence of kidney slices according to the technique developed by Krebs.[2] A dinitrophenylhydrazone of the keto acid melting at 149° was obtained in about 20% yield.[3]

Anal. Calcd. for $C_{11}H_{12}O_6N_4S$: C, 40.24; H, 3.68; N, 17.07; S, 9.77. Found: C, 40.40; H, 3.81; N, 16.57; S, 9.80.

Solutions of methionine which had been similarly incubated with kidney slices were deproteinized and the filtrates containing the free keto acid and unchanged methionine were digested with acid and with alkali. Under both conditions methyl mercaptan was produced copiously. The liberated methyl mercaptan was identified by its yellow silver compound and by the melting point and analysis of the mercury mercaptide. In one experiment 400 mg. of *dl*-methionine was metabolized by kidney slices. After deproteinization the keto acid was determined in an aliquot of the solution as the dinitrophenylhydrazone (yield, calculated to the total sample, 210 mg. of the hydrazone). To another aliquot sufficient 10 *N* sodium hydroxide was added to make the solution 2 *N*. The solution was refluxed under nitrogen for one hour and the liberated mercaptan was absorbed in a solution of mercuric cyanide. Most of the methyl mercaptan was liberated during the first twenty minutes. The mercaptan weighed as mercury mercaptide corresponded to 72% of the keto acid in the solution (68 mg. $Hg(SCH_3)_2$). Since the original solution contained negligible amounts of mercaptan and as methionine does not yield mercaptan under these conditions, the reaction is ascribed to the decomposition of the keto acid. This finding may be explained on the basis of the instability of β-keto sulfides investigated by Nicolet.[4]

To establish the possible physiological significance of our findings we are continuing our studies with other sulfur-containing compounds.

(1) This work was made possible through a grant from the Friedsam Fund donated to the Division of Child Neurology, Neurological Institute, New York, N. Y.

(2) Krebs, *Z. physiol. Chem.*, **217**, 216 (1933).

(3) Bernheim, *J. Biol. Chem.*, **114**, 657 (1936), obtained a phenylhydrazone by incubating methionine with a kidney extract.

(4) B. H. Nicolet, THIS JOURNAL, **53**, 3066 (1931).

FROM THE DEPARTMENT OF BIOCHEMISTRY
NEW YORK STATE PSYCHIATRIC INSTITUTE
AND HOSPITAL AND THE DEPARTMENT OF
NEUROLOGY, COLUMBIA UNIVERSITY HEINRICH WAELSCH
NEW YORK, N. Y. ERNEST BOREK

RECEIVED JULY 19, 1939

THE VERATRINE ALKALOIDS. VI. THE OXIDATION OF CEVINE

Sir:

In previous work on the degradation of cevine, high temperature pyrolytic procedures (soda lime distillation or selenium dehydrogenation) have been rewarding in the search for degradation products. These, however, have been limited in number and their nature has made them difficult to relate to the parent substance with the exception of those derived from its basic portion. More recently it has been possible, for the first time, to achieve a crystalline oxidation product. Chromic acid in dilute sulfuric acid has given a mixture from which an acid fraction in good yield has been separated. This fraction, still a mixture, could not be directly crystallized. However, when heated to 180° evolution of carbon dioxide occurred, with production in good yield of a crystalline product which was non-nitrogenous (m. p. 273–278°), $[\alpha]^{25}D$ +47.6° (c = 0.925 in pyridine). Analysis indicated a formula $C_{14}H_{14}O_6$. Calculated: C, 60.41; H, 5.07. Found: C, 60.51; H, 5.20.

Diazomethane gave a product which crystallized readily from acetone (m. p. 165–166°). Analysis indicated 2 methoxyl groups. Calcd. for $C_{16}H_{18}O_6$: C, 62.75; H, 5.92; OCH_3, 20.26. Found: C, 62.96; H, 6.07; OCH_3, 19.90. The

molecular weight by the Rast method was found to be 326. Calculated for $C_{16}H_{18}O_6$, 306.14.

15.06 mg. of the acid in 2.5 cc. of alcohol was titrated against phenolphthalein. Found 1.014 cc. of 0.1 *N* NaOH; calculated for 2 equivalents, 1.082 cc. No additional alkali was consumed after boiling with excess 0.1 *N* sodium hydroxide.

14.96 mg. of the ester required 0.478 cc. of 0.1 *N* NaOH for direct titration in the cold. Calculated for one equivalent: 0.488 cc. After boiling for two hours an additional 0.437 cc. of alkali was consumed.

From these data it appears likely that the substance contained a labile lactone group and that one of the two methyl groups introduced with diazomethane involved a phenolic or enolic hydroxyl. Presence of a phenolic or enolic group was indicated by a prompt, deep red-purple color obtained with ferric chloride. The acid as well as the ester coupled with diazotized sulfanilic acid. On hydrogenation with platinum approximately 3 moles of hydrogen was absorbed, but the product could not be crystallized. It no longer gave the original color reactions.

These properties suggest that the substance contained a benzene ring and is possibly the lactone of a substituted tetrahydronaphthalene. However, the substance when treated with alkali gave a solution from which carbon dioxide was liberated on acidification. From this solution crystalline degradation products could be isolated which suggested that the original acid is capable of undergoing decomposition similar to that of β-ketonic acids. The phenolic or enolic character may therefore be due to such a grouping and thus the unsaturation of the substance to the presence of ketonic linkages rather than to a benzene ring. The details of this further degradation must be left to a later communication.

Our previous studies [*J. Biol. Chem.*, **119,** 141 (1937); **120,** 447 (1937)] have indicated that the basic portion of the cevine molecule is a substituted octahydropyridocholine. The substance, $C_{14}H_{14}O_6$, must be derived from that portion of the molecule all or in part distinct from the basic portion.

THE LABORATORIES OF
THE ROCKEFELLER INSTITUTE
FOR MEDICAL RESEARCH
NEW YORK, N. Y.

LYMAN C. CRAIG
WALTER A. JACOBS

RECEIVED JULY 5, 1939

NEW BOOKS

The Principles of Electrochemistry. BY DUNCAN A. MACINNES, Associate Member, Rockefeller Institute for Medical Research. Reinhold Publishing Corporation, 330 West 42d Street, New York, N. Y., 1939. 478 pp. Price, $6.00.

This book treats the conductive and thermodynamic properties of electrolytic solutions and is not concerned with metallic and gaseous conduction, which the author considers a branch of electrophysics. After a brief historical introduction, there follows an excellent treatment of transference phenomena embodying the masterly researches of the author and his collaborators on the moving boundary method and precision conductance determinations; several well written chapters on the thermodynamics of galvanic cells, standard electrode potentials and the ramifications of Debye–Hückel theory. The vexing problem of liquid junction potentials receives a critical and modern treatment. The practical determination and meaning of *p*H, conductance methods, oxidation potentials, potentiometric titrations with the glass and other electrodes which have found wide application, are adequately presented. Conductance in non-aqueous and mixed solvents is treated in an up-to-date fashion. The book closes with chapters on ionization constants and structure, effects of centrifugal forces, dielectric constants, passivity and overvoltage, and the latest accepted developments in electrokinetic phenomena.

A comparison of the tables with those of previous texts gives ample evidence of the discrimination that has been exercised in assembling these data. The expert will notice the omission or correction of many of the time-honored values of the pioneers but he will be gratified to learn that these omissions and corrections are the result of painstaking recomputation and critical evaluation of the data from the original sources. Misprints and errors of statement are rare. On page 142, eq. 19, "extremely dilute" instead of "infinitely dilute" would be a more concrete expression. On page 143, *kappa* is to be held constant in the Güntelberg–Müller charging process. The reviewer has not found a single meaningless sentence. The format and printing are in keeping with the high standard of presentation.

Readers interested in locating the very latest theoretical contributions or commercial applications will be disappointed. The author consistently refrains from including theories which have not been adequately verified by experiment, and makes no pretense of dealing with the patent literature.

The artifice of eliminating both liquid junction potentials and activity coefficient corrections in concentration cells by "swamping" with an inert electrolyte deserved mention by the author at least as a simple practical device for determining ionic concentrations. It is unfortunate that the author, in presenting Güntelberg's data (pp. 170–171), did not seize the opportunity to demonstrate the excellent agreement of these data in each case with the specific osmotic properties of the solvent. By introducing the Gibbs–Duhem equation, electrochemistry, instead of appearing as a separate subject, can be correlated with general solution theory in a comprehensive manner. However, like Donnan membrane potentials, some important topics had to be eliminated to keep the book within reasonable compass. The book should prove to be an excellent treatise in Theoretical Electrochemistry.

VICTOR K. LA MER

An Introduction to the Principles of Physical Chemistry. By O. MAASS, Macdonald Professor of Physical Chemistry, and E. W. R. STEACIE, Associate Professor of Chemistry, McGill University. Second edition. John Wiley and Sons, Inc., 440 Fourth Avenue, New York, N. Y., 1939. ix + 395 pp. 102 figs. 15.5 × 23.5 cm. Price, $3.00.

The second edition of this text is considerably larger and more complete than the first edition. Many matters which were passed over too rapidly and superficially have now been elucidated in more detail. The discussions are clear and understandable, being particularly adapted to those students who have not had any mathematics beyond algebra. The discussion of electrolytic solutions has now been brought up to date although it is a little unfortunate to begin with the laws of osmotic pressure.

The treatment of reaction rates is now much more rigorous than formerly. While on page 291 the statement is made that "the chemical equation, therefore, does not necessarily represent the true course of reaction," the student might obtain an erroneous idea from the previous two pages. The statement is made on page 290 that the initial rate of a reaction

$$A + B + C + \ldots \longrightarrow \text{(Products)}$$

is given in its initial stages by

$$\text{Rate} = kC_AC_BC_C \ldots$$

The discussion on this and the next page creates, therefore, a rather unfortunate impression which may not be completely eradicated by the more correct statements on the following pages.

On the whole, however, the book is exceedingly well and clearly written and is admirably adapted to give an introduction in physical chemistry to those students who have not had much previous experience with physics and mathematics.

W. ALBERT NOYES, JR.

BOOKS RECEIVED

June 15, 1939 to July 15, 1939

D. BALAREW. "Der disperse Bau der festen Systeme. Allgemeine Theorie der Verunreinigung fester Systeme." Verlag von Theodor Steinkopff, Residenzstrasse 32, Dresden-Blasewitz, Germany. 240 pp. RM. 10; bound, RM. 11.50.

GARDNER L. CARTER and JAMES W. COLE. "A Laboratory Course in General Chemistry," Second edition. D. Van Nostrand Co., Inc., 250 Fourth Ave., New York, N. Y. 225 pp. $2.00.

BERND EISTERT. "Tautomerie und Mesomerie. Gleichgewicht und 'Resonanz'." Verlag von Ferdinand Enke, Hasenbergsteige 3, Stuttgart W, Germany. 204 pp. RM. 14; bound, RM. 15.80.

C. A. ELVEHJEM and P. W. WILSON, Editors. "Respiratory Enzymes." Mimeoprinted by Burgess Publishing Co., 426 South Sixth St., Minneapolis, Minn. 236 pp.

JAMES MURRAY LUCK and JAMES H. C. SMITH, Editors. "Annual Review of Biochemistry, Vol. VIII." Annual Reviews, Inc., Stanford University P. O., California. 676 pp. $5.00.

J. W. MELLOR and G. D. PARKES. "Modern Inorganic Chemistry." Revised edition. Longmans, Green and Co., Inc., 114 Fifth Ave., New York, N. Y. 915 pp. $4.50.

A. MITTASCH. "Schopenhauer und die Chemie." Carl Winter's Universitätsbuchhandlung, Lutherstrasse 59, Heidelberg, Germany. 90 pp. RM. 2.50.

HERMANN STAUDINGER. "Über die makromolekulare Chemie." Hans Speyer Verlag, Hans Ferdinand Schulz, Albertstrasse 16, Freiburg im Breisgau, Germany. 32 pp. RM. 1.40.

"Analyses of Pennsylvania Bituminous Coals." Technical Paper 590, U. S. Bureau of Mines. Superintendent of Documents, Government Printing Office, Washington, D. C. 503 pp. $0.50.

"Index to the Literature of Food Investigation. Vol. 10, No. 2." (British) Department of Scientific and Industrial Research. British Library of Information, 50 Rockefeller Plaza, New York, N. Y. 102 pp. $1.35.

"Report for the Year 1937–1938." (British) Department of Scientific and Industrial Research. British Library of Information, 50 Rockefeller Plaza, New York, N. Y. 203 pp. $0.90.

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Baron Joji Sakurai

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BARON JOJI SAKURAI*

1858–1939

BY KOICHI MATSUBARA

Joji Sakurai was born in Kanazawa, Ishikawa Prefecture, on August 18, 1858. Coming to Tokyo in 1871, he entered Daigaku Nanko, the forerunner of the Tokyo Imperial University, where he received general education in modern sciences, specifying himself, later, in chemistry. In 1876, he was sent to England by the government to study under Professor A. W. Williamson in University College, London. Soon Sakurai distinguished himself by carrying off the gold medal in chemistry at the end of the first year, and secured the Clothworker Scholarship for two following years. In 1879, he was elected a Fellow of the Chemical Society, London, of which he has been a life member, and elected an Honorary Fellow in 1931.

Returning home in 1881, Dr. Sakurai was appointed lecturer in the newly established Tokyo University and, in the following year, promoted to a full professorship which he held until 1919, when he reached the traditional age limit and retired from the University, after serving the cause of science and education for nearly forty years, not only as a teacher but also as a University Councillor, Dean of the Faculty of Science and Acting President of the University. The title of Honorary Professor of the Tokyo Imperial University was conferred on him soon after.

The Degree of Rigakuhakusi (D.Sc.) was conferred upon Prof. Sakurai in 1888. In 1901, the Honorary Degree of Doctor of Laws was conferred upon him by the University of Glasgow, when he attended the celebration of the Ninth Jubilee of the University as a representative of the Tokyo Imperial University. He was elected a member of the Imperial Academy of Tokyo in 1898, in which he was elected the President in 1926, after assiduous service as Secretary during the preceding thirteen years. He was reëlected several times and remained in the post until his death.

Professor Sakurai was, in brief, the founder of Scientific Chemistry in Japan. He worked at first in the field of organic chemistry, but his natural bent of mind was in the direction of theoretical and physical chemistry. When the brilliant researches of van't Hoff, Ostwald, Arrhenius, Nernst and a host of others were published in succession, he recognized at once their immense importance, and endeavored to take up the new

(*) This Obituary is based on a note left by Professor Sakurai himself. A notice nearly the same as this was contributed by Professor Yukichi Osaka to the *Proceedings of the Imperial Academy, Tokyo*, **15**, No. 2, February (1939). Here my name is affixed both as one of those who were pupils of Professor Sakurai in the last decade of the nineteenth century and were near him ever since, and as a present member of the American Chemical Society.—K. M.

principles and introduce them in all stages of chemical education. Among the scientific contributions of Prof. Sakurai, special mention may be made of his modification of Beckmann's ebullition method for the determination of molecular weight, published in 1892. To avoid superheating, he passed the vapor of the solvent through the solution, and succeeded in overcoming the difficulty. This idea was followed by several other investigators.

Professor Sakurai was one of the most active members of the Chemical Society of Japan almost since its foundation as the Tokyo Chemical Society in 1878, and served as its president for several terms of office. When he completed twenty-five years of his professorship in 1907, the occasion was celebrated by his friends and former pupils. On this occasion, a respectable sum of money was raised to be used as a fund in association with his name under the direction of the Chemical Society.

Important as were the contributions to chemistry and chemical education in the earlier years of his career, Prof. Sakurai was destined to be an outstanding promoter of research activities in Japan and her international cultural relations. Indeed, he left imperishable footprints in both of these fields.

The bitter experience in the World War, which deprived Japan of several necessities, which had been imported from Germany, taught the nation a valuable lesson in the importance of self-supply. Professor Sakurai and his colleagues lost no time in embarking upon a movement with the object of realizing an independent research organization. This movement, strongly backed by influential men of business, succeeded in raising an ample fund, including a subsidy from the government, and in consequence Rikwagaku Kenkyusho (Institute of Physical and Chemical Research) was established in 1917. At the same time, H. M. The Emperor graciously made a contribution to the fund of the Institute. The Institute is now, as is well known, one of the most important and active centers of research in Japan, in the field of exact sciences and their applications.

When the International Research Council, renamed afterwards International Council of Scientific Unions, was organized as the result of the conferences held in London and Paris in 1918, in which Prof. Sakurai was a representative of the Imperial Academy, that Academy proceeded at once to organize a National Research Council. It was Prof. Sakurai who drafted the Constitution and actively promoted its organization. He was elected the President of the National Research Council shortly after its foundation, and remained in the position until his death.

Professor Sakurai was always looking to another sort of organization of a much wider scope, namely, an organization having for its main object the general promotion of research in all branches of science, pure and applied, by giving aids in research funds to competent scholars. The movement for its realization was started in 1931 by convening a meeting of the representatives of all the Universities, important research organizations and other like bodies. As the most important effect of the meeting, two Houses of the Imperial Diet soon adopted by a unanimous vote a resolution aiming at the speedy promotion of scientific research. Those directly concerned in the movement were deeply moved when, in August, 1932, it was officially announced that H. M. The Emperor was graciously pleased to make a magnificent gift toward the fund of the proposed organization for the encouragement of scientific research. The government was now determined to take definite steps to help the organization with an ample subsidy, and the Nippon Gakujutu Shinkokwai (Japan Society for the Promotion of Scientific Research) came into existence with H. I. H. Prince Chichibu as Patron and Viscount Saito, then Premier, as President. Professor Sakurai was elected Chairman of the Board of Directors, and the Society started its work from the fiscal year commencing April 1, 1933. At its seventh general meeting on January 19, 1939, Prof. Sakurai gave an eloquent official address to the meeting. On the next day he took cold, suffered pneumonia and passed away after eight days.

His long stay in London and his attendance at many international scientific meetings, combined with his extended tours in the world gave him splendid opportunities of studying men and world affairs, of which his knowledge was both deep and wide. This knowledge and his love of mankind, besides his being President of the Imperial Academy and of the National Research Council for so many years, made him a figure particularly suited to promoting Japan's international cultural relations.

In recognition of the valuable services rendered to the State, Prof. Sakurai was, in 1920, appointed by the Throne a member of the House of Peers

and, six years later, Privy Councillor, this being the first occasion on which a man of purely scientific career has been raised to the high post of supreme adviser to the Throne. Further, in 1916, the Order of the First Class of the Sacred Treasure was conferred upon him and in addition, in 1929, that of the Grand Cordon of the Rising Sun. Shortly before his death, Prof. Sakurai was decorated with the Order of the Grand Cordon of the Rising Sun and Paulownia and was created a Baron in recognition of his meritorious services to the State.

Professor Sakurai's work was also widely recognized abroad. In addition to his election as an Honorary Member of the American Chemical Society in 1926, he received the Honorary Degree of LL.D. from the University of Glasgow in 1901, was elected an Honorary Member of the Chemical Society of France in 1923, the Society of Chemical Industry (of London) also in 1923, the Royal Institution of Great Britain in 1925, the Academy of Sciences of U. S. S. R. in 1927, the Chemical Society of Poland in 1929 and the Chemical Society (of London) in 1931. On the occasion of his last visit to London in 1937, he was elected by his *alma mater* an Honorary Member of University College, London, an honor which had never before been bestowed upon a foreigner.

[CONTRIBUTION FROM THE LABORATORIES OF THE SCHOOL OF CHEMISTRY, RUTGERS UNIVERSITY, AND RESEARCH DEPARTMENT, THE CALCO CHEMICAL COMPANY, INC.]

The Polyhydric Alcohol–Polybasic Acid Reaction. III. Further Studies of the Glycerol–Phthalic Anhydride Reaction[1]

BY R. H. KIENLE,[1] P. A. VAN DER MEULEN AND F. E. PETKE

Since the appearance of the first paper of this series,[2] the polyhydric alcohol–polybasic acid reaction has become the basis for a large number of industrial products. Several excellent scientific treatments have been published covering the simple bi-bi functional or non-convertible type polyester polymerides, that is, those obtained from dihydric alcohols and dibasic acids.[3] The glyceryl phthalate reaction,[4] however, still remains the only convertible or higher functional saturated polyester polymeride to which scientific attention has been directed in spite of the clarification that a study of other similar systems should have offered to the problem of resin formation.

In the previous paper on glyceryl phthalate, the data seemed to indicate that the reaction was simple esterification. Such being the case, it followed that all polyester polymerides might be studied by carefully determining the rate and amount of water formed as the reaction proceeded, then directly calculating acid values and percentage esterifications therefrom. Several of the recent investigations on glyceryl phthalate,[5] however, raised some doubt as to the validity of this deduction that only esterification was involved. It was decided, therefore, prior to investigating other polyester systems, to reinvestigate thoroughly the glyceryl phthalate reaction under more rigidly controlled conditions than was done previously, to collect continuously all the products evolved, and to examine in detail resin samples representative of the progress of the reaction.

Recently several kinetic treatments, particularly for the non-convertible polyester polymerides, have been presented principally by Chalmers,[6] Dostal, Mark and Raff,[7] Alatman and Kedrinski,[8] Flory,[9] and Davies.[10] These treatments, with the exception of that by Davies, have all been made on fairly limited experimental data. Very little has been done kinetically, however, with the convertible polyester polymerides, especially when the reaction is carried out under conditions as usually encountered in practice, that is, where the condensation products are removed as formed. In obtaining our experimental data an attempt was made so that sufficient evidence would be available to allow subsequent presentation of a kinetic treatment.

Experimental

Apparatus and Procedure.—After considerable experimentation and many changes, during which time a number of physical factors governing polyester reactions were examined and placed under control, an apparatus was finally developed wherein polyester formation could be carried out under carefully controlled and exactly reproducible conditions and in which the water formed could be instantly and accurately determined. Because this apparatus will be referred to in later papers of this series, it will be described at this time in some detail. The apparatus is illustrated in Fig. 1.

In the experiments on glyceryl phthalate the charge used was such as to theoretically produce $^1/_4$ mole of resin calculated as glyceryl triphthalate, *i. e.*, $^1/_2$ mole or 46.0 g. of glycerol, $^3/_4$ mole or 111.0 g. of phthalic anhydride. In the relating experiments with other polybasic anhydrides, the charges were adjusted to yield an equivalent volume. Whenever polybasic acids were employed, because of the limitation effected by the size of the water-collecting chamber (E) and the increased volume of water evolved, a charge approximately one-half that employed for the anhydride experiments was used.

The water evolved could, of course, have been determined gravimetrically by using a suitable absorbent medium in an absorbent train attached to the outlet of the reaction flask. This would, however, have required continual weighings which would have made rapid readings very difficult. Therefore, a volumetric method was employed. It was essential in the design of the water-collecting chamber that immediately any water was evolved in the reaction flask (A) it was condensed and appeared

(1) Portion of a dissertation submitted to the Graduate Faculty of Rutgers University in partial fulfilment of the requirements for the degree of Doctor of Philosophy, June, 1938.

(2) Kienle and Hovey, THIS JOURNAL, **51**, 509 (1929).

(3) Carothers and Arvin, *ibid.*, **51**, 2566 (1929); Dostal and Raff, *Monatsh.*, **68**, 117 and 188 (1936); Flory, THIS JOURNAL, **59**, 466 (1937); Kogan, *J. Applied Chem. Russ.*, **10**, 900 (1937); Davies, *Trans. Faraday Soc.*, **34**, 410 (1938); Bradley, Kropa and Johnson, *Ind. Eng. Chem.*, **29**, 1270 (1937).

(4) Hönel, *Paint, Oil, Chem. Rev.*, **91**, 19 (1931); Savard and Diner, *Bull. soc. chim.*, **51**, 597 (1932); Kogan, *C. A.*, **31**, 7047 (1937); Carothers, *Trans. Faraday Soc.*, **32**, 39 (1936); Schlenker, *Allgem. Oel- u Fett-Ztg.*, **29**, 658 (1932); Wornum, *J. Oil Colour Chem. Assoc.*, **16**, 231 (1933); **17**, 119 (1934); Houwink and Klaassens, *Kolloid. Z.*, **70**, 329 (1935).

(5) Bozza, *Giorn. Chim. Ind. Applicata*, **14**, 294 and 400 (1932); Scheiber, "Kunststoffe," Leipzig, 1934, pp. 217.

(6) Chalmers, THIS JOURNAL, **56**, 912 (1934).

(7) Dostal, Mark and Raff, *Ind. Eng. Chem.*, **29**, 595 (1937).

(8) Alatman and Kedrinski, *C. A.*, **31**, 6219 (1937).

(9) Flory, THIS JOURNAL, **59**, 466 (1937).

(10) Davies, *Trans. Faraday Soc.*, **34**, 410 (1938).

in (E). The calibrated tube used to read the water evolved in (E) had, therefore, to be as close to the reaction flask as possible and the condensation in (E) had to occur with little or no time lag. Furthermore, many of the polybasic acids, particularly in the early stages, possessed subliming tendencies. It was therefore necessary that (E) be filled with a liquid which would dissolve and remove any of such sublimate that might be formed and carried over by the inert gas. It was also recognized that whatever liquid was used in (E), water must be insoluble therein and readily form a sharp distinct meniscus. After considerable experimentation, it was found that a mixture of three parts by volume of toluene to one part by volume of acetophenone was a suitable liquid to use.

It was realized that the gas flow and speed of stirring might have an important effect on the rate of the polyester reaction. These factors were therefore investigated and both were found to be important. In order to obtain reproducible results, a certain optimum definite gas flow and speed of stirring had to be used.

The gas flow was adjusted by observing the rate at which the gas bubbled through the sulfuric acid drying bottle (H). It was found that a rate of three bubbles per second was the optimum for use. With this gas flow, a stirring rate of 400 r. p. m. for stirrer (S) was found to be satisfactory.

The experimental technique was first carefully to weigh out the acid or anhydride into the reaction flask (A). The apparatus was then assembled and the proper amount of polyhydric alcohol carefully introduced into the dropping funnel. In order to prevent any contamination from the exterior and in order thoroughly to seal the apparatus, all the ground glass joints on assembling were lubricated with a small amount of glycerol. The apparatus, once assembled, was placed in the constant temperature bath (D) and with gas very slowly flowing through, heated until the polybasic acid or anhydride was at the temperature at which it was intended to carry out the reaction. The polyhydric alcohol in the dropping funnel, in the meanwhile, was brought to this same temperature by means of a free flame played on the outside thereof. When both the polybasic acid or anhydride and the polyhydric alcohol were at the reaction temperature, the gas was stopped momentarily and the polyhydric alcohol run into the flask. This addition was taken as the zero time for the reaction. Upon the completion of the addition of the polyhydric alcohol, which rarely took more than fifteen seconds, the glass stopper of the dropping funnel was closed and the gas flow adjusted to the proper rate.

When phthalic anhydride was used, because of its subliming tendency, a small amount was transferred by the gas stream to the toluene–acetophenone in the water-collecting chamber. The actual amount thus carried over was determined at the end of any run by analyzing the toluene–acetophenone mixture.

As water was evolved, it was transferred immediately into the water-collecting chamber where it was condensed, dropping to the bottom of the collecting tube where the amount given off could be accurately read as a function of the time of reaction. The small amount of water vapor carried in the gas stream was trapped by means of the anhydrone, the increase in weight of the anhydrone being determined for each run, at regular intervals, by removing the absorption bottle (G_2) and weighing it. In order to eliminate any possibility of loss during the weighing operation, a second pre-weighed (G_2) absorption bottle was used as a replacement, while the first absorption bottle was out of the system. The increase in weight of the anhydrone was thus plotted as a function of time, from which curve corrections were made to the amount of water evolved as read in the collecting tube, giving the true water evolved.

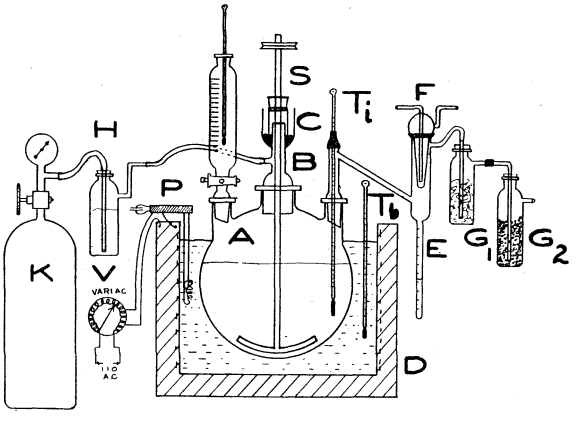


Fig. 1.—Apparatus for preparation of glyceryl phthalate. A, Pyrex reaction flask (500 cc.); B, adapter with side-arm; C, mercury seal stirrer (S); D, constant temperature wax bath; E, 10-ml. water-collecting chamber; F, condenser; G_1, absorption bottle (glass wool); G_2, absorption bottle (anhydrone); H, gas drier (sulfuric acid); K, gas cylinder (nitrogen or carbon dioxide); P, de Khotinsky thermo-regulator; V, variac (General Radio Company).

In order to prevent any condensation of moisture in the upper part of the reaction flask, adapter (B), or that part of the water-collecting chamber connected to the reaction flask, all these parts were heated during a run by continually playing a Bunsen burner thereon.

It was thus possible to carry out reproducible polyester formation reactions accurately and determine the rate at which the water was evolved. It was also possible to carry out these reactions so that samples could be taken out at regular intervals and the reactions studied by subsequently studying the composition of these samples at the various stages. And, finally, it was possible to carry any of the desired polyester resin-forming reactions along to some particular predetermined end-point and to be reasonably assured that the rate at which that end-point was achieved was, to all purposes, the same as passed through in carrying out the complete reaction.

Materials.—The phthalic anhydride for this investigation was resublimed C. P. phthalic anhydride obtained from the Selden Division, American Cyanamid Company, which material itself had already been sublimed in its preparation.

The glycerol was obtained by twice distilling Procter and Gamble C. P. water-white glycerin at 6 mm. pressure in an atmosphere of nitrogen. A small portion was then frozen rapidly in carbon dioxide and alcohol with continual

stirring until small crystals were obtained. These crystals were used to seed the specially distilled glycerol and the entire product crystallized by maintaining in a sealed container and a thermostat set at 17°. This crystallized glycerol was then brought to room temperature and the first portion melted, decanted and discarded. The remaining portion was used in the experiments. Its constants were: specific gravity at 20°, pycnometer corrected for vacuum, 1.2631; index of refraction at d_{20} 1.4741. This compared with the data given by Bozart and Snoddy[11] for 100% glycerol: specific gravity at 20° 1.2633; index of refraction at d_{20} 1.4740.

The Reaction at 200°

The glycerol–phthalic anhydride reaction was studied in detail at 200°. This temperature was chosen because experience showed that at 200° the reaction progressed at a rapid rate but not at such a rapid rate that it could not be followed accurately; also, it represented an average temperature at which alkyd resins are prepared commercially.

TABLE I

GLYCERYL PHTHALATE (ANHYDRIDE)

Experiment 39: complete experimental data at T, 200°. Glycerol, 46.0 g.; phthalic anhydride, 111.0 g.; temperature of mixing, 200°.

Time, min.	Temp., °C.	Water evolved, cc. V_0	G_2	V_a	Acid value[a]
0	200	..	..	..	535.7
1	236	..	..	..	
2	227	0.10	..	0.10	
3	222	0.40	..	0.40	247
4	217	0.85	..	0.85	241
6	212	1.42	..	1.42	229
7	210	1.72	..	1.72	223
8	208	2.02	..	2.02	218
9	206	2.28	..	2.28	213
10	203	2.50	..	2.50	208
11	203	2.62	..	2.62	206.5
12	202	2.85	..	2.85	201
13	202	2.93	..	2.93	200
14	201	3.12	..	3.12	197
16	201	3.30	..	3.30	193
18	200	3.52	..	3.53	188
20	200	3.72	0.01	3.73	184.5
22	199	3.92	..	3.93	182
24	199	4.17	..	4.19	176
26	199	4.30	..	4.32	173
28	199	4.48	..	4.50	170
30	200	4.68	.03	4.71	166
32	200	4.82	..	4.85	164
36	201	5.12	..	5.16	157
40	201	5.40	..	5.45	153
45	200	5.72	..	5.78	147
50	200	6.10	.08	6.18	143.5
55	200	6.30	..	6.39	141
60	199	6.52	..	6.61	139
65	199	6.70	..	6.82	136
70	200	6.90	..	7.03	134
75	200	7.10	..	7.24	133
80	200	7.15	.16	7.31	132

Experiment No. 40

0	200	..	..	..	535.7
1	230				
	233				
	228	Trace		..	
2	225	0.20		0.20	...
3	220	.40		.40	247
4	216	.85		.85	240
5	212	1.30		1.30	232
6	211	1.55		1.55	227
7	209	1.80		1.80	222
8	208	2.02		2.02	218
9	206	2.20		2.20	214.5
10	204	2.38		2.38	210.8
11	204	2.55		2.55	208
12	202	2.65		2.65	206
14	202	2.90		2.90	201
16	201	3.18		3.18	195
18	200	3.45	.01	3.46	190
20	200	3.70		3.71	185
22	200	3.90		3.91	181.5
24	200	4.12		4.14	177
28	200	4.50	.02	4.52	169
30	200	4.63		4.65	166
35	200	5.03		5.07	158.5
40	200	5.41		5.46	152
45	200	5.72		5.78	147.5
50	200	6.02		6.09	144
55	200	6.30	.09	6.39	140.5
60	200	6.50		6.60	139
65	200	6.80		6.90	135.5
70	200	6.90	.12	7.02	134
75	200	7.08		7.21	132.5
80	200	7.15		7.31	131
86	200	7.38		7.55	128.5
90	200	7.46	.19	7.65	127
95	201	7.56		7.76	126

[a] Calculated at each point from the water evolved–acid value curve, which curve was established carefully by a large number of individual determinations.

Studies were made to determine whether the reaction could be carried out quantitatively. A large number of experiments revealed that the loss in weight obtained after the reaction had been completed equalled the sum of the amount of water evolved and collected in the water-collecting chamber, plus such correction as it was necessary to make for the water carried off by the inert gas, and the amount of phthalic anhydride that had been carried over into the toluene–acetophenone mixture.

In order to determine whether or not the liquid which was collected and measured in the water-collecting chamber was actually water, at the end of one of the runs the entire contents of the water-collecting chamber was placed in a separatory

(11) Bozart and Snoddy, *Ind. Eng. Chem.*, **19**, 506 (1927).

funnel. After allowing sufficient time for complete separation, the lower layer was then removed and examined. It was neutral to litmus and tasteless. The index of refraction was determined in an Abbe refractometer and found to be $n^{22}D$ 1.333 which agrees very well with the value for pure water as given in the "International Critical Tables."

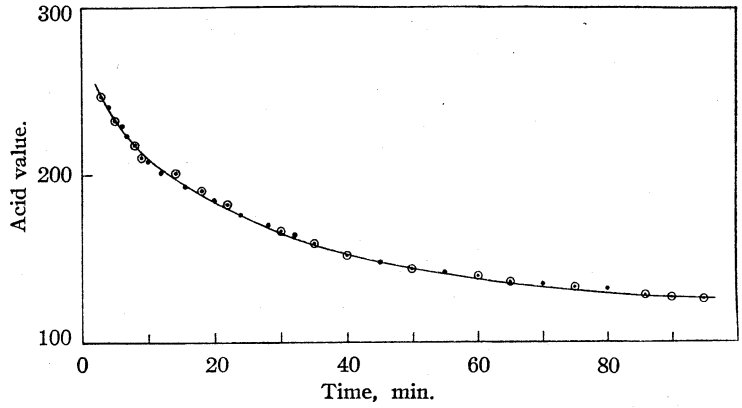


Fig. 2.—Glyceryl phthalate: variation of acid value with time at T = 200°; ●, expt. 39; ⊙, expt. 40.

It was observed, as in previous studies of this reaction, that when the reactants were brought together at 200°, an almost instantaneous exothermic interaction occurred, the temprature rising approximately 35°. In this interaction, no evolution of water was obtained, but the acid value dropped from an initial one of 535.7 to approximately 267. In other words, an initial 50% esterification occurred.

A detailed study of the water evolved–acid value relationship was undertaken. In order accurately to establish this relationship, it was necessary to make individual experimental runs to certain water evolved values and, on the resulting samples, to determine the acid values, having previously established the fact that experimental runs carried to the same water evolved values gave substantially identical acid values. This gave a series of samples of sufficiently large size that such properties as ultimate composition, molecular weight, viscosity characteristics, etc., could then be determined readily as a function of the progress of the reaction. But it was necessary to be certain that no change occurred in the samples on standing. A study was therefore made of what effect aging for several weeks had on the samples from various stages of the reaction. Except for a slight change in the early stages, the samples were apparently unaffected.

The complete water evolved–time data for the reaction at 200° are given in Table I. The corresponding acid values attained are included. As the reaction proceeded, the bath temperature (T_b), the temperature of the reaction itself (T_i), and the amount of water collected in the water-collecting chamber (V_0), were recorded carefully at every time interval that readings were taken. From the water–correction curve, V_0 was corrected to give V_a, the actual amount of water evolved. It is obvious that at the temperature of 200° very little correction in V_0 is necessary.

The change in acid value as a function of time, T, 200°, is plotted in Fig. 2, the complete data for experiments 39 and 40 being included. It is evident that both runs give exactly the same curve, showing that the reaction is accurately reproducible. In Fig. 3, the water evolved–time curve is plotted similarly.

From these two curves, Fig. 4 has been constructed which shows the water evolved–acid value relationship. In addition, the experimentally determined values of a number of individual runs also have been given. It will be seen that these individual values quite accurately fit the curve obtained by combining Figs. 2 and 3, showing that the water evolved–acid value relationship

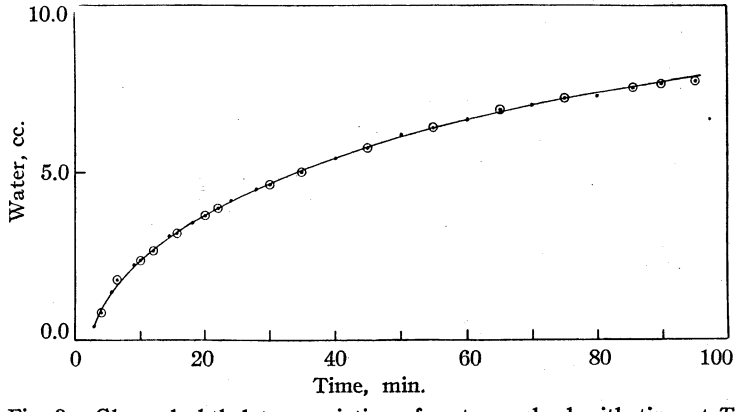


Fig. 3.—Glyceryl phthalate: variation of water evolved with time at T = 200°; ●, expt. 39; ⊙, expt. 40.

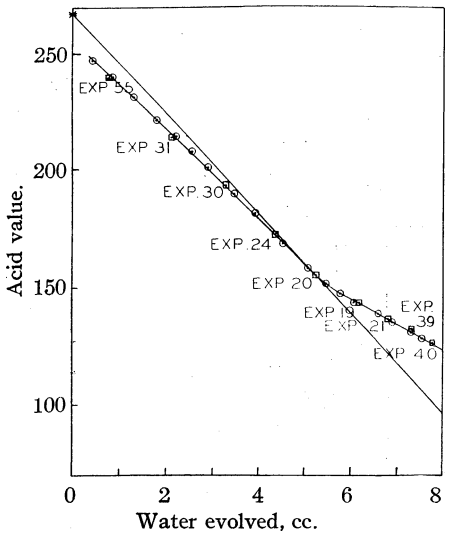


Fig. 4.—Glyceryl phthalate (anhydride): water evolved—acid value relationship.

is the same whether obtained by the method of individual runs or by the graphical method of combining the complete acid value–time run with the water evolved–time run. In Fig. 4 there is shown also the theoretical relationship between the volume of water evolved and the acid number on the assumption that, immediately after 50% esterification had been attained without loss of water, subsequent resinification occurred with evolution of water and with only esterification occurring at all times. The equation representing this theoretical relationship is

$$A = 378.9\frac{P - P_c}{W - P_c} - 3110\frac{V}{W - T} \qquad (1)$$

wherein A is acid number; P, weight of phthalic anhydride used; W, the total weight of ingredients; T, total weight loss in experiment; V, cc. of water evolved; and P_c, weight of phthalic anhydride lost in the experiment.

It is evident, when Fig. 4 is examined, that in the early stages of a glyceryl phthalate reaction there is less water evolved than is required on the assumption that only esterification has taken place. In the later stages of the reaction, more water is evolved which suggests that over this portion of the reaction some anhydride formation occurs.

Numerous attempts were made to treat water evolved and acid value data for glyceryl phthalate kinetically. It is sufficient to indicate at this point that no simple kinetic relationship was found applicable to the entire data.

In order to get some idea of the "beyond the gel" state, an experiment was made in which the rate of water evolution was followed well beyond the gel state. That portion of the data which covers the portion of the reaction just prior to and beyond gelation, is shown in Fig. 5. The point at which gelation occurred is indicated clearly by an arrow. It is evident from this curve that condensation continues beyond gelation with such change of rate as takes place seemingly resulting from the physical limitations of intercontact of the molecules brought about by the state of arrested motion that occurred at gelation.

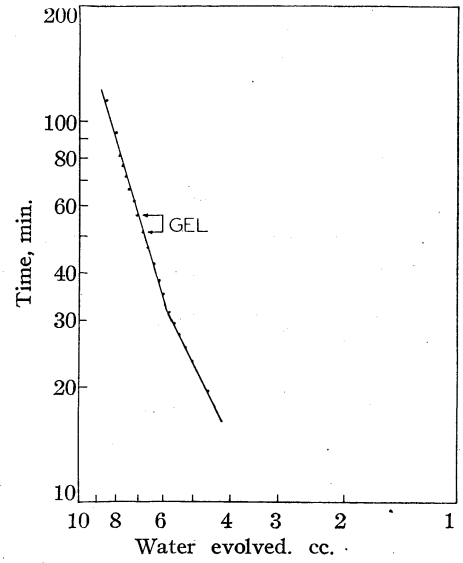


Fig. 5.—Glyceryl phthalate: water evolved, V_0, before and after gelation.

Effect of Temperature

The reaction was studied over the temperature range 160–215°. A number of individual experiments revealed that over this temperature range the same acid value is attained for any given water loss independent of the temperature. This having been established, detailed quantitative water evolved–acid value–time runs were carried out at 160, 185 and 215°. The data obtained, as well as those given in Table I, are plotted as a log acid value–log time relationship in Fig. 6.

In Table II are summarized for the various temperatures, the time for gelation to occur and the water evolved. It will be noted that the amount of water evolved at gelation appears to be independent of the temperature. Using the gel point, therefore, as a common reference state for the reaction, the heat of activation has been calculated and found to be 21,600 cal. per g. mole.

TABLE II

EFFECT OF TEMPERATURE

Temp., °C.	Time, min. gelation	Water evolved, cc.
160	860	7.98
185	255	7.99
200	105	7.99
215	50	7.98

Physical and Chemical Variations as Reaction Progresses

Analytical.—In Table III are summarized the analytical data of the various glyceryl phthalate samples prepared in the 200° temperature studies. The methods used in determining the acid value and saponification value already have been described[2]; carbon and hydrogen were determined by the standard micro-chemical methods now in use for these elements.[12] The values given for the sample marked "gel" are only approximate. The sample marked "degelled" was prepared by taking a portion of the gelled resin, placing in a Pyrex tube, sealing the tube and heating in an oven overnight at a temperature of approximately 150°. A fusible, amber, resinous product resulted which was now soluble in acetone and which cured only very, very slowly when a small portion was placed on a hot-plate at 200°. Data on the degelled sample are included for whatever bearing such data might have on the later theoretical speculations.

TABLE III

ANALYTICAL DATA

VARIOUS GLYCERYL PHTHALATES (ANHYDRIDE) AT 200°

Expt.	Acid value	Saponification value	%, E	H_2O, cc. V_a	Ultimate analyses C, %	H, %
55	240	536	55.2	0.85	..	..
29	204.5	536.7	61.9	2.70	58.6	4.74
27	193.1	537.8	64.2	3.30	58.9	4.52
28	183.8	537	65.9	3.80	59.3	4.59
24	172.7	542.5	68.2	4.37	59.7	4.71
20	155.4	549.8	71.8	5.25	59.4	5.01
21	136.6	551	75.0	6.80	59.2	4.43
40	126.0	552	77.2	7.76	60.2	4.37
Gel	(107)	556.8	..	7.99	60.0	4.39
Degel	141.8	538.9	73.6	..	59.7	4.44

Infrared Spectra.—Infrared spectra on the samples described in Table III and covering the range from 1–15 μ have been measured. The details of this investigation will be reported elsewhere.[13] The spectra showed that the glyceryl phthalate samples for the various acid values fell into groups rather than varying continuously, the spectra of the several samples in a given group being quite similar one with another.

Of special interest in the infrared investigation were the spectra of the degelled samples. These were found to be similar to the corresponding polymeride of the same acid value obtained when approaching gelation, making the assumption that gelation is the result of the formation of a gigantic molecule very questionable.

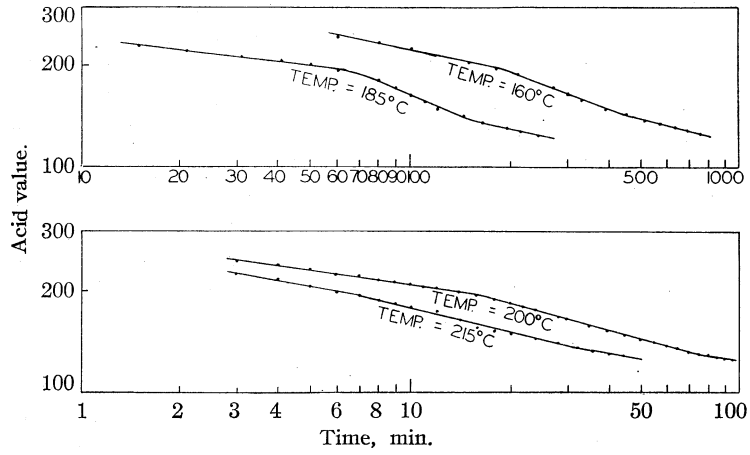


Fig. 6.—Glyceryl phthalate: acid value–time isotherms.

Molecular Weight.—For the determination of the average molecular weights, a cryoscopic solvent was sought in which the polyesters were all very soluble, in which water was immiscible, and in which duplicate values, unaffected by moderate changes in concentration of resin used, could be obtained. Acetophenone (K = 5650) was found to answer these requisites. In the experimental data presented, carefully distilled acetophenone was employed throughout, its suitability being checked with specially purified naphthalene.

The average molecular weights found for the various glyceryl phthalate samples are given in Table IV together with the concentrations at which the measurements were made and the depressions observed. In Fig. 7, these average molecular weights are plotted against the corresponding acid values.

How the molecular weight would vary with the acid value if any ideal (2,3) continuous interesterification alone occurred is shown as the so-called theoretical curve in Fig. 7. The deviation of the

(12) Acknowledgment is made to Dr. G. L. Royer for carrying out these determinations.

(13) R. H. Kienle and R. B. Barnes, Presented before American Chemical Society Meeting at Chapel Hill, N. C., April, 1937.

TABLE IV

AVERAGE MOLECULAR WEIGHTS
GLYCERYL PHTHALATES (ANHYDRIDE)
SOLVENT: ACETOPHENONE

Expt.	Acid value	Concn., %	ΔT,°C.	M
55	240	5.38	0.713	418
29	204	3.12	.402	437
28	184	3.94	.463	482
24	173	5.46	.565	545
20	155	4.36	.420	590
21	137	4.52	.325	790
40	126	3.02	.152	1120
Degel	142	3.98	.227	680

actual data from the theoretical shows that other molecular species in variance with simple interesterification must be forming. The fact that the experimental curve falls below the theoretical, and in keeping with the general evidence that the reaction is essentially esterification, strongly suggests intraesterification. These average molecular weights must be dovetailed with the other data such as acid value, water loss, etc., in modifying the reaction and structural consideration.

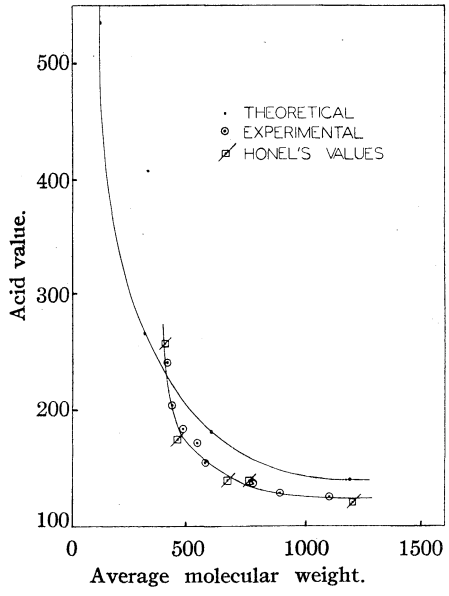


Fig. 7.—Glyceryl phthalate.

Viscosity Studies.—As a further possible adjunct to information concerning the molecular changes in the glyceryl phthalate reaction, viscosity measurements were undertaken.

Working in dioxane, Kienle and Race[14] reported the viscosity characteristics of a series of glyceryl phthalate samples at various acid values. A similar investigation was later made by Houwink and Klaassens.[4] There is a fair agreement between the values reported in both these papers for the samples taken at the early stages of the reaction. Houwink and Klaassens, however, were not able to obtain the high value reported by Kienle and Race for the very last stages. But Houwink and Klaassens, in their measurements, used as a final sample one which was a considerable time period away from gelation, while Kienle and Race used a sample just prior to gelation. All of these values reported, however, were low as compared with numerous specific viscosity values given by Staudinger for other synthetic polymerides, such as polystyrene. If the contention of Staudinger, that specific viscosity bears relation to the molecular size, has the importance he attributes thereto, this would indicate that glyceryl phthalate is definitely a small polymeric molecule.

The present measurements were made using C. P. acetone (A. V. = 0) as a solvent at a concentration of 15.0% by weight. The measurements were made in a vacuum capillary type viscometer described by Gregory, Ressweiler and Lampert,[15] and were carried out at 35°. The average values of several determinations have been corrected for the density of the solution in each case. The values obtained for the different glyceryl phthalate samples are given in Table V. It will be noted that until an acid value of less than 137 is reached, only a small steady increase in the specific viscosity is observed. From then on, the increase is rapid in line with Kienle and Race's original observations. The rather rapid increase in specific viscosity that begins at an acid value of approximately 137 indicates that a change in molecular complexity occurs when this acid value is reached. Up to this time, the molecules probably were of such small size that they had some, although little,

TABLE V

VISCOSITY CHARACTERISTICS OF VARIOUS
GLYCERYL PHTHALATE (ANHYDRIDE) SAMPLES

Solvent, acetone; concentration, 15.0% by weight; temperature, 35°; viscosity of acetone, η_0 = 0.00278 poise.

Acid value	$\eta \times 10^5$ poise	Relative viscosity, η_r	Specific viscosity, η_s
204	574	2.065	1.065
193	598	2.150	1.150
184	568	2.044	1.044
173	560	2.018	1.018
155	560	2.255	1.255
137	654	2.350	1.350
123	930	3.420	2.420

(14) Kienle and Race, *Trans. Electrochem. Soc.*, **65**, 231 (1934).

(15) Gregory, Ressweiler and Lampert, *J. Rheol.*, **1**, 30 (1929)

effect on the viscosity. Beyond this point, the reaction started to produce large enough molecules to be effective in causing a pronounced increase in viscosity.

Monomolecular Films.—It was found that the various glyceryl phthalate samples readily formed monomolecular films. These have been studied in detail and will be reported upon later. Although Moss[16] and Harkins[17] investigated some of the linear polymerides in this manner, as far as is known, no measurements have been reported on convertible polymerides.

By means of the usual method of intercepts, it was possible to determine an area which represented the area per molecule of the average molecular species, A_{max}, present in any given sample. The values of A_{max} and the corresponding acid values are given in Table VI and are shown in curve form in Fig. 8.

TABLE VI

AREA PER AVERAGE MOLECULE, A_{max}, OF SEVERAL GLYCERYL PHTHALATES AS MONOMOLECULAR FILMS ON 0.001 *N* HCl

Acid value	Area/molecule, A_{max} (Å.)²
240	31.1
204	35.5
184	52.0
155	74.0
137	129.2
126	138.8

Fractionation.—While studying the various glyceryl phthalate samples in glacial acetic acid solution, it was observed that when this solution was drowned in a large volume of water, white amorphous precipitates frequently resulted. It was found that if the water was made slightly acid with hydrochloric acid, the precipitate obtained was readily filterable and often granular in nature. Undoubtedly low molecular weight portions were separated from the larger molecules by this treatment. Thus some idea of obtaining the size of the latter seemed a possibility. A fractionation was therefore made, using glyceryl phthalate, A. V. 130.

Fifteen grams of the resin was dissolved in 150 g. of glacial acetic acid. This solution was added slowly to 1500 cc. of water which had been acidified with hydrochloric acid. The resulting precipitate was reslurried in distilled water, washed several times by decantation, filtered, and dried at 60°. The acid value was found to be 92.2, and

(16) Moss, THIS JOURNAL, **56**, 41 (1934).
(17) Harkins, Ries and Carman, *ibid.*, **57**, 776 (1935).

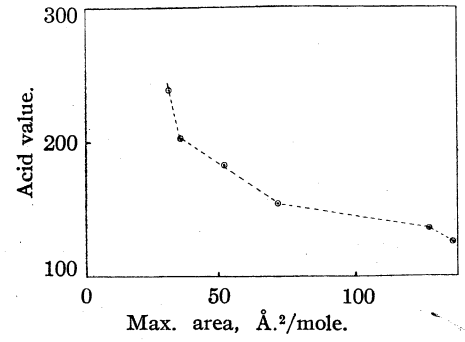


Fig. 8.—Glyceryl phthalate: monomolecular area per average molecule as function of acid value.

the molecular weight in acetophenone was 2580. It is interesting to compare these values with the theoretical values calculated if only interesterification were involved. On the assumption that a condition of interesterification equivalent to tetramer formation has occurred, which is required by the molecular weight and other data, the acid value resulting would be 117 and the molecular weight 2384. If intraesterification occurred at one position on the molecule along with the interesterification, the acid value would be 94.5 and the molecular weight 2366. These latter values are in fair agreement with the values found experimentally.

It has been known for some time that if polyester resins are dissolved in acetone, water can be added slowly and, at a certain point, precipitation or turbidity occurs. The amount of water that can be added to any given solution and the character of the precipitate obtained seemingly depend on the extent to which the resin has been carried in its preparation. Thus a solution of a partially formed resin will tolerate a large amount of water and will give a very gummy precipitate while a resin near the gel point will tolerate little water and will yield a precipitate quite granular in character.

TABLE VII

PRECIPITATION STUDIES OF GLYCERYL PHTHALATE (ANHYDRIDE) AT 20–21°

Sample	A. V.	Weight, g.	Water used, cc.	H_2O/g. to ppt.	Character of ppt.
55	240	1.0125	66.50	65.50	Colloidal
29	204	1.0040	62.40	62.30	Colloidal
27	193	1.0007	46.20	46.20	Soft, gummy
28	184	1.0006	45.25	45.25	Soft, gummy
24	173	1.0036	41.40	41.30	Soft, gummy
20	155	1.0316	33.60	32.60	Soft, gummy
21	137	1.0065	23.36	23.26	Granular
40	126	1.0050	20.50	20.50	Granular

Approximately 1 g. of each of the glyceryl phthalate resins was dissolved in 50 cc. of C. P. acetone, the actual amount used being carefully weighed and recorded. Each solution was then titrated with distilled water to the point at which cloudiness was first observed. It was possible to obtain this end-point to within 0.05 cc. The data obtained are given in Table VII, and plotted in Fig. 9.

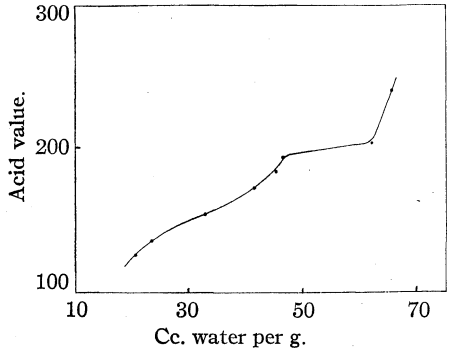


Fig. 9.—Glyceryl phthalate: water required for precipitation.

Theoretical

It has been shown by all the chemical examinations and supported by the infrared spectra data that only C–O–C linkages are formed.[18] Therefore, in modifying the assumption that interesterification was the only reaction involved, the possible secondary reactions to consider were ether formation, anhydride formation, and intraesterification. In the case where equivalent quantities of reactants are involved, as in the present investigation, there was little evidence for ether formation. Anhydride formation and intraesterification, however, appeared to be definite possibilities. A number of glyceryl phthalate samples for which the acid value, saponification value, average molecular weight, and water evolved had been determined were taken and examined as to whether or not possible combinations of polyesters could be postulated, following a common pattern, which would correlate all the data. On the basis of interesterification as the primary reaction with anhydride and intraesterification as secondary reaction possibilities, it has been found possible to derive approximate theoretical compositions which satisfy all of the determined values. In arriving at these calculations, a schematic postulation of the progress of reaction, such as is shown diagrammatically in Fig. 10, was used.

(18) Kienle, *J. Soc. Chem. Ind.*, **55**, 229T (1936).

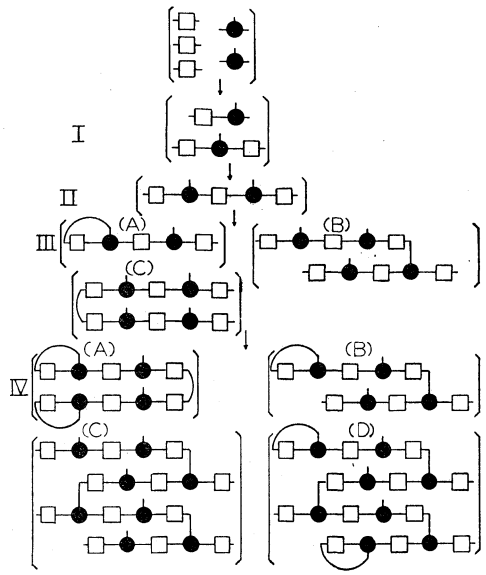


Fig. 10.—Glyceryl phthalate reaction, postulated progress: ratio of 2 moles of glycerol to 3 moles of phthalic anhydride.

Four typical glyceryl phthalate samples have been examined in detail, namely, those with acid values of 235, 184, 137 and 126. It has been possible to propose approximate compositions for each of these samples. These compositions, as well as the agreement between the calculated and the observed analytical data, are given in Table

TABLE VIII

CALCULATED COMPOSITIONS OF VARIOUS GLYCERYL PHTHALATES

Observed	Composition: Species (Fig. 10)	Composition: Approximate mol. fraction	Calcd.
A. V. = 235			A. V. = 235
V_a = 1.00 cc.	I	0.60	V_a = 1.80
M = 425	II	.40	M = 480
			v = 1.7
M_v = 406			
A. V. = 184			A. V. = 190
V_a = 3.80 cc.			V_a = 4.00
M = 482	I	.40	M = 488
	II	.30	v = 1.5
	IIIa	.30	
M_v = 460			
A. V. = 137			A. V. = 140
V_a = 6.70 cc.			V_a = 6.70
M = 795	II	.33	M = 801
	IIIa	.33	v = 2.0
	IIIb	.33	
M_v = 800			
A. V. = 126			A. V. = 125
V_a = 7.60 cc.			V_a = 7.60
M = 1120	II	.167	M = 1190
Sap. value = 551	IIIa	.167	v = 2.6
	IIIb	.333	Sap. value = 552
	IVa	.084	
	IVb	.083	
	IVc	.084	
	IVd	.083	
M_v = 1150			

VIII. Examination of this table shows that the agreement between the observed and calculated values is surprisingly good.

The value of M_v in this table requires explanation. It will be observed by examining Fig. 10 that every postulated polymeric molecule is a polybasic acid with a characteristic basicity. Thus the basicity of the molecule represented by IIIb is 3. Any given individual glyceryl phthalate sample will, therefore, have an average basicity, v, depending on the number and kind of polymeric molecules present. Carothers[4] has shown in linear systems, in which the basicity of the polymeric molecules remains essentially constant, that the molecular weights can be determined either by the usual methods or from the acid value. When the molecular weight is determined from the acid value, the following equation applies

$$MA_t = 56.1 \times 10^3 v \qquad (2)$$

wherein M is the average molecular weight, A_t is the acid value at time t, and v is the basicity. In linear polyesters, v is 1, therefore v did not appear in Carothers' calculations. But in the convertible polyesters, the value of v is important. In Table VIII the Mv value was obtained by using equation (2), first determining the average value of v from the composition finally suggested, then substituting this together with the acid value experimentally determined, and solving. It is seemingly additional evidence in favor of the compositions suggested that the molecular weights thus calculated agree very well with the average molecular weights, M, actually determined.

The compositions of the several glyceryl phthalate samples as calculated are in surprisingly good agreement with the various experimental facts observed. Thus, only when an acid value around 190 is reached in the reaction, do molecules of the species III type seemingly appear. From this point on to approximately an acid value of 135, molecules of the species III type are apparently forming. Further on, molecules of the species IV type, with their three dimensional complexities, begin to appear until finally their concentration is sufficiently great to cause arrested motion, that is, gelation. The grouping of the various samples with respect to the infrared spectra is now understandable. The marked change in the character of the precipitate from a gummy to that of a granular, easily filterable type at an acid value of 137 as acetone solutions are diluted with water is explained. When the basicities are taken into account and it is assumed that in monomolecular films the point of attachment to water is through the carboxyl groups, which all prior work on complex acids has indicated is the case, the changing character of the monomolecular areas is also understandable. The non-appearance of the complex three-dimensional polyester molecules of the species IV type, until acid values less than approximately 137 are reached, offers an explanation for the change in specific viscosity that was observed in the neighborhood of this acid value. The introduction of the intraesterification and anhydride modification also accounts for the character of the acid value–water loss relationship. In other words, the general schematic postulation of the progress of the reaction presented in Fig. 10 is consistent with the experimental data that have been obtained for glyceryl phthalate.

It must not be concluded that the polyester compositions developed above are being presented as definite fixed structures. Thus it is suggested that in a glyceryl phthalate resin, such as one represented by an acid value of 126, small amounts of polyesters of even higher degrees of polymerization or complexity than those postulated might well be present.

The possibility that the reaction proceeds entirely in a heterogeneous manner, governed completely by the random chance contact of active groups on the interacting molecules, each active group acting independently and in no organized molecular manner, is therefore questioned. When, however, the reaction has proceeded so that essentially tetramers are being formed and the concentration thereof has approximated 33 mole %, gelation occurs seemingly because, at this concentration, a sufficient complexity of three-dimensional molecules has been built up to bring about a state of arrested motion. It follows that gelation in polymerides is not necessarily attendant with the formation of gigantic macromolecules. Macromolecules may appear later, but gelation apparently occurs, or can occur, when there has formed a sufficient concentration of suitably complex three dimensional molecules of a relatively low degree of polymerization which are capable of intertwining. This may be thought of as analogous to a log jam which always results when a certain minimum concentration of logs becomes permanently interlocked.

Other convertible polyester systems also have

been investigated recently. It was found that the data obtained for these systems could be treated in a manner analogous to the glyceryl phthalate data. It is, therefore, suggested that the essential concepts developed herewith are applicable generally to convertible polymeric systems.

Summary

1. The reaction between glycerol and phthalic anhydride was reinvestigated. A special apparatus, designed so that the reaction could be carried out under controlled reproducible conditions, was used.

2. The reaction was studied in detail at 200°. Samples were taken at various stages of the reaction and their acid value, saponification value, ultimate analysis, and molecular weight determined. The infrared spectra, rheological properties, and spreading characteristics as monomolecular films were ascertained for each of the samples.

3. As the reaction proceeded at 200°, it was shown that the water evolved was greater than calculated from simple interesterification considerations.

4. A schematic progress of the reaction is suggested wherein it is proposed that the underlying reactions are essentially interesterification, modified by intraesterification and anhydride formation. Application of these concepts allowed approximate compositions of glyceryl phthalate polymerides to be derived at various stages of polymerization. The several constants calculated from these postulated compositions were found to agree very well with those measured experimentally.

5. Gelation has been shown to occur at a relatively low average molecular weight, suggesting that molecular growth proceeds until a sufficient concentration of intertwined three dimensional molecules has formed, whence arrested motion occurs.

6. Limited data are presented on precipitation and fractionation studies.

BOUND BROOK, N. J. RECEIVED MAY 4, 1939

[CONTRIBUTION FROM THE LABORATORIES OF THE SCHOOL OF CHEMISTRY, RUTGERS UNIVERSITY, AND RESEARCH DEPARTMENT, THE CALCO CHEMICAL COMPANY, INC.]

The Polyhydric Alcohol–Polybasic Acid Reaction. IV. Glyceryl Phthalate from Phthalic Acid

BY R. H. KIENLE, P. A. VAN DER MEULEN AND F. E. PETKE

All the studies on the glyceryl phthalate reaction thus far reported in the literature have been carried out with phthalic anhydride. In the present investigation, data are presented wherein phthalic acid was substituted for the anhydride.

The apparatus used and experimental technique employed already have been described fully.[1] The phthalic acid was obtained from resublimed phthalic anhydride (Selden Division, American Cyanamid Company) by dissolving in carbonate free sodium hydroxide solution, then precipitating with hydrochloric acid, thoroughly washing until the wash water tested free from chloride ion, and finally drying carefully at 60° in the air.

The present investigation was carried out at 190°. This temperature was chosen because it was found that at this temperature no anhydride formation occurred during the preheating period employed before the glycerol was added.

(1) Kienle, van der Meulen and Petke, THIS JOURNAL, **61**, 2258 (1939).

Experimental Data

The detailed data obtained for the glycerol–phthalic acid reaction at 190° are given in Table I.

In Fig. 1 the variations of both the acid value and the water evolved with time of reaction have been plotted. In the case of the water evolved–time curve, the observed points of a second independent experiment under identical conditions have been included to show how well the data could be duplicated. On the acid value–time curve, the values obtained from several independent determinations are also shown. Again they fall quite well on the curve.

The log acid value–log time relationship is shown in Fig. 2. It is strikingly similar in shape to the same relationship for glyceryl phthalate (anhydride) except that for glyceryl phthalate (acid) it has been possible to extend the relationship to much higher acid values.

In Fig. 2 changes in slope are observed at ap-

TABLE I

GLYCERYL PHTHALATE FROM PHTHALIC ACID

Glycerol (2/8 mol.), 23.0 g. Phthalic acid (3/8 mol.), 62.3 g. Temperature of mixing, 190°. Experiment 63.

Time, min.	Temp., °C.	Water evolved,[a] V_0	V_a	Acid value
0	190	..	..	494
2	189	..		
5	174	0.31	0.31	
8	174	1.46	1.47	
10	174	2.31	2.31	350
14	185	3.68	3.70	
16	187	4.19	4.21	
18	187	4.77	4.80	
20	187	5.00	5.04	294
24	189	5.44	5.48	
26	189	5.65	5.70	
28	189	6.04	6.09	
30	190	6.19	6.24	259
35	190	6.49	6.55	
40	191	6.71	6.78	235
50	191	7.22	7.31	218
60	190	7.68	7.70	203
70	187	8.08	8.23	190
80	190	8.38	8.55	177
90	191	8.71	8.92	164
100	191	9.28	9.52	155
110	190	9.49	9.72	145
120	190	9.78	10.07	137
130	191	9.90	10.22	132
140	190	10.12	10.48	128

[a] V_0 = cc. observed. V_a = cc. when corrected for water loss in gas stream.

proximate acid values 275, 185 and 140. These agree rather well with the approximate acid values at which similar changes are found in the case of glyceryl phthalate (anhydride), namely, 190 and 138. In addition, acid value 275 is reasonably close to acid value 266, the instantaneous initial acid value always obtained when phthalic anhydride is employed.

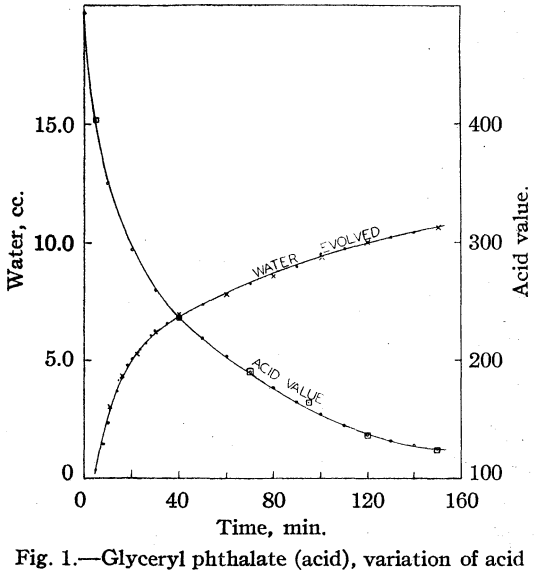


Fig. 1.—Glyceryl phthalate (acid), variation of acid value–water evolved with time, T = 190°.

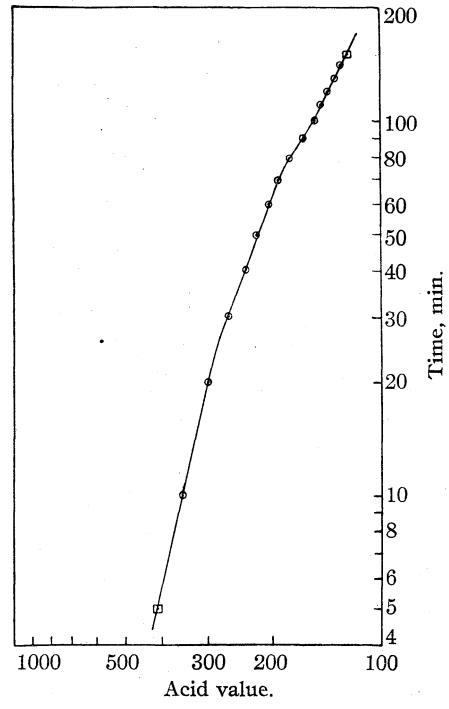


Fig. 2.—Glyceryl phthalate (acid); temperature, 190°.

The water evolved–acid value relationship is

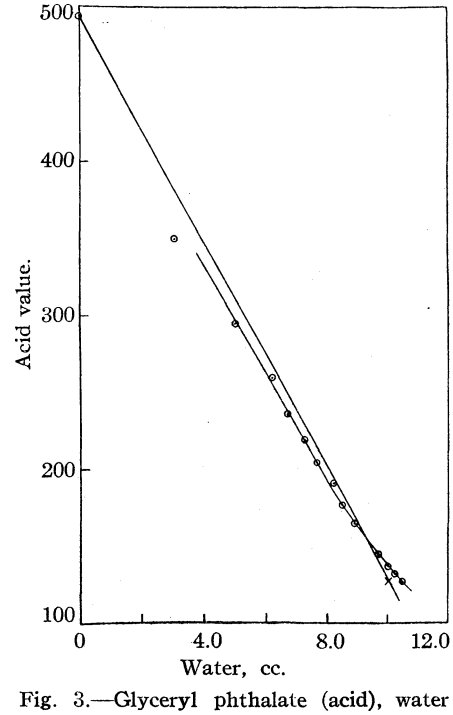


Fig. 3.—Glyceryl phthalate (acid), water evolved–acid value relationship.

given in Fig. 3. There is also included the theoretical relationship for glyceryl phthalate (acid) that should have resulted if the reaction had proceeded by interesterification only. It is interesting to note that the deviations from the theoretical are similar to that observed for glyceryl phthalate (anhydride). This is particularly true from an acid value of 266 on, the acid value representing 50% esterification. In the case of glyceryl phthalate (acid) the curve crosses the theoretical at acid value 155 as compared with acid value 158 observed for glyceryl phthalate (anhydride).

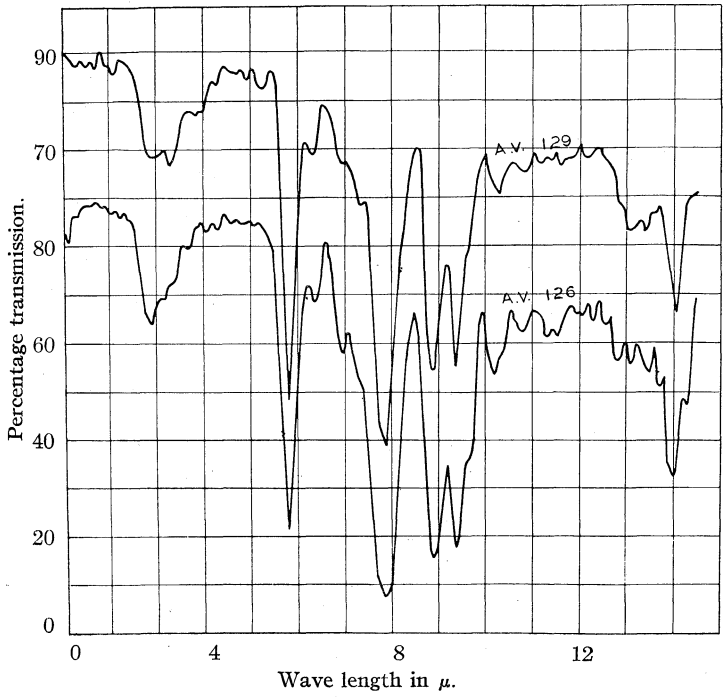


Fig. 4.—Infrared spectra: glyceryl phthalate (acid), A. V. = 129; glyceryl phthalate (anhydride), A. V. = 126.

Analytical.—The polymeride obtained just prior to gelation was a light amber, brittle resin similar in physical appearance to that from glyceryl phthalate (anhydride). Its analytical values are given in Table II. In this table there also are included data for an actual glyceryl phthalate (anhydride) sample of nearly the same acid value and, in addition, the calculated analytical values for glyceryl phthalate (anhydride) of exactly the same acid value determined, by extrapolation, from the curves of the recent glyceryl phthalate (anhydride) study. The water evolved data shown in parentheses for the anhydride samples were obtained by adding to the actual water evolved the water required theoretically to convert the phthalic anhydride to phthalic acid.

TABLE II

ANALYTICAL DATA

	Glyceryl phthalate (acid)	Glyceryl phthalate (anhydride) Calcd.	Exptl.
Acid value	129	129	126
Saponification value	560	551	552
% esterification	76.2	76.6	77.2
Av. molecular weight	910	920	1120
Water evolved, cc.	10.48	(10.51)	(10.63)
Ultimate analysis % C	59.5	59.9	60.2
Ultimate analysis % H	4.4	4.4	4.3

The infrared spectrum[2] from 1–15 μ of the glyceryl phthalate (acid) sample is shown in Fig. 4. There is also included the spectrum obtained for the glyceryl phthalate (anhydride) sample, acid value 126. The general closeness of the two spectra with respect to the over-all shape and positions of the absorption maxima is apparent.

Discussion

In the glyceryl phthalate reaction, when phthalic acid is substituted for phthalic anhydride, no initial temperature rise is observed and time is necessary to attain 50% esterification. When, however, 50% esterification has been attained, the reaction proceeds further in a manner quite analogous to that observed when phthalic anhydride is used. It appears that equivalent polymerides are eventually formed with quite similar degrees of molecular complexity. This perhaps is illustrated best by the comparison of the various analytical values and is further shown by comparing the water evolved for similar acid values, Table III. In setting up this table, the experimental values for glyceryl phthalate (anhydride) have again been corrected for the amount of water evolved to 50% esterification had phthalic acid been used.

TABLE III

Acid value	Water evolved, cc. Glyceryl phthalate acid	Glyceryl phthalate anhydride
190	8.10	8.47
150	9.50	9.55
129	10.48	10.51
Gel	10.80	10.74

(2) Acknowledgment is made to Mr. R. R. Brattain for determining this spectrum.

It appears that polybasic acids can be substituted for anhydrides in the polyester reaction to yield finally fairly equivalent polymerides.

Summary

The glyceryl phthalate reaction has been investigated substituting phthalic acid for phthalic anhydride. Differences in the early stages of the reaction were observed but the later portions of the reaction to gelation are comparable.

BOUND BROOK, N. J. RECEIVED JUNE 17, 1939

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, No. 709]

The Hydration of Unsaturated Compounds. VII. The Rate of Hydration of Crotonic Acid; the Rate of Dehydration of β-Hydroxybutyric Acid; the Equilibrium between Crotonic Acid and β-Hydroxybutyric Acid in Dilute Aqueous Solution

BY D. PRESSMAN AND H. J. LUCAS

Introduction

Crotonic acid has been shown to hydrate slowly in the presence of boiling 20% sulfuric acid to form β-hydroxybutyric acid.[1] This reaction is unlike the hydration of acrylic acid, since the latter occurs in the presence of hydroxide ion[2] while crotonic acid is not affected under these conditions. Moreover, only about 80% of the crotonic acid hydrates, for it appears that at this point it is in equilibrium with the hydroxy acid. The fact that the hydroxyl group enters into the β-position during the hydration is shown by the identical properties of the acid obtained by this method and of β-hydroxybutyric acid obtained by other methods. Also the ethyl ester of the hydroxybutyric acid prepared by this method is identical with that from hydroxybutyric acid obtained by other syntheses.[3]

It was desirable to extend the study of the hydration on unsaturated compounds to an investigation of the kinetics of the hydration of crotonic acid, of the kinetics of dehydration of β-hydroxybutyric acid, and of the equilibrium between crotonic acid, β-hydroxybutyric acid, and water. Since it was known that crotonic acid is not hydrated at an appreciable rate at 25° in 1 normal nitric acid,[4] the reaction was carried out in 1.06 and 2.06 normal perchloric acid solutions at 90.03 and 111.31° in order to obtain a measurable rate. These solutions were of 2.06 molal ionic strength. Nitric acid could not be used since its oxidizing power at the elevated temperature was appreciable, as evidenced by the liberation of the oxides of nitrogen.

(1) Kaufel and Basel, *Monatsh.*, **53**, 122 (1929).
(2) Linnemann, *Ber.*, **8**, 1095 (1875); Erlenmeyer, *Ann.*, **191**, 281 (1878).
(3) Dewael, *Bull. soc. chim. Belg.*, **34**, 341 (1925).
(4) Winstein and Lucas, THIS JOURNAL, **59**, 1461 (1937).

Data and Discussion

Kinetics of the Reaction.—The hydration was found to be first order with respect to crotonic acid since the plots against time of the fraction of crotonic acid unreacted, C_t/C_0, are practically identical for two runs at hydrogen ion concentration of 1.06 molal where the initial crotonic acid concentration has the values 0.0128 molal and 0.0249 molal. Here C_0 and C_t are the molar concentrations of crotonic acid at the respective times, zero and t (Fig. 1). That the reaction is first order with respect to hydrogen ion concentration is evidenced through a comparison of the initial slopes of the plots of C_t/C_0 against t when the hydrogen ion concentrations are 1.06 and 2.06 molal. The slope at the higher concentration corresponds to a rate constant of 0.014, which is twice that of the lower, approximately 0.007. However, hydrogen ion is not used up in the reaction and thus is constant during any one run.

The independence of the equilibrium value with respect to the hydrogen ion concentration, except for small second order differences, is clearly evident from Fig. 2, which shows the complete runs of which Fig. 1 contains only the first portions. The equilibrium value of the crotonic acid fraction remaining is practically identical for both acid concentrations. The reaction then may be considered to be

$$H_3O^+ + H_2O + CH_3CH{=}CHCOOH \underset{k_2}{\overset{k_1}{\rightleftharpoons}} CH_3CHOHCH_2COOH + H_3O^+$$

where k_1 is the specific reaction rate constant of

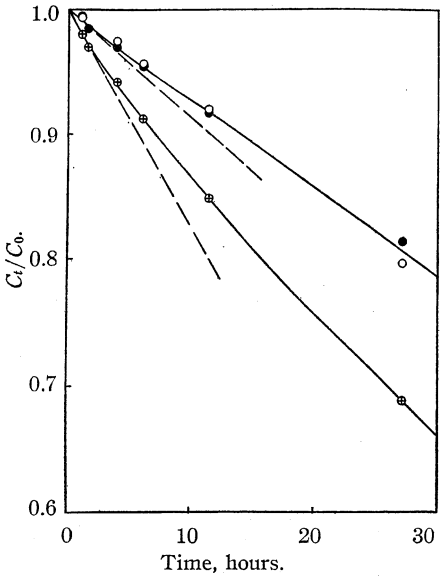


Fig. 1.—Hydration of crotonic acid showing the effect of hydrogen ion concentration and initial crotonic acid concentration on the initial slope of a plot of C_t/C_0 against time: T, 90.03°; μ, 2.06 molal.

	○	●	⊕
Crotonic acid, C_0 molal	0.02487	0.01282	0.01248
(H^+), molal	1.060	1.060	2.056

the forward reaction and k_2 is the specific reaction rate constant for the reverse reaction considering

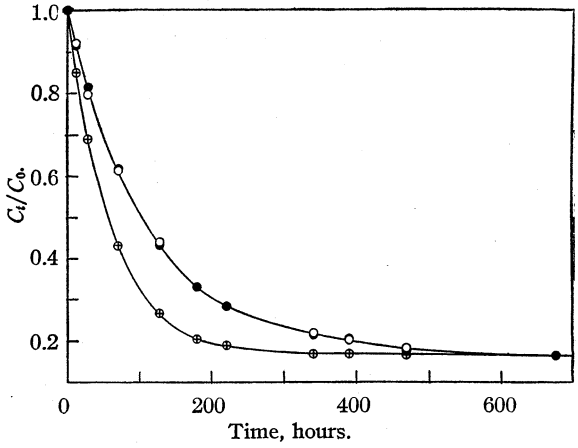


Fig. 2.—Hydration of crotonic acid showing the effect of hydrogen ion concentration and initial crotonic acid concentration on the equilibrium between crotonic acid and β-hydroxybutyric acid. Plot of C_t/C_0 against time. The last point is common to the three runs. T, 90.03°; μ, 2.06 molal.

	○	●	⊕
Crotonic acid, C_0, molal	0.02487	0.01282	0.01248
(H^+), molal	1.060	1.060	2.056

both reactions to be monomolecular with respect to the organic reactant.

$$-\text{d(crotonic acid)}/dt = k_1(\text{crotonic acid}) \quad (1)$$

$$-\text{d(hydroxybutyric acid)}/dt = k_2(\text{hydroxybutyric acid}) \quad (2)$$

Rather than calculate k_1 from the initial slope of the reaction rate curve, it was calculated by the analytical method which involves the integrated expression for a unimolecular reaction approaching equilibrium (equation 3) and the equilibrium constant (equation 4).

$$\log_{10}\frac{\epsilon}{\epsilon - x} = \frac{(k_1 + k_2)t}{2.303} \quad (3)$$

$$K = \frac{k_1}{k_2} = \frac{\epsilon}{1 - \epsilon} \quad (4)$$

Here ϵ is the fraction of the crotonic acid hydrated at equilibrium, x is the fraction hydrated at the time t, and K is the equilibrium constant. When the correct value of ϵ is chosen, a straight line results in a plot of $\log_{10}\epsilon/(\epsilon - x)$ against time. An example of this calculation is given in Table I, the data of which are plotted in Fig. 3. In order

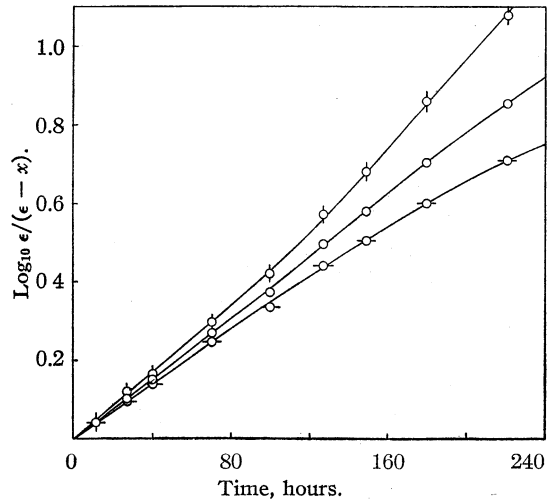


Fig. 3.—Effect of variation of ϵ on $\log_{10}\epsilon/(\epsilon - x)$ in the hydration of crotonic acid: initial crotonic acid, C_0, 0.01282 molal; T, 90.03°; (H^+), 1.060 molal; μ, 2.06 molal: ○, ϵ = 0.775; ○, ϵ = 0.834; -○-, ϵ = 0.892.

to show the effect of a variation of ϵ, the value was changed from the experimental value of 0.834 to 0.892 and 0.775. It can be seen that the experimental value produces a straight line but the variations induce marked curvature in the plots of $\log_{10}\epsilon/(\epsilon - x)$ against t. It will be noted that the values very close to equilibrium were discarded since very slight titration errors at these points in

TABLE I

EFFECT OF VARIATION OF ε ON $\text{LOG}_{10}\ \epsilon/(\epsilon - x)$ IN THE HYDRATION OF CROTONIC ACID AT 90.03°

$HClO_4$ = 1.060 molal; μ = 2.06 molal; initial crotonic acid = 0.01282 molal.

Time, hrs.	$1 - x$	ϵ = 0.834 $\log \frac{\epsilon}{\epsilon - x}$	ϵ = 0.892 $\log \frac{\epsilon}{\epsilon - x}$	ϵ = 0.775 $\log \frac{\epsilon}{\epsilon - x}$
0	1.000			
0.5	1.000			
1.1	0.995	0.003	0.003	0.003
1.6	.985	.008	.008	.0085
4.0	.970	.0155	.0145	.017
6.1	.955	.024	.022	.026
11.4	.917	.0445	.042	.048
27.1	.815	.1085	.101	.118
31.5	.795	.124	.115	.136
39.8	.756	.149	.138	.163
47.6	.714	.182	.168	.199
56.9	.665	.222	.204	.245
69.8	.616	.267	.244	.296
99.6	.520	.372	.335	.419
127.1	.482	.496	.439	.572
148.8	.385	.579	.506	.681
179.8	.331	.703	.601	.860
221	.282	.854	.708	1.079
340	.212			
389	.204			
468	.177			
677	.165			

the determination of the crotonic acid concentration would cause very appreciable errors in the value of $\log_{10} \epsilon/(\epsilon - x)$. In every case, the experimentally determined value for ε from the equilibrium constant gave an excellent straight line. The slope of this line is $(k_1 + k_2)/2.303$. The data of the several runs made are plotted in Figs. 4 and 5 as $\log_{10} \epsilon/(\epsilon - x)$ against time.

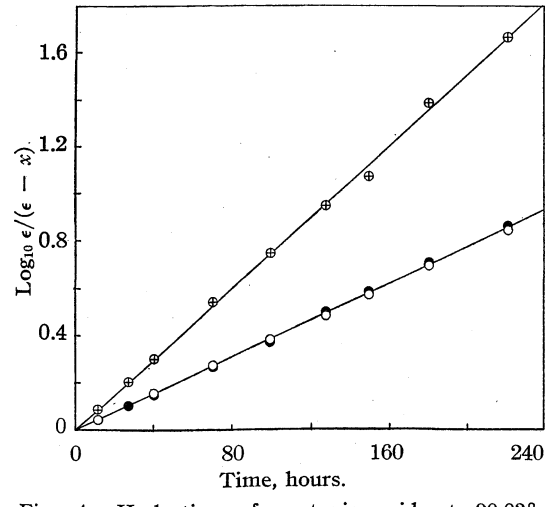


Fig. 4.—Hydration of crotonic acid at 90.03°. Plot of $\log_{10} \epsilon/(\epsilon - x)$ against time.

	●	○	⊕
μ, molal	2.06	2.06	2.06
(H^+), molal	1.060	1.060	2.056
C_0, molal	0.01282	0.02487	0.01248
	.835	.836	.829

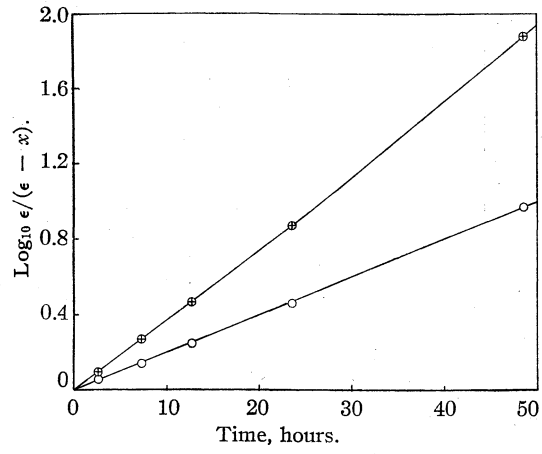


Fig. 5.—Hydration of crotonic acid at 111.31°. Plot of $\log_{10} \epsilon/(\epsilon - x)$ against time.

	○	⊕
μ, molal	2.06	2.06
(H^+), molal	1.060	2.056
C_0, molal	0.0186	0.0200
ε	.774	.760

As a test of the stability of the system at equilibrium one run was permitted to stand for three hundred and fourteen hours, whereas the system apparently had come to equilibrium after seventy-three hours. However, there was no observable shift in the equilibrium value of the system. These data are shown in Table II and plotted in Fig. 6.

TABLE II

STABILITY OF EQUILIBRIUM IN THE HYDRATION OF CROTONIC ACID

T = 111.3°; μ = 2.06 molal; $HClO_4$ = 2.06 molal; initial crotonic acid, C_0 = 0.0200 molal.

Time, hrs.	0	0.4	0.98	1.63	2.62	4.25
C_t/C_0	1	.983	.948	0.910	0.855	0.774
Time, hrs.		7.33	12.75	23.57	48.57	73.1
C_t/C_0		0.649	0.499	0.342	0.250	0.236
Time, hrs.		96.6	120.9	145.6	169.6	314.6
C_t/C_0		0.238	0.238	0.238	0.238	0.240

The calculation of the specific reaction rate constants for the dehydration of β-hydroxybutyric acid was carried out in a similar manner. In this case ε is the fraction of β-hydroxybutyric acid decomposed at equilibrium and x is the fraction decomposed at the time, t. A plot of $\log_{10} \epsilon/(\epsilon - x)$ against time for β-hydroxybutyric acid is found in Fig. 7. The specific reaction rate constants and

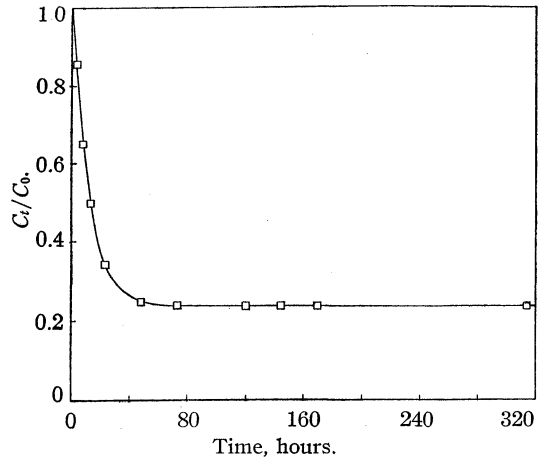


Fig. 6.—Stability of equilibrium between β-hydroxybutyric acid and crotonic acid when approached from crotonic acid. Plot of C_t/C_0 against time. Initial crotonic acid, C_0, 0.0200 molal; T, 111.31°; (H^+), 2.06 molal; μ, 2.06 molal.

the equilibrium constant determined in the dehydration run on β-hydroxybutyric acid are in excellent agreement with those obtained in the hydration of crotonic acid. This proves that a true equilibrium occurs since it can be approached from both sides.

The kinetic data obtained are listed in Table III. Experiments 1 to 5 deal with the hydration of crotonic acid while experiment 6 is concerned with the dehydration of β-hydroxybutyric acid. The specific reaction rate constants, k_1 and k_2, for the forward and reverse reactions are listed along with the constants which have been corrected for hydrogen ion concentration. The latter are listed as $k_1/(H^+)$ and $k_2(H^+)$. The constancy of these corrected values with acid concentration checks the observation that the reaction is first order with respect to hydrogen ion concentration.

The equilibrium constants, 5 at 90° and 3.4 at 111°, correspond to 84 and 78% hydration, respectively. These data substantiate the value of 80% hydration observed by Kaufel and Basel,[1] in boiling 20% sulfuric acid.

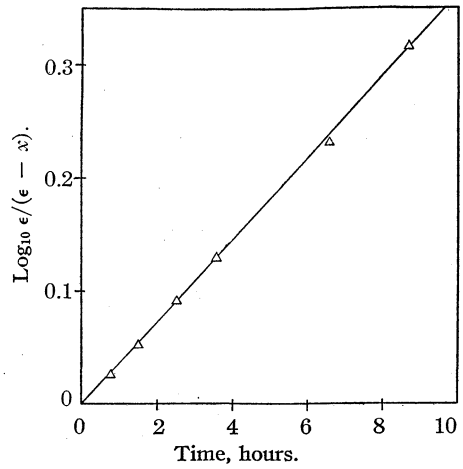


Fig. 7.—Dehydration of β-hydroxybutyric acid. Plot of $\log_{10} \epsilon/(\epsilon - x)$ against time. Initial β-hydroxybutyric acid, C_0, 0.0225; ϵ, 0.228; T, 111.31°; (H^+), 2.01 molal; μ, 2.01 molal.

Effect of Salt.—It is interesting to note that the equilibrium is shifted to the right when hydrogen ions are replaced by sodium ions. This shows that there is a relative increase in the activity coefficient of crotonic acid over the activity coefficient of β-hydroxybutyric acid when sodium ions replace hydrogen ions. This effect was also observed in the case of crotonaldehyde.[4] In Table IV a comparison is made of these effects in the two cases, crotonaldehyde and crotonic acid. It is evident that the equilibrium constant, at constant ionic strength, increases with decreasing hydrogen ion concentration.

TABLE III

KINETIC DATA CONCERNING THE HYDRATION OF CROTONIC ACID (1 TO 5) AND DEHYDRATION OF β-HYDROXYBUTYRIC ACID (6)

	Temp., °C.	(H^+)	(μ), M	Initial crotonic acid, M	$k_1 \times 10^2$	$k_2 \times 10^2$	$k_1/(H^+) \times 10^2$	$k_2/(H^+) \times 10^2$	K
1	90.03	1.06	2.06	0.01282	0.752	0.1485	0.710	0.140	5.05
2	90.03	1.06	2.06	.02487	.745	.1445	.703	.1365	5.14
3	90.03	2.06	2.06	.01248	1.43	.299	.696	.145	4.80
						Average	.703	.140	5.00
4	111.31	1.06	2.06	.01860	3.485	1.025	3.29	.97	3.41
5	111.31	2.06	2.06	.0200	6.765	2.135	3.28	1.03	3.16
						Average	3.29	1.00	3.28
6	111.31	2.01	2.01	.02249[a]	6.48	1.915	3.23	0.955	3.38

[a] Concentration of initial β-hydroxybutyric acid.

TABLE IV

EFFECT OF ACID CONCENTRATION AT CONSTANT IONIC STRENGTH ON THE EQUILIBRIUM CONSTANTS FOR THE HYDRATION OF CROTONALDEHYDE AND CROTONIC ACID

Crotonaldehyde $T = 25°$			Crotonic Acid $T = 90°$		
μ	(H^+)	K	μ	(H^+)	K
1.90	1.905	0.795	2.06	2.06	4.80
1.93	1.432	.816	2.06	1.06	5.10
1.96	0.956	.873		$T = 111.3°$	
1.98	.478	.930	2.06	2.06	3.16
			2.06	1.06	3.41

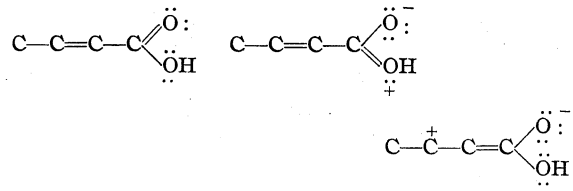
Thermochemistry of the Reaction.—Table V contains the thermal data for the reactions involved. The heat of the reaction, ΔH, the heats of activation, Q_1 and Q_2 of the forward and reverse reactions, and the temperature coefficients are listed individually for the runs in the solvents of different acid concentration. The values of k_1, k_2 and K for the two runs at 90.03° in 1.06 N perchloric acid were averaged in this calculation. This averaging accounts for the discrepancy between the difference in the heats of activation and the heat of the reaction, since the latter was calculated from the temperature coefficient of the averaged equilibrium constants and the former from the averaged values of the rate constants. The heat of activation of the forward reaction is smaller than that of the reverse reaction. Thus, there results a ΔH of -10.1 kcal. for the reaction. However, the heat of activation of 38.0 kcal. for the forward reaction is larger than any of those observed previously for unsaturated compounds, which were 23.4 kcal. for isobutene[5]; 21.04 kcal. for methylethylethylene[6]; 18.92 kcal. for trimethylethylene[7]; and 18.3 kcal. for crotonaldehyde.[4] The heat of activation for the reverse reaction is 48.1 kcal. for crotonic acid as compared with 24.5 kcal. for crotonaldehyde.

TABLE V

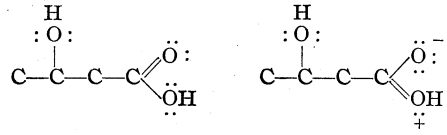
THERMAL DATA CONCERNING THE HYDRATION OF CROTONIC ACID

(H^+)	μ	Heats of activation Q_1, kcal.	Q_2, kcal.	ΔH, kcal.	Temp. coefficient 90–100° Hyd.	Dehyd.
1.06	2.06	37.85	47.85	− 9.8	4.08	5.94
2.06	2.06	38.15	48.4	−10.3	4.14	6.05
	Average	38.00	48.1	−10.1	4.11	6.00

The fact that the hydration of crotonic acid liberates 10 kcal. while the hydration of crotonaldehyde liberates only 6 kcal. indicates that β-hydroxybutyric acid is relatively more stable in aqueous solution with respect to crotonic acid than aldol is with respect to crotonaldehyde. Resonance explains the relatively lower stability of the aldol. Crotonic acid in the acid solution can resonate between the unexcited forms

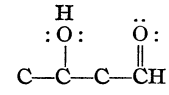


while β-hydroxybutyric acid resonates between the unexcited forms



On the other hand, crotonaldehyde can resonate between the unexcited forms

while the hydration product, aldol, can exist only in the single unexcited form



Thus, when crotonic acid hydrates it goes from a structure of principally three resonating forms to one of two, while crotonaldehyde loses nearly all of its resonance energy upon hydration. Hence, it would be expected that the evolution of energy during hydration would be less in the case of crotonaldehyde than in the case of crotonic acid, since each must retain energy equivalent to its loss of resonance energy and since the loss for the former is greater than for the latter. The difference in the heats of reaction, *viz.*, 4 kcal., is the difference in the resonance energy changes.

Ester Formation.—Gehrke and Willrath[8] have shown that β-hydroxybutyric acid loses water by itself to form a compound of lower free carboxyl content. This could be a linear ester, lactide or lactone since saponification of the compound of lower free carboxyl content liberates all these bound groups. In any case, it was stated that in a 0.1 molal solution of the hydroxy acid at 100° only 95.5% of the carboxyl groups are free. This would mean that 9% of the molecules are com-

(5) Eberz and Lucas, THIS JOURNAL, **56**, 1230 (1934).
(6) Lucas and Liu, *ibid.*, **56**, 2138 (1934).
(7) Liu and Wei, *J. Chinese Chem. Soc.*, **4**, 297 (1936).
(8) Gehrke and Willrath, *Z. physik. Chem.*, **A142**, 301 (1929).

bined as linear ester molecules or 4.5% are in the lactide or lactone form. Linear ester formation would be essentially negligible because of the high dilution, if it is assumed that in the pure acid, the extent of this reaction would be about 50%, as generally is the case in the formation of simple esters. At the concentration of 0.1 molal, esterification of this type would be only about 0.05%. Likewise, lactide formation and esterification of the β-hydroxy acid by crotonic acid would be negligible. However, lactone formation and lactone hydrolysis are essentially unimolecular reactions, and thus the equilibrium would not be affected by dilution. The formation of a four-membered ring as in the lactone would result in a low value of the lactone formation which may well be of the order of 5%.

Thus the equilibrium values as listed in Table III may be as much as 4.5% in error, due to the uncertainty of the β-hydroxybutyric acid concentration. However, in the important calculation, that of the heat of reaction, a ratio of equilibrium constants is taken and these errors occur then as second order corrections and are thus negligible.

Experimental

Materials. Crotonic Acid.—The crotonic acid used was the Eastman Kodak Co. product which had been recrystallized from water. It melted at 70.5–71.0° uncorr., and analysis for unsaturation showed 1.000 double bonds per mole.

β-Hydroxybutyric Acid.—This was prepared by the method of Kaufel and Basel[1] in which crotonic acid is hydrolyzed in the presence of boiling 20% sulfuric acid. The reaction mixture was neutralized to methyl orange with a freshly prepared paste of calcium hydroxide in order to remove sulfuric acid. The solution was filtered from the solid calcium sulfate and concentrated by vacuum distillation. This also removed most of the unconverted crotonic acid. A solid separated and was filtered. This was most likely a mixture of calcium sulfate and calcium β-hydroxybutyrate. The resulting sirup was extracted several times with ether to remove remaining crotonic acid. This was continued until the sirup indicated negligible unsaturation when analyzed by bromination. Upon standing in a vacuum desiccator over sulfuric acid, a precipitate of calcium hydroxybutyrate separated from the sirup. This was washed with alcohol and dried in a vacuum desiccator. An ash determination showed 15.9 and 16.0% calcium; calculated for calcium hydroxybutyrate 16.2% calcium. Since difficulties would occur in obtaining a known sample of the hydroxybutyric acid itself due to its self esterification and water loss, the calcium salt was used in its place since it could easily be weighed out quantitatively.

Perchloric Acid Solution of Constant Ionic Strength.—Equal portions of 60% perchloric acid were weighed out. To one was added enough sodium hydroxide to neutralize one-half of the acid. These portions were made up to equal volumes with distilled water. They were of equal ionic strength but unequal acidity.

Method of Analysis.—The solutions were analyzed by a quantitative bromination method. The solution to be analyzed was added to an excess of 0.05 normal bromate–bromide solution in an iodometric flask. If the solution to be analyzed did not contain a strong acid, 5 ml. of 6 *N* sulfuric acid was added at this time to liberate bromine. Potassium iodide solution was then added and the liberated iodine titrated with 0.02 *N* sodium thiosulfate solution. In the analysis of crotonic acid, it was found that a 50% excess of bromine gave theoretical bromination in five minutes while a 300% excess introduced an error of only 2% after one hour of standing. Experiments concerning the effect of bromine on hydroxybutyric acid showed that it substituted at the rate of 0.04%/minute when the mole ratio of bromine to β-hydroxybutyric acid was unity. Thus, the error incurred by the bromination of hydroxybutyric acid would be negligible under the conditions of analysis using a five-minute bromination period and a 50 or 100% excess of bromine.

Procedure of the Reaction.—Standard solutions of crotonic acid in perchloric acid were made up by roughly weighing the crotonic acid into an approximate volume of standard perchloric acid and then analyzing 20-ml. aliquots by bromination. The solutions of β-hydroxybutyric acid were made up gravimetrically by weighing out accurately a portion of calcium hydroxybutyrate and then making it up accurately to volume with perchloric acid solution. The runs were made by sealing off 20-ml. aliquots in test-tubes. These were placed in a thermostat at either 90.03° or 111.31 ± 0.05°. Tubes were withdrawn from time to time, quenched in water and the contents analyzed by bromination.

Summary

A study of the reversible hydration of crotonic acid to β-hydroxybutyric acid in 1.06 and 2.06 normal perchloric acid solutions of ionic strength 2.06 at temperatures of 90.03° and 111.31 ± 0.05° was made.

The hydration is first order with respect to crotonic acid and hydrogen ion. The dehydration is first order with respect to β-hydroxybutyric acid and hydrogen ion. The equilibrium is shown to be approachable from either the crotonic acid or the β-hydroxybutyric acid side. The equilibrium constant is 5.0 at 90° and 3.4 at 111°.

In solutions of constant ionic strength the equilibrium shifts toward crotonic acid with increasing acid concentration, thus showing that the replacement of sodium ion by hydrogen ion relatively increases the activity coefficient of β-hydroxybutyric acid over that of crotonic acid.

The energy of activation is 38.0 kcal. for the hydration and 48.1 kcal. for the dehydration.

The heat of the reaction is thus 10.1 kcal. The 4 kcal. greater heat of reaction than that which accompanies the hydration of crotonaldehyde is explained by a lower loss of resonance energy in the hydration of crotonic acid.

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[A CONTRIBUTION FROM THE YALE-IN-CHINA SCHOOL OF SCIENCE, HUA CHUNG COLLEGE]

The Reaction of Wijs Solution with Tung Oil

BY S. W. WAN AND D. B. HU

Tung oil contains mainly the glycerides of eleostearic acid and oleic acid and its drying power is due to the former unsaturated acid. In estimating the degree of unsaturation of tung oil with Wijs solution, the presence of eleostearic glyceride causes much uncertainty because the iodine value thus obtained varies with experimental conditions such as temperature, concentration and relative amount of reagent, and time of contact between reagent and oil.[1] Various methods have been tried for determining the percentage of eleostearic acid glyceride in tung oil, but have given no concordant results. Among the most recent methods may be mentioned the combined bromine vapor and Wijs method,[2] the differential halogen absorption method,[3] the polymerization method,[4] and the diene number method.[5] The peculiar properties of eleostearic acid giving rise to analytical difficulties have been explained by Böeseken and co-workers by assigning to it the molecular constitution $CH_3(CH_2)_3CH{=}CHCH{=}CHCH{=}CH(CH_2)_7COOH$,[6] which, in the light of Thiele's theory of partial valency, is expected to absorb halogens in two stages represented as

$$CH_3(CH_2)_3CH{=}CHCH{=}CHCH{=}CH(CH_2)_7COOH + 2X_2 \longrightarrow CH_3(CH_2)_3CHXCHXCH{=}CHCHXCHX(CH_2)_7COOH \quad (I)$$

$$CH_3(CH_2)_3CHXCHXCHXCHXCHXCHX(CH_2)_7COOH + X_2 \longrightarrow \quad (II)$$

With Wijs solution, X_2 being a molecule of iodine monochloride, the first stage reaction is much faster and produces a chloro compound.[6] On the other hand, compounds with non-conjugate double bonds take up the theoretical amount of iodine chloride in a short time, forming iodochloro compounds.

(1) Boughton, *Seventh Int. Congr. Appl. Chem.*, London (1909); Ho and co-workers, *Ind. Eng. Chem., Anal. Ed.*, **7**, 96 (1936).
(2) Toms, *Analyst*, **53**, 69 (1928).
(3) Croxford, *ibid.*, **54**, 445 (1929).
(4) Bolton and Williams, *ibid.*, **55**, 360 (1930).
(5) Kaufmann and Baltes, *Fette u. Seifen*, **43**, 93 (1936).
(6) Böeseken and Gelber, *Rec. trav. chim.*, **46**, 158 (1927); Böeseken, Hoogl, Broek and Smit, *ibid.*, **46**, 619 (1927).

This paper gives an account of the authors' attempt to apply the above-mentioned property of eleostearic acid to the determination of the concentration of its glyceride in tung oil, and an account of their investigation in the chemical kinetics of reaction (II).

Materials.—Glacial acetic acid, C. P., tested free from reducible substances. Iodine, C. P., twice resublimed. Sodium oxalate, C. P., giving an assay of 99.98%. Sodium thiosulfate, potassium iodide, carbon tetrachloride, oleic acid, potassium permanganate, all C. P. grade. Tung oil, supplied from the Chinese Vegetable Oil Corporation, Hankow. α-Eleostearic acid, prepared according to the method of Thomas and Thomson,[7] m. p. 48.3°. Wijs solution, prepared according to the procedure given by Griffin[8] with the important modification that the iodine and chlorine contents in the solution were adjusted to be exactly equivalent in amount.

The sodium thiosulfate solutions used in these experiments were standardized against potassium permanganate as a secondary standard and sodium oxalate as a primary standard.

Experimental

Part I.—Approximately equal weights of the carbon tetrachloride solution of a sample were placed in glass-stoppered conical flasks. To each was then added a weighed amount of Wijs solution and the mixture allowed to react for a definite length of time by shaking in a thermostat maintained at 25 ± 0.1°. All reagents also had been allowed previously to reach temperature equilibrium in the same thermostat. The reaction in each mixture was stopped promptly by adding 20 cc. of 15% potassium iodide solution and the reaction mixture was immediately diluted with water and titrated with sodium thiosulfate solution from a weighing buret. A number of runs were made by following the above procedure and using samples of: (a) pure α-eleostearic acid with a reaction period of five minutes; (b) pure α-eleostearic acid with a reaction period of two minutes; (c) pure α-eleostearic acid with a reaction period of ten minutes; (d) pure oleic acid with a reaction period of ten minutes; (e) a known mixture of α-eleostearic and oleic acids with a reaction period of five minutes; (f) tung oil with a reaction period of five minutes.

Part II.—α-Eleostearic acid was weighed into a 100-cc. volumetric flask and carbon tetrachloride was added, mak-

(7) Thomas and Thomson, THIS JOURNAL, **56**, 898 (1934).
(8) Griffin, "Technical Methods of Analysis," McGraw-Hill Book Co., Inc., New York, N. Y., p. 310.

ing up to volume at 25.0°. This solution was transferred into a glass-stoppered conical flask containing the Wijs solution previously set in the same thermostat maintained at 25.0 ± 0.1°. While beginning the delivery of the carbon tetrachloride solution of α-eleostearic acid two stopwatches were started simultaneously, one of them being stopped just when the delivery was completed, and the time of half delivery was taken as the starting point of the reaction. The flask containing the reaction mixture was well shaken at the start and also occasionally as the reaction went on. At definite intervals, 25-cc. portions of the reaction mixture were withdrawn with a pipet and each portion was delivered into one of a series of 120-cc. cork-stoppered conical flasks containing about 20 cc. of 15% potassium iodide solution. The duration for this delivery was noted and its half value was considered as the stopping point of the reaction. Each flask had been weighed with the potassium iodide solution in it and was again weighed after adding the reaction mixture. The exact volume of a portion of the mixture thus withdrawn was calculated from its weight and the density of the reaction mixture. (The densities of the eleostearic acid solution and that of Wijs solution were found to be additive.) The contents of the flask were transferred quickly and washed into a 300-cc. flask and titrated with sodium thiosulfate solution from a weighing buret. By following the above procedure the following investigations were performed: (g) reaction between α-eleostearic acid and Wijs solution in conventional proportions; (h) reaction between α-eleostearic acid and an equivalent amount of Wijs solution just sufficient for the first stage saturation; (i) reaction between α-eleostearic acid and an excess of Wijs solution; (j) comparison of halogen absorption by α-eleostearic acid and by tung oil.

Results

For experiments in part (I), solutions of α-eleostearic acid were of the concentration of about 0.015 millimole per gram of solution; solutions of oleic acid were of the concentration of about 0.022 millimole per gram of solution; the concentration of Wijs solution was 0.1450 millimole of iodine monochloride per gram of solution and 1 g. of the sodium thiosulfate solution was equivalent to 0.06295 millimole of halogen. All original data have been converted into millimoles of iodine monochloride used per millimole or gram of sample, and millimoles of halogen absorbed or left over per millimole or gram of sample, respectively; these results are given in Table I.

Results of Part II are given in Tables II to VI, where a is the molar concentration of α-eleostearic acid in the mixture or in other words the initial concentration of α-eleostearic acid tetrachloride at the beginning of the second stage reaction; b is the initial molar concentration of iodine monochloride at the beginning of the second stage; b' which is equal to $2a$ is the initial molar concentration of free iodine liberated during the first stage; B is the sum of b and b'; x' is the molar concentration of the iodochloride of α-eleostearic acid tetrachloride and x'', that of the di-iodide of α-eleostearic acid tetrachloride formed during time t of the reaction; x is the sum of x' and x''; k_1, k_1^*, k_2, k_2^*, and k_3 are specific reaction rates described in another section of this paper (see Discussion).

TABLE I[9]

RESULTS OF EXPERIMENTS

Run	Millimoles used: ICl per mmol. α-eleost. acid	Halogen abs. per mmol. acid
	Expt. (a)	
101	2.1306	1.0358
102	2.5400	1.2619
103	2.9461	1.4998
104	3.3753	1.7206
105	4.2076	2.0039
106	4.5855	2.0527
107	4.7605	2.1142
108	5.0209	2.1257
	Expt. (c)	
301	3.856	2.008
302	3.570	1.906
303	3.187	1.715
304	2.904	1.550
305	4.225	2.081
306	4.505	2.100
	Expt. (e)	
	ICl per g. acid mixt.	Halogen abs. per g. acid mixt.
501	11.002	5.970
502	11.318	6.116
503	11.743	6.292
504	12.168	6.415
505	12.544	6.601
506	13.505	6.799
507	12.956	6.808
508	13.830	6.844
509	14.231	6.888
510	14.696	6.904
511	13.078	6.683

Actual compn. of mixt.:
α-Eleostearic acid, 84.57%
Oleic acid, 15.43%
Calcd. compn. of mixt.:
α-Eleostearic acid, 84.51%
Oleic acid, 17.77%

Run	Millimoles used: ICl per mmol. α-eleost. acid	Halogen abs. per mmol. acid
	Expt. (b)	
201	1.8173	0.9442
202	2.2790	1.1369
203	2.5285	1.2198
204	3.5789	1.6671
205	3.9596	1.8128
206	5.0272	2.0480
207	5.4495	2.0652
208	5.9313	2.0889
209	6.4945	2.0940
	Expt. (d)	
	ICl per mmol. oleic acid	Halogen left per mmol. acid
401	1.1358	0.1393
402	1.2372	.2208
403	1.3688	.3546
404	1.4672	.4522
405	1.5893	.5699
406	1.8165	.8001
407	2.0182	1.0000
408	2.2607	1.2370
	Expt. (f)	
	ICl per g. tung oil	Halogen abs. per g. of oil
601	8.962	5.052
602	9.290	5.239
603	9.558	5.397
604	9.936	5.610
605	10.216	5.751
606	10.546	5.925
607	10.886	5.994
608	11.161	6.186
609	11.582	6.353
610	11.958	6.461
611	12.262	6.537
612	9.352	5.351
613	11.445	6.344
614	12.533	6.583

Calcd. % α-eleostearic acid glyceride, 72.2.

(9) These data were obtained with the assistance of Miss K. L. Lu, while working on her undergraduate thesis in this College during 1937–1938.

TABLE II

RESULTS OF EXPERIMENT (g)

Original concentration of ICl, 0.07072 M; a, 0.007953 M; b, 0.038908 M; initial halogen concentration for second stage, $2a + b = 0.05481$ M.

t, minutes	Halogen concn.	x	k_1	k_1^*
30.7	0.05270	0.00211	0.211	89.2
68.5	.05198	.00283	.172	27.3
90.6	.05178	.00303	.142	26.5
125.5	.05161	.00320	.111	24.7
157.0	.05150	.00331	.0925	19.9
189.3	.05132	.00349	.0827	16.9
262.9	.05118	.00363	.0632	12.4

TABLE III

RESULTS OF EXPERIMENT (h)

Original concentration of ICl, 0.067891 M; a, 0.016972 M; b', 0.033944 M.

t, minutes	Concn. of I_2	x''	Log $\frac{(b'-x)}{(a-x)}$	$K_3 \times 10^3$
23.95	0.033807	0.000137	0.3028	9.99
47.45	.033679	.000265	.3045	9.81
80.45	.033546	.000398	.3062	8.74
117.5	.033365	.000579	.3086	8.78
160.2	.033260	.000684	.3101	7.64
204.8	.033035	.000909	.3132	8.03
351.3	.032604	.001340	.3198	7.23
466.0	.032371	.001573	.3227	6.18

Calculated log $b'/a = 0.3010$.

Extrapolated log $b'/a = 0.3022$.

TABLE IV

RESULTS OF EXPERIMENT (i)

Original concentration of ICl, 0.11960; a, 0.005303 M; b, 0.098390 M.

t, minutes	Halogen concn.	x'	Log $\frac{(b-x)}{(a-x)}$	$k_2 \times 10^2$	$k_2^* \times 10^2$
50.1	0.10742	0.00156	1.413	7.13	6.42
78.3	.10712	.00186	1.448	5.69	1.52
105.6	.10694	.00205	1.471	4.76	1.66
142.1	.10667	.00231	1.493	3.92	1.62
186.2	.10674	.00224	1.497	3.04	1.00
230.1	.10658	.00240	1.520	2.71	1.29
269.1	.10653	.00245	1.527	2.38	1.17
329.7	.10608	.00290	1.600	2.49	1.50
377.1	.10597	.00301	1.620	2.31	1.44
512.6	.10585	.00313	1.642	1.81	1.17
632.1	.10549	.00349	1.724	1.79	1.27

Calculated log $b/a = 1.268$.

Extrapolated log $b/a = 1.400$.

TABLE V

RESULTS OF EXPERIMENT (g)

Showing the relation between t and log $(B - x)/(a - x)$, where $B = b + b' = 0.038908 + 0.015906 = 0.054814$.

t, minutes	Log $(B - x)/(a - x)$
30.7	0.9554
68.5	1.007
90.6	1.021
125.5	1.037
157.0	1.045
189.3	1.060
262.9	1.075

TABLE VI

RESULTS OF EXPERIMENT (j)

Weight of tung oil sample, 1.7286 g.; original concentration of ICl, 0.07775 M.

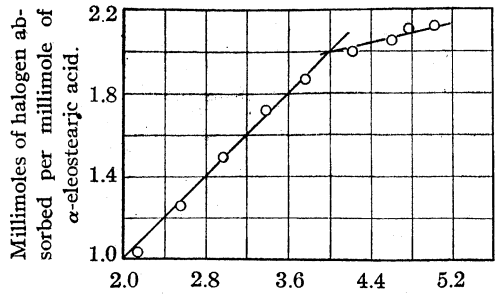
t, minutes	Halogen concn.
16.0	0.04647
37.3	.04606
85.0	.04553
138.3	.04528
187.8	.04503
235.2	.04470
353.0	.04429
450.0	.04414

Discussion

The interpretation of the results from the experiments of part (I) is based on the following consideration. When x, representing the number of millimoles of iodine monochloride added to one millimole of acid, is plotted against y, the number of millimoles of halogen absorbed, then in the case of α-eleostearic acid, a linear relation, $y = x/2$, will be obtained until the point, $y = 2$, $x = 4$, is reached, because this acid absorbs chlorine and not iodine in the first stage reaction, each millimole of acid requiring two of chlorine obtainable from four of iodine monochloride. Beyond this point the plot will become a horizontal straight line, $y = 2$.

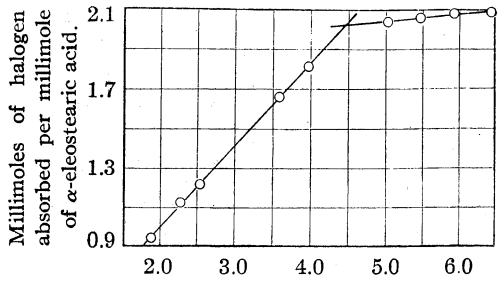
However, the above relation is valid only when the reaction period is long enough for completing the first stage absorption but not too long lest the second stage reaction become appreciable. If the second stage reaction takes place to an appreciable extent along with the first stage reaction, the plot will not be linear; if the reaction period is too short for the first stage saturation, the first part of the plot will have a slope less than $^1/_2$; and if the reaction period is too long for the first stage saturation, the first part of the plot will have a slope greater than $^1/_2$. Furthermore, if the second stage reaction can be detected in the presence of excess iodine monochloride, the second part of the plot will not be horizontal and not necessarily linear. These phenomena are clearly illustrated by Figs. 1, 2 and 3, in which are plotted the results of experiments (a), (b) and (c).

The results obtained from the reaction of oleic acid and iodine monochloride when treated in the same manner give a decisive answer to the question whether oleic acid absorbs chlorine alone or a whole molecule of iodine monochloride. Since oleic acid contains one double bond, the plot, in the former case, will be $y = {}^1/_2x$ up to $x = 2$,



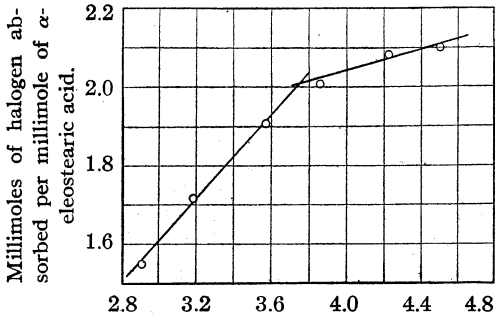
Millimoles of iodine chloride per millimole of α-eleostearic acid.

Fig. 1.



Millimoles of iodine chloride per millimole of α-eleostearic acid.

Fig. 2.



Millimoles of iodine chloride per millimole of α-eleostearic acid.

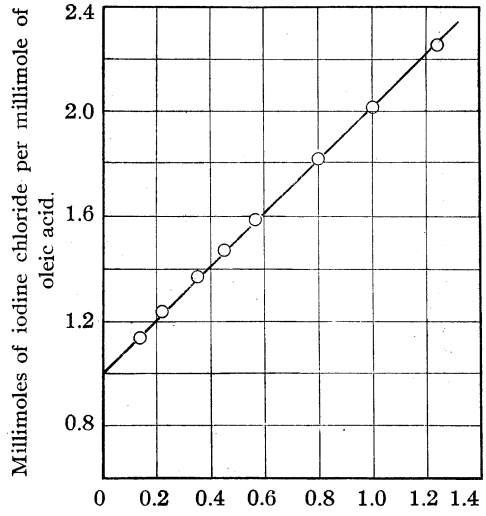
Fig. 3.

$y = 1$, and become $y = 1$ beyond that, while in the latter case it will be simply $y = x$ up to $x = 1$, $y = 1$ and then become $y = 1$ beyond that. On the other hand, if u represents the millimoles of iodine monochloride added to one of acid, and v, the millimoles of halogen left over, the plot will be $u = 2v$ up to $u = 2$ and $v = 1$, and become $u = v$ further on, in the former case; in the latter case, $u = v + 1$ throughout. The intercept of 1 on the u-axis is clearly brought out in Fig. 4.

With a mixture of the two acids, the results have been plotted on the basis of x millimoles of iodine monochloride added per gram of sample against y millimoles of halogen absorbed. Let r and s be the weight fractions; m_e and m_o, the millimolecular weights of α-eleostearic acid and oleic acid, respectively; p, the point at which just enough iodine monochloride has been used to satisfy both the oleic acid and the eleostearic acid first stage saturation. From the knowledge gained in these experiments concerning the behavior of iodine monochloride toward the two acids, it is evident that

$$x_p = 4\frac{r}{m_e} + \frac{s}{m_o} \quad \text{and} \quad y_p = 2\frac{r}{m_e} + \frac{s}{m_o}$$

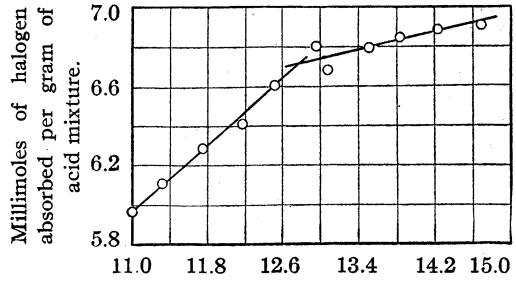
Hence r and s can be solved for simultaneously from the above equations.



Millimoles of halogen left per millimole of oleic acid.

Fig. 4.

In our analysis of a known mixture by this method, there has been good agreement between the actual and the calculated values for α-eleostearic acid (see Fig. 5). Only one determination



Millimoles of iodine chloride per gram of acid mixture.

Fig. 5.

has been made with tung oil (see Fig. 6) but further investigation is in progress because on the

whole the method thus developed seems very promising.

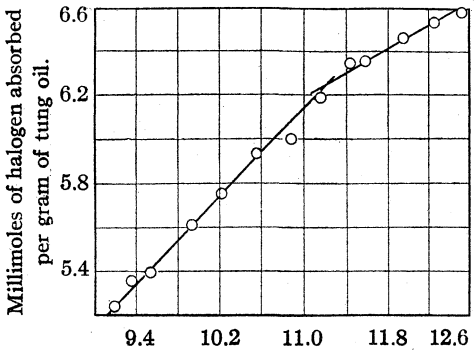


Fig. 6.

The data of experimental part (II) are the first of the kind making possible a study of the chemical kinetics for the reaction between α-eleostearic acid and iodine monochloride. For this reaction Böeseken[6] has proposed the scheme

$$CH_3(CH_2)_3CH{=}CHCH{=}CHCH{=}CH(CH_2)_7COOH + 4\ ICl \longrightarrow CH_3(CH_2)_3CHClCHClCH{=}CHCHClCHCl\text{-}(CH_2)_7COOH + 2I_2 \xrightarrow{+\ ICl} CH(CH_2)_3CHClCHClCHI\text{-}CHClCHClCHCl(CH_2)_7COOH \quad (III)$$

The second stage reaction according to the above scheme is bimolecular and therefore its reaction rate k_1 can be expressed by the second order relation

$$k_1 = 1/t(a - b) \ln b(a - x)/a(b - x) \quad (IV)$$

However, if the absorption involves the addition of chlorine or iodine (from iodine monochloride), instead of iodine monochloride itself, the specific reaction rate k_1^* of a third order reaction would be obtained from the equations

$$dx/dt = k_1^*(a - x)(b - 2x)^2 \quad (V)$$

and

$$k_1^* = 1/t(b - 2a)\{1/(b - 2a) \ln a(b - 2x)/b(a - x) - 1/(b - 2x) + 1/b\} \quad (VI)$$

There is still another possibility, namely, the absorption of iodine (liberated in the first stage) and iodine monochloride simultaneously in the second stage. In this case, the reaction rate would be governed by the relation

$$dx/dt = k_2(a - x)(b - x') - k_3(a - x)(b' - x'') \quad (VII)$$

The integration of equation (VII) would be a laborious process but as a first approximation the calculation may be simplified by either one of the following conditions. (1) The iodine monochloride concentration is just sufficient to complete the first stage absorption, so that $b = 0$ and $x' = 0$ and equation (VII) reduces to

$$dx/dt = k_3(a - x)(b' - x'') = k_3(a - x)(b' - x) \quad (VIII)$$

and

$$k_3 = 1/t(b' - a) \ln a(b' - x)/b'(a - x) \quad (IX)$$

(2) When excess of iodine monochloride is used, the relatively small amount of iodine liberated in the first stage may be disregarded so that equation (VII) becomes

$$dx/dt = k_2(a - x)(b - x') = k_2(a - x)(b - x) \quad (X)$$

and

$$k_2 = 1/t(b - a) \ln a(b - x)/b(a - x) \quad (XI)$$

The fact that values of k_1 and k_1^* given in Table II fail to correlate with equations (IV) and (VI), respectively, indicates that the mechanism suggested by Böeseken for the second stage reaction between iodine monochloride and α-eleostearic acid is incorrect, and that it is neither bimolecular nor trimolecular but most probably a combination of two simultaneous bimolecular reactions, one between the acid and the iodine liberated in the first stage and the other between the acid and iodine monochloride. This statement is supported by the data given in Table III and Table IV and plotted in Fig. 7 and Fig. 8 to show the linear relation between t and ln $(b' - x)/(a - x)$ and between t and ln $(b - x)/(a - x)$, respectively. It should be noted that when the

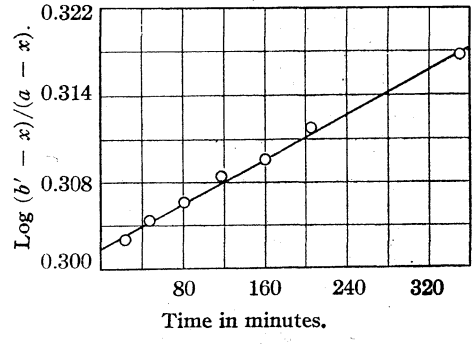


Fig. 7.

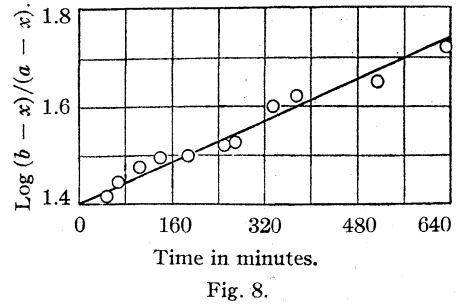


Fig. 8.

above plots are extrapolated to zero time, the values of ln (b/a) and ln (b'/a) are higher than the corresponding computed values. This may be accounted for by the presence of the beta form of eleostearic acid produced from the alpha acid on standing, the beta acid having a lower halogen-absorption rate.[10] Furthermore, the prompt stopping of a reaction in these experiments was done through adding to the reaction mixture, an excess of potassium iodide solution which might react with the iodo-chloride of α-eleostearic acid addition product forming a di-iodide which in turn might liberate iodine and restore the last-saturated double bond.[6]

The specific reaction rates k_2 and k_3 of the above-mentioned simultaneous bimolecular reactions are both small and of the same order of magnitude. If they could be assumed equal, equation (VII) would become

$$\begin{aligned} dx/dt &= k_4(a - x)(b + b') - (x' + x'') \\ &= k_4(a - x)(B - x) \end{aligned} \qquad \text{(XII)}$$

which is equivalent to a second order equation. As a matter of fact, a linear relation is obtained between t and log $(B - x)/(a - x)$ as shown in Fig. 9, which apparently confirms the contention made previously on the absorption of halogen by α-eleostearic acid in Wijs solution that the mechanism of the reaction is bimolecular.

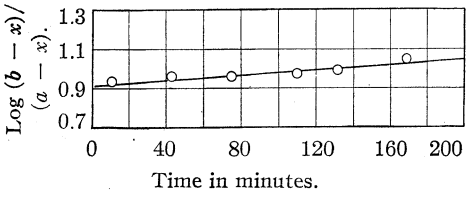


Fig. 9.

The similarity of the two curves in Fig. 10 serves to indicate that the reaction of halogen in Wijs solution with tung oil is much of the same nature as that with α-eleostearic acid. This property also has been applied in experimental part (I).

The increase of iodine value of the oil with increase of temperature or time of contact with Wijs solution can be explained easily in the light of what has been found from these experiments. The absorption of chlorine from iodine monochloride in the first stage explains the requirement of a minimum excess of Wijs solution for obtaining a normal iodine value.[1] The slight decrease of iodine value with increased amount of oil when the same amount of Wijs solution is used[11] may be accounted for by the fact that a relatively larger amount of α-eleostearic acid glyceride absorbs a correspondingly larger amount of iodine monochloride in the first stage and leaves a smaller excess of halogen which because of the kinetic relations mentioned above decreases the rate of halogen absorption in the second stage.

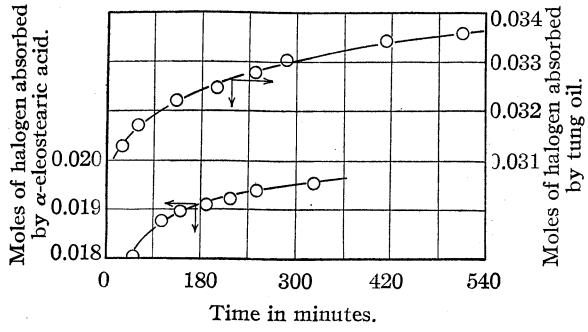


Fig. 10.

Finally, attention should be called to the fact that although experiment (i) was aimed at using a large excess of iodine monochloride relative to α-eleostearic acid so that b' and x'' might become insignificant compared with b and x', yet practical limitations made it possible to realize only a ratio of about 10 to 1 between b and b'. This ratio may not justify the process of simplifying equation (VII) to equation (X). Most probably errors have been introduced into the values of k_2 by this simplifying process which makes it necessary to use an extrapolated value for log (b/a) in order to obtain a fairly constant k_2^*. A more direct and accurate determination of both k_2 and k_3 is highly desirable. The authors are making this investigation.

Summary

1. The behavior of Wijs solution toward α-eleostearic acid, oleic acid and a mixture of the two acids has been studied by varying the proportion of Wijs solution to acid and the time of contact.

2. The two-stage halogen absorption from Wijs solution by α-eleostearic acid forming a tetrachloro addition product in the first stage, and the addition of iodine monochloride to oleic acid have been quantitatively established.

3. The difference in halogen absorption between α-eleostearic acid and oleic acid has been applied to the analysis of a mixture of the two acids and to the analysis of α-eleostearic acid

(10) Van Loon, *Chem. Umschau, Fette, Oele, Wachse, Harze*, **37**, 269 (1930).

(11) *Chemistry* (China), **1**, 1 (1934).

glyceride in tung oil, further work being carried on for developing the latter analysis into a reliable method.

4. The chemical kinetics for the absorption of halogen from Wijs solution by α-eleostearic acid has been studied and two specific reaction rates have been determined.

5. Böeseken's assumption of a bimolecular reaction for the second stage halogen absorption by α-eleostearic acid from Wijs solution has been found incorrect. A combination of two simultaneous bimolecular reactions has been suggested

$$CH_3(CH_2)_3CHClCHClCH{=}CHCHClCHCl(CH_2)_7COOH$$

$$\xrightarrow{+ICl} CH_3(CH_2)_3CHClCHClCHICHClCHClCHCl(CH_2)_7COOH$$

$$\xrightarrow{+I_2} CH_3(CH_2)_3CHClCHClCHICHICHClCHCl(CH_2)_7COOH$$

6. The variation of the iodine value of tung oil with temperature, excess of reagent and time of contact with reagent has been explained.

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[A CONTRIBUTION FROM THE YALE IN CHINA SCHOOL OF SCIENCE, HUA CHUNG COLLEGE]

Physicochemical Studies of Alpha and Beta Eleostearic Acids. I. Molar Refractivity and Parachor

BY S. W. WAN AND M. C. CHEN

Alpha and beta eleostearic acids were names suggested by Maquenne[1] for the isomeric eleomargaric and eleostearic acids so named and first isolated from the oil of *Eleococca Vernicia* by Cloez.[2] Tung oil is mainly a triglyceride of the alpha acid, and because of its special properties which make tung oil a highly important and useful material, a large amount of data has been accumulated. However, there were differences in opinion concerning its constitution[3] until Böeseken and co-workers[4] suggested the formula, $CH_3(CH_2)_3CH{=}CHCH{=}CHCH{=}CH(CH_2)_7COOH$ which has correlated many important phenomena not satisfactorily explained before. Although experimental findings from different sources have not entirely converged toward a common conclusion, most investigations seem to confirm this constitution.

One of the arguments put forth by Böeseken and co-workers[4] for suggesting the above formula was based upon the molar refractivity of the eleostearic acids. Melting points of 47 and 67° were given, respectively, for the specimens of alpha and beta isomers prepared for their experiments. Since then the method of preparation has been much improved. The authors have followed the method of Thomas and Thomson[5] with increased repetition of recrystallization, and have obtained from a large batch of original crystals a small crop of highly purified product with melting points higher than the previously reported values. A series of physicochemical determinations is being made with the highly purified alpha and beta eleostearic acids thus obtained.

Experiments and Data.—Alpha and beta eleostearic acids were prepared from their corresponding glycerides in tung oil, the beta-glyceride being formed when tung oil was allowed to stand in contact with a trace of sulfur. Density, surface tension and index of refraction of the alpha and beta acids were determined, respectively, at 50 ± 0.01° and 75 ± 0.01°. The surface tension of each was measured by the capillary rise method and the index of refraction by the use of an Abbe refractometer. The following data were obtained.

TABLE I

Acid	α-Eleostearic	β-Eleostearic
Melting point, °C.	49.0–49.2	71.5–72.0
Density	0.9028 at 50°	0.8909 at 75°
Surface tension	33.42 at 50°	31.04 at 75°
Refractive index	1.5112 at 50°	1.5022 at 75°

Results and Discussion

From the above data the parachor, P, and molar refractivity, R, of the eleostearic acids were calculated and are given in Tables II and III. P' and R' in the tables are, respectively, the theoreti-

(1) Maquenne, *Compt. rend.*, **135**, 696 (1902).

(2) Cloez, *ibid.*, **81**, 469 (1875); **82**, 501 (1876); **83**, 943 (1877).

(3) Kametaka, *J. Chem. Soc.*, **83T**, 104 (1903); Mania, *Chem. Inst., Univ. Kiel. Ber.*, **42**, 674 (1909); Vercruysse, *Bull. soc. chim. Belg.*, **32**, 151 (1923); Nicolet, THIS JOURNAL, **43**, 938 (1921); Ishio, *J. Pharm. Soc., Japan*, **529**, 228 (1926); Eibner, Merz and Munzert, *Chem. Umschau*, **31**, 69 (1924).

(4) Böeseken and Ravenswaay, *Rec. trav. chim.*, **44**, 241 (1925); *Verslag. Akad. Wetenschappen, Amsterdam*, **34**, 204 (1925); Böeseken and Gelber, *Rec. trav. chim.*, **46**, 158 (1927); Böeseken, Hoogl, Broek and Smit, *ibid.*, **46**, 619 (1927).

(5) Thomas and Thomson, THIS JOURNAL, **56**, 898 (1934).

cal parachor, and the theoretical molar refractivity less exaltation due to conjugation of double bonds between carbon atoms. In calculating the theoretical values, Böeseken's formula for eleostearic acid and the data compiled by Sugden[6] and Smyth,[7] respectively, for parachor and molar refractivity were adopted. In Table III are also given for comparison the data of Böeseken and Ravenswaay, those of Ishio, and those of Toyama and Tsuchiyu for punicic and trichosanic acids, considered as stereoisomers of eleostearic acid.

TABLE II

Acid	P	P'	Diff.
α-Eleostearic	741.0	709.0	32.0
β-Eleostearic	736.9	709.0	27.0

TABLE III

R for α-eleostearic acid	92.36
R for β-eleostearic acid	92.20
R' for above acids	85.47
Böeseken's R for α-acid	93.05
Ishio's value for α-acid	98.62
R for punicic acid	92.4
R for trichosanic acid	92.4

An explanation is desirable for the difference between P and P' since it cannot be accounted for by the conjugation of double bonds which, although having a large influence upon many other physical constants, shows no measurable effect on parachor. Interpretation of these results has to be postponed until further investigation in this Laboratory throws more light on the nature and amount of exaltation in molar refractivity due to conjugated double bonds in general. Nevertheless, the technique of the present procedure has been tested with a sample of purified oleic acid giving the results in Table IV.

TABLE IV

	Molar refractivity of oleic acid	Parachor of oleic acid
Observed value	86.6	731.4
Calculated value	86.4	731.0

Maleic anhydride was suggested by Kaufmann and Baltes[8] for detection and determination of conjugated double bonds in fats and oils. However, it does not seem satisfactory in distinguishing between the presence of two and of three conjugated double bonds. Incidentally, it may be pointed out that the reaction products between maleic anhydride and the alpha and beta eleostearic acids reported by Kaufmann and Baltes were, respectively, the reverse of those reported by Morrel and Samuels[9] and Morrel.[10] As a rule, it is very difficult to obtain clear-cut results from eleostearic acid by chemical methods alone.

Summary

Highly purified specimens of alpha and beta eleostearic acids having melting points higher than previously reported values were prepared, and their molar refractivity and parachor were determined accurately. The molar refractivity of the alpha acid was compared with data from other sources. For the molar refractivity and parachor of the beta acid and the parachor of the alpha acid, no previous data were available. Other physicochemical measurements are being made with both eleostearic acids.

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(6) Sugden, "The Parachor and Valency," Routledge, London, 1930.

(7) Smyth, "Dielectric Constant and Molecular Structure," Reinhold Publishing Corp., New York, N. Y., 1931.

(8) Kaufmann and Baltes, *Fette Seifen*, **43**, 93 (1936).

(9) Morrel and Samuels, *J. Chem. Soc.*, 2251 (1932).

(10) Morrel, *Chemistry & Industry*, **56**, 795 (1937).

On the Properties of Dipicrylaminates

BY JACOB KIELLAND

Very little has been published about the chemical and physical properties of dipicrylaminates, though dipicrylamine (2,4,6-hexanitrodiphenylamine) has been known as an explosive for many years, and its sodium or ammonium salt ("Aurantia") has been used on account of its dyeing properties, and as a light filter in photography.

Recently, dipicrylamine has been shown to be of importance for the quantitative determination of potassium[1]; consequently, these compounds and their properties are of some interest. Further, it has been shown by the author that specific attraction forces, of interest for the theory of strong electrolytes, occur even in very dilute solutions of dipicrylaminates. Hence, he feels justified in presenting some measurements recently made.

Purification of Material.—The hexanitrodiphenylamine (made by Skaanska Bomullskrutsaktiebolaget) was dissolved by the equivalent amount of alkali to give an aqueous solution (at about 50°) containing 15 to 20% dipicrylaminate. After filtration, a crude mass of sodium dipicrylaminate was salted out by the addition of an equal volume with concentrated (50°) aqueous sodium nitrate. In order to remove any impurities still present, the red crystalline mass was then treated three times with an excess of 65–70% nitric acid, leaving a yellow crystalline mass of dipicrylamine.[2] The washed crystals (solubility product about 10^{-10}, according to Kielland[1]) were dissolved in alkali and salted out as described above, filtered and washed rapidly with a little chilled water. After recrystallizing twice from conductivity water, the brilliant red crystal mass finally was dried to constant weight in a desiccator at room temperature.

Color

Solutions.—Dipicrylaminate solutions are strongly colored, yellow at high dilutions, and orange to red at intermediate and high concentrations. The solvent effect is of minor importance, as was found from preliminary absorption measurements, carried out with a Zeiss Stufenphotometer.

The molecular extinction coefficient at 463 mμ was in all cases about 2.2×10^4, but the curves in acetone, etc., appeared a little steeper than in water. For dilute solutions in water, Bouguer–Beer's law was found approximately valid, but since the Stufenphotometer does not work with monochromatic light, one does not feel justified in presenting more extensive data.

In order to give an idea of the color of the aqueous solutions, in the "fundamental, universal color language,"[3] a chromatic analysis was carried out, on the basis of measured extinction curves at different concentrations. Hardy's method of ten selected ordinates[3] was applied, and the computation based upon ICI normal observer, ICI illuminant C and ICI primary stimuli. From Table I, the pronounced change in hue at about 10^{-4} N is easily seen; the color is typical orange between 10^{-4} and 10^{-3} N, red at higher, and yellow at lower concentrations. The very high excitation purity of all solutions above 10^{-4} N, together with the relatively high corresponding brightness figures, is of importance for the use of dipicrylaminates as light filters.

TABLE I

CHROMATIC ANALYSIS OF AQUEOUS SOLUTIONS OF DIPICRYLAMINATES

		(Concentration 10^6 × moles per liter) 0	5	10	20	40	60	100	200	500	1000
Dominant wave length, mμ		...	573.8	574.1	574.8	576.3	577.7	580.3	585	593	600
Relative brightness, %		100.0	96.3	93.5	88.7	81.0	75.5	67.5	54.0	38.4	28.3
Excitation purity, %		0	14	26	47	76	90	98	99.6	99.8	99.9
Trichromatic coefficients	red	0.310	0.332	0.352	0.389	0.446	0.478	0.511	0.549	0.595	0.628
	green	.316	.343	.368	.415	.468	.484	.482	.448	.403	.371
	violet	.374	.325	.280	.196	.086	.038	.007	.003	.002	.001

Solids.—The color of solid dipicrylamine is yellow to orange (according to purity and particle size), that of the solid dipicrylaminates red. Using the Zeiss Stufenphotometer with Kugel-reflector, some spectral reflection curves were measured, and the resulting chromatic analysis (Table II) may serve as an illustration (based on ICI illuminant C).

TABLE II

COLOR OF SOLIDS

		Commercial dipicrylamine, amorphous powder	Potassium dipicrylaminate crystals
Dominant wave length, mμ		587	650
Relative brightness, %		19	10
Excitation purity, %		47	22
Trichromatic coefficients	red	0.425	0.305
	green	.375	.415
	violet	.200	.280

(1) (a) Winkel and Maas, *Angew. Chem.*, **49**, 827 (1936); (b) Kielland, *Ber.*, **71**, 220 (1938); (c) Kolthoff and Dendix, *Ind. Eng. Chem., Anal. Ed.*, **11**, 94 (1939).

(2) Microscopic examination showed that the exchange of sodium by hydrogen proceeded fairly rapidly inward, the crystal shape apparently not being distorted.

(3) Hardy, "Handbook of Colorimetry," Technology Press, Boston, 1936.

Particle Size

Ultrafiltration.—Ultrafiltration analysis according to Ferry[4] was carried out with 10^{-3} N potassium dipicrylaminate in water at 20°. As filters were used Membran- and Ultrafeinfilter from Membranfiltergesellschaft in Göttingen, membranes of the Elford type made according to the directions given by Bauer and Hughes,[5] as well as cellophane, swollen in concentrated zinc chloride as suggested by McBain and Stuewer.[6] Normal filtration was effected in all experiments, with no blocking effects detectable. The maximum relative concentration[7] was 100% even at mean pore diameters of only 10 mμ, and very near to 100% at about 4 mμ. The end-point consequently was so low as to justify the conclusion that the dipicrylaminate did not appear in colloidal dispersion.

Dialysis.—The dialysis coefficient of the dipicrylaminate anion in 10^{-3} N aqueous solution was measured by a Cuprophane membrane at 18°, by the method of Brintzinger.[8] The solvent was in all cases 0.5 N sodium nitrate; concentrations were measured photometrically, and ferricyanide and thiosulfate were employed as reference substances.

The resulting ionic weight was found equal to the formula weight (438) ± 10%. Hence, in very dilute solutions, the dipicrylaminate anion probably carries no complex bound water in the sense described by Brintzinger,[9] nor is it associated or polymerized in such a manner as to affect the process of dialysis. In this connection perhaps it may be mentioned that Brintzinger and Schall[10] also found the theoretical molecular weight for most of the ionic dyes studied by them.

The precision of measurement, however, does not exclude the possibility that a small fraction of the anions may have been present as double ions.

Density and Molal Volume.—The densities $d^{18}{}_4$ of sodium dipicrylaminate solutions were measured at molalities from 0.01 to 0.13, using a pycnometer (volume about 30 ml.) of the Sprengel type, as modified by Riiber.[11] All solutions were made up by weight, and all weighings corrected to vacuum. Temperature was maintained with a precision of ±0.01°. The results are given in Table III.

TABLE III

MEASURED DENSITIES OF SODIUM DIPICRYLAMINATE SOLUTIONS

G. per 1000 g. of water	Molality	$d^{18}{}_4$
5.68	0.01232	1.00140
6.885	.01493	1.00198
13.66	.02963	1.00526
35.90	.0779	1.01582
60.45	.1311	1.02710

Since the work of Masson[12] it has been known that for most electrolytes the apparent molal volume of a solute is a linear function of $c^{1/2}$, and a convenient method of computation has been suggested by Gucker.[13] In the present case there results the equation

$$\Phi(V_2) = 235 + 3.0c^{1/2} \text{ ml. per mole} \qquad (1)$$

The densities of solutions obeying Masson's rule are found from

$$d = d_1 + c(M_2 - d_1\,\Phi^0)/1000 - c^{3/2}\,(d_1/1000)(\partial\Phi/\partial c^{1/2}) \qquad (2)$$

Hence, for sodium dipicrylaminate at 18°

$$d^{18}{}_4 = 0.99862 + 0.2263c - 0.0030c^{3/2} \qquad (3)$$

The densities at other temperatures may be calculated similarly, taking[14] the molal volume at 0 and 10° approximately 4 and 2.5 ml. lower than the figure at 18°.

Freezing Point Depression.—The freezing points of aqueous solutions of sodium dipicrylaminate at concentrations from 5×10^{-3} to 5×10^{-2} N were measured, using a platinum resistance thermometer[15] for calorimetric purposes, of the type described by Dickinson and Mueller,[16] and made by the Leeds and Northrup Company.

A differential method of measurement was used. The arrangement made it possible to detect temperature variations of about 1 to 2 × 10^{-4}°. Samples for analysis were taken with a chilled pipet immediately after the final readings, and the concentrations determined[17] by measuring the conductivity at 0°. The results are reported in Table IV.

TABLE IV

FREEZING POINT DEPRESSIONS OF SODIUM DIPICRYLAMINATE IN WATER

Concn., moles per liter c	Density $d^0{}_4$	Depression ϑ, °C.	Depression Per mole ϑ/m	Function j
0.00572	1.0012	0.0196	3.43	0.078
.00986	1.0022	.0325	3.30	.114
.01021	1.0022	.0333	3.27	.123
.01087	1.0023	.0347	3.18	.144
.01337	1.0029	.0415	3.09	.169
.01696	1.0037	.0510	3.00	.193
.02149	1.0048	.0620	2.88	.225
.02840	1.0063	.0780	2.74	.264
.02982	1.0067	.0783	2.62	.295
.03450	1.0077	.0900	2.60	.301
.03625	1.0082	.0919	2.52	.319
.03765	1.0084	.0948	2.50	.325
.05005	1.0113	.1138	2.25	.393

(4) Ferry, *Chem. Rev.*, **18**, 373 (1936).
(5) Bauer and Hughes, *J. Gen. Physiol.*, **18**, 143 (1935).
(6) McBain and Stuewer, *J. Phys. Chem.*, **40**, 1157 (1936).
(7) Optical analysis with Zeiss Stufenphotometer.
(8) Brintzinger, *Z. anorg. allgem. Chem.*, **232**, 415 (1937).
(9) Brintzinger and Osswald, *ibid.*, **225**, 312 (1935).
(10) Brintzinger and Schall, *ibid.*, **225**, 213 (1935).
(11) Riiber, *Z. Elektrochem.*, **29**, 334 (1923).
(12) Masson, *Phil. Mag.*, [7] **8**, 218 (1929); see also Gucker, *Chem. Rev.*, **13**, 111 (1933).
(13) Gucker, *J. Phys. Chem.*, **38**, 306 (1934).
(14) Compare the variation with temperature of $\overline{V}^\circ{}_2$ for other sodium salts, see La Mer and Gronwall, *J. Phys. Chem.*, **31**, 393 (1927).
(15) The writer is indebted to the Institute of Organic Chemistry, Trondheim, for the loan of thermometer with accessories.
(16) Dickinson and Mueller, *Bull. Bur. Standards*, **9**, 483 (1913).
(17) Compare Lange, *Z. physik. Chem.*, **168**, 169 (1934).

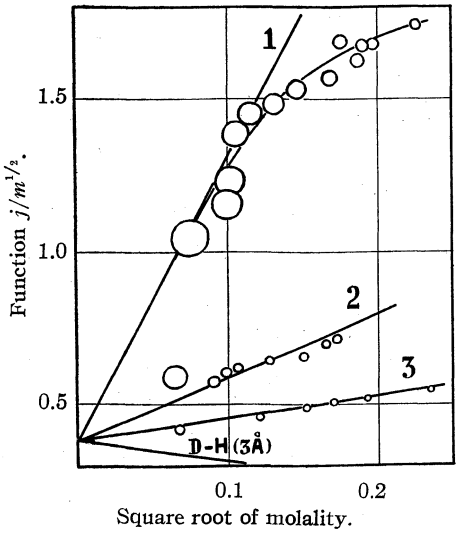


Fig. 1.—Freezing point measurements of sodium dipicrylaminate (1); picric acid (2); and sodium dinitrophenolate (3).

Activity Coefficients.—The activity coefficients of the solute at 0° were computed from plottings (Fig. 1) of $j/m^{1/2}$ against $m^{1/2}$, according to the method of Abel, Redlich and Lengyel[18]

$$-\log_{10}\gamma_{\pm} = (j + 2\int_0^{m^{1/2}} (j/m^{1/2})\, dm^{1/2})/2.303 \quad (4)$$

where j is the Lewis–Randall function $[1 - \vartheta/(3.718\ m)]$. The values at even molalities are given in Table V, and may be represented by the equation

$$-\log_{10}\gamma_{\pm} = 0.486\mu^{1/2}/(1 + \mu^{1/2}) + (9.0 - 50m)m \quad (5)$$

where μ denotes the ionic strength $\mu = {}^1/_2\Sigma m_i z_i^2$.

TABLE V

MEAN STOICHIOMETRIC ACTIVITY COEFFICIENTS OF SODIUM DIPICRYLAMINATE IN WATER AT 0°

Concn., moles per 1000 g. of water	Activity coefficient $\gamma_{\pm}$
0.001	0.947
.002	.916
.005	.840
.01	.739
.02	.602
.03	.509
.04	.440
.05	.387

In Fig. 2 are also plotted the activity coefficients at 0° for the related compounds sodium dinitrophenolate, sodium picrate and picric acid, calculated from the freezing points measured by Lange and Herre.[19] The dipicrylaminates obviously have such low activities that some strong association effects must be present. From pH measurements it is evident, however, that dipicrylamine is not a typical weak electrolyte. Thus, it is most probable that strong forces appear between the anions, a view which is confirmed by the measurements below.

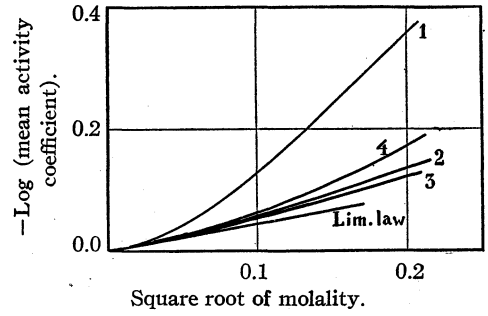


Fig. 2.—Activity coefficients at 0° for sodium dipicrylaminate (1); sodium picrate (2); sodium dinitrophenolate (3); and picric acid (4).

Equivalent Conductivity

Experimental.—Conductivity measurements were carried out in a 20-ml. cell of the pipet type designed by Washburn.[20] The cell constants were determined with the 0.1 and 0.01 D solutions of potassium chloride described by Parker and Parker.[21] The measurements were made with an improved Wheatstone bridge described by Jones and Josephs.[22] Measurements at 700 and 2000 cycles gave identical results within ±0.05%.

All solutions were made up by weight from purified (see above), dried sodium dipicrylaminate and doubly distilled "equilibrium" water.[23] Since the carbonic acid present may produce some colloidal dipicrylamine which may disturb the electrode functions and sound minima, a little sodium carbonate was usually added to the distilled water; the conductivity of the latter thus was increased from about 0.5 to 1.0 × 10^{-6} mhos, the proper correction of which was allowed for.

Results.—The conductance measurements were carried out at 0° with solutions of concentrations ranging from 10^{-3} to 10^{-1} N, and the results are presented in Table VI and in Fig. 3.

Up to concentrations about 0.03 N, the measurements may be given by the equation

$$1 - f_{\mu} = (0.219 + 29.5/\Lambda_0)c^{1/2} - Bc \quad (6)$$

(18) Abel, Redlich and Lengyel, *Z. physik. Chem.*, **132**, 189 (1928).

(19) Lange and Herre, *ibid.*, **181**, 329 (1938).

(20) Washburn, THIS JOURNAL, **38**, 2431 (1916).

(21) Parker and Parker, *ibid.*, **46**, 312 (1924).

(22) Jones and Josephs, *ibid.*, **50**, 1049 (1928). The writer wishes to thank Dr. L. Tronstad and K. Stokland at the Institute of Applied Inorganic Chemistry, Trondheim, for the loan of the generator as well as the cells.

(23) Kendall, *ibid.*, **38**, 2460 (1916).

TABLE VI

CONDUCTIVITY OF SODIUM DIPICRYLAMINATE IN WATER AT 0°

Concn. moles per liter	Density d^0_4	Conductivity $10^3 \times K$	Equiv. cond. Λ_c
0.00138	1.0002	0.0515	37.3
.00582	1.0012	.2120	36.45
.00667	1.0014	.2427	36.35
.00936	1.0020	.3370	36.0
.01480	1.0032	.527	35.6
.0211	1.0047	.744	35.3
.0294	1.0066	1.022	34.75
.0426	1.0096	1.450	34.0
.0475	1.0107	1.600	33.65
.0764	1.0173	2.458	32.15
.1177	1.0268	3.521	29.9

The coefficient $B = 2.5$ is probably larger than for any other uni-univalent electrolyte, the highest value reported being given by Lange and Herre[19] as $B = 1.7$ for sodium picrate.

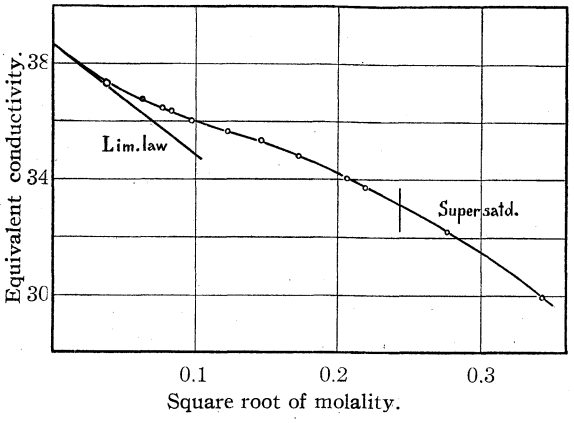


Fig. 3.—Equivalent conductivity of sodium dipicrylaminate in water at 0°.

The large conductivity of the dipicrylaminate at intermediate concentrations, together with the very low activity coefficients given above, must probably be interpreted as a pronounced association of anions, increasing with increasing concentration.

At about 0.025 N, however, we have an inflection point of the conductivity curve, perhaps caused by the interaction between associated anions and the cations.

Ion Mobilities.—The extrapolation to infinite dilution was made by the method of Shedlovsky.[24] The plotting of $\Lambda_0' = (\Lambda_c + 29.5c^{1/2})/(1 - 0.219c^{1/2})$ against c gave a straight line below $c = 0.025$, with the result $\Lambda_0 = 38.7$ for sodium dipicrylaminate. If 25.85 be taken[25] as Λ_0 for sodium ion at 0°, one obtains the limiting equivalent conductivity for the dipicrylaminate anion at 0° equal to 12.8, which is a fairly probable figure (compare the known figure for picrate anion, 15.2).

Mobility values at other temperatures may be computed from the empirical Johnston–Angel[26] formula

$$\Lambda_0(t) = \Lambda_0(t_1) \times [\varphi_t/\varphi t_1]^m \qquad (7)$$

where φ denotes the fluidity of water; $m = c/a$, where c equals the temperature coefficient of ion mobility, and a that of the fluidity of water. Since m represents the deviation from Stokes' law, a deviation which decreases with decreasing mobility and also with increasing size of the hydrated ions, we have from plottings of c against mobilities extrapolated to a probable figure $m = 0.98 \pm 0.01$ for the dipicrylaminate anion. Then we have

$$\Lambda_{0t} = 21.5\ [1 + 0.0251(t - 18) + 0.000125(t - 18)^2]^{0.98} \qquad (8)$$

Heat of Solution

The integral heat of solution of sodium dipicrylaminate in water was determined at 0.005 and 0.01 N, also the heat of dilution of a 0.125 N solution. The measurements were carried out at 20° in a Dewar vessel of 1.5-liter capacity, with 2- to 4-g. samples of sodium dipicrylaminate crystals. The temperature curves were taken with the platinum resistance thermometer described above. Calibration of the calorimeter was made with potassium chloride, the heat of solution of which was obtained from the tables of Bichowsky and Rossini.[27] The results are seen from Table VII (in the last column is shown the error caused by an uncertainty of 3×10^{-4} degree in the original temperature measurements).

TABLE VII

INTEGRAL HEAT OF SOLUTION OF SODIUM DIPICRYLAMINATE IN WATER

Concn., moles per liter	Heat of soln., kcal. per mole
0.005	−12.35 ± 0.06
.010	−12.32 ± 0.04
.125	−10.9 ± 0.1

The absorption of heat is seen to be fairly high, reaching about twice the figure for sodium picrate.

(24) Shedlovsky, THIS JOURNAL, **54**, 1405 (1932).

(25) Landolt–Börnstein–Roth, "Physikalisch-chemische Tabellen," 5 Aufl., III Erg. bd., Verlag von Julius Springer, Berlin, 1936, p. 2059.

(26) Angel, *Z. physik. Chem.*, **170**, 81 (1934).

(27) Bichowsky and Rossini, "The Thermochemistry of the Chemical Substances," Reinhold Publishing Corp., New York, N. Y., 1936.

Discussion.—The figures above indicate a relative partial molal heat content at 0.05 N equal to $\bar{L}_2 \doteq -0.8$ kcal., while the non-ideal free energy change is calculated to $\bar{F}_2 \doteq -0.5$ kcal. Hence,[28] we can conclude that in such solutions some molecule-molecule effect must be quite overwhelming. Taking into consideration also the results of the activity and conductance measurements, we see that, owing to strong van der Waals forces between the two large organic, polarizable anions, considerable association occurs between ions of equal sign, in spite of electrostatic repulsion. A more quantitative treatment of the degree of association will appear elsewhere.[29]

Phase Phenomena

The writer recently happened to make some interesting observations, a preliminary report of which might be mentioned here.

On mixing at room temperature perhaps 1 g. of sodium dipicrylaminate crystals with 10 ml. of a 1 N aqueous sodium chloride solution, part of the crystal mass is dissolved, while the remainder sinks to the bottom, still in the crystalline state. Making the same experiment with calcium chloride instead of sodium chloride, part of the crystals dissolve readily, but the remainder after some minutes will have changed into a *heavy, clear and red colored liquid.* Heating to 53° causes complete miscibility. On cooling below 52°, the dark colored liquid phase again separates as a turbidity which soon collects to larger drops, subsiding to the bottom. As an example may be mentioned that the separated liquid phase from one of the experiments had a specific gravity of 1.33 and contained about 45% of water, the rest being calcium dipicrylaminate together with some chloride.

Such systems, with definite temperatures of complete miscibility (the same result obtained by increasing as by decreasing the temperature), were also observed at other normalities of calcium chloride, as well as with different weights of dipicrylaminate added. The results of these preliminary experiments, carried out in sealed glass tubes of 1-ml. capacity, are given in Fig. 4.

(28) Scatchard, *Chem. Rev.*, **13**, 23 (1933).
(29) Kielland, to be published in *J. Chem. Education.*

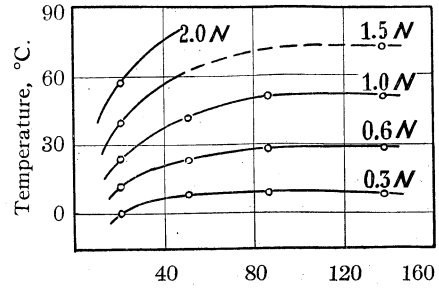


Fig. 4.—Curves of complete miscibility of dipicrylaminate in calcium chloride solutions of different normalities.

At present the writer is not able to give a satisfactory explanation of the astonishing distribution of the electrolyte dipicrylaminate on *two* aqueous solutions in equilibrium with each other, though it is in accordance with the phase rule. An extensive and thorough study of the problem seems very desirable, particularly because, on account of the strong specific forces observed in dilute solutions, interesting structural relationships are likely to occur in such concentrated solutions as obtained during the miscibility experiments.

Acknowledgments.—The writer wishes to acknowledge his indebtness to Norsk Hydro-Elektrisk Kvælstofaktieselskab, Oslo, to Norges Tekniske Höiskole (Chemistry Department), Trondheim, and to "Nansenfondet" for a grant.

Summary

1. A short color analysis of dipicrylaminates is given.

2. The molal volume of sodium dipicrylaminate in water has been determined, and density figures of aqueous solutions are reported.

3. Freezing point depressions and equivalent conductivities of sodium dipicrylaminate have been measured at 0°, also its heat of solution.

4. Strong association effects due to van der Waals forces have been found to exist between the dipicrylaminate anions even in dilute aqueous solutions.

5. An interesting case of partial miscibility has been discovered in mixtures of dipicrylaminates with aqueous calcium chloride solutions.

PORSGRUNN, NORWAY RECEIVED DECEMBER 10, 1938

[CONTRIBUTION FROM THE CHEMISTRY LABORATORIES OF NEW YORK UNIVERSITY]

The Rate of Dissolution of Iron in Acids

BY MORRIS B. ABRAMSON AND CECIL V. KING

Previous work in this Laboratory has indicated that a modified Nernst diffusion layer theory accounts, in large part at least, for the dissolution rates of magnesium and marble in acids, of zinc and cadmium in acids with certain depolarizers present, of copper in ferric salt solutions (but not in acids with depolarizers), of benzoic acid in dilute alkali and for the rate of heat transfer from solid to solution.[1] Other work on magnesium in aqueous solutions[2] can for the most part be interpreted on this basis, though in ethyl alcohol solutions the rate for magnesium seems to be partly diffusion, partly chemically, controlled.[3]

Van Name and his co-workers[4] have shown very clearly the conditions under which dissolution rates are controlled by diffusion rates or by chemical rates, and have studied cases believed to be of each type. They point out that if the chemical rate is very rapid compared to the physical transport rate, the reagent concentration falls to zero at the surface and a diffusion gradient equal to the full reagent concentration will be set up; if the chemical rate is very slow, no concentration gradient between the surface and the bulk of the solution will exist; and finally if chemical and physical transport rates are comparable in magnitude, a definite reagent concentration will exist at the solid surface, less than that in the bulk of the solution. The intermediate case where both the physical and chemical factors are operative has been treated theoretically by Roller.[5]

The general criteria of a diffusion-controlled rate are: (1) Various solids dissolve in the same reagent at the same rate. (2) In different reagents the rate is an exponential function of the diffusion coefficient.[1b] (3) The rate increases with stirring speed, the exact function depending on the type of stirring. (4) The rate follows the same function of the viscosity as the diffusion coefficient. (5) The temperature coefficient is in general less than 1.5 per 10°. If the chemical reaction is slow and controls the observed rate, then (1) the rate should be independent of stirring speed, viscosity and diffusion coefficient; and (2) the temperature coefficient should be, in general, greater than 2.0 per 10°.

Iron was chosen for the present investigation because it is less active than zinc, and its chemical reaction rate should be lower; also it was known that the metal dissolves faster in nitric acid than other dilute acids, indicating that nitrate acts as a depolarizer; and nitro compounds are reduced by iron and acid without hydrogen evolution. The disadvantages are that salts of weak acids hydrolyze and form insoluble films, and the dual valence leads to some complication, fortunately found not to be serious.

The dissolution rate of iron has not been measured previously with the present objectives in mind. The rate in more concentrated acid, with no depolarizer but with other metals as coupling agents, has been measured by Centnerszwer and Straumanis.[6]

Friend and Dennett[7] found that the rate of dissolution from a rotating iron disk, in dilute acid with no depolarizer, was linear with rotational speed up to 4000 r. p. m., and that the temperature coefficient was about 2 per 10°. Huber and Reid[8] also measured the effect of rotational speed with an iron disk, in 0.1 *N* sulfuric acid with no depolarizer, up to 11,360 r. p. m., and the rate of reduction of nitrobenzene in acid with the iron disk rotating up to 10,560 r. p. m.

Experimental.—Cylinders of the purest iron available commercially[9] of dimensions given in the figures, were rotated in 250 cc. of solution for all experiments at the lower speeds; at speeds above 6000 r. p. m. in 2000 cc. of solution. In most of the experiments the cylinders were removed, dried and weighed after five minutes in the solution at 25 ± 0.5°, and were repolished with fine emery paper before using again. The reproducibility was in general ±2 to 4% except in those cases where visible films formed on the metal.

1.—The rates were measured in four concentrations of hydrochloric acid at 2000 r. p. m., 25°, with increasing

(1) (a) King and Cathcart, THIS JOURNAL, **59**, 63 (1937); (b) King and Howard, *Ind. Eng. Chem.*, **29**, 75 (1937). Earlier references are given in these papers.

(2) Kilpatrick and Rushton, *J. Phys. Chem.*, **34**, 2180 (1930); **38**, 269 (1934).

(3) Sclar and Kilpatrick, THIS JOURNAL, **59**, 584 (1937).

(4) Van Name and Edgar, Bosworth, Hill, *Am. J. Sci.*, **29**, 237 (1910); **32**, 207 (1911); **42**, 307 (1916).

(5) Roller, *J. Phys. Chem.*, **39**, 221 (1935).

(6) Centnerszwer and Straumanis, *Z. physik. Chem.*, **A128**, 369 (1927).

(7) Friend and Dennett, *J. Chem. Soc.*, **121**, 41 (1922).

(8) Huber and Reid, *Ind. Eng. Chem.*, **18**, 535 (1936).

(9) Svea metal furnished by the Swedish Iron and Steel Co., New York City, to whom we acknowledge our thanks. The analysis furnished indicated 99.92–99.96% Fe.

amounts of potassium nitrate added until maximum rates were reached. In one series the cylinder was polished after each run; in another series it was allowed to become fully etched. It showed a fine, uniform crystalline structure with no inhomogeneities. These maximum rates were considerably higher than with the polished cylinder. In both cases yellow films appeared at low nitrate concentrations, and the rates were quite erratic with the etched metal. No films were visible at higher nitrate concentrations and the rates became reproducible. Under similar conditions the dissolution rate of zinc is linear with nitrate concentration, and less nitrate is necessary to reach the maximum rate.

Typical rates are plotted in Figs. 1 and 2 up to the nitrate concentration at which they become constant.

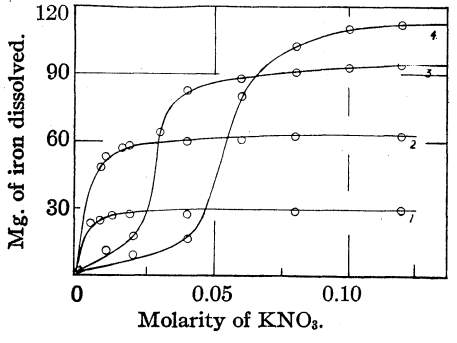


Fig. 1.—Mg. of iron dissolved in five minutes in 250 cc. of hydrochloric acid and potassium nitrate at 2000 r. p. m., at 25°: iron polished; cylinders about 1.8 cm. in diameter, 2.6 cm. in length; 1, 0.01 *N* HCl; 2, 0.025 *N* HCl; 3, 0.04 *N* HCl; 4, 0.05 *N* HCl.

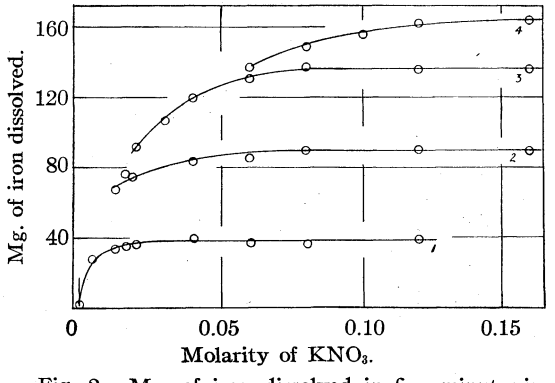


Fig. 2.—Mg. of iron dissolved in five minutes in 250 cc. of hydrochloric acid and potassium nitrate at 2000 r. p. m. at 25°: iron etched; cylinders 1.8 cm. in diameter, 2.6 cm. in length; 1, 0.01 *N* HCl; 2, 0.025 *N* HCl; 3, 0.04 *N* HCl; 4, 0.05 *N* HCl.

2.—Similar experiments were carried out with the polished cylinders in perchloric, nitric, sulfuric, acetic and tartaric acids with added potassium nitrate. Rates with the sulfuric and perchloric acids are shown in Figs. 3 and 4. No satisfactory maxima are reached with the higher acid concentrations, the rate increasing steadily with

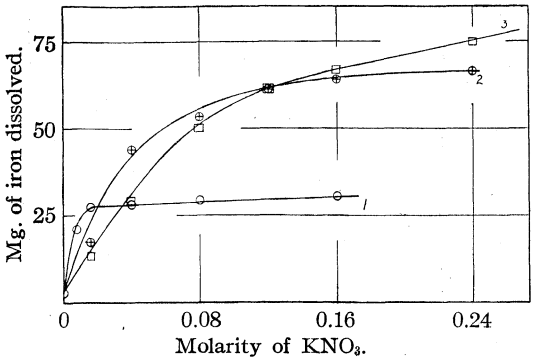


Fig. 3.—Mg. of iron dissolved in 250 cc. of solution in five minutes at 25° and 2000 r. p. m.: cylinders 1.8 cm. diameter, 2.6 cm. long; polished between runs; 1, 0.01 *N* H_2SO_4; 2, 0.025 *N* H_2SO_4; 3, 0.05 *N* H_2SO_4.

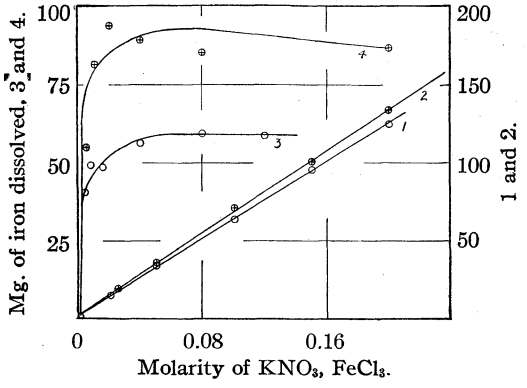


Fig. 4.—Mg. of iron dissolved in 250 cc. of solution in five minutes at 25°, at 2000 r. p. m.: cylinders 1.8 cm. diameter, 2.6 cm. long; polished between runs; 1, $FeCl_3$ + 0.01 *N* HCl; 2, $FeCl_3$ + 0.05 *N* HCl; 3, 0.025 *N* $HClO_4$ + KNO_3; 4, 0.05 *N* $HClO_4$ + KNO_3.

sulfuric, and decreasing with perchloric, acid after reaching a maximum which is lower than that in hydrochloric acid. The rates in 0.01 *N* acids, however, are about the same as in hydrochloric acid, and those at 0.025 *N* are only slightly lower. Added potassium nitrate did not have a very large effect on the rate in nitric acid; this is shown in Fig. 5, where the maximum rates, or the highest rates obtained, in these three acids and also in hydrochloric acid, are plotted. Only the rates in hydrochloric acid are linear with acid concentration, and none of them extrapolate to zero. The extrapolated rate may be due to a solvent reaction, which cannot be obtained experimentally at zero acid concentration because of insoluble reaction products.

The rates in acetic and tartaric acids were about one-tenth as great as in the strong acids. Visible films were formed and the rates were not very reproducible. These rates are not tabulated or shown in the figures.

3.—Experiments carried out in various solutions showed that the rate follows the unimolecular law over at least half the reaction in all the solutions mentioned, except those of very low nitrate concentration. The cylinders were rotated for two- or three-minute periods in the same

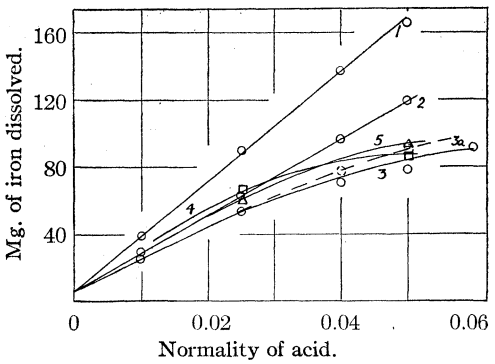


Fig. 5.—Effect of acid concentration on maximum rates of iron dissolving in 250 cc. of solution at 25° and 2000 r. p. m.: 1, HCl + KNO_3, etched iron; 2, HCl + KNO_3, polished iron; 3, HNO_3, polished iron; 3a, HNO_3 + KNO_3; 4, H_2SO_4 + KNO_3; 5, $HClO_4$ + KNO_3.

solution until most of the acid was used up. In calculating rate constants from the equation $k = \frac{2.3V}{At} \log \frac{a}{a-x}$ (where the symbols have the usual significance) it was assumed that two equivalents of hydrogen are used per atom of iron. The deviation from the equation in the later stages shows that this is not strictly true. Tests after the runs showed that one-tenth to one-fifth of the dissolved iron was in the ferric state, probably due to oxygen absorption or oxidation of ferrous ion by nitrate and hydrogen ion. The nitrate reduction also probably requires more than two hydrogen ion equivalents per iron atom. On the other hand, any ferric ion formed will begin to dissolve iron without using up hydrogen ion.

The highest rate constants thus obtained are given in Table I.

4.—Hydrogen peroxide and potassium nitrite were tried as depolarizers with hydrochloric acid. The rates obtained are shown in Fig. 6. The initial rates are nearly linear with peroxide concentration, but the maxima are not as high as with nitrate and tend to fall off with increasing peroxide at the higher acid concentrations. With nitrite the maxima are still lower and the rates fall off rapidly with higher nitrite concentration. In both cases heavy yellow or brown films account for these results. Neither substance can be considered a satisfactory depolarizer.

A few experiments showed that *p*-nitrophenol was even less satisfactory. Iron dissolves to some extent in persulfates; addition of hydrochloric acid had little effect on the rate.

5.—The rates were measured in ferric chloride solutions, with 0.01 and 0.05 *M* hydrochloric acid present. These rates are plotted in Fig. 4. They are linear with ferric chloride concentration at least to 0.2 *M*, are not greatly influenced by added acid, and follow the unimolecular law at all concentrations.

6.—In an attempt to explain irregularities in the preceding curves, the effect of various salts on the rate in nitric acid was determined. These rates are shown in Fig. 7. Small amounts of chloride and bromide increase the rate somewhat, while larger amounts have a remarkable depressing effect. Sulfate ion has only a retarding effect. The rates were unimolecular at low salt concentration, but in the presence of 0.08 *N* salt showed an autocatalytic trend where repeated runs were made in the same solution even though the iron cylinder was repolished between runs. Addition of 0.04 *M* potassium nitrate to 0.05 *M* nitric acid, 0.08 *M* potassium chloride nearly doubled the rate, which still was autocatalytic; addition of 0.08 *M* potassium nitrate increased the rate from 15 to 106 mg. dissolved in five minutes and caused the rate to become unimolecular again.

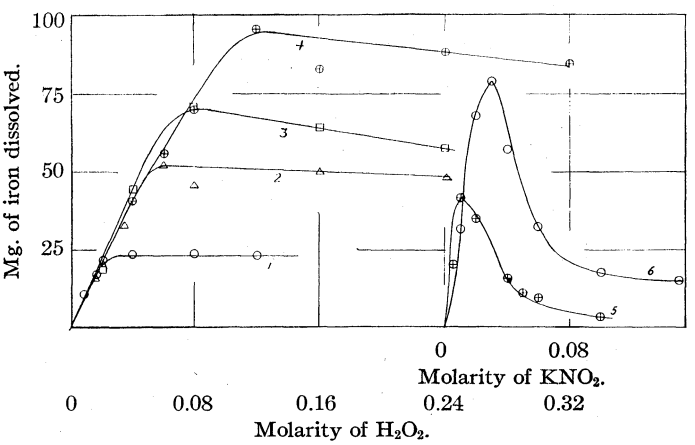


Fig. 6.—Mg. of iron dissolved in five minutes in 250 cc. of HCl with either KNO_2 or H_2O_2 at 2000 r. p. m. and 25°: 1, 0.01 *N* HCl + H_2O_2; 2, 0.025 *N* HCl + H_2O_2; 3, 0.04 *N* HCl + H_2O_2; 4, 0.05 *N* HCl + H_2O_2; 5, 0.025 *N* HCl + KNO_2; 6, 0.05 *N* HCl + KNO_2.

7.—The effect of rotational speed on the dissolution rate was determined in a number of solutions. These rates are plotted in Figs. 8, 9 and 10. Only in ferric chloride solution is the rate proportional to the speed up to the highest values of the latter. In all other cases the rate reaches a maximum and in hydrochloric acid decreases again at higher speeds. In the hydrochloric, perchloric and sulfuric acids, sufficient nitrate was present to give the maximum rate at 2000 r. p. m. In the more concentrated hydrochloric acid, and in nitric acid with the higher sulfate ion concentrations, the maximum rate is reached at lower stirring speeds. Apparently ions which

TABLE I

REACTION RATE CONSTANTS FOR IRON DISSOLVING IN SEVERAL MEDIA. AVERAGE VALUES FOR THE FIRST HALF OF THE REACTION

Reagent	Per. speed, cm./min.	Diff. coeff. $D \times 10^3$ cm.²/min.[1a]	k 0.025 *N*	k 0.05 *N*
Perchloric acid	11,960	3.60	1.340	
Hydrochloric acid	11,310	3.30	1.89	1.47
Sulfuric acid	11,436	2.10	1.48	0.884
Nitric acid	11,184	1.57[a]	1.06	
Acetic acid	11,686	0.76	0.170	.116
Ferric chloride	10,932	0.215[12]		.367

[a] Taken from "Int. Crit. Tables" for 20° (in water).

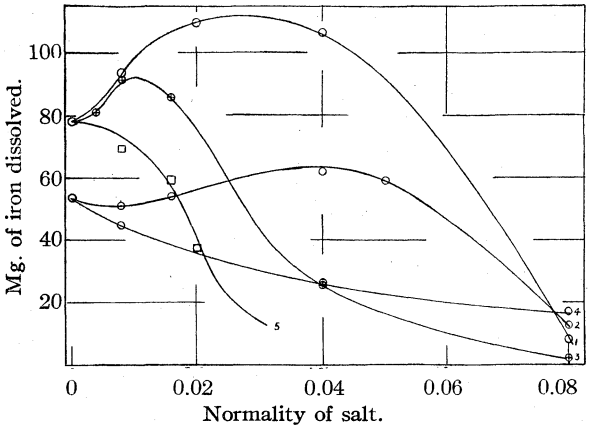


Fig. 7.—Effect of added salts on mg. of iron dissolved in 250 cc. of HNO_3 in five minutes at 2000 r. p. m., 25°: 1, 0.025 *N* HNO_3 + KCl; 2, 0.05 *N* HNO_3 + KCl; 3, 0.05 *N* HNO_3 + KBr; 4, 0.025 *N* HNO_3 + K_2SO_4; 5, 0.05 *N* HNO_3 + K_2SO_4.

retard the rate at low speeds also lower the speed at which the maximum rate is attained.

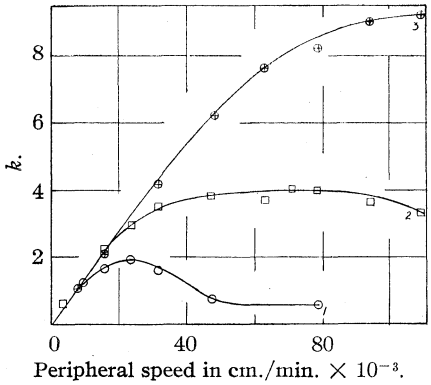


Fig. 8.—Effect of stirring on iron dissolving in HCl + KNO_3 in five minutes at 25°: 1, 0.05 *N* HCl; 2, 0.025 *N* HCl; 3, 0.01 *N* HCl.

8.—Finally, temperature coefficients were determined in ferric chloride and in nitric and hydrochloric acid solutions at typical low and high stirring speeds; *i. e.*, below and above speeds at which the maximum rates are reached in the acid solutions. Rates were run at approximately 15, 25, 35° and in some cases at 45°. The rate constants are plotted in Fig. 11 and average values of the Arrhenius "*A*" are given in Table II with the temperature coefficients from 15–25°.

TABLE II

ENERGIES OF ACTIVATION FOR IRON DISSOLVING IN VARIOUS SOLUTIONS. THE SOLUTIONS ARE NUMBERED TO CORRESPOND TO THE CURVES OF FIG. 11

	Solution	R. p. m.	*A*, cal.	$\frac{k_{298}}{k_{288}}$
1	0.025 *N* HCl + 0.10 *M* KNO_3	2,000	5,194	1.35
2	.025 *N* HCl + 0.10 *M* KNO_3	12,000	13,020	2.14
3	.05 *N* HCl + 0.18 *M* KNO_3	1,500	4,576	1.29
4	.05 *N* HCl + 0.18 *M* KNO_3	3,000	12,240	2.05
5	.05 *N* HCl + 0.18 *M* KNO_3	8,000	14,480	2.34
6	.025 *M* $FeCl_3$	10,000	6,109	1.43
7	.05 *M* $FeCl_3$	2,000	5,491	1.38
8	.05 *N* HNO_3	12,000	12,120	2.04

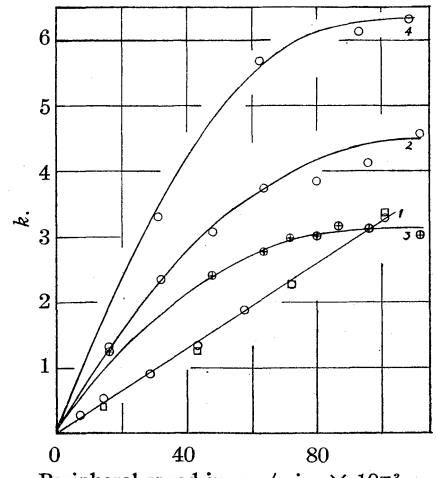


Fig. 9.—Effect of stirring on iron dissolving in several media in five minutes at 25°: 1, 0.025 *M* $FeCl_3$ ⊙, and 0.05 *M* $FeCl_3$ □; 2, 0.025 *M* HNO_3; 3, 0.05 *M* HNO_3; 4, 0.025 *N* $HClO_4$ + KNO_3.

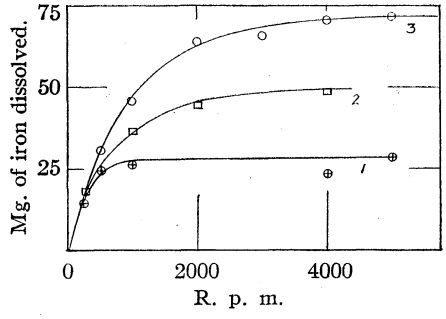


Fig. 10.—The effect of stirring on the amounts of iron dissolving in 250 cc. of solution in five minutes at 25°: 1, 0.025 *N* HNO_3 + 0.04 *N* K_2SO_4; 2, 0.025 *N* HNO_3 + 0.008 *N* K_2SO_4; 3, 0.025 *N* H_2SO_4 + 0.16 *M* KNO_3.

These temperature coefficients evidently fall into two distinct groups. In ferric chloride at low and high stirring speeds and in the other solutions at low stirring speeds, the temperature coefficients lie between 1.29 and 1.43; in the acid solutions at higher speeds, at which the maximum dissolution rates have been reached, the temperature coefficients lie between 2.04 and 2.34. Obviously two different reaction mechanisms are involved.

Discussion

According to the criteria given in the introduction, the effect of stirring speed and the low and high temperature coefficients indicate that these two mechanisms which control the dissolution rates are (a) diffusion and (b) chemical reaction.

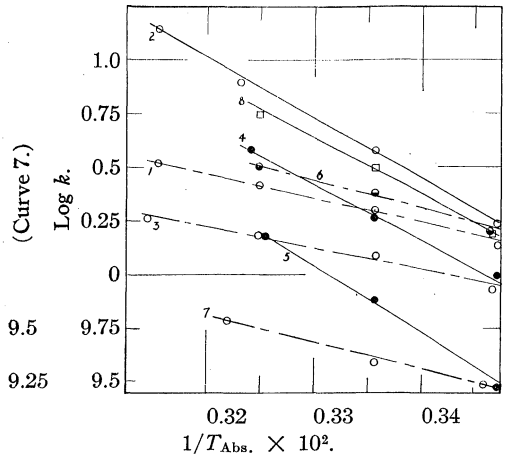


Fig. 11.—Effect of temperature on the rate constants. For legend, see Table IV.

The maximum rates for the polished cylinders in dilute hydrochloric acid at 2000 r. p. m. (Fig. 1), agree well with those found previously for zinc and magnesium. For example, from a cylinder of zinc 2.44 cm. in diameter, 1.88 cm. long, 3.75 mg. of zinc dissolves per sq. cm. in five minutes in 500 cc. of 0.0142 *M* hydrochloric acid at 25°, 1440 r. p. m.[10] From this we calculate $k = 1.87$, in excellent agreement with the value 1.89 of Table I obtained at the same peripheral speed. Comparison with the work of King and Schack[11] at higher peripheral speeds also shows good agreement.

In ferric chloride at 2000 r. p. m. (Fig. 4), the value of k is 0.357. A copper cylinder of similar diameter, in dilute ferric chloride at 2000 r. p. m., gives a somewhat higher value, $k = 0.500$.[12] In ferric chloride at a peripheral speed of 24,000 cm./min. (about 4000 r. p. m., Fig. 9), the rate constant for iron is about 0.755; at the same peripheral speed the rate constant for copper in ferric chloride with no added acid is 0.829 (ref. 12, Table VI). The rate of dissolution of copper in ferric nitrate is lower and under similar conditions the rate constant is 0.666 (ref. 12, Table V).

The etched iron dissolves considerably faster than the polished metal and we must attribute this to the increased surface, in spite of statements frequently made to the effect that etching or pitting has little effect on these diffusion-controlled rates. Such tests usually have been made at comparatively low stirring speeds. Experiments in this Laboratory have shown that magnesium is little affected by polishing or etching, while c. p. zinc dissolves more slowly if not frequently cleaned and polished, due to accumulation of impurities on the surface.

If the rates are actually controlled by the chemical reaction at higher stirring speeds, it is difficult to see why the rate should decrease as the speed increases, in certain solutions (Fig. 8). This is in some way connected with the retarding effect of chloride ion, as shown at 2000 r. p. m. (Fig. 7). The more chloride or sulfate ion present, the lower the speed at which the maximum rate is reached (Figs. 8 and 10). Undoubtedly the rate at 2000 r. p. m., 0.08 *N* chloride or sulfate (Fig. 7) would be "chemically controlled" (high temperature coefficient). This chloride ion effect is sufficient to obscure the effect, at the maximum, of increasing the hydrogen ion concentration (Fig. 8).

It is evident that the rate in hydrochloric acid at low nitrate concentrations (Fig. 1) is influenced both by film formation and by a slow "chemical rate." The maximum rate is not reached sharply and the excess nitrate necessary for the maximum rate increases with the acid concentration. The rate is also lower in stronger than in more dilute acid in this region, at the same nitrate concentration. This indicates that considerable excess nitrate must be present at the immediate surface of the metal if hydrogen ion is to react as rapidly as it reaches the surface, *i. e.*, if the hydrogen ion concentration is to fall to zero at the surface.

The same thing is true of sulfuric though not of perchloric acid. It seems probable that this need for excess nitrate ion and also the retarding effect of chloride, bromide and sulfate ions is connected with the efficiency of nitrate as a depolarizer. The oxidizing potential of nitrate may be barely high enough to overcome the overvoltage of hydrogen on iron under the conditions present, and either this potential or the overvoltage may be influenced by various ions, or the latter by the rotational speed; it seems unlikely that a true chemical rate would vary in this way with salt concentration and stirring speed, with otherwise constant conditions. Also the large increase in rate on addition of excess nitrate (to 0.05 *M* nitric acid, 0.08 *M* potassium chloride, already noted) indicates that the effect of chloride and other ions is to diminish the depolarizing action of nitrate.

A few experiments showed that addition of sucrose has the normal effect in those solutions giving definitely diffusion-controlled rates (*i. e.*, rate inversely proportional to viscosity). Sucrose

(10) King and Braverman, THIS JOURNAL, **54**, 1744 (1932).
(11) King and Schack, *ibid.*, **57**, 1212 (1935).
(12) King and Weidenhammer, *ibid.*, **58**, 602 (1936).

added to sulfuric acid (plus potassium nitrate) at a stirring speed high enough to give the maximum rate, diminishes the rate to the same extent, which does not indicate a chemically-controlled rate.

For these reasons we hesitate to call the rate at higher stirring speeds a true chemical rate until it has been investigated further. It is probable that a very high stirring speed, or a sufficiently high concentration of certain salts, would reduce the rate to the value it has with no depolarizer present, where the temperature coefficient is also high[7]; in this case the mechanism might also be identical.

The increase in the rate in nitric acid on addition of small amounts of chloride and bromide (Fig. 7) may be ascribed to an increase in the diffusion coefficient of the acid. While the diffusion coefficient of nitric acid has not been determined in the presence of salts, it is lower than that of hydrochloric acid in water ("International Critical Tables").

The maximum rates in the various acids at 2000 r. p. m. are roughly proportional to the diffusion coefficients, except for perchloric acid, as shown in Table I. Because of the irregularities found, including film formation with the weaker acids, a quantitative comparison would be impossible.

Summary

The rate of dissolution of very pure iron has been measured in solutions of several acids, with potassium nitrate, hydrogen peroxide, potassium nitrite and *p*-nitrophenol as depolarizers. Of these only the nitrate was found to be reasonably satisfactory as a depolarizer.

The rate was studied as a function of the depolarizer concentration, the acid concentration, the concentration of various added salts, the stirring speed and the temperature. The rate was also measured in ferric chloride solutions of various concentrations, at various stirring speeds and temperatures, with and without added acid.

The rate is shown to be diffusion-controlled under all conditions in ferric chloride; at low stirring speeds in hydrochloric acid with sufficient nitrate present, and approximately so in nitric acid with certain chloride concentrations. Under other conditions (higher stirring speeds, higher salt concentrations, low nitrate concentrations) it is in whole or part controlled by a slower reaction perhaps of chemical nature at the metal surface.

Under conditions where the rate is diffusion-controlled, the temperature coefficient is about 1.35 per 10°; where it is "chemically" controlled, the temperature coefficient is 2.0–2.4 per 10°. The activation energies vary accordingly.

WASHINGTON SQUARE COLLEGE
NEW YORK, N. Y. RECEIVED APRIL 20, 1939

Studies of Purified Palladium Sols Prepared by Electric Sparking

BY W. PAULI, W. HOFF AND F. LICHTENSTERN[1]

The series of investigations of different purified and concentrated Bredig sols of the noble metals,[2] carried out at this Institute over a period of years, has been continued with the study of palladium sols. As in the previous studies our concern was to observe the relations between origin of charge and stability on the one hand and inorganic chemical properties of palladium on the other by physical-chemical methods of analysis. Thus it was possible to make comparisons in the same way with the other sols of noble metals already investigated.

The methods of preparing, purifying and concentrating were disintegration by the electric spark and an improved process of electrodecantation.[2]

One of the first results was that it is impossible to prepare a palladium sol by electrodispersion in *conductivity water* (spec. cond. 7×10^{-7} mho). Regardless of the dispersion time, in every case precipitates are formed instantly. This behavior contrasts with that of platinum and silver.[2b,c] The explanation is that pallado oxide is less acid than platino oxide[3]; a hydroxo acid of palladium is not known, while a hydroxo acid of platinum

(1) The experiments were carried out at the Institut für medizinische Kolloidchemie der Universität Wien in 1936 and 1937.

(2) (a) Gold sols: Pauli, *Naturwissenschaften*, **20**, 551 and 573 (1932), with many references to literature; Pauli and Russer, *Kolloid. Z.*, **58**, 22 (1932); Eirich and Pauli, *ibid.*, **67**, 186 (1934); Pauli, Russer and Brunner, *ibid.*, **72**, 26 (1935); (b) platinum sols: Pauli and Schild, *ibid.*, **72**, 165 (1935); Pauli and Baczewski, *Monatsh.*, **69**, 204 (1936); (c) silver sols: Löffler and Pauli, *Kolloid. Z.*, **60**, 146 (1932); Hoff and Pauli, to be published, with list of literature.

(3) P. Pascal and P. Baud, "Traité de Chimie Minérale," Tome XI, Masson et Cie, Paris, 1932, p. 793.

has been shown to be the charging group of Bredig platinum sols in conductivity water.[4] On the other hand, palladium is more noble than silver (silver oxide is a strong base). In the case of silver the anodic oxidation (during electrodispersion) furnishes the stabilizing complex by forming ultimately silver hydroxide,[2c] which in the case of palladium in conductivity water is not possible. This demonstrates a similarity with gold, which for analogous reasons does not form a electrodispersion sol in conductivity water.[5]

We found similar conditions by electrodispersion in sulfuric acid (1×10^{-3} N). An adhering surface complex could not be expected because of the high solubility of palladium sulfate in water.[3] Since the formation of an oxo complex (as a result of electrolysis) is not possible either, we have no sol formation. Silver and gold form very instable colloids in dilute aqueous sulfuric acid solutions. The corresponding experiments with platinum have not yet been undertaken. Such experiments would be interesting because of the great number of complex acids known to be formed by platinum and the sulfate radical.

The behavior of palladium when dispersed in solutions of potassium chloride was unexpected. Within the concentration range 1×10^{-4} to 1×10^{-2} N a dark brown sol is formed, but it coagulates within one day at the most. These sols, therefore, are still less stable than the corresponding silver sols. The explanation probably is that the reaction of palladium metal while being dispersed in potassium chloride solutions does not lead to a noticeable complex formation. The formation of silver sols (dispersed under the same circumstances) was favored by the simultaneous formation of oxo complexes. Thus one may consider the Bredig silver sols in potassium chloride solutions as stabilized by chloro hydroxo mixed complexes (Löffler–Pauli[2c]), so that the extraordinary sensitiveness of the pure hydroxo silver sols to carbon dioxide was considerably decreased.

The question was raised, therefore, to what extent the behavior of palladium would prove analogous. For this purpose the electrodispersion in sodium hydroxide solutions (optimal concentration 1×10^{-3} N) was tried. We obtained dark brown sols which were stable for months if sufficiently protected against carbon dioxide. As hydroxo sols (which they obviously are) they showed a high sensitiveness to carbon dioxide and electrodialysis, just as do the corresponding silver sols. The exchange of sodium ion for hydrogen ion forced by membrane hydrolysis processes during electrodialysis leads again to rapid discharge by complex decomposition. The reaction is the same as of silver sol (Löffler–Pauli[2c]), namely, a neutralization of the hydrogen ions by the complex hydroxo groups (see also the silver nitrate titration of a chloro hydroxo palladium sol discussed later in this paper).

Sols dispersed in nitric acid solutions proved not to be resistant to carbon dioxide or electrodialysis in spite of the fact that the nitrate ion is a favored complex partner of palladium. They were even less resistant than the sols dispersed in sodium hydroxide. This behavior would suggest the presence of hydroxo nitrato mixed complexes. If perfectly protected from carbon dioxide, the sols are stable for a long time. This demonstrates that the coagulation is due not only to the high solubility of the palladium complex mentioned, but also to its decomposition. This decomposition is caused by hydrolytical processes aided by reaction with carbon dioxide or electrolysis.

By far the best sols were obtained by electrodispersion in hydrochloric acid solutions. In the optimal concentration (1×10^{-3} N) the time of dispersion may be extended to three hours. Excellent sols with a content up to 0.2 g. of palladium per liter are attainable directly; they are not sensitive to carbon dioxide and laboratory air. Only sols with a smaller content (0.12 g. of palladium per liter and one to two hours time of dispersion) which may easily be concentrated to more than 1 g. of palladium per liter are suitable for electrodecantation. The conductivity of the dispersion medium decreases during dispersion (by 5–8%) and continues to decrease after completing the electrodispersion.[6] After eighteen to twenty days the limiting value of conductivity (equilibrium) is reached. In case the primary sols were too concentrated (0.2 g. of palladium per liter), the period of decreasing conductivity is interrupted by an increase about the thirteenth day after dispersion. Shortly thereafter these sols coagulate spontaneously.

(4) S. W. Pennycuick [*J. Chem. Soc.*, 2108 (1928); 623 (1929)] has postulated a hexahydroxo platini acid as charging complex. A platino hydroxo acid $H_2Pt(OH)_4$ is more probable. This acid possibly is in oxidation and detachment equilibrium with a platini complex (Pauli and Baczewski[2b]). For further details, see Pennycuick, *Kolloid Z.*, **49**, 407 (1929); *Z. physik. Chem.*, **148**, 413 (1930).

(5) Beans and Eastlack, THIS JOURNAL, **37**, 2667 (1915) and [2a].

(6) Under certain favorable circumstances observations have been made of an analogous behavior of gold and platinum sols. After dispersion the complexes are filled up by consumption of free acid.

The electrodispersion sols (before electrodecantation) contain nearly the same concentration of chlorine and hydrogen ions (about 8×10^{-4} N), ascertained by conductometrical titration. But this amount of ions is not yet sufficient to explain the total conductivity. Therefore we have to assume a further amount of electrolyte (about 3–6 $\times 10^{-4}$ N). We suppose it is the colloid electrolyte with the "gegenions" (contra-ions) H^+ and Pd^{++} which is present besides molecularly disperse hydrochloric acid and pallado chloride. The molecularly disperse contaminations are removed to a large extent by electrodecantation. In order to avoid an entire hydrolysis of the complexes the electrodecantation has to be stopped at the right moment. Besides, a decomposition equilibrium seems to exist between the charging groups and pallado chloride. In sols purified and concentrated by electrodecantation, a small amount of pallado chloride therefore is always present.

The sols concentrated and purified by electrodecantation show a continual increase of conductivity with time, accompanied by spontaneous layer formation and partial flocculation. Nevertheless, among our number of specimens were some sols with nearly constant conductivity after concentrating. These sols show the same amount of (free) hydrogen ions titrated either by sodium hydroxide or barium hydroxide. On the other hand, all sols the conductivity of which increases with time show a sodium hydroxide consumption greater than the concentration of free (conductance-active) hydrogen ions and a consumption of barium hydroxide still larger than that of sodium hydroxide. The greatest number of our sols obviously possess further heteropolar surface groups which may be filled up to chlorohydroxo mixed complexes, besides the charging complexes. In this respect they are similar to the chloro platinum sols (Pauli–Schild[2b]).

With our concentrated sols which are freed to a large extent from molecular electrolytes (in so far as these are not re-formed by complex decomposition), we also found the amount of titrated hydrogen ions insufficient to explain the total conductivity. They contain on the average the same concentration of other cations (Pd^{++}). Less highly purified sols are more strongly charged (the membrane hydrolysis of surface complexes is not so far advanced), but they contain up to twenty times as many other cations as hydrogen ions. A part (up to one-half) of this amount of cations can be ascribed to molecularly disperse pallado chloride, as may be ascertained by simultaneous determination of free chlorine ions by conductometrical titration.

This may be illustrated by some results:

	Sol VII	Sol XXII	Sol X
Content, g. Pd/liter	0.35	0.66	1.10
k of last upper layer, mho $\times 10^6$	7.0	2.7	5.7
k of sol, mho $\times 10^5$	2.36	1.09	2.80
Concn. of active H^+, $N \times 10^5$	0.92	2.1	4.6
Concn. of cations other than H^+, $N \times 10^5$	20	1.5	9.6
Concn. of free chloride ion, $N \times 10^5$	8.9	<1	~3.1

Sol VII incompletely purified, sol XXII highly purified, sol X middle degree of purification; k = specific conductivity at 25°.

As one may see from this table, continued purification causes removal of molecularly disperse pallado chloride and exchange of the "gegenion" (contra-ion) Pd^{++} for H^+. This is in agreement with the previous experience with other negative colloids. Simultaneously the absolute amount of charging ionogen groups is decreased by the accompanying complex decomposition.

Coagulation by freezing produces a decrease of conductivity in the freezing liquid (liquid produced by thawing the frozen colloid and by separation from the coagulum, without Tyndall phenomenon). The sols mentioned above as of constant conductivity are exceptions: they maintain their constant conductivity in the freezing liquid also after coagulation. In all cases where the conductivity of the freezing liquid is lower than that of the sol, the hydrogen ion concentration of the sol is decreased in the freezing liquid. The cations present other than H^+ are in some cases increased, in some decreased, by freezing. This leads to the conclusion that the bulk of hydrogen ions, being "gegenions," goes into the coagulum or vanishes by reaction with the hydroxyl groups of the charging chloro hydroxo complex which is partially destroyed, and pallado chloride is set free. But the amount of pallado chloride liberated by freezing in some cases may be ten times as much as could be produced by complex decomposition at the maximum. This abundance of pallado chloride is probably originated by non-ionogen heteropolar surface groups of the sol particles which are rich with chlorine. In other cases, on the contrary, the amount of pallado chloride is considerably decreased by

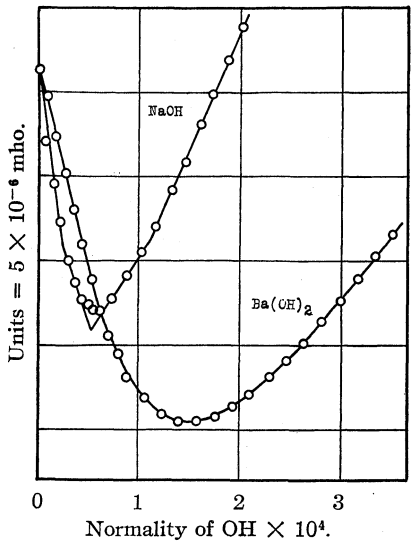


Fig. 1.—Correlative sodium hydroxide and barium hydroxide titrations of 3 cc. of sol X.

freezing. This may be due to a filling up of non-ionogen heteropolar surface groups that are low in chlorine. Thereby the cation (Pd^{++}) will be inactivated. This behavior is in agreement with the results of the barium hydroxide titration. Figure 1 shows an example of a characteristic pair of correlative sodium hydroxide and barium hydroxide titrations.

The existence of non-charging heteropolar surface groups in addition to the charging groups had been proved in the case of platinum sols (Pauli–Baczewski,[2b] Pennycuick[4]) by comparison of sodium hydroxide and barium hydroxide titrations. A filling up of the heteropolar surface groups to ionogen complexes is more favored in the presence of barium hydroxide than of sodium hydroxide because of the more strongly inactivating and associating divalent barium ion.

The presence of palladium ions in the freezing liquid could be proved in all cases by a special palladium test.

This palladium test is analogous to the platinum test of Pauli–Schild.[2b] The procedure is reduction of the palladium compound by formic acid under special conditions and addition of phosphorous–molybdenic acid. The blue color of the solution indicates palladium concentrations of 0.2–1 γ per cc.; green color.

The determination of the colloid equivalent—number of palladium atoms per one free charge—was possible only in cases where nearly all gegenions were hydrogen ions. The calculated values varied between 100 and 300.

The conductometrical determination of chlorine had to be carried out by silver sulfate titration instead of the usual silver nitrate titration, for some sols had the capacity of taking the nitrate radical into their complexes. This could be proved by titration with potassium nitrate, nitric acid and by the comparison of silver sulfate and silver nitrate titrations. This behavior was obvious with freezing liquids which had been reduced by hydrogen gas. If titrated by silver nitrate they showed a less consumption of the reagent after reduction than before. The explanation is that the complex present in the freezing liquid and capable of adding the nitrate radical, loses this capacity by reduction.

A further interesting result of titration analysis was also found by silver nitrate titration. The charging complexes of some sols are destroyed by reaction with silver ion, *i. e.*, after removal of chlorine, a reaction between hydrogen ion and complex hydroxyl groups takes place. The nitrate radical instead of chlorine cannot form a stable complex. In such cases the silver nitrate titration diagrams show the particular character of acid–base titration plots, since during titration the hydrogen ion is stoichiometrically consumed (Fig. 2). There seems to be only one equation possible for the corresponding reaction: $[Pd(OH)_2Cl_2]H_2 + 2AgNO_3 = 2AgCl + Pd(NO_3)_2 + 2H_2O$, because for one hydrogen ion conductivity equivalent that vanishes, one salt conductivity equivalent has been found to be set free.

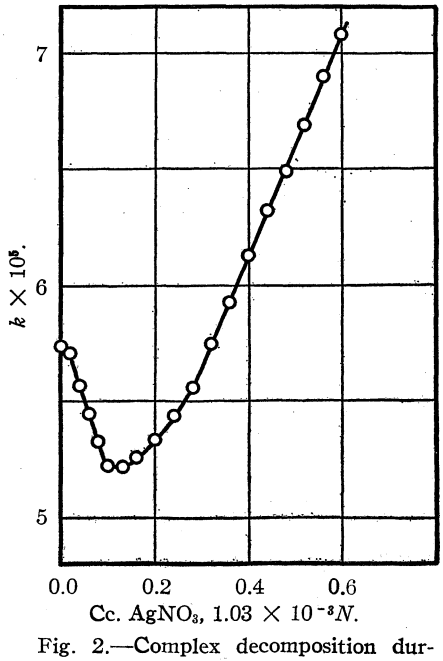


Fig. 2.—Complex decomposition during silver nitrate titration: sol IX, 3 cc.

The chlorohydroxo palladium sols (even if not concentrated and purified) are coagulated by boiling. The conductivity is then slightly increased, the charging groups are probably detached entirely, and the titrable hydrogen ion is transferred completely into the "boiling liquid."

Summary

1. Preparations of palladium sols by sparking under the solvents: conductivity water, and 10^{-3} normal solutions of sulfuric acid, sodium hydroxide, nitric acid, potassium chloride, hydrochloric acid, are related and discussed briefly.

2. The charging group of the sols prepared in the case of the chlorides very probably is a chlorohydroxo mixed complex of varying constitution. This complex maintains a decomposition equilibrium with molecularly disperse pallado chloride. Besides there are heteropolar groups on the particle surface that are non-ionogen and therefore not charging. These groups may react in a variety of ways.

ZOLLIKON, SWITZERLAND RECEIVED MARCH 11, 1939

[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF STANFORD UNIVERSITY]

The Quantum Yield of Monochloroacetic Acid Hydrolysis

BY R. NELSON SMITH, PHILIP A. LEIGHTON AND WESLEY G. LEIGHTON

A direct comparison of the uranyl oxalate and monochloroacetic acid photolyses at 2537 Å. shows, on the basis of the published quantum yields for these reactions, a startling discrepancy. Since both reactions have been widely used as chemical actinometers and results interpreted on the basis of the existing quantum yields, it seemed necessary to find the source of this discrepancy. In a recent note[1] the authors reported a redetermination of both yields. A solution 0.01 *m* in uranyl sulfate and 0.05 *m* in oxalic acid gave an average quantum yield at 2537 Å. of 0.60, in agreement with the value reported by W. G. Leighton and Forbes[2] for this wave length. For a solution 0.5 *m* in monochloroacetic acid at room temperature and 2537 Å. the quantum yield was found to lie between 0.3 and 0.4, as compared with the value of 1.07 given by Rudberg.[3] We, accordingly, have reinvestigated this reaction, and now find the quantum yield to be strongly dependent on temperature.

Experimental

Monochloroacetic acid was purified by a series of distillations in an all-glass apparatus, starting samples from several sources being employed. Freshly prepared solutions, before exposure to light, showed no chloride ion. Quantum yields were based on the amount of chloride ion produced, which was determined by potentiometric titration against standard (0.0075 *m*) silver nitrate. The cell consisted of a calomel electrode connected to an Ag–AgCl electrode by a saturated potassium nitrate bridge (Cl^- free). The method was checked by titration of standard chloride solutions. Radiation at 2537 Å. was supplied by a mercury arc in conjunction with a quartz monochromator. The rectangular reaction cell was entirely of fused silica and contained 8.23 cc. of solution in which the average light path was 25 mm. Absolute energies were determined by thermopile, calibrated against U. S. B. S. radiation standards. In the course of the investigation, two independent monochromators, four light sources, including lamps giving both reversed and non-reversed lines at 2537 Å., as well as lamps giving both continuous and intermittent radiation (with respect to time), two thermopiles, one surface and one linear, and four U. S. B. S. standard lamps were used, all with uniform results.

Energy measurements were carried out by the method of horizontal integration[4] taking thermopile readings at 2-mm. intervals across the back of the cell. The length of the monochromator slit was adjusted so that the divergent beam, after passing through the cell filled with water or solution, fell entirely within the vertical limits of the thermopile surface. Variations in arc intensity during a run and between different series of integration measurements were followed by placing the thermopile in a fixed and reproducible position at the front of the cell. The methods of applying corrections and of computation were those employed by the authors in previous work.[2,5]

For runs at elevated temperatures the cell, with the exception of the front window, was enclosed in an insulated heating jacket and energy measurements were made as before except that variations in intensity were not followed during the course of the run. Rates of decomposition by the dark reaction were determined for several different temperatures, and from a plot of log k *vs.* $1/T$ the correction for the amount of decomposition due to the dark reaction during a photolysis was determined.

(1) W. G. Leighton, R. N. Smith and P. A. Leighton, THIS JOURNAL, **60**, 2566 (1938).

(2) W. G. Leighton and G. S. Forbes, *ibid.*, **52**, 3139 (1930).

(3) Rudberg, *Z. Physik*, **24**, 247 (1924).

(4) Leighton and Leighton, *J. Phys. Chem.*, **36**, 1900 (1932).

(5) P. A. Leighton and G. S. Forbes, THIS JOURNAL, **51**, 3549 (1929).

TABLE I

MONOCHLOROACETIC ACID AT λ = 2537 Å.

	Molar conc.	Temp., °C.	Exposure time, min.	Average I, ergs/mm.^{2} sec.	Quanta absorbed	Total moles Cl^- formed	Moles Cl^- formed in dark react.	Molecules photolyzed	Φ
1	0.50	25	808	73.7	4.06×10^{19}	2.22×10^{-5}	3.0×10^{-7}	1.32×10^{19}	0.325
2	.50	25	822	75.3	4.22×10^{19}	2.30×10^{-5}	3.0×10^{-7}	1.37×10^{19}	.325
3	.50	25	771	76.5	4.04×10^{19}	2.10×10^{-5}	2.8×10^{-7}	1.25×10^{19}	.310
4	.50	25	796	76.0	4.04×10^{19}	2.18×10^{-5}	2.9×10^{-7}	1.30×10^{19}	.321
5	.50	25	837	76.5	4.39×10^{19}	2.325×10^{-5}	3.1×10^{-7}	1.38×10^{19}	.314
6	.50	25	2774	8.32	1.52×10^{19}	0.863×10^{-5}	10.0×10^{-7}	0.495×10^{19}	.303
7	.50	25	1101	97.3	7.38×10^{19}	3.69×10^{-5}	4.1×10^{-7}	2.20×10^{19}	.298
8	.50	25	551	7.62	0.314×10^{19}	0.190×10^{-5}	2.0×10^{-7}	1.02×10^{19}	.326
9	.50	25	1335	7.60	0.781×10^{19}	0.455×10^{-5}	4.9×10^{-7}	2.445×10^{19}	.317
								Average	.315
10	2.00	25	541	97.6	3.70×10^{19}	1.92×10^{-5}	8.0×10^{-7}	1.11×10^{19}	.301
11	0.50	32	835	86.0	5.10×10^{19}	3.19×10^{-5}	0.06×10^{-5}	1.88×10^{19}	.369
12	.50	41	1013	91.2	6.22×10^{19}	4.65×10^{-5}	0.21×10^{-5}	2.68×10^{19}	.432
13	.50	56	1024	101.2	7.16×10^{19}	8.21×10^{-5}	1.42×10^{-5}	4.09×10^{19}	.571
14	.50	56	1063	101.0	7.65×10^{19}	9.70×10^{-5}	1.48×10^{-5}	4.95×10^{19}	.647
15	.50	56	717	89.8	4.35×10^{19}	5.18×10^{-5}	1.00×10^{-5}	2.52×10^{19}	.579
16	.50	56	1146	80.5	6.23×10^{19}	8.40×10^{-5}	1.59×10^{-5}	4.10×10^{19}	.658
								Average	.611
17	.50	69	563	90.0	3.62×10^{19}	9.30×10^{-5}	5.18×10^{-5}	2.48×10^{19}	.688

Results

Numerical results are given in Tables I and II. Percentages decomposed ranged from 0.04 to 2. Runs 5 to 8 show that Φ is constant over a 13-fold variation in light intensity, and runs 7 and 10 that it is constant over a 4-fold variation in chloroacetic acid concentration. The variation in quantum yield of the photolysis with temperature is shown in Fig. 1. The rate of the dark reaction is given by the equation

$$\log k = 5.40 - (5240/T),\ k = \text{moles cc.}^{-1}\ \text{sec.}^{-1}$$

This corresponds to an activation energy of 24,000 cal./mole. While at 25° the dark reaction rate was only about 1% of the rate during photolysis, at 69° it amounted to 57% of the total rate and at higher temperatures became so large as to make quantum yield determinations uncertain.

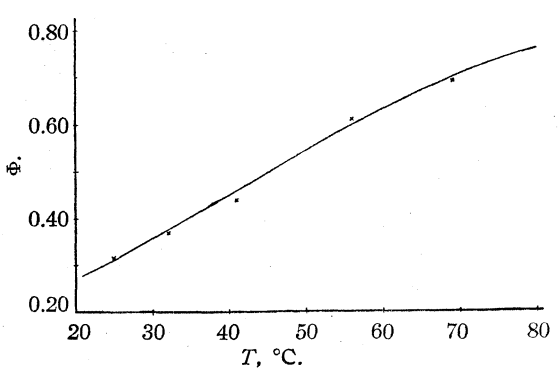


Fig. 1.—Variation in quantum yield of monochloroacetic acid hydrolysis with temperature. The points are experimental, the curve calculated.

TABLE II

0.01 M UO_2SO_4 + 0.05 M $H_2C_2O_4$ AT λ = 2537 Å.

Temp., °C.	Exposure time	Av. I_1, ergs/mm.^{2} sec.	Quanta absorbed	Molecules photolyzed	Φ
25	976	34.6	2.50×10^{19}	1.58×10^{19}	0.632
25	816	35.9	2.29×10^{19}	1.30×10^{19}	.566

Discussion

The variation in quantum yield with temperature may be accounted for by a mechanism which assumes a competition between secondary reactions which lead to deactivation or to decomposition, *viz.*

(1) $CH_2ClCOOH + h\nu \longrightarrow CH_2ClCOOH^*$ ϕI_a

(2) $CH_2ClCOOH^* + M \longrightarrow CH_2ClCOOH + M$ k'_2

(3) $CH_2ClCOOH^* + 2H_2O \longrightarrow CH_2OHCOOH + H_3O^+ + Cl^-$ k'_3

Assuming a steady state concentration for $CH_2ClCOOH^*$ and including (M) and (H_2O) with the values of k'_2 and k'_3, this mechanism gives for the over-all quantum yield

$$\Phi = \frac{+d(Cl^-)/dt}{I_a} = \frac{\phi}{1 + k_2/k_3} \qquad (1)$$

If now

$$k_2 = A_2 e^{-E_2/RT} \text{ and } k_3 = A_3 e^{-E_3/RT}$$

equation (1) becomes

$$\Phi = \frac{\phi}{1 + \frac{A_2}{A_3} e^{(E_3 - E_2)/RT}} \qquad (2)$$

The curve in Fig. 1 was obtained from this equation by setting $\phi = 1$, $A_2/A_3 = 8.3 \times 10^{-6}$, and $E_3 - E_2 = 7400$ cal./mole. It fits the observed points within experimental error. The value of 7400 cal. for the difference in activation energies between reactions 3 and 2 appears reasonable. The ratio of the temperature independent factors, A_2/A_3, implies that in the deactivating step the excited chloroacetic acid molecules must withstand at least 10^5 collisions before deactivation occurs. Although direct evidence indicating that activated molecules can enter into secondary reactions is very meager in photochemistry, in this instance a free radical mechanism appears unlikely and the reactions given are the simplest which will fit the facts.

The results of this investigation are definitely at variance with those of Rudberg[3] and of Harris and Kaminsky.[6] The difference between our values and that of Rudberg may be due first to the fact that he used a Hefner lamp for calibration of his thermopile and second to the extremely small amounts of photolysis which he obtained, requiring only about 0.2 ml. of 0.0002 *m* silver nitrate for titration.

Harris and Kaminsky, by a comparison of the rate of coloration of malachite green leucocyanide with the monochloroacetic acid hydrolysis found $\Phi_{HClAc} = 1.05$ at 2537 Å. and 26–29°. The source of the variation between their result and ours is not apparent.

Farkas[7] determined Φ for monochloroacetic acid in the region 1850–2000 Å. by comparison with the photolysis of ammonia. The temperature of the solution was not given. Assuming $\Phi_{NH_3} = 0.25$, he obtained $\Phi_{HClAc} = 0.9$. From the newer work of Wiig[8] the value of Φ_{NH_3} at the pressure used by Farkas (1 atm.) is $\sim$0.16. Making this correction one obtains $\Phi_{HClAc} \sim 0.58$.

Farkas, and Farkas and Hirschberg[9] used the monochloroacetic acid reaction, assuming $\Phi = 0.9$, as an actinometer for determination of quantum yields in the photolysis of ethyl alcohol and of various aldehydes and acids. Again the temperatures were not given, but assuming that they were the same as in the comparison of monochloroacetic acid with ammonia, the yields given by Farkas, and Farkas and Hirschberg should be reduced by the ratio 0.58/0.9. In addition, in the equation used by Farkas and Hirschberg[9] (p. 2452) the factor 0.9 should be in the numerator rather than the denominator. Making both corrections, the yields reported by these authors should be reduced by approximately one-half.

Frankenburger and Klinkhardt[10] assumed a quantum yield of unity in using the monochloroacetic acid hydrolysis as an actinometer in a study of the photosensitized hydrogen–oxygen reaction. The temperature of the actinometer solution was 65°. Using our value of $\Phi_{HClAc} = 0.67$ at 65°, the quantum yields given by them for the H_2–O_2 reaction should be reduced by the ratio 0.67/1. This change would not appear appreciably to affect their interpretation of results.

Lyons and Dickinson[11] used the monochloroacetic acid hydrolysis as an actinometer in a careful study of the photoöxidation of liquid carbon tetrachloride at 2537 Å. and room temperature. Using Rudberg's value for Φ_{HClAc}, they found an over-all yield of close to unity for the oxidation, which in turn led to difficulty in explaining the very low yield ($\Phi < 0.01$) in the photolysis of pure carbon tetrachloride. On the basis of our results the yield for the oxidation of carbon tetrachloride becomes *ca.* 0.33, which removes the difficulty.

Summary

The quantum yield of the monochloroacetic acid hydrolysis is found to be considerably lower than the previously established values, and to vary with temperatures, at 2537 A., from 0.31 at 25° to 0.69 at 69°. The yield is independent of light intensity and concentration over the ranges studied. A mechanism involving competition between deactivation and decomposition is suggested. The relation of these results to publications in which this reaction has been used as an actinometer is discussed.

STANFORD UNIVERSITY, CALIF. RECEIVED MAY 19, 1939

(6) Harris and Kaminsky, THIS JOURNAL, **57**, 1154 (1935).
(7) L. Farkas, *Z. physik. Chem.*, **B23**, 89 (1923).
(8) Wiig, THIS JOURNAL, **57**, 1559 (1935); **59**, 827 (1937).
(9) Farkas and Hirschberg, *ibid.*, **59**, 2450, 2453 (1937).
(10) Frankenburger and Klinkhardt, *Z. physik. Chem.*, **B15**, 421 (1932).
(11) Lyons and Dickinson, THIS JOURNAL, **57**, 443 (1935).

[CONTRIBUTION FROM THE DEPARTMENT OF LEATHER RESEARCH, INSTITUTE OF SCIENTIFIC RESEARCH, UNIVERSITY OF CINCINNATI]

The Isoelectric Point of Collagen

BY JOHN H. HIGHBERGER

Although the isoelectric point of collagen is usually given as *p*H 4.7, a second critical point in the behavior of collagen and gelatin has frequently been noted at *p*H 7.7. Wilson and Gallun[1] found two points of minimum plumping of limed calf skin, at *p*H 5.1 and 7.6, and Wilson and Kern[2] located similar points at *p*H values of 4.7 and 7.7 in studying the swelling of gelatin. Davis and Oakes[3] found a minimum in the viscosity of 1% gelatin sols at about *p*H 8, when measured at 40°, but none at 4.7. Just the opposite result was obtained by Hitchcock,[4] whose curves show a minimum viscosity at 4.7, but not at 8. Hitchcock attributed the difference between his results and those of Davis and Oakes to the practice of the latter workers of heating their sols to 75° in the course of their preparation. Higley and Mathews[5] studied the absorption of light by gelatin sols as a function of *p*H, and found two sharply defined minima in the wave lengths absorbed, at *p*H values of 4.7 and 7.7. Kraemer and Dexter,[6] on the other hand, found a maximum in the light scattering of gelatin at *p*H 8 only in the case of pig skin gelatin, while for other gelatins it was found close to *p*H 5. Electrophoretic studies[7] have established the isolectric point of commercial calf skin gelatin as close to *p*H 4.7 to 4.8, the exact location depending upon the nature and ionic strength of the buffer salts present.

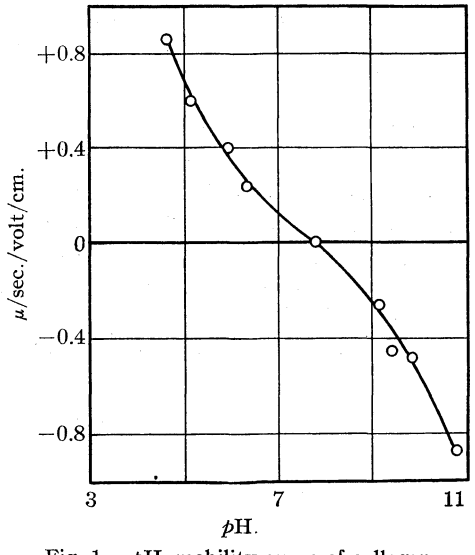


Fig. 1.—*p*H–mobility curve of collagen.

Experimental

A study of the electrophoresis of the collagen of animal skin, using the technique described by Moyer,[8] has been in progress in this Laboratory for some time. Several lots of collagen prepared from fresh steer hide by a process previously described by the writer,[9] and varying in ash content from 0.05 to 0.08%, have been used in this work. Powdered material which had passed a 100-mesh sieve was used to make suspensions in acetate, phosphate, and borate buffers of ionic strength 0.005, and covering the *p*H range from 4 to 11. Relatively dilute buffer systems were found necessary on account of the unusually small slope of the mobility curve over a considerable range of *p*H.

All measurements were made in the vertical microelectrophoresis cell of Abramson, Moyer and Voet,[10] which was found to be very satisfactory for use with these rather rapidly settling suspensions. At least ten particles were timed at each of the stationary cell levels 0.2 and 0.8, and the results averaged. The particles measured ranged in size from about 15 to about 75 μ. No temperature correction was made. Room temperature varied between 23 and 26° during the observations. Hydrogen electrode measurements were made in duplicate, using Clark rocking electrode vessels and a saturated calomel electrode. The reference standard was "standard acetate," of *p*H 4.65.[11]

The *p*H–mobility curve thus obtained is given in Fig. 1, from which it will be seen that this collagen is isoelectric at *p*H 7.8 under the experimental conditions mentioned. This observation is in accord with swelling data already reported[12] for similar collagen preparations, which showed a pronounced minimum zone between *p*H 7 and 10 in unbuffered solutions. An experiment by Beek[13] indicates that the isoionic point of this collagen is also close to *p*H 7.7.

Preliminary observations on a mixed gelatin made by extracting a similar collagen preparation several times with distilled water at 100° indicate that this gelatin is isoelectric at *p*H 6.1, when adsorbed on collodion particles and observed in buffers of ionic strength 0.005. Qualita-

(1) Wilson and Gallun, *Ind. Eng. Chem.*, **15**, 71 (1923).
(2) Wilson and Kern, THIS JOURNAL, **44**, 2633 (1922); **45**, 3139 (1923).
(3) Davis and Oakes, *ibid.*, **44**, 464 (1922).
(4) Hitchcock, *J. Gen. Physiol.*, **6**, 457 (1924).
(5) Higley and Mathews, THIS JOURNAL, **46**, 852 (1924).
(6) Kraemer and Dexter, *J. Phys. Chem.*, **31**, 764 (1927).
(7) Hitchcock, *J. Gen. Physiol.*, **14**, 685 (1931); Abramson, *ibid.*, **15**, 575 (1932).
(8) Moyer, *J. Bact.*, **31**, 531 (1936).
(9) Highberger, *J. Am. Leather Chem. Assoc.*, **31**, 93 (1936).
(10) Abramson, Moyer and Voet, THIS JOURNAL, **58**, 2362 (1936).
(11) Hitchcock and Taylor, *ibid.*, **59**, 1812 (1937).
(12) Highberger, *J. Am. Leather Chem. Assoc.*, **31**, 345 (1936).
(13) Beek, *J. Research Natl. Bur. Standards*, **21**, 117 (1938).

tive observations on a sample of standard hide powder[14] showed it to be isoelectric in the neighborhood of *p*H 5.

Discussion

Wilson has interpreted the two critical points, at *p*H values of 4.7 and 7.7, as the respective isoelectric points of the gel and the sol forms of collagen and gelatin.[15] The fact that the collagen used in the present work received only a mild alkaline treatment with half-saturated calcium hydroxide solution in the course of its preparation, while commercial hide powder and gelatin are given a much more drastic alkaline treatment, suggests that the isoelectric point of native collagen is near *p*H 7.8, and that treatment with alkaline solutions causes some structural change the effect of which is to lower the isoelectric point of the collagen and of the gelatin made from it.[16] The work of Briefer,[17] who found that gelatin made from alkaline pretreated collagen possesses minimum jelly consistency and maximum turbidity at about *p*H 5, while that made from acid pretreated collagen has similar properties at about *p*H 8, is recalled in this connection.

In addition to its unusually small slope, the curve of Fig. 1 displays a further feature of interest when compared to similar curves for other proteins. The curvature in such cases, while slight, is usually convex in the region of positive mobilities and concave in the negative. Just the opposite relations are found in the curve of Fig. 1. No explanation of this difference in shape, which is undoubtedly related to the mode of linkage of the polar groups of the protein, will be attempted at this time. Further work on the cause of the shift in the isoelectric points of collagen and gelatin is in progress in this Laboratory.

The author wishes to acknowledge the valuable assistance of Dr. H. J. Kersten in mounting the vertical microelectrophoresis cell. The cell itself was made by Mr. J. D. Graham of Haddonfield, New Jersey, to whom the author's thanks are also due.

Summary

The isoelectric point of collagen prepared from steer hide with a minimum alkaline treatment has been shown, by measurements of electrophoretic mobility, to be at *p*H 7.8 in buffers of ionic strength 0.005. It is suggested that the shift of the isoelectric point to *p*H 4.7 in the case of commercial gelatin and hide powder is due to some structural change in the protein caused by the alkaline treatment given these materials.

CINCINNATI, OHIO RECEIVED MAY 17, 1939

(14) Kindly furnished by Mr. Louis Cuthbert of The Standard Hide Powder Mfg. Co., Ridgway, Penna.

(15) For further discussion and references see J. A. Wilson, "The Chemistry of Leather Manufacture," Vol. I, The Chemical Catalog Company, New York, N. Y., 1928.

(16) After the completion of this work a paper on the electrophoresis of collagen was presented by Beek and Sookne at the meeting of The American Leather Chemists Association at Shawnee-on-Delaware, Penna., June 7, 1939. Using a horizontal cell and buffers of ionic strength 0.02, they located the isoelectric point of collagen similar to that used in the present work at about *p*H 7, and attributed the shift to a more acid value in the case of commercial gelatins to the hydrolysis of the amide groups during the liming treatment.

(17) Briefer, *Ind. Eng. Chem.*, **21**, 266 (1929).

[CONTRIBUTION FROM CALIFORNIA FRUIT GROWERS EXCHANGE RESEARCH DEPARTMENT]

A Study of the Boric Acid Color Reaction of Flavone Derivatives

BY C. W. WILSON[1]

It was observed in this Laboratory that lemon juice dried in the presence of boric acid produced a brilliant yellow color. Later the color reactive substance was identified as a constituent of Szent-Györgyi's citrin.[2]

This color reaction is sufficiently sensitive to detect 0.004 mg. of citrin or 0.002 mg. of quercitrin in 0.5 ml. of solution. The work here reported is an attempt to determine the specificity of the boric acid color reaction.

Experimental

Several representative flavones[3] and flavanones were purified by recrystallization from dilute alcohol at least three times. Table I shows the structural formulas of some of these substances and their boric acid color reactions.

The hydroxychalcones shown in Table I were prepared by alkaline treatment of naringin and hesperidin. A suspension of 2 g. of naringin or hesperidin with 25 ml. of water was placed in a 50-ml. flask equipped with a stopcock, the flask

(1) Corona Laboratory of California Fruit Growers Exchange, Research Department.

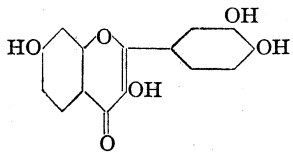
(2) Armentano, Bentsath Beres, St. Rusznyak and Szent-Györgyi, *Deut. med. Wochschr.*, **62**, 1326 (1936).

(3) The flavones used in this work were obtained by Mr. A. J. Lorenz from Dr. C. E. Sando of the U. S. Bureau of Chemistry and Soils.

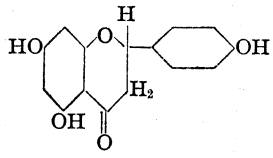
TABLE I

CONFIGURATION OF VARIOUS ORGANIC SUBSTANCES, AND CORRELATION WITH BORIC ACID COLOR REACTION

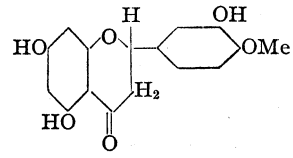
NEGATIVE REACTIONS



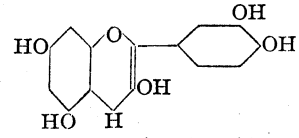
Fisetin



Naringenin

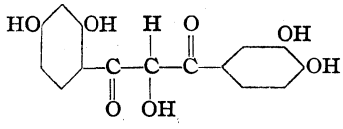


Hesperetin

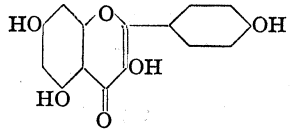


Cyanidin (as glycoside from apple)

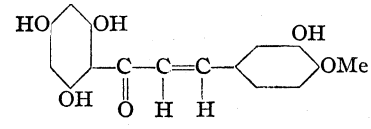
POSITIVE REACTIONS



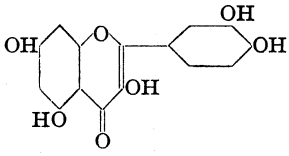
Alkali treated fisetin



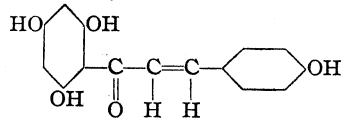
Kaempferol



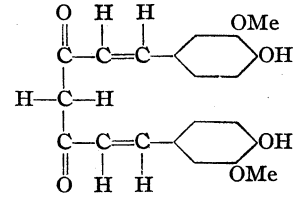
2′,4′,5,6′-Tetrahydroxy-4-methoxychalcone (from hesperetin)



Quercetin



2′,4,4′,6′-Tetrahydroxychalcone (from naringenin)



Curcumin. The positive color is pink and not confusable with the flavone color

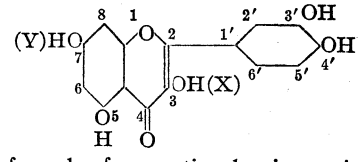
evacuated until the liquid boiled and the stopcock then closed. Into the flask was drawn 25 ml. of 2.5 *N* sodium hydroxide solution. The dark reddish solution was mixed thoroughly and allowed to stand for twenty-four hours at room temperature. It was then poured into 12.5 ml. of 5 *N* hydrochloric acid. The very slightly acid solution was evaporated to dryness in vacuum, and the hydroxychalcone extracted from the residue with absolute methyl alcohol.

The compounds so obtained were water soluble, orange powders.

The reagent used for determining the boric acid reactivity of a compound was made by mixing equal parts of two separate solutions, one composed of 100 ml. of absolute acetone saturated with boric acid, and the other 100 ml. of absolute acetone containing 10 g. of anhydrous citric acid.[4] Sufficient of the mixed solutions was prepared for each day's requirements, since it was found that while each solution was stable indefinitely, a very slow color formation took place in the acidified boric acid solution. This color was sometimes observable after as short an interval as two days.

For carrying out the determination of reactivity, approximately 0.5 mg. of the flavone derivative or other substance was dissolved in about 1 ml. of dry acetone, and the solution divided into two equal portions. To one portion was added about 2 ml. of the boric acid–citric acid–acetone reagent, and the other portion was diluted to an equal volume with a mixture of equal parts of the citric acid–acetone solution and acetone. The colors of the two tubes were compared at the end of a few minutes, and any definitely stronger color in the boric acid containing tube was reported in Table I as a positive reaction.

In addition to testing the aglycones (non-sugar parts) shown in Table I, the effect of the presence of sugar groups was checked by comparing the reactivity of two of the glycosides of quercetin; isoquercitrin (sugar group in the position marked X)[5] and quercimeritrin (sugar group in the position marked Y). With quercetin all three gave positive reactions. In these cases, the presence or position of the sugar group was without influence.



Structural formula of quercetin, showing position of sugar group in isoquercitrin (X) and quercimeritrin (Y)

(4) Made by allowing crystalline acid to effloresce completely in air at 30–40°, then heating in a thin layer to 100° for two hours.

(5) Attree and Perkin, *J. Chem. Soc.*, 234–240 (1927).

Since treatment of naringenin and hesperetin with dilute sodium hydroxide caused formation of a substance that gave a positive reaction with the borocitric acid reagent, it was decided to try the effect of the same treatment on fisetin. In this case, also, a positive reacting compound was formed.

Hesperetin heated with 1 volume of concentrated hydrochloric acid in 2 volumes of alcohol formed an orange solution which was carefully neutralized with sodium hydroxide solution and the liquid was evaporated over a steam-bath. The residue was extracted with acetone, and the extract gave a positive reaction with borocitric acid reagent.

U. S. P. tannic acid gave no reaction when treated directly with the borocitric acid reagent, nor after alkaline or acid treatment as described above.

Other substances not shown in Table I but tested in view of their possible occurrence in nature with flavones gave negative reactions. These included coumarin, coumarinic acid, dextrose, alkali treated dextrose, phloroglucinol, quinhydrone, salicylic acid, sucrose, and alkali treated sucrose.

Discussion of Results

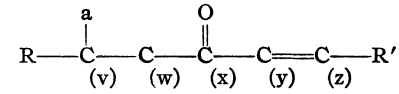
Of the flavone derivatives tested, the flavanones give no color reaction with boric acid, whereas all of the flavones except fisetin gave a reaction. With this one exception, if a substance is established as being a flavone or a flavanone by the cyanidin test, but does not give a color with borocitric acid reagent, the supposition would be that it was a flavanone.

Comparing the lack of reaction of fisetin with the reactivity of quercetin, the importance of the hydroxyl (or some other auxochromic) group in the 5-position is evident.

Comparing the reactivity of kaempferol with the lack of reactivity of naringenin leads to the speculation of whether the OH in the 3-position or the double bond between the 2 and 3 carbon atoms is responsible for the difference.

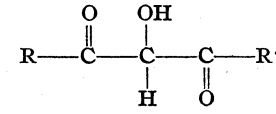
Opening the pyran ring to give the equivalent chalcone definitely establishes the importance of the double bond, and indicates that the pyran ring is unnecessary for color formation.

The configuration of a chalcone suggests that of curcumin, and causes one to feel that the color formation of curcumin with boric acid under similar conditions may be further indicative of the configuration required. If this reactivity is comparable, the benzene ring near the ketone (or quinone) group is unnecessary provided an auxochromic group is attached to the second carbon atom from the C=O group. The indicated configuration for reactivity is

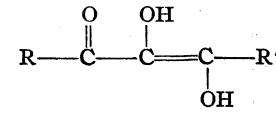


in which "a" is an auxochromic group which may probably be =O, OH, OCH_3, etc., and in which R, C_v and C_w may form a benzene ring, and C_x, C_y and C_z may form a portion of a pyran ring. In all of this work, R′ has been a benzene ring containing either methoxyl or hydroxyl groups.

When the pyran ring of fisetin is opened by treatment with an alkali, the formation of the hydroxyl group in the ortho position on one of the benzene rings fulfils the boric acid color forming requirement of having an OH (or other auxochromic) group on the second carbon atom from a C=O group. The double bond between carbon atoms on the other side of the C=O group is missing in the formula shown in Table I. Compounds of this type, however, are known to exist at least to some extent in enolic forms,[6] and instead of



the enolic form would be



which, when R and R′ have the proper configurations, as is the case in the present instance, would be expected to yield the observed coloration.

Another possible explanation is that in the alkali treatment of the fisetin there are formed other secondary compounds responsible for the color reaction.

Acknowledgment.—The author wishes to express his appreciation to the California Fruit Growers Exchange for the opportunity to carry on and publish this work and to Mr. W. E. Baier, Manager of the Research Department, for his suggestions and interest.

(6) A. M. Buswell, W. H. Rodebush and M. F. Roy, THIS JOURNAL, **59**, 1767 (1937).

Summary

Citrus juices have been observed to give a yellow color when dried with boric acid.

This yellow color forming substance is concentrated in the citrin fraction of Szent-Györgyi.

Many flavone derivatives have been found to give the color reaction. Of non-flavone substances commonly found in plant tissues, none have so far been found to give a confusable color reaction.

The color reaction has been correlated with molecular constitution.

ONTARIO, CALIF. RECEIVED MAY 2, 1939

[CONTRIBUTION FROM THE AVERY LABORATORY OF CHEMISTRY OF THE UNIVERSITY OF NEBRASKA]

Organoselenium Compounds. I. Diphenylselenium Dihydroxides and Diphenylselenides

BY C. KENNETH BANKS[1] AND CLIFF S. HAMILTON

In order to investigate some of the therapeutic properties of organoselenium compounds, a series of compounds in which the effect of the valence of selenium could be studied, as well as the effect of changes in substituent groups, was prepared. This paper deals with some of the derivatives of diphenylselenium dihydroxide and diphenylselenide derived from the phenoxyalkanols, as these compounds have led to some therapeutically valuable arsenicals.

The reaction of Alquist and Nelson[2] and Kunckell[3] by which anisole and its homologs were condensed with selenium oxychloride to give *bis*-(*p*-alkyloxyphenyl)-selenium dichlorides was extended to three other ethers, β-phenoxyethanol, γ-phenoxypropanol and α-methyl-β-phenoxyethanol. The first two gave ether insoluble gums, while the last gave a crude crystalline mass. The crude products were purified by dissolving in chloroform, treatment with activated charcoal and "Celite," and reprecipitation with benzene. By means of this procedure all three crystallized in stable forms. The dichlorides hydrolyzed to the dihydroxides in the presence of sodium carbonate, all three of which were white crystalline solids.

The above dihydroxides, as well as *bis*-(4-methoxyphenyl)-selenium dihydroxide, were then nitrated using fuming nitric acid (sp. gr. 1.5) at 0° as the nitrating agent. A large excess of acid was required for complete nitration, probably due to the formation of an alcohol dinitrate of the dinitrodietherdiphenylselenium dinitrate. The gum formed when the nitration mixture was poured over ice was solidified by neutralizing the excess acid with sodium carbonate and boiling. These compounds proved to be of the formula *bis*-(3-nitro-4-R-phenyl)-selenium dihydroxide, R representing the ether group. The position of the nitro group was shown by cleaving with hydriodic acid, giving *o*-nitrophenol.

The nitro compounds were reduced catalytically to the diamines, using Raney catalyst.[4] At 40 pounds (2.67 atm.) pressure and room temperature the selenium was also reduced. The amines were of the general formula *bis*-(3-amino-4-R-phenyl) selenide.

Of theoretical interest was the extension of the reaction to another type of compound, acetanilide. The reaction was first tried in ether but it was found that the product was a double salt of acetanilide and selenium oxychloride. As the salt was soluble in chloroform, the reaction was run in that medium. After five days, a thick gum separated. This gum was hydrolyzed with sodium carbonate, giving a water insoluble white compound which, on purification, proved to be *bis*-(4-acetaminophenyl)-selenium dihydroxide. This compound was reduced to the corresponding diphenyl selenide and then hydrolyzed to the free amine. The last two compounds have been prepared by Theobald[5] from sulfonamide and selenic acid. The acetylated compound was obtained in two crystalline modifications, one melting at 216° as reported by Theobald, the other at 176°. The two forms were chemically identical.

Experimental

1. Diphenylselenium Dichlorides.—One-half mole of the aromatic ether was treated with selenium oxychloride according to the procedure of Alquist and Nelson.[2] The solvent was decanted from the gum or crystals formed and

(1) Parke, Davis and Company Fellow.

(2) F. N. Alquist and R. E. Nelson, THIS JOURNAL, **53**, 4033 (1931).

(3) Kunckell, *Ber.*, **28**, 609 (1895).

(4) M. Raney, U. S. Patent 1,628,190 (1927).

(5) E. Theobald and P. Theobald, French Patent 794,192 (1936); German Patents 631,100, 631,570, 631,571, 631,572, 632,073, 633,344 (1936).

TABLE I

	Compound	Color	M. p., °C.	% Yield	Formula	% Se Calcd.	% Se Found
1	*bis*-(4-Methoxyphenyl)-selenium dichloride	Yellow	163	84	.....	..	..
2	*bis*-(4-β-Hydroxyethoxyphenyl)-selenium dichloride	Yellow	172	74	$C_{16}H_{18}O_4Cl_2Se$	18.6	18.7
3	*bis*-(4-γ-Hydroxypropoxyphenyl)-selenium dichloride	Yellow	159	66	$C_{18}H_{22}O_4Cl_2Se$	17.5	17.5
4	*bis*-(4-β-Hydroxypropoxyphenyl)-selenium dichloride	Yellow	147	80	$C_{18}H_{22}O_4Cl_2Se$	17.5	17.4
5	*bis*-(4-Methoxyphenyl)-selenium dihydroxide	White	134	90	.....	..	..
6	*bis*-(4-β-Hydroxyethoxyphenyl)-selenium dihydroxide	White	99	78	$C_{16}H_{20}O_6Se$	20.4	20.5
7	*bis*-(4-γ-Hydroxypropoxyphenyl)-selenium dihydroxide	White	140	67	$C_{18}H_{24}O_6Se$	19.0	19.1
8	*bis*-(4-β-Hydroxypropoxyphenyl)-selenium dihydroxide	White	56	63	$C_{18}H_{24}O_6Se$	19.0	19.1
9	*bis*-(3-Nitro-4-methoxyphenyl)-selenium dihydroxide	Cream	203	95	$C_{14}H_{14}O_8N_2Se$	18.9	19.0
10	*bis*-(3-Nitro-4-β-hydroxyethoxyphenyl)-selenium dihydroxide	Cream	175	84	$C_{16}H_{18}O_{10}N_2Se$	16.6	16.5
11	*bis*-(3-Nitro-4-γ-hydroxypropoxyphenyl)-selenium dihydroxide	Yellow	117	62	$C_{18}H_{22}O_{10}N_2Se$	15.6	15.7
12	*bis*-(3-Nitro-4-β-hydroxypropoxyphenyl)-selenium dihydroxide	Yellow	128	52	$C_{18}H_{22}O_{10}N_2Se$	15.6	15.7
13	*bis*-(3-Amino-4-methoxyphenyl) selenide	White	112	>90	$C_{14}H_{16}O_2N_2Se$	23.8	23.9
14	*bis*-(3-Amino-4-β-hydroxyethoxyphenyl) selenide	White	132	>90	$C_{16}H_{20}O_4N_2Se$	22.2	22.3
15	*bis*-(3-Amino-4-γ-hydroxypropoxyphenyl) selenide	Pink	104	>90	$C_{18}H_{24}O_4N_2Se$	20.6	20.5
16	*bis*-(3-Amino-4-β-hydroxypropoxyphenyl) selenide	Brown	128	>90	$C_{18}H_{24}O_4N_2Se$	20.6	20.6
17	Dihydrochloride of 13	White	>250	78	$C_{14}H_{16}O_2N_2Se \cdot 2HCl$	20.1	20.0
18	Selenium oxychloride salt of acetanilide	White	135	80	$(C_8H_9N)_2 \cdot SeOCl_2$	18.1	18.0
19	*bis*-(4-Acetaminophenyl)-selenium dihydroxide	White	223	90	$C_{16}H_{18}O_4N_2Se$	20.6	20.5
20	*bis*-(4-Acetaminophenyl) selenide	White	176, 216	>90	$C_{16}H_{16}O_2N_2Se$	22.7	22.7
21	*bis*-(4-Aminophenyl) selenide	White	117	60	$C_{12}H_{12}N_2Se$	30.0	29.9

purified by solution in chloroform, treatment with activated charcoal and "Celite" and reprecipitation with benzene.

2. Diphenylselenium Dihydroxides.—The above dichlorides (0.2 mole) were added to an excess of sodium carbonate in water (30 g. in 200 ml.) and the mixture heated for half an hour. On cooling, if the dihydroxide crystallized, it was filtered off; if it remained an oil, the water was decanted, fresh water added, heated and cooled. This was repeated until a solid was obtained. The crude dihydroxides were recrystallized from ethyl alcohol.

3. Nitro Compounds.—The dihydroxide was added slowly with stirring to fuming nitric acid (sp. gr. 1.5) at 0° (0.025 mole to 25 ml. of acid). After the addition was complete, the stirring was continued for fifteen minutes and the nitration mixture then poured over chipped ice. Water was added and the acid neutralized with an excess of sodium carbonate. The mixture was boiled and then cooled. The nitro compounds solidified on stirring. The methoxy and γ-hydroxypropoxy compounds were recrystallized from ethyl alcohol, the β-hydroxyethoxy compound from ethyl cellosolve and the β-hydroxypropoxy compound from methyl cellosolve.

4. Amines.—The nitro compounds were suspended in ethyl alcohol (10 g. in 50 ml.), Raney nickel prepared by the method of Adkins[6] was added and the reduction carried out with electrolytic hydrogen at 40 pounds (2.67 atm.) pressure and room temperature. The solution and suspended amine were removed from the reduction container, heated to boiling and the catalyst filtered off. Most of the alcohol was removed by evaporation under reduced pressure, water and hydrochloric acid added and the solution decolorized with charcoal. The amine was then precipitated with ammonium hydroxide. Water–alcohol mixtures were used to recrystallize the amines.

5. *bis*-(3-Amino-4-methoxyphenyl) Selenide Dihydrochloride.—The corresponding amine (10 g.) was dissolved in an excess of 6 *N* hydrochloric acid and the solution evaporated until precipitation started to occur while hot. On cooling the hydrochloride crystallized out; yield 9.5 g.

6. Double Salt of Acetanilide and Selenium Oxychloride.—Eight grams of acetanilide was dissolved in 200 ml. of dry ether and an equal weight of selenium oxychloride added with shaking. A white precipitate formed almost immediately. It was purified by solution in chloroform and reprecipitation with ligroin.

7. *bis*-(4-Acetaminophenyl)-selenium Dihydroxide.—One-fifth mole of acetanilide was treated with selenium oxychloride in chloroform as in procedure 1. The excess solvent was decanted from the gum formed, an excess of sodium carbonate in water was added and the temperature raised to the boiling point. The solution was filtered hot, removing any excess acetanilide. The precipitate was dissolved in alcohol, decolorized with charcoal and reprecipitated with water.

8. *bis*-(4-Acetaminophenyl) Selenide.—Ten grams of the dihydroxide was dissolved in warm alcohol, Raney catalyst added, and the reduction carried out under the same conditions as for the reduction of nitro compounds. After the reduction was complete, the catalyst was removed and the solution reduced in volume, and water was added, precipitating the diphenyl selenide. The product was recrystallized from a water–alcohol mixture.

9. *bis*-(4-Aminophenyl) Selenide.—Ten grams of the above product was refluxed with 100 ml. of 20% hydrochloric acid. When all the material had gone into solution, the solution was charcoaled and filtered. On cooling and making basic with sodium hydroxide, the amine precipitated.

Analytical

A modification of the method of Arne Fredga[7] was used in determining the percentage of selenium. A tenth-gram sample was digested with 5 ml. of concd. sulfuric acid until it was well charred. Fuming nitric acid was added (about 1 ml.) until the solution cleared. The excess nitric acid was boiled off, the digestion transferred to a beaker containing 50 ml. of water and the whole diluted to 150 ml. Hydrazine sulfate was added and the solution heated on a hot-plate until the precipitated selenium coagulated. The precipitate was collected in a semi-

(6) Covert and Adkins, THIS JOURNAL, **54**, 4116 (1932).

(7) A. Fredga, *Uppsala Univ. Arsskrift*, No. 5, 232 (1935).

micro sintered glass crucible containing a thin layer of asbestos. After washing well with water, alcohol and ether, the crucible was dried and weighed on a semi-micro balance. The nitric acid must not be added until the compound is well charred or polynitro compounds resisting digestion will be formed. The precision of this method of analysis is ±0.0%.

Summary

1. Three new *bis*-(4-hydroxyalkyloxyphenyl)-selenium dichlorides and their corresponding dihydroxides were prepared by the condensation of selenium oxychloride with mixed ethers.

2. The dinitro derivatives of the above compounds and the corresponding methoxy compound were obtained. These compounds were reduced catalytically to the *bis*-(3-amino-4-R-phenyl) selenide.

3. The condensation of selenium oxychloride with benzene derivatives was extended to acetanilide, resulting in *bis*-(4-acetaminophenyl)-selenium dihydroxide. On reduction, *bis*-(4-acetaminophenyl) selenide was formed. The corresponding amine also was prepared.

LINCOLN, NEBRASKA RECEIVED MAY 8, 1939

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

Studies in the Sitosterol Complex. The Structure of α_1-Sitosterol

BY SEYMOUR BERNSTEIN[1] AND EVERETT S. WALLIS

In their experiments on α-sitosterol, Wallis and Fernholz[2] showed that this material first described as a compound by Anderson and his coworkers[3] was in reality a mixture of at least two new sterols, α_1- and α_2-sitosterol.

Besides recording the physical properties of these two new compounds and their derivatives, these investigators[2] made the following observations. Neither α_1- nor α_2-sitosterol are isomers of β- and γ-sitosterol. α_1-Sitosterol is an isomer of stigmasterol, $C_{29}H_{48}O$, and α_2-sitosterol is in all probability a homolog, $C_{30}H_{50}O$. By titration with perbenzoic acid they showed that two double bonds are present in both sterols. They give the same Liebermann color reaction. The final color is a dark blue with a reddish tint. The Salkowski reaction for both α_1- and α_2-sitosterol was found to be similar to that of ergosterol, the sulfuric acid layer becomes colored, while the chloroform stays colorless. The opposite is true for cholesterol, γ-sitosterol and stigmasterol. They also noted that both α_1- and α_2-sitosterol are precipitated by digitonin.

In this paper we wish to report the results of further experiments on α_1-sitosterol which to us seem pertinent to the elucidation of its structure. That the two double bonds in α_1-sitosterol are not conjugated was shown by an absorption spectrum study. No maxima were observed. It is also to be noted that α_1-sitosterol does not form an addition compound with maleic anhydride. Taken together these two facts indicate that this sterol cannot have its double bonds conjugated within one ring or between two adjacent rings.

The results which we obtained from a hydrogenation study on α_1-sitosterol are of special interest. From preliminary experiments we learned that only one of the two double bonds can be hydrogenated under ordinary conditions. If the hydrogenation, however, be carried out at a higher temperature (65–70°) in the presence of a small amount of concentrated hydrochloric acid, complete saturation is possible. It was further observed that the double bond originally resistant to hydrogenation can be isomerized by dry hydrogen chloride into a position which is easy to hydrogenate under ordinary conditions.

With the above facts in mind, α_1-sitosteryl acetate (I) was hydrogenated with a platinum catalyst at room temperature and atmospheric pressure. As a result, α_1-dihydrositosteryl acetate (II) was obtained. This acetate was then isomerized in a chloroform solution with dry hydrogen chloride at 0°. A new acetate, α_1-isodihydrositosteryl acetate (III), was isolated and characterized. On hydrogenation at room temperature and atmospheric pressure this compound gave a completely saturated acetate, α_1-sitostanol acetate (IV). This same substance was also obtained when α_1-sitosteryl acetate was hydrogen-

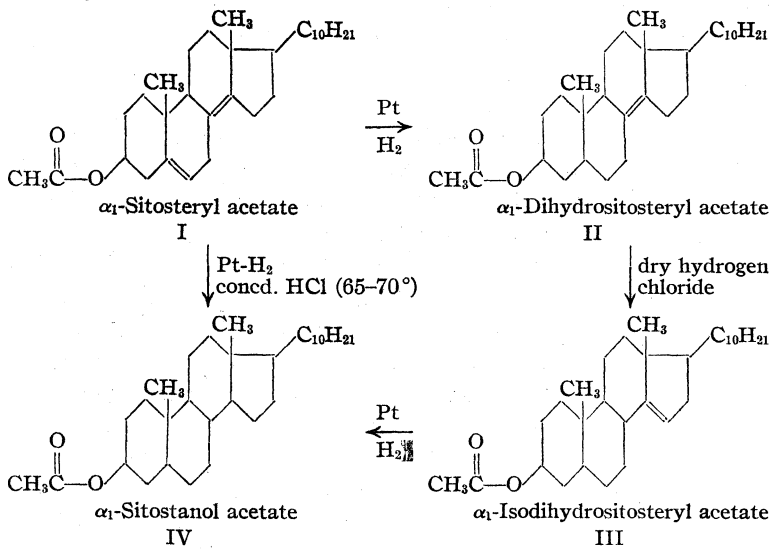
(1) Research Assistant on Special Funds from the Rockefeller Foundation.

(2) Wallis and Fernholz, THIS JOURNAL, **58**, 2446 (1936).

(3) Anderson, Shriner and Burr, *ibid.*, **48**, 2987 (1926); see also Anderson, *ibid.*, **46**, 1450 (1924).

ated with a platinum catalyst at 65–70°, and at atmospheric pressure in the presence of a small amount of concentrated hydrochloric acid.

These results may be explained as follows



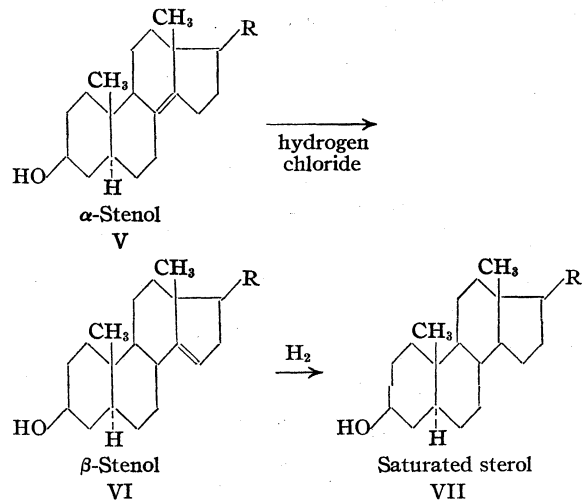
In Table I there are also listed the properties of α_1-sitosterol and its various hydrogenation products.

TABLE I

Compound	M. p., °C.	$[\alpha]_D$(CHCl3)
α_1-Sitosteryl acetate	137	+29
α_1-Sitosterol	164–166	− 1.7
α_1-Dihydrositosteryl acetate	108.5–110.5	+35.1
α_1-Dihydrositosterol	152–154.5	+10.9
α_1-Isodihydrositosteryl acetate	137.5–138.5	+42.0
α_1-Isodihydrositosterol	152–154	+31.0
α_1-Sitostanol acetate	147–148	+39.4
α_1-Sitostanol	185–186	+27.0

The structures which we have proposed for this sterol and its hydrogenation products may be supported by the following arguments. All natural sterols whose structures are known have been found to have an hydroxyl at the C_3-position. That the hydroxyl group in α_1-sitosterol is *cis* to the C_{10} methyl group is supported by the formation of an insoluble digitonide, a characteristic property of all sterols of this type. The proposed non-conjugation of the double bonds in α_1-sitosterol is supported by the negative Diels–Alder reaction and by the results of the absorption spectrum study. All natural sterols which are unsaturated have been found to have one double bond at the 5,6-position. It is also to be recalled that a $\Delta^{5,6}$-sterol is hydrogenated easily. One double bond in α_1-sitosterol is hydrogenated easily under ordinary conditions.

The fact that the second double bond in α_1-sitosterol is resistant to hydrogenation but can be isomerized into a position in which it can be hydrogenated easily is a phenomenon not unknown in sterol chemistry. The naturally non-occurring sterols α-ergostenol[4] (V) and α-cholestenol[5] (V) have been found to be resistant to hydrogenation under ordinary conditions but can be isomerized with dry hydrogen chloride to give β-ergostenol (VI) and β-cholestenol (VI), respectively. These products then can be hydrogenated easily to give the corresponding saturated compounds (VII). The fact that the cholestanol obtained from α-cholestenol by this method is identical

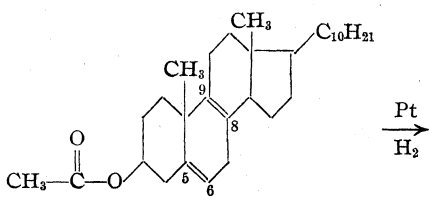


with the cholestanol obtained by hydrogenation of cholesterol shows that rearrangement with hydrogen chloride and subsequent hydrogenation do not produce epimerization at any asymmetric center. Therefore it may be argued that rearrangement of α_1-dihydrositosterol and subsequent hydrogenation, likewise, does not produce any epimerization. If such be the case, it therefore follows that α_1-sitostanol and stigmastanol differ solely due to isomerism of the hydrocarbon side chain.

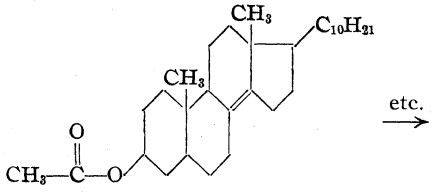
(4) Reindel, Walter and Rauch, *Ann.*, **452**, 34 (1927); Reindel and Walter, *ibid.*, **460**, 212 (1928); Achtermann, *Z. physiol. Chem.*, **225**, 141 (1934); Laucht, *ibid.*, **237**, 236 (1935).

(5) (a) Schenck, Buchholz and Wiese, *Ber.*, **69B**, 2696 (1936), (b) Windaus, Linsert and Eckhardt, *Ann.*, **543**, 22 (1938).

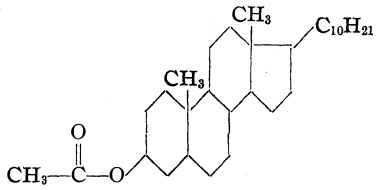
In this connection it should be recalled that a δ-stenol, such as δ-cholestenol, also has been found to be resistant to hydrogenation, and that during the course of attempted hydrogenation with palladium it is converted into the α-stenol[5b] modification. Hence the possibility presents itself that α_1-sitosterol may be in reality unsaturated at the 5,6- and 8,9-positions. The course of hydrogenation would then become



α_1-Sitosteryl acetate



α_1-Dihydrositosteryl acetate



α_1-Sitostanol acetate

Against this formulation may be cited our observation that in our hands α_1-sitosteryl acetate does not give a ketone at C_7 on oxidation with chromic acid, as would be expected if its double bonds were located at the 5,6- and 8,9-positions.

TABLE II

Unsaturated at $\Delta^{5,6}$	$[\alpha]_D$ ($CHCl_3$)	Saturated at $\Delta^{5,6}$	$[\alpha]_D$ ($CHCl_3$)
Stigmasterol	−45°	Stigmastanol	+23.8
β-Sitosterol	−37°		
α_1-Sitosterol	− 1.7°	α_1-Sitostanol	+27.0

Our assignment of the positions of the double bonds in α_1-sitosterol and its intermediate hydrogenation products may be strengthened further by considering the relation of optical rotatory power and constitution.[6] It has been observed, qualitatively, that a compound unsaturated at the 5,6-position always will have a levo or a lower dextro rotation than the corresponding saturated compound which will always have an appreciable dextro-rotation. α_1-Sitosterol fits very well into this observation, as may be seen in Table II.

That α_1-dihydrositosterol and α_1-isodihydrositosterol are α- and β-stenols, respectively, is likewise indicated by a qualitative interpretation of the optical activity of these compounds. An α-stenol, in general, will have a positive rotation lower in degree than the corresponding saturated compound. A β-stenol will, in general, have a positive rotation, higher in degree than the corresponding saturated compound. These two statements are borne out by Table III.

Further evidence for the proposed structure of α_1-isodihydrositosteryl acetate (III) (which is represented as a β-stenol) has also been obtained. We have found that if α_1-isodihydrositosteryl acetate be treated with perbenzoic acid, an oxide (VIII) is obtained. Hydrolysis of the oxide ring with glacial acetic acid and concentrated sulfuric acid gives a doubly unsaturated compound (IX), and not a triol diacetate (X).

The formation of this doubly unsaturated compound from the oxide is in accordance with the experimental observations of other investigators on similar compounds. For example, Morrison and Simpson[7] have found that when β-ergostenol oxide (XI) is dissolved in hot ethyl alcohol and treated with dilute sulfuric acid with subsequent heating for fifteen minutes on the steam-bath, a doubly unsaturated sterol, dehydroergostenol (XII), is produced. They[8] also have reported that α-ergostenol oxide (XIII) under similar treatment gives the same dehydroergostenol. Since Callow[9] has shown experimentally that the most probable formula for this latter doubly un-

TABLE III

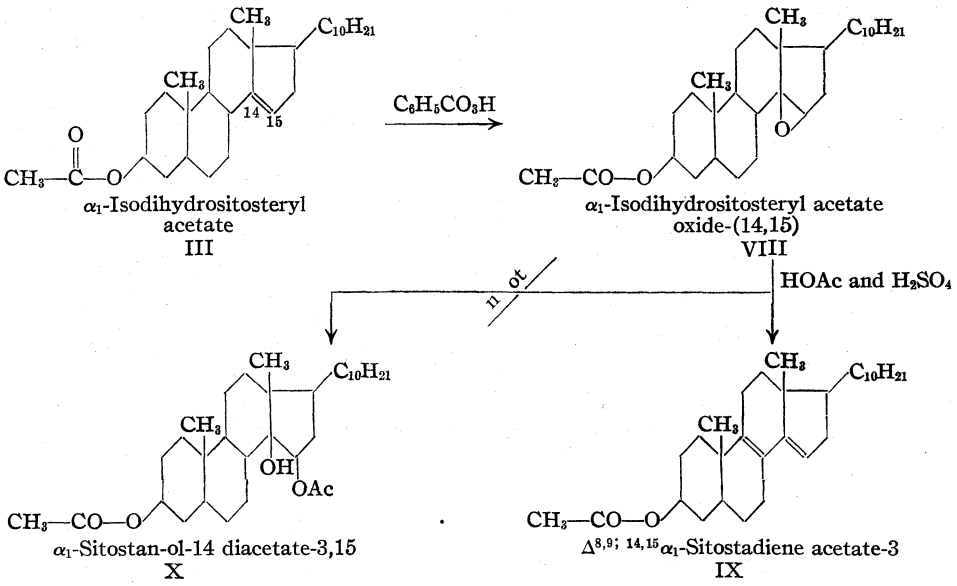
α-Stenol	$[\alpha]_D$ ($CHCl_3$)	β-Stenol	$[\alpha]_D$ ($CHCl_3$)	Satd. sterol	$[\alpha]_D$ ($CHCl_3$)
α-Ergostenol	+13.1	β-Ergostenol	+20.3	Ergostanol	+15.5
α-Ergostene	+11.0	β-Ergostene	+21.3	Ergostane	+19.0
α-Cholestenol	+20.7	β-Cholestenol	+34.0	Cholestanol	+29.7
α_1-Dihydrositosterol	+10.9	α_1-Isodihydrositosterol	+31.0	α_1-Sitostanol	+27.0

(6) Callow and Young, *Proc. Roy. Soc.* (London), **A157**, 194 (1936).

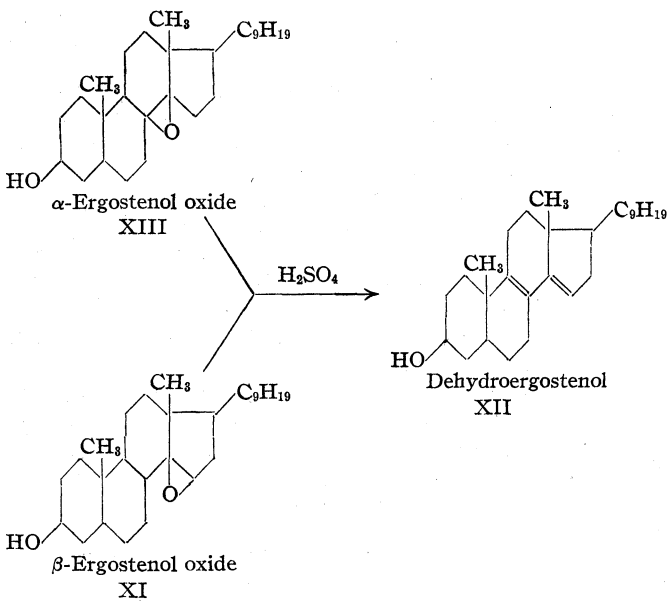
(7) Morrison and Simpson, *J. Chem. Soc.*, 1710 (1932).

(8) Ref. 7; see also Windaus and Luttringhaus, *Ann.*, **481**, 119 (1930).

(9) Callow, *J. Chem. Soc.*, 462 (1936).



saturated sterol is as indicated below, it follows that the doubly unsaturated compound obtained by us from α_1-isodihydrositosteryl oxide is to be represented as given and therefore is, accordingly, $\Delta^{8,9;\ 14,15}$ α_1-sitostadiene acetate-3.



Experimental Part

Preparation of α_1-Sitosteryl Acetate.—Two and one-half grams of α_1-sitosterol (m. p. 159–166°) isolated from the sitosterol complex (1627 g.) of wheat germ oil by the method of Wallis and Fernholz[2] was heated on the water-bath for one hour with acetic anhydride. Crystallization from methyl alcohol gave 2 g. of α_1-sitosteryl acetate, m. p. 136–137°.

The Reaction of α_1-Sitosteryl Acetate with Maleic Anhydride (Diels–Alder Reaction).—A mixture of 50 mg. of α_1-sitosteryl acetate, 20 mg. of maleic anhydride and 10 cc. of acetic anhydride was refluxed for eight hours. During this time a brown coloration appeared. The reaction mixture was evaporated to dryness *in vacuo*. The residue was crystallized from ethyl alcohol and gave a material melting at 137–138°. A mixed melting point determination with α_1-sitosteryl acetate (136–137°) indicated identity since no depression was observed.

The Diels–Alder reaction was repeated, with xylene as the solvent. The starting material was again recovered and no indication of a positive addition reaction was observed.

An absorption spectrum study of α_1-sitosterol (m. p. 166°) was carried out by Dr. T. J. Webb of the Research Laboratories, Merck and Company, Inc. It was found not to have any maxima in the ultraviolet region of the spectrum.

Hydrogenation of α_1-Sitosteryl Acetate at 60° and Atmospheric Pressure.—One-tenth of a gram of α_1-sitosteryl acetate dissolved in glacial acetic acid was hydrogenated for five hours at 60° and atmospheric pressure, with a previously reduced platinum catalyst prepared according to Adams. The catalyst was then filtered off and the acetic acid was removed by vacuum distillation. After four crystallizations from ether and methyl alcohol needles were obtained which melted at 107–108°, $[\alpha]^{25}D$ +36.6° (0.0191 g. in 2 cc. of chloroform solution gave $\alpha^{25}D$ +0.35°). The Liebermann test was positive. The Salkowski test was similar to that for ergosterol, α_1- and α_2-sitosterol; the chloroform layer was colorless, while the sulfuric acid layer became colored.

Hydrogenation of α_1-Sitosteryl Acetate at 65–70° in the Presence of Concentrated Hydrochloric Acid.—Two-tenths of a gram of α_1-sitosteryl acetate was dissolved in glacial acetic acid to which was added 0.5 cc. of concd. hydrochloric acid. It was then hydrogenated at 65–70° and atmospheric pressure for five and one-half hours with a platinum catalyst prepared according to Adams. The

catalyst was reduced in the presence of the sterol acetate. The hydrogenation mixture took up the calculated amount for the complete saturation of the two double bonds. The catalyst was filtered off, and the reaction mixture was evaporated to dryness *in vacuo*. The residue gave a negative Liebermann test. After several crystallizations from dilute alcohol needles were obtained which melted at 147–148°, $[\alpha]^{19}D$ +39.4 (0.0208 g. in 2 cc. of chloroform solution gave $\alpha^{19}D$ +0.41°).

Anal. Calcd. for $C_{31}H_{54}O_2$: C, 81.16; H, 11.87. Found: C, 80.89; H, 11.71.

Preparation of α_1-Sitostanol.—α_1-Sitostanol acetate was hydrolyzed by refluxing it for one hour with a 5% alcoholic solution of potassium hydroxide. The sterol was then worked up in ether in the usual manner. Recrystallization from dilute alcohol gave needles which melted at 185–186°, $[\alpha]^{25}D$ +27.0 (10.4 mg. in 2 cc. of chloroform solution gave $\alpha^{25}D$ +0.14).

Anal. Calcd. for $C_{29}H_{52}O$: C, 83.58; H, 12.58. Found: C, 83.71; H, 12.48.

Preparation of α_1-Dihydrositosteryl Acetate.—Nine hundred and sixty milligrams of α_1-sitosteryl acetate dissolved in glacial acetic acid was hydrogenated at room temperature and atmospheric pressure with 0.14 g. of a platinum catalyst prepared according to Adams. The catalyst was reduced in the presence of the sterol acetate. Only one mole of hydrogen was taken up, and the hydrogenation was complete in fifteen minutes. The catalyst was filtered off, and the solvent was evaporated *in vacuo*, leaving an oily residue which crystallized on cooling. Recrystallization from ethyl alcohol gave needles of m. p. 108.5–110.5° $[\alpha]^{20}D$ +35.1 (0.0442 g. in 5 cc. of chloroform solution gave $\alpha^{20}D$ +0.31°). The Liebermann test was positive. This material is identical with that obtained by hydrogenation of α_1-sitosteryl acetate at 60° and atmospheric pressure. A melting point determination showed no depression.

Anal. Calcd. for $C_{31}H_{52}O_2$: C, 81.52; H, 11.48. Found: C, 81.30; H, 11.33.

Preparation of α_1-Dihydrositosterol.—One hundred and two milligrams of α_1-dihydrositosteryl acetate was hydrolyzed by refluxing it on the water-bath with 5% alcoholic potash solution. The sterol was precipitated with water and filtered. Purification was obtained by crystallization from ethyl acetate and methyl alcohol; needles m. p. 152–154°, $[\alpha]^{20}D$ +10.9° (0.0238 g. in 2 cc. of chloroform solution gave $\alpha^{20}D$ +0.13°).

Anal. Calcd. for $C_{29}H_{50}O$: C, 83.98; H, 12.15. Found: C, 83.9; H, 11.9.

Acetylation of α_1-dihydrositosterol with acetic anhydride gave back α_1-dihydrositosteryl acetate, m. p. 108°. The melting point was not depressed by α_1-dihydrositosteryl acetate previously prepared by hydrogenation of α_1-sitosteryl acetate.

Preparation of α_1-Isodihydrositosteryl Acetate.—Dry hydrogen chloride was passed for two hours into a chloroform solution of α_1-dihydrositosteryl acetate kept at 0°. The reaction mixture was then evaporated to dryness *in vacuo*. The oily residue gave a negative Beilstein test. Since the residue had a slight coloration it was taken up in ether and decolorized with animal charcoal. Recrystallization from ethyl alcohol gave pure α_1-isodihydrositosteryl acetate in the form of plates m. p. 137.5–138.5°, $[\alpha]^{20}D$ +42.0° (0.0572 g. in 5 cc. of chloroform solution gave $\alpha^{20}D$ +0.48°).

α_1-Isodihydrositosteryl acetate gives a positive Liebermann test. It gives a depression of the melting point when intimately mixed with α_1-sitosteryl acetate (m. p. 136–137°).

Anal. Calcd. for $C_{31}H_{52}O_2$: C, 81.52; H, 11.48. Found: C, 81.4; H, 11.6.

Preparation of α_1-Isodihydrositosterol.—One hundred and thirty milligrams of α_1-isodihydrositosteryl acetate was hydrolyzed by refluxing it for one hour with a 5% alcoholic potash solution. The sterol was worked up in ether. Recrystallization from ethyl alcohol gave needles melting at 152–154°, $[\alpha]^{20}D$ +31.0° (0.0452 g. in 5 cc. of chloroform solution gave $\alpha^{20}D$ +0.28°). The melting point is depressed by α_1-dihydrositosterol.

Anal. Calcd. for $C_{29}H_{50}O$: C, 83.98; H, 12.15. Found: C, 83.7; H, 11.9.

Acetylation of a sample of α_1-isodihydrositosterol with acetic anhydride again gave back α_1-isodihydrositosteryl acetate, m. p. 137°.

Hydrogenation of α_1-Isodihydrositosteryl Acetate.—α_1-Isodihydrositosteryl acetate dissolved in glacial acetic acid was hydrogenated at room temperature and atmospheric pressure with a platinum catalyst prepared according to Adams. The catalyst was reduced in the presence of the sterol acetate. α_1-Sitostanol acetate was again obtained, m. p. 147°.

Preparation of α_1-Isodihydrositosteryl Acetate Oxide-(14,15).—Sixty-five milligrams of α_1-isodihydrositosteryl acetate (m. p. 137.5–139) was treated for ten days at room temperature with a large excess of a chloroform solution of perbenzoic acid. The reaction mixture was washed once with water, twice with dilute sodium hydroxide, and then with water until neutral. The chloroform solution was dried with anhydrous sodium sulfate, and evaporated to dryness *in vacuo*. The residue was crystallized from methyl alcohol. Needles were obtained which melted at 152–154°.

Anal. Calcd. for $C_{31}H_{52}O_3$: C, 78.76; H, 11.09. Found: C, 78.71; H, 10.97.

α_1-Isodihydrositosteryl acetate oxide was dissolved in dry pyridine and treated with acetic anhydride for one-half hour on the water-bath. The reaction mixture was worked up in ether in the usual manner. Recrystallization from methyl alcohol gave back the starting material, m. p. 152°.

Preparation of $\Delta^{3,9;14,15}$-α_1-Sitostadiene Acetate-3.—α_1-Isodihydrosteryl acetate oxide was treated with 1 cc. of glacial acetic acid and one small drop of concentrated sulfuric acid. The reaction mixture was warmed on the water-bath for a very short time to dissolve completely the oxide. The reaction mixture was allowed to stand at room temperature for twenty-four hours. Small needles separated. The product was taken up in ether. The ether solution was washed successively with water, sodium bicarbonate, and water, and dried with anhydrous sodium sulfate. The ether solution was decolorized with animal charcoal. Evaporation of the ether left an oil which was crystallized from petroleum ether (30–60°) and methyl

alcohol, and methyl alcohol. Needles were obtained which melted at 121.5–122°.

Anal. Calcd. for $C_{31}H_{50}O_2$: C, 81.88; H, 11.08. Found: C, 81.62; H, 10.90.

We wish to take this opportunity to express our thanks to the Rockefeller Foundation for a grant-in-aid for this work, to Merck & Co., Inc., of Rahway, New Jersey, for the analytical and absorption spectrum data and to Dr. O. H. Emerson of the University of California for kindly furnishing part of the crude sterol from wheat germ oil from which the α_1-sitosterol used in these experiments was isolated.

Summary

1. Certain experimental results on the determination of the structure of α_1-sitosterol are described.

2. An absorption spectrum study, and the non-formation of an addition compound with maleic anhydride, indicate that the two double bonds in α_1-sitosterol are not conjugated.

3. Only one of the double bonds in α_1-sitosteryl acetate can be hydrogenated under ordinary conditions. α_1-Dihydrositosterol and its acetate have been prepared and characterized. Evidence is offered to show that α_1-dihydrositosterol is an *α-stenol.*

4. The second double bond which is resistant to hydrogenation can be isomerized by dry hydrogen chloride into a position which is easy to hydrogenate. α_1-Isodihydrositosterol and its acetate have been prepared and characterized. Evidence is offered to show that α_1-isodihydrositosterol is a *β-stenol.*

5. Hydrogenation of α_1-isodihydrositosteryl acetate gives α_1-sitostanol acetate. Certain characteristic properties of this latter compound have also been described and we have observed that it may be obtained also by the direct complete hydrogenation of α_1-sitosteryl acetate at 65–70° in the presence of a small amount of concentrated hydrochloric acid.

6. α_1-Sitostanol and stigmastanol are not identical. This difference is probably the result of isomerization in the hydrocarbon side chain.

7. A structural formula for α_1-sitosterol has been proposed.

PRINCETON, N. J. RECEIVED JUNE 19, 1939

[CONTRIBUTION FROM THE EXPERIMENT STATION OF THE HAWAIIAN SUGAR PLANTERS' ASSOCIATION]

Electrolytes and the Viscosity of Pectin Solutions[1]

BY HUGO P. KORTSCHAK

Introduction

That the addition of electrolytes to certain colloidal solutions will cause marked changes in the viscosity is well known, but no explanation has been offered that seems completely satisfactory for all cases. This paper describes the effect of electrolytes on pectin sols, and shows that the colloidal character of the solutions is not a determining factor.

Experimental.—The pectin used was Eastman Citrus, practical. This was not the same sample used in the previous paper;[2] solutions prepared from it had a somewhat higher viscosity, indicating greater purity. The equivalent weight was 1500–2000. Other reagents were C. P. grade. Ordinary distilled water was used. No precautions were taken to prevent contamination by atmospheric carbon dioxide, except for boiling before use with substances containing calcium.

Since it is difficult to reproduce pectin sols exactly, a correction factor (always less than 2%) was applied to values at 0.1% pectin, to make them more easily comparable. Correction was made for density at salt concentrations above 0.1 *N* but no other correction factors were applied. For other experimental details see previous paper.[2] Viscosities reported are relative to water at the temperature of measurement, 27.5 ± 0.5°.

TABLE I

VISCOSITY OF 0.1% PECTIN SOLS

N added base	NaOH		$Ca(OH)_2$		KOH	NaOH + 0.001 *N* NaCl	
	η	*p*H	η	*p*H	η	η	*p*H
0	1.414	3.83	1.414	3.83	1.414	1.309	3.87
5×10^{-5}	1.424	3.93	1.419	3.82	1.434	1.323	4.00
1×10^{-4}	1.445	4.03	1.421	3.84	1.457	1.333	4.13
2×10^{-4}	1.474	4.32	1.428	3.91	1.504	1.339	4.52
5×10^{-4}	1.513	7.15	1.423	4.09	1.484	1.300	8.50
1×10^{-3}[a]	1.43	10.2	1.31	4.56	1.41	1.29	10.3
2×10^{-3}[a]	1.34	11.2	...	..	1.30	1.19	11.1
5×10^{-3}[a]	1.29	12.0	...	..	1.22	1.17	11.7

[a] Pectin hydrolyzes rapidly in alkaline solution; viscosities at these concentrations are therefore inaccurate.

(1) Experimental work reported in this paper was done as part of Project ST-P-5 of the H.S.P.A. Experiment Station.

(2) H. P. Kortschak, THIS JOURNAL, **61**, 681 (1939).

Discussion

It is evident that substances which increase the hydroxyl ion concentration raise the viscosity at low concentrations. Where the added substance is a strong base, as with sodium and potassium hydroxides, the maximum occurs when base and pectin are present in approximately equivalent concentration. This increase may be explained very simply. Pectin is an acid which is not completely ionized in the concentrations used. When neutralized with sodium hydroxide, the more highly ionized sodium salt is formed. If we admit that an increase in the electric charge causes increased hydration, and thus increased viscosity, the results are as would be expected.

A comparison of the viscosities of pectin and sodium–pectin sols supports this viewpoint (Table II). At great dilutions, where the acid would be largely dissociated, there is little difference between the two.

The increased viscosity at high salt concentrations is not, in most part, due to the presence of the pectin, as can be seen by a comparison between the viscosities of salt solutions with and without pectin (Table IV). Table V shows the behavior with varied pectin concentration. With higher salt concentration, a greater viscosity increase is to be noted in the series containing pectin than in the series of sodium chloride in water. Except for the most concentrated solution with 0.5% pectin, however, this effect is small when compared to the total viscosity increase, or to the viscosity decrease in more dilute solution. Some additional viscosity increase is to be expected

TABLE II

DILUTION OF PECTIN AND NA-PECTIN

% P	η P	η NaP	Ratio
0	1.000	1.000	1.00
0.0016	1.016	1.016	1.00
.0031	1.033	1.031	1.00
.0062	1.066	1.059	0.99
.0125	1.106	1.104	1.00
.025	1.161	1.183	1.02
.05	1.260	1.302	1.03
.10	1.414	1.504	1.06

TABLE III

VISCOSITIES OF 0.1% PECTIN SOLS

N added salt	HCl	$CaCl_2$	$KClO_4$	Aconitic acid	NaCl + 0.005 *N* NaOH
0	1.414	1.414	1.414	1.414	1.476
2×10^{-5}	1.409	1.407	1.410	1.407	1.468
5×10^{-5}	1.406	1.399	1.405	1.402	1.457
1×10^{-4}	1.386	1.380	1.398	1.397	1.439
2×10^{-4}	1.353	1.352	1.380	1.381	1.426
5×10^{-4}	1.289	1.310	1.345	1.350	1.380
1×10^{-3}	1.263	1.284	1.313	1.315	1.339
2×10^{-3}	1.242	1.266	1.282	1.288	1.299
5×10^{-3}	1.235	1.254	1.253	1.258	1.267
1×10^{-2}	1.240	1.248	1.235	1.243	1.250
2×10^{-2}	1.237	1.248	1.223	1.233	1.236
5×10^{-2}	1.242	1.245	1.210	1.239	1.227
1×10^{-1}	1.246	1.256	1.203	1.247	1.231
2×10^{-1}	1.255	1.275	1.189		1.238
5×10^{-1}		1.322			1.273

TABLE IVa

VISCOSITIES OF ELECTROLYTE SOLUTIONS WITH AND WITHOUT 0.1% PECTIN

N salt	KCl[a]	KCl + Pectin	NaCl[b]	NaCl + Pectin
0		1.414		1.414
1×10^{-5}		1.412		1.415
2×10^{-5}		1.410		1.414
5×10^{-5}		1.404		1.402
1×10^{-4}		1.391		1.398
2×10^{-4}		1.379		1.388
5×10^{-4}		1.340		1.351
1×10^{-3}		1.306		1.318
2×10^{-3}	1.000	1.277	1.000	1.282
5×10^{-3}	1.000	1.251	1.001	1.259
1×10^{-2}	1.000	1.241	1.002	1.243
2×10^{-2}	1.000	1.231	1.003	1.238
5×10^{-2}	1.000	1.222	1.005	1.232
1×10^{-1}	1.000	1.220	1.010	1.233
2×10^{-1}	0.999	1.216	1.019	1.236
5×10^{-1}	.998	1.211	1.046	1.276
1×10^{0}	.997	1.212	1.096	1.340
2×10^{0}	1.008	1.224	1.219	1.488

[a] G. Jones and S. K. Talley, THIS JOURNAL, **55,** 624, 4124 (1933). [b] G. Jones and S. M. Christian, *ibid.*, **59,** 484 (1937).

TABLE IVb

VISCOSITIES OF ELECTROLYTE SOLUTIONS WITH AND WITHOUT 0.1% PECTIN

N added salt	LiCl[c]	LiCl + pectin	$NaNO_3$[c]	$NaNO_3$ + pectin	Citric acid[d]	Citric acid + pectin[e]
0		1.414		1.414		1.414
1×10^{-5}		1.410		...		...
2×10^{-5}		1.408		1.405		1.413
5×10^{-5}		1.400		1.405		1.406
1×10^{-4}		1.400		1.387		1.399
2×10^{-4}		1.387		1.374		1.385
5×10^{-4}		1.359		1.343		1.355
1×10^{-3}		1.331		1.312		1.323
2×10^{-3}		1.301		1.287		1.286
5×10^{-3}		1.274		1.270		1.259
1×10^{-2}		1.257		1.259		1.242
2×10^{-2}		1.249		1.252		1.234
5×10^{-2}		1.243		1.243		1.234
1×10^{-1}	1.014	1.249	1.005	1.243	1.021	1.236
2×10^{-1}	1.028	1.260	1.010	1.249	1.039	1.255
5×10^{-1}	1.069	1.313	1.025	1.267	1.077	1.315
1×10^{0}	1.142	1.381	1.062	1.328	1.154	1.425

[c] "International Critical Tables." [d] Apparently not previously reported. At higher concentrations: 2 *N*, 1.330; 5 *N*, 2.23; 10 *N*, 7.4. [e] Note difference in quantitative values from those previously reported,[2] due to different pectin sample.

when pectin is present, since the pectin concentration, referred to water alone, is significantly greater in such concentrated salt solutions.

If the electric charge on the pectin micelle were reversed to any appreciable extent, one would expect the viscosity to remain at a value approximately that of a pectin sol containing no added electrolyte.

It is not suggested that the effect of the salt on water alone will suffice to explain all similar viscosity minima, but in some cases[3,4] the possibility apparently has not been considered.

The viscosity increase found here cannot be the same phenomenon as has been noted in the case of hydrophobic sols, for instance by Dhar.[5] In that case even potassium chloride produced an increase in viscosity, which is not the case here, and in all cases the rise commenced at salt concentrations which were far too low to give a measurable viscosity effect in water alone.

The decrease in viscosity which occurs at low salt concentrations is most probably due to a decrease in hydration.

From the data presented it can be seen that variation of the anion has no effect (with the exception of OH^-, due to the acid character of the pectin). Variation of the cation produces some change, but the minimum viscosity is nearly the same for all salts and acids.[6] The order of increasing effectiveness of the different cations follows the lyotropic series, Li, Na, K, Ca; the same order as is found, for instance, in solubility measurements.[7,8] This is the order of increasing hydration, and of increase in size of the ions.

TABLE V

VARIED PECTIN CONCENTRATION

	% pectin			
N NaCl	0	0.01	0.1	0.5
0	1.000	1.064	1.414	2.862
0.0001	1.000	1.040	1.398	
.0002	1.000	1.037	1.388	
.0005	1.000	1.030	1.351	
.001	1.000	1.025	1.318	2.781
.002	1.000	1.024	1.282	2.714
.005	1.001	1.023	1.259	2.679
.01	1.002	1.021	1.243	2.633
.02	1.003	1.023	1.238	2.601
.05	1.005	1.029	1.232	2.575
.1	1.010	1.030	1.233	2.580
.2	1.019	1.034	1.236	2.590
.5	1.046	1.067	1.276	2.676
1	1.096	1.113	1.340	2.736
2	1.219	1.236	1.488	3.116

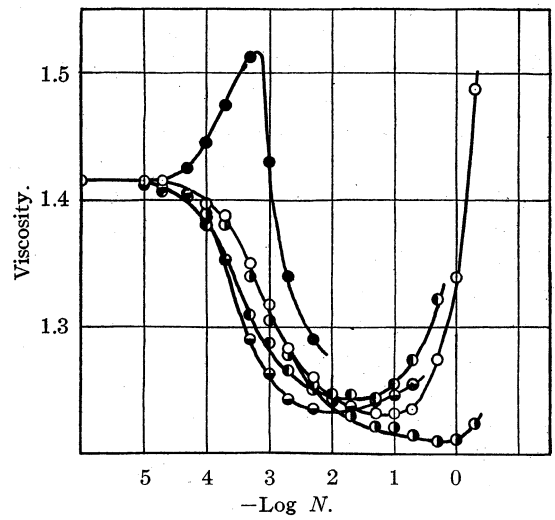


Fig. 1.—Viscosity of 0.1% pectin sols: ●, NaOH; ◒, HCl; ◐, $CaCl_2$; ◑, KCl; ○, NaCl.

Since the original purpose for which these measurements were made required only relative accuracy, no effort was made to obtain absolutely accurate values. For this reason it seems unprofitable to apply the concept of activity, or, especially in view of the uncertain equivalent weight of pectin, to attempt a test of the applicability of the Debye–Hückel equation.

This decrease in viscosity conceivably could be due to any of several different influences: (1) A solvent effect, the pectin remaining unchanged except for loss of water of hydration. In this case, the salt concentration required to produce minimum viscosity should be almost independent of the pectin concentration, which is not the case (see also the previous article). (2) Change in the acid dissociation of the pectin. The addition of electrolytes increases the dissociation constant of weak acids.[8] Also, the fact that the addition of alkalies will lower the viscosity, after a maximum has been reached, would make this explanation impossible. In view of the similarity of the curves for a strong acid, as hydrochloric acid, and for neutral salts, there can be no question of the effect being due to change in *p*H. (3) Adsorption

(3) H. Erbring, *Kolloid Z.*, **80**, 20 (1937); *C. A.*, **31**, 6948 (1937).

(4) R. Haller and B. Frankfurt, *Kolloid Z.*, **80**, 68 (1937); *C. A.*, **31**, 6950 (1937).

(5) D. N. Chakravarti and N. R. Dhar, *J. Phys. Chem.*, **29**, 1556 (1925).

(6) That an amount of citrate equal in weight to the pectin present produced the solutions of minimum viscosity,[2] must be purely a coincidence, due to the ratio of the equivalent weights of the citrates and the pectin, and to the concentrations employed.

(7) H. v. Halban, G. Kortum and M. Seiler, *Z. physik. Chem.*, **A173**, 449 (1935).

(8) H. v. Halban and H. P. Kortschak, *Helv. Chim. Acta*, **21**, 392 (1938).

of ions, causing changes in the electric charge of the pectin micelle, or (4) the formation of undissociated salts of the pectin.[9]

These last two are very much the same thing, except that in the case of adsorption no definite limit to the amount of ion which can be adsorbed is to be expected, whereas with salt formation a definite limit exists, when the stoichiometric quantity of cation has combined with the pectin. It is this latter type of combination which seems to represent the facts most closely. Were more than an equivalent amount of cation to combine with the pectin, it would be expected that a considerable increase would occur in the viscosity. However, as has been pointed out above, no such large increase was found.

It is in accordance with this explanation, of the formation of an undissociated salt, that NaCl + NaOH, NaCl, $CaCl_2$, and HCl are progressively more effective in the order given. This agrees with the findings of Stuewer,[10] that calcium pectin is more highly dissociated than pectin itself, and sodium pectin still more so.

That the minimum ratio of electrolyte to pectin, which is necessary in order to attain the minimum viscosity, decreases with increasing pectin concentration (Table V), would be expected with both adsorption and salt formation.

When the viscosity has first been lowered with sodium chloride, subsequent addition of sodium hydroxide raises it only slightly (Table I), showing that there is less undissociated pectin acid present than in the absence of sodium chloride. The presence of additional ions does, of course, increase the dissociation constant of a weak acid,[8] which would account for this, but increased ionization appears to be associated with increased viscosity (see above). One must conclude that Na has replaced acid H in the pectin micelle (compare the conclusions of Rabinovich[11]).

Comparison of Pectin and Electrolyte Solutions.—The neutralization of an acid generally results in increased viscosity, *i. e.*, a sodium chloride solution has a greater viscosity than an equivalent hydrochloric acid solution. Similarly, the viscosity of a pectin sol increases when the pectin is neutralized (Table I).

(9) By "undissociated salt" is meant only that the entire hydrated pectin micelle contains no excess of either positive or negative ions. To economize space, the well-known references to McBain, Loeb, Pauli, *et al.*, will not be given here.

(10) R. F. Stuewer, *J. Phys. Chem.*, **42**, 305 (1938).

(11) A. I. Rabinovich, *Z. physik. Chem.*, **116**, 97 (1925); *cf. C. A.*, **19** 3048 (1925).

It has been noted previously that the viscosities of solutions containing two electrolytes are lower than would be expected on the assumption of a purely additive effect.[12] Since the viscosities of electrolyte solutions are low compared to those of equivalent pectin sols, an actual decrease in viscosity rarely has been noted, when a second salt has been added to an electrolyte solution. The data of Ruby and Kawai[12] show this effect when the measurements of 0.4 *N* hydrochloric acid solutions are examined (Table VI).

TABLE VI

VISCOSITY OF 0.4 *N* HYDROCHLORIC ACID (RUBY AND KAWAI)

c KCl	η	Calcd.
0[a]	1.0257	1.0257
0.1	1.0250	1.0260
.6	1.0221	1.0238
1.6	1.0285	1.0298

[a] Interpolated.

On the assumption that an electrolyte giving more viscous solutions than hydrochloric acid would show the effect more clearly, the data of Table VII were measured. (About ten measurements were made at each concentration, and the average reported. The average deviation of the individual measurements was 0.0015. Assuming statistical significance of the data, the probable error is less than 0.001 at each concentration.)

TABLE VII

VISCOSITY OF 1 *N* CITRIC ACID

c KCl	η	*c* KCl	η
0[a]	1.151	0.20	1.146
0.01	1.149	.50	1.147
.02	1.148	1.00	1.153
.05	1.148	2.00	1.183
.10	1.146		

[a] Interpolated.

It is evident that the behavior of citric acid is qualitatively similar to that of pectin. The viscosity is increased by 1 *N* potassium chloride, a concentration which decreases the viscosity of water. This would seem to be similar to the behavior of the more concentrated pectin sols (Table V).

Combination of some kind has been postulated in many papers reporting the conductivities of mixed electrolytes, whereas others use the "mixture rule" and its modifications.[13] It would seem that any satisfactory explanation must also account for the viscosity effects.

(12) C. E. Ruby and J. Kawai, THIS JOURNAL, **48**, 1119 (1926).

(13) See, for instance, R. W. Bremner, T. G. Thompson and C. L. Utterback, THIS JOURNAL, **61**, 1222 (1939), and literature there cited.

Summary

1. The viscosity of pectin sols as affected by the addition of various electrolytes has been determined.

2. Three separate effects are present with increasing electrolyte concentrations: (a) An increase in viscosity at low electrolyte concentration, when an alkaline substance is added. This is due to the formation of the more highly ionized pectin salt from the pectin acid. (b) A decrease in viscosity to a minimum, further increase in electrolyte concentration having no apparent effect on the pectin. The formation of practically uncharged, undissociated salts of pectin is suggested, causing dehydration, and thus decreased viscosity. (c) Increase in viscosity at high salt concentration, due to interaction of the added electrolyte and water; an increase greater than this being due, in part at least, to the increased concentration of pectin with respect to water alone.

3. Any increase in viscosity which could be ascribed to reversal of charge on addition of excess electrolyte is either absent or very small.

4. The viscosities of solutions of pectin and of truly soluble electrolytes change in similar manner with increasing electrolyte concentration.

HONOLULU, T. H. RECEIVED MARCH 20, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

The Preparation of Acetyl-5-fluorosalicylic Acid

BY C. M. SUTER AND ARTHUR W. WESTON[1]

As a part of a program of preparing various aromatic fluorine compounds[2] for the purpose of determining their pharmacological properties, it has seemed of interest to synthesize 5-fluorosalicylic acid and its acetyl derivative (fluoroaspirin). 4-Fluorosalicylic acid (4-fluoro-2-hydroxybenzoic acid) was prepared some time ago by Hodgson and Nixon[3] but its physiological properties were not investigated.

5-Fluorosalicylic acid was prepared by carbonation of the Grignard reagent obtained from 2-bromo-4-fluorophenetole,[2] followed by deëthylation of the ethoxy acid by hydriodic acid. It was noted by Hodgson and Nixon[3] that while 4-methoxy-2-fluorobenzoic acid could not be demethylated, the 2-methoxy-4-fluoro isomer reacted readily with hydrogen iodide. It is evident from the behavior of 5-fluoro-2-ethoxybenzoic acid that the position of the fluorine has little effect upon the ease of dealkylation when the alkoxy group is ortho to carboxyl.

Preliminary data obtained in a comparison of the toxicity of the 5-fluorosalicylic acid and its acetyl derivative with the fluorine-free compounds[4] using white mice as test animals show that 5-fluorosalicylic acid is approximately twice as toxic as salicylic acid while the acetylfluoro acid is about 50% more toxic than aspirin. Although it has been reported[5] that 5-bromosalicylic acid is twice as effective against several types of bacteria as the chlorine compound, no experiments on animal toxicity have been carried out. 5-Chlorosalicylic acid has the same germicidal action as salicylic acid.

(1) Sharp and Dohme Post-doctorate Fellow, 1938–1939.

(2) Suter, Lawson and Smith, THIS JOURNAL, **61**, 161 (1939).

(3) Hodgson and Nixon, *J. Chem. Soc.*, 1632 (1929).

(4) We are indebted to Dr. Maurice L. Moore, Research Laboratories of Sharp and Dohme, for these results.

Experimental

2-Ethoxy-5-fluorobenzoic Acid.—A Grignard reagent was prepared using ethyl bromide as a starter from 35 g. (0.16 mole) of 2-bromo-4-fluorophenetole and 4 g. (0.17 mole) of magnesium and the ether solution dropped with stirring into a beaker containing 40 g. of crushed dry ice. After the excess carbon dioxide had evaporated, ice and dilute hydrochloric acid were added, the ether layer separated and the water again extracted with ether. The combined portions of ether were extracted several times with 10% sodium bicarbonate and the latter acidified. There resulted 19 g., a 64.5% yield, of a slightly yellow solid which after crystallization from dilute alcohol or a mixture of benzene and petroleum ether melted at 65.5–66.5°. The acid is soluble in benzene, alcohol, acetic acid and slightly soluble in carbon tetrachloride.

Anal. Calcd. for $C_9H_9O_3F$: neut. equiv., 184.1. Found: neut. equiv., 184.6.

5-Fluorosalicylic Acid.—The ethoxy compound was deëthylated by refluxing 17 g. with 150 ml. of hydriodic acid (d. 1.7) for ten hours. The white solid which separated as the reaction proceeded was filtered off on a sintered glass funnel. Dilution of the filtrate with water and extraction with ether gave only a little more product. 5-Fluoro-2-hydroxybenzoic acid crystallizes from water in fine white needles which melt at 178.5–179.5°. It is

(5) Rochaix and Pinet, *Bull. sci. pharmacol.*, **34**, 486 (1927).

soluble in ether and alcohol. The yield was 12.5 g. or 87% of the theoretical amount. A purple-violet color was obtained with ferric chloride solution. The methyl ester has the "oil of wintergreen" odor.

Anal. Calcd. for $C_7H_5O_3F$: neut. equiv., 156. Found: neut. equiv., 157.4.

Acetyl-5-fluorosalicylic Acid.—Acetylation was effected by warming 4.5 g. of the hydroxy acid with 10 ml. of acetic anhydride and a few drops of sulfuric acid. After cooling the mixture, adding 100 ml. of water, and filtering there was obtained 3.2 g. (56% yield) of product which crystallized from benzene as fine needles melting at 130–131° which gave no ferric chloride color test. The compound is soluble in alcohol, ether, hot benzene and insoluble in ligroin.

Anal. Calcd. for $C_9H_7O_4F$: neut. equiv., 198.1. Found: neut. equiv., 198.4.

Summary

5-Fluorosalicyclic acid and its acetyl derivative have been prepared. These are more toxic than the unfluorinated compounds.

EVANSTON, ILL. RECEIVED APRIL 24, 1939

[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY, THE UNIVERSITY OF CHICAGO]

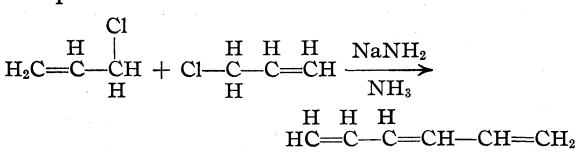
Syntheses of Polyenes. I. Hexatriene and its Polymers

BY M. S. KHARASCH AND E. STERNFELD[1]

Introduction

In the course of an investigation on highly unsaturated compounds containing conjugated systems, the need of a simple and efficient method of synthesis became apparent. The general method now in use (the reduction of unsaturated carbonyl compounds to pinacols, replacement of the hydroxyl groups by halogens, and elimination of the halogens by zinc) necessitates the use of large quantities of materials, involves difficult experimental procedures, and usually the over-all yield of the polyene is poor.

Preparation of Hexatriene and its Polymers.—Ordinarily, when organic halides are treated with bases, halogen acids are eliminated and ethylene derivatives are formed. In certain cases, however, two molecules of the halide condense in the course of the reaction to form an unsaturated dimer. Specifically, 9-fluorenyl bromide reacts with potassium hydroxide in acetone solution to yield bifluorenylidene.[2] In our laboratory sodamide in liquid ammonia has been used successfully as a condensing agent. The equation below represents the reaction of allyl chloride with sodamide in liquid ammonia.



Our hypothesis which has now been verified in a number of cases is that halides of weakly electronegative radicals[3] will condense when treated with sodamide in liquid ammonia if there is a hydrogen atom on the carbon atom to which the halogen atom is attached.

Since the electronegativity of the allyl radical would be decreased by substituents on the α-carbon atom and only very little affected by substituents on the β-carbon atom, this general method applies to the preparation of many substituted hexatrienes.

Our method of preparing hexatrienes has many advantages over the methods of van Romburgh, namely, the decomposition of *s*-divinylglycol diformate,[4] or the dehydration of 1,5-hexadien-4-ol. The operations involved are simple and rapid. The sodamide used is produced preferably by the action of sodium on liquid ammonia in the presence of finely divided iron as a catalyst.[5] It is then added to a liquid ammonia solution of allyl chloride as rapidly as the violence of the reaction permits, and the products are isolated as described in the experimental part.

It was found that the yield of hexatriene was dependent upon the order of addition; thus sodamide added to allyl chloride gave 30% hexatriene, whereas when the allyl chloride was added to sodamide only a 10% yield of hexatriene was obtained along with a proportionately greater amount of a high boiling material. This is accounted for on the basis that a concentrated solu-

(1) Eli Lilly Fellow. The authors wish to thank the Eli Lilly Company for generous support which made this work possible.

(2) Thiele and Wahnscheidt, *Ann.*, **376**, 278 (1910).

(3) Kharasch and Flenner, THIS JOURNAL, **54**, 674 (1932); Kharasch and Swarts, *J. Org. Chem.*, **3**, 405 (1938).

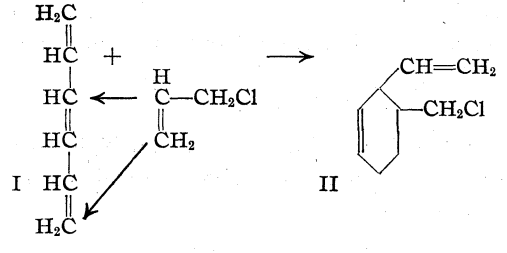
(4) Van Romburgh, *J. Chem. Soc.*, **90**, 130 (1906); *Proc. Roy. Acad. Amsterdam*, **15**², 1184 (1913).

(5) Vaughn, Vogt and Nieuwland, THIS JOURNAL, **56**, 2120 (1934).

tion of sodamide causes the hexatriene to polymerize.

We are not prepared to state whether the hexatriene made from allyl chloride in this manner is *cis* or *trans;* in our opinion there is not sufficient evidence to show that either pure *cis*- or pure *trans*-hexatriene has ever been isolated. The constants of our hexatriene are nearer to those obtained by Farmer and co-workers[6] for the *cis*-hexatriene.

The nature of the higher boiling material obtained by the reaction of allyl chloride with sodamide in liquid ammonia is dependent upon the experimental conditions. When three moles of allyl chloride was dissolved in liquid ammonia and two moles of sodamide added, the main product (50%) was a compound boiling at 44–48° at 8 mm., containing one chlorine atom. The molecular weight of the substance was 156 and it was identified as 1-chloromethyl-2-vinyl-cyclohexene-3. The product undoubtedly is formed by the condensation of allyl chloride with hexatriene as indicated in the following schematic representation



The structure of the substance (II) was proved by hydrogenation to 1-ethyl-2-methylcyclohexane. The boiling point and index of refraction of this substance agreed with those recorded in the literature.[7]

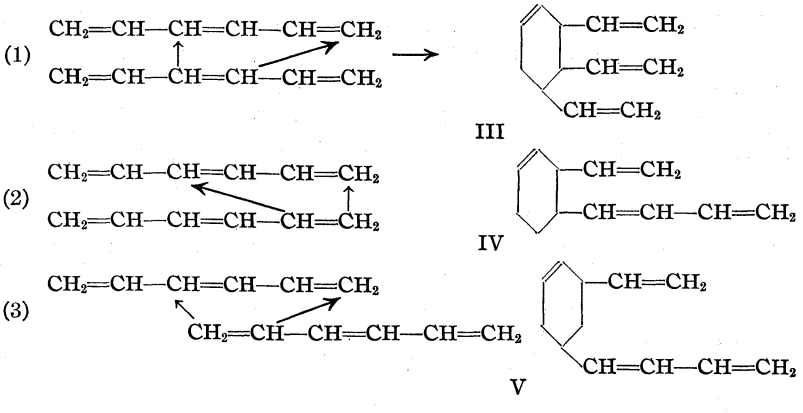
This type of condensation has been discussed recently by Alder and Windemuth,[8] who condensed cyclopentadiene and anthracene with a number of allyl compounds, including allyl chloride. They found that temperatures about 150–180° and fairly high pressures were necessary to bring about the condensations. Compound II is formed readily under our experimental conditions at −33° and atmospheric pressure.

(6) Farmer, Larola, Switz and Thorpe, *J. Chem. Soc.*, 2949 (1927).
(7) Signaigo and Cramer, THIS JOURNAL, **55**, 3326 (1933).
(8) Alder and Windemuth, *Ber.*, **71B**, 1939 (1938).

However, if an excess of sodamide is employed, polymers of hexatriene can be isolated uncontaminated with halogen compounds. In particular one fraction can be isolated which boils 50–55° at 3 mm., in over 40% of the calculated yield. The only investigation of the polymers of hexatriene mentioned in the literature was conducted by van Romburgh[4] who distilled a five-year-old sample of hexatriene and obtained a liquid which boiled at 99.5° at 16 mm. The molecular weight indicated that it was a dimer of hexatriene. Because of the density of the liquid van Romburgh assumed that a ring had been formed with the elimination of two double bonds. However, he made no attempt to establish the structure of his dimer.

Upon hydrogenation of the dimer a saturated hydrocarbon (molecular weight 168) is obtained. The fact that the substance absorbs eight hydrogen atoms corresponding to four double bonds indicates a ring structure for the molecule, since the straight chain molecule would have five double bonds. The index of refraction of the saturated dimer is much too high for a straight chain paraffin hydrocarbon but is normal for a cyclohexane derivative.

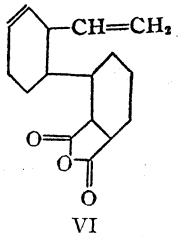
Dimerization of hexatriene to give a ring compound may take place in two ways: 1,4-addition of a medial double bond of a hexatriene molecule to another hexatriene molecule as in scheme 1, or 1,4-addition of a terminal double bond, as in scheme 2 or 3.



Of the three dimers, IV and V contain conjugated systems and will react with maleic anhydride. Since the dimer gives a well-defined crystalline derivative with maleic anhydride, its structure is either IV or V.

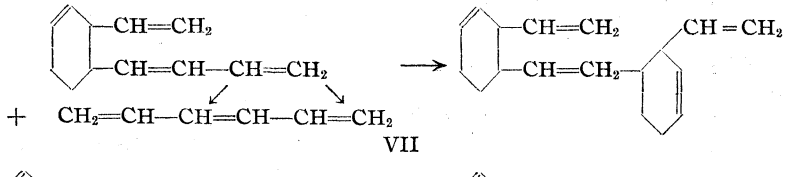
Hydrogenation of the dimer yields a liquid which is either 1-butyl-2-ethyl or 1-butyl-3-

ethylcyclohexane. Neither of these cyclohexanes is recorded in the literature. We synthesized the 1-butyl-2-ethylcyclohexane using the procedure suggested by Signaigo and Cramer.[7] α-Ethylcyclohexanone from α-chlorocyclohexanone and ethylmagnesium bromide was added to butylmagnesium bromide and the mixture, upon hydrolysis, gave 1-butyl 2-ethylcyclohexanol. This substance was dehydrated by distillation with iodine and then hydrogenated to the saturated hydrocarbon. The constants of 1-butyl-2-ethylcyclohexane agreed with those of the saturated hexatriene dimer. The unsaturated compound is, therefore, 1-butadienyl-2-vinylcyclohexene-3 (IV) and the maleic anhydride derivative is represented by VI. The dimerization of hexatriene is analogous to the dimerization of butadiene to vinylcyclohexene, and of phenylbutadiene to phenylstyrylcyclohexene. These conjugated systems, therefore, as well as hexatriene upon condensation give rise to six-membered rings by 1,4-addition of a terminal double bond in preference to the addition of a medial double bond.

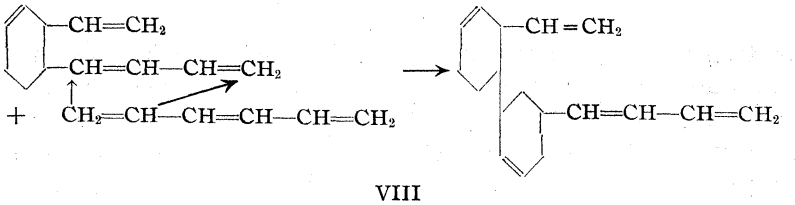


VI

With the aid of a molecular still we isolated the trimer and tetramer of hexatriene. The structure of the trimer, which has five double bonds, may be represented by two different formulas, according to two possible reactions by which it may be formed



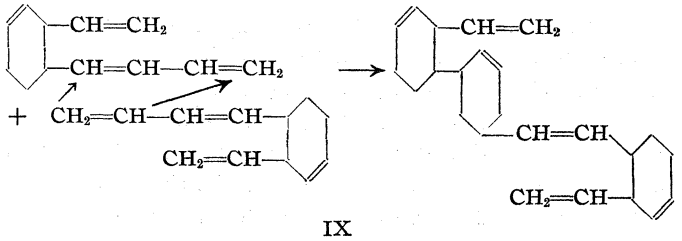
VII



VIII

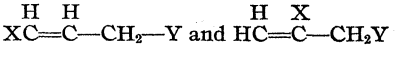
That VII is probably the correct structure is indicated by the fact that the trimer does not react with maleic anhydride.

The tetramer of hexatriene was obtained as a light-yellow viscous liquid whose color became darker in air. It has six double bonds and a molecular weight of 320. It does not react with maleic anhydride. These facts, in conjunction with the observation that the tetramer is formed under conditions that favor the presence of large concentrations of the dimer, indicate that the tetramer results from the 1,4-addition between two molecules of dimer as follows.



IX

This work is being continued. We are also engaged in an extensive study of other polyenes prepared by treating sodamide in liquid ammonia with substituted allyl compounds of the type



in which Y is a halogen atom and X is either a halogen atom, a hydrocarbon radical, or a carbethoxy group.

Experimental Part

Preparation of Hexatriene and Butadienylvinylcyclohexene.—The sodamide was prepared in an 800-cc. unsilvered Dewar flask (equipped with a stirrer and a dropping tube) from 23 g. of sodium in 600 cc. of liquid ammonia. About half a gram of ferric nitrate was dissolved in the ammonia and then the sodium added in 2–3 g. portions, each piece being allowed to react before the next was added. The sodamide suspension was forced over into a 3-liter Dewar, equipped with a good stirrer and containing 1 liter of liquid ammonia and 76 g. (1 mole) of allyl chloride. The flow of sodamide suspension had to be regulated carefully and only small portions added at a time as the reaction was very violent.

In later runs the sodamide was made in large quantities by the above procedure and stored, after evaporation of the ammonia, in a sealed bottle until used. It was added to the reaction mixture by means of an adapter cut short at the narrow end and connected to a glass tube of the same diameter in the

rubber stopper of the Dewar flask by a short piece of rubber tubing. This procedure allowed much greater control of the speed of the reaction and was more convenient than the earlier method in the reactions where the sodamide was added to the allyl chloride.

After all the sodamide was added the mixture was poured into a 3-liter round-bottomed flask and the ammonia evaporated on the steam-bath. Water was then added to dissolve the sodium chloride, and the mixture extracted successively with several portions of ether. The combined ether portions were washed thoroughly with water, dried over anhydrous sodium sulfate, and the ether removed. The remaining material was separated into fractions. Two different procedures were used. In the first experiments the product was fractionated with the aid of a column. The low boiling material was hexatriene (8.6 g., 24%), b. p. 76–80°, $n^{20}D$ 1.4330, d^{20}_4 0.7182. This material, dissolved in methyl alcohol, hydrogenated smoothly in the presence of platinum oxide to *n*-hexane, b. p. 68°, $n^{20}D$ 1.3748.

The second fraction was the dimer, 14 g. (41%), b. p. 50–55° at 3 mm., $n^{20}D$ 1.5137.

Anal. Calcd. for $C_{12}H_{16}$: C, 89.92; H, 10.08; mol. wt., 160. Found: C, 89.20; H, 9.75; mol. wt. (in triphenylmethane), 174.

Upon hydrogenation 0.4234 g. of liquid in absolute methyl alcohol absorbed 254.1 cc. of hydrogen (corr.). Calcd. for $C_{12}H_{16}$ and four double bonds, 264 cc. The ethylbutylcyclohexane had a b. p. 208°, $n^{20}D$ 1.4493.

Anal. Calcd. for $C_{12}H_{24}$: C, 85.71; H, 14.29. Found: C, 85.42; H, 14.19.

By using a column the liquid is kept at 75–80° for some time during the distillation of the hexatriene and polymerization takes place. To avoid this the product was sealed in a system containing a flask and several bomb tubes and connected to a vacuum line by a yoke. The liquid was cooled, the system evacuated to the limits of a three-stage mercury pump, degassed, and sealed off. The flask containing the liquid was allowed to come to room temperature while one of the tubes was cooled. In this way a 30% yield of hexatriene was obtained after twenty-four hours. The remaining liquid was distilled on an oil pump, yielding 33% of the dimer.

Preparation of Hexatriene Dimer, Trimer, and Tetramer.—The yield of butadienylvinylcyclohexene was increased to 50% by adding 100 g. (1.33 moles) of allyl chloride to a solution of 70 g. (2 moles) of sodamide in 2 liters of liquid ammonia and stirring the mixture for thirty to forty-five minutes after the addition of the halide. The aforementioned procedure was then followed and the ether-free product distilled in a molecular still. Twenty-seven grams of dimer distilled at 20–35° at 10^{-4} mm.

Five grams of trimer distilled at 70–80° at 10^{-4} mm., $n^{20}D$ 1.5232.

Anal. Calcd. for $C_{18}H_{24}$: C, 89.92; H, 10.08; mol. wt., 240. Found: C, 89.27; H, 9.84; mol. wt. (in triphenylmethane), 227. *Hydrogenation:* 0.2450 mg. in methyl alcohol absorbed 113.1 cc. of hydrogen (corr.). Calcd. for $C_{18}H_{24}$ and five double bonds, 114.3 cc.

Five grams of tetramer distilled at 120–133° at 10^{-4} mm., $n^{20}D$ 1.5330.

Anal. Calcd. for $C_{24}H_{32}$: C, 89.92; H, 10.08; mol. wt., 320. Found: C, 88.98; H, 9.72; mol. wt. (in triphenylmethane), 341. *Hydrogenation:* 0.2837 g. in methyl alcohol absorbed 126 cc. hydrogen (corr.). Calcd. for $C_{24}H_{32}$ and six double bonds, 119.5 cc.

Preparation of Chloromethylvinylcyclohexene.—Forty grams of sodamide was added over a period of one and one-half hours to a solution of 100 g. of allyl chloride in liquid ammonia. After the usual treatment the following fractions were obtained: 13 g., b. p. 70–85° (hexatriene contaminated with halogenated compounds) and 23 g. of chloromethylvinylcyclohexene, b. p. 44–48° at 8 mm., $n^{20}D$ 1.4670.

Anal. Calcd. for $C_9H_{13}Cl$: Cl, 22.66; mol. wt., 156.45. Found: Cl, 22.91; mol. wt. (in camphor), 156.

It was hydrogenated under pressure of 40 pounds (2.7 atm.) in presence of platinum oxide. The resulting liquid, after some purification, yielded a fraction b. p. 156°, $n^{20}D$ 1.4412, which is identical with 1,2-ethylmethylcyclohexane.

Synthesis of 1,2-Butylethylcyclohexane.—Twenty grams of ethylcyclohexanone was added to butylmagnesium bromide from 4.5 g. of magnesium and 23 g. of butyl bromide in 150 cc. of ether at 0°. The mixture was allowed to warm up to room temperature, then hydrolyzed with dilute sulfuric acid and ice. The layers were separated, the ether solution was washed with saturated sodium bisulfite and water, dried over anhydrous sodium sulfate, and distilled. The carbinol left after distillation of the ether, 20 g., was distilled immediately with 0.5 g. of iodine and gave a mixture of olefin and water boiling from 100–200°. The olefin, 15 g., was separated, dried, dissolved in glacial acetic acid and hydrogenated at an initial pressure of 36 pounds (2.5 atm.) in the presence of 0.3 g. of platinum oxide. The saturated hydrocarbon was separated by the addition of water, washed with cold concentrated sulfuric acid, dried and distilled. Upon fractionation was obtained 7 g. of pure 1,2-butylethylcyclohexane, b. p. 205–206°, $n^{20}D$ 1.4479.

Reaction of Hexatriene and its Dimer with Maleic Anhydride.—By heating equivalent amounts of hexatriene and maleic anhydride in benzene at 90–100° for three hours the vinyl (or ethylidene) tetrahydrophthalic anhydride, m. p. 45°, described by Farmer and Warren[9] was obtained. The free acid, m. p. 160°, was hydrogenated; 0.2108 g. absorbed 45.64 cc. of hydrogen (corr.). Calcd. for vinyl tetrahydrophthalic acid, 47.93 cc. Ethyl hexahydrophthalic acid, m. p. 117°, was the product.

Butadienylvinylcyclohexene reacted smoothly in benzene with maleic anhydride at 90–100°. The resulting anhydride was not crystallized, but was converted to the free acid, m. p. 178°.

Anal. Calcd. for $C_{16}H_{20}O_4$: C, 69.70; H, 7.26; neut. equiv., 138. Found: C, 70.05; H, 7.65; neut. equiv., 138.

Summary

1. A simple method of obtaining hexatriene and compounds derived from hexatriene in comparatively good yields by the condensation of allyl chloride is described.

(9) Farmer and Warren, *J. Chem. Soc.*, 897 (1929).

2. The structures of the hexatriene polymers are elucidated.

3. Work is being continued on the chemistry of these compounds and also on the synthesis of similar compounds containing substituent groups.

CHICAGO, ILLINOIS RECEIVED MAY 26, 1939

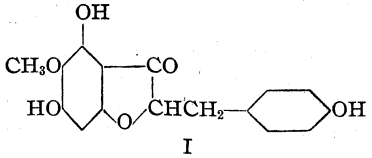
[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Derivatives of Coumaran. IV. The Structure of Tectorigenin

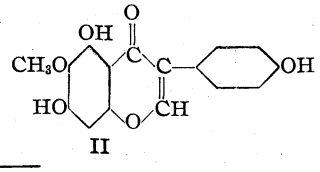
BY R. L. SHRINER, EDWARD J. MATSON AND R. E. DAMSCHRODER

The glucoside, tectoridin, was isolated by Shibata[1] from the rhizomes of *Iris tectorum* Maxim. Recently Mannich, Schumann and Lin[2] have shown that the glucoside, shekanin, in the rhizomes of the blackberry lily, *Belamcanda chinensis* (L.) Leman, is identical with tectoridin. Hydrolysis of tectoridin produced glucose and tectorigenin. Since the products of alkaline decomposition of tectorigenin were *p*-hydroxyphenylacetic acid, formic acid and iretol (V), Shibata first proposed the coumaran-3-one structure shown in formula I. Later, on the basis of the absorption spectrum, Asahina, Shibata and Ogawa[3] suggested the isoflavone structure of formula II. It is obvious that the isomeric formulas III and IV also represent possible structures which would yield the same degradation products.

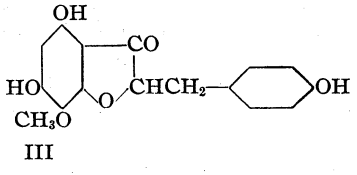
The coumaranone structures I and III have two atoms of hydrogen more than the isoflavone structures but the combustion analyses were not sufficiently accurate to distinguish between them. None of these structures has been synthesized previously. This paper reports the synthesis of the two isomeric coumaranone structures, I and III, and of their completely methylated derivatives.



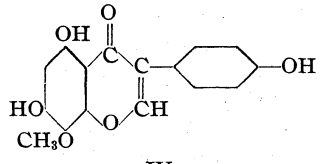
I



II



III



IV

The general method[4] of synthesis used involved the preparation of the coumaranones properly substituted in the benzene nucleus, condensation of the active methylene group in the heterocyclic ring with an aldehyde followed by reduction. The necessary coumaranones are most conveniently made by treating phenols with chloroacetonitrile followed by hydrolysis and ring closure.

Application of this method to iretol (V) yielded two isomeric coumaranones which were separated by fractional crystallization. The structure of the two isomeric coumaranones produced by hydrolysis and ring closure of α-chloro-2,4,6-trihydroxy-3-methoxyacetophenonimine hydrochloride (VI) was established by methylation and synthesis of each of the methylated compounds. The less soluble isomer was 4,6-dihydroxy-5-methoxycoumaran-3-one (VII); the more soluble was 4,6-dihydroxy-7-methoxycoumaran-3-one (X).

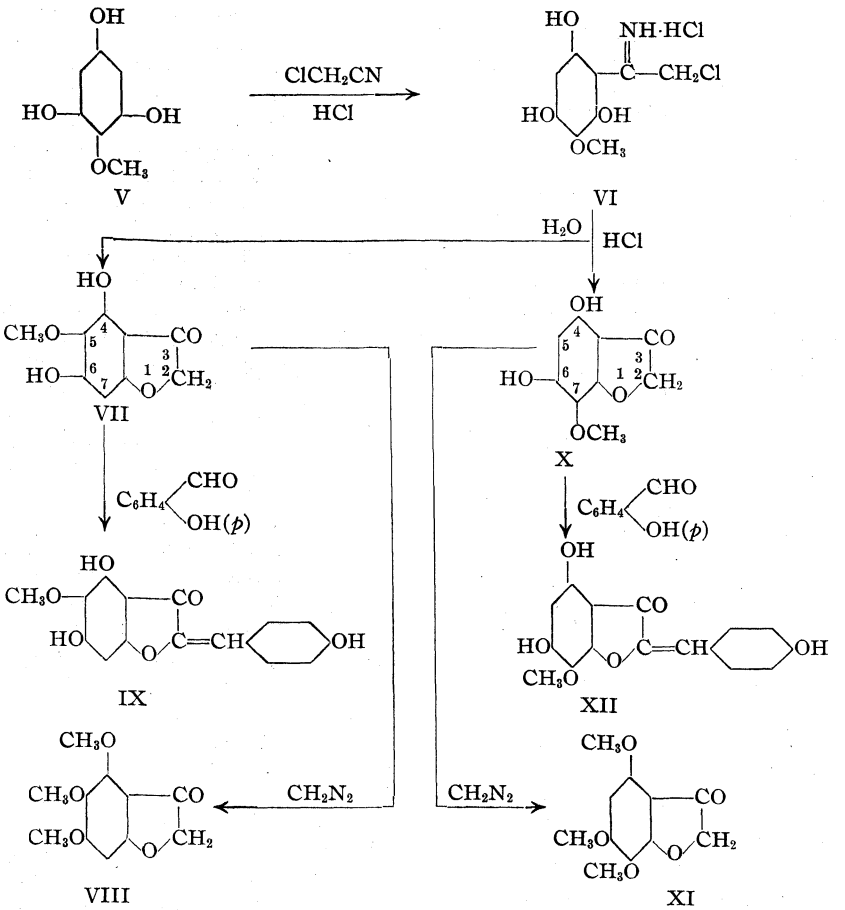
The methylated isomer, 4,5,6-trimethoxycoumaran-3-one (VIII), was prepared from antiarol (XIII), which underwent a Hoesch reaction with chloroacetonitrile to yield the α-chloroacetophenone (XIV). Ring closure gave the desired coumaranone (VIII). In a similar fashion the isomeric methylated compound, 4,6,7-trimethoxy-

(1) Shibata, *J. Pharm. Soc. Japan*, **47**, 380 (1927).

(2) Mannich, Schumann and Lin, *Arch. Pharm.*, **275**, 317 (1937).

(3) Asahina, Shibata and Ogawa, *J. Pharm. Soc. Japan*, **48**, 1087 (1928).

(4) Shriner and Damschroder, THIS JOURNAL, **60**, 894 (1938); Shriner and Anderson, *ibid.*, **60**, 1415 (1938).



coumaran-3-one (XI), was synthesized from 2,5-dimethoxyresorcinol (XVII).

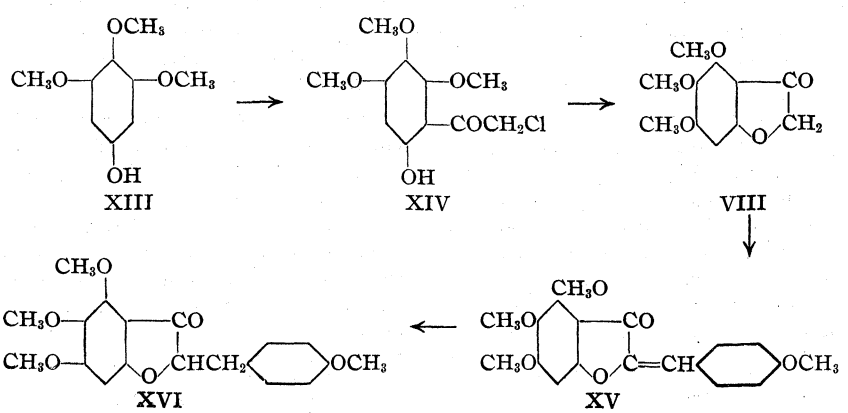
A Hoesch reaction gave the α-chloroacetophenone (XVIII), which was cyclized to the coumaranone (XIX). Methylation with diazomethane gave the completely methylated ether (XI).

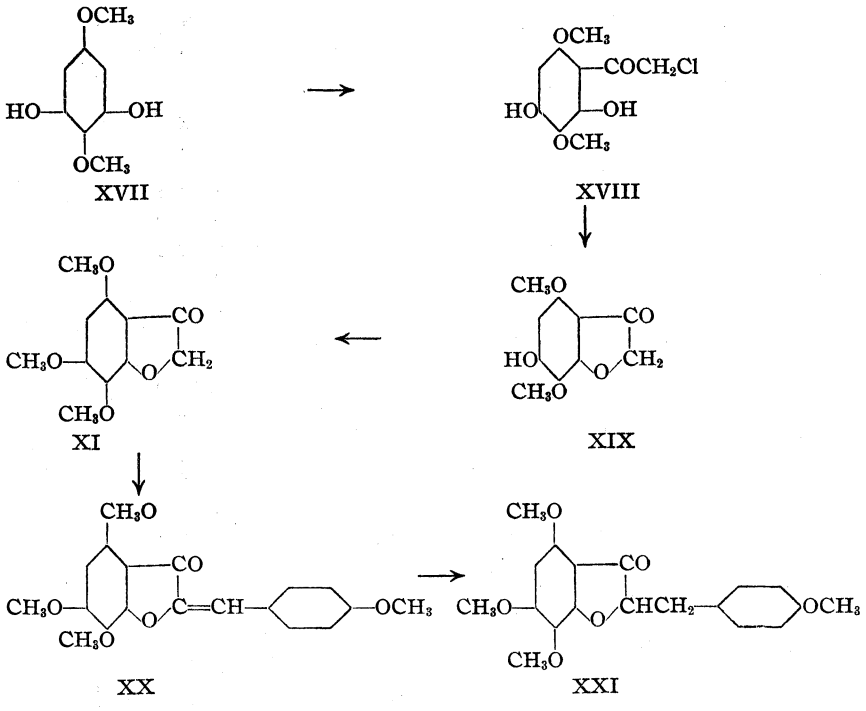
In order to obtain the 2-(*p*-hydroxybenzyl)-coumaranones (I and III) each of the isomeric coumaranones (VII and X) was condensed with *p*-hydroxybenzaldehyde and the benzal derivatives were reduced catalytically. The products of reduction proved to be very unstable and could not be isolated in the pure state but their properties were totally different from those of the natural product, tectorigenin.

The synthesis of the methylated derivatives was accomplished by condensing the trimethoxycoumaranones (VIII and XI) with anisaldehyde and reducing the anisal derivatives. The two isomeric methylated coumaranones (XVI and XXI) were isolated.

For purposes of comparison, tectoridin was isolated from the rhizomes of *Iris tectorum* and hydrolyzed to tectorigenin. Methylation of the latter yielded dimethyltectorigenin, which could not be methylated to trimethyltectorigenin although eleven different methylation procedures were used. Mannich, Schumann and Lin[2] also found that only a dimethyl derivative of tectorigenin could be obtained.

Although it was not possible to make a direct comparison with trimethyltectorigenin, the properties of the two synthetic trimethoxycoumaranones are quite different from those of the known methylated derivatives of tectorigenin. Compound XVI melts at 93–94°, and compound XXI at 116°. The melting points of tectorigenin and





its derivatives are: demethylated tectorigenin,[2] 270°; tectorigenin,[1] 230°; monomethyltectorigenin,[2] 191–192°; dimethyltectorigenin,[2] 188°.

The remarkable resistance to complete methylation exhibited by tectorigenin is probably due to the fact that the hydroxyl group ortho to the carbonyl group is strongly chelated as well as sterically hindered. This constitutes some evidence that the heterocyclic ring is six-membered rather than five-membered. It will be noted that the 4-hydroxyl group in the coumaranone (VII) was readily methylated.

The instability of the unmethylated coumaranones (I and III) obtained by reduction of IX and XII, and the differences in ease of methylation exhibited by all these coumaranones in comparison with tectorigenin show that the natural product is not a coumaranone derivative and favors the isoflavone structure II.

Experimental

α - Chloro - 2,4,6 - trihydroxy - 3 - methoxyacetophenonimine Hydrochloride (VI).—Dry hydrogen chloride gas was passed into a solution of 3 g. of iretol[5] and 1.5 g. of chloroacetonitrile[6] dissolved in about 300 cc. of dry ether. After forty-five minutes the solution became warm and after one hour yellow crystals began to be formed on the walls of the flask. The stream of hydrogen chloride was maintained eight hours longer, at which time the volume of ether had decreased to 100 cc. The flask was stoppered and allowed to stand overnight. The yellow crystals were then collected on a filter and washed quickly with dry ether. The yield of the crude product was 4.5 g. (87.5%).

The sample analyzed was purified by dissolving it in absolute alcohol into which dry hydrogen chloride had been passed for fifteen minutes. This solution was diluted with five volumes of dry ether. After the solution had stood for several hours, golden-yellow crystals precipitated. These were collected and dried in a vacuum desiccator over calcium chloride. The pure compound decomposed at 164–165°.

Anal. Calcd. for $C_9H_{11}Cl_2NO_4$: N, 5.22. Found: N, 5.37.

Hydrolysis of the Ketimine Hydrochloride.—A solution of 4 g. of the ketimine hydrochloride (VI) in 50 cc. of water was refluxed for one hour. The light-yellow solution gradually became red. The solvent was then removed slowly by surrounding the flask containing the hydrolysis mixture with calcium chloride in a vacuum desiccator. The pressure was reduced carefully until the water began to boil. After twenty-four hours the calcium chloride was replaced. When one-half the solvent had been removed in this manner, the rose-colored precipitate was removed by filtration. This less soluble fraction was recrystallized twice from water using norit and 0.9 g. of colorless needles of 4,6-dihydroxy-5-methoxycoumaran-3-one (VII) melting at 208.5 to 209.5° obtained.

Anal. Calcd. for $C_9H_8O_5$: C, 55.09; H, 4.11. Found: C, 55.29; H, 4.30.

The dark red filtrate from the above was concentrated to a volume of 8 cc. and the red precipitate filtered. Two recrystallizations from water using norit gave 1.5 g. of colorless crystals of 4,6-dihydroxy-7-methoxycoumaran-3-one (X) which melted at 177–178°.

Anal. Calcd. for $C_9H_8O_5$: C, 55.09; H, 4.11. Found: C, 55.05; H, 4.32.

Methylation of 4,6-Dihydroxy-5-methoxycoumaran-3-one.—A dioxane solution of diazomethane was prepared according to the method of Arndt.[7] Thirty-five milligrams of the coumaranone was dissolved in 25 cc. of dioxane and to this was added 1 cc. of the diazomethane solution containing about 90 mg. of the reagent, four times the theoretical amount necessary. The solution was allowed to stand overnight, and then the same amount of diazomethane was added again. After the solution had stood for ten hours longer it was evaporated to dry-

(5) Damschroder and Shriner, THIS JOURNAL, **59**, 931 (1937).
(6) Steinkopf, *Ber.*, **41**, 2541 (1908).
(7) Arndt, *Org. Syn.*, **15**, 4 (1935).

ness. The yield of colorless needles of 4,5,6-trimethoxycoumaran-3-one (VIII) was quantitative. The material was purified by repeated crystallization from absolute alcohol. It melted at 142.5–143.5°.

Anal. Calcd. for $C_{11}H_{12}O_5$: C, 58.93; H, 5.36. Found: C, 59.03; H, 5.48.

Methylation of 4,6-Dihydroxy-7-methoxycoumaran-3-one (X).—Sixty milligrams of this coumaranone was dissolved in 4 cc. of dioxane and 1.7 cc. of the above diazomethane solution was added. This contained about 150 mg. of diazomethane, four times the theoretical amount required. The procedure followed was the same as above and quantitative methylation resulted. The colorless needles of 4,6,7-trimethoxycoumaran-3-one (XI) melted at 153.5–154.5°.

Anal. Calcd. for $C_{11}H_{12}O_5$: C, 58.93; H, 5.36. Found: C, 59.28, 59.24; H, 5.25, 5.21.

Antiarol (3,4,5-Trimethoxyphenol) (XIII).—Antiarol was prepared from pyrogallol trimethyl ether according to the procedure of Chapman, Perkin and Robinson[8] except that the reduction of the intermediate 2,6-dimethoxyquinone was accomplished with sulfur dioxide instead of hydrogen sulfide, as recommended by Hattori.[9] The product used melted at 148°.

α - Chloro - 2 - hydroxy - 4,5,6 - trimethoxyacetophenone (XIV).—In 25 cc. of dry ether were suspended 5 g. of antiarol, 1.5 g. of chloroacetonitrile, and 2 g. of powdered anhydrous zinc chloride. Dry hydrogen chloride was passed into the mixture. Almost at once a paste began to form and heating occurred. The stream of hydrogen chloride was continued six hours, during which time half the ether evaporated. The flask was stoppered and allowed to stand overnight, then 25 cc. of cold water was added slowly. The resulting solution was shaken thoroughly with 25 cc. of ether, and the water layer was separated and refluxed one-half hour. The flask was cooled in ice and the voluminous precipitate which had formed was removed by filtration. The yield was 3 g. (42%). The sample analyzed was purified by repeated recrystallization, each time with the aid of norit. The crystals were dissolved in hot absolute alcohol, norit was added and the solution was warmed for a few minutes. The solution was filtered and then warmed again to boiling, and warm water was added until the solution was permanently cloudy. The flask was allowed to stand until it had reached room temperature. The pure product consisted of small colorless needles which, in the mass, had a faint greenish tinge. The m. p. was 107–107.5°.

Anal. Calcd. for $C_{11}H_{13}ClO_5$: C, 50.67; H, 4.99; Cl, 13.60. Found: C, 50.82; H, 4.93; Cl, 13.31.

4,5,6-Trimethoxycoumaran-3-one (VIII).—In a 25-cc. Erlenmeyer flask were mixed 0.71 g. of the above chloro ketone, 0.83 g. of powdered sodium acetate, and 7 cc. of alcohol. The mixture was refluxed two hours, becoming rose-colored, and was then poured into 110 cc. of a cold saturated sodium chloride solution. The voluminous rose-colored precipitate, collected on a filter, contained some sodium chloride. It was extracted with boiling absolute alcohol which was then treated twice with norit. The final filtrate was cooled in a dry ice–ether mixture, and the colorless needles formed were separated by filtration. A recrystallization gave no change in the m. p. of 142.5–143.5°. Decomposition occurred at the melting point. The yield of pure product was 0.55 g. (91%).

Anal. Calcd. for $C_{11}H_{12}O_5$: C, 58.93; H, 5.36. Found: C, 58.79; H, 5.37.

A mixed melting point with the methylation product of 4,6-dihydroxy-5-methoxycoumaran-3-one (VII) showed no depression.

2,5-Dimethoxyresorcinol (XVII).—This compound was prepared from pyrogallol tribenzyl ether by the method of Baker, Nodzu and Robinson[10] as modified by Shah, Mehta and Wheeler.[11]

α - Chloro - 2,4 - dihydroxy - 3,6 - dimethoxyacetophenone (XVIII).—About 3.5 g. of 2,5-dimethoxyresorcinol was dissolved in 40 cc. of dry ether, along with 1.55 g. of chloroacetonitrile. Dry hydrogen chloride was passed into the solution for six hours, crystals appearing on the walls of the flask a short time after the reaction was started. The reaction mixture was allowed to stand overnight, and then the ether was decanted. The brownish mass was washed with dry ether and then was treated with 40 cc. of water. The mixture was warmed on a steam-bath for one hour and then cooled, when the oil which had separated solidified. A small amount of pink crystals, weighing 0.16 g., remained suspended in the water. This was collected on a filter and recrystallized by dissolving in absolute alcohol, treating the solution with norit, and reprecipitating by adding 3 volumes of water to the filtrate. The total yield of product, after one recrystallization, was 1.3 g. (about 25%). The colorless needles of the pure compound had a m. p. of 150.5–151.5°.

Anal. Calcd. for $C_{10}H_{11}ClO_5$: C, 48.70; H, 4.50. Found: C, 48.53; H, 4.66.

4,7-Dimethoxy-6-hydroxycoumaran-3-one (XIX).—In 12 cc. of alcohol were put 1.1 g. of the above chloro ketone and 1.2 g. of powdered sodium acetate. The solution was refluxed two and one-half hours, during which time it gradually became red, and then was poured into 190 cc. of cold saturated sodium chloride solution. After standing overnight in a refrigerator, the precipitate was removed by filtration. It consisted of a mixture of cubic sodium chloride crystals and the colorless monoclinic prisms of the product. This mixture was extracted with 40 cc. of boiling absolute alcohol. This extract was treated with norit, concentrated to 5 cc., and cooled. This solid was collected on a filter and was recrystallized to constant melting point from absolute alcohol. The pure compound melted at 180–181° with decomposition. The yield of purified material was 0.4 g. (43%).

Anal. Calcd. for $C_{10}H_{10}O_5$: C, 57.15; H, 4.80. Found: C, 57.31; H, 4.94.

4,6,7-Trimethoxycoumaran-3-one (XI).—In 25 cc. of dioxane was dissolved 0.32 g. of the above hydroxycoumaranone. Seven cubic centimeters of the diazomethane solution previously mentioned was added; this contained about 0.45 g. of diazomethane, four times the theoretically required amount. The solution was allowed to

(8) Chapman, Perkin and Robinson, *J. Chem. Soc.*, 3028 (1927).
(9) Hattori, *Acta Phytochim. (Japan)*, **5**, 226 (1931).
(10) Baker, Nodzu and Robinson, *J. Chem. Soc.*, 77 (1929).
(11) Shah, Mehta and Wheeler, *ibid.*, 1557 (1938).

stand overnight, and then the same amount of diazomethane solution was added again. Seven hours later the solution was evaporated to dryness *in vacuo* to give 0.27 g. (80%) of colorless needles, which were recrystallized from absolute alcohol to give a product melting at 153.5–154.5°.

A mixed melting point with the methylation product of 4,6-dihydroxy-7-methoxycoumaran-3-one (X) showed no depression.

4,6 - Dihydroxy - 2 - (*p* - hydroxybenzal) - 5 - methoxycoumaran-3-one (IX).—The method of von Auwers and Pohl[12] was employed. A solution of 0.5 g. of 4,6-dihydroxy-5-methoxycoumaran-3-one and 0.4 g. of *p*-hydroxybenzaldehyde in 10 cc. of absolute alcohol was warmed to 65–70°. Five drops of concentrated hydrochloric acid was then added, the solution immediately becoming red. The temperature was kept at 65–70° for two hours, and the solution was then poured into 200 cc. of water. After the mixture had stood for two days the brown precipitate which had formed was removed by filtration and was dissolved in a few cubic centimeters of alcohol. This red solution was treated with norit and then filtered. The orange filtrate was diluted with 5–10 volumes of water. After the flask had been cooled and scratched with a glass rod, yellow needles formed which weighed 0.55 g. (72%). The sample analyzed was recrystallized again as described. The golden-yellow needles were dried in a vacuum desiccator at 2 mm. over calcium chloride for twenty-four hours, and then for three hours in an Abderhalden drier over phosphorus pentoxide at 2 mm. and 110°. The product so prepared decomposed at 291° on a Maquenne block.

Anal. Calcd. for $C_{16}H_{12}O_6$: C, 63.98; H, 4.03. Found: C, 64.18; H, 3.99.

A small amount of this material in alcoholic solution was treated with hydrogen at 3 atm. pressure and with an equal weight of platinum oxide catalyst present. Reduction occurred rapidly; the solution on evaporation to dryness under reduced pressure in a nitrogen atmosphere gave a white residue melting at 114–117° which decomposed rapidly and could not be purified.

2 - (*p* - Anisal) - 4,5,6 - trimethoxycoumaran - 3 - one (XV).—In 5.5 cc. of warm absolute alcohol was dissolved 0.6 g. of 4,5,6-trimethoxycoumaranone, 0.42 g. of anisaldehyde, and 2 drops of concentrated hydrochloric acid. The mixture was heated at 60–70° for two hours, the solution gradually becoming red. It was poured into 60 cc. of water and the mixture was allowed to cool. The reddish-brown solid formed was separated by filtration and after one recrystallization from alcohol weighed 0.7 g. (77%). Repeated recrystallization from alcohol, with the aid of norit, gave golden-yellow crystals melting at 148–149°. The solid quickly assumed an orange color on exposure to air.

Anal. Calcd. for $C_{19}H_{18}O_6$: C, 66.65; H, 5.30. Found: C, 66.63; H, 5.18.

2 - (*p* - Anisyl) - 4,5,6 - trimethoxycoumaran - 3 - one (XVI).—One-tenth gram of the above anisalcoumaranone and 0.1 g. of platinum oxide catalyst were suspended in 30 cc. of absolute alcohol, and the mixture was shaken with hydrogen at 3 atm. pressure. Absorption was complete and the solution was colorless in five minutes. The alcohol was distilled *in vacuo* to 1 cc., low-boiling petroleum ether was added, and the solution was cooled in an acetone–dry-ice bath. Seventy milligrams (70%) of colorless needles was collected on a filter and was recrystallized with absolute alcohol and low-boiling petroleum ether to give 6 mg. of a product melting at 93–94°. Some decomposition seemed to occur at each crystallization, since the alcoholic solution became slightly yellow when heated.

Anal. Calcd. for $C_{19}H_{20}O_6$: C, 66.25; H, 5.85. Found: C, 65.73; H, 5.95.

4,6 - Dihydroxy - 2 - (*p* - hydroxybenzal) - 7 - methoxycoumaran-3-one (XII).—To a solution of 1 g. of 4,6-dihydroxy-7-methoxy-coumaranone and 0.8 g. of *p*-hydroxybenzaldehyde in 10 cc. of absolute alcohol at 65–70°, 10 drops of concentrated hydrochloric acid was added. The deep red solution was kept at 65–70° for two hours and was then poured into 200 cc. of water. The brick-red precipitate weighed 1.4 g. (92%).

The sample analyzed was purified by dissolving in 75% alcohol, treating the solution with norit, filtering, and diluting the filtrate with 4 volumes of water. The mixture was allowed to stand in the refrigerator for two days. The red crystals formed were removed by filtration and again dissolved in alcohol. Addition of 10 volumes of water caused rapid precipitation of the product as an orange powder. This was dried in an Abderhalden drier over phosphorus pentoxide at 2 mm. and 110° for eighteen hours. The product so prepared decomposed at 282° on a Maquenne block.

Anal. Calcd. for $C_{16}H_{12}O_6$: C, 63.98; H, 4.03. Found: C, 64.16; H, 4.25.

A small amount of this material in alcoholic solution was treated with hydrogen at 3 atm. pressure in the presence of an equal weight of platinum oxide catalyst. Reduction took place rapidly; the solution on evaporation to dryness under reduced pressure in a nitrogen atmosphere gave a light-yellow solid which melted with decomposition at about 155–170°. The material decomposed when manipulated and could not be purified.

2 - (*p* - Anisal) - 4,6,7 - trimethoxycoumaran - 3 - one (XX).—In 3.5 cc. of absolute alcohol were suspended 0.26 g. of 4,6,7-trimethoxycoumaranone, 0.18 g. of anisaldehyde, and 2 drops of concentrated hydrochloric acid. This mixture was held at 65–70° for one and one-half hours. The red solution was then poured into 35 cc. of water, and the mixture was allowed to stand for one hour. The red solid was collected on a filter; it weighed 0.3 g. (76%). The solid was dissolved with difficulty in 125 cc. of boiling absolute alcohol; the solution was filtered and concentrated *in vacuo* to 5 cc. On cooling a greenish-yellow precipitate was formed which was separated by filtration. Water added to the filtrate caused the formation of another precipitate which after several recrystallizations decomposed over a wide range at about 180°; it was discarded. The first precipitate was recrystallized by dissolving in a large volume of boiling absolute alcohol and reprecipitating by adding water. The yellow prisms, melting at 195–196°, tended to take on a greenish tinge on exposure to air.

(12) Von Auwers and Pohl, *Ann.*, **405**, 243 (1914).

Anal. Calcd. for $C_{19}H_{18}O_6$: C, 66.65; H, 5.30. Found: C, 66.61; H, 5.27.

2 - (*p* - Anisyl) - 4,6,7 - trimethoxycoumaran - 3 - one (XXI).—A suspension of 85 mg. of the above anisalcoumaranone and 85 mg. of platinum oxide catalyst in 30 cc. of absolute alcohol was treated with hydrogen at 3 atm. pressure. Reduction was practically complete in two minutes. After ten minutes the platinum catalyst was removed by filtration and the filtrate was concentrated *in vacuo* to 1 cc. Low-boiling petroleum ether was added, causing precipitation of colorless needles. After two hours 70 mg. (82%) of product was collected on a filter. The material was recrystallized by dissolving in hot absolute alcohol and precipitating with low-boiling petroleum ether. Since this was a rather complete precipitation, there were also precipitated the products of the serious decomposition caused by heating the alcoholic solution. Consequently, the last two recrystallizations were carried out by cooling the alcohol solution in a dry ice–acetone bath and collecting the crystals which formed. This materially improved the product, but the loss of product in each crystallization was great and only two such manipulations could be employed. The final product, weighing 2 mg., melted at 116°.

Anal. Calcd. for $C_{19}H_{20}O_6$: C, 66.25; H, 5.85. Found: C, 65.87; H, 6.06.

Isolation of Tectoridin.—Difficulty was experienced in attempting to follow the procedure given by Shibata.[1] The following modification proved satisfactory. A 2950-g. quantity of the fresh rhizomes of *Iris tectorum* Maxim was trimmed of sprouts and adventitious roots, leaving 1985 g. of the stripped rhizomes. These were cut in 1/4-in. (6-mm.) slices and were dried at 80° for thirty hours under a 25-in. vacuum. They then weighed 675 g. This material was ground to a fine powder by passing the dried rhizomes three times through a colloid mill.

The powder was extracted twice for one and one-half hours with 1400-cc. portions of ethyl alcohol. The volume of the alcoholic solution was reduced *in vacuo* to 700 cc. The tannin impurities were then precipitated by adding a 5% alcoholic solution of lead acetate in portions until no further precipitation was observed. The lead tannate precipitate was removed by filtration and the excess lead in the filtrate was precipitated with hydrogen sulfide. The filtrate from the lead sulfide was evaporated to dryness under reduced pressure.

The residue was treated twice with 500-cc. portions of boiling ethyl acetate, for one hour. The extract was discarded. The mass remaining was stirred into 500 cc. of water. The white solid left suspended in the water was collected on a filter and was washed with absolute alcohol and then ether. The tectoridin thus obtained weighed 5.4 g. and melted at 258°.

A further 55 mg. of tectoridin was recovered from the lead tannate precipitate by suspending it in alcohol, removing the lead with hydrogen sulfide, and adding benzene to the concentrated alcoholic filtrate.

By the above procedure a total of 9.4 g. of tectoridin was isolated from 4550 g. of fresh rhizomes.

Tectorigenin.—One gram of crude tectoridin was heated with 75 cc. of 20% sulfuric acid, with stirring, in an oil-bath maintained at 90°. After the mixture was cooled, 0.83 g. of tectorigenin, m. p. 230°, was separated by filtration.

Dimethyltectorigenin.—Tectorigenin was methylated by the reaction with methyl sulfate and alkali according to the method of Mannich, Schumann and Lin.[2] This ether was also made by methylation with diazomethane. It melted at 188°.

Attempts to convert dimethyltectorigenin into trimethyltectorigenin were made by treatment with an excess of methyl sulfate and alkali, treatment with an excess of diazomethane in methanol and dioxane solutions, methyl iodide and silver oxide, methyl iodide and sodium in liquid ammonia, methyl iodide and phenyllithium, methyl iodide and triphenylmethylsodium. Acetylation of dimethyltectorigenin by acetic anhydride and pyridine yielded the acetyl derivative which melted at 213–214°. Attempts to convert this acetyl derivative to the methyl derivative according to Nierenstein's method[13] were not successful.

Summary

The structure of the two isomeric coumaranones produced by ring closure of α-chloro-2,4,6-trihydroxy-5-methoxyacetophenone was established by methylation and synthesis of each of the methylated compounds. One of these methylated isomers, 4,5,6-trimethoxycoumaran-3-one, was obtained by the following sequence: pyrogallol trimethyl ether → 2,6-dimethoxyquinone → 2,6-dimethoxyhydroquinone → 3,4,5-trimethoxyphenol (antiarol) → α-chloro-2-hydroxy-4,5,6-trimethoxyacetophenone → 4,5,6 - trimethoxycoumaran-3-one. The isomeric product, shown to be 4,6,7-trimethoxycoumaran-3-one, was synthesized as follows: pyrogallol tribenzyl ether → 2,6-dibenzyloxyquinone → 2,6-dibenzyloxyhydroquinone → 2,6-dibenzyloxy-1,4-dimethoxybenzene → 2,5-dimethoxyresorcinol → α-chloro-2,4-dihydroxy - 3,6 - dimethoxyacetophenone → 6 - hydroxy-4,7 - dimethoxycoumaran - 3 - one → 4,6,7-trimethoxycoumaran-3-one.

Condensation of each of these trimethoxycoumaranones with anisaldehyde yielded the 2-anisal derivatives, which were reduced and the two isomers 2-(*p*-anisyl)-4,5,6-trimethoxycoumaran-3-one and 2-(*p*-anisyl)-4,6,7-trimethoxy-coumaran-3-one were isolated.

Tectoridin was isolated from the rhizomes of *Iris tectorum* Maxim and hydrolyzed to tectorigenin. Methylation of tectorigenin yielded only a dimethyl derivative. No trimethyltectorigenin could be obtained, even under drastic conditions. Comparison of the properties of the known methyl derivatives of tectorigenin with those of the above synthetic coumaranones showed that tectorigenin does not possess the coumaranone structure.

URBANA, ILLINOIS RECEIVED JUNE 23, 1939

(13) Nierenstein, THIS JOURNAL, **52**, 4012 (1930).

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

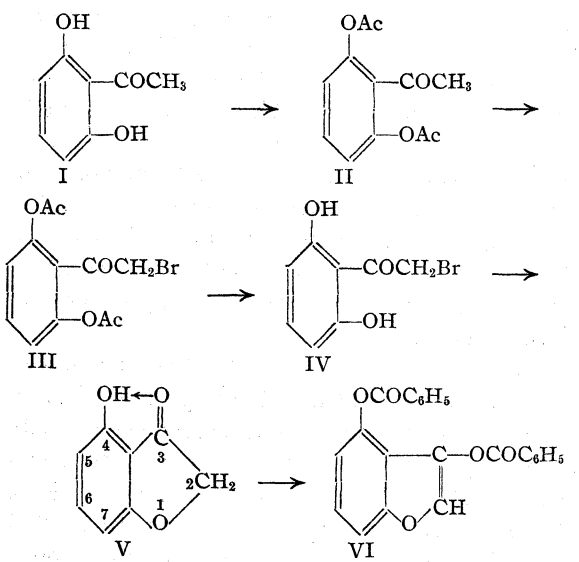
Derivatives of Coumaran. V. Synthesis of 4-Hydroxycoumaran-3-one

BY R. L. SHRINER AND MICHAEL WITTE

The synthesis of many substituted coumaranones has been accomplished by the reaction of phenols with α-halo acid chlorides[1] or with α-halonitriles.[2] These methods have proven useful for the synthesis of coumaranones with hydroxyl groups in the 6- and 7-positions. This paper reports the synthesis and properties of 4-hydroxycoumaran-3-one (V).

Acetylation of 2,6-dihydroxyacetophenone[3] (I) yielded the diacetoxy derivative (II).[4] When this 2,6-diacetoxyacetophenone was treated with bromine in carbon disulfide solution, substitution took place in the side chain giving an 80% yield of the monobromo compound (III). If 2,6-dihydroxyacetophenone is brominated without acetylation nuclear substitution takes place as well as side chain halogenation and a mixture is produced. If acetic acid is used instead of carbon bisulfide, a dibromo derivative is produced. Kröhnke[5] has pointed out that monohalo ketones are in equilibrium with dihalo ketones.

Hydrolysis of the 2,6-diacetoxy-α-bromoacetophenone with dilute hydrobromic acid yielded the 2,6-dihydroxy-α-bromoacetophenone (IV) which underwent ring closure upon treatment with sodium acetate to produce 4-hydroxycoumaran-3-one (V). Benzoylation by the Schotten–Bauman method yielded the dibenzoate, (VI). This is analogous to the oxygen acetylation of coumaran-3-ones previously reported.[6]



The physical properties of 4-hydroxycoumaran-3-one (V) are quite different from those of other monohydroxycoumaranones. It began to sublime at 85° and melted at 120°. 6-Hydroxycoumaran-3-one[7] melts at 243° and the 7-hydroxy isomer[8] at 184°. The 4-hydroxy isomer is also more soluble than the others. This suggests that the hydroxyl group is chelated with the carbonyl group as shown in Formula V. The chelated conjugated system in this structure is in agreement with the suggestion of Mills and Nixon[9] that the two carbon atoms common to the benzene ring and a five-membered ring are joined by a single bond.

Experimental

2,6-Diacetoxyacetophenone.[10]—A solution of 15 g. of 2,6-dihydroxyacetophenone[11] and 45 cc. of acetic anhydride was refluxed for five hours; then, while still hot, it was poured into ice water. A greenish oil separated which upon standing crystallized. The crude compound was recrystallized twice from isoamyl alcohol to give 19 g. of white platelets melting at 60° (corr.).

Anal. Calcd. for $C_{12}H_{12}O_5$: C, 61.01; H, 5.10. Found: C, 60.99; H, 5.47.

2,6-Diacetoxy-α-bromoacetophenone.—Four grams of 2,6-diacetoxyacetophenone was dissolved in 75 cc. of carbon disulfide and 2.8 g. of bromine dissolved in 25 cc. of carbon disulfide was added dropwise with stirring. The addition took one hour and sometimes heating was required to initiate the reaction. The reaction went to completion at room temperature. The carbon disulfide was then removed from the reaction mixture by distillation and the resulting crude brominated compound was twice recrystallized from isopropyl alcohol to give 4.3 g. (80%) of white crystals, m. p. 112° (corr.).

Anal. Calcd. for $C_{12}H_{11}O_5Br$: C, 45.71; H, 3.49; Br, 25.43. Found: C, 45.71; H, 3.60; Br, 25.30.

(1) Auwers and Pohl, *Ann.*, **405**, 243, 294 (1914).
(2) Hoesch, *Ber.*, **48**, 1122 (1915).
(3) Baker, *J. Chem. Soc.*, 1953 (1934).
(4) Dattatraya, Balkrishna, Limaye and Gorind, *J. Ind. Chem. Soc.*, **12**, 788 (1935).
(5) Kröhnke, *Ber.*, **69**, 921–935 (1936).
(6) Shriner and Anderson, THIS JOURNAL, **60**, 1418 (1938).
(7) Brüll and Friedlaender, *Ber.*, **30**, 297 (1897).
(8) Mostmann and Tambor, *ibid.*, **49**, 1261 (1916).
(9) Mills and Nixon, *J. Chem. Soc.*, 2510 (1930).
(10) Dattatraya, Balkrishna, Limaye and Gorind, *J. Ind. Chem. Soc.*, **12**, 788 (1935), prepared this compound, but reported that they had to distil the above at 180° and 10 mm. and inferred that they had an oil. No mention of a solid was made by these authors although their compound analyzed correctly for C and H.
(11) This compound was prepared by modification of Baker's[3] method developed by Alfred Russell of the University of North Carolina. The details will be published by him.

2,6-Diacetoxy-α,α-dibromoacetophenone.—Four grams of 2,6-diacetoxyacetophenone was dissolved in 50 cc. of glacial acetic acid and 5.6 g. of bromine dissolve in 25 cc. of glacial acetic acid was added dropwise with stirring. The addition took one hour and sometimes heating was required to initiate the reaction which then continued to completion at room temperature. The reaction mixture was then poured into ice water with stirring and the crude brominated compound separated in greenish crystals. These were filtered and twice recrystallized from isopropyl alcohol to give 5.3 g. of white crystals which melted at 113° (corr.).

Anal. Calcd. for $C_{12}H_{10}O_5Br_2$: C, 36.54; H, 2.53; Br, 40.50. Found: C, 36.79; H, 2.66; Br, 39.82.

Both of the above halogen compounds gave an active halogen test by first heating with alcoholic sodium ethoxide solution, then testing the resulting solution after acidification with silver nitrate.

2,6-Dihydroxy-α-bromoacetophenone.—A mixture of 3 g. of 2,6-diacetoxy-α-bromoacetophenone, 80 cc. of 60% ethanol, 20 cc. of hydrobromic acid (40%) and 1 mg. of sodium hydrosulfite was refluxed for one hour. The solvent was then distilled at 30° and 30 mm. pressure to leave yellow platelets which were recrystallized twice from benzene to give a yield of 1.6 g. It melted at 143° (corr). This compound gave a green ferric chloride test.

Anal. Calcd. for $C_8H_7O_3Br$: C, 41.55; H, 3.03. Found: C, 41.84; H, 2.99.

4-Hydroxycoumaran-3-one.—A solution of 1 g. of 2,6-dihydroxy-α-bromoacetophenone, 1 g. of sodium acetate trihydrate, 1 mg. of sodium hydrosulfite and 50 cc. of ethanol was refluxed for one hour. Twenty cubic centimeters of water was added and 30 cc. of ethanol was distilled from the reaction mixture. The resulting solution was allowed to cool and placed in a refrigerator overnight. Brown crystals separated and were filtered and recrystallized twice from high boiling petroleum ether to give 0.4 g. of brown granular crystals. This compound began subliming at 85° and finally melted at 120° (corr.). It gave a violet ferric chloride test for phenols.

Anal. Calcd. for $C_8H_6O_3$: C, 64.00; H, 4.00. Found: C, 64.21; H, 4.17.

In this last reaction a few milligrams of sodium hydrosulfite was added to the reaction mixture to minimize oxidation of the rather unstable 2,6-dihydroxy-α-bromoacetophenone.

3,4-Dibenzoxybenzofuran.—A solution of 0.5 g. of 4-hydroxycoumaran-3-one, 1 g. of benzoyl chloride, 1 g. of sodium carbonate, 10 cc. of water and 15 cc. of acetone was warmed gently for thrity minutes, then poured into ice water. The benzoylated compound separated and was filtered. It was recrystallized from ethyl acetate to give 1.0 g. of colorless needles; m. p. 183° (corr.).

Anal. Calcd. for $C_{15}H_{10}O_4$: C, 73.74; H, 3.91. Found: C, 73.47; H, 4.03.

Summary

4-Hydroxycoumaran-3-one has been synthesized by the following sequence: 2,6-dihydroxyacetophenone ⟶ 2,6-diacetoxyacetophenone ⟶ 2,6-diacetoxy-α-bromoacetophenone ⟶ 2,6-dihydroxy-α-bromoacetophenone ⟶ 4-hydroxycoumaran-3-one. The low melting point and tendency to sublime exhibited by this compound indicate that the hydroxyl group is probably chelated with the carbonyl group.

URBANA, ILLINOIS RECEIVED JUNE 26, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF THE GENERAL ELECTRIC CO.]

Electrical Properties of Solids. IV.* The Influence of Thermal History on Polyvinyl Chloride Plastics

BY RAYMOND M. FUOSS

I. Introduction.—Plastics containing polyvinyl chloride have two characteristics which sharply differentiate them from most of the systems ordinarily studied by physico-chemical methods: the electrical properties of a given sample depend on the method of preparing the sample[1] and, after preparation, the properties of a given sample change with time. Obviously the influence of the corresponding variables must be eliminated before any correlation between properties and chemical composition and structure is attempted. The most important item in the preparation of the sample is the thermal history; two samples of the same composition with identical thermal histories will give results which check as precisely as might be desired (assuming that trivial variables, such as those due to surface effects and humidity, are eliminated).[2]

The changes with time are of at least two kinds: (1) a slow decrease of dielectric constant, amounting to several per cent., while the density remains constant and (2) a slow increase of d. c. conductance, which in turn induces an increase in dielectric constant and a. c. absorption. These two effects combine to produce a minimum in the dielectric constant–time curve.

It is the purpose of this paper to present and

(*) Paper III, THIS JOURNAL, **60**, 456 (1938).

(1) Fuoss, *Trans. Electrochem. Soc.*, **74**, 91 (1938).

(2) Fuoss, THIS JOURNAL, **59**, 1703 (1937).

discuss some experimental results of a study of the properties outlined above. Not enough data are yet available to give a complete description of the plastic solid, because so very much more remains to be done. Enough has been accomplished, however, to show several promising lines of attack on the general problem, and it is believed that the results are sufficiently interesting and suggestive to be made available to other workers in this field.

II. Experimental Methods.—All measurements were made on disks of plastic 10 cm. in diameter and 6 mm. in thickness. All samples were surfaced in some way to eliminate series capacity due to air films between the sample and electrodes. Diluted aquadag, powdered graphite, or tin foil, the latter rubbed on with a minute amount of petrolatum, all gave satisfactory results; depending on the composition and flexibility of the sample, one or another method was preferred. (It might be well to point out that *tin* must be used in the foil method: all other available foils were too hard to give adequate contact.)

The cell[1] and bridges[1-3] used in the measurements have been described previously.

In general, the samples were prepared by cold mixing a weighed amount of polyvinyl chloride and plasticizer. (The polyvinyl chloride was from the same lot as that used in preparing samples for the two previous papers of this seiries.[3,4]) The mixture was then worked on a rubber mill under controlled and recorded conditions (time and temperature of milling, thickness of sheet, speed of rolls and size of batch) Disks about 0.5 mm. thick and 9.84 cm. in diameter were stamped from the final mill sheet. These disks will shrink much more parallel to the milling direction (as much as 40%) on heating to 150° than perpendicular to this direction, but heating above 100° under pressure will gradually destroy this elastic memory. In order to obtain samples for electrical measurements which would remain circular, 15–20 disks from the mill sheet were stacked with mill directions crossed on consecutive sheets and compressed to a single disk in a hot closed mold under hydraulic pressure. Time and temperature of pressing were always recorded. After pressing, the sample was weighed, surfaced, placed in the cell and allowed to come to temperature equilibrium in an oil thermostat held at 40.00 ± 0.01°.

Electrical measurements were then made. Thickness of cell plus sample was determined before and after the electrical measurements, and also during them, if the run lasted more than an hour. (As previously pointed out,[1] the dimensions change with time, and since the thickness enters the calculation of dielectric constant and conductance explicitly, it must be determined accurately.)

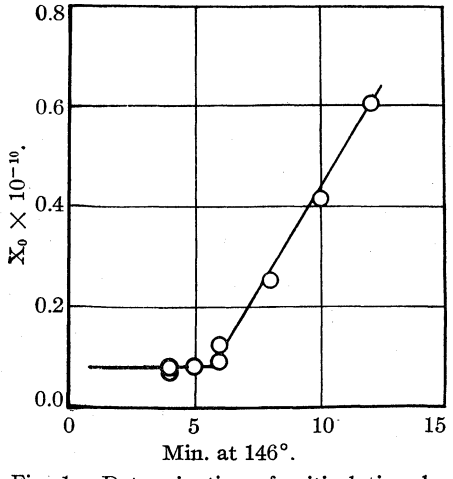


Fig. 1.—Determination of critical time by conductance method.

III. Results and Discussion.—It has been shown[1] that the d. c. conductance of plastics containing polyvinyl chloride plasticized with tricresyl phosphate increases on exposure to heat. The preparation of the sample involves two heat treatments, milling and pressing. The relation between d. c. conductance, which is a measure of the hydrogen chloride produced by pyrolysis, and the time and temperature of heating, is given by the equation

$$\kappa_0 = A \int_0^t \exp.\,[-B/T(t)]\,dt \qquad (1)$$

where A depends on the composition of the plastic and on the temperature at which the electrical measurement is made.

In order to find a correlation between conductance and the actual amount of hydrogen chloride present, a series of samples was made up, with various amounts of lead abietate dissolved in the plasticizer. These samples were then heated for different times at different temperatures. A typical result is shown in Fig. 1, which is for a set of samples containing 0.5% lead abietate in the tricresyl phosphate. The composition was 60% polyvinyl chloride by weight. After milling fifteen times at 105°, which was sufficient to plasticize the polymer, the samples were pressed at 145° for times ranging from four to twelve minutes. As will be seen in the figure, the d. c. conductance, measured at 40°, was low (0.08×10^{-10}) and independent of heating time up to six minutes; beyond this time, however, the conductance increased rapidly with further heating. The break in the curve clearly corresponds to the time required for the lead present initially as abietate to be converted into chloride. After the lead is consumed, the conductance rises parallel to the conductance–time curve for the blanks (similar sample containing no dissolved lead).

(3) Fuoss, THIS JOURNAL, **60**, 451 (1938).
(4) Fuoss, *ibid.*, **60**, 456 (1938).

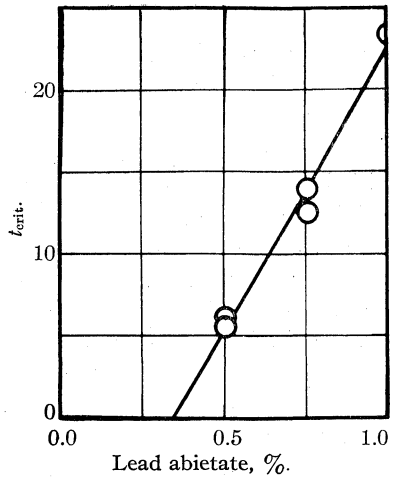


Fig. 2.—Dependence of critical time on lead content.

Figure 2 is a summary of data referring to samples heated at 145°, containing various percentages of lead abietate. The ordinate is the time required to consume the lead added. Since the line does not go through the origin, we conclude that the components of the plastic contained some material which reacts with lead abietate before the pressing. The intercept at zero time in Fig. 2 corresponds to 0.35% of lead abietate; 100 parts per million of hydrogen chloride originally in the polyvinyl chloride would use up this quantity of lead. An aqueous extract of the polyvinyl chloride gave a turbidity with silver nitrate solution, which indicated this order of magnitude of extractable chloride. After allowing for the lead consumed initially, 1.00 g. of lead abietate per 100 g. of plasticizer corresponds to 60 mg. of hydrogen chloride per 100 g. of polyvinyl chloride in the 40:60 plastic.

The dependence of lead consumption on temperature of heating is shown in Fig. 3, where data covering the range 130–160° are presented. The times were obtained as the breaks in the conductance–heating time curves; these samples contained 0.7% lead abietate in the tricresyl phosphate. Assuming that the amount of lead chloride formed is measured by the time to the break in the heating curve, the slope of the line in Fig. 3 gives 33 kcal. as the energy associated with the reaction between the products of pyrolysis and the lead abietate in the plastic. This value is practically the same as that found by Dr. M. M. Sprung[5] for the pyrolysis of dry polyvinyl chloride in a stream of nitrogen. The rate of evolution of hydrogen chloride at various temperatures was plotted against reciprocal of absolute temperature; a straight line was obtained, whose slope gave 35 kcal. In a typical experiment, 47 mg. of hydrogen chloride was obtained per 100 g. of polyvinyl chloride in fifteen minutes at 150°. This is about twice as much as was found by the lead abietate (21 mg. hydrogen chloride per 100 g. polyvinyl chloride in twelve minutes at 146°) method in the plastic, and suggests that several reactions, competing for hydrogen chloride, are taking place in the presence of tricresyl phosphate containing lead abietate.

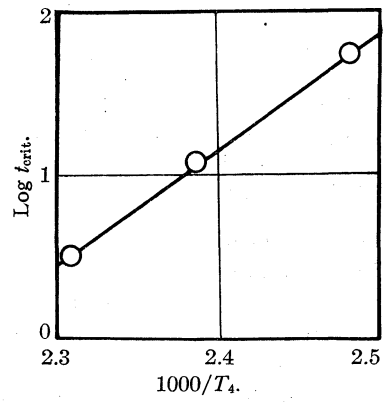


Fig. 3.—Temperature coefficient of pyrolysis.

There is other experimental evidence that the chain of reactions in the plastic is not simple pyrolysis of polyvinyl chloride to give hydrogen chloride, followed by metathesis between hydrogen chloride and lead abietate. If samples are made up containing 60 parts polyvinyl chloride and 40 parts of another plasticizer, such as dibenzyl sebacate, dibutyl phthalate, diphenyl ether, amylnaphthalene and so on, their d. c. conductance is always much higher (regardless of the intrinsic conductance of the plasticizer) for a given thermal history than that of samples made with tricresyl phosphate. This suggests the possible explanation that the hydrogen chloride set free by pyrolysis of the polymer reacts with the tricresyl phosphate, forming phosphorus oxychloride as the ultimate end-product of reaction by the reverse of the usual synthesis of tricresyl phosphate. Then the products of this reaction in turn react with the lead abietate. This assumption was checked by adding 10% octyl borate to a sample made up with dibenzyl sebacate: the resulting sample gave a conductance as low as that obtained with tricresyl phosphate, and octyl borate is a compound

(5) Unpublished work done in this Laboratory.

which one would expect to react with hydrogen chloride to give non-electrolytic products.

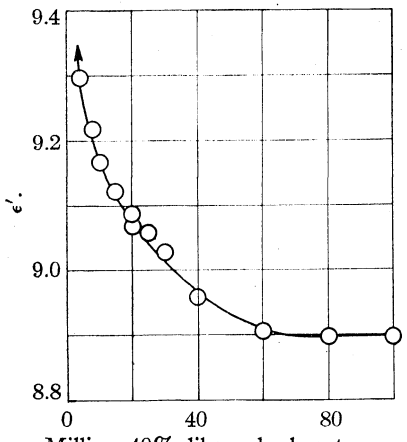


Fig. 4.—Dependence of dielectric constant on milling for polyvinyl chloride–dibenzyl sebacate.

It should be mentioned that the milling was kept to the minimum for thorough mixing in the above set of samples where press time and temperature were under investigation. Separate experiments showed that the d. c. conductance produced by the milling alone was 0.02×10^{-10}, or about 25% of the lowest and 2% of the highest d. c. conductance involved. The minimum value of 0.08×10^{-10} at 40° is due to the presence of electrolyte which will not react with lead abietate; the latter is an extremely weak electrolyte.[6,7]

For plastics made with tricresyl phosphate as plasticizer, the primary effect on electrical properties of milling is an increase of d. c. conductance due to pyrolysis. This is not in general true, however; for example, with dibenzyl sebacate as plasticizer, the dielectric constant decreases with increased number of millings, and becomes constant after about fifty times through the mill at 105° as is shown in Fig. 4. Apparently different plasticizers require different amounts of milling to reach homogeneity. With tricresyl phosphate, the dielectric constant was independent of the number of times the mixture was milled; in fact, samples made by hot pressing an unmilled mixture of polyvinyl chloride and tricresyl phosphate, which had been thoroughly rubbed together cold in a mortar, gave the same dielectric constant as milled material, if allowance for differences in d. c. conductance were made.

The density was the same for the various samples of Fig. 4, and the dielectric constant *decreased* with increased milling; hence the action of the mill in the plasticization process is more than mere mixing for the case of dibenzyl sebacate. The rate at which the dielectric constant–milling curve reaches its asymptote at a fixed milling temperature might be used as a measure of plasticizing power of a given liquid. On this basis, tricresyl phosphate is a more effective plasticizer than dibenzyl sebacate.

Practically all of the plastics studied so far show a small but systematic change of dielectric constant with time. An example is shown in Fig. 5 for 60 and 1000 cycle measurements at 40° on a sample containing 40% tricresyl phosphate and 60% polyvinyl chloride. If the logarithm of the difference between the dielectric constant at time t and its asymptotic value is plotted against the square root of the age of the sample, reckoned from the time it was cooled in the disk mold, a straight line is obtained. The slope depends upon frequency.

A similar relation between logarithm of relaxation and time elapsed after elastic strain has been observed by Dr. W. I. Patnode of this Laboratory in a study of the mechanical properties of plastics. When the samples considered here are taken from the disk mold, there is an immediate shrink of about 1% in diameter, together with an increase in thickness. These changes continue for days, but occur in such a way that the density, within an experimental error of 0.1%, is con-

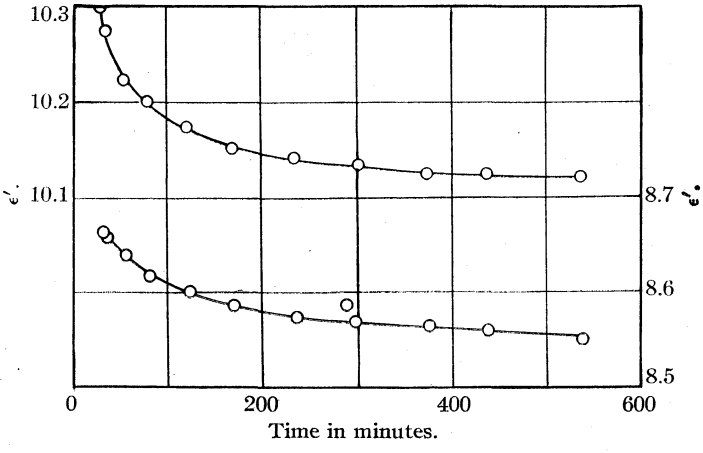


Fig. 5.—Aging curves at 60 (top) and 1000 (bottom) cycles.

(6) Deitz and Fuoss, THIS JOURNAL, **60**, 2394 (1938).
(7) Elliott and Fuoss, *ibid.*, **61**, 294 (1939).

served. The change in dielectric constant is therefore due to an internal rearrangement of some sort. Polyvinyl chloride molecules are chains of enormous length, held together in the chain direction by C–C bonds. When a sample is pressed, local strains are set up, as shown by the colored patterns which appear in polarized light. If the sample has a fairly high viscosity (less than 70% plasticizer), these strains can relax only slowly, because freedom of orientation comparable to that in liquids is made impossible by the chain structure. Relative motion of whole molecules is impossible in general, but segments of chains can slip past one another, given sufficient energy, so that there exists in the plastic the analog of liquid viscosity, but one dimension of freedom of motion is lost. Adjacent parts of the same or different molecules in a given configuration may have a position of lower potential energy available, but can reach it only when a positive fluctuation in kinetic energy gives them sufficient energy to get over the potential barrier between the metastable and the stable positions. Obviously at the start of the relaxation process, there will be many strained regions which can easily rearrange, irreversibly, of course; therefore the initial change in dielectric constant, which is a measure of internal orientation, is rapid. But as more and more energy is required to rearrange the remaining strained regions, the number of probable transitions per unit time must necessarily decrease, and the system asymptotically approaches a state in which all molecules occupy stable mutual positions. Similar arguments based on increase of entropy have been advanced to explain the relaxation of stress in stretched rubber and like compounds.[8]

After several days, the dielectric constant of a polyvinyl chloride plastic slowly starts to increase again. This change is quite different from the initial decrease, and can be correlated with the simultaneous increase in d. c. conductance. The production of hydrogen chloride which occurs in the pressing continues at room temperature (although at a very much reduced rate), and as hydrogen chloride concentration increases, the dielectric constant increases with it. Simultaneously, the pure a. c. absorption, as measured by the loss factor, ϵ'', increases.

The loss factor is defined for our present work by the equation

$$\epsilon'' = 18 \times 10^{11}(\kappa - \kappa_0)/f \qquad (2)$$

where κ is the specific conductance at frequency f and κ_0 is the d. c. conductance measured on a d. c. bridge.

Equation (2) tacitly implies that the electrolytic conductance is independent of frequency and that its value is determined by d. c. measurement; obviously any variation of electrolytic conductance with frequency would induce a spurious change in apparent a. c. loss factor as defined above. This assumption may require later scrutiny; certainly in the range of high frequencies, it is known that electrolytic conductance is a function of frequency due to relaxation effects.

The correlation between a. c. and d. c. properties is shown in Figs. 6 and 7, where ϵ' and ϵ'' are plotted against the *square root* of d. c. conductance. (It was found empirically that the data approximate linearity with this choice of coördinates; we are at present unable to say whether this form is significant or coincidental.) The important fact shown by Figs. 6 and 7 is that the a. c. properties can be correlated directly with the d. c. conductance; since the latter is determined by the thermal history; we have in the d. c. conductance a variable which summarizes the thermal history as far as electrical properties are concerned.

The samples whose constants are shown in Figs. 6 and 7 were all 40% tricresyl phosphate–60% polyvinyl chloride. Different thermal histories were obtained by varying time and temperature of milling and pressing. It will be noted that data, self-consistent within a few tenths per cent. in dielectric constant, were obtained. In order to eliminate the effect of aging, all data for Figs. 6 and 7 were interpolated to two hours after preparation, from a series of measurements made on each sample. The rate of change of ϵ' and ϵ'' with electrolytic conductance decreases with increasing frequency; details of this behavior will be presented in a later paper.

The data of Figs. 6 and 7 show that we may write

$$\epsilon' = \epsilon_0 + A\sqrt{\kappa_0} \qquad (3)$$

$$\epsilon'' = \epsilon_0'' + B\sqrt{\kappa_0} \qquad (4)$$

where ϵ_0' and ϵ_0'' are the a. c. constants referring to the hypothetical electrolyte-free plastic. The terms in $\sqrt{\kappa_0}$ represent the contributions to a. c. mechanism due to the presence of electrolyte. It is planned to study this question further by using known concentrations of known electrolytes in plastics of various compositions. Incidentally,

(8) Meyer, *Chemistry & Industry*, **57**, 439 (1938).

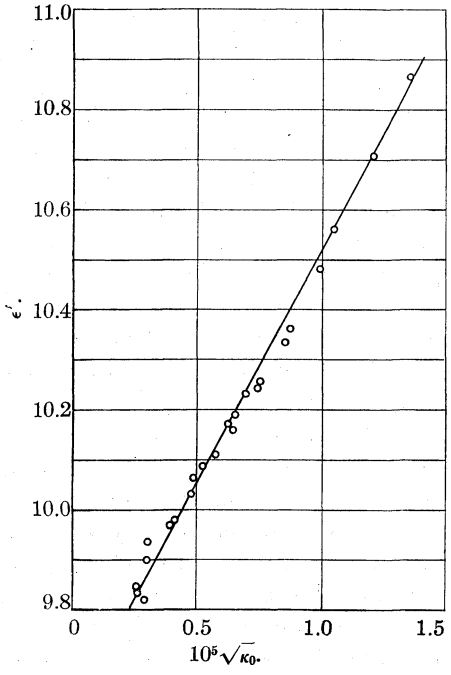


Fig. 6.—Dependence of 60 cycle dielectric constant on d. c. conductance.

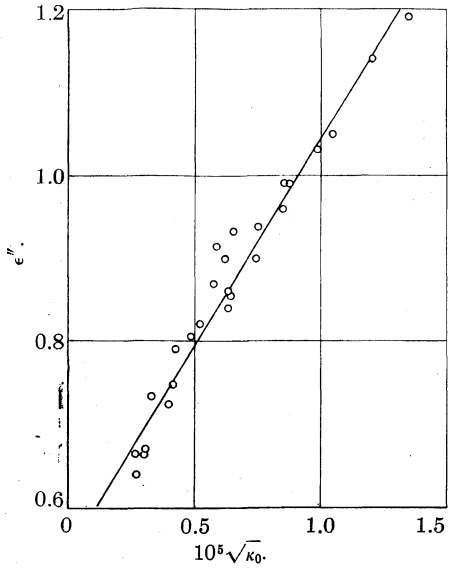


Fig. 7.—Dependence of 60 cycle loss factor on d. c. conductance.

this will permit a study of electrolytic conductance in the range of very high viscosities ($\eta \sim 10^6$ poises).

Summary

1. The electrical properties of polyvinyl chloride plastics depend on thermal history. Increased time and temperature of heating give increased d. c. conductance.

2. The amount of pyrolysis can be followed by adding a soluble lead compound such as lead abietate to the plasticizer and determining the conductance for various heating times and temperatures.

3. The dielectric constant changes with time in a way which suggests a relaxation mechanism.

4. There is a one to one correlation between d. c. conductance, dielectric constant and loss factor.

SCHENECTADY, N. Y. RECEIVED JUNE 3, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF THE GENERAL ELECTRIC COMPANY]

Electrical Properties of Solids. V. Their Variation at 40° with Frequency and Composition in the System Polyvinyl Chloride–Tricresyl Phosphate

BY RAYMOND M. FUOSS

I. Introduction

Polyvinyl chloride as ordinarily obtained is an amorphous white powder, which can be converted under hydraulic pressure at 120° into a transparent brittle solid. By the addition of various liquids, such as tricresyl phosphate, it can be softened or "plasticized," to give solids ranging from glass-like to jelly-like substances, going through a tough rubber-like form at about 35–45% plasticizer. Dilute solutions of the polymer in plasticizers are very viscous liquids. The two-phase system polymer–plasticizer thus permits a study of electrical properties over an enormous range of macroscopic viscosity. By varying the chemical nature of the two components, or by adding a third, a wide range of conductance and dielectric constant can then be investigated.

In previous papers in this series, experimental methods[1] for obtaining electrical data of reasonable precision on solids have been described, and a preliminary account of some of the properties of the system polyvinyl chloride–tricresyl phosphate

(1) (a) Fuoss, THIS JOURNAL, **59**, 1703 (1937); (b) **60**, 451 (1938); (c) **60**, 456 (1938); (d) **61**, 2329 (1939).

TABLE I

DIELECTRIC CONSTANTS OF POLYVINYL CHLORIDE–TRICRESYL PHOSPHATE PLASTICS AT 40°

Polyvinyl chloride, %	Frequency 20 ~	60 ~	120 ~	250 ~	500 ~	1000 ~	2000 ~	5000 ~	10,000 ~
100	3.454	3.435	3.419	3.397	3.370	3.338	3.306	3.263	3.231
95	3.300	3.268	3.257	3.239	3.223	3.204	3.182	3.154	3.132
90	3.320	3.275	3.250	3.225	3.195	3.170	3.145	3.115	3.085
85	3.640	3.510	3.440	3.375	3.320	3.270	3.220	3.165	3.120
80	4.760	4.395	4.190	4.010	3.840	3.695	3.580	3.425	3.310
75	6.50	5.87	5.48	5.10	4.79	4.50	4.23	3.88	3.64
70	8.29	7.56	7.10	6.62	6.17	5.72	5.27	4.67	4.21
65	9.47	9.02	8.64	8.14	7.65	7.14	6.62	5.82	5.24
60	10.00	9.69	9.42	9.08	8.62	8.32	7.78	6.97	6.37
55	10.33	10.00	9.80	9.59	9.37	9.09	8.75	8.08	7.57
50	10.46	10.19	10.02	9.85	9.68	9.50	9.25	8.76	8.30
45	10.45	10.21	10.06	9.90	9.75	9.60	9.40	9.06	8.70
40	10.38	10.18	10.05	9.92	9.80	9.65	9.48	9.22	8.97
35	(12.25)	(11.00)	(10.38)	(10.88)	9.55	9.40	9.28	9.08	8.86
20	....	8.99	....	....	8.90	8.72	..	..	..
0	....	6.92	....	....	6.89	6.89	..	..	..

TABLE II

LOSS FACTORS OF POLYVINYL CHLORIDE–TRICRESYL PHOSPHATE PLASTICS AT 40°

Polyvinyl chloride, %	Frequency 20 ~	60 ~	120 ~	250 ~	500 ~	1000 ~	2000 ~	5000 ~
100	0.031	0.040	0.046	0.053	0.060	0.066	...	...
95	.033	.035	.035	.037	.038	.040	0.042	...
90	.060	.058	.056	.054	.052	.049	.045	...
85	.133	.131	.127	.124	.116	.107	.097	0.079
80	.451	.441	.405	.368	.330	.294	.256	.208
75	.752	.810	.778	.726	.664	.598	.530	.440
70	.920	.978	.994	.992	.972	.930	.880	(.820)
65	.720	.836	.904	.976	1.056	1.090	1.084	1.080
60	.550	.630	.686	.770	0.860	0.952	1.040	1.160
55	.45	.46	.49	.55	.63	.71	0.82	0.98
50	.37	.38	.40	.45	.51	.60	.70	.85
45	.3	.345	.3	.30	.34	.38	.44	.55
40	...	.348	...	.27	.29	.30	.32	....
35	...	1.39	1.05	.80	.60	.45	.35	....

has been presented.[1b] This paper represents the first part of a systematic study of the properties of plastic solids. The conductance and dielectric constant have been determined at 40° over the frequency range 20 to 10^4 cycles (low voltage[1c]) for the system polyvinyl chloride–tricresyl phosphate, over the entire concentration range.

II. Experimental Methods

Cells, bridges, materials, method of preparing and measuring samples and experimental precautions already have been described.[1,2]

Milling was the minimum necessary for thorough mixing, and pressing was only ten minutes at 120°. By using mild thermal conditions in the preparation of this series of samples, pyrolysis of the polyvinyl chloride was kept small, so that the accompanying d.c. conductance due to hydrogen chloride from pyrolysis would not be too serious a disturbing factor.

III. Results

Measurements were made at a number of frequencies between 15–20 cycles and 10 kilocycles. In order to save space in presentation, values of dielectric constant ϵ' and a. c. loss factor ϵ'' have been interpolated from the data to round frequencies in the above range, and are given in Tables I and II. The d. c. conductance was also measured; these values are summarized in Table III.

The a. c. loss factor is defined as

$$\epsilon'' = 18 \times 10^{11} (\kappa - \kappa_0)/f \qquad (1)$$

where κ is the conductance at frequency f and κ_0 is the electrolytic conductance as measured on a d. c. bridge. It is assumed, for the present, that κ_0 is independent of frequency.

(2) Fuoss, *Trans. Electrochem. Soc.*, **74**, 91 (1938).

TABLE III

D. C. CONDUCTANCES OF POLYVINYL CHLORIDE–TRICRESYL PHOSPHATE PLASTICS

Polyvinyl chloride, %	$\kappa \times 10^{10}$	Polyvinyl chloride, %	$\kappa \times 10^{10}$
90	0.001	55	0.198
85	.010	50	.510
80	.014	45	1.462
75	.025	40	3.23
70	.028	35	3.63
65	.014	20	12.40
60	.064	0	0.75

Densities were determined by weighing the samples and measuring their dimensions with vernier scales. For the 60 polyvinyl chloride–40 tricresyl phosphate samples some densities were also determined by weighing under water; the two methods checked within several tenths of one per cent., the experimental precision of the former method. As nearly as we can conclude from the data, polyvinyl chloride and tricresyl phosphate mix to form a plastic without volume change.

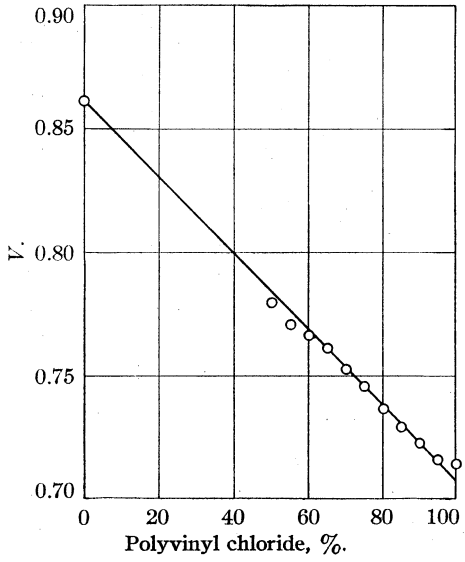


Fig. 1.—Specific volumes of polyvinyl chloride–tricresyl phosphate plastics.

In Fig. 1 the specific volume is plotted against composition by weight; the circles are observed and the solid line is that corresponding to

$$v = p_1 v_1 + p_2 v_2 \quad (2)$$

$$p_1 + p_2 = 1 \quad (3)$$

where $v_1 = 0.706$ and $v_2 = 0.861$ cc./g. are, respectively, the specific volumes of pure polyvinyl chloride and of tricresyl phosphate. This result is in accord with Brönsted's view[3] that all solutions of high polymers are very dilute solutions from the thermodynamic point of view, on account of the enormous molecular weight of the polymer.

IV. Discussion

In general, most polar substances show a high dielectric constant at low frequencies, and a small dielectric constant approaching the square of the index of refraction at high frequencies. The transition from high to low values usually occurs over a fairly narrow range of frequency; about 90% of the inflection region of the ϵ'–f curve lies within two decades of frequency. In this frequency range, the loss factor goes through a maximum, and approaches zero for higher or lower frequencies. The plastic solid, as exemplified by the system under discussion here, shows a markedly different behavior. The dielectric constant decreases (Fig. 2) with increasing frequency,

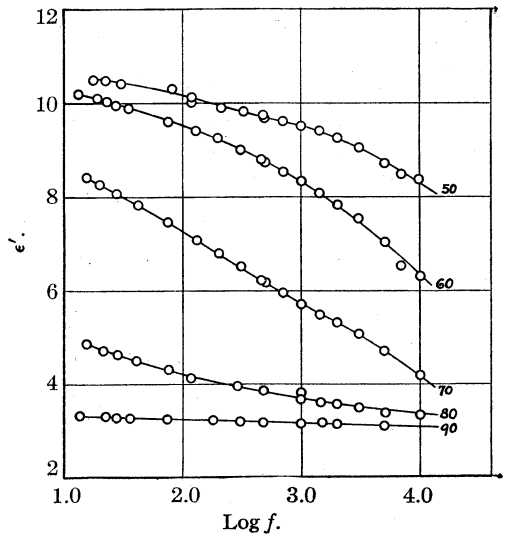


Fig. 2.—Dependence of dielectric constant on frequency and composition.

but only very slowly as compared to normal polar systems. The loss factor shows a maximum (Fig. 3) in the range 80–65% polyvinyl chloride within our present frequency range, which is nearly three decades wide, but is still relatively far from zero at the extreme frequencies. In other words, the plastic system roughly resembles ordinary systems in that the dielectric constant decreases with increasing frequency, and the loss factor has a maximum at some definite frequency (for a given temperature), but differs from them in the width of the dispersion region. The inflection slope on an ϵ'–f plot is much shallower for the plastic, and the ϵ'' maximum is very much broader.

(3) Brönsted, *Compt. rend. trav. Lab. Carlsberg, Sér. chim.*, **22**, 99 (1937).

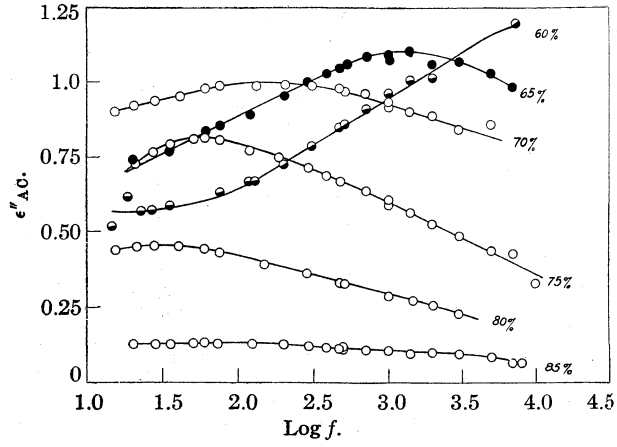


Fig. 3.—Dependence of loss factor on frequency and composition.

If a much wider range of frequency were available, an S-shaped ϵ'–f curve would probably have been obtained for all the systems of Table I. As it is, those containing between 90 and 70% polyvinyl chloride give concave-up ϵ'–log f curves in the range 0.01–10 kc. (inflection at lower frequencies). The 70% sample gives a practically linear ϵ'–log f curve, which indicates an inflection point within this range of frequency (at about 150 cycles, judging from the maximum in the ϵ''–log f curve). Those containing less than 70% polyvinyl chloride give curves that are concave-down, which suggests that their inflection points lie at higher frequencies than 10 kc. The loss factor curves similarly show a shift of the absorption maxima to higher frequencies as the plasticizer content increases.

Another reversal in curvature appears near the pure polyvinyl chloride end of the composition range. Pure polyvinyl chloride gives a concave-down ϵ'–log f curve, and an ϵ''–log f curve which rises with frequency in the 0.01–10 kc. range, indicating a center of dispersion at higher frequencies than 10 kc. The addition of 5% tricresyl phosphate decreases the dielectric constant, converts the ϵ'–log f curve almost to a straight line and decreases the rate of increase of ϵ'' with frequency; the center of the dispersion is therefore at lower frequencies than for the 100% sample, although still beyond 10 kc. At 10% plasticizer, the ϵ'–log f curve is nearly linear, and ϵ'' now decreases with increasing frequency in the experimental range, corresponding to a center of dispersion *below* 10 cycles. At 15% tricresyl phosphate, the center of dispersion appears to be just about at 10 cycles. Then with increasing plasticizer, the dispersion moves regularly to higher frequencies. The critical region between 95 and 85% polyvinyl chloride, where the dispersion crosses the frequency band from high to low frequencies and back again, will require further study.

Attention has already been called to the bluntness of the absorption maxima and the width of the dispersion on a frequency scale. There is further experimental evidence that the dispersion is much broader than can be shown by actual a. c. measurement by our present methods. If the

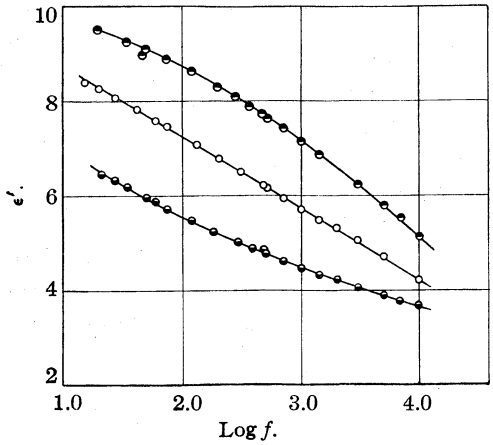


Fig. 4.—Transition region in dispersion—polyvinyl chloride: ◓, 65%; ○, 70%; ◒, 75%.

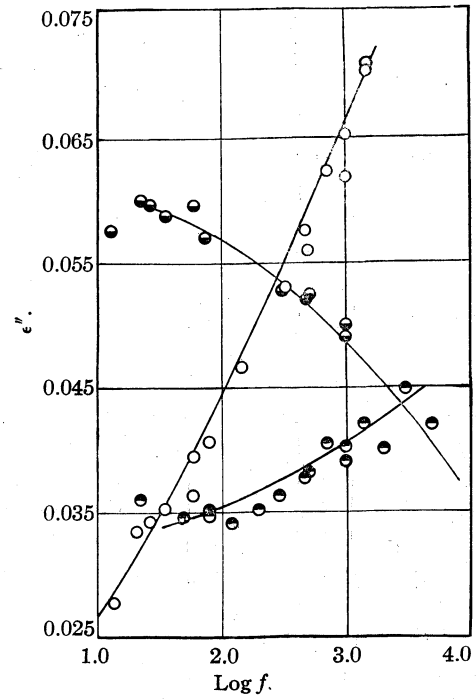


Fig. 5.—Loss factor in high polymer plastics: ○, 100%; ◓, 95%; ◒, 90%.

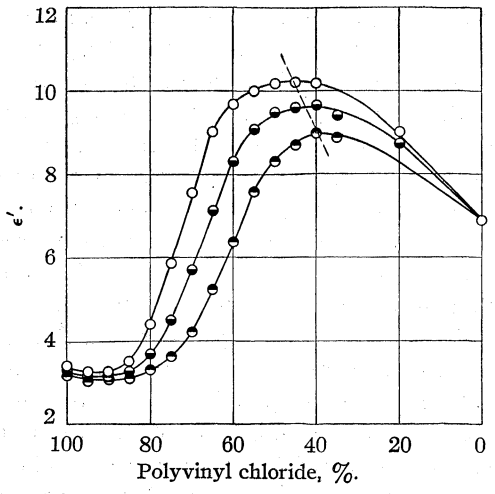


Fig. 6.—Dependence of dielectric constant on composition: ○, 60∼; ◒, 1000∼; ◓, 10 kc.

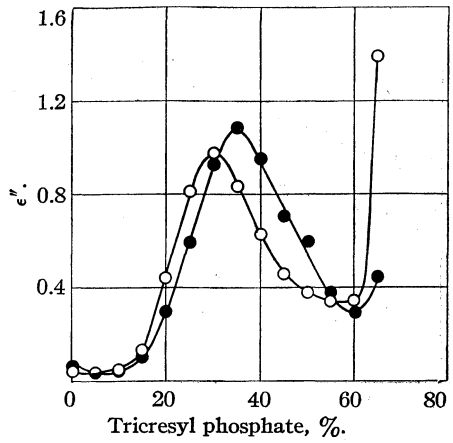


Fig. 7.—Dependence of loss factor on composition: ○, 60 ∼; ●, 1000 ∼.

observed conductance is plotted against frequency for the samples of Table II, approximate straight lines are obtained *which extrapolate linearly to the d. c. conductance.*[1b] Even for those samples for which a maximum in ϵ'' was found, the per cent. change in ϵ'' was nevertheless small; the fact that the a. c. data extrapolate *linearly* to the d. c. conductance (*cf.* eq. 1) is equivalent to saying that ϵ'' will not change much with frequency until extremely low frequencies are reached. On the basis of any of the present theories of absorption, ϵ'' must reduce to zero at zero frequency; *i. e.*, the κ–f plots must approach κ_0 with a horizontal tangent in the limit. No evidence of curvature was observed at 40°; at higher temperatures, the κ–f curves do, however, become concave-up in the low (10–100 cycles) frequency range.

A number of possible explanations of the width of the dispersion have been suggested, but no general theory with only a small number of arbitrary constants with assignable physical significance has been advanced. The fundamental difference between a solution of simple dipole molecules such as ethyl chloride and a plastic containing polyvinyl chloride is, aside from the obvious difference in viscosity, the fact that the ethyl chloride molecules are free to assume a normal distribution of orientations in thermal equilibrium, while the dipoles of polyvinyl chloride are constrained to fluctuations about orientations fixed by the accidental convolutions of the chain molecule which carries them. The components of moment in the direction of the field are thus subject to a different distribution law than for free dipoles. An eventual theory of the electrical properties of dipolar polymers must include explicitly this influence of structure on distribution.

The influence of such a distribution on the a. c. absorption can be qualitatively described. Under the action of the field, adjacent parts of the same or different chain molecules can be irreversibly twisted into new positions, in much the same way as elastic strains relax in the plastic. This process corresponds to a loss factor independent of frequency. If a second frequency-sensitive absorption (Debye relaxation or Maxwell–Wagner polyphase dielectric) were also present, curves like those of Fig. 3 would be obtained; these curves would resemble normal absorption curves, if the frequency axis were higher. In other words, the plastic behaves as if the loss factor could be broken up into two terms

$$\epsilon'' = \epsilon_s'' + \epsilon''(f) \qquad (4)$$

where ϵ_s'' is the power absorption due to irreversible slipping of molecules in the field against a static friction, and $\epsilon''(f)$ is a frequency-sensitive absorption which reduces to zero in a normal way for both very high and very low frequencies.

As a function of composition at fixed frequency, very interesting curves are obtained. These are shown in Figs. 6 and 7. As plasticizer content increases, the flexibility (plasticity, viscosity) increases, and has its most obvious change in the region centering around 30% plasticizer, where the transition from brittle to soft takes place. In the same range of composition, the dielectric constant has its maximum rate of change, and the loss factor goes through a sharp maximum. This region corresponds to a dispersion which is produced by varying the time of relaxation through

change of internal viscosity, as contrasted to the usual dispersion curves which are obtained by varying frequency at fixed temperature or *vice versa*. A rough estimate of the viscosity of the 60 polyvinyl chloride–40 tricresyl phosphate from the dispersion gives 10^6 poises, which is a reasonable order of magnitude.

The rapid change of viscosity is best illustrated by the change of d. c. conductance with composition, as is shown in Fig. 8. All the samples had as nearly as possible the same thermal history; consequently the hydrogen chloride concentration should be of about the same order in each, and any gross change of κ_0 with composition can be ascribed to changing viscosity. As seen in the figure, the conductance increases exponentially with increasing plasticizer content in the middle of the concentration range.

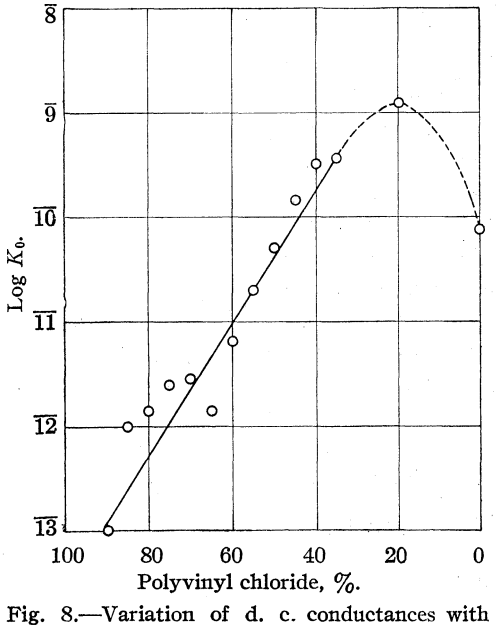


Fig. 8.—Variation of d. c. conductances with composition.

The two ends of the curves of Figs. 6 and 7 exhibit several striking characteristics. The dielectric constant of polyvinyl chloride is at first decreased by the addition of tricresyl phosphate. The decrease is greater than simple volume replacement of relatively more polarizable halogen compound by a compound containing only carbon, hydrogen, oxygen and phosphorus atoms. The index of refraction of tricresyl phosphate at 40° is 1.5494, which gives a specific refractivity.

$$r = (n^2 - 1)/\rho \qquad (5)$$

equal to 1.210; for polyvinyl chloride, $n = 1.565$ and $r = 1.023$. As a function of composition, the electrical susceptibility

$$\sigma = (\epsilon' - 1)/\rho \qquad (6)$$

shows a minimum; and even after subtracting $(p_1r_1 + p_2r_2)$ to allow for the greater polarizability of chlorine atoms, the non-optical susceptibility

$$\sigma^* = (\epsilon' - 1)/\rho - (p_1r_1 + p_2r_2) \qquad (7)$$

still shows a minimum. This may indicate a coupling between the dipoles of polymer and plasticizer.

After this initial decrease in dielectric constant, a minimum appears, followed by the rapid rise already discussed. The maximum which next appears is described most easily as a viscosity effect: starting with pure tricresyl phosphate, we obtain an increase in dielectric constant because we are increasing the content of polar solute, but simultaneously the viscosity increases, so that the two competing influences finally produce a maximum. It is impossible, of course, to consider the properties on a mole fraction scale, because the molecular weight of the polymer is unknown, but we can plot the results on a mole ratio scale, which is proportional to the mole fraction scale. If the susceptibility of the polyvinyl chloride in the plastic, defined by the equation

$$\sigma_1 = (\sigma - p_2\sigma_2)/p_1 \qquad (8)$$

where σ_2 is the total susceptibility of the pure plasticizer, is plotted against the mole ratio, approximate linearity is obtained in the range 0–70% polymer (Fig. 9). The quantity σ_1 extrapolates to 14.5 cc./g. at zero concentration. In order of magnitude, this is a very reasonable figure, if the electrical behavior of the plastic were primarily due to chlorine dipoles in a viscous medium. If we assume that E/F, the ratio of external and in-

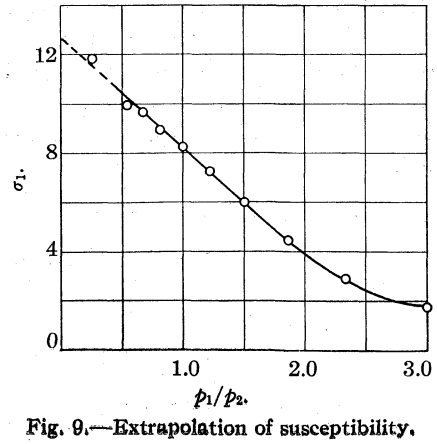


Fig. 9.—Extrapolation of susceptibility.

ternal fields, is of order unity, the molecular polarization per —CH_2CHCl— group is 30 cc., because

$$p = \frac{E}{F}\frac{\epsilon' - 1}{3} \qquad (9)$$

This corresponds to a moment equal to 1.2×10^{-18}, which compares favorably with the values found for Cl-dipoles in simple molecules, where liquid friction is the only restraint on molecular rotation.

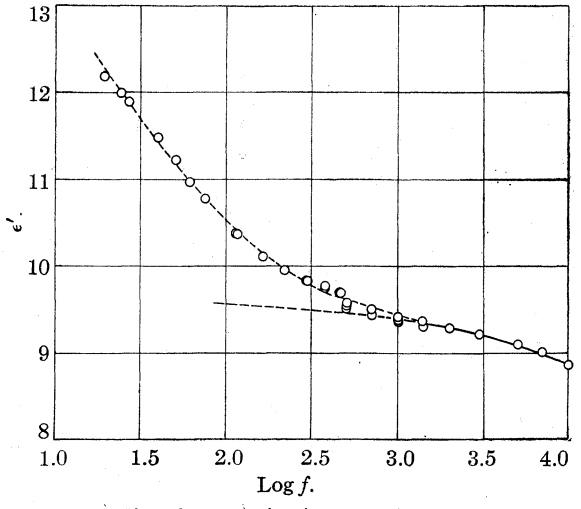


Fig. 10.—Polarization capacitance.

Two other interesting facts are contained in the data. The first is the sudden increase (Fig. 10) with decreasing frequency of the dielectric constant of the 35 polyvinyl chloride–65 tricresyl phosphate sample. This may be due to polarization capacity acting at the electrodes; more data are needed to decide the question. The second is the corresponding rise in loss factor for this sample. If these two properties really are volume properties and not surface effects, the system polyvinyl chloride–tricresyl phosphate has two dispersion regions. The region from the gel stage through the viscous solutions to dilute solutions of polymers in plasticizer needs considerable more investigation, which must be prefaced by a study of experimental methods for handling these materials.

Summary

1. Dielectric constants and loss factors at 40° and 20 cycles to 10 kilocycles under low voltage are reported for the system polyvinyl chloride–tricresyl phosphate, over the entire concentration range.

2. As a function of composition, the maximum absorption and the dielectric dispersion appear in the range 70–50% polymer, where the macroscopic viscosity has its most rapid rate of change with composition.

3. A characteristic difference between free dipoles and dipolar polymers is pointed out: the former can assume a normal distribution of orientations, while the latter have a distribution determined by the chain orientation.

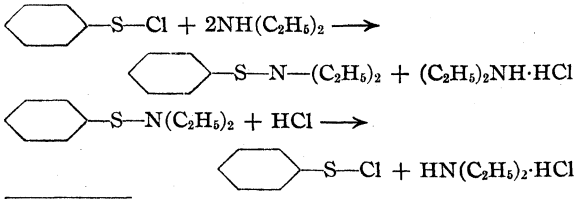
SCHENECTADY, NEW YORK RECEIVED JUNE 3, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

The Use of *o*-Nitrobenzenesulfenyl Chloride in the Identification of Amines

BY JOHN H. BILLMAN AND EUGENE O'MAHONY

It has been reported by Zincke[1] and Lecher[2] that amines would react with aromatic sulfenyl chlorides to produce amides of sulfenic acid which upon treatment with hydrochloric acid could be hydrolyzed. In certain cases, solid amides were obtained.



(1) T. Zincke and F. Farr, *Ann.*, **391**, 57–88 (1912).
(2) H. Lecher and F. Holschneider, *Ber.*, **57**, 755–758 (1924).

The purpose of our work was to investigate further these reactions using substituted benzenesulfenyl chlorides in an attempt to produce suitable solid derivatives of amines for means of identification and to examine the ease of hydrolysis of the amides back to the amines.

It was found that *o*-nitrobenzenesulfenyl chloride was quite satisfactory as a reagent. The compound is easily prepared and does not react readily with water or alcohol, thereby affording the identification of amines in water solution.

The reactions between reagent and amines were carried out in ether solution and in all cases took place spontaneously. However, no reaction could

be obtained when *o*-nitrobenzenesulfenyl chloride was treated with *o*-nitroaniline or diphenylamine. All of the derivatives were insoluble in 10% alkali.

TABLE I

PROPERTIES OF AMINE DERIVATIVES

Amine	M. p.[a] of amide, °C.	M. p. of hydrochloride, °C.	Analyses of amide, % Calcd.	Found
Ammonia[2]	124–125 dec.	350 dec.		
Aniline[b]	88.5–89	198	S, 13.00	12.95
p-Anisidine	138–138.5	220 dec.	N, 10.00	10.15
p-Bromoaniline	146–146.5	Dec.	N, 8.62	8.73
n-Butylamine	27–28	142–142.5	S, 14.16	14.00
p-Chloroaniline	143.5–144	194 dec.	N, 9.98	10.01
Cyclohexylamine	51.5–52	206–207	N, 11.12	11.09
Diethylamine	Oil	215–223		
Dimethylamine	62.5–63	171	N, 14.14	13.93
Ethylamine	32.5–33	108	S, 16.15	15.92
Methylamine	35.5–36	225–226	S, 17.38	17.11
N-Methylaniline	86–86.5	121–122	N, 10.78	10.85
α-Naphthylamine[c]	130.5–131	260 dec.	N, 9.46	9.30
β-Naphthylamine[b]	202–202.5	254	N, 9.46	9.33
n-Propylamine	Oil	157–158		
o-Toluidine	115.5–116	215	S, 12.31	12.20
m-Toluidine	106.5–107	228	N, 10.77	10.90
p-Toluidine	136–136.5	243	N, 10.77	10.86

[a] Melting points are corrected. [b] Melting points differ from those previously reported in the literature. [c] Softens at 125°.

These solid amides of *o*-nitrobenzenesulfenic acid, when dissolved in ether and treated with gaseous hydrogen chloride, for three minutes, regenerated the sulfenyl chloride and gave an approximately quantitative recovery of the amine in the form of its hydrochloride.

TABLE II

AMIDES HYDROLYZED

Amide of	% recovery of amine hydrochloride
Cyclohexylamine	98.5
m-Toluidine	95.0
Dimethylamine	97.4
Aniline	98.7

Further experiments are being carried out using other sulfenyl chlorides in an attempt to obtain derivatives of tertiary amines and higher melting amides of the aliphatic amines.

Experimental

The *o*-nitrobenzenesulfenyl chloride was prepared from *o,o'*-dinitrodiphenyl disulfide and chlorine by the method described in "Organic Syntheses."[3]

The amides described in this paper were all prepared by the addition of an ether solution of *o*-nitrobenzenesulfenyl chloride to an ether solution of the amine. When an aqueous solution of the amine, as dilute as 25%, was used, enough ether was added to produce a homogeneous solution before treatment. The amount of reagent required for the reaction was determined by slowly adding the sulfenyl chloride and observing whether or not further precipitation of the hydrochloride occurred. The hydrochloride formed was filtered and washed thoroughly with dry ether. The filtrates were collected and the ether evaporated off. The remaining material was easily solidified and recrystallized from 95% alcohol.

The hydrolysis of the amides was accomplished by dissolving the amide in a slight excess of dry ether and passing in dry hydrogen chloride. At the end of three minutes the gas was turned off and the solution filtered. The insoluble amine hydrochloride was then washed with dry ether and weighed. To recover the amine, sodium hydroxide was added to the hydrochloride.

Summary

1. *o*-Nitrobenzenesulfenyl chloride has been found to form a large number of solid derivatives of amines.

2. The reaction goes quickly and gives sharp melting compounds.

3. The amide derivatives are readily hydrolyzed to the amine hydrochloride in three minutes.

4. Anhydrous and aqueous amines were both used in the experiment without difficulty.

URBANA, ILLINOIS RECEIVED MAY 10, 1939

(3) *Org. Syntheses*, **15**, 45 (1935).

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS, AND JOHNS HOPKINS UNIVERSITY MEDICAL SCHOOL]

Sulfanilamide Derivatives. I

BY ROGER ADAMS, P. H. LONG AND A. J. JOHANSON[1]

The intensive study of sulfanilamide derivatives during the past few years has been with the objective of discovering compounds of higher activity, lower toxicity and more advantageous physical properties. The work described in this communication involved especially the preparation of a variety of *p*-acylamidobenzenesulfonalkanolamides and *p*-aminobenzenesulfonalkanolamides in order to determine, (1) the effect of the alkanolamine, (2) the effect of the acyl radical, and (3) the effect of changes in water solubility on the toxicity and antistreptococcal activity of the molecules. A few of these compounds have been described by other investigators[2] since the initiation of the research but they are included in order to show the general comparisons. The description of certain simple amides,[3] morpholides and double ring compounds is also included.

The compounds were prepared by condensation of the proper substituted *p*-aminobenzenesulfonyl chloride (Table I) and an alkanolamine, ammonia, morpholine, or *p*-aminobenzenesulfonalkanolamide, according to the equation

$$RNHC_6H_4SO_2Cl + NH_2CH_2CHOHR \longrightarrow RNHC_6H_4SO_2NHCH_2CHOHR$$

The individual compounds are listed in Tables II–X.

The following general statements can be made concerning these various compounds:

(a) The aminobenzenesulfonalkanolamides are more soluble in water than sulfanilamide. The antistreptococcal activity of these compounds is from slight to moderate but lower in every instance than that of sulfanilamide. The least activity is found in the 2,3-dihydroxypropylamine derivative. The therapeutic ratio is more favorable in many of the derivatives than in sulfanilamide.

(b) The acylamidobenzenesulfonalkanolamides were less soluble in water than the unacylated analogs. The antistreptococcal activity was usually lower though not so in all instances. The toxicity, however, was greatly reduced so that in many of these compounds the therapeutic ratio was more favorable than in sulfanilamide. As the acyl group increased in size, the water solubility decreased and the antistreptococcal activity was less. The toxicity, however, remained very low except in the isobutyryl derivative.

Several compounds in the series of acylamidobenzenesulfonmorpholides showed slight to moderate activity and materially reduced water solubility.

Carbethoxyaminobenzenesulfonalkanolamides were similar in solubility, effectiveness and toxicity to the lower acyl derivatives.

The *p*-acylamidobenzenesulfonamides were less effective than sulfanilamide with the valeryl derivative somewhat more effective than the propionyl.

The substituted benzenesulfonanilide derivatives were all ineffective.

A few compounds in which an alkyl or a benzyl group was substituted for one of the hydrogens in the amino group of an aminobenzenesulfonalkanolamide showed properties not very dissimilar to those of the analogous unsubstituted amino compound.

Several 4-methoxy-3-aminobenzenesulfonamides and the analogous alkanolamides showed essentially no antistreptococcal activity.

The various compounds were also tested for antimeningococcal activity. There appeared to be no correlation with antistreptococcal activity. On the other hand, a large number of the compounds possessed antimeningococcal activity equivalent to that of sulfanilamide. Since the toxicity of most of these compounds was much less than that of sulfanilamide, the therapeutic ratio in respect to antimeningococcal activity of the new compounds is much more favorable than in sulfanilamide.

These preliminary toxicity, antistreptococcal and antimeningococcal tests were carried out in Johns Hopkins University Medical School by Dr. P. H. Long. In the tables, ++++ is the equivalence in activity to sulfanilamide.

(1) An abstract of a thesis submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy in chemistry, 1938.

(2) Kharasch and Reinmuth, U. S. Patent 2,097,414.

(3) Miller, Rock and Moore, THIS JOURNAL, **61**, 1198 (1939).

TABLE I

SUBSTITUTED *p*-AMINOBENZENESULFONYL CHLORIDES

No.	Sulfonyl chloride	M. p., °C.	Formula	Nitrogen analyses, % Calcd.	Found
1	*p*-Propionamidobenzene-	113	$C_9H_{10}O_3NSCl$	5.66	5.89
2	*p*-*n*-Butyramidobenzene-	120–121	$C_{10}H_{12}O_3NSCl$	5.35	5.53
3	*p*-Isobutyramidobenzene-	131–132	$C_{10}H_{12}O_3NSCl$	5.35	5.53
4	*p*-*n*-Valeramidobenzene-	115–116	$C_{11}H_{14}O_3NSCl$	5.08	5.32
5	*p*-Isovaleramidobenzene-	120–121	$C_{11}H_{14}O_3NSCl$	5.08	5.22
6	*p*-Methylacetamidobenzene-	136–137	$C_9H_{10}O_3NSCl$	5.66	5.81
7	*p*-Ethylacetamidobenzene-	142–143	$C_{10}H_{12}O_3NSCl$	5.35	5.39
8	*p*-Carbethoxyamidobenzene-	103	$C_9H_{10}O_4NSCl$	5.32	5.39
9	4-Methoxy-3-acetamidobenzene-[4]	149			

Experimental

Substituted (*p*)-Aminobenzenesulfonyl Chlorides.—*p*-Acetamidobenzenesulfonyl chloride was prepared by the method of Stewart.[4] A series of *p*-acylamidobenzenesulfonyl chlorides (Table I) was synthesized in essentially the same manner, by the reaction of chlorosulfonic acid with the appropriate anilide. In each case, 1 mole of the anilide was added to 5 moles of chlorosulfonic acid at 10–20° with stirring. The reactions were, with the exception of numbers 6 and 7, allowed to proceed, with stirring, from one to five hours at room temperature followed by a final period of from one to five hours at 50–60°. In the cases of numbers 6 and 7 the mixtures gradually were heated to 80° and the reactions continued at that temperature for three hours.

p-Carbethoxyaminobenzenesulfonyl chloride was prepared by adding 1 mole of phenylurethan to 5 moles of chlorosulfonic acid and stirring for five hours at room temperature followed by heating at 60° for one hour.

In no case was hydrogen chloride evolution as extensive as with *p*-acetamidobenzenesulfonyl chloride. Most of the sulfonyl chlorides tended to separate when poured into the ice–water mixture, as sticky gummy masses, light tan in color. After standing from fifteen minutes to one hour, these masses solidified and could be filtered. In most cases the solidification could be hastened by transferring the gum to a fresh ice–water mixture, and stirring and kneading.

4-Methoxy-3-acetamidobenzenesulfonyl chloride[5] was prepared in the same manner as the *p*-acetamidobenzenesulfonyl chloride except that the mixture was stirred at room temperature for twenty hours and then poured into the ice–water mixture.

The crude, moist sulfonyl chlorides were used directly in the condensation reactions. Small portions were purified for characterization by recrystallization from benzene and were obtained as small white crystals. In contrast to Stewart's acetyl compound, these sulfonyl chlorides were all found to be very soluble in hot benzene.

Although no exact determinations were made on a pure basis, the yields, excepting in the cases of numbers 6 and 7 in Table I, appeared to be about the same as with the acetyl compound. The yields of numbers 6 and 7 were not more than 15 to 20% of theoretical.

(4) Stewart, *J. Chem. Soc.*, **121**, 2558 (1922); "Org. Syntheses," Coll. Vol. I, p. 8.

(5) German patent 573,193 (1931); *Friedlaender*, **19**, (I), 699 (1934).

Condensation of the Substituted *p*-Aminobenzenesulfonyl Chlorides with Amino Compounds.—The substituted *p*-aminobenzenesulfonyl chlorides were condensed with the various amino compounds using molar portions of each and one of the following as a condensing agent to take up hydrogen chloride: (1) an additional mole of the amine (plus a small excess to neutralize hydrochloric and sulfuric acids not removed from the crude sulfonyl chloride in the washing process); (2) potassium hydroxide in 10 to 20% aqueous solution, in sufficient quantity to maintain alkalinity throughout the reaction (about 1.5 moles); (3) an excess (3 or 4 moles) of pyridine; (4) in the case of the unsubstituted sulfonamides a large excess of concentrated aqueous ammonia.

For the preparation of *p*-acetamidobenzenesulfon-(β-hydroxyethyl)-amide and *p*-acetamidobenzenesulfon-di-(β-hydroxyethyl)-amide and all the morpholides, method 1 was found satisfactory. Method 3 was most satisfactory for the substituted benzenesulfonanilide derivatives. All the other compounds were prepared using method 2.

General Procedure.—The amino compound and the condensing agent were placed in an open beaker. To the mixture was added, with stirring, a quantity of the crude damp benzenesulfonyl chloride derivative estimated to contain the desired amount of pure substance. Heat usually was evolved, but the temperature of the mixture was held below 45° by means of an ice-bath. In some cases the sulfonyl chloride dissolved to form a clear yellow solution. In others, as the sulfonyl chloride dissolved, the product separated immediately in solid form or as a heavy dark oil. The mixture was heated about thirty minutes at 70–80°, cooled to room temperature and neutralized with concentrated hydrochloric acid to brilliant yellow as indicator. At this point, the product if not already in suspension in solid form or present as an oily layer in the bottom of the beaker, usually separated, either in crystalline form or as an oil which upon cooling and standing eventually solidified. Evaporation to small volume, cooling and standing caused separation in cases where precipitation did not occur directly when the mixture was neutralized.

The products were usually recrystallized from water or aqueous ethanol of various dilutions. In almost every case one or more treatments with norite was necessary to remove color.

Hydrolysis of Acetamidobenzenesulfonamides.—The compounds shown in Tables V and VI were prepared by acid hydrolysis of the corresponding acetamido compounds.

The acetamido compound (1 mole) was added to dilute

hydrochloric acid (4–6 *N*) containing at least 1.4 moles of the acid. The mixture was heated under reflux for two to five hours at 70–80°. If the material did not dissolve completely on heating, a small quantity of ethanol was added to bring about solution. After completion of the hydrolysis, the solution was cooled and neutralized to litmus with solid sodium carbonate. In nearly every case the amine separated as a heavy oil, which after stirring, cooling and standing became solid. Purification was effected by recrystallization from water or dilute ethanol. Treatment with norite to remove color was necessary in most cases.

TABLE II

p-ACYLAMIDOBENZENESULFONAMIDES[a]

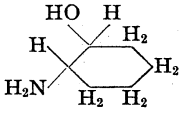
Compounds 1, 2, 3 and 4 have been described recently by Miller, Rock and Moore.[3] The melting points reported differed considerably from those given here. Compound 4 has also been described in French Patent 820,546: *C. A.*, **32**, 2958 (1938).

No.	Acyl group	M. p., °C.	Anti-strep. activity	Anti-mening. activity	Formula	Nitrogen analyses, % Calcd.	Found
1[b]	CH_3CH_2CO	226.5–227.5	++	+++	$C_9H_{12}O_3N_2S$	12.28	12.23
2[c]	$CH_3CH_2CH_2CO$	236–237	+	++++	$C_{10}H_{14}O_3N_2S$	11.57	11.61
3[d]	$(CH_3)_2CHCO$	248–249	±	++++	$C_{10}H_{14}O_3N_2S$	11.57	11.18
4[e]	$CH_3CH_2CH_2CH_2CO$	209–210	+++		$C_{11}H_{16}O_3N_2S$	10.94	10.95

[a] White microcrystalline powders very slightly soluble in water. Yields varied from 53 to 86%. [b] Recrystallized from 25% ethanol. [c] Recrystallized from a mixture of acetone and 95% ethanol. [d] Recrystallized from an acetone–water mixture. [e] Recrystallized from 50% ethanol.

TABLE III

p-ACETAMIDOBENZENESULFONALKANOLAMIDES[a]

No.	Alkanolamine	M. p., °C.	Anti-strep. activity	Anti-mening. activity	Formula	Nitrogen analyses, % Calcd.	Found
1	$NH_2CH_2CH_2OH$	150–151	0	++++	$C_{10}H_{14}O_4N_2S$	10.81	10.86
2[b]	$NH(CH_2CH_2OH)_2$	158–159	0	+	$C_{12}H_{18}O_4N_2S$	9.27	9.53
3	$NH_2CH_2CH_2CH_2OH$	133.5–135	0	+	$C_{11}H_{16}O_4N_2S$	10.30	10.45
4[c]	$NH_2CH_2CHOHCH_3$	166–167	+	0	$C_{11}H_{16}O_4N_2S$	10.30	10.61
5	$NH_2CH_2COH(CH_3)_2$	185–187	±	++	$C_{12}H_{18}O_4N_2S$	C, 50.35 H, 6.29	51.01 6.44
6	$NH_2CH_2CHOHCH_2OH$	132–133	0	0	$C_{11}H_{16}O_5N_2S$	9.72	10.07
7	$NH(CH_3)CH_2(CHOH)_4CH_2OH$	87–91	0	±	$C_{15}H_{24}O_8N_2S$	7.14	6.93
8		218	0	0	$C_{14}H_{20}O_4N_2S$	8.97	8.88

[a] White crystalline powders of varying solubility in water. With the exception of number 8, all recrystallized from water. Number 8 from dilute ethanol. Yields from 50 to 75%. [b] Kolloff, THIS JOURNAL, **60**, 950 (1938). [c] U. S. Patent 2,097,414, Oct. 26 (1937).

TABLE IV

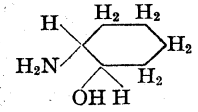
p-ACYLAMIDOBENZENESULFONALKANOLAMIDES[a]

No.	Acyl group	Alkanolamine	M. p., °C.	Anti-strep. activity	Anti-mening. activity	Formula	Nitrogen analyses, % Calcd.	Found
1	CH_3CH_2CO	$NH_2CH_2CHOHCH_3$	148	0	+++	$C_{12}H_{18}O_4N_2S$	9.79	9.87
2	CH_3CH_2CO	$NH_2CH_2COH(CH_3)_2$	172–172.5	+	+++	$C_{13}H_{20}O_4N_2S$	9.33	9.45
3	$CH_3CH_2CH_2CO$	$NH_2CH_2CH_2OH$	139	0	+	$C_{12}H_{18}O_4N_2S$	9.79	9.79
4	$CH_3CH_2CH_2CO$	$NH(CH_2CH_2OH)_2$	114–115	0	+	$C_{14}H_{22}O_5N_2S$	8.48	8.44
5	$CH_3CH_2CH_2CO$	$NH_2CH_2CHOHCH_3$	127–128	0	++	$C_{13}H_{20}O_4N_2S$	9.33	9.65
6	$CH_3CH_2CH_2CO$	$NH_2CH_2COH(CH_3)_2$	166	±	++++	$C_{14}H_{22}O_4N_2S$	8.91	8.80
7	$(CH_3)_2CHCO$	$NH_2CH_2CH_2OH$	116.5	++	+	$C_{12}H_{18}O_4N_2S$	9.79	9.68
8	$(CH_3)_2CHCO$	$NH_2CH_2CHOHCH_3$	144	±	+++	$C_{13}H_{20}O_4N_2S$	9.33	9.23
9	$(CH_3)_2CHCO$	$NH_2CH_2COH(CH_3)_2$	173	±	++++	$C_{14}H_{22}O_4N_2S$	8.91	9.10
10	$CH_3(CH_2)_3CO$	$NH_2CH_2CHOHCH_3$	121.5	±	++++	$C_{14}H_{22}O_4N_2S$	8.92	8.89
11	$CH_3(CH_2)_3CO$	$NH_2CH_2COH(CH_3)_2$	136–136.5	±	+++	$C_{15}H_{24}O_4N_2S$	8.54	8.56
12	$(CH_3)_2CHCH_2CO$	$NH_2CH_2COH(CH_3)_2$	146–147	0	0	$C_{15}H_{24}O_4N_2S$	8.54	8.63

[a] White microcrystalline powders, slightly soluble in water. Recrystallized from 25 to 50% aqueous ethanol. Yields ranged from 30 to 60%.

TABLE V

p-AMINOBENZENESULFONALKANOLAMIDES[a]

No.	Alkanolamine	M. p., °C.	Antistrep. activity	Antimening. activity	Formula	Nitrogen analyses, % Calcd.	Found
1	$NH_2CH_2CH_2OH$	95–97	++	+++	$C_8H_{12}O_3N_2S$	12.98	13.16
2[b]	$NH(CH_2CH_2OH)_2$	109–110	++	±	$C_{10}H_{16}O_4N_2S$	10.77	10.52
3	$NH_2CH_2CH_2CH_2OH$	123–124	±	++++	$C_9H_{14}O_3N_2S$	12.18	12.18
4	$NH_2CH_2CHOHCH_3$[2]	115–116	+	++++	$C_9H_{14}O_3N_2S$	12.18	12.20
5	$NH_2CH_2COH(CH_3)_2$	102–103	0	++++	$C_{10}H_{16}O_3N_2S$	11.48	11.69
6	$NH_2CH_2CHOHCH_2OH$	102–104	0	++++	$C_9H_{14}O_4N_2S$	11.39	11.11
7		141–142	0	0	$C_{12}H_{18}O_3N_2S$	10.36	10.22

[a] White crystalline powders soluble in water, number 7 only slightly. Yields varied from 48 to 67%. Recrystallized from water with the exception of number 7, which was recrystallized from 20% aqueous ethanol. [b] *Cf.* Kolloff.

TABLE VI

p-ALKYL- AND *p*-ARALKYLAMINOBENZENESULFONALKANOLAMIDES[a]

No.	Alkyl or aralkyl group	Alkanolamine	M. p., °C.	Antistrep. activity	Formula	Nitrogen analyses, % Calcd.	Found
1	CH_3	$NH_2CH_2CHOHCH_3$	90–91	..	$C_{10}H_{16}O_3N_2S$	11.48	11.40
2	$C_2H_5(COCH_3)$	$NH_2CH_2COH(CH_3)_2$	134	..	$C_{14}H_{22}O_4N_2S$	8.92	8.81
3	C_2H_5	$NH_2CH_2COH(CH_3)_2$	131.5	0	$C_{12}H_{20}O_3N_2S$	10.29	10.36
4	$CH_2C_6H_5$	$NH_2CH_2CH_2OH$	115–116	±	$C_{15}H_{18}O_3N_2S$	9.15	9.05

[a] White crystalline solids slightly soluble in water. Yields varied from 35 to 60%. All were recrystallized from water except number 4 for which benzene containing 5% methanol was used.

TABLE VII

SUBSTITUTED *p*-CARBETHOXYAMINOBENZENESULFONAMIDES[a]

No.	Amide	M. p., °C.	Antistrep. activity	Antimening. activity	Formula	Nitrogen analyses, % Calcd.	Found
1[b]	$NH_2CH_2CH_2OH$	176	+	++++	$C_{11}H_{16}O_5N_2S$	9.72	9.65
2[c]	$NH_2CH_2CHOHCH_3$	132	±	++	$C_{12}H_{18}O_5N_2S$	9.27	9.26
3[d]	$NH(CH_2CH_2)_2O$	157–158	0	++	$C_{13}H_{18}O_5N_2S$	8.91	8.89
4[e]	NH_3	241–242	+	+	$C_9H_{12}O_4N_2S$	11.48	11.58

[a] White microcrystalline solids, very slightly soluble in water. Estimated yields varied from 50 to 86%. [b] Recrystallized from 60% ethanol. [c] Recrystallized from hot water. [d] Recrystallized from 50% ethanol. [e] Recrystallized from acetone and water (1:1).

TABLE VIII

p-ACYLAMIDOBENZENESULFONMORPHOLIDES AND *p*-AMINOBENZENESULFONMORPHOLIDE[a]

No.	Acyl group	M. p., °C.	Antistrep. activity	Antimening. activity	Formula	Nitrogen analyses, % Calcd.	Found
1	CH_3CO	165–166	+	++	$C_{12}H_{16}O_4N_2S$	9.86	9.77
2	CH_3CH_2CO	189–190	+	+	$C_{13}H_{18}O_4N_2S$	9.40	9.49
3	$CH_3CH_2CH_2CO$	191–193	+	++	$C_{14}H_{20}O_4N_2S$	8.97	8.75
4	$(CH_3)_2CHCO$	147	±	±	$C_{14}H_{20}O_4N_2S$	8.97	8.93
5	H	217	±	±	$C_{10}H_{14}O_3N_2S$	11.57	11.51

[a] White crystalline solids usually as small glistening plates. Very slightly soluble in water. Yields varied from 50 to 82%. Recrystallized from 20 to 50% ethanol.

TABLE IX

SUBSTITUTED BENZENESULFONANILIDE DERIVATIVES:[a]

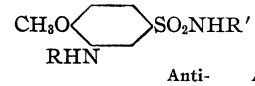
$RNHC_6H_4SO_2NHC_6H_4SO_2NHR'$

No.	R	R′	M. p., °C.	Antistrep. activity	Antimening. activity	Formula	Nitrogen analyses, % Calcd.	Found
1	CH_3CO	$CH_2CHOHCH_3$	127–128	0	0	$C_{17}H_{21}O_6N_3S_2$	9.88	9.58
2	H	$CH_2CHOHCH_3$	123–125	0	++++	$C_{15}H_{19}O_5N_3S_2$	10.97	11.00
3	CH_3CO	$CH_2COH(CH_3)_2$	213	0	0	$C_{18}H_{23}O_6N_3S_2$	9.52	9.46
4	H	$CH_2COH(CH_3)_2$	184–185	±	++++	$C_{16}H_{21}O_5N_3S_2$	10.52	10.74
5	C_2H_5OCO	$CH_2CHOHCH_3$	175–177	0	++++	$C_{18}H_{22}O_7N_3S_2$	9.19	8.99

[a] White microcrystalline powders very slightly soluble in water. Yields varied from 60 to 77%. Recrystallized from 30 to 50% ethanol.

TABLE X

DERIVATIVES OF 4-METHOXY-3-AMINOBENZENESULFONAMIDE:[a]



No.	R	R′	M. p., °C.	Anti-strep. activity	Anti-mening. activity	Formula	Nitrogen analyses, % Calcd.	Found
1	CH_3CO	H	225.5	0	±	$C_9H_{12}O_4N_2S$	11.47	11.34
2	CH_3CO	CH_2CH_2OH	152–153	0	0	$C_{11}H_{16}O_5N_2S$	9.72	9.85
3	CH_3CO	$CH_2CHOHCH_3$	146–147	0	0	$C_{12}H_{18}O_5N_2S$	9.27	9.36
4	CH_3CO	$CH_2COH(CH_3)_2$	125	0	±	$C_{13}H_{20}O_5N_2S$	8.86	9.09
5	H	H	142–142.5	0	0	$C_7H_{10}O_3N_2S$	13.86	13.53
6	H	$CH_2CHOHCH_3$	102	0	0	$C_{10}H_{16}O_4N_2S$	10.77	10.90

[a] Usually small glistening white crystals. Yields varied from 60 to 84%. Slightly soluble in water. Recrystallized from water, excepting number 4 which was recrystallized from dilute ethanol.

Summary

A variety of *p*-acylamidobenzenesulfonamides, *p*-acylamidobenzenesulfonalkanolamides, *p*-aminobenzenesulfonalkanolamides, *p*-alkyl- and *p*-aralkylaminobenzenesulfonalkanolamides, *p*-carbethoxyaminobenzenesulfonamides, *p*-acylamidobenzenesulfonmorpholides, *p*-aminobenzenesulfonmorpholide, *p*-acyl- and *p*-aminobenzenesulfonanilides and derivatives of 4-methoxy-3-aminobenzenesulfonamide have been prepared.

All show less antistreptococcal activity than sulfanilamide but practically all are much less toxic.

The antimeningococcal activity of many is equivalent to that found in sulfanilamide.

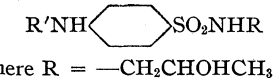
URBANA, ILLINOIS RECEIVED JUNE 16, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS, AND JOHNS HOPKINS UNIVERSITY MEDICAL SCHOOL]

Sulfanilamide Derivatives. II

BY ROGER ADAMS, P. H. LONG AND ALLENE JEANES[1]

In the previous paper[2] it was demonstrated that the acyl groups in acylamidobenzenesulfonalkanolamides greatly reduced the toxicity of the molecule. The antistreptococcal activity was generally lower than that of sulfanilamide but the therapeutic ratio in many instances was more favorable. Consequently, a variety of other substituted acyl substituents has been introduced either directly or indirectly into the molecule. The compounds studied are shown below.



where R = $—CH_2CHOHCH_3$ and

R′ = $HOOC(CH_2)_2CO—$ I

$C_2H_5OOC(CH_2)_2CO—$ II

$CH_3CHOAcCO—$ III

where R = $—CH_2CH_2OH$ and

R′ = $HOCH_2CH_2NHCO(CH_2)_2CO—$ IV

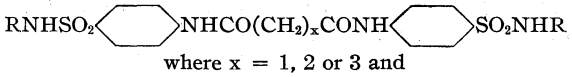
$CH_3OCH_2CO—$ V

where R = H and

R′ = $NH_2CO(CH_2)_2CO—$ VI

$CH_3CHOAcCO—$ VII

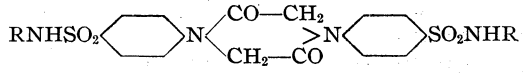
$CH_3CHOHCO—$ VIII



where x = 1, 2 or 3 and

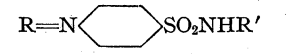
R = $—CH_2CH_2OH$ or

$—CH_2CHOHCH_3$

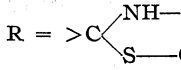


where R = H or $—CH_2CH_2OH$ or

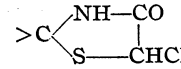
$—CH_2CHOHCH_3$



where R′ = $—CH_2CHOHCH_3$ and

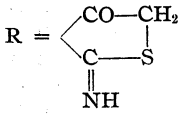


IX



X

where R′ = H and



XI

All the compounds were prepared either (1) by introduction of the sulfonyl chloride grouping into

(1) The authors are indebted to The Chemical Foundation for grants which made possible the work described in this communication.

(2) Adams, Long and Johanson, THIS JOURNAL, 61, 2342 (1939).

the properly substituted anilide followed by treatment with ammonia or an amine, or (2) by introduction of the proper acyl group into sulfanilamide or into sulfonalkanolamide.

Only a few of the products showed any antistreptococcal activity. Compound II and the isopropanol derivative of the diketopiperazide showed very slight, and compound V, moderate activity.

Experimental

Succinanil.—This was prepared by a modification of the method of Tingle and Cram.[3]

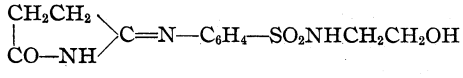
A mixture of 170 cc. of freshly distilled aniline and 225 g. of pulverized succinic acid was heated in an open flask in an oil-bath at 140–150° for four hours. The mixture was then distilled at atmospheric pressure which, due to the high temperature necessary, converted the succinic acid monoanilide into the anil. The distillate was crystallized from 95% ethanol: colorless needles, m. p. 156–158°; yield, 246 g. (75%). Menschutkin[4] reports the same melting point.

Mono-(*p*-aminosulfonylphenyl)-succinamide (VI).—Succinanil was treated with five moles of chlorosulfonic acid according to the method in "Organic Syntheses."[5] After heating to 60–65° for two hours, the product was poured slowly into well-stirred crushed ice and water. The crude sulfonyl chloride was washed and used directly.

To an excess of ice-cold 28% aqueous ammonia, 60 g. of the crude, moist sulfonyl chloride was added. The chloride dissolved and a mass of white crystals separated. The mixture was heated to 70° for a half hour and was then cooled. The product was purified by recrystallization from water, using norite; white needles, m. p. 234–238° with decomposition.

Anal. Calcd. for $C_{10}H_{13}N_3O_4S$: N, 15.50. Found: N, 15.55.

Succinamide Derivative (IV).—The crude acid chloride from chlorosulfonic acid and succinanil was treated with 2 molecules of ethanolamine dissolved in 7% aqueous potassium hydroxide (containing 2.5 moles of potassium hydroxide for each mole of acid chloride) and heated to 70° for a half hour. After neutralization and concentration to small volume, a thick oil was obtained. This was dissolved in butanol and two crystalline products separated. The first and main fraction was a granular product which formed slowly in the undisturbed solution; the second, a by-product, glistening plates which formed rapidly after removal of the first fraction. This by-product was probably the compound



as shown by analysis. After recrystallization from butanol, and washing with dry ether, the first product melted at 137–142°; the second at 85–93°.

Anal. (m. p. 137–142°). Calcd. for $C_{14}H_{21}N_3O_6S$: N, 11.70. Found: N, 11.35 (m. p. 85–93°) Calcd. for $C_{12}H_{15}N_3O_4S$: N, 14.14. Found: N, 14.20.

Succinamide Derivative (I).—The product from the acid chloride and isopropanolamine was obtained in the same manner as described for the ethanolamine. It remained as an oil, however, and was hydrolyzed directly by boiling for ten minutes with the calculated quantity of 10% aqueous potassium hydroxide and then acidifying with concentrated hydrochloric acid. Addition of a small amount of water gave a gummy precipitate which was dried and then crystallized from water, using norite: colorless needles, m. p. 179–192° with decomposition; yield, 30 g. from 60 g. of succinanil.

Anal. Calcd. for $C_{13}H_{18}N_2O_6S$: N, 8.48. Found: N, 8.71.

The ethyl ester (II), produced by the action of ethanol and a drop of sulfuric acid, was purified from very dilute ethanol; white crystals, m. p. 125–128°.

Anal. Calcd. for $C_{15}H_{22}N_2O_6S$: N, 7.82. Found: N, 7.94.

(*p*) - Methoxyacetamidobenzenesulfon - (β - hydroxyethyl)-amide (V).—The *p*-methoxyacetamidobenzene sulfonyl chloride was prepared in the usual way from methoxyacetanilide and chlorosulfonic acid. It was condensed with ethanolamine (2 moles) in 7% aqueous potassium hydroxide and the mixture heated to 60° during the course of five minutes. On cooling the product separated. The reaction mixture was neutralized, the substance filtered and purified from water; white crystals, m. p. 125–127°.

Anal. Calcd. for $C_{11}H_{16}N_2O_5S$: N, 9.72. Found: N, 9.80.

p **- (α - Acetoxypropionamido) - benzenesulfonamide (VII).**—A solution of 16 g. of α-acetoxypropionyl chloride (1 mole) in dry ether was added slowly to 35 g. of sulfanilamide (2 moles) in dry ether. After stirring overnight, the precipitate was filtered and treated with water, followed by dilute hydrochloric acid. The product was purified from water, using norite; white crystals, m. p. 192.5°.

Anal. Calcd. for $C_{11}H_{14}N_2O_5S$: N, 9.79. Found: N, 9.70.

The same product was also obtained from α-acetoxypropionanilide and chlorosulfonic acid, followed by treatment with aqueous ammonia.

p **- (α - Hydroxypropionamido) - benzenesulfonamide (VIII).**—A mixture of 0.75 g. (1 mole) of the acetoxy compound just described and 4 cc. of 1.5 *N* aqueous sodium hydroxide was heated at 50–55° for three and one-half hours. At the end of the reaction, the solution was made slightly acid, and the product filtered. It was purified by recrystallization from water; transparent prisms, m. p. 196°.

Anal. Calcd. for $C_9H_{12}N_2O_4S$: N, 11.47. Found: N, 11.50.

p **- (α - Acetoxypropionamido - N - (2 - hydroxy - 1-propyl)-benzenesulfonamide (III).**—Addition of 25 g. of α-acetoxypropionanilide to 73 g. of chlorosulfonic acid according to the usual procedure gave little evolution of gas until the mixture was heated to 30°, when the reaction became vigorous. The reaction mixture was held be-

(3) Tingle and Cram, *Am. Chem. J.*, **37**, 596 (1907).
(4) Menschutkin, *Ann.*, **162**, 166 (1872).
(5) "Org. Syntheses," Coll. Vol. I, p. 7.

TABLE I

DERIVATIVES OF DIBASIC ACIDS

	M. p., °C.	Solvent	Nitrogen analyses, % Calcd.	Found
[(*p*)-$HOCH_2CH_2NHSO_2C_6H_4NHCO]_2CH_2$	203–208 (dec.)	H_2O	11.20	11.36
[(*p*)-$CH_3CHOHCH_2NHSO_2C_6H_4NHCO]_2CH_2$	173–176 (dec.)	H_2O	10.60	10.80
[(*p*)-$HOCH_2CH_2NHSO_2C_6H_4NHCOCH_2]_2$	243–250 (dec.)	EtOH	10.89	11.26
[(*p*)-$CH_3CHOHCH_2NHSO_2C_6H_4NHCOCH_2]_2$	265–270 (dec.)	EtOH	10.33	10.50
[(*p*)-$HOCH_2CH_2NHSO_2C_6H_4NHCOCH_2]_2CH_2$	196–198	H_2O	10.60	10.70
[(*p*)-$CH_3CHOHCH_2NHSO_2C_6H_4NHCOCH_2]_2CH_2$	187–190	EtOH	10.07	10.04

tween 30–60° for three hours, cooled and added very slowly to a well-stirred mixture of ice and water. The sticky gum which formed was washed with ice water, then condensed immediately. The sulfonyl chloride was assumed to be 50% pure.

The sulfonyl chloride was added gradually in the cold to a cold solution of 2 moles of isopropanolamine in 30 cc. of 7% aqueous potassium hydroxide. The mixture was warmed to 60° during the course of ten minutes, filtered and neutralized with hydrochloric acid. Concentration of the solution at room temperature to a small volume resulted in the separation of an oil. By cooling and standing, this solidified and was purified from water using norite; white crystals, m. p. 97–103°.

Anal. Calcd. for $C_{14}H_{20}N_2O_6S$: N, 8.13. Found: 8.03.

Dibasic Acid Derivatives of the Type (*p*)-$RNHSO_2C_6H_4NHCO(CH_2)_xCONHC_6H_4SO_2NHR$(*p*).—These were all prepared by the same general method. The dianilides of malonic, succinic and glutaric acids were synthesized, the first by the action of aniline on diethyl malonate,[6] the latter two by the action of aniline on the dibasic acid chlorides in dry ether. The dianilides were converted to the corresponding disulfonyl chlorides by the method described in "Organic Syntheses."[5] These products were then condensed with ethanolamine and isopropanolamine dissolved in 7% aqueous potassium hydroxide and more alkali was added during the course of the reaction to maintain alkalinity. The reactions were completed by heating for a half hour at 70°. Neutralization caused precipitation of the products which were then recrystallized, using norite, from water or alcohol. The products separated as white crystals upon slow cooling.

Diketopiperazine Derivatives of the Type

(*p*)-$RNHSO_2C_6H_4$—N(CO—CH_2 / CH_2—CO)N—$C_6H_4SO_2NHR$-(*p*)

Compound in which R = —CH_2CH_2OH.—N,N'-Diphenyldiketopiperazine[7] was converted into the corresponding disulfonyl chloride and then condensed with ethanolamine in the usual way. The product was purified from water; white microcrystals, m. p. 260–270° with decomposition.

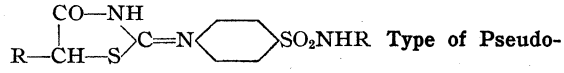
Anal. Calcd. for $C_{20}H_{24}N_4O_8S_2$: N, 10.93. Found: N, 11.00.

Compound in which R = —$CH_2CHOHCH_3$.—This substance was prepared like the above using isopropanolamine; white needles, m. p. 280–284° with decomposition.

Anal. Calcd. for $C_{22}H_{28}N_4O_8S_2$: N, 10.37. Found: N, 10.66.

Compound in which R = H.—Made in a similar manner with ammonia, the product was purified from water; white microcrystals, m. p. 325° with decomposition.

Anal. Calcd. for $C_{16}H_{16}N_4O_6S_2$: N, 13.20. Found: N, 13.20.



Type of Pseudothiohydantoin Derivatives.—The above structure for the following compounds was assigned on the basis of those suggested by Wheeler and Johnson[8] for the stable and labile forms of aryl-substituted pseudothiohydantoins.

Isopropanolamine Compound (IX).—*p*-Chloroacetamidobenzenesulfonyl chloride was prepared from *p*-chloroacetanilide and chlorosulfonic acid in the usual way and then condensed with isopropanolamine. An oil which separated from the reaction mixture was removed and the desired isopropanolamine derivative obtained by concentration of the solution. On purification from water, it formed colorless needles, m. p. 125–129°.

Anal. Calcd. for $C_{11}H_{15}N_2O_4SCl$: N, 9.13. Found: N, 9.10.

This product was treated with 1.5 moles of ammonium thiocyanate in sufficient absolute ethanol to dissolve it. The mixture was boiled gently for one and one-half hours and then the solvent removed by means of a current of air. The resulting product was crystallized from water, using norite; yellow needles, m. p. 209–212°.

Anal. Calcd. for $C_{12}H_{15}N_3O_4S_2$: N, 12.76. Found: N, 12.87.

Isopropanolamine Compound (X).—α-Bromopropionanilide was converted with chlorosulfonic acid to the sulfonyl chloride and then condensed with isopropanolamine. The product melted at 140–143° after purification from ethanol. It was then dissolved in absolute ethanol and refluxed gently for one and one-half hours with one and one-half moles of ammonium thiocyanate. Much longer heating caused no further change. Removal of the solvent at room temperature gave a mixture of an oil and a solid, which was converted into a solid by agitation with 2.5% sodium carbonate solution. Acidification of the basic filtrate from this treatment gave more of the same substance as a white solid.

The combined solids from the sodium carbonate treatment were dissolved in boiling water, a small amount of a highly insoluble yellow product was removed, and the solution allowed to cool. The desired compound sepa-

(6) Reissert and Moré, *Ber.*, **39**, 3300 (1906).

(7) Kuhara, *Am. Chem. J.*, **24**, 168 (1900).

(8) Wheeler and Johnson, *ibid.*, **28**, 121 (1902).

rated slowly, sometimes only after agitation and concentration of the solution. A second recrystallization from water gave white needles, m. p. 190–192°.

Anal. Calcd. for $C_{13}H_{17}N_3O_4S_2$: N, 12.24. Found: N, 12.22.

3 - (*p* - Aminosulfonylphenyl) - pseudothiohydantoin (XI).—A mixture of 7.5 g. of *p*-chloroacetamidobenzenesulfonamide[9] in 150 cc. of absolute ethanol and 3.5 g. of ammonium thiocyanate was refluxed for thirty minutes. Longer heating produced no further change. The precipitate that formed was filtered, washed with 5 g. of aqueous sodium carbonate and recrystallized from water with norite. From the slow cooling of the solution, a colorless non-crystalline precipitate was obtained which darkened from 238°, melted at 258°, with decomposition.

Anal. Calcd. for $C_9H_9N_3O_3S_2$: N, 15.49. Found: N, 15.26.

(9) Jacobs and Heidelberger, THIS JOURNAL, **39**, 2429 (1917).

Summary

A number of sulfanilamide derivatives was prepared in which the amino group was substituted by various complex acyl groups and the amido group by ethanol and isopropanolamine. None showed activity comparable with sulfanilamide.

URBANA, ILLINOIS RECEIVED JUNE 16, 1939

[CONTRIBUTION FROM THE INTERNATIONAL LEPROSY CENTER, RIO DE JANEIRO]

Alepric, Aleprylic, Aleprestic and Aleprolic Acids, New Homologs of Chaulmoogric Acid

BY HOWARD IRVING COLE AND HUMBERTO T. CARDOSO

In analyzing *Hydnocarpus wightiana* oil by the method described by us[1] the high optical rotation and iodine numbers of the lower boiling fractions of ethyl esters indicated that there must be present at least one more optically active fatty acid besides those already known (chaulmoogric, hydnocarpic and gorlic[2] acids). By repeated fractional vacuum distillation of 200 l. of *H. wightiana* ethyl esters and fractional crystallization of the free acids we have succeeded finally in isolating two new homologs of chaulmoogric acid. The presence of two other homologs has been proved and they have been obtained 70.5 and 42% pure, respectively. Lack of sample prevented further purification. Because of their relationship to the treatment of leprosy we have named these four new homologs, alepric, aleprylic, aleprestic and aleprolic acids.

Alepric acid is the next lower homolog to hydnocarpic acid, differing from it by C_2H_4, having the formula $C_{14}H_{24}O_2$. Our final sample still contained a small amount of another unsaturated acid as indicated by the iodine number and optical rotation. The acid is colorless when liquid, white when solid, almost odorless and melts at 48°. The melted acid upon solidifying forms characteristic beautiful branching crystals rising above the surface of the acid. They are very similar to those already reported by us as characteristic of hydnocarpic and chaulmoogric acids.[3] Our purest sample of alepric acid gave a specific optical rotation of +77.12°. The theoretical value from the molecular weight–optical rotation curve is +80°.

Aleprylic acid is the next lower homolog to alepric acid containing two carbon atoms and four hydrogen atoms less than the latter. It has the formula $C_{12}H_{20}O_2$. It was obtained absolutely pure. It crystallizes in the same characteristic manner as the other homologs. Aleprylic acid melts sharply at 32° and has a specific optical rotation of +90.78°. It is colorless when liquid, white when solid and has a slight aromatic odor when warmed.

Aleprestic acid is the next lower homolog to aleprylic acid differing from it by C_2H_4 and having the formula $C_{10}H_{16}O_2$. It was obtained only 70.5% pure (Table I, 51W, 2) based upon its specific optical rotation which would be +100.5° as determined from the curve for the other homologs of this series of acids.

Although the next homolog to aleprestic acid may be present, our experimental data neither prove nor disprove its presence (Table I, 49W, 3, 4 and 5). On the other hand the second homolog below aleprestic acid is definitely proven to be present by the boiling point of the ethyl ester and the optical rotation and iodine number (Table I, 49W, 1). Computed from its rotation value we have obtained it 42% pure. We have named this lowest homolog aleprolic acid. It differs from aleprestic acid by C_4H_8 and has the

(1) Cole and Cardoso, THIS JOURNAL, **60**, 614 (1938).
(2) *Ibid.*, **60**, 612 (1938).
(3) *Ibid.*, **59**, 963 (1937).

TABLE I

FRACTIONAL DISTILLATION OF LOW BOILING ETHYL ESTERS OF *H. Wightiana* OIL

Fraction	Run	B. p., °C. (10 mm.)	Cc.	Rotation α	Specific rotation $[\alpha]^{25}D$	Iodine no.
1[a]	49W	58–66	1.5	42.4	42.68	100.2
2	49W	66–88	8.2	5.6	...	....
3	49W	88–100	2.1	8.6	...	....
4	49W	100–118	11.0	20.7	...	....
5	49W	118–120	10.0	44.0	...	....
6[b]	49W	120–122	5.0	51.0	...	....
7	49W	122–127	10.0	40.7	...	....
8	49W	127–129	5.2	24.7	...	....
9	49W	129–140	8.0	25.5	...	....
10	49W	140–146	7.0	33.1	...	....
11[c]	49W	146–148	44.0	52.6	...	....
		Fractions 49W, 2–5, redistilled				
1	50W	58–82	1.1	15.2	...	....
2[d]	50W	82–86	4.0	2.8	...	....
3	50W	86–100	5.0	6.4	...	....
4	50W	100–114	4.0	8.8	...	....
5	50W	114–120	7.0	25.3	...	....
6	50W	120–120	7.0	49.6	...	....
		Fractions 49W, 6 and 50W, 6, redistilled				
1	51W	114–122	5.0	44.8	...	....
2[e]	51W	122–122	7.0	54.6	60.94	96.64
		Ethyl aleprate (final distillation)				
1	53W	160–174	2.0	..	66.25	....
2[f]	53W	174–174	7.0	..	66.54	100.70
3	53W	174–174	2.5	..	65.41	....
		Ethyl aleprylate (final distillation)				
1[g]	31W	148	20.0	71.7	79.14	113.4
2	31W	148	20.0	71.7	79.14	113.4

[a] Ethyl aleprolate 42% pure. [b] Impure ethyl aleprestate. [c] Impure ethyl aleprylate. [d] Unidentified acids. [e] Ethyl aleprestate 70.5% pure. [f] Ethyl aleprate 94.2% pure. [g] Pure ethyl aleprylate.

formula $C_6H_8O_2$. From the curve of the other homologs its specific optical rotation would be +120.5° when pure.

In these low boiling fractions of *H. wightiana* ethyl esters there is also present an optically inactive unsaturated acid containing one double bond and probably a saturated acid. The sample at our disposal was not large enough to isolate and identify these acids (Table I, 49W, 2 and 50W, 2).

Experimental

The *H. wightiana* oil used was obtained from Ernakulam, India. The ethyl esters were made in the usual manner by esterifying with ethyl alcohol and sulfuric acid and washing to remove glycerol and acid. Two hundred liters of the ethyl esters was fractionally distilled in a 2-l. still at 10 mm. The first 10% (20 l.) fractions were redistilled in the same manner. The 2 liters of low boiling esters thus obtained was refractionated carefully several times in a Podbielniak Model B high temperature fractionating apparatus at 10 mm. The apparatus and technique used were described in a previous paper.[1] Plateaus in the distillation curves were finally obtained at 122, 148 and 174° (Table I). These fractions upon being changed to acids and recrystallized several times from acetone proved to be three new homologs of chaulmoogric acid (Table I, 51W, 2; 31W, 2; 53W, 2). The fourth and lowest homolog is clearly shown to be present in fraction 49W, 1 by the very sharp drop in rotation in the next higher fraction, 49W, 2.

Alepric Acid.—Alepric acid was much more difficult to isolate than aleprylic acid as it was impossible to free it entirely from the other unsaturated acid and from palmitic acid without very great loss. We finally obtained it 96.4% pure as calculated from actual and theoretical rotations (77.1 and 80.0). The constants for alepric acid and for ethyl aleprate are given in Tables II and III.

TABLE II

CONSTANTS OF OPTICALLY ACTIVE FATTY ACIDS FOUND IN CHAULMOOGRA OILS

Acids	Mol. wt.	M. p., °C.	Sp. rot. $[\alpha]^{25}D$	Iodine no.
Chaulmoogric acid	280.2	68.5	60.3	90.5
Hydnocarpic acid	252.2	60.5	69.3	100.7
Alepric acid	224.2	48.0	77.1	113.4
Aleprylic acid	196.2	32.0	90.8	129.7
Aleprestic acid	168.1	..	100.5[a]	151.2
Homolog not found	140.1	..	110.5[a]	181.5
Aleprolic acid	112.1	..	120.5[a]	226.7
Gorlic acid	278.2	6.0	60.7	182.5

[a] Calculated.

TABLE III

CONSTANTS OF ETHYL ESTERS OF OPTICALLY ACTIVE ACIDS FOUND IN CHAULMOOGRA OILS

Compound	Mol. wt.	B. p. °C. (10 mm.)	Sp. rot. $[\alpha]^{25}D$	Iodine no.	R. index $n^{25}D$	Sp. gr. 25°/25°
Ethyl chaulmoograte	308.3	222	55.4	82.5	1.4592	0.901
Ethyl hydnocarpate	280.2	200	61.9	90.5	1.4578	.907
Ethyl aleprate	252.2	174	66.5	100.7	1.4562	.915
Ethyl aleprylate	224.2	148	79.1	113.4	1.4550	.925
Ethyl aleprestate	196.2	122[a]	86.5[a]	129.7	1.4538[a]	...
Homolog not found	168.1	96[a]	94.1[a]	151.2	1.4526[a]	...
Ethyl aleprolate	140.1	70[a]	101.8[a]	181.5	1.4514[a]	...
Ethyl gorlate	306.3	232	55.6	167.0	1.4667	.912

[a] Calculated.

Anal. Calcd. for $C_{14}H_{24}O_2$: C, 74.93; H, 10.78; iodine no., 113.4; mol. wt., 224.2. Found: C, 74.86; H, 10.86; iodine no. (Hanus), 116.7; mol. wt., 224.5.

Aleprylic Acid.—Aleprylic acid was purified fairly easily by several fractional distillations of the ethyl ester and fractional crystallizations of the acid. The latter must be done in an electric refrigerator as the acid melts at 32°. The constants for aleprylic acid and ethyl aleprylate are given in Tables II and III. They indicate that the acid and ester were 100% pure.

Anal. Calcd. for $C_{12}H_{20}O_2$: C, 73.41; H, 10.27; iodine no., 129.7; mol. wt., 196.15. Found: C, 73.54; H, 10.24; iodine no. (Hanus), 129.6; mol. wt., 196.2.

CALCULATIONS FOR SPECIFIC OPTICAL ROTATION

Compound	Grams	$CHCl_3$, cc.	Ang. rotn. 100-mm. tube	$[\alpha]^{25}D$
Alepric acid	2.2703	25	7.00	77.12
Ethyl aleprate	2.5562	25	6.80	66.54
Aleprylic acid	2.6712	50	4.85	90.78
Ethyl aleprylate	4.0433	50	6.40	79.14

Aleprestic Acid.—Since this acid was obtained only 70.5% pure we can determine its constants only from the curves made with the other pure homologs. These probable constants are shown in Tables II and III.

Aleprolic Acid.—Fraction 49W, 1, Table I, clearly indicates the presence of this very low homolog of chaulmoogric acid. The boiling point of ethyl aleprolate should be 70° at 10 mm.; being impure it boiled slightly lower.

The homolog between ethyl aleprestate and ethyl aleprolate should boil at 96° at 10 mm. It is probably present but our final fractions were too small to attempt further fractionation to prove its presence.

An optically inactive unsaturated acid with one double bond must be present in fraction 50W, 2 to account for the iodine number found. There may also be present a saturated acid of low molecular weight.

For purposes of comparison the constants of the other known optically active acids and their ethyl esters are included in Tables II and III.

Summary

Four optically active fatty acids hitherto unknown have been discovered in *Hydnocarpus wightiana* oil. They have been named alepric, aleprylic, aleprestic and aleprolic acids.

The characteristics of these new acids and their ethyl esters are given and their relationship to their previously known homologs, hydnocarpic and chaulmoogric acids, is shown.

RIO DE JANEIRO, BRAZIL RECEIVED APRIL 20, 1939

[CONTRIBUTION FROM THE INTERNATIONAL LEPROSY CENTER, RIO DE JANEIRO]

Analysis of Chaulmoogra Oils. III. *Hydnocarpus Wightiana* Oil

BY HOWARD IRVING COLE AND HUMBERTO T. CARDOSO

Of the various chaulmoogra oils used in the treatment of leprosy, that expressed from the seeds of *Hydnocarpus wightiana* is by far the most generally employed. This is largely due to the fact that an oil of excellent quality is easily obtainable in large quantities at a reasonable price. *H. wightiana* occurs abundantly in southwestern India. The tree grows to a height of 7 to 10 meters. The fruit measures 6 to 12 cm. in diameter. The seed is about 2 cm. long with longitudinal grooves and a knot on the end. The species is one of the most abundant and easily accessible of the *Hydnocarpaceae*. Although *H. wightiana* oil has been so widely used for the past fifteen years in the treatment of leprosy, no accurate qualitative or quantitative analysis has ever been made due to the difficulty in separating the constituents. In 1905 Power and Barrowcliff[1] reported that the total fatty acids of this oil consisted chiefly of hydnocarpic and chaulmoogric acids and that they found evidences of a still lower homolog of the same series having the formula $C_{14}H_{24}O_2$ in the mother liquor but were unable to isolate it. Since the iodine number of the final mother liquor was so large (140.7) they concluded that it indicated the presence of an acid or acids belonging to the linolic or linolenic series. Our analysis shows that acids of neither of these series are present but that the high iodine number (and high rotation, 50.4) that they obtained are due to gorlic acid.[2] No evidence of the presence of palmitic acid was found by them and they make no mention of oleic acid. Since their analysis was made practically nothing has been added to our knowledge of the composition of this important medicinal oil. A single reference has been made to the possible presence of gorlic acid.[3] We have succeeded in analyzing *H. wightiana* oil by the method for chaulmoogra oils given in the first article of this series.[4] Our analysis is shown in Table I. It shows six fatty acids not previously reported in this oil, four of which are new homologs of chaulmoogric acid.

Experimental

The sample of oil was taken from a 300-liter drum of *H. wightiana* oil, cold-pressed from fresh, selected seeds imported for the routine production of leprosy drugs for Brazil from the Ernakulam Trading Co., Ernakulam, South India. The characteristics of the oil were as follows: sp. gr. $^{25}/_{25}$, 0.9549; F. F. A. (as % oleic), 2.7; sapon. no., 201; iodine no. (Hanus), 98.4; sp. rotn.,

(1) Power and Barrowcliff, *J. Chem. Soc.*, **87**, 884 (1905).

(2) Cole and Cardoso, THIS JOURNAL, **60**, 612 (1938).

(3) Anon., *Bull. Imp. Inst.*, **34**, 145 (1936).

(4) Cole and Cardoso, THIS JOURNAL, **60**, 614 (1938).

+55.0°; ref. index (at 25°), 1.4799; unsaponifiable matter, 0.25%.

Method of Analysis.—Since the medicinal properties of chaulmoogra oils depend on the percentage of optically active acids, the analysis is reported in percentage of the various fatty acids present. The sample of oil was saponified and the fatty acids liberated and washed in the usual manner. The solid acids were separated from the liquid acids by crystallization from 80% ethyl alcohol. The two fractions were changed to ethyl esters and then fractionally distilled in a Podbielniak Model B high temperature fractionating apparatus. The details of the separation and distillation were given in the first article of this series, the only change being that the two final crystallizations for the separation of the liquid acids were made with 80% acetone to prevent the formation of ethyl esters.

Qualitative Analysis

The fatty acids of *H. wightiana* oil contain hydnocarpic, chaulmoogric, gorlic, oleic, palmitic, alepric, aleprylic and aleprestic acids besides a very small amount of a low-boiling, optically inactive, unsaturated acid with one double bond and another homolog of chaulmoogric acid containing only six carbon atoms which we have named aleprolic acid. The acids were identified as follows.

Hydnocarpic Acid.—This acid was isolated easily from fraction 2, Table III, by repeated crystallization from 80% ethyl alcohol. It gave the correct optical rotation, iodine number, neutralization equivalent and melting point for pure hydnocarpic acid as well as the characteristic crystalline growth previously described.[5]

Chaulmoogric Acid.—Pure chaulmoogric acid was obtained readily from fraction 4, Table III, by crystallization to constant melting point from 80% ethyl alcohol. It gave the correct optical rotation, iodine number, neutralization equivalent and melting point for pure chaulmoogric acid.[5]

Gorlic Acid.—Ethyl gorlate was isolated by several fractional distillations of fraction 4, Table II. It gave the correct optical rotation, iodine number and boiling point for ethyl gorlate. Changed to acid it also gave the correct constants for gorlic acid.[2]

Oleic Acid.—Oleic acid was not obtained pure but its presence was indicated in the liquid fraction by the distillation curve of the ethyl esters and by the correct iodine numbers for mixtures containing ethyl oleate in fractions 2, 3 and 4, Table II. The elaidic acid test could not be used as gorlic acid gives a similar reaction. Hydrogenation tests were equally unsatisfactory in the presence of hydnocarpic and chaulmoogric acids.

Palmitic Acid.—It is practically impossible to separate ethyl palmitate from hydnocarpate by distillation but the separation can be accomplished easily by cooling a fraction of esters high in palmitate in the icebox. By separating the solid ethyl palmitate and crystallizing it twice from alcohol it was obtained pure (m. p. 24°). Upon changing it to palmitic acid and crystallizing two or three times the correct melting point and neutralization equivalent for palmitic acid was obtained.

Alepric Acid.—This acid is the next lower homolog to hydnocarpic acid, differing from the latter by C_2H_4 and having the formula $C_{14}H_{24}O_2$. It occurs in very small amount (less than 0.5%) in *H. wightiana* oil. No attempt was made to isolate it in the sample here analyzed but it was isolated from a much larger sample (200 liters) and its properties were determined. The method of separation of this homolog and the determination of its properties as well as those of the following homologs of chaulmoogric acid form the subject of another paper.[6]

Aleprylic Acid.—This acid is a homolog of chaulmoogric acid next lower in the series to alepric acid having the formula $C_{12}H_{20}O_2$. In the same sample about ten times as much of this acid can be isolated as of alepric or aleprestic acid. *H. wightiana* oil contains about 3% of aleprylic acid. It was isolated from the large sample mentioned above and its properties were determined.[6]

Aleprestic Acid.—This is the next lower homolog to aleprylic acid having the formula $C_{10}H_{16}O_2$. It occurs in very small amounts in *H. wightiana* oil (less than 0.5% and was not isolated from this sample but was obtained 70.5% pure from the large sample mentioned above.

Aleprolic Acid.—This is the lowest homolog of chaulmoogric acid yet discovered, being the second lower homolog after aleprestic acid having the formula $C_6H_8O_2$. Even from the large sample mentioned above we obtained only a very small amount of this acid, but the boiling point of its ethyl ester (65° at 10 mm.) and its specific rotation indicated its presence and from the latter we were able to determine its purity (42%). From our distillation curves we were unable to say whether or not the homolog between aleprestic and aleprolic acids was present.

In the sample at our disposal we were unable to isolate the optically inactive unsaturated acid with one double bond indicated as present by the iodine number.

Quantitative Analysis

The total fatty acids of *H. wightiana* oil when separated into liquid and solid acids by the method described by us consisted of 84.3% solid acids and 15.7% liquid acids. Although the separation is by no means complete, the breaks in the distillation curves of the ethyl esters made from these two fractions are much more distinct than when the whole esters are used. Complete separation is not necessary as the amounts of the various constituents can be computed by taking advantage

TABLE I

PERCENTAGE COMPOSITION OF THE FATTY ACIDS OF *H. Wightiana* OIL (FROM TABLES II AND III)

Acids	%
Hydnocarpic	48.7
Chaulmoogric	27.0
Gorlic	12.2
Oleic	6.5
Palmitic	1.8
Lower homologs of chaulmoogric acid (alepric, aleprylic, aleprestic, aleprolic and unidentified acids)	3.4
Loss	0.4

(5) Cole and Cardoso, THIS JOURNAL, **59**, 963 (1937).

(6) Cole and Cardoso, *ibid.*, **61**, 2349 (1939).

TABLE II

FRACTIONAL DISTILLATION OF ETHYL ESTERS FROM LIQUID ACIDS OF *H. Wightiana* OIL (15.7% OF TOTAL FATTY ACIDS)

Fraction	B. p., °C. (10 mm.)	Cc.	Sp. rotn. $[\alpha]^{25}D$	Iodine no.	Percentage in liquid fraction: Hydnocarpate	Chaulmoograte	Gorlate	Oleate	Palmitate	Lower homologs
1	120–187	3.3	50.64	86.7	..	..	..	..	0.9	2.4[a]
2	187–203	24.0	46.79	95.4	15.2	..	3.3	4.5	1.0	...
3	203–207	14.0	46.25	121.7	5.0	..	6.1	2.9	...	..
4	207–212	55.7	49.01	142.0	..	13.3	39.3	3.1	...	...
Residue	.....	3.0	...	...	..	..	..	..	...	...
			% in liquid fraction		20.2	13.3	48.7	10.5	1.9	2.4
			% in total fatty acids		3.2	2.1	7.7	1.6	0.3	0.4

[a] Alepric, aleprylic, aleprestic, aleprolic and unidentified acids.

TABLE III

FRACTIONAL DISTILLATION OF ETHYL ESTERS FROM SOLID ACIDS OF *H. Wightiana* OIL (84.3% OF TOTAL FATTY ACIDS)

Fraction	B. p., °C. (10 mm.)	Cc.	Sp. rotn. $[\alpha]^{25}D$	Iodine no.	Percentage in solid fraction: Hydnocarpate	Chaulmoograte	Gorlate	Oleate	Palmitate	Lower homologs
1	117–189	5	53.13	83.3	..	..	...	...	1.4	3.6[a]
2	191–202	55	57.57	91.3	49.7	..	1.6	3.3	0.4	...
3	202–210	5	54.75	93.6	4.2	..	0.3	0.5	...	...
4	210–214	35	52.38	90.3	..	29.6	3.4	2.0	...	...
			% in solid fraction		53.9	29.6	5.3	5.8	1.8	3.6
			% in total fatty acids		45.5	24.9	4.5	4.9	1.5	3.0

[a] Alepric, aleprylic, aleprestic, aleprolic and unidentified acids.

of the boiling points, optical activity and iodine numbers or absence of one or both of the two latter constants as described in part one of this series. The results of these computations are given in Tables II and III and these are summarized in Table I. Fraction 1 of Table II and of Table III were too small to be further divided but we know from distillation of much larger samples that there is about ten times as much aleprylic acid in this first fraction as there is of the homolog above and below it or of the optically inactive, unsaturated acid. We have therefore figured these two fractions on the basis of the specific optical rotation of ethyl aleprylate (79.14) which gives us 0.9% for the amount of saturated ester present in fraction 1, Table II, and 1.4% in fraction 1, Table III. This is admittedly only an approximation.

Summary

The qualitative and quantitative analyses of the total fatty acids of *H. wightiana* oil have been made by the method described in the first article of this series.

This is the first quantitative analysis that has been made of this oil. Six constituents not previously reported have been found, four of which are new homologs of chaulmoogric acid.

This analysis shows *H. wightiana* oil to be quite similar in composition to *Carpotroche braziliensis oil.*

RIO DE JANEIRO, BRAZIL RECEIVED APRIL 20, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE COLLEGE OF LIBERAL ARTS AND SCIENCES OF TEMPLE UNIVERSITY]

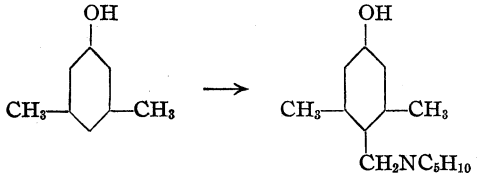
A Study of Orientation of Nuclear Methylation in Phenols and Naphthols

BY WILLIAM T. CALDWELL AND THOMAS R. THOMPSON

We described recently[1] a simple method for the introduction of one or more methyl groups into the nucleus of phenols, a method requiring merely treatment of the phenol with dimethylamine and formaldehyde and subsequent fission of the substituted benzylamine by catalytic high pressure hydrogenation.

In all reactions carried out at that time, we obtained only ortho substitution as proved by the structure of the methylated phenol formed. Indeed, the ease with which we were always able to purify these phenols indicated that they were substantially free of isomers or homologs which might have formed had any intramolecular rearrangements occurred during the hydrogenation, an unlikely possibility at best.

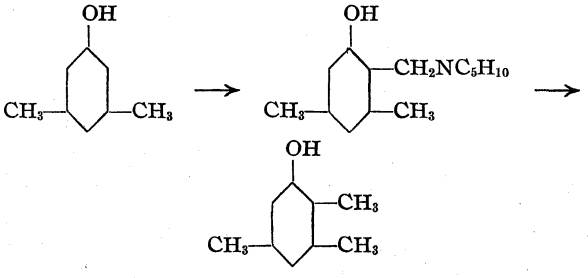
In 1906, Auwers and Dombrowski[2] prepared a number of analogously constituted benzylpiperidines by the action of piperidine and formaldehyde upon various phenols. They assumed that the piperidinomethyl groups entered the nucleus preferentially in the para position to the hydroxyl and that ortho substitution took place only when the para position was blocked. Thus, they formulated the reaction with 3,5-dimethylphenol to give a substituted piperidinomethyl derivative as follows



We already had prepared, in the course of our work, substituted benzylamines by using secondary amines other than dimethylamine; for example, 3,5-dimethylphenol formed a beautifully crystalline product with morpholine and formaldehyde which gave the same trimethylphenol on hydrogenolysis as did the dimethylaminomethyl derivative, namely, 2,3,5-trimethylphenol.

Although it appeared improbable that the use of piperidine instead of morpholine would bring about a different orientation in the product, this was not impossible; furthermore, if such were the case, we would have a desirable method of influencing the direction of nuclear methylation of phenols in which para and ortho positions are open.

We, therefore, prepared piperidinomethyl-3,5-dimethylphenol according to the directions given by Auwers and Dombrowski[2] and subjected it to hydrogenolysis. Again we obtained 2,3,5-trimethylphenol in accord with the steps indicated



Since this proved that the assumption of Auwers and Dombrowski had been erroneous in this particular case, we subjected additional piperidinomethyl phenols, for which they had assumed para substitution, to hydrogenolysis in order to ascertain whether or not this assumption was generally incorrect. In this way, we were able to prove that, although their assumption of para substitution was also wrong in the piperidinomethyl derivatives of *m*-cresol and of naphthol-1, it was correct in 4-piperidinomethyl-3-methyl-6-isopropylphenol and in 4-piperidinomethyl-2,5-dimethyl phenol. In addition, we subjected to hydrogenolysis some of the morpholinomethyl phenols described by Bruson[3] in order to determine their orientations. All of these methylations are summarized as follows

3-Methylphenol ⟶ 3,6-dimethylphenol
4-Methylphenol ⟶ 2,4-dimethylphenol
3,5-Dimethylphenol ⟶ 2,3,5-trimethylphenol
2,3,5-Trimethylphenol ⟶ 2,3,5,6-tetramethylphenol
2,5-Dimethylphenol ⟶ 2,4,5-trimethylphenol
3-Methyl-6-isopropylphenol ⟶ 3,4-dimethyl-6-isopropylphenol
Hydroquinone ⟶ 2,5-dimethylhydroquinone
Catechol ⟶ 2,4-dimethylcatechol
Naphthol-1 ⟶ 2-methylnaphthol-1
Naphthol-2 ⟶ 1-methylnaphthol-2

(1) Caldwell and Thompson, THIS JOURNAL, **61**, 765 (1939).
(2) Auwers and Dombrowski, *Ann.*, **344**, 285 (1906).
(3) H. Bruson, U. S. Patent 2,040,039 and 2,040,040 (May, 1936).

We have thus shown that, although para substitution does not occur preferentially, our surmise that ortho substitution would prove general is equally without foundation.

The formation of 3,4-dimethyl-6-isopropylphenol from 3-methyl-6-isopropylphenol is interesting when viewed in the light of what happens when this reaction is applied in two successive stages to 3,5-dimethylphenol. Attempts to introduce two dimethylaminomethyl or two morpholinomethyl groups into 3,5-dimethylphenol have not been successful in our hands; however, once we obtained 2,3,5-trimethylphenol we had no difficulty in converting it to 2,3,5,6-tetramethylphenol. Yet, to our surprise, we found that the piperidinomethyl group enters the para position in thymol. From this observation it appears that, although the ortho position is open, some factor other than a steric one causes preferential reaction in the para position. In view of the fact that 3,5-dimethylphenol had undergone successive methylations in the ortho positions, it seemed interesting to us to treat similarly 2,5-dimethylphenol, which differs from thymol only in having a methyl instead of an isopropyl group ortho to the hydroxyl. Here, too, substitution occurred in the para position although the ortho was as open as in 3,5-dimethylphenol or 2,3,5-trimethylphenol, and steric factors were alike.

Methylcarvacrol was prepared from carvacrol but has not been described in the literature. Its empirical formula has been proved by analysis and it is assumed that since carvacrol has a structure analogous to that of thymol and of 2,5-dimethylphenol, the methyl group enters para to the hydroxyl. The evidence at our disposal at this point, then, indicates that while the directional influences at play produce a single isomer, no simple prediction of orientation appears feasible, for comparatively slight changes in the constitution of the original phenol are, at times, sufficient to change the direction of the reaction.

An attempt was made to introduce an additional aminomethyl group into 2,5-dimethylhydroquinone and 3,4-dimethyl-6-isopropylphenol, in each of which an ortho position was still open, and into methylcarvacrol in which an ortho position was presumably open—at least an ortho or para position was certainly free. In none of these cases was any evidence of reaction obtained, and the original phenols were recovered and identified.

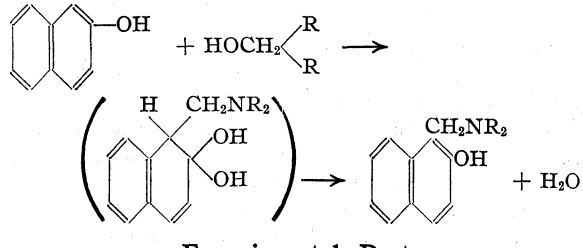
Again, 2,3,5,6-tetramethylphenol, in which only a para position is open, was submitted to the same treatment, but was recovered after giving no evidence of reaction.

The results obtained with catechol are particularly interesting in that one group entered the nucleus ortho to one hydroxyl while the other went into the para position with respect to the second hydroxyl. We have not been able to isolate, as yet, a product from catechol containing only one substituted aminomethyl group; hence, we cannot say whether the first substituent enters the ortho or para position, nor whether it does so exclusively in one way or to form a mixture of isomers. In any event, when disubstitution occurs, although both para positions as well as both ortho positions are free, the product formed indicates that one of each of these positions is involved.

In the naphthalene series we found that substitution took place with naphthol-2 in the position indicated by Auwers and Dombrowski, but not with naphthol-1. With the former, 1-methylnaphthol-2 was obtained in which an unhindered ortho position is still open. Therefore an attempt was made to introduce another piperidinomethyl group into this position, C_3. No evidence of reaction was obtained and the original material was recovered. Since steric factors do not seem to be involved, we believe that this observation properly may be regarded as additional evidence for the point of view[4] that the two ortho positions in naphthol-2 are not equivalent.

The reaction between a phenol, formaldehyde and a secondary amine apparently involves first the formation of a substituted aminomethanol which then reacts with the phenol, for we have not been able to obtain a substituted benzylamine by treating 2,6-dimethylol-4-methylphenol with morpholine.

Corresponding then to one formulation of the coupling of a diazo compound with naphthol-2, we may write



Experimental Part

The following piperidinomethyl phenols were made ac-

(4) Fieser and Lothrop, THIS JOURNAL, **57**, 1459 (1935).

cording to Auwers and Dombrowski,[5] the yields being essentially quantitative.

	M. P., °C. Obsd.	A. and D.
2-Piperidinomethyl-4-methylphenol	44.5–45.0	46
2-Piperidinomethyl-5-methylphenol	Oil	57
2-Piperidinomethyl-3,5-dimethylphenol	99	98.5
4-Piperidinomethyl-6-isopropyl-3-methylphenol	152–153	149.5
2-Piperidinomethyl-naphthol-1	137	133–134
1-Piperidinomethyl-naphthol-2	93–94	92–93
4-Piperidinomethyl-2,5-dimethyl	130–131	131.5–132.0
Piperidinomethylcarvacrol, (see text)	184–185	183

3,5-Dimorpholinomethyl Catechol.—One-quarter mole (27.5 g.) of practical catechol was mixed with 42 g. (0.5 mole) of morpholine and enough 95% alcohol added to keep the ingredients in solution; 45 ml. (0.5 mole) of formalin was added slowly and the mixture set aside. Crystals formed overnight and, after five days, were filtered off, giving a nearly quantitative yield; large, colorless prisms crystallized from 95% alcohol, m. p. 173–174°.

Anal. Calcd. for $C_{16}H_{24}O_4N_2$: N, 9.1. Found: N, 9.1.

2-Morpholinomethyl-3,5-dimethylphenol.—To one mole of technical 3,5-dimethylphenol were added one mole of morpholine and, then, while keeping the temperature between 25–35°, one mole of formaldehyde (as formalin) with vigorous stirring. On cooling in an ice-bath with continued agitation the product solidified in small aggregates which were filtered off and washed with water, giving an almost quantitative yield. Recrystallized from methyl alcohol, it melts at 96.5–97.0°.

Anal. Calcd. for $C_{13}H_{19}O_2N$: N, 6.3. Found: N, 6.3.

6-Morpholinomethyl-2,3,5-trimethylphenol.—Two and three-tenths grams of 2,3,5-trimethylphenol was treated with 5 g. of morpholine and 5 ml. of formalin and heated on the steam-bath for three hours. After adding some water, an oil formed which solidified on standing. Colorless needles crystallized from benzene: yield 70%; m. p. 78°.

Anal. Calcd. for $C_{19}H_{24}O_2N$: N, 5.88. Found: N, 5.81.

All hydrogenations were carried out in the following manner. The aminomethylphenol and copper chromite catalyst were placed in the copper liner of the high pressure hydrogenation apparatus and the dioxane solvent added. Under a pressure of 1500 lb. (102 atm.) and, with the rocker in motion, the electric heating element was adjusted so that in the course of one and one-half hours the temperature was 165°, at which it was kept constant for an additional hour and a half. Upon opening the bomb the odor of regenerated amine was quite noticeable. After filtering off the catalyst and removing the solvent, the mixture was acidified with hydrochloric acid and the phenol distilled with steam.

2,4-Dimethylphenol.—Eight and five-tenths grams of 2-piperidinomethyl-4-methylphenol, 1 g. of catalyst and 100 ml. of dioxane were hydrogenated. A colorless oil separated from the steam distillate and was extracted with ether, dried, and distilled: yield 1 g.; b. p. 205–206°. Jacobsen[6] gives b. p. 211.5° (corr.). The phenoxyacetic acid was made by condensing with monochloroacetic acid in 33% sodium hydroxide solution; m. p. 141°. Gluud and Breuer[7] give m. p. 141.6° for 2,4-dimethylphenoxyacetic acid.

2,5-Dimethylphenol.—Thirty-five grams of 2-piperidinomethyl-5-methylphenol, 5 g. of catalyst, and 200 ml. of dioxane were hydrogenated. Four grams of product solidified from the steam distillate and was crystallized from petroleum ether; m. p. 75°. Jacobsen[6] gives m. p. 74.5° for 2,5-dimethylphenol. A mixed melting point with an authentic sample showed no depression.

2,3,5-Trimethylphenol.—Eleven and five-tenths grams of 2-piperidinomethyl-3,5-dimethylphenol, 2 g. of catalyst, and 150 ml. of dioxane were hydrogenated. The white needles that crystallized from the steam distillate and also collected in the condenser were crystallized from petroleum ether; m. p. 93°; when mixed with an authentic sample of 2,3,5-trimethylphenol no depression of melting point occurred.

3,4-Dimethyl-6-isopropylphenol.—Eleven and five-tenths grams of 4-piperidinomethyl-3-methyl-6-isopropylphenol, 1.5 g. of catalyst, and 100 ml. of dioxane were hydrogenated. Six grams of product solidified from the steam distillate and, after crystallization from petroleum ether, the colorless needles melted at 70–71°; yield, 78%. Clemmensen[8] gives m. p. 70–71° for 3,4-dimethyl-6-isopropylphenol.

Methylcarvacrol.—Twenty grams of piperidinomethylcarvacrol, 2 g. of catalyst, and 200 ml. of dioxane were hydrogenated. An oil separated from the steam distillate and was extracted with ether. Distillation of the dried ether solution gave a colorless liquid which turned light brown on standing, b. p. 244–246°. The product became very viscous on cooling to −15°: yield 4 g., or 30%.

Anal. Calcd. for $C_{11}H_{16}O$: C, 80.5; H, 9.75. Found: C, 80.3; H, 9.70.

The phenoxyacetic acid derivative was made by condensing with monochloroacetic acid in the presence of 33% sodium hydroxide solution; colorless needles from benzene, m. p. 173°.

2-Methyl-1-hydroxynaphthalene.—Sixteen and one-tenth grams of 2-piperidinomethylnaphthol-1, 1.6 g. of catalyst, and 200 ml. of dioxane were hydrogenated. Two grams of product was volatile with steam; after crystallization from petroleum ether, fluffy needles were obtained, m. p. 61.5–62°; yield, 19%. Lesser[9] gives m. p. 62°.

1-Methyl-2-hydroxynaphthalene.—Fifteen grams of 1-piperidinomethyl-naphthol-2, 2 g. of catalyst, and 200 ml. of dioxane were hydrogenated. Two and eight-tenths

(5) Auwers and Dombrowski, *Ann.*, **344**, 280 (1906).

(6) Jacobsen, *Ber.*, **11**, 24 (1878).

(7) Gluud and Breuer, *Chem. Zentr.*, **90, I**, 626 (1919).

(8) Clemmensen, *Ber.*, **47**, 62 (1914).

(9) Lesser, *Ann.*, **402**, 8 (1914).

grams of substance was volatile with steam and after crystallization from petroleum ether melted at 107–108°. A sublimed portion melted at 109°. Betti and Mundici[10] give m. p. 110° for sublimed 1-methyl-2-hydroxynaphthalene. The acetate was found to melt at 65°; Betti and Mundici give m. p. 66°.

3,5-Dimethylcatechol.—Twenty-five grams of 3,5-dimorpholinomethylcatechol, 3 g. of catalyst, and 200 ml. of dioxane were hydrogenated. The product was not volatile with steam; it was therefore extracted three times with ether. The dried, ethereal solution gave, on distillation, 3 g. of colorless oil, b. p. 235–240°, which solidified on cooling to room temperature. Crystallization from petroleum ether–benzene mixture gave yellow needles, m. p. 73.5–74.0°; yield, 36%. Hodgkinson[11] gives m. p. 73–74°.

Anal. Calcd. for $C_8H_{10}O_2$: C, 69.6; H, 7.25. Found: C, 69.5; H, 7.25.

2,3,5,6-Tetramethylphenol.—Two and three-tenths grams of 2-morpholinomethyl-3,5,6-trimethylphenol, 0.5 g. of catalyst, and 50 ml. of dioxane were hydrogenated. Nine-tenths gram was volatile with steam and after crystallization from petroleum ether–benzene mixture melted at 117.5–118°. A sublimed portion melted at 118°. Jacobsen and Schnapauff[12] give m. p. 117°. Bromination in acetic acid gave the bromide, m. p. 117.5–118.5°. Jacobsen and Schnapauff give m. p. 118° for bromodurenol.

2,3,5-Trimethylphenol.—Twenty-five grams of 2-morpholinomethyl-3,5-dimethylphenol, 3 g. of catalyst, and 150 ml. of dioxane were hydrogenated. Four and five-tenths grams of product was volatile with steam and after crystallization from petroleum ether melted at 94°; yield, 29%.[1] The residual liquor from the steam distillation was filtered from a small amount of resinous material, and neutralized with sodium carbonate, giving a light brown precipitate weighing 15 g. After recrystallization from methyl alcohol, the melting point was 96–97° (2-morpholinomethyl-3,5-dimethylphenol). The yield, based on the amount of 2-morpholinomethyl-3,5-dimethylphenol converted, was 73%.

2,4,5-Trimethylphenol.—Six grams of 4-piperidinomethyl-2,5-dimethylphenol, 1 g. of catalyst, and 100 ml. of dioxane were hydrogenated. The product separated from the steam distillate and also in the condenser. Crystallization from petroleum ether gave needles, m. p. 70°. Auwers and Marwedel[13] give m. p. 70°. The yield, 0.8 g., was 21%.

Attempted Preparation of Certain Aminomethyl Derivatives.—As previously stated, we were unable to obtain aminomethyl derivatives of several phenols. As an example, we may record here our experience with 2-isopropyl-4,5-dimethylphenol: 1.6 g. (m. p. 70–71°) was mixed with equivalent amounts of piperidine and formalin in 75% alcohol. After standing for several days, no separation of oil or crystals occurred; the mixture then was acidified and, upon steam distillation, 1.2 g. of crystals, m. p. 70–71°, was recovered.

Summary

Although the formation of a substituted benzylamine from a phenol by the action of a secondary amine and formaldehyde occurs in such fashion that the ortho position generally is preferentially affected, contrary to the assumptions of Auwers and Dombrowski, nevertheless some factor or factors not always of a steric nature bring about para substitution in certain cases.

The failure of this reaction to take place with 1-methylnaphthol-2 is adduced as additional evidence bearing upon the nature of the two ortho positions and the disposition of the double bonds in naphthol-2.

A formulation of the reaction between a phenol, secondary amine and formaldehyde is suggested.

PHILADELPHIA, PENNA. RECEIVED JUNE 17, 1939

(10) Betti and Mundici, *Gazz. chim. ital.*, **36**, II, 657 (1905).
(11) Hodgkinson and Limpach, *J. Chem. Soc.*, **63**, 108 (1893).
(12) Jacobsen and Schnapauff, *Ber.*, **18**, 2843 (1885).
(13) Auwers and Marwedel, *ibid.*, **28**, 2902 (1895).

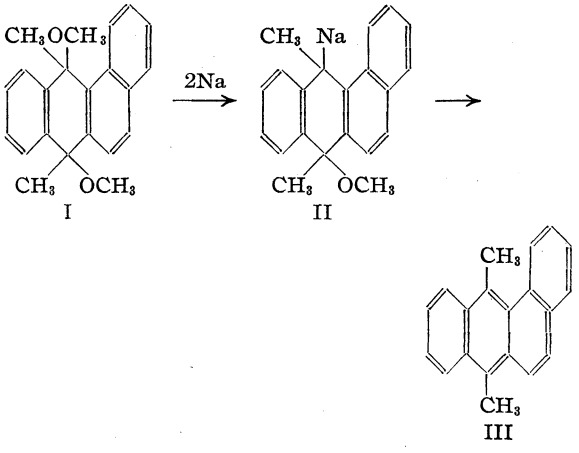
[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF THE UNIVERSITY OF MICHIGAN]

The Synthesis of 9,10-Dialkyl-1,2-benzanthracenes

BY W. E. BACHMANN AND J. M. CHEMERDA[1]

Recently[2] we described the synthesis of 9,10-dimethyl-1,2-benzanthracene and two other hydrocarbons containing alkyl groups in the 9,10-positions of the 1,2-benzanthracene molecule.[3] The mechanism by which 9,10-dimethyl-9,10-dimethoxy-9,10-dihydro-1,2-benzanthracene (I) is converted to 9,10-dimethyl-1,2-benzanthracene (III) by reaction with sodium has now been investigated.

In considering a mechanism the following facts must be kept in mind: (1) the reaction occurs between one mole of the dimethyl ether of the diol and two equivalents of sodium; (2) the 9,10-dimethyl-1,2-benzanthracene is present in the reaction mixture as the hydrocarbon and not in the form of a derivative; (3) the reaction mixture remains practically colorless throughout the reaction, an indication that no disodio derivative of the hydrocarbon is present. All of these facts receive a satisfactory explanation if we assume that the diol dimethyl ether reacts with sodium to give the intermediate II, which yields 9,10-dimethyl-1,2-benzanthracene by transannular elimination of sodium methylate.



We consider this reaction more probable than the simultaneous elimination of both methoxy groups by reaction with sodium.

Apparently the hydrocarbon begins to be formed as soon as the reaction is initiated. Since the solution remains practically colorless, our mechanism implies that none of the hydrocarbon which is formed reacts with the sodium as long as any diol dimethyl ether is present. Although this did not seem reasonable in view of the rapidity with which the 9,10-dimethyl-1,2-benzanthracene reacts with sodium in the absence of the diol dimethyl ether, an experiment designed to test this point showed that this is indeed the case. When equimolar amounts of 9,10-dimethyl-1,2-benzanthracene and 9,10-dimethyl-9,10-dimethoxy-9,10-dihydro-1,2-benzanthracene were allowed to compete for two equivalents of sodium, no disodio addition product was formed and the diol dimethyl ether was converted completely to the hydrocarbon. One other mechanism, involving the intermediate formation of 9,10-dimethyl-9,10-disodio-9,10-dihydro-1,2-benzanthracene and its subsequent reaction with the diol dimethyl ether, was excluded from consideration when it was found that the two compounds did not react to produce any appreciable quantity of 9,10-dimethyl-1,2-benzanthracene.

We also examined the utilization of other ethers for the sodium reaction. Of the four alcohols, ethyl, *n*-propyl, isopropyl, and *n*-butyl alcohol, only the ethyl alcohol yielded an ether under the conditions employed for the preparation of the dimethyl ether. From the diethyl ether and sodium, 9,10-dimethyl-1,2-benzanthracene was obtained although in lower yield. The diol dimethyl ethers are undoubtedly the best intermediates as they form easily and crystallize readily. In the case of the product from the interaction of 1,2-benzanthraquinone and *n*-propylmagnesium bromide the diol has not been obtained crystalline[4]; the diol dimethyl ether, however, crystallizes readily and yields 9,10-di-*n*-propyl-1,2-benzanthracene by reaction with sodium.

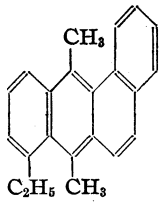
We have employed our method of synthesis to prepare 5-ethyl-9,10-dimethyl-1,2-benzanthracene (IV) and 5-*n*-propyl-9,10-dimethyl-1,2-benzanthracene (V). For the preparation of the intermediate 5-ethyl-1,2-benzanthracene we employed the reaction between 5-keto-tetrahydro-

(1) From the Ph.D. dissertation of J. M. Chemerda.

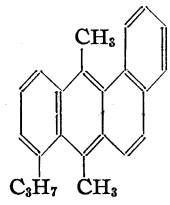
(2) Bachmann and Chemerda, THIS JOURNAL, **60**, 1023 (1938).

(3) For the carcinogenic properties of these compounds see Bachmann, Kennaway and Kennaway, *Yale J. Biol. Med.*, **11**, 97 (1938).

(4) Bachmann and Bradbury, *J. Org. Chem.*, **2**, 175 (1937).

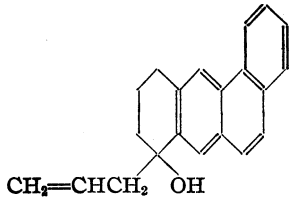


IV

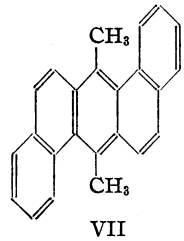


V

1,2-benzanthracene and ethylmagnesium bromide, followed by treatment of the resulting carbinol with palladium on charcoal as was done in the preparation of 5-methyl-1,2-benzanthracene.[5] When the cyclic ketone was treated with *n*-propylmagnesium bromide, considerable reduction took place. The 5-*n*-propyl-1,2-benzanthracene was best prepared by the catalytic dehydration and isomerization of the carbinol VI, which was obtained in good yield by interaction of the cyclic ketone and allylmagnesium bromide.



VI



VII

Our reaction also offers a convenient preparation of 9,10-dimethyl-1,2,5,6-dibenzanthracene (VII). This hydrocarbon has been prepared previously by Cook[6] by cautious reduction of the corresponding diol and by Akin and Bogert[7] by means of the Pschorr synthesis.

Experimental

Reaction of Sodium with a Mixture of 9,10-Dimethyl-1,2-benzanthracene and Diol Dimethyl Ether.—A mixture of 1.0 g. of 9,10-dimethyl-9,10-dimethoxy-9,10-dihydro-1,2-benzanthracene and 0.80 g. of 9,10-dimethyl-1,2-benzanthracene (equimolar proportions) in 25 cc. of benzene and 25 cc. of ether was shaken with 0.14 g. of powdered sodium and some sharp glass particles. After one day's shaking, a nearly colorless solution was obtained and all of the sodium had reacted. From the solution 1.59 g. (99%) of the calculated amount of the 9,10-dimethyl-1,2-benzanthracene was isolated; m. p. 122–123°.

Reaction of 9,10-Dimethyl-9,10-disodio-9,10-dihydro-1,2-benzanthracene with Diol Dimethyl Ether.—The disodium derivative was prepared by shaking 1.25 g. of 9,10-dimethyl - 9,10 - dimethoxy - 9,10 - dihydro - 1,2 - benzanthracene with 0.36 g. of powdered sodium in 30 cc. of ether and 30 cc. of benzene. After a week, the solution had a color reminiscent of the permanganate ion. The addition of 1.25 g. of the diol dimethyl ether did not decolorize the solution; the solution seemed to take on a brighter tinge of red. After a week, no further change was observed and the solution was treated with carbon dioxide to remove the disodium derivative. From the benzene–ether solution 0.75 g. (58%) of pure diol dimethyl ether was isolated. The mother liquor gave lower melting material from which no 9,10-dimethyl-1,2-benzanthracene could be isolated.

In another experiment, the disodium derivative was prepared by shaking the hydrocarbon with the theoretical amount of sodium. In the same manner as described above, 80% of the added diol dimethyl ether was recovered.

9,10 - Dimethyl - 9,10 - diethoxy - 9,10 - dihydro - 1,2-benzanthracene.—A suspension of 1.0 g. of 9,10-dimethyl-9,10-dihydroxy-9,10-dihydro-1,2-benzanthracene[4] in 5 cc. of absolute alcohol was treated with 0.05 cc. of sulfuric acid in 1 cc. of absolute alcohol. In ten minutes a clear solution was obtained and the diol diethyl ether crystallized out. After standing at room temperature for one hour the diol diethyl ether was collected, dissolved in benzene and washed with ammonium hydroxide to remove traces of sulfuric acid. It is highly essential that the ether be as pure as possible for the successful preparation of the hydrocarbon in the sodium reaction. The benzene solution was concentrated, alcohol was added and the diol diethyl ether crystallized in clumps of colorless narrow prisms; yield 0.84 g., m. p. 167.5–171°. After two recrystallizations from benzene–alcohol the **9,10-dimethyl-9,10-diethoxy-9,10-dihydro-1,2-benzanthracene** melted at 172–173.5°.

Anal. Calcd. for $C_{24}H_{26}O_2$: C, 83.2; H, 7.6. Found: C, 83.1; H, 7.4.

A mixture of 0.84 g. of the above diol diethyl ether and 0.11 g. of powdered sodium in 15 cc. of benzene and 20 cc. of ether was shaken with a half-dozen sharp glass particles. In the course of a day, a greenish-blue mixture was obtained. The mixture was decolorized with methanol and washed with dilute hydrochloric acid. By recrystallization of the product from acetone–alcohol, 0.38 g. (61%) of 9,10-dimethyl-1,2-benzanthracene was obtained.

9,10-Di-*n*-propyl-1,2-benzanthracene.—The reaction mixture from 5.16 g. of 1,2-benzanthraquinone and *n*-propylmagnesium bromide, obtained according to the procedure of Bachmann and Bradbury,[4] was hydrolyzed and the solvent evaporated at room temperature. Treatment of the oil with a solution of 0.25 cc. of sulfuric acid in 50 cc. of methanol resulted in an immediate crystallization of the diol dimethyl ether. After standing overnight at room temperature, the diol dimethyl ether (3.9 g.) was filtered off and treated in the manner already described. From benzene–methanol, 3.25 g. of **9,10-di-*n*-propyl-9,10-dimethoxy-9,10-dihydro-1,2-benzanthracene** was obtained as colorless needles; m. p. 174–176°. One recrystallization from benzene–ethyl acetate raised the melting point to 176.5–177.5°. The compound gives a brown color with sulfuric acid.

Anal. Calcd. for $C_{26}H_{30}O_2$: C, 83.4; H, 8.1. Found: C, 83.5; H, 8.2.

A mixture of 2.31 g. of the diol dimethyl ether in 25 cc.

(5) Bachmann and Wilds, THIS JOURNAL, **60**, 624 (1938).
(6) Cook, *J. Chem. Soc.*, 489 (1931).
(7) Akin and Bogert, THIS JOURNAL, **59**, 1564 (1937).

of benzene and 25 cc. of ether shaken with 0.28 g. of powdered sodium for one day gave 1.83 g. (95%) of **9,10-di-*n*-propyl-1,2-benzanthracene;** m. p. 98.5–100°. After purification through the picrate and recrystallization from benzene–alcohol, the hydrocarbon formed thick colorless needles; m. p. 100.5–101°.

Anal. Calcd. for $C_{24}H_{24}$: C, 92.3; H, 7.7. Found: C, 92.1; H, 7.5.

The **picrate** of the hydrocarbon crystallized from absolute alcohol in black needles; m. p. 107.5–108°.

Anal. Calcd. for $C_{24}H_{24}\cdot C_6H_3O_7N_3$: N, 8.1. Found: N, 8.0.

5-Ethyl-1,2-benzanthracene.—To a solution of the Grignard reagent prepared from 22 g. of ethyl bromide and 50 cc. of ether was added 50 cc. of benzene. To the ice-cold solution was added 13.8 g. of 5-keto-5,6,7,8-tetrahydro-1,2-benzanthracene. After standing at room temperature for half an hour, the mixture was hydrolyzed with ice-cold ammonium chloride solution. The reaction product obtained by evaporation of the solvent was heated with 1.0 g. of palladium on charcoal[8] at 310–320° for half an hour in an atmosphere of nitrogen. The cooled solid was extracted with acetone–benzene. After concentrating and adding alcohol, 9.95 g. of slightly yellow hydrocarbon was obtained; m. p. 115–117°. An additional 1.3 g. of hydrocarbon was obtained by treating the product in the mother liquor once more with the catalyst making a total yield of 79% based on the cyclic ketone. After distillation at 0.4 mm. the hydrocarbon crystallized from acetone–alcohol in colorless plates; yield, 9.3 g. (65%); m. p. 118–119°. Cook and his co-workers[9] reported a melting point of 120° for the compound prepared from 5-keto-dodecahydro-1,2-benzanthracene.

In another run with 5.0 g. of the cyclic ketone, the product was heated with 10 g. of powdered potassium bisulfate at 150–160° for one hour. The benzene extract of the hydrocarbon was clarified and concentrated, by addition of alcohol giving 3.46 g. of **5-ethyl-7,8-dihydro-1,2-benzanthracene.** A sample of the hydrocarbon after sublimation under reduced pressure crystallized from alcohol in colorless prisms; m. p. 110–112°.

Anal. Calcd. for $C_{20}H_{18}$: C, 93.0; H, 7.0. Found: C, 92.9; H, 7.1.

Dehydrogenation of the dihydro derivative by palladium on charcoal[8] at 330–340° for one hour gave the hydrocarbon in 70% yield.

5 - Ethyl - 9,10 - dimethyl - 1,2 - benzanthracene.—Five grams of 5-ethyl-1,2-benzanthracene was dissolved in 50 cc. of hot acetic acid. After cooling to 70°, 5.81 g. of pure sodium dichromate dihydrate was added in portions and the mixture was heated on the steam-bath for an hour. The quinone was precipitated by the addition of 15% sulfuric acid. Recrystallization from acetone–alcohol gave 4.1 g. of 5-ethyl-1,2-benzanthraquinone; m. p. 96–98°. A second recrystallization gave 3.75 g.; m. p. 97–98° (Cook,[9] 97–98°).

5-Ethyl-1,2-benzanthraquinone (3.75 g.) was added to an ice-cold solution of the Grignard reagent prepared from 4 cc. of methyl iodide and 12 cc. of ether and 12 cc. of benzene. After hydrolysis with ice-cold ammonium chloride solution, 3.54 g. of the diol was isolated. Recrystallized twice from ethyl acetate the **5-ethyl-9,10-dimethyl - 9,10 - dihydroxy - 9,10 - dihydro - 1,2 - benzanthracene** formed microscopic needles; m. p. 201.5–204.5°. It gives a purple color with sulfuric acid. Since the diol retains solvent of crystallization tenaciously, it was analyzed as the dimethyl ether. The latter was prepared by treating a suspension of the diol (3.0 g.) in 15 cc. of methanol with a solution of 0.15 cc. of sulfuric acid in 5 cc. of methanol. After one hour at room temperature the diol dimethyl ether was filtered off and purified in the usual manner. Recrystallization from benzene–methanol gave colorless needles of **5-ethyl-9,10-dimethyl-9,10-dimethoxy-9,10-dihydro-1,2-benzanthracene;** yield, 2.36 g.; m. p. 194–195°. Two more recrystallizations raised the melting point to 197–200°.

Anal. Calcd. for $C_{24}H_{26}O_2$: C, 83.2; H, 7.6. Found: C, 83.4; H, 7.9.

A mixture of 2.36 g. of the above diol dimethyl ether (m. p. 194–196°) and 0.31 g. of powdered sodium in 25 cc. of ether and 25 cc. of benzene was shaken with a half-dozen sharp glass particles for one day. Worked up in the usual manner, 1.56 g. (80%) of the hydrocarbon was obtained. The hydrocarbon does not form a stable picrate. After purification by passage of a benzene solution through a tower of anhydrous alumina, **5-ethyl-9,10-dimethyl-1,2-benzanthracene** crystallized from acetone in light yellow plates; m. p. 107–108°.

Anal. Calcd. for $C_{22}H_{20}$: C, 92.9; H, 7.1. Found: C, 92.6; H, 6.8.

5-*n*-Propyl-1,2-benzanthracene.—(a) A mixture of 10 g. of 5-keto-5,6,7,8-tetrahydro-1,2-benzanthracene, 2 g. of magnesium, 20 cc. of ether and 40 cc. of benzene was placed in a dry flask equipped with a reflux condenser. When 10 cc. of allyl bromide was added, a vigorous reaction was initiated in a few minutes. The contents were swirled occasionally until all the cyclic ketone dissolved (ten to twenty minutes) the mixture being cooled in a pan of cold water when necessary. The product began to crystallize from the hot mixture. After twelve hours in a refrigerator, the product was filtered off, washed with benzene and hydrolyzed with ice-cold ammonium chloride solution. The carbinol which crystallized out was filtered off, dissolved in benzene to free it from magnesium salts and returned to the benzene solution of the carbinol. Spontaneous evaporation of the solution gave practically colorless carbinol; yield 9.87 g. (84%). From dilute methanol, **5-allyl-5-hydroxy-5,6,7,8-tetrahydro-1,2-benzanthracene** crystallizes in colorless needles; m. p. 82–82.5°. With sulfuric acid it gives a brown color.

Anal. Calcd. for $C_{21}H_{20}O$: C, 87.5; H, 7.0. Found: C, 87.3; H, 7.0.

Five grams of the allylcarbinol was heated with 0.5 g. of palladium on charcoal[8] for half an hour at 300° in an atmosphere of nitrogen. At this temperature there was a sudden evolution of hydrogen which was reabsorbed for the most part by the end of the experiment. The cooled malodorous melt was extracted with acetone, filtered and allowed to evaporate spontaneously. A gum settled out on the bottom and crystalline material along the

(8) Zelinsky and Turowa-Pollak, *Ber.*, **58**, 1295 (1925).
(9) Cook, Robinson and Gulden, *J. Chem. Soc.*, 393 (1937).

sides. These portions, distilled separately at 0.4 mm. and recrystallized from acetone–alcohol, gave pure colorless needles of 5-*n*-propyl-1,2-benzanthracene; yield 3.55 g.; m. p. 90–92°. Cook and Haslewood[10] prepared the compound (m. p. 92°) from 5-keto-dodecahydro-1,2-benzanthracene.

(b) Five grams of 5-keto-5,6,7,8-tetrahydro-1,2-benzanthracene was added to an ice-cold solution of the Grignard reagent prepared from 4 cc. of *n*-propylmagnesium bromide and 20 cc. of ether followed by the addition of 20 cc. of benzene. The mixture was kept in a refrigerator for twenty-four hours and the crystalline product was filtered off and washed with benzene. The crystalline material was hydrolyzed with ice-cold ammonium chloride solution containing a little benzene. By spontaneous evaporation of the benzene solution and trituration of the residue with benzene–ligroin, 2.2 g. of **5-*n*-propyl-5-hydroxy-5,6,7,8-tetrahydro-1,2-benzanthracene** was obtained. The carbinol crystallized from benzene–ligroin in colorless threads; m. p. 107–108.5°. With sulfuric acid it gives a brownish-yellow color. It was not obtained analytically pure. By dehydrating the carbinol by heating with formic acid and dehydrogenating the product with palladium on charcoal, a 69% yield of 5-*n*-propyl-1,2-benzanthracene (m. p. 86–88°) was obtained.

5-*n*-Propyl-9,10-dimethyl-1,2-benzanthracene.—In the same manner as described for the ethyl homolog, 4.42 g. of 5-*n*-propyl-1,2-benzanthraquinone (obtained in 66% yield by the oxidation of 5-*n*-propyl-1,2-benzanthracene) was treated with methylmagnesium iodide. The clear yellow gum obtained was scratched until crystallization set in and the diol triturated with benzene–ligroin; yield 3.9 g.; m. p. 160–161°. **5-*n*-Propyl-9,10-dimethyl-9,10-dihydroxy-9,10-dihydro-1,2-benzanthracene** crystallized from ligroin–ethyl acetate in microscopic needles; m. p. 161.5–163°. With sulfuric acid it gives a purple color. It retains solvent of crystallization tenaciously and was analyzed as the dimethyl ether. In the manner previously described, 3. 0 g. of the diol dimethyl ether was obtained from 3.4 g. of the diol. **5-*n*-Propyl-9,10-dimethyl-9,10-dimethoxy-9,10-dihydro-1,2-benzanthracene** crystallizes from benzene–methanol in colorless rectangular prisms; m. p. 157–159°.

Anal. Calcd. for $C_{25}H_{28}O_2$: C, 83.3; H, 7.8. Found: C, 83.3; H, 7.9.

A mixture of 2.23 g. of the diol dimethyl ether reacted with 0.29 g. of powdered sodium in 25 cc. of ether and 25 cc. of benzene in the manner previously described to give 1.64 g. (89%) of **5-*n*-propyl-9,10-dimethyl-1,2-benzanthracene.** Purified by passage of a benzene solution of the hydrocarbon through anhydrous alumina and crystallized from acetone–alcohol, the hydrocarbon formed yellowish nacreous plates; m. p. 84–85°.

Anal. Calcd. for $C_{23}H_{22}$: C, 92.6; H, 7.4. Found: C, 92.4; H, 7.7.

(10) Cook and Haslewood, *J. Chem. Soc.*, 428 (1934).

9,10-Dimethyl-1,2,5,6-dibenzanthracene.—One and one-half grams of the crude methyl diol, obtained according to Cook's[6] procedure, was treated with a solution of 0.2 cc. of sulfuric acid in 10 cc. of methanol and 20 cc. of benzene. The diol dissolved and the diol dimethyl ether crystallized in fine needles. After purification in the usual manner the **9,10-dimethyl-9,10-dimethoxy-9,10-dihydro-1,2,5,6-dibenzanthracene** (1.2 g.) crystallized from benzene in fine narrow colorless prisms; m. p. 310–320° with decomposition.

Anal. Calcd. for $C_{26}H_{24}O_2$: C, 84.8; H, 6.6. Found: C, 84.7; H, 6.7.

A mixture of 0.092 g. of powdered sodium and 0.74 g. of the diol dimethyl ether in 20 cc. of ether and 20 cc. of benzene was shaken for two days. A yield of 0.52 g. (85%) of hydrocarbon was obtained; m. p. 202–205°. From the mother liquor an additional 0.06 g. was obtained which gave 0.07 g. of fairly pure picrate; m. p. 174–176°.

The first crop was picrated in benzene and the benzene solution of the regenerated hydrocarbon passed through anhydrous alumina. From benzene the 9,10-dimethyl-1,2,5,6-dibenzanthracene crystallized in glistening yellow plates; m. p. 205.5–206.5°, the same melting point reported by Cook.[6]

9,10-Dimethyl-1,2,5,6-dibenzanthracene and picric acid dissolved in hot alcohol containing a little benzene deposited bright red needles of a **dipicrate;** m. p. 175°.

Anal. Calcd. for $C_{24}H_{18}\cdot 2C_6H_3O_7N_3$: N, 11.0. Found: N, 11.0.

Care must be exercised to avoid undue exposure of solutions of the hydrocarbon to light, for the hydrocarbon readily forms a peroxide. In one experiment, after purification, colorless needles of the peroxide were obtained instead of the usual yellow plates; m. p. 206–207° with decomposition. When placed in a bath at 200°, a melting point of 218–219° with bubbling and complete decomposition was observed. This same compound was prepared by exposure to sunlight of a solution of 0.10 g. of the hydrocarbon in 5 cc. of benzene. After forty-five minutes, 0.07 g. of clumps of colorless needles of **9,10-dimethyl-1,2,5,6-dibenzanthracene peroxide** was filtered off; m. p. 212–213° with decomposition when placed in the bath at 200°.

Anal. Calcd. for $C_{24}H_{18}O_2$: C, 85.2; H, 5.4. Found: C, 84.4; H, 5.5.

Summary

The mechanism by which 9,10-dimethyl-1,2-benzanthracene is formed by interaction of sodium and 9,10-dimethyl-9,10-dimethoxy-9,10-dihydro-1,2-benzanthracene has been investigated.

5-Ethyl- and 5-*n*-propyl-9,10-dimethyl-1,2-benzanthracene, 9,10-di-*n*-propyl-1,2-benzanthracene and 9,10-dimethyl-1,2,5,6-dibenzanthracene have been prepared.

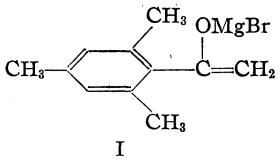
ANN ARBOR, MICHIGAN RECEIVED JULY 10, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

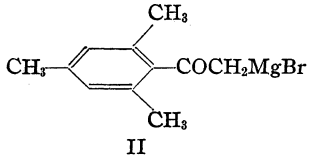
Reactions of Bromomagnesium Enolates of Mesityl Ketones. II. Condensation

BY REYNOLD C. FUSON, W. O. FUGATE AND C. H. FISHER

The bromomagnesium derivative of acetomesitylene may be formulated as an enolate (I) or as a compound of the RMgBr type (II).



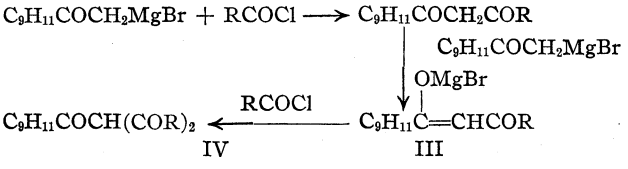
I



II

A study of its reactions has revealed the somewhat surprising fact that in all cases it behaves as though it were a true Grignard reagent. This is perhaps most striking in connection with condensation with carbonyl compounds. In the work presently reported condensation has been effected with acid chlorides, esters, carbon dioxide, aldehydes and ketones. The product in each instance is that which is predicated by formula II.

Acid chlorides and *esters* proved to be especially interesting in this connection for they reacted to give carbonyl compounds rather than carbinols. The reason for this interruption was that the newly formed aldehyde or ketone reacted in the enolic form, decomposing the excess of the original bromomagnesium derivative:



Indeed, if the amount of acid chloride present is not controlled carefully the bromomagnesium derivative of the diketone (III) is transformed to a triketone (IV).[1]

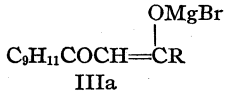
However, acetyl chloride and benzoyl chloride give satisfactory yields of the corresponding diketones when one mole of the chloride is added gradually to two moles of the bromomagnesium compound (II). Similar results were obtained with propiomesitylene and benzoyl chloride.

(1) Kohler and Baltzly, THIS JOURNAL, **54**, 4015 (1932).

With hindered acid chlorides such as 2,4,6-trimethylbenzoyl chloride this control was unnecessary; evidently the bromomagnesium derivative of the diketone in these cases had no appreciable tendency to undergo further acylation with the hindered acid chloride.

That esters also yield diketones is explained in a similar manner. The product with ethyl formate–oxymethyleneacetomesitylene showed remarkable stability.

It should be pointed out in passing that formula IIIa is less probable than III for the postulated enolate. It is known that the mesityl radical promotes enolization to a greater degree than do other radicals; this would favor III over IIIa.



IIIa

Aldehydes and *ketones* condense with the bromomagnesium derivative of acetomesitylene (II) to give carbinols. This seems to be a general property of the bromomagnesium derivatives of hindered ketones for it also has been observed with α - benzohydrylacetomesitylene,[2] propiomesitylene[3] and isobutyromesitylene.[3] Actually, in the present work carbinols were isolated only from benzaldehyde and benzophenone. When 2-methoxy-1-naphthaldehyde and acetophenone were used the products were the corresponding substituted vinyl mesityl ketones.

Carbon dioxide reacted with the bromomagnesium derivatives of acetomesitylene, propiomesitylene, isobutyromesitylene and 3,5-dibromoisobutyromesitylene to give the corresponding β-keto acids. While this type of reaction seems to proceed with unusual ease with these highly hindered substances, it is by no means novel.[4] The acids were identified by decarboxylation to the original ketones.

Coupling was effected by treating the bromomagnesium derivative with anhydrous cupric chlo-

(2) Kohler, Tishler and Potter, *ibid.*, **57**, 2517 (1935).

(3) Fuson, Fisher, Ullyot and Fugate, *J. Org. Chem.*, **4**, 111 (1939).

(4) (a) Malmgren, *Ber.*, **36**, 2608 (1903); (b) Umnova, *J. Russ. Phys.-Chem. Soc.*, **45**, 881 (1913); (c) Ivanoff and Spossoff, *Bull. soc. chim.*, [4] **49**, 19 (1931); (d) Kohler and Tishler, THIS JOURNAL, **54**, 1594 (1932); (e) Ivanoff and Pchenitchny, *Bull. soc. chim.*, [5] **1**, 223 (1934).

ride. However, the yield of the resulting ethane was small. Bromine induced no coupling but led to the formation of α-bromoacetomesitylene.

Experimental

Condensation with Acid Chlorides and Esters.—The same general procedure was employed with slight modifications in all of the reactions studied. For a 0.1 mole run the bromomagnesium derivative was prepared by adding a solution of 0.1 mole of the mesityl ketone in 25 cc. of dry ether during thirty minutes to 100 cc. of an ethereal solution of a slight excess of ethylmagnesium bromide. The bromomagnesium derivative began to precipitate when about half of the ketone had been added. Refluxing was continued for thirty minutes after all of the ketone had been added.

An ether solution of the acylating agent was added to the mixture and, after the reaction was complete, the resulting mixture was decomposed with iced hydrochloric acid. The ether layer was then washed with 10% sodium carbonate solution. The diketone was usually obtained as the copper derivative by shaking the ether solution with a saturated solution of cupric acetate for several minutes and subsequently removing the ether.

The diketones or β-keto aldehydes were obtained easily by shaking an ether suspension of the copper derivative with dilute hydrochloric acid.

2,4,6,2′,4′,6′-Hexamethyldibenzoylmethane.—In a 0.031-mole run equivalent amounts of the reagent and 2,4,6-trimethylbenzoyl chloride were employed. The reaction was complete after five hours of gentle refluxing. Acidification of the sodium carbonate solution gave 1.5 g. of 2,4,6-trimethylbenzoic acid. The yield of copper derivative was 6.5 g. (64%). The dark green copper derivative was recrystallized from benzene.

Anal. of the copper derivative. Calcd. for $C_{42}H_{46}O_4Cu$: C, 74.34; H, 6.84. Found: C, 74.74; H, 7.04.

The diketone, which melted at 96–97°, was identical with that previously reported.[5]

2,4,6-Trimethyl-2′,4′,6′-triethyldibenzoylmethane.—Four hundredths mole of the bromomagnesium derivative of acetomesitylene was treated with an equivalent amount of 2,4,6-triethylbenzoyl chloride and the resulting mixture refluxed overnight. Three grams of the acid was recovered from the sodium carbonate solution. After recrystallization from a mixture of carbon tetrachloride and ligroin, the olive green copper derivative melted at 287°; yield 6.5 g. (49%).

Anal. of the copper derivative. Calcd. for $C_{48}H_{58}O_4Cu$: C, 75.59; H, 7.66. Found: C, 75.72; H, 7.68.

The diketone was a pale yellow oil, b. p. 188–190° (2 mm.), $n^{20}D$ 1.5697. It gave a red color with ferric chloride.

Anal. Calcd. for $C_{24}H_{30}O_2$: C, 82.28; H, 8.57. Found: C, 82.07; H, 8.75.

In a similar experiment the same copper derivative was prepared by treating 0.1 mole of the bromomagnesium derivative of 2,4,6-triethylacetophenone with an equivalent amount of 2,4,6-trimethylbenzoyl chloride. The yield of the copper derivative was 15 g. (46%).

(5) Fisher, Snyder and Fuson, THIS JOURNAL, **54**, 3665 (1932).

α-Benzoylacetomesitylene.—A suspension of 0.1 mole of the bromomagnesium derivative of acetomesitylene was cooled in a salt–ice bath and 0.05 mole of benzoyl chloride added during ten minutes. Stirring was continued at this temperature for ten minutes and the mixture decomposed. Steam distillation of the ether layer gave 8 g. of acetomesitylene. The residue was taken up in ether, the ether solution dried over magnesium sulfate and evaporated to dryness. A small amount of the triketone (IV) crystallized during the evaporation. The residue was recrystallized from petroleum ether; yield 10 g. (75%); m. p. 76–78.5°. The α-benzoylacetomesitylene was identical with that prepared by cleavage of the corresponding enol methyl ether.[6]

α-Benzoylpropiomesitylene.—A solution of 0.025 mole of benzoyl chloride was added to a cold suspension of the bromomagnesium derivative of propiomesitylene and the mixture stirred for two hours at room temperature. The yield of the copper derivative of α-benzoylpropiomesitylene was 5 g. (65%). Distillation of the residue gave 4.4 g. of propiomesitylene. The residue in the distilling flask gave, after recrystallization, 0.7 g. of the enol benzoate of α-benzoylpropiomesitylene. Both the diketone and its enol ester were identified by comparison with the compounds previously reported.[3]

α-Acetylacetomesitylene.—(a) One-tenth mole of the enolate was cooled in an ice–salt bath and a solution of 0.05 mole of acetyl chloride added during five minutes. Stirring and cooling were continued for one hour. After decomposition the ether layer was dried, the ether removed and the residue distilled. Eight grams of acetomesitylene was recovered and 7 g. (69%) of the diketone boiling at 143–146° (8 mm.) obtained. After recrystallization from methanol the diketone melted at 45–46°. It was identified by a mixed melting point with an authentic specimen.[7]

(b) A solution of 0.1 mole of ethyl acetate in 25 cc. of ether was added during two and one-half hours to a suspension of 0.1 mole of the bromomagnesium derivative of acetomesitylene. The mixture was then refluxed overnight.

The diketone was isolated in the manner described above. Ten and five-tenths grams of acetomesitylene was recovered and 5.5 g. (26%) of the acetyl derivative was obtained.

Hydroxymethyleneacetomesitylene.—To a suspension of 0.1 mole of the bromomagnesium derivative of acetomesitylene, 7.4 g. (0.1 mole) of ethyl formate in 25 cc. of ether was added during the course of one hour. The enolate dissolved during this time and refluxing was continued for several hours. The copper derivative of the aldehyde was recrystallized from a mixture of carbon tetrachloride and ligroin; yield, 7.2 g. (33%). Nine grams of acetomesitylene was recovered from the filtrate.

Anal. of the copper derivative. Calcd. for $C_{24}H_{26}O_4Cu$: C, 65.22; H, 5.88. Found: C, 64.86; H, 6.05.

The hydroxymethylene compound was a colorless oil, b. p. 108–110° (3 mm.); $n^{20}D$ 1.5641. It gave a blood red color with ferric chloride and dissolved slowly in 10% sodium hydroxide solution.

(6) Kohler and Barnes, *ibid.*, **55**, 690 (1933).

(7) Woodward and Fuson, *ibid.*, **55**, 3472 (1933).

Formula	M. p., °C.	Analysis, % Calcd. C	H	Br	Found C	H	Br
$C_9H_{11}COCH_2COOH$[a]	104–105	69.90	6.79		69.6	6.8	
$C_9H_{11}COCH(CH_3)COOH$[a]	111.5–112.5	70.91	7.27		71.17	7.29	
$C_9H_{11}COC(CH_3)_2COOH$[a]	86–87	71.79	7.69		72.16	8.07	
$C_9H_9Br_2COC(CH_3)_2COOH$[b]	108–110	42.86	4.08	40.82	42.81	4.37	40.2

[a] These acids were identified by thermal decomposition to give the corresponding ketones. The ketones were identified as the 3,5-dinitro derivatives. [b] Decomposition of α-3,5-dibromo-2,4,6-trimethylbenzoylisobutyric acid gave 3,5-dibromoisobutyromesitylene; m. p. 69.5–70.5°.

Anal. Calcd. for $C_{12}H_{14}O_2$: C, 75.79; H, 7.37. Found: C, 75.81; H, 7.74.

Preparation of the β-Keto Acids.—The procedure used in the preparation of α-2,4,6-trimethylbenzoylisobutyric acid is typical. A solution of 19 g. of isobutyromesitylene in 25 cc. of ether was added during thirty minutes to 100 cc. of a solution containing a slight excess of ethylmagnesium bromide. The resulting mixture was then refluxed for thirty minutes and transferred to a catalytic reduction[8] machine whose tank contained carbon dioxide which passed into the mixture under pressure. During the first forty-five minutes the mixture was shaken by hand and cooled in a freezing mixture. The pressure dropped from 38 to 24 lb. (2.5 to 1.7 atm.). Mechanical shaking was then commenced and the mixture shaken at room temperature for twelve hours.

The mixture was then chilled in an ice-bath and poured very slowly into iced hydrochloric acid. The ether layer was extracted with cold sodium carbonate solution and the sodium carbonate extract acidified carefully with iced hydrochloric acid. The yield of α-2,4,6-trimethylbenzoylisobutyric acid was 18 g. (77.4%). The acid was recrystallized by dissolving it at room temperature in ether, adding a small amount of petroleum ether and then removing the solvent slowly under reduced pressure; m. p. 86–87° with decomposition. The original mesityl ketone was obtained when the acid was heated on a steam-cone for two hours.

2-(2,4,6-Trimethylbenzoyl)-1-phenylethanol.[9]—To a suspension of 0.2 mole of the bromomagnesium derivative of acetomesitylene in approximately 275 cc. of ether, 22 g. of freshly distilled benzaldehyde in 100 cc. of dry ether was added over a period of one hour. During this time the enolate gradually disappeared. Refluxing was continued for three hours.

The mixture was poured into iced hydrochloric acid, the ether layer separated and the aqueous layer extracted twice with ether. The combined ether solution was dried over sodium sulfate. Evaporation of the ether left a reddish-brown oil which deposited crystals of the carbinol on addition of a few cubic centimeters of ligroin. The yield of 2-(2,4,6-trimethylbenzoyl)-1-phenylethanol was 25 g. (47%). Recrystallization from petroleum ether gave 22 g. of the pure material, m. p. 77–77.5°.

Anal. Calcd. for $C_{18}H_{20}O_2$: C, 80.59; H, 7.46. Found: C, 80.13; H, 7.42.

Distillation of the residual oil gave small amounts of benzaldehyde and acetomesitylene and 13 g. (26%) of benzalacetomesitylene, b. p. 215–221° (16 mm.).

(8) Adams and Voorhees, *Org. Syntheses*, **8**, 10 (1928).

(9) This synthesis was carried out by Mr. R. V. Lindsey, Jr.

β-(2-Methoxy-1-naphthyl)-vinyl Mesityl Ketone.—A solution of 9.5 g. of 2-methoxy-1-naphthaldehyde in a mixture of 25 cc. of dry ether and 75 cc. of benzene was added dropwise during three hours to a suspension of 0.05 mole of the bromomagnesium derivative of acetomesitylene. During the addition, the enolate was converted to a chrome yellow solid. To ensure complete reaction, the mixture was then refluxed gently for three hours. The complex was decomposed with iced hydrochloric acid, the ether–benzene layer washed once with water and dried. After removal of the solvent by distillation, an oil remained which solidified when its solution in hot methyl alcohol was allowed to cool slowly, yield 13.5 g. (82%) of β-(2-methoxy-1-naphthyl)-vinyl mesityl ketone melting at 100–103°. After two recrystallizations from methanol the product melted at 107–108°. It reacted slowly with bromine in carbon tetrachloride.

Anal. Calcd. for $C_{23}H_{22}O_2$: C, 83.64; H, 6.67. Found: C, 83.43; H, 7.07.

α,β-Dibromo-β-(2-methoxy-1-naphthyl)-propiomesitylene.—To an ice-cold solution of 1.5 g. of β-(2-methoxy-1-naphthyl)-vinyl mesityl ketone in 3 cc. of carbon tetrachloride a solution of bromine in carbon tetrachloride was added in small portions until the red color of the bromine solution persisted. Crystallization began before the bromination was complete. After all the bromine was added, 1.5 g. of α,β-dibromo-β-(2-methoxy-1-naphthyl)-propiomesitylene melting at 145–147° with decomposition was collected on a filter. The product was recrystallized by dissolving in the minimum of hot carbon tetrachloride and adding ligroin; m. p. 148–149°.

Anal. Calcd. for $C_{23}H_{22}O_2Br_2$: C, 56.33; H, 4.49; Br, 32.65. Found: C, 56.17; H, 4.80; Br, 32.75.

β-Methylbenzalacetomesitylene.—During a period of one and one-half hours, 96 g. (0.8 mole) of acetophenone in 100 cc. of ether was added to a suspension of 0.7 mole of the bromomagnesium derivative of acetomesitylene in 400 cc. of ether. During this time the enolate was converted to a thick gum. Refluxing was continued for six hours.

The mixture was decomposed by pouring it into 1 kg. of cracked ice and 200 cc. of concentrated hydrochloric acid, the ether layer washed with water and dried over magnesium sulfate. After removal of the ether, no product could be induced to crystallize. However, when distillation was attempted a solid began to form and, on addition of a small amount of petroleum ether, β-methylbenzalacetomesitylene, a pale yellow solid melting at 79–82°, began to crystallize. Sixty-three grams of the solid was collected on a filter. Distillation of the mother liquor gave 38 g. of acetophenone, 20 g. of acetomesitylene, and an additional 35 g. of the α,β-unsaturated ketone. After

three recrystallizations from alcohol the compound melted at 85.5–87°. Kohler and Barnes[6] reported the melting point as 84°. The yield of β-methylbenzalacetomesitylene was 98 g. (69%).

Anal. Calcd. for $C_{19}H_{20}O$: C, 86.36; H, 7.55. Found: C, 86.15; H, 7.51.

The identification was completed by conversion to β,β-dimethyl-β-phenylpropiomesitylene by the method of Kohler and Barnes.[6]

1,1 - Diphenyl - 2 - (2,4,6 - trimethylbenzoyl)-ethanol.—To a suspension of 0.05 mole of the bromomagnesium derivative of acetomesitylene in 120 cc. of ether, 10 g. of benzophenone in 60 cc. of ether was added during the course of two hours. The enolate dissolved completely as the last of the ketone was added. The mixture was then refluxed gently overnight.

The ether solution was poured slowly with stirring into iced hydrochloric acid, the ether layer separated, dried and the ether allowed to evaporate spontaneously. The nearly colorless residual oil was taken up in warm methyl alcohol. When the solution was allowed to cool 13.2 g. (76.5%) of 1,1-diphenyl-2-(2,4,6-trimethylbenzoyl)-ethanol was obtained, m. p. 70–72°. After recrystallization from methanol, the product melted at 74–75°. A mixture with an authentic sample prepared by the method of Kohler and Barnes[6] showed no depression in melting point.

α - Bromoacetomesitylene.—Three and three-tenths grams of acetomesitylene was converted to the bromomagnesium derivative, the mixture cooled in a salt–ice bath and a slight excess of bromine in 15 cc. of ether added dropwise. The reaction was complete in twenty minutes.

The reaction mixture was treated with dilute hydrochloric acid, the ether layer separated, dried over magnesium sulfate, and the ether removed. After recrystallization from petroleum ether, 2.7 g. (56%) of α-bromoacetomesitylene was obtained, m. p. 52–55°. After purification the product melted at 55–56°, and was identified by a mixed melting point with an authentic sample.

1,2-Di(2,4,6-trimethylbenzoyl)-ethane.—Seven and five-tenths grams of anhydrous cupric chloride was added in small portions to an ether suspension of 0.05 mole of the bromomagnesium enolate of acetomesitylene in 125 cc. of dry ether and the mixture refluxed gently for twenty hours. During this time a crimson solid appeared in the reaction flask. The mixture was cooled in an ice-bath, decomposed by slowly adding iced hydrochloric acid, the ether layer dried over anhydrous magnesium sulfate and the ether removed by distillation. When the resulting liquid was distilled, 6.1 g. (75.4%) of acetomesitylene was recovered.

The residual oil was left standing for several days during which a solid began to form. The solid, after two recrystallizations from alcohol melted at 137–139°, the melting point of the ethane reported by Kohler and Baltzly[1] and by Conant and Lutz.[10]

1,3-Di-(2,4,6-trimethylbenzoyl)-propane.—Three and two-tenths grams of acetomesitylene was converted to the bromomagnesium enolate. To the resulting vigorously stirred suspension of the enolate in about 40 cc. of ether, a solution of 3.5 g. of vinyl mesityl ketone[11] in 20 cc. of dry ether was added during a period of thirty minutes. The resulting clear solution was refluxed gently for one hour. After the complex was decomposed with iced hydrochloric acid, the ether layer was separated and dried. When the ether was evaporated, there remained 5.5 g. (82%) of 1,3-di-(2,4,6-trimethylbenzoyl)-propane. After recrystallization from methanol the diketone melted at 131–132°. It was identical with the product previously reported.[12]

Summary

The bromomagnesium derivative of acetomesitylene reacts as a true Grignard reagent. This behavior has been observed in the condensations of this derivative with acid chlorides, esters, carbon dioxide, aldehydes and ketones.

URBANA, ILLINOIS RECEIVED JUNE 26, 1939

(10) Conant and Lutz, THIS JOURNAL, **45**, 1303 (1923).

(11) This compound was supplied by Mr. C. H. McKeever; it will be described in a forthcoming communication.

(12) Fuson, Ross and McKeever, THIS JOURNAL, **61**, 414 (1939).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

Propylene. The Heat Capacity, Vapor Pressure, Heats of Fusion and Vaporization. The Third Law of Thermodynamics and Orientation Equilibrium in the Solid

BY T. M. POWELL AND W. F. GIAUQUE

Several cases are known where molecules containing somewhat similar atoms in otherwise equivalent positions enter the crystal lattice without appreciably distinguishing between the similar atoms. This situation which corresponds to thermodynamic equilibrium at the freezing point is sometimes unable to readjust itself to an ordered molecular arrangement as the temperature of the solid is lowered sufficiently to make this the stable state.

This effect was first observed by Johnston and Giauque[1] in the case of nitric oxide which polymerizes to N_2O_2. They showed that a residual entropy of R ln 2 per mole of N_2O_2 remained near the absolute zero. The above explanation was advanced by Clayton and Giauque,[2] who investigated the similar effect in carbon monoxide. These authors pointed out that this was the usual case in molecules containing isotopes and was to be expected in other cases where the atoms are of somewhat similar size. In addition to the above cases this effect has been observed in the case of nitrous oxide NNO by Clusius[3] and Blue and Giauque.[4] Clayton and Giauque[2] also pointed out that this effect was to be expected in the case of certain carbon compounds.

The experimentally investigated cases mentioned above involve only lack of discrimination between atoms but it is evident that cases may occur where false equilibrium may exist at low temperatures with respect to groups of atoms. This paper is a report on a calorimetric investigation of propylene, $CH_2{=}CH{-}CH_3$, which shows that the CH_3 and CH_2 groups are located without discrimination when they enter the crystal lattice under equilibrium conditions at the freezing point. Propylene lacks the mechanism to rotate the molecule within the solid so as to produce an ordered arrangement corresponding to zero entropy as the absolute zero of temperature is approached.

The apparatus and method of measurement have been described previously.[4-8] The measurements were made in a calorimeter with the laboratory designation Gold Calorimeter II.

Preparation and Purity of the Propylene.—A sample of propylene was donated by the Shell Development Company. Several heat capacity measurements in the region just below the melting point were made on the original sample and from the heat effect due to premelting the liquid soluble–solid insoluble impurity was estimated at 0.2 mole %. The material was then fractionated and subsequent calorimetric measurements of the premelting indicated that the impurity had been reduced to 0.02 mole %. Table I shows the several estimates of impurity as obtained by the total premelting which occurred up to the several temperatures.

TABLE I

PREMELTING DATA ON THE SAMPLE OF PROPYLENE

Δ, $T°$ below m. p.	Premelting cal. mole^{-1}	% melted	Impurity mole %
3.77	0.94	0.132	0.022
2.34	1.49	.208	.022
1.06	3.06	.428	.021
0.265	9.76	1.37	.017
.109	34.2	4.8	.024
.063	60.4	8.5	.024
		Average	.022

The Vapor Pressure of Propylene.—The vapor pressure of propylene was measured by means of a mercury manometer and a standard meter with a cathometer used as a comparison instrument. The acceleration of gravity was taken as 979.973 cm. sec.$^{-2}$ for this location and the standard acceleration as 980.665 cm. sec.$^{-2}$.

The results have been represented by the equation, 165.8 to 225.9°K.

$$\log_{10} P_{(\text{inter. cm. Hg})} = -\frac{1196.9}{T} - 3.92 \times 10^{-3} T + 8.07544 \quad (1)$$

The vapor pressure observations are compared with Equation 1 in Table II.

The temperatures are given to 0.001° only because the high relative accuracy permits the data to be used in obtaining derivatives.

From Equation 1 the boiling point of propylene was found to be 225.35°K.

A summary of observations on the melting point is given in Table III. The gradual increase with

(1) Johnston and Giauque, THIS JOURNAL, **51**, 3194 (1929).
(2) Clayton and Giauque, *ibid.*, **54**, 2610 (1932).
(3) Clusius, *Z. Elektrochem.*, **40**, 99 (1934).
(4) Blue and Giauque, THIS JOURNAL, **57**, 991 (1935).
(5) Giauque and Wiebe, *ibid.*, **50**, 101 (1928).
(6) Giauque and Johnston, *ibid.*, **51**, 2300 (1929).
(7) Giauque and Egan, *J. Chem. Phys.*, **5**, 45 (1937).
(8) Giauque and Powell, THIS JOURNAL, **61**, 1970 (1939).

TABLE II

VAPOR PRESSURE OF PROPYLENE 0°C. = 273.10°K.

T, °K.	$P_{obsd.}$ int. cm. Hg.	$P_{obsd.} - P_{calcd.}$	$T_{obsd.} - T_{calcd.}$
165.764	1.598	−0.006	+0.039
172.721	2.941	− .001	+ .005
176.465	3.992	.002	− .005
179.951	5.232	− .001	+ .003
184.486	7.319	− .000	+ .001
189.451	10.354	+ .001	− .002
195.583	15.452	+ .002	− .003
202.665	23.731	+ .008	− .006
207.395	30.996	− .002	+ .001
213.343	42.547	− .002	+ .001
220.228	59.830	− .051	+ .018
225.925	77.992	+ .001	− .000

the % melted corresponds to the 0.02 mole % of impurity mentioned above.

TABLE III

MELTING POINT OF PROPYLENE 0°C. = 273.10°K.

% melted	T, °K. Thermocouple	T, °K. Resistance thermometer
4.8	87.76	87.748
8.5	87.81	87.794
45	87.82	87.836
82	87.84	87.849
94	87.85	87.852
Accepted value	87.85	

In Table IV the melting and boiling points are compared with those obtained by previous observers.

TABLE IV

MELTING AND BOILING POINTS OF PROPYLENE

M. p., T, °K.	B. p., T, °K.	Observer
..	225.3	Burrell and Robertson[9] (1915)
87.9	226.1	Maass and Wright[10] (1921)
..	225.3	Trautz and Winkler[11] (1922)
88.2	....	Huffman, Parks and Barmore[12] (1931)
..	225.34	Kistiakowsky, *et al.*[12a] (1935)
..	225.45	Ashdown, Harris and Armstrong[13] (1936)
87.85	225.35	This research

The Calorimetric Observations.—The heat capacity measurements on solid and liquid propylene are recorded in Table V. The results on the liquid were corrected for vaporization into the small gas space when the vapor pressure made the effect appreciable. In making this correction the measurements of Maass and Wright[10] on the density of liquid propylene were utilized. A small pressure of helium gas was used to facilitate thermal equilibrium in the solid. The amount of propylene taken for the measurements was determined by condensing the material in a steel bomb equipped with a valve and weighing at room temperature: 64.227 g. equivalent to 1.5264 moles was used for the measurements; 4.1832 international joules was taken equal to 1 calorie (15°).

(9) Burrell and Robertson, THIS JOURNAL, **37**, 2188 (1915).

(10) Maass and Wright, *ibid.*, **43**, 1098 (1921).

(11) Trautz and Winkler, *J. prakt. Chem.*, **104**, 37 (1922).

(12) Huffman, Parks and Barmore, THIS JOURNAL, **53**, 3876 (1931).

(12a) Kistiakowsky, Ruhoff, Smith and Vaughan, THIS JOURNAL, **57**, 876 (1935).

(13) Ashdown, Harris and Armstrong, *ibid.*, **58**, 850 (1936).

TABLE V

THE HEAT CAPACITY OF PROPYLENE

0°C. = 273.10°K. Molecular weight = 42.078. 1.5264 moles were in the calorimeter.

T, °K.	ΔT approx.	C_p cal. deg.$^{-1}$ mole^{-1}	T, °K.	ΔT approx.	C_p cal. deg.$^{-1}$ mole^{-1}
14.18	1.3	1.141	87.85	Melting point	
16.66	3.6	1.588	93.91	4.4	22.03
19.63	2.4	2.201	98.66	5.1	21.76
22.81	3.9	3.057	104.18	5.8	21.49
26.23	2.9	3.891	109.98	5.7	21.35
29.87	4.2	4.686	115.64	5.5	21.14
33.62	3.3	5.607	128.09	6.0	20.99
37.46	4.3	6.468	134.56	6.6	20.93
41.29	3.8	7.175	141.21	6.4	20.81
45.53	4.7	7.85	154.97	6.8	20.83
50.66	5.5	8.71	161.88	6.6	20.82
55.96	4.9	9.44	169.01	7.2	20.87
61.25	5.6	10.26	176.71	7.0	20.98
66.61	5.0	10.98	187.77	6.7	21.06
71.45	4.6	11.61	194.66	6.5	21.19
76.49	5.4	12.29	201.77	7.0	21.42
76.59	5.3	12.41[a]	209.18	6.8	21.55
81.69	4.8	13.40[a]	216.41	6.6	21.61
84.87	1.4	14.20[a]	223.40	6.3	21.86
86.17	1.3	16.10[a]	225.35	Boiling point	

[a] Values include premelting heat effect.

Results taken from a smooth curve through the data are given in Table VI. The curve should represent the heat capacity to 0.1–0.2% above 35°K. At 20°K. the error may be 1% and at 15°K. several %.

The data are shown graphically in Fig. 1 where the dotted curve below the melting point shows the rise in heat capacity due to the premelting resulting from 0.02 mole % of impurity.

The heat capacity of propylene, above 68.9°K., has been measured by Huffman, Parks and Barmore.[12] The observations agree well with the present results, as may be seen from a comparison included in Table VI.

The observations on the heat of fusion are given in Table VII. The runs started several degrees below the melting point and ended somewhat

TABLE VI

THE HEAT CAPACITY OF PROPYLENE

0°C. = 273.10°K. Molecular weight = 42.078.

T, °K.	C_p cal. deg.$^{-1}$ mole^{-1}	% dev., H. P. and B. This research	T, °K.	C_p cal. deg.$^{-1}$ mole^{-1}	% dev., H. P. and B. This research
15	1.27		100	21.70	−0.3
20	2.29		110	21.33	−0.7
25	3.59		120	21.08	−1.3
30	4.78		130	20.93	−1.1
35	5.92		140	20.85	−1.1
40	6.92		150	20.82	−0.9
45	7.78		160	20.83	− .8
50	8.56		170	20.89	− .6
60	10.05		180	20.98	− .2
70	11.45	0.9	190	21.13	.0
80	12.79		200	21.32	.0
			210	21.52	.0
87.85	13.83	Melting point	220	21.75	
87.85	22.33		225.35	21.89	(B. p.)
90	22.21	0.0	230	22.01	

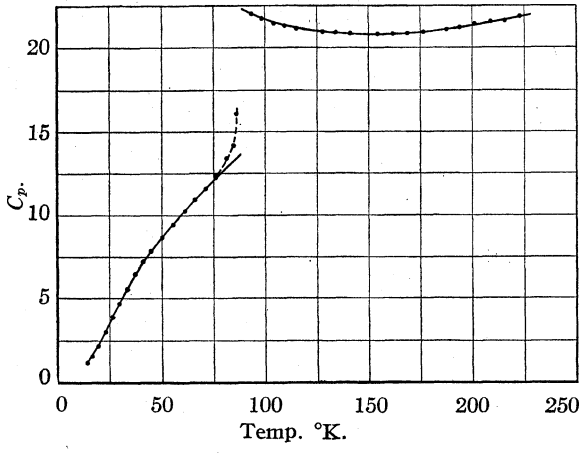


Fig. 1.—Heat capacity in calories per degree per mole of propylene.

above. The correction for the heat capacity was of course made on the basis that premelting as shown in Table I is included in the heat of fusion.

TABLE VII

HEAT OF FUSION OF PROPYLENE

Melting point, 87.85°K. Molecular weight, 42.078.

Run	T_1° − T_2°	Heat input cal. mole^{-1}	$\int C_p\,dT$ cal. mole^{-1}	Premelting at T_1, cal. mole^{-1}	ΔH Fusion cal. mole^{-1}
1	83.131–93.912	914.59	198.69	1.38	717.2
2	82.812–91.626	868.75	152.35	1.30	717.7
3	84.398–92.692	871.17	154.37	2.06	718.1
4	83.099–91.698	865.95	149.95	1.38	717.3
				Average	717.6

The heat of fusion also has been measured by Huffman, Parks and Barmore,[12] who obtained the value 701.4 cal. mole^{-1}. This value is 2% less than the one obtained in the present research. As the heat capacity in the earlier work had not been measured to temperatures sufficiently below the melting point to permit an estimate of the effect of impurity, it is presumed that the deviation is due to unconsidered premelting rather than to error in the actual calorimetric observation.

For measurements of the heat of vaporization the amount evaporated was measured by means of a 5-liter thermostatted bulb, initially filled with mercury which was removed automatically as the gas was accepted at constant pressure. This apparatus has been described previously.[6] At the conclusion of energy input the line leading from the calorimeter was closed, the mercury was lowered to a suitable calibration mark and a pressure observation was taken. The propylene from three such observations was collected and weighed in the steel bomb mentioned above. From these data a value of the gas density was calculated. The data are collected in Table VIII.

TABLE VIII

GAS DENSITY OF PROPYLENE AT 25°

Bulb volume, cc.	Pressure inter. cm. Hg	Total amt., g.
5330.9	71.574	
5358.5	73.233	26.823
5320.9	74.120	

$$P_0V_0 = RT = 22411.5 \times \frac{298.10}{273.10} \text{ cc. atm.}$$

$$PV = RT(1 + \lambda P)$$

$$\lambda = -0.0149 \text{ atm.}^{-1}$$

The density calculated to 1 atmosphere was 1.7461 g./l. at 25.00°. Before and after the measuring bulb was connected to the calorimeter the temperature was not exactly the vaporization temperature and suitable corrections were applied for the effect of temperature change on calorimetric heat content and the small amount of gas in the connecting line. The measurements of the heat of vaporization are given in Table IX.

TABLE IX

HEAT OF VAPORIZATION OF PROPYLENE

Boiling point, 225.35°K.

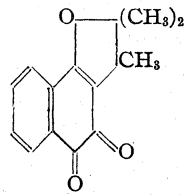
Run	Moles evaporated	Time of energy input, min.	ΔH vap. cal. mole^{-1}
1	0.20483	54	4400
2	.21618	57	4405
3	.21744	57	4405
4	.20770	56	4399
		Average	4402

The entropy calculation from 0°K. to the boiling point is summarized in Table X.

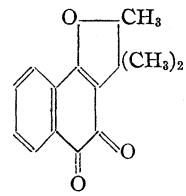
No red color will result when R^1 is in any of the following:

(a) $-CH_2CH_2COOH$ (b) $-CH{=}C(COOH)COOC_2H_5$
(c) $-CH_2COCH_3$ or the tautomeric form $-CH{=}C(OH)CH_3$
(d) $-COCH_2COCH_3$ or the tautomeric forms
(e) $-CH_2Cl$ (f) CH_3 (g) C_2H_5

It is interesting in connection with structure IV for the red compounds that Price and Robinson[15] have investigated a naturally occurring *red* pigment, dunnione, for which they propose structure XII or XIII, and that as a result of their study of the absorption spectra of naphthoquinone derivatives, Cook, Macbeth and Winzor[10] agree with Price and Robinson that dunnione is either XII or XIII.



XII



XIII

Experimental Part[16]

The apparatus and procedure used for obtaining the absorption curves have been described in a previous paper.[1b]

2,2,7,8-Tetramethylchroman-5,6-quinone (IV, R^1 = CH_3; R^2 = H).—A solution of 2,2,5,7,8-pentamethyl-6-hydroxychroman (I, $R^1 = CH_3$; R^2 = H) (500 mg.) in absolute ethanol (500 cc.) and concd. nitric acid (100 cc.) was warmed for ten minutes on the steam-bath. The solution was cooled rapidly, diluted with water (1800 cc.) and extracted thoroughly with ether (six times). The combined extracts were washed with water until the washings were neutral to litmus, then once with dilute sodium carbonate and finally twice with water. The ether was removed on the steam-bath, the last traces being taken off under reduced pressure. The residue solidified to a red solid which was crystallized, first from petroleum ether (b. p. 28–38°) and then from ether–petroleum ether. The substance formed red needles which melted at 109–110° and which did not depress the melting point of a specimen made by the action of silver nitrate upon the chroman according to the directions of John.[2a]

The red compound forms deeply colored, red-violet solutions with cold, concd. hydrochloric acid, cold concd. sulfuric acid, or with hot dilute aqueous alkali. When hydrochloric acid is used, the solution finally deposits a brown amorphous solid melting above 200°. This brown solid gives a yellow solution in ether and a deep red solution in alcohol. All of these yellow and colorless transformation products are very soluble and so far we have not been able to isolate any pure compounds from them. These color changes with acids and alkali parallel strongly those observed by Hooker[17] in the lapachol series when an *o*-quinone of the type of IV (red) was transformed, by opening the hetero ring and recyclizing, into a *p*-quinone of type III (yellow), and the new pigment, dunnione, shows a similar series of color changes under the same circumstances.[10]

Phenazine.—The crude, moist quinone (0.43 g.) was dissolved in acetic acid (25 cc.) and warmed on the steam-bath. To this solution was added *o*-phenylenediamine (0.25 g.) and the solution was heated for ten minutes. It was then diluted with water to incipient cloudiness, and cooled. The fine yellow needles (0.11 g.) were removed and crystallized twice from dilute acetic acid. The substance formed glistening yellow needles which melted at 151–151.5°; the compound could be sublimed *in vacuo*, but this did not result in a higher melting point.

Anal. Calcd. for $C_{19}H_{20}ON_2$: C, 78.08; H, 6.85; N, 9.59. Found: C, 77.43; H, 7.10; N, 9.51.

Tetramethylphenazine.—To a boiling solution of the red quinone (50 mg.) in acetic acid (2 cc.) was added a solution of prehnitenediamine hydrochloride (60 mg.) in acetic acid (5 cc.) containing a crystal of sodium acetate. On cooling, a yellow granular solid precipitated, which was removed and crystallized twice from acetic acid. It melted at 204–205°, but the amount of it was too small to crystallize to analytical purity.

Anal. Calcd. for $C_{23}H_{28}ON_2$: C, 79.31; H, 8.05. Found: (2 mg. sample) C, 77.1; H, 8.04.

In ultraviolet light, these phenazines show a powerful green fluorescence, which is visible, though much fainter, even in daylight. Neither of these phenazines gives a positive phenol test (Folin). When, however, the phenazine of m. p. 151–151.5° is reduced catalytically (platinum oxide), the colorless solution gives a positive phenol test. The colorless solution of the reduction product is re-oxidized rapidly in the air.

Bisulfite Reduction of IV.—When shaken with 20% aqueous sodium bisulfite, the red quinone dissolved, giving a pale straw colored solution. Acidification and boiling to remove sulfur dioxide regenerated the deep red color; similarly, the red color reappears on boiling with a little nitric acid or alkali. In the latter case, the solution becomes red, then purple.

Reaction of IV with Alkali.—The quinone IV (1.7 mg.) was added to potassium hydroxide solution (1 cc., 5%). On warming, the solution became deep violet. It was boiled for ten seconds, then cooled and acidified with acetic acid (0.2 cc.). The color at once became yellow. Water was added and the solution was extracted with ether. Evaporation of the ether left an oil, soluble in benzene and insoluble in petroleum ether. This oil gave a positive phenol test but it could not be crystallized.

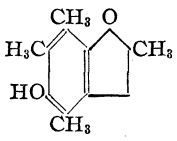
Cleavage of IV.—When the red quinone was boiled with acetic acid, potassium acetate and hydrogen peroxide (3%), the solution decolorized completely. An attempt was made to isolate the cleavage product as the barium salt, but no product could be obtained.

Addition of Isoprene to *o*-Xylohydroquinone.—Isoprene (2.2 cc.) was added to a hot solution of the hydroquinone

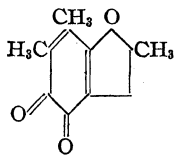
(15) Price and Robinson, *Nature*, **142**, 147 (1938).
(16) Microanalyses by J. W. Opie, C. O. Guss and H. H. Hoehn.
(17) Hooker, THIS JOURNAL, **58**, 1202, 1207 (1936); *J. Chem. Soc.*, **65**, 76, 321. 717 (1894).

$R^1 = CH_3$; $R^2 = C_{15}H_{31}$)[12] from α-tocopherol (I, $R^1 = CH_3$; $R^2 = C_{15}H_{31}$) gives a phenazine, which is also an oil, but which shows the same strong green fluorescence in ultraviolet light as is shown by the simpler phenazine of IV ($R^1 = CH_3$; $R^2 = H$).[13]

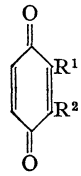
Formation of the red ortho quinones by oxidation is not limited to 6-hydroxychromans. It has been shown by Furter[14] and in a previous paper from this Laboratory[1b] that the reaction occurs also in the case of 5-hydroxycoumarans such as IX. By analogy the red compounds derived from these substances would have structures such as X, although this point has not yet been investigated thoroughly.



IX



X



XI

With regard to the mechanism whereby these red compounds are produced from the chromans (I) and the related quinones (II), it is not possible at present to do more than speculate. Certain facts, however, have been discovered which must be taken into account in formulating a mechanism; since these facts have a bearing upon the applicability of the Furter and Meyer method of photometric analysis, they are given here.

An alcohol or possibly a phenol is necessary as a solvent in order to produce the red solutions from the tocopherols and related substances. Using 2,4,6,7 - tetramethyl - 5 - hydroxycoumaran (IX) as the test substance, red solutions were obtained in methanol, ethanol, 2-propanol, *t*-butyl alcohol, and mesitol. The *intensity* of the color developed in the alcohols in a given time, however, decreased in the order they are named—that is, primary alcohols were more effective than secondary, and these more so than tertiary. Red solutions are not formed in petroleum ether, acetic acid, or acetone, although Furter and Meyer observed that a mixture of ethanol and acetone could be used in the case of the tocopherols. It appears from these results that alcohols are essential for the production of the red color, and this leads to the suspicion that the alcohol plays the role of a reagent as well as that of a solvent in the reaction, especially when taken along with the fact that acetone (negative) is the oxidation product of isopropyl alcohol (positive). There is definite evidence that the alcohol is oxidized during the reaction: in methanol, formaldehyde was detected, and in ethanol, acetaldehyde. Naturally these oxidation products might have been produced by the nitric acid in the absence of any substance capable of giving a red solution, but it is perhaps significant in this connection that the color in *t*-butyl alcohol was developed *very* much more slowly than in the other three alcohols tested, and all of the solvents giving negative results are substances quite resistant to the action of nitric acid over fairly short periods of time.

As to the nature of the substances capable of giving the red colors, the following can now be added to those previously reported:[1b,4] *m*-xylotocopherol (synthetic), 2,4,6-trimethyl-7-allyl-5-hydroxycoumaran, *o*-allyl-*p*-aminophenol, tetramethyl-*o*-benzohydroquinone, catechol, and the substances described in this paper. The positive reaction with catechol is important in connection with the Furter and Meyer method of analysis for tocopherols when applied to preparations or concentrates obtained from natural sources, for catechol derivatives are very common among certain classes of natural products. In the case of the *o*-quinones and catechol the red color is developed in the cold, as soon as the nitric acid is added, but it fades to yellow on standing, a behavior which also is shown by the red *o*-quinones such as IV, although here the color persists for a day or so. These substances did not give a red color under the conditions of the Furter and Meyer reaction: duroquinone, trimethylethylquinone, 2,5,7,8 - tetramethyl - 6 - hydroxychromone, 2,4,5-trimethyl-3,6-diacetoxybenzyl chloride, trimethyl-(β-carboxy ethyl)-*p*-benzoquinone, mesitol.

When the results obtained from all of the compounds so far tested are assembled, they lead to the conclusion that if the heterocyclic compound can be oxidized readily to a quinone of type XI (vacant positions may be occupied by alkyl or substituted alkyl groups), *a positive reaction* (formation of a red ortho quinone of type IV, with elimination of the group R^2) will occur when the group R^1 is any of the following:

(a) $-CH_2CH_2CH(OH)CH_3$ (b) $-CH_2CH_2C(OH)(CH_3)_2$
(c) $-CH_2CHOHCH_3$ (d) $-CH(CH_3)CHOHCH_3$
(e) $-CH(C_2H_5)CHOHCH_3$ (f) $-CH_2CH_2C(OH)(CH_3)R$
(g) allyl

(12) Dr. H. M. Evans has assayed this red oil for vitamin E activity; it is inactive at 3 and 6 mg. doses.

(13) Furter and Meyer[4] carried out this reaction with α- and β-tocopherols; our experiments were limited to α- and γ-tocopherols.

(14) Private communication.

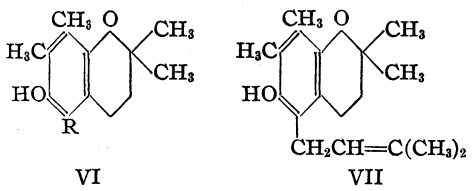
lished the results of a thorough investigation of the absorption spectra of some naphthoquinones and their derivatives. They conclude that a maximum of about 4000–4400 Å. is characteristic of ortho-naphthoquinones, while it is absent in the para-quinones. Our curve for β-lapachone is identical with theirs in the range accessible to us. The location of the characteristic maximum in ortho-benzo- and β-naphtho-quinones is not identical, but involves a slight shift to the longer wave lengths in the case of the benzoquinones, which accounts for the deeper color of these substances. The fact that the red oxidation products absorb most strongly in the region of 4500 Å. may be taken as good evidence that the *o*-quinoid structure is present.

On the chemical side, the results are decisively in favor of the *o*-quinoid structure IV for these red oxidation products. The red substance, m. p. 109–110° (IV, $R^1 = CH_3$; $R^2 = H$), forms a phenazine with m. p. 151–152° with *o*-phenylenediamine, and a tetramethylphenazine of m. p. 204–205° with tetramethyl-*o*-phenylenediamine. These phenazines are yellow and their alcoholic solutions show a pale green fluorescence; in ultraviolet light the fluorescence is quite brilliant.[11] Hooker found that most of the azines of the lapachol group exhibited this greenish fluorescence. The phenazine from tetramethyl-*o*-benzoquinone[8] also exhibits a strong green fluorescence in ultraviolet light although this is lacking in ordinary light. When reduced the bright red solution of IV ($R^1 = CH_3$; $R^2 = H$) becomes completely decolorized in a few minutes. The reduction product, however, is oxidized in the air with extreme rapidity—so rapidly that the compound becomes reoxidized and the solution turns bright red before the insoluble material (catalyst, zinc, etc.) can be filtered off.

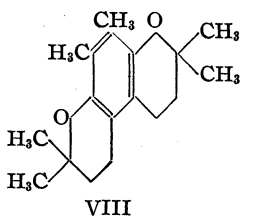
In order to prove structure IV, it was necessary to locate definitely the position occupied by the methyl group eliminated in the conversion of the quinone II to the red compound IV. This methyl group must be one of those in the benzene ring, for Karrer, Fritzsche and Escher showed that 2,5,7,8-tetramethyl-6-hydroxychroman (I, $R^1 = R^2 = H$) gave a red compound $C_{12}H_{14}O_3$ which was a lower homolog of IV, $C_{13}H_{16}O_3$. Since all of the substituents in the benzene ring of the pentamethylchroman are alike, structure V for the red compound, although improbable, is not rigidly excluded.

(11) Hooker, *J. Chem. Soc.*, **63**, 1376 (1893).

It is obvious that, if structure IV is correct, the same red compound must result from any 6-hydroxychroman of the type of VI. Accordingly, *o*-xylohydroquinone was condensed with isoprene. The product was a mixture, as is usual in these condensations when the hydroquinone possesses more than one vacant position ortho to the hydroxyl groups. Unchanged hydroquinone was removed from this product by extraction with



VI VII



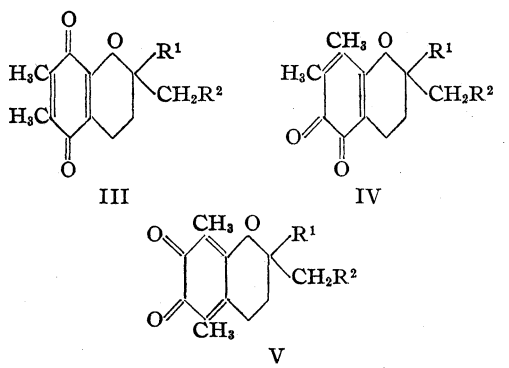
VIII

aqueous sodium hydroxide, and the insoluble portion was then separated by extraction with Claisen's alkali into (a) a phenolic constituent, the chroman VI, R = H, possibly containing also the chroman VII and (b) a non-phenolic constituent, the double chroman VIII. These materials were not further purified, but were subjected directly to oxidation, the non-phenolic constituent by silver nitrate, and the phenolic constituent by nitric acid under the conditions of the Furter reaction. *Both of these substances gave in excellent yield, the same red compound IV*, m. p. and mixed m. p. 109–110°. In fact, the red compound from the phenolic constituent melted at 109.5–110.5°, the highest melting point so far recorded for this compound. It is thus apparent that the group eliminated in these oxidations of 6-hydroxychromans is the one in the 5-position, and that this reaction will occur even though both oxygen atoms of the hydroquinone are involved in heterocyclic systems; furthermore, when hydrogen occupies the 5-position, the composition of red compound IV will be that of the quinone II minus two hydrogen atoms only.

α-, β- and γ-tocopherols give deep red compounds when they are oxidized by nitric acid in alcohol solution. These substances are obtained in good yield, but they are oils which we have so far been unable to crystallize. The red oil (IV,

ever, the reproducibility of the Furter and Meyer reaction under standard conditions is very good.

John and his associates[2a] established that the red compounds differed in composition from the para-quinones II by one carbon atom and four hydrogen atoms; thus the red compound from the pentamethylchroman had the composition $C_{13}H_{16}O_3$, and Karrer and his associates[2b] established that there was a similar change in composition when the quinone (II, $R^1 = R^2 = H$) from 2,5,7,8-tetramethyl-6-hydroxychroman (I, $R^1 = R^2 = H$) was converted into the analogous red compound $C_{12}H_{14}O_3$, m. p. 140°. In their recent paper, Karrer, Fritzsche and Escher[2b] have shown that the red compound obtained from 2,5,7,8-tetramethyl-6-hydroxychroman (I, $R^1 = R^2 = H$) contains no active hydrogen atoms and that it is a quinone, for on reduction it absorbs two atoms of hydrogen to give a colorless hydroquinone. They have proposed a tentative structure for this red compound, which by analogy would become III ($R^1 = CH_3$; $R^2 = H$) when applied to the pentamethylchroman I ($R^1 = CH_3$; $R^2 = H$).



The red substance, however, is not a para-quinone, but is an ortho-quinone. First of all, the red color is in itself a strong argument against such a formulation as III. It has been shown by Hooker and his associates, in a series of remarkable papers, that in the naphthoquinone series all of the hydroxy-α-quinones and the chromans and coumarans derived from them are yellow, the only exceptions being those 2-hydroxy-α-naphthoquinones with a side chain in the 3-position containing a double bond α,β- to the ring—these, and only these, are red, whereas *all* of the derivatives of 4-hydroxy-β-naphthoquinone, as well as the chromans and coumarans derived from them, are red.[7] In Fig. 2 are given the absorption curves for

(7) Hooker, *et al.*, THIS JOURNAL, **58**, 1163, 1168, 1179, 1181, 1198, 1202 (1936). References to previous work by Hooker are given in these papers. See also Fieser, *ibid.*, **49**, 857 (1927).

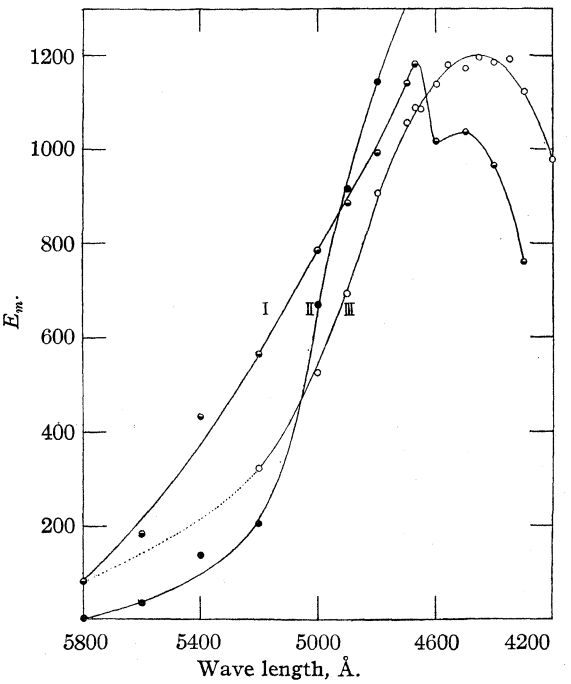


Fig. 2.—◒, Curve I, $C_{13}H_{16}O_3$ (IV), m. p. 109–110°, in absolute ethanol; ●, Curve II, β-lapachone in absolute ethanol; ○, Curve III, tetramethyl-*o*-benzoquinone.

the red compound (pure; m. p. 109–110°) in ethanol, together with curves for two known ortho-quinones—tetramethyl-*o*-benzoquinone[8] and β-lapachone.[9] The curves for the red compound (curve I) and tetramethyl-*o*-benzoquinone (curve III) show good agreement, particularly with respect to the molecular extinction coefficient at the maximum. The shift of the maximum from about 4460 Å. in curve III to 4670 Å. in curve I may be ascribed to the 6-membered hetero ring, because this maximum is characteristic of the red oxidation products of all 6-hydroxychromans which have so far been investigated. The curves reported previously for the red solutions obtained in the Furter reaction from 5-hydroxycoumarans[1b] show a maximum at 4400 Å., which agrees well with an *o*-quinone structure as for instance with tetramethyl-*o*-benzoquinone. Our absorption curve for β-lapachone (curve II, Fig. 2) does not allow for inferences as to structural units, because the range of our instrument was not sufficiently great to include all of the significant parts of the curve. However, while this work was under way, Cook, Macbeth and Winzor[10] have pub-

(8) Smith and Hac, *ibid.*, **56**, 477 (1934).

(9) The authors are greatly indebted to Dr. L. F. Fieser for generous samples of β-lapachone and lapachol.

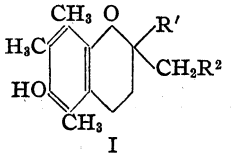
(10) Cook, Macbeth and Winzor, *J. Chem. Soc.*, 878 (1939).

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

The Chemistry of Vitamin E. XVII. The Oxidation Products of α-Tocopherol and of Related 6-Hydroxychromans[1]

BY LEE IRVIN SMITH, WILLA B. IRWIN AND HERBERT E. UNGNADE

When α-tocopherol (I, $R^1 = CH_3$; $R^2 = C_{15}H_{31}$), 2,2,5,7,8-pentamethyl-6-hydroxychroman (I, $R^1 = CH_3$; $R^2 = H$) and similar substances are oxidized by ferric chloride, gold chloride or, under certain circumstances by silver nitrate, the products are yellow para-quinones, II.[2]



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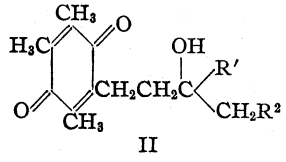

II

When, however, the action of silver nitrate is prolonged, the oxidation proceeds beyond the yellow para-quinone stage and brilliant red solutions are obtained.[2,3] Red solutions also result when nitric acid is used as the oxidizing agent, and Furter and Meyer[4] have developed an elegant photometric method of analysis for tocopherols based upon the production of these red solutions with nitric acid. This reaction has been extended in this Laboratory to para hydroxy coumarans and chromans in general.[5]

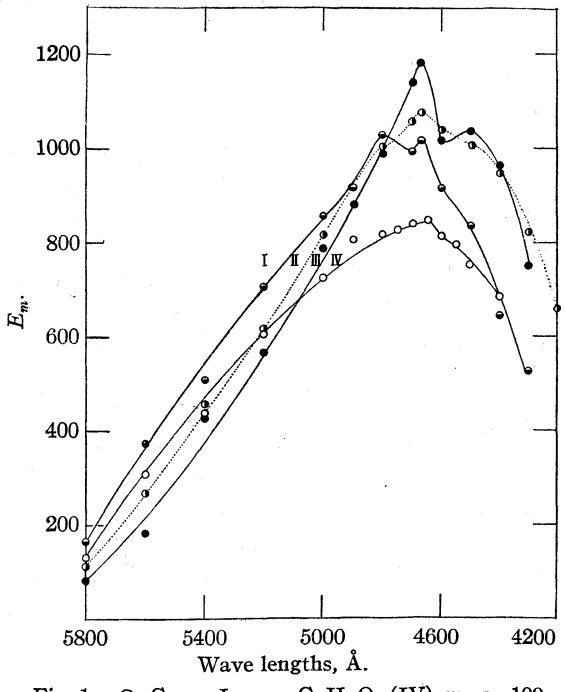

Fig. 1.—◒, Curve I, pure $C_{13}H_{16}O_3$ (IV) m. p. 109–110° in 5 cc. abs. ethanol + 1 cc. concd. HNO_3; ◑, Curve II, $C_{13}H_{16}O_3$ (IV) m. p. 107.5–108.5° from $AgNO_3$ method in abs. ethanol; ●, Curve III, pure $C_{13}H_{16}O_3$ (IV) in absolute ethanol; ○, Curve IV, further reaction on pure 2,2,5,7,8-pentamethyl-6-hydroxychroman.

We have obtained, from the chroman I ($R^1 = CH_3$, $R^2 = H$), the same red crystalline compound using either silver nitrate or nitric acid as the oxidizing agent. The substance forms brilliant red needles which have a melting point (and mixed melting point) of 109–110°.[6] These results show that this compound, m. p. 109–110°, is the substance responsible for the color in the Furter and Meyer reaction with the pentamethylchroman. This is also shown by the curves in Fig. 1. In these curves, the molecular extinction coefficient, E_m, is plotted against the wave length in Ångström units. Curve IV represents the data obtained when the pentamethylchroman was analyzed photometrically by the method of Furter and Meyer; curve III represents the data for the pure (m. p. 109–110°) red substance in absolute ethanol; curve II represents the data for a slightly less pure specimen (m. p. 107.5–108.5°, obtained by silver nitrate oxidation of the chroman) in absolute ethanol, while curve I was obtained using a solution of the pure substance (m. p. 109–110°) in absolute ethanol (5 cc.) containing nitric acid (1 cc.) in the proportions in which they are used in the photometric method of analysis. Comparison of the curves shows that the effect of the nitric acid is to decrease the maxima at 4670 and 4500 Å. (curve III) and to produce a new maximum at 4800 Å. (curve I). These effects, however, are not sufficient to account for the curve obtained in the Furter reaction (curve IV), and it appears that in the Furter reaction the yield of the red compound is not quantitative, due either to incomplete reaction or to the slow destruction of the red compound by the nitric acid, a reaction which is known to occur. How-

(1) (a) XVI, *Science*, in press (1939); (b) XV, *J. Org. Chem.*, **4**, 298 (1939).

(2) (a) John, Dietzel and Emte, *Z. physiol. Chem.*, **257**, 173 (1939); (b) Karrer, Fritzsche and Escher, *Helv. Chim. Acta*, **22**, 661 (1939).

(3) Evans, Emerson and Emerson, *Science*, **88**, 38 (1938).

(4) Furter and Meyer, *Helv. Chim. Acta*, **22**, 240 (1939); see also ref. 2b.

(5) Paper XV in this series, ref. 1b.

(6) John, Dietzel and Emte, ref. 2a, give the m. p. as 109°.

suggests a number of reactions that the "isodione" should undergo and the investigation will be continued at the first opportunity.

Experimental

Absorption Spectra.—The spectra were taken with a Bausch and Lomb medium quartz spectrograph in conjunction with a Hilger Spekker photometer and a hydrogen discharge tube. The alkaline solutions of "isonorechinocystenedione" were prepared by adding to a solution of 7.1 mg. in 9 cc. of ethanol, 0.1 cc. of 3 *N* aqueous sodium hydroxide and allowing the solutions to stand for fifteen minutes before beginning the photographing of the spectra. In the case of norechinocystenedione, 0.1 cc. of 2 *N* sodium hydroxide in 90% ethanol was added to a solution of 3.9 mg. of the dione in 5 cc. of ethanol. The dilution effect of this addition of alkali was neglected in the calculation of the molecular extinction coefficients.

The preparation of a suitable alkaline solution of norechinocystenone was difficult because of the low solubility of this substance. A clear solution containing 0.1 ml. of a 2 *N* sodium hydroxide solution in 90% ethanol was finally obtained but as the precise concentration with respect to the ketone was uncertain, exact molecular extinction coefficients could not be calculated. The curve therefore is not reproduced although qualitatively it is similar to that obtained in the absence of alkali (maximum at 2930 Å.) and of the same order of intensity.

Isomerization of "Isonorechinocystendione."—A solution of 0.5 g. of the "isodione" and 0.5 g. of potassium hydroxide in 50 cc. of 95% ethyl alcohol was refluxed for one and one-half hours. The solution became yellow in color and later a deep amber. It was poured into water, most of the alcohol removed by boiling and the precipitate filtered. The crude material after drying melted at 169–181° and after three crystallizations from methyl alcohol the melting point remained constant at 199–200°. A mixed melting point with norechinocystenedione, m. p. 200–203°, gave no depression. The specific rotation was $[\alpha]^{24}D$ −93.2° in dioxane compared with the previously recorded value for norechinocystenedione[2] of −92.7°.

Monoxime of "Isonorechinocystenedione."—A solution of 0.5 g. of the "isodione," 0.1 g. of fused sodium acetate and 0.5 g. of hydroxylamine hydrochloride in 75% aqueous ethyl alcohol was refluxed for two hours. Hot water then was added to turbidity and the solution cooled. The crude product weighed 0.44 g. and melted at 248–252° with some decomposition. After four crystallizations from methyl alcohol the melting point remained constant at 254–257° when the bath was preheated to 240°.

Anal. Calcd. for $C_{29}H_{45}O_2N$: C, 79.21; H, 10.33; N, 3.18. Found: C, 79.12; H, 10.28; N, 3.33.

Dioxime of Norechinocystenedione.—To the alkali insoluble material from the saponification of 1 g. of the diketomethyl ester was added 5 g. of hydroxylamine hydrochloride in 10 cc. of water and 20 cc. of 1% sodium hydroxide solution and then methyl alcohol was added until complete solution had taken place at the boiling point. After refluxing for two hours, concentrating and cooling a product was obtained which after four crystallizations from methyl alcohol melted at 248–249°.

Anal. Calcd. for $C_{29}H_{46}O_2N_2$: C, 76.60; H, 10.20; N, 6.16. Found: C, 76.41; H, 9.89; N, 6.28.

Oxime of Norechinocystenone.—The oxime was prepared as above in methyl alcohol solution from 0.045 g. of norechinocystenone, 0.25 g. of hydroxylamine hydrochloride and 1 cc. of 1% sodium hydroxide. The crude product melted at 253–253.5° and the melting point was unchanged on recrystallization from methyl alcohol.

Anal. Calcd. for $C_{29}H_{47}ON$: C, 81.82; H, 11.13; N, 3.29. Found: C, 82.01; H, 10.62; N, 3.45.

Summary

1. The ultraviolet absorption spectra of norechinocystenone and norechinocystenedione confirm the presence of isolated carbonyl groups. That of "isonorechinocystenedione" indicates the absence of carbonyl groups in ether solution but the presence of one or more carbonyl groups in alkaline ethyl alcohol solution.

2. Norechinocystenone and norechinocystenedione form a monoxime and dioxime, respectively, whereas "isonorechinocystenedione" forms only a monoxime.

3. On heating with alcoholic alkali "isonorechinocystenedione" is converted into norechinocystenedione. A possible interpretation of the isomerization is suggested.

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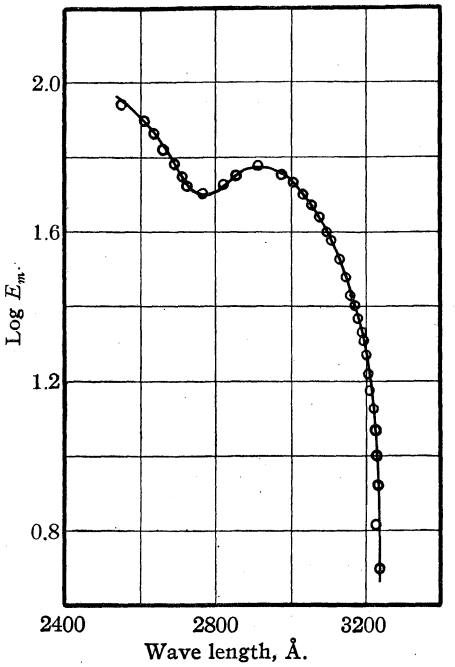

Fig. 1.—Absorption spectrum of norechinocystenone in ethanol.

abnormal behavior cannot be due to a keto–enol type of equilibrium since in the presence of the excess alkali (approximately eighteen moles) one would expect the enolic form to predominate whereas alkali seems to favor the production of the keto form.

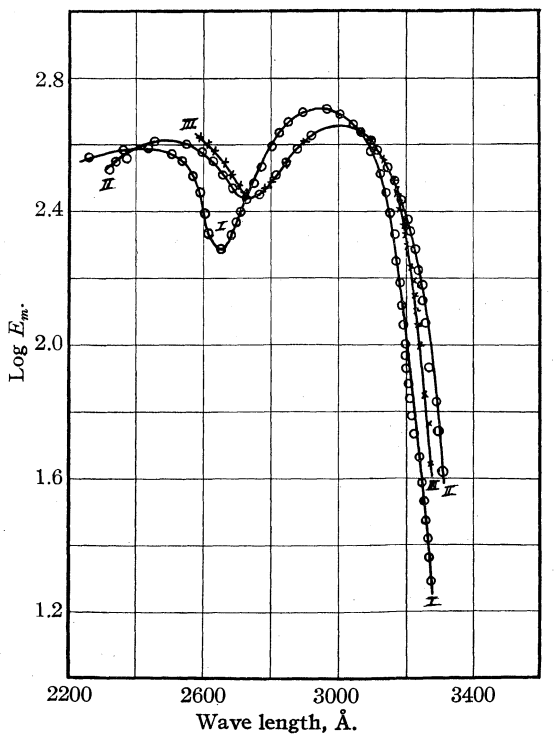

Fig. 2.—Absorption spectra of norechinocystenedione: Curve I in ether, II in ethanol, III in alkaline ethanol.

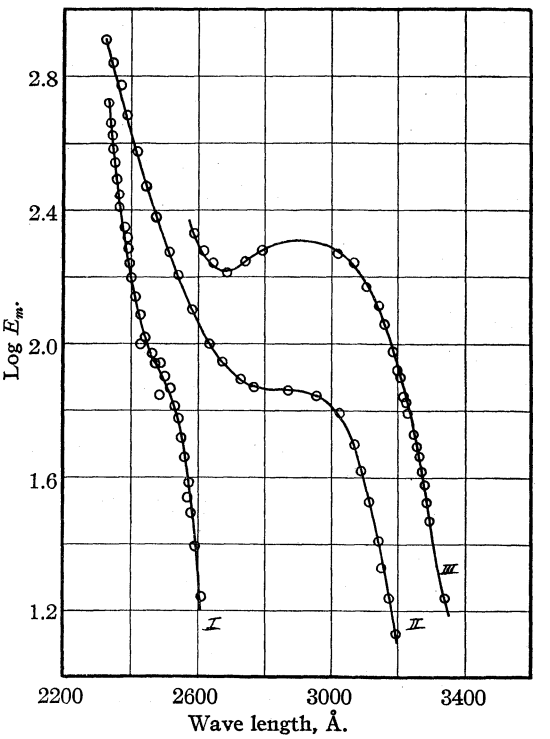

Fig. 3.—Absorption spectra of "isonorechinocystenedione": Curve I in ether, II in ethanol, III in alkaline ethanol.

The above observations led us to return to the chemical investigation of "isonorechinocystenedione." On boiling it with alcoholic potassium hydroxide, it was converted into norechinocystenedione as shown by melting point, mixed melting point and optical rotation. In spite of the spectrographic evidence against the presence of a carbonyl group, the "isodione" reacts with aqueous alcoholic hydroxylamine acidified with acetic acid to give a product the analysis of which is that of a monoxime. Norechinocysteneone and norechinocystenedione give the expected mono- and dioximes, respectively. While the results so far obtained are not sufficient to give a clear picture of the reactions involved, the conversion by alkali of a substance lacking a carbonyl group into a diketone suggests that the "isodione" may be a cyclic hemiacetal of a monoenol form of the diketone. The reaction product with hydroxylamine in acid solution would then be formed by loss of water between hydroxylamine and the hydroxyl group of the cyclic hemiacetal. Such a structure

ether. The ether solution was washed with 5% sodium carbonate solution and evaporated to dryness. The residue was boiled with 5 cc. of ligroin (b. p. 60–70°), the solution decanted and concentrated to approximately 1 cc. Cooling gave needles, m. p. 196–205°. After three recrystallizations from acetone platelets were obtained melting at 211–214°. Neotigogenone when mixed with tigogenone, m. p. 201–207°, melted at 191–205°.

Anal. Calcd. for $C_{27}H_{42}O_3$: C, 78.21; H, 10.21. Found: C, 78.24; H, 9.90.

A solution of 0.0233 g. in 3 cc. of chloroform gave $\alpha = -0.47°$ in a 1-dm. tube; $[\alpha]^{25}D$ −60.6°.

Neotigogenone Oxime.—A mixture of 23 mg. of neotigogenone, m. p. 205–210°, with 0.04 g. of hydroxylamine hydrochloride, 0.46 g. of sodium acetate, 1 cc. of water and 4 cc. of ethyl alcohol was boiled for one hour. Water was added and the mixture was filtered, dried, and recrystallized by dissolving in 7 cc. of acetone, concentrating to 1.5 cc. and allowing to cool slowly. This gave 12 mg. of fine needles which melted with decomposition at 224.5°. Repeated recrystallization from acetone raised the melting point to 231–232° with decomposition.

Anal. Calcd. for $C_{27}H_{43}O_3N$: C, 75.48; H, 10.09; N, 3.25. Found: C, 75.20; H, 9.87; N, 3.33.

Attempted Isomerization of Tigogenin.—One gram of tigogenin, m. p. 200–202.5°, was dissolved in 100 cc. of 95% ethyl alcohol and this was added to a mixture of 66 cc. of 95% ethyl alcohol and 30 cc. of concentrated hydrochloric acid. After heating for thirty-six hours the mixture was concentrated, cooled and filtered. On fractional crystallization from ethyl alcohol almost all of the material was separated into fractions which melted close to the melting point of tigogenin and gave no depression when mixed with tigogenin. However, about 5 mg. of material melting from 189.5–194.5° was obtained from the mother liquors. This gave no Beilstein test for halogen and a mixture with tigogenin, m. p. 206.5–209°, melted at 193–206°.

Summary

A new steroid sapogenin has been obtained which is isomeric with tigogenin and has been named "neotigogenin." It has been isolated as the acetate and characterized by oxidation to a monoketone and conversion of the ketone into the oxime.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Saponins and Sapogenins. XII. The Product of Direct Oxidation of Echinocystic Acid with Dichromic Acid

BY R. NORMAN JONES,[1] DAVID TODD AND C. R. NOLLER

When methyl echinocystate is oxidized with dichromic acid in glacial acetic acid solution, a diketo ester is formed which on saponification loses carbon dioxide to give a diketone, norechinocystenedione.[2] However, if free echinocystic acid is oxidized under the same conditions, one obtains instead of the expected norechinocystenedione an isomeric compound which was believed to be an isomeric diketone and was named "isonorechinocystenedione."

In the hope that a clue would be provided as to the difference in structure of these two compounds we have determined their ultraviolet absorption spectra (Figs. 2 and 3) as well as that of the monoketone, norechinocystenone (Fig. 1). All three compounds contain a carbon–carbon double bond and the nature of the absorption precludes the possibility that this is conjugated with a carbonyl group since such a structure would give an intense absorption band with a maximum near 2350 Å. (log E_m about 4.2) and a second band of lower intensity with a maximum near 3200 Å.[3] An α-diketone is excluded also since such a structure causes absorption in or near the visible region of the spectrum.

Norechinocystenone and norechinocystenedione gave typical carbonyl absorption bands in ethanol (Fig. 1 and Curve II, Fig. 2) with low-intensity maxima between 2900 and 3000 Å. This was not appreciably altered by the addition of alkali (Curve III, Fig. 2) or, in the case of the dione, by changing the solvent to ethyl ether (Curve I, Fig. 2). The second low-intensity maximum in the spectrum of the dione at 2450 to 2500 Å. cannot be attributed to simple carbonyl absorption and will be investigated further.

In the case of "isonorechinocystenedione" it was surprising to find no evidence of carbonyl absorption in ethyl ether (Curve I, Fig. 3). In absolute ethanol, however, it appeared as an inflection (Curve II) which developed in moist alcoholic sodium hydroxide solution into a clearly defined maximum at 2930 Å. (Curve III). This

(1) Commonwealth Fund Fellow.

(2) White and Noller, THIS JOURNAL, **61**, 983 (1939).

(3) Fieser, Fry and Jones, *ibid.*, **61**, 1849 (1939).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Saponins and Sapogenins. XI. Neotigogenin, a New Steroid Sapogenin

BY L. H. GOODSON AND C. R. NOLLER

During the course of the preparation of tigogenin acetate using acetic anhydride and pyridine,[1] a low melting fraction was accumulated which appeared to be a mixture of two or more components and could not be separated readily by repeated crystallization. When solutions of this fraction in ethyl alcohol were allowed to evaporate spontaneously, two types of crystals separated, a fine white powder and small regular octahedra. After mechanical separation it was found that the powder was chiefly tigogenin acetate. The octahedra were recrystallized from isopropyl alcohol and were found by melting point and mixed melting point to be a different compound. Analysis of this compound showed that it is isomeric with tigogenin acetate. Saponification of the new acetate gave a sapogenin which, although it has a melting point very close to that of tigogenin, produced a marked melting point depression when mixed with tigogenin. Oxidation of the sapogenin gave a ketone which was not identical with tigogenone[2] so the isomerism does not involve the carbon atom bearing the hydroxyl group. Moreover, the properties of the new compound and its derivatives are different from those of sarsasapogenin,[3] isosarsapogenin,[4] *epi*-sarsasapogenin[5] and smilagenin.[6] The compound does not appear to be related to tigogenin as isosarsasapogenin is related to sarsasapogenin[4] because tigogenin was practically unchanged by boiling with alcoholic hydrochloric acid. This conclusion is only tentative, however, because the tigogenin was altered partially to give a small amount of low melting material, but we have not yet succeeded in isolating the new compound from this altered tigogenin. Because the new sapogenin has been obtained in relatively small amounts and is difficult to isolate, we are unable to state at the present time whether it is one of the original hydrolysis products of the extract of *Chlorogalum pomeridianum* or is formed by isomerization during the acetylation. Because of the uncertainty concerning the seat of the isomerism we prefer to name the new compound "neotigogenin."

(1) Noller, Goodson and Synerholm, THIS JOURNAL, **61**, 1707 (1939) (paper X).
(2) Jacobs and Fleck, *J. Biol. Chem.*, **88**, 545 (1930).
(3) Jacobs and Simpson, *ibid*, **105**, 501 (1934).
(4) Marker and Rohrmann, THIS JOURNAL, **61**, 846 (1939).
(5) Marker and Rohrmann, *ibid.*, **61**, 943 (1939).
(6) Askew, Farmer and Kon, *J. Chem. Soc.*, 1399 (1936).

Experimental

Neotigogenin Acetate.—The acetylation of tigogenin, m. p. 198–203°, obtained from *Chlorogalum pomeridianum* was carried out at temperatures below 50° using acetic anhydride and pyridine. The yield of easily purified tigogenin acetate in this acetylation varied from 80–85%. The lower melting fractions which were more soluble in ethyl alcohol than tigogenin acetate were collected from several acetylations and combined. Fractional crystallization from ethyl alcohol yielded only a small amount of tigogenin acetate together with fractions melting over ranges of 10 to 30° and as low as 135°. Solutions of these low-melting fractions on spontaneous evaporation at room temperature over a period of weeks yielded two types of crystals, a white powder which appeared amorphous through a low-power microscope and small regular octahedra. The octahedra were separated mechanically and washed with isopropyl alcohol, when they melted at 172–174°. After one crystallization from isopropyl alcohol they melted at 174–176° and further crystallization from this solvent did not change the melting point. Approximately 40 mg. of neotigogenin acetate was obtained from the acetylation of 10 g. of tigogenin.

Anal. Calcd. for $C_{29}H_{46}O_4$: C, 75.94; H, 10.11. Found: C, 76.10, 76.02; H, 10.21, 10.21.

A solution of 0.0414 g. in 3 cc. of chloroform gave $\alpha = -1.01°$ in a 1-dm. tube; $[\alpha]^{25}D$ −73.4°.

When this substance was mixed with tigogenin acetate, m. p. 202–208°, the mixture melted at 163.5–185°.

Neotigogenin.—A solution of 41 mg. of neotigogenin acetate, m. p. 174–176°, and 0.08 g. of potassium hydroxide in methyl alcohol was boiled under reflux for forty-five minutes and then a small quantity of water was added. On cooling needles separated which after recrystallization from 4 cc. of methyl alcohol weighed 35 mg. and melted at 200–203°. Further crystallization from methyl alcohol narrowed the melting point range to 202–203°. Neotigogenin when mixed with tigogenin, m. p. 206.5–209°, melted at 182–188° while a mixture with a sample of sarsasapogenin, m. p. 193.5–197.5°, melted below 140°. Neotigogenin separated with alcohol of crystallization and was dried for analysis at 135° and 2 mm.

Anal. Calcd. for $C_{27}H_{44}O_3$: C, 77.83; H, 10.64. Found: C, 77.96; H, 10.45.

A solution of 0.0537 g. in 3 cc. of chloroform gave $\alpha = -1.16°$ in a 1-dm. tube; $[\alpha]^{26}D$ −64.9°.

Neotigogenone.—To a solution of 72 mg. of neotigogenin (alcohol-free) in 2 cc. of acetic acid at room temperature was added dropwise a solution of 0.012 g. of chromium trioxide in 2 cc. of 80% acetic acid. The mixture was allowed to stand until the solution was a light clear green in color. This was diluted with water and extracted with

alkaline solution of formaldehyde should give a greater increase in the yield of hydrocarbon. This expectation was realized and the following table shows that quite a wide variety of compounds have been deaminated in yields of 50–80%. Some substances such as 2,5-dichloroaniline and anthranilic acid, which are deaminated in the poorest yields by this method, are the ones which succeed best by the time-honored alcohol method. Thus the two processes supplement each other. A typical experiment is described and the table shows the yields obtained with other compounds by using the same procedure.

Experimental Part

Deamination of *p*-Toluidine to Toluene.—A solution of 0.5 mole (53.5 g.) of *p*-toluidine in 150 cc. of concentrated hydrochloric acid and 400 cc. of water was chilled by the addition of 400 g. of ice and diazotized in the usual manner with 36 g. of sodium nitrite. A solution of 100 g. of commercial sodium hydroxide in 600 cc. of water was then prepared and placed with 500 g. of shaved ice into a 5-liter flask which was fitted with a mechanical stirrer. The stirrer was started and 75 cc. of formalin (37% formaldehyde) added. The solution of *p*-tolyldiazonium chloride was then poured in a slow stream into the rapidly stirred alkaline solution of formaldehyde. The rapid escape of nitrogen caused considerable frothing. After all of the diazonium chloride solution had been added the stirring was continued for two to three minutes, after which the stirrer was removed, the mouth of the flask covered with a watch glass and the reaction mixture allowed to stand with occasional shaking for thirty to forty minutes. The toluene in the upper oily layer was then removed by distillation in steam, separated from the water, dried and distilled. The yield of toluene, b. p. 108–111°, was 36–38 g. (78–82%).

TABLE I

YIELD OF DEAMINATED PRODUCTS FROM DIAZONIUM SALTS

Amino compound	Product and % yield	
Aniline	Benzene	60
o-Toluidine	Toluene	80
p-Toluidine	Toluene	80
o-Anisidine	Anisole	75
p-Anisidine	Anisole	72
o-Phenetidine	Phenetole	75
p-Phenetidine	Phenetole	65
2,4-Dimethylaminobenzene	*m*-Xylene	80
p-Chloroaniline	Chlorobenzene	50
o-Chloroaniline	Chlorobenzene	55
4-Aminodiphenyl ether	Diphenyl ether	60
2-Aminodiphenyl ether	Diphenyl ether	60
2-Amino-4′-methyldiphenyl ether	4-Methyl diphenyl ether	50
4-Amino-4′-methyldiphenyl ether	4-Methyl diphenyl ether	50
2,5-Dichloroaniline	*p*-Dichlorobenzene	10
Anthranilic acid	Benzoic acid	25
o-Nitraniline	Nitrobenzene	20
m-Nitraniline	Nitrobenzene	10
p-Nitraniline	Nitrobenzene	10

Discussion.—The addition of the diazonium salt to the alkaline formaldehyde may produce both the *syn* and *anti* diazotates, the former of which might be reduced more rapidly than the latter. However, after the reduction had proceeded for five minutes, reacidification of the solution and again making it alkaline did not increase the yield. Neither was the yield of toluene increased by addition of sodium stannite, zinc dust or ferrous sulfate to the alkaline solution of formaldehyde. The use of alkaline pyrogallol in place of alkaline formaldehyde gave a little toluene but chiefly an azo dye (coupling reaction) with excessive frothing. Since no alcohol is used in the method, the formation of an ether is avoided. The loss of material in each experiment was accounted for by the formation of tarry substances which were chiefly polymers of the aromatic radical and remained in the flask after steam distillation. Replacement of *p*-tolyldiazonium chloride by the sulfate reduced the yield of toluene from 80 to 75% and an increase in the concentration of the sulfate ion by the addition of 1 g. mole of sodium sulfate further reduced the yield of toluene to 55%. The low yield of nitrobenzene from the three nitroanilines is explained by the fact that the nitro group is largely reduced by the alkaline formaldehyde to a mixture of azo compounds. The reaction of phenyldiazonium chloride with alkaline acetaldehyde in place of formaldehyde gave a red dye as reported by Bamberger and Müller.[8] In our experiments the yield of benzene by this reaction was less than 5%.

Summary

The reduction of a number of diazonium salts with alkaline formaldehyde has been found to produce good yields of hydrocarbons. This procedure often gave the best yields of hydrocarbons in cases where the classical reduction with alcohol gave the poorest yields and vice versa. Hence the two methods supplement each other.

LAWRENCE, KANSAS RECEIVED JUNE 30, 1939

(8) Bamberger and Müller, *J. prakt. Chem.*, [2] **64**, 199 (1901).

Acetone precipitation was most satisfactory for the preparation of concentrates. The fraction soluble at 50% but insoluble in 55% aqueous acetone was redissolved in water. This solution had a "Kat. f." of 1800, representing a threefold concentration of the original activity. Stern has used acetone in the preparation of liver catalase concentrates.[7]

A cottonseed extract (*p*H 6.4) was only slightly affected by heating at 50° for thirty minutes. At 60° the catalase was destroyed completely in fifteen minutes, and at 70° no activity remained after five minutes. However, dry ether-extracted cottonseed meats could be heated at 105° for several hours without destruction of the enzyme. Commercial cottonseed meal contained no catalase; this material is generally subjected to a steaming process for twenty to forty minutes prior to the pressing operation.

The activity of concentrates was almost entirely repressed in 0.02 *N* sodium cyanide solution.

During the first forty-eight hours of germination, the catalase concentration of whole seeds increased from 120 to 140% of the original content.

The characteristics of this enzyme are not essentially different from those of other plant catalases.[3] The availability of a plant source of somewhat greater original catalase content should facilitate its further investigation.

(7) K. J. Stern, *J. Biol. Chem.*, **112**, 661 (1935–36).

Summary

Cottonseeds contain appreciably more catalase than do a number of other seeds examined. Some properties of the enzyme have been described.

PITTSBURGH, PENNA. RECEIVED JUNE 29, 1939

[CONTRIBUTION FROM THE BAILEY CHEMICAL LABORATORY OF THE UNIVERSITY OF KANSAS]

Reduction of Diazonium Salts to Hydrocarbons with Alkaline Formaldehyde

BY RAY Q. BREWSTER AND JOHN A. POJE

It is well known that the classical method[1] for the reduction of a diazonium salt such as phenyldiazonium chloride or sulfate to a hydrocarbon by reaction with an alcohol produces an ether as well as the hydrocarbon. In most cases the ether is the major product. An experiment by Hantzsch and Jochem,[2] which is typical of many recorded in the literature, produced 1.6 g. of benzene and 34.1 g. of phenetole from the reaction of ethyl alcohol upon 64 g. of phenyldiazonium chloride. Similar results with varying proportions in the yield of hydrocarbon (hydrogen reaction, I) and ether (alkoxy reaction, II) have been obtained by a large number of investigators.[3] The extent to which the reaction between any given diazonium salt and an alcohol will follow one course or the other depends upon the character of the radical (R) and upon the nature of the alcohol. In general the yield of hydrocarbon increases with the

$$RNNCl + C_2H_5OH \longrightarrow RH + CH_3CHO + HCl + N_2 \quad (I)$$

$$RNNCl + C_2H_5OH \longrightarrow ROC_2H_5 + HCl + N_2 \quad (II)$$

substitution of a carboxyl, halogen or nitro group ortho to the diazonium radical, and the hydrogen reaction becomes quite predominant in the case of 2,4,6-tribromophenyldiazonium sulfate where the yield of tribromobenzene[4] is 75–78% of the theoretical quantity. The alcohols used most commonly are methyl and ethyl, of which the latter usually gives the better yield of hydrocarbon. Some experiments using other alcohols are to be found in the literature and they are being extended in this Laboratory.

In the deamination of certain aminodiphenyl ether derivatives in which we were interested, the alkoxy reaction occurred almost exclusively and it was necessary to devise some other method for replacement of the amino group by hydrogen. Inasmuch as the hydrogen reaction involves a reduction of the carbon atom to which the diazonium salt is joined, it would seem that a reducing agent considerably stronger than an alcohol should be used. Such reducing agents as sodium alcoholate,[5] stannous chloride[6] and hypophosphorous acid[7] in certain cases have increased somewhat the yield of the hydrocarbon but it would seem that the more effective reducing action of an

(1) Griess, *Ann.*, **137**, 69 (1866).
(2) Hantzsch and Jochem, *Ber.*, **34**, 3340 (1901).
(3) A. W. Hofmann, *Ber.*, **17**, 1919 (1884); Remsen and Orndorff, *Am. Chem. J.*, **9**, 387 (1887); Cameron, *ibid.*, **20**, 229 (1898); Franklin, *ibid.*, **20**, 455 (1898), and many others.
(4) *Org. Syntheses*, **13**, 96 (1933).
(5) Beeson, *Am. Chem. J.*, **16**, 250 (1894).
(6) Friedländer, *Ber.*, **22**, 587 (1889).
(7) Mai, *ibid.*, **35**, 163 (1902).

[CONTRIBUTION FROM THE MULTIPLE FELLOWSHIP OF THE COTTON RESEARCH FOUNDATION, MELLON INSTITUTE]

Composition of Cottonseeds. II. Catalase

BY H. S. OLCOTT AND C. D. W. THORNTON

During an investigation of cottonseed proteins, hydrogen peroxide was added to an aqueous extract of cottonseeds in an attempt to bleach the colored extractives. The extensive foaming which occurred suggested that a catalase was present in appreciable amounts. The results of further experiments indicated that cottonseeds contained more catalase than any of several other seeds examined.

The following routine method of assay for catalase activity was used.[1] To 5 cc. of approximately 0.02 *N* hydrogen peroxide solution were added 1 cc. of 0.067 *N* phosphate buffer (*p*H 6.85) and 1 cc. of catalase extract suitably diluted so that 10 to 20% of the peroxide was decomposed in two minutes at room temperature (25–28°). At the end of this period 10 cc. of 10% sulfuric acid was added. The peroxide remaining was determined iodimetrically; 10 cc. of 10% potassium iodide and three drops of 1 *N* ammonium molybdate solution were added, and the liberated iodine was titrated with 0.005 *N* sodium thiosulfate with starch for an indicator.

In most cases parallel determinations were run at four- and six-minute intervals. The computed monomolecular reaction constant diminished with increased time of reaction. Activity indices were calculated from the reaction constant at two minutes rather than from that obtained by extrapolation to 0 time in order to obtain minimum values. The index of catalase activity ("Kat. f." of von Euler and Josephson[2]) was obtained by dividing the reaction constant by the weight of solids added in the catalase extract. Approximate indices were obtained experimentally with crude aqueous extracts of a number of ground whole seeds (dehulled in the case of cottonseed, hempseed, and soybean), and rat and beef liver (Table I). Zeile[3] reported that an extract of pumpkin seeds was one-fifteenth as effective as one prepared from horse liver by the same method. According to Sumner and Dounce[4] the "Kat. f." (0°) of crystalline beef liver catalase is 35,000.

TABLE I

CATALASE CONTENT OF AQUEOUS EXTRACTS FROM VARIOUS SOURCES

Source of extract	Kat. f.
Cottonseed[a]	600
Corn	90
Hempseed[a]	60
Wheat	40
Flaxseed[a]	15
Soybean[b]	15
Rapeseed[a]	1
Beef liver	5,000
Rat liver	3,000

[a] Ether extracted. [b] Petroleum ether extracted.

Ether-extracted cottonseed meats[5] were leached with water to obtain the active enzyme solutions. Preserved with chloroform, the extracts retained their activity for several days at 0°. A number of experiments designed to concentrate the catalase fraction were only partially successful.

In the extraction of catalase from cottonseed meal by dilute acids and alkalies, the most active preparations were obtained with neutral or slightly alkaline extractants. Acids destroyed the catalase activity. Aqueous extracts were most effective at a *p*H of 6.8 to 7.2 (phosphate and borate buffers). However, there was no sharp peak in the *p*H–activity curve; the preparations were almost equally active in the *p*H range 6 to 9.

The addition of ammonium sulfate to 0.6 saturation did not precipitate the enzyme, but at 0.75 saturation most of the activity could be accounted for in the precipitate. During the dialysis procedure used to remove the ammonium sulfate, the catalase content spontaneously decreased so that no marked concentration was effected by this method.

Several attempts to concentrate the enzyme by adsorption on moist alumina[6] were unsuccessful, as was the dioxane precipitation method described by Sumner and Dounce.[4]

The catalase was partially precipitated from its aqueous solution by the addition of an equal part of anhydrous alcohol. With 60% alcohol precipitation was complete. The total activity rapidly decreased in the presence of this solvent.

(1) Adapted from K. G. Stern, *Z. physiol. Chem.*, **204**, 259 (1932), and others.

(2) H. V. von Euler and K. Josephson, *Ann.*, **452**, 158 (1927).

(3) K. Zeile, *Ergebnisse Enzymforschung*, **3**, 265 (1934).

(4) J. B. Sumner and A. L. Dounce, *J. Biol. Chem.*, **121**, 417 (1937); *ibid.*, **127**, 439 (1939).

(5) H. S. Olcott and T. D. Fontaine, THIS JOURNAL, **61**, 2037 (1939).

(6) K. G. Stern, *J. Biol. Chem.*, **114**, 473 (1938).

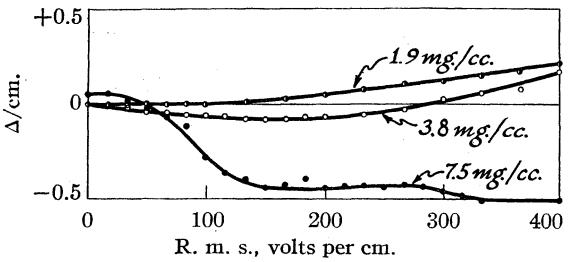


Fig. 5.—The double refraction of several concentrations of tobacco mosaic virus (preparation A) at *p*H 5.1 ± 0.1, plotted as a function of field strength.

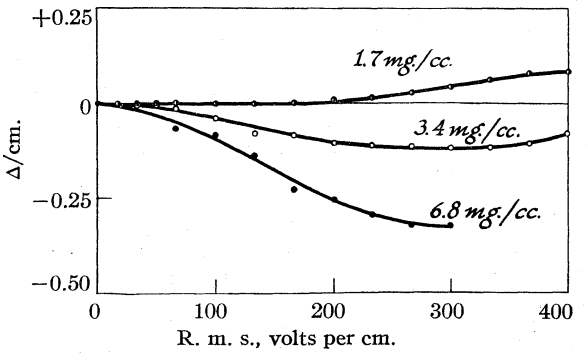


Fig. 6.—The double refraction of several concentrations of aucuba mosaic virus at *p*H 5.2 ± 0.1, plotted as a function of field strength.

higher field strength, just as could have been predicted from the foregoing considerations. By comparing Figs. 3 and 6, it may be seen that, in general, the aucuba mosaic virus responds to the addition of acid in a similar manner. The effect on the inversion point of aging of tobacco mosaic virus at *p*H 5, already described, may be accounted for in a similar manner, for it is known that upon long standing under such conditions the virus undergoes partially irreversible linear aggregation.

The point of view just outlined could be subjected to further tests by studying the phenomenon in viruses with alternating fields of various frequencies. If it is correct, raising the frequency should tend to result in an apparent increase of the negative effect for weak fields and in an inversion point at a higher field strength. It is recognized that many obstacles remain in the path of the complete acceptance of the proposed interpretation of the electrical double refraction of the viruses. Nevertheless, it is hoped that the observations and suggestions herein presented eventually may prove of use in understanding the nature of the electro-optical effect in colloidal solutions.

Summary

It has been found that solutions of tobacco mosaic virus, aucuba mosaic virus, and potato latent mosaic virus exhibit the Kerr electro-optical effect. In dilute solutions in an alternating electric field of 60 cycles, the double refraction of tobacco mosaic virus appears to be positive for all values of the field strength, but for more concentrated solutions the effect becomes negative in weak electric fields, passes through an inversion point for stronger fields, becomes positive for still stronger fields, and finally attains a maximum value. The inversion point occurs at higher field strengths in more concentrated solutions. By bringing the virus nearer its isoelectric point, the negative effect is generally increased and the inversion point is shifted to stronger fields. Aging the virus has a similar effect. In an attempt to explain these observations, it was suggested that two opposing forces control the orientation of the particles. One of these may be a negative orienting effect which varies with the first power of the field strength and which does not follow the alternations of the field. Opposing it and eventually overcoming it in strong fields, there was assumed to be a positive orienting effect, perhaps due to a permanent dipole moment, an effect which varies with the second power of the field strength, but which does follow the alternations of the field, and which is, therefore, affected by interparticle attraction.

PRINCETON, N. J. RECEIVED JUNE 23, 1939

trical double refraction of these materials would seem to be due to the orientation of rod-shaped particles, parallel to the electrical field for the case of positive birefringence, and perpendicular to the field for the case of negative birefringence.

It would seem reasonable to assume that the positive orientation of the virus particles is due, at least in part, to a dipole moment in the direction of the long axis of the rods. In such a case, in sufficiently weak fields, the positive double refraction should be proportional to the second power of the field strength. In order to explain the negative double refraction at low field strengths, it is necessary to assume further that opposing the positive orienting tendency is some negative orienting tendency which is greater than the positive one for weak fields, but which increases less rapidly than the positive effect as the field strength is increased, and which is thereby finally overtaken by the positive effect. This condition would be satisfied if the negative double refraction varied with approximately the first power of the field strength. This would suggest some type of mechanical force, perhaps one associated with the electrokinetic properties of the viruses. However, whatever the nature of the orienting tendencies may be, by postulating a negative tendency proportional to the first power of the field strength which is opposed by a positive tendency proportional to the second power of the field strength, it is possible to explain the existence of negative double refraction in weak fields and positive double refraction in strong fields. In fact, except for the higher values of the field strength, many of the data obtained in this study can be described moderately well by equations of the form, $y = Ax^2 - Bx$. However, the change in inversion point with change of concentration of the virus solutions still remains unexplained. Hence, a consideration of other properties of virus solutions which depend upon concentration becomes necessary.

At concentrations of tobacco virus somewhat greater than the highest shown in Fig. 1, the material is spontaneously doubly refracting, *i. e.*, the particles spontaneously orient themselves parallel to each other in small doubly refracting elements of volume.[16] This means that between the particles there exist forces of attraction which should vary in some manner inversely with the interparticle distance.[17] If the positive orientation of the viruses is due largely to a permanent dipole moment in the direction of the long axis of the particles, it would have to follow the alternations of the field. In such a case, forces of attraction between the particles and actual aggregation of particles should tend to increase the relaxation time of positive orientation. From the estimates of the rotational diffusion constant of tobacco mosaic virus obtained by Mehl,[18] it follows that the critical frequency for the virus is of the same order of magnitude as the frequency here employed. Under such circumstances, an increase in relaxation time will result in a decrease in average positive orientation for a given orienting force. If we assume further that the negative orientation does not follow the alternations of the field, as it should not if it were due to mechanical causes, the negative birefringence should not be diminished by forces of attraction between particles. Hence, the net result of imposing interparticle attraction upon the system should be an apparent increase in the negative double refraction and an inversion point at a higher field strength, all of which would be due mainly to the decrease of the positive birefringence. Dilution of the solution, which results in a decrease of the interparticle attraction, should result in an apparent decrease in the negative effect and a corresponding lowering of the inversion point. As Fig. 1 shows, this is consistent with the experimental observations.

There is considerable evidence[8] which indicates that when a solution of tobacco mosaic virus is acidified to *p*H 5 there is an end to end aggregation of rod-like particles. This has the effect of decreasing the ratio of mean interparticle distance to particle length and should, therefore, result in more interaction between particles. As a matter of fact, changing a relatively concentrated sol from neutrality to *p*H 5 causes it to acquire the properties of a gel. The particles in an acidified solution, then, should have an increased relaxation time and should, therefore, show a retarded positive orientation. By comparing Fig. 5 with Fig. 1, it may be seen that bringing the acidity of a solution of tobacco mosaic virus from *p*H 6.4 to 5.1 results in a general increase of the negative effect and in an inversion point at a

(16) Bawden and Pirie, *Proc. Roy. Soc.* (London), **B123**, 274 (1937). See also refs. 7 and 15.

(17) For a theoretical treatment of this question, see Langmuir, *J. Chem. Phys.*, **6**, 873 (1938).

(18) Mehl, *Cold Spring Harbor Symp. Quant. Biol.*, **6**, 218 (1938).

In a superficial way, at least, this phenomenon resembles the magnetic double refraction of ferric oxide sols, known as the Majorana effect, which has been described and studied by Cotton and Mouton.[11] However, the electrical double refraction of the viruses is perhaps more closely related to the behavior of bentonite sols as described by Mueller[5] and by Norton.[6] Norton

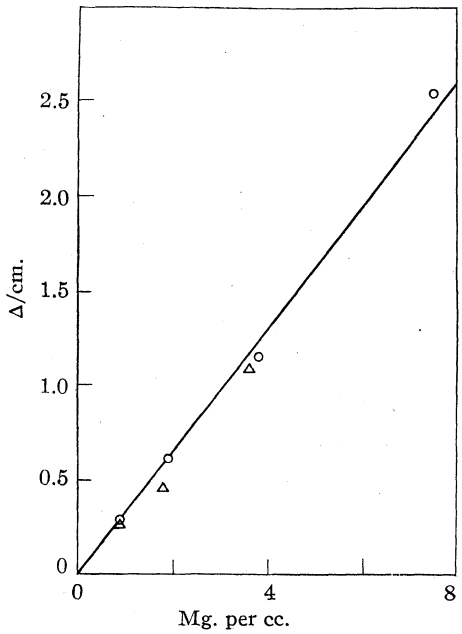


Fig. 2.—The electrical double refraction of tobacco mosaic virus in an electric field of 400 r. m. s. volts/cm., plotted as a function of the concentration of virus: ○, preparation A; △, preparation B.

found that the electrical double refraction of a 1% bentonite sol varied in sign and magnitude with the frequency of alternation of the electric field, it being negative for frequencies up to 630 cycles and positive at higher frequencies. Mueller extended this observation by demonstrating that, at a given frequency, a 1% bentonite sol may show negative double refraction, but that as the sol is diluted the double refraction decreases to zero and finally becomes positive. The transition point varies with the frequency. These observations were made in relatively weak electric fields. It may be seen from Fig. 1 that in fields weaker than 100 volts per cm., the phenomenon here reported seems to be identical with that just described for bentonite sols.

A considerable body of physical evidence, recently reviewed,[12] shows that the particles of tobacco mosaic virus are rod-shaped bodies about 12–15 mμ in thickness and about 400–500 mμ in length. Recent studies with the electron microscope[13] substantiate the conclusions concerning the shape and thickness of the particles and indicate a probable length of about 300 mμ. The amount of double refraction of flow shown by all three of the viruses here studied is about the same,[14] indicating that the conclusions concerning the physical nature of the tobacco mosaic virus probably apply, in general, to the other two. The double refraction of flow of tobacco mosaic virus is always positive, and it has been shown by the author to be due to the orientation of rod-shaped particles which are themselves isotropic or nearly so.[15] In view of these facts, the elec-

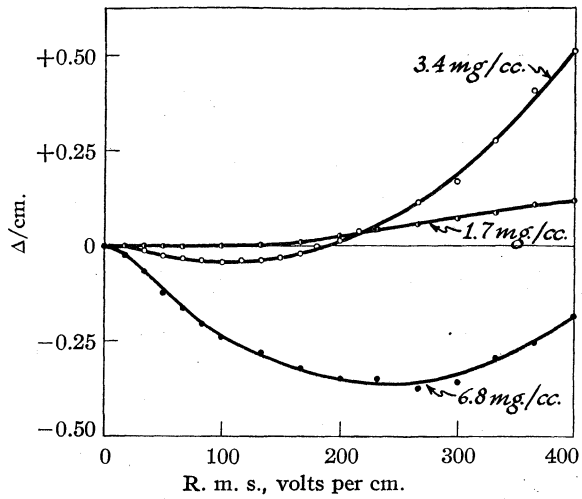


Fig. 3.—The double refraction of several concentrations of aucuba mosaic virus at *p*H 6.7 ± 0.1, plotted as a function of field strength.

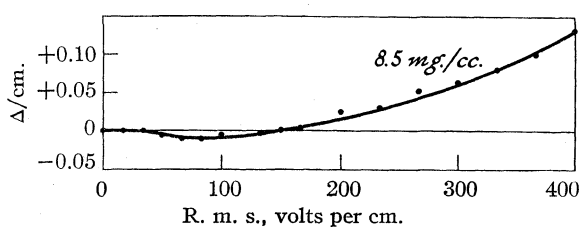


Fig. 4.—The double refraction of latent mosaic virus (concentration of 8.5 mg./cc.) at *p*H 6.7, plotted as a function of field strength.

(11) Cotton and Mouton, *Ann. chim. phys.*, [8] **11**, 145, 289 (1907).

(12) Lauffer and Stanley, ref. 8. For recent papers, see also Kausche, Guggisberg, and Wissler, *Naturwissenschaften*, **27**, 303 (1939), and Robinson, *Proc. Roy. Soc.* (London), **A170**, 519 (1939); *Nature*, **143**, 923 (1939).

(13) Kausche, Pfankuch and Ruska, *Naturwissenschaften*, **27** 292 (1939).

(14) Lauffer and Stanley, *J. Biol. Chem.*, **123**, 507 (1938).

(15) Lauffer, *J. Phys. Chem.*, **42**, 935 (1938).

Description of the Method and the Materials.—The apparatus used for measuring double refraction resembled somewhat that described by Kunitz.[9] It consisted of a polarizing microscope equipped with a Babinet compensator and external analyzer. A mercury quartz lamp provided with filters which transmit only the mercury 5461 Å. green band was used as the source of illumination. The Kerr cell consisted of a flat-bottomed glass tube 2.5 cm. deep and 1.5 cm. in diameter containing 2 platinum electrodes 5 mm. wide and long enough to reach nearly to the bottom of the tube. In order to facilitate mounting onto the stage of the microscope, the glass tube was fitted into a hollow hard rubber cylindrical housing. The electrodes were firmly held 3 mm. apart by a second housing, which acted as a cap for the first, and were thus permitted to dip into the solution in the glass tube. As a source of potential, 120-v., 60-cycle alternating current was used, and fractional parts of this voltage were obtained by employing the principle of the potentiometer. The voltages actually applied across the terminals of the Kerr cell were measured with a Weston a. c. voltmeter. During the course of actual measurements, the light from the polarizer passed between the platinum electrodes of the Kerr cell in such a manner that the direction of the electric field made an angle of 45° with the plane of polarization of the incident light. With an experimental arrangement of the type described, good comparative data may be obtained on systems showing as much double refraction as that shown by reasonably concentrated tobacco mosaic virus solutions, but no great precision may be claimed for the absolute magnitudes of the quantities measured.

The viruses used in this study were purified by ultracentrifugation and then dissolved in distilled water. Preparation A of tobacco mosaic virus was stored for about two months in the cold at about *p*H 6.5. Preparation B was dialyzed against distilled water and stored for about six months at about *p*H 5. It was brought to neutrality before using. The aucuba mosaic virus was stored for about four months at about *p*H 6.5, and the latent mosaic virus for two months at about *p*H 6.7.[10]

Presentation and Discussion of Results.—The electrical double refraction shown by each of the 3 viruses was determined for electric fields ranging from 0 to 400 root mean square volts per cm. In the case of tobacco mosaic and aucuba mosaic viruses, these measurements were carried out for various concentrations of virus and at acidities near neutrality and near the isoelectric zones. The data are presented in Figs. 1–6. In these figures, field strengths in root mean square volts per cm. or concentration of virus in milligrams per milliliter are plotted as abscissas and displacements in wave lengths per cm. of solution as ordinates. The latter is equal to the quotient of the double refraction divided by the wave length of the light used. An inspection of Fig. 1 reveals that in relatively concentrated solutions of tobacco mosaic virus (preparation A) the electrical double refraction is negative for the lower values of the field strength, but reverses in sign and finally appears to approach a maximum for higher values of the field strength. By simply diluting the solution, the negative effect gradually disappears, until in the more dilute solutions the double refraction appears to be positive for all values of the field strength. Preparation B of tobacco mosaic virus, which had been allowed to age for six months instead of two months as in the case of A, behaved in a manner very similar to that just described, except that the transition points from positive to negative double refraction were more than twice those of the first preparation. However, as may be seen in Fig. 2, the maximum values of the positive double refraction approached by both preparations are approximately proportional to the virus concentration and are the same on a concentration basis. As is revealed by Figs. 3 and 4, the unusual type of reversal found for tobacco mosaic virus is common to all 3 of the viruses examined.

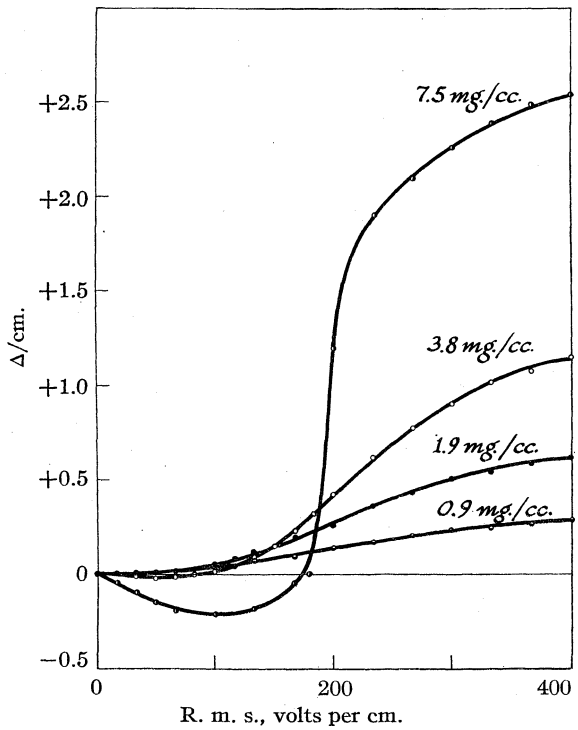


Fig. 1.—The double refraction of several concentrations of tobacco mosaic virus (preparation A) at *p*H 6.4 ± 0.2, plotted as a function of the field strength.

(9) Kunitz, *J. Gen. Phys.*, **13**, 565 (1930). The author wishes to acknowledge his gratitutde to Dr. Kunitz for making much of the apparatus described in this publication available to him.

(10) The author wishes to acknowledge his gratitude to Dr. Loring for supplying the latent mosaic virus protein.

were obtained with benzene and dioxane. Ethanol, glacial acetic acid and acetonitrile were better and only occasionally showed a tendency to form a precipitate. Methanol, dimethylformamide and excess pyridine all were free from this objectionable feature.

Analytical Methods Used.—In the absence of sulfur dioxide, analyses for strong acidity as hydriodic or sulfuric acid were obtained by titration with standard 0.5 *N* sodium hydroxide to a phenolphthalein end-point. The samples were then titrated back to the brom phenol blue end-point with 0.5 *N* hydrochloric acid to obtain a measure of pyridine. This titrimetric procedure was found by control experiments to be reproducible within ±0.2% and to account for at least 99% of the pyridine and inorganic acid added. Sulfate was determined by Raschig's benzidine method[15] and iodide argentimetrically using fluorescein as an adsorption indicator,[16] in both cases removing most of the pyridine by making alkaline to phenolphthalein with sodium hydroxide and boiling for fifteen to twenty minutes before proceeding with the analysis. Free and "periodide" iodine was obtained by thiosulfate titration after acidification to a *p*H of 4. In the presence of sulfur dioxide, the sample was boiled for ten to fifteen minutes with a known excess of standard hydrochloric or sulfuric acid, depending on whether sulfate or iodide was being determined. This modified analytical scheme was applicable to spent Fischer reagent. The alkali and acid titrations of mixtures containing free or "periodide" iodine were made successfully after destroying the iodine with sodium thiosulfate. The presence of this salt and its reaction product, sodium tetrathionate, did not interfere with the double titration procedure for strong acids and pyridine. When analyzing for sulfate and iodide ions, hydrazine hydrate in neutral or slightly alkaline solution was used instead of sodium thiosulfate to reduce iodine.

(15) Treadwell-Hall, "Analytical Chemistry," 8th ed., John Wiley and Sons, Inc., New York, N. Y., 1935, Vol. II, p. 660.

(16) Kolthoff and Sandell, "Textbook of Quantitative Inorganic Analysis," The Macmillan Co., New York, N. Y., 1936, p. 542.

Summary

1. The stoichiometric relations and mechanism of the reaction of water with Karl Fischer reagent have been investigated.

2. Crystalline intermediates and products of the reaction have been identified by optical crystallographic methods.

3. The nature of a parasitic reaction affecting the stability of the reagent has been clarified.

4. The effect of substituting other amines for pyridine and other solvents for methanol has been investigated.

WILMINGTON, DELAWARE RECEIVED JULY 11, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF ANIMAL AND PLANT PATHOLOGY OF THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH]

The Electro-optical Effect in Certain Viruses

BY MAX A. LAUFFER

Introduction

Kerr[1] was the first to observe that many substances become doubly refracting when placed in a strong electrical field, behaving like uniaxial crystals with optic axes in the direction of the field. As a result of the studies of Raman and Sirkar[2] and of Kitchin and Mueller,[3] it is now known that this effect in homogeneous liquids is due to the orientation of molecules. Colloidal solutions containing rod-like or plate-like particles, such as those of vanadium pentoxide, benzopurpurin, ferric oxide, and bentonite, also show the Kerr effect. It is thought that this is due to the orientation of the anisometric colloidal particles. However, the studies of Errera, Overbeek, and Sack[4] on vanadium pentoxide and benzopurpurin sols and those of Mueller[5] and of Norton[6] on bentonite sols show that the phenomenon in colloids is rather complex and not as yet encompassed by a single simple theory.

Bawden and associates[7] first reported that the particles of tobacco mosaic virus can be oriented by an electric field, *i. e.*, that the material exhibits electrical double refraction. This double refraction was reported recently by the author[8] to be positive with respect to the direction of the electric field. However, more detailed studies have substantiated this observation only in part, for it has been found that under some circumstances the electrical double refraction shown by the viruses may be negative. It is the purpose of this communication to describe further studies on the electrical double refraction of tobacco mosaic virus, the closely related aucuba mosaic of tomato virus, and latent mosaic of potato virus.

(1) Kerr, *Phil. Mag.*, [4] **50**, 337, 446 (1875).

(2) Raman and Sirkar, *Nature*, **121**, 794 (1928).

(3) Kitchin and Mueller, *Phys. Rev.*, **32**, 979 (1928).

(4) Errera, Overbeek, and Sack, *J. chim. phys.*, **32**, 681 (1935).

(5) Mueller, *Phys. Rev.*, **55**, 508, 792 (1939).

(6) Norton, *ibid.*, **55**, 668 (1939).

(7) Bawden, Pirie, Bernal and Fankuchen, *Nature*, **138**, 1051 (1936).

(8) Lauffer and Stanley, *Chem. Rev.*, **24**, 303 (1939).

nary compound, no appreciable thermal change was observed to accompany the mixing of the two binaries, although appreciable heat was evolved during the formation of the individual compounds. The two binary compounds deserve some attention because of the great confusion in the literature regarding their composition and physical properties. Pyridine diiodide was obtained from a 20% solution of iodine in pyridine both by spontaneous evaporation of the solution on a micro slide and also by precipitation by the gradual addition of several volumes of water or hexane. The compound was obtained in glistening orange plates or scales of probable monoclinic symmetry. The crystals decomposed rapidly in air to form a deep brown derivative of greater iodine content, probably $C_5H_5N \cdot I_4$. The compound was more stable under water, hexane or Nujol but gradually darkened. The structure is probably $\left[I \begin{smallmatrix} C_5H_5N \\ I \end{smallmatrix} \right]$,[6] involving an atom of positive monovalent iodine. The identity of the above preparations with a crystalline phase isolated from concentrated Fischer reagent was readily established by measurement of the optic axial angle and observation of the characteristic horizontal dispersion. The compound of pyridine with sulfur dioxide has been formulated both as $C_5H_5NSO_2$[7] and $(C_5H_5N)_2SO_2$.[2] Observations of the melting points in the vicinity of these compositions disclosed a 1:1 compound melting sharply at -4.4 to $-4.8°$ while the 2:1 mixture melting over the range -11 to $-50°$ was obviously not homogeneous. André's 1:1 compound[7] was described as a solid at room temperature, hence was probably polymeric. A small amount of a similar material of unknown composition was obtained on adding about 1% of water to the 1:1 compound.

Nature of Parasitic Side Reactions.—The deterioration of Fischer's reagent on standing was investigated in an effort to discover the reactions responsible and, if possible, prevent their occurrence. Considerable light was thrown upon the side reactions, although no method of inhibiting their progress was found. Chemical analyses of the strong reagent immediately after preparation and after standing for one month disclosed the following facts: (1) essentially complete recovery of iodine as iodide ion regardless of standing time; (2) a pronounced disappearance of both pyridine and total acidity after standing. In freshly prepared reagent, treatment with water and distillation from excess sodium hydroxide permitted a recovery of 97% of the initial pyridine. After standing for one month, similar treatment accounted for only 71% of the pyridine. After the distillation residue became more concentrated, a small amount of distillate with a very sharp amine odor somewhat like piperidine was obtained. This material was alkaline, and reduced potassium permanganate solution rapidly but did not form a crystalline picrate. A considerable amount of brown tarry material remained in the flask. A sample of methylpyridinium iodide distilled with aqueous sodium hydroxide apparently produced the same volatile base, hence it is assumed the methylpyridinium ion was present in both samples. According to Meyer and Jacobson[14] N-alkyldihydropyridines are formed when alkylpyridinium salts are distilled with strong alkali. These are reducing substances. It is not certain whether reaction 5 or 6 is responsible for the formation of the methylpyridinium ion. Reaction 6 is supported by the fact that pyridine and diethyl sulfite on heating reacted sufficiently to give an alkyldihydropyridine on subsequent distillation with alkali.

Substitution of Other Nitrogen Bases for Pyridine.—Separate solutions were prepared by dissolving 42.3 g. of iodine in 50 ml. of methanol and 125 ml. of one of a group of dry nitrogen bases, then cautiously adding 25 ml. of liquid sulfur dioxide to the mixture cooled in a bath of methanol and "dry ice." The solutions were finally made up to 250 ml. with methanol. Each solution was used at intervals to titrate known quantities of water in methanol. The relative stability of the different mixtures was found in this way. The bases tried were quinoline, aniline, dimethylaniline, tri-*n*-butylamine and triethanolamine, with pyridine as a control. All of the above bases had some value as substitutes for pyridine but the reagent employing aniline decomposed almost completely in twenty-four hours. Dimethylaniline was somewhat better. Decomposition of the reagent during preparation was difficult to avoid in the case of triethanolamine. Quinoline and tri-*n*-butylamine closely paralleled pyridine. Other experiments, however, showed that more of the aliphatic amine was required on a molal basis than in the case of pyridine. All of the above amines were analyzed carefully for water content.

Substitution of Other Solvents for Methanol.—Samples of iodine weighing 8.5 g. were each dissolved in 25 ml. of pyridine and 5 ml. of liquid sulfur dioxide carefully added. Each sample was diluted with 50 ml. of one of the following solvents: benzene, dioxane, glacial acetic acid, ethanol, acetonitrile, dimethylformamide, pyridine or methanol. On using these samples to titrate a standard solution of water in methanol, precipitates obscuring the end-point

(14) Meyer and Jacobson, "Lehrbuch der organischen Chemie," Walter de Gruyter and Co., Berlin, 1920, Vol. II, Part 3, p. 799.

TABLE I

OPTICAL PROPERTIES AND MELTING POINTS OF CRYSTALLINE COMPOUNDS ISOLATED

Formula	M. p., °C.[a]	Optic axial angle[b]	Optical character	Dispersion	Miscellaneous observations
$C_5H_5N \cdot I_2$	62	$2H_a = 59 \pm 1°$; $2E = 96.5 \pm 1°$	+	$r > v$, moderate; distinct horizontal dispersion	Orange plates elongated $\parallel \alpha$
$C_5H_5N \cdot HI$	231 (slow dec. at 195°)	Uniaxial	−		Compact colorless or pale yellow crystals
$C_5H_5N \cdot HI \cdot I$	193–195	Uniaxial	+		ω & $\epsilon > 1.75$; pleochroism yellow $\parallel \omega$; red-brown to black $\parallel \epsilon$
$C_5H_5N \cdot H_2SO_4$	101–105	$2H_a = 51 \pm 1°$	−	$r > v$, moderate	$\alpha = 1.430^c \pm 0.005$; $\beta = 1.615 \pm .005$
$C_5H_5N \cdot SO_3$		$2H_0 = 135 \pm 10°$	−		$\alpha = 1.470 \pm .003$; $\beta = 1.690 \pm .003$
$C_5H_5N \cdot HSO_4CH_3$	112–117	$2H_a = 24 \pm 1°$; $2H_0 = 135 \pm 5°$		$r > v$, moderate	Needles and plates elongated $\parallel \beta$

[a] Corrected melting points by Kofler–Hilbck micro heating stage. [b] For details regarding this constant see Bryant, THIS JOURNAL, **60**, 1394 (1938). [c] All refractive indices referred to 5461 Å. Hg light at 25 ± 3°.

$(C_5H_5N)_2H_2SO_4$. Repeated attempts to prepare a "neutral" sulfate of pyridine were unsuccessful. Evaporation of sulfuric acid with large excesses of pyridine invariably gave the acid salt, $C_5H_5NH_2SO_4$, confirming the smaller ratios found in the above experiments. Although the absence of methanol did not prevent the removal of the brown iodine color by water, an abrupt change in the actual amount of water absorbed occurred as the molal ratio of methanol to iodine was reduced below one, while above this ratio only minor differences were observed. In the absence of methanol the water absorbed per mole of iodine at the characteristic end-point varied from 1.1 moles, when water was added to the reagent, to 1.9 moles in the reverse process. In the presence of one mole or more of methanol, about 0.7 mole of water was absorbed regardless of the order of mixing. This is preliminary evidence that, (a) the combination of the reagent with water occurs in two stages, and (b) that methanol can replace water in one stage. The nature of the intermediate and final products will be considered in the following section.

Isolation and Identification of Crystalline Phases.—A mixture of iodine, sulfur dioxide and pyridine in the stoichiometric ratios was not homogeneous at room temperatures but contained some $C_5H_5NI_2$ as a solid phase. Even after the addition of sufficient excess pyridine to produce a homogeneous solution, crystalline solid phases were obtained on the addition of water. When water was added directly to this mixture much heat was evolved and a slightly yellowish crystalline phase was obtained consisting of pyridine hydriodide and pyridine hydrogen sulfate. When, however, the reagent mixture was poured slowly onto chopped ice and stirred to prevent local heating, fine buff-colored plate-like crystals were formed. This material was identified as pyridine-sulfur trioxide, and is undoubtedly the intermediate compound predicted in the molal composition studies. In agreement with Baumgarten,[3] the compound was difficultly soluble and stable for an hour or two in ice water. It was converted rapidly to pyridine hydrogen sulfate by hot water and to pyridine methyl sulfate by methanol at room temperature. The action of methanol is evidently much less at 0°, since the "inner salt" was obtained by ice treatment of strong reagent containing up to ten moles of methanol. Vacuum evaporation of partly "spent" reagent also yielded some pyridine-sulfur trioxide along with brown crystals of pyridine hydroperiodide, $C_5H_5NHI \cdot I$.

Identification of the above crystalline materials was made by comparing the optical crystallographic properties with those of the known salts. This did not involve a complete optical study but simply observation or measurement of a sufficient number of optical properties to ensure identification (Table I).

Analytical data for the compounds included in Table I are as follows

Compound	Calculated, %	Found, %
$C_5H_5N \cdot I_2$	I, 76.3	I, 75.4, 75.7
$C_5H_5N \cdot HI$	HI, 61.8; C_5H_5N, 38.2	HI, 62.1; C_5H_5N, 37.4
$C_5H_5N \cdot HI \cdot I$	I, 38.0	I, 38.5
$C_5H_5N \cdot H_2SO_4$	H_2SO_4, 55.4; C_5H_5N, 44.6	H_2SO_4, 53.8; C_5H_5N, 44.5; H_2O, 0.6
$C_5H_5N \cdot SO_3$	SO_3/C_5H_5N, 1.000	SO_3/C_5H_5N, 1.002
$C_5H_5N \cdot HSO_4CH_3$	HSO_4CH_3, 58.7; C_5H_5N, 41.3	HSO_4CH_3, 57.8; C_5H_5N, 41.1

Analyses of $C_5H_5NSO_3$ indicated the presence of a considerable amount of "adsorbed" water. Consequently the observed SO_3/C_5H_5N ratio is given instead of the weight composition.

Chemical Nature of the Reagent.—It was first believed that the active constituents of Fischer's reagent were present as a complex compound of pyridine with sulfuryl iodide analogous to acetylpyridinium chloride formed from pyridine and acetyl chloride. However, all evidence to this effect has so far been negative and the reagent is now believed to be a mixture of the two binary compounds $C_5H_5NI_2$ and $C_5H_5NSO_2$. In addition to the failure to isolate a crystalline ter-

line, aniline, dimethylaniline, tri-*n*-butylamine and triethanolamine can be used although not with equal success. Close to four moles of tri-*n*-butylamine instead of three are necessary. The stability of the reagents prepared with aniline, dimethylaniline and triethanolamine was very poor. All factors considered, pyridine was the most satisfactory base employed.

The principal disadvantage of most organic solvents when incorporated in the reagent is their failure to dissolve the amine salts produced by the action of water. Where salts are thrown out of solution, the end-point is obscured to a serious degree. Only a few solvents were found free from this objection. Methanol, dimethylformamide and pyridine are satisfactory. Ethanol is fairly good but shows some tendency to deposit pyridine hydriodide crystals.

Fischer has discussed applications of his analytical technique in the determination of water in liquids and solids, both organic and inorganic, including benzene, liquid sulfur dioxide, methanol, acetone, petroleum fractions, fuller's earth, hydrated copper sulfate and calcium carbonate.[9] As a result of three years' laboratory experience with the method, the present writers recommend it for the determination of water in the following classes or organic compounds: alcohols, hydrocarbons, including saturated, ethylenic and aromatic types, carboxylic acids (except formic acid) and esters. Some weak tertiary amines can be titrated directly, but a better and more general procedure for amines involves the solution of the amine in an excess of glacial acetic acid of known water content, before titration. On titration with the regular reagent, the behavior of aldehydes and ketones is unsatisfactory due to the formation of acetals and ketals with the large excess of methanol in the reagent and the attendant liberation of water. Rapidly fading end-points and erroneously high apparent water contents are characteristic.[10] By greatly reducing the methanol content and increasing the pyridine in regular Fischer reagent, a modified reagent is obtained which reacts normally in the presence of ketones provided large amounts of the lower alcohols are absent. The writers have confirmed Fischer's surprising observation that the iodine in the reagent shows practically no tendency to react with ethylenic double bonds.

(9) Kaufmann and Funke [*Fette und Seifen*, **44**, 345 (1937)] describe the use of the reagent in determining water in fats.

(10) Fischer's apparent success with acetone is difficult to explain.

Experimental

Preparation of the Reagent.—One-liter quantities of Karl Fischer reagent are prepared by dissolving 84.7 g. (0.33 mole) of Mallinckrodt resublimed U. S. P. iodine in a mixture of 269 ml. (3.3 moles) of pyridine and 667 ml. of du Pont synthetic methanol. The above solution is cooled in a slurry of chopped ice and 64 g. (1 mole) of liquid sulfur dioxide cautiously added. The final dark brown solution is about twice as strong as Fischer employed but is essentially the same in other respects. The water content of the solvents used should not exceed 0.1% since the presence of as much as 6 g. of water per liter will completely exhaust the reagent. (The color of the spent reagent is chromate yellow.) The solution deteriorates rapidly during the first week but more slowly thereafter.[11] The special reagent for use in the presence of ketones is prepared as above but using 860 ml. of pyridine and 90 ml. of methanol per liter instead of the quantities originally specified. A suction-filling reservoir buret[12] protected by calcium chloride towers is the most satisfactory dispensing device.

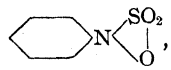
Standardization of the Reagent.—A supply of dry methanol (<0.1% water) is reserved for the preparation of a standard water solution. Several 10-ml. samples of it are titrated with the unstandardized reagent and the average titer recorded. About 18 ml. of distilled water is weighed carefully into a 1-liter volumetric flask, made up with the methanol and adjusted to volume after standing in a thermostat at 25 ± 1°. Ten-ml. samples of this solution are titrated with the reagent until the brown color of iodine persists. The average titer is recorded. It can be assumed with sufficient precision that this titer corresponds to the aliquot of the water weighed in, plus 98% of the titer of the original methanol. Deduction of the titer due to water originally present with the methanol gives the titer due solely to the added water, which constitutes a standardization of the Fischer reagent. Reference to the uncorrected titer of the water solution now permits a calculation of the water in the final methanol solution. The latter solution is preserved as a standard for daily evaluation of the reagent.

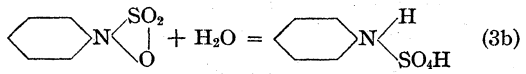
Establishment of the Stoichiometric Composition.—Since the brown color of Fischer reagent evidently is due to the presence of free iodine, its disappearance on the addition of water affords a means of verifying the stoichiometric ratios of the individual constituents of the reagent. Starting with aliquots of a dimethylformamide solution each containing 8.5 g. of iodine (33 mmol.), the relative amounts of the other constituents, sulfur dioxide and pyridine were decreased individually until titration with a molar solution of water in dimethylformamide just failed to discharge the brown color of the solution. The minimum ratios were: $I_2:SO_2:C_5H_5N = 1:1:3$. Fischer's equation corresponds to the ratios, 1 : 1 : 4[13] and is based on the assumption that pyridine forms a "neutral" sulfate,

(11) Little if any loss of strength occurs before the addition of sulfur dioxide, hence it is convenient to store the solution in this form and defer adding sulfur dioxide until a day or two before use. The reagent is conveniently prepared in 3-liter quantities.

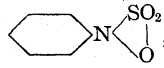
(12) Item No. 750, supplied by Eck and Krebs, 131 West 24th St., New York, N. Y.

(13) The regular reagent contains a considerable excess of sulfur dioxide and pyridine, corresponding to ratios of 1:3:10.

Only the first involves water absorption, and the stoichiometric amount of this substance is but half that required for Fischer's reaction 1. The intermediate compound,  , can be isolated,[3] especially if methanol is omitted from the reagent. It was found possible to prepare a modified reagent (without methanol) by which the water absorbed approached the two moles required by equation 1

 (3b)

The general use of such a reagent, however, appears undesirable for the following reasons. First, reaction 3b is not specific for water as is reaction 2 but also takes place with alcohols (reaction 3a) and presumably with other compounds containing active hydrogen. Second, reaction 3b may be used only indirectly since it is not accompanied by a color change. (The indicator action of reaction 2 may be utilized in certain cases to follow the course of 3b.) Third, the water equivalence of the reagent varies greatly with minor differences of technique. Fourth, in the absence of methanol the reagent soon discolors.

By reducing the ratios of sulfur dioxide and pyridine to iodine, until in each case the iodine color no longer could be discharged on titration with a standard water solution, the stoichiometric ratios were found to be $I_2:SO_2:3C_5H_5N$, in support of equation 2. Further it was found that the presence of as much as one mole of methanol per mole of iodine would completely inhibit absorption of the second mole of water according to equation 3b, in support of equation 3a. In addition to the compound  , all of the other products of reactions 2, 3a and 3b have been isolated and identified by comparison with the synthetic materials.

The literature gives little indication of the chemical nature of solutions of iodine and sulfur dioxide in pyridine. Since according to Mellor[4] iodine and sulfur dioxide do not combine appreciably to form sulfuryl iodide

$$I_2 + SO_2 = SO_2I_2 \qquad (4)$$

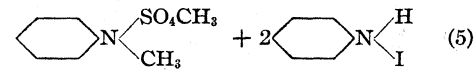
(3) This substance is really the "inner salt" of pyridinium hydroxide-N-sulfonic acid. It has been prepared previously by other methods. Baumgarten, *Ber.*, **59**, 1166 (1926); **64**, 1502 (1931); **64**, 1582 (1931).

(4) Mellor, "A Comprehensive Treatise on Inorganic and Theoretical Chemistry," Longmans, Green and Co., Ltd., London, 1930, Vol. X, p. 676.

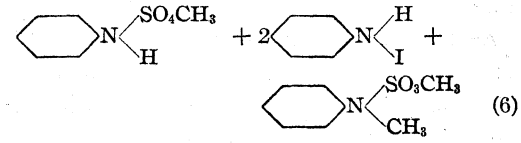
this iodide as such is not regarded as a likely constituent of the reagent although it may possibly be involved in the mechanism.

Binary combinations of pyridine with both iodine[5,6] and sulfur dioxide[2,7] are known, although accounts of their composition are conflicting. The existence of the binary compounds $C_5H_5NI_2$ and $C_5H_5NSO_2$ was verified in this Laboratory and some of their physical constants observed. The composition of the sulfur dioxide compound was established by melting point studies, and the formula $2(C_5H_5N)_2SO_2$ postulated by Karl Fischer shown to be incorrect. It is believed that the iodine and sulfur dioxide in Fischer reagent are present largely as the 1:1 compounds with pyridine. No ternary compounds have as yet been isolated.

While equations 2 and 3a fix the maximum absorption of water by the regular reagent at one mole per mole of iodine, this theoretical efficiency is rarely attained because of side reactions. Freshly prepared reagent is usually equivalent to 70% of the theoretical water but in the course of a month or two its strength falls to about 40%. The side reactions have been found to involve the reduction of iodine to the iodide ion and the formation of quaternary methylpyridinium salts, probably as follows

$I_2 + SO_2 + 3C_5H_5N + 2CH_3OH =$  (5)

or

$I_2 + 2SO_2 + 4C_5H_5N + 3CH_3OH =$  (6)

Contrary to earlier assumptions on this subject,[8] no evidence of the iodination of pyridine has been observed, since practically all of the iodine can be recovered from the spent reagent as iodide. The reagent is so readily standardized empirically that the lack of stability is only a minor consideration in connection with its analytical use.

Substitution of other bases for pyridine in the preparation of Fischer reagent proved feasible although not advantageous. For example, quino-

(5) Carlsohn, "Über eine neue Klasse von Verbindungen des positiv einwertigen Iods," S. Hirzel, Leipzig, 1932, p. 6.

(6) M. Chatelet, *Ann. chim.*, [2] **2**, 5 (1934).

(7) André, *Compt. rend.*, **130**, 1714 (1900).

(8) Ref. 2, p. 395; ref. 5, p. 45.

This equation indicates that titanium is somewhat more effective as a deoxidizer in steel than would be calculated from the equation of Chipman, which gives for the reaction

$$\Delta F^\circ = -151{,}000 + 57.3T$$

The deoxidation constants usually are expressed as the reciprocals of the constants of the deoxidation reactions; *i. e.*, $K = [\%\text{Ti}] \times [\%\text{FeO}]^2$. The values of these constants calculated from the authors' and from Chipman's equations are compared in Table II at several temperatures.

TABLE II

DEOXIDATION CONSTANTS

Temp., °C.	1500	1600	1700
Chipman	8.2×10^{-7}	8.1×10^{-6}	6.2×10^{-5}
Authors	3.2×10^{-9}	4.3×10^{-8}	4.4×10^{-7}

The authors wish to thank Professor J. G. Aston of Pennsylvania State College who made available the standard couple, S-6, for calibration of our calorimeter; Dr. C. S. Barrett of the Metals Research Laboratory of this Institute for the X-ray photographs of the oxide used in this investigation; and Mr. J. W. Stewart, of the same laboratory, for the spectroscopic analysis.

Summary

1. The heat capacity of titanium dioxide (rutile) has been determined from 68–298°K.

2. The entropy of titanium dioxide has been computed from these measurements and found to be 12.45 e. u. at 298.1°K.

3. The thermodynamic properties of titanium dioxide have been evaluated, and applied to the problem of the deoxidation of steel by titanium.

PITTSBURGH, PENNA. RECEIVED JUNE 28, 1939

[CONTRIBUTION FROM THE AMMONIA DEPARTMENT OF E. I. DU PONT DE NEMOURS & COMPANY, INC.]

Analytical Procedures Employing Karl Fischer Reagent. I. Nature of the Reagent

BY DONALD MILTON SMITH, W. M. D. BRYANT AND J. MITCHELL, JR.

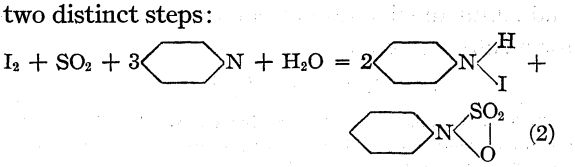
The determination of water in mixtures by specific chemical methods has become an essential part of analytical chemistry. The senior authors[1] described such a procedure based on the hydrolysis of acetyl chloride in the presence of pyridine. Almost simultaneously another water method of unusual simplicity and range of application but based on a different chemical reaction was described by Karl Fischer.[2] The latter method involves a direct titration of the wet material with a solution of iodine, sulfur dioxide and pyridine in methanol, the reagent serving as its own indicator. The two methods have unique advantages in specific types of analysis, but the general analytical value of Fischer's method is sufficiently great to render desirable a detailed study of its underlying chemistry and a presentation of some of its significant applications.

Fischer has given a good practical discussion of the preparation and use of his reagent but has only briefly outlined the reactions involved. The latter, however, while partly correct as given, do not adequately explain the observed quantitative results. For example, his reaction

$$2H_2O + I_2 + SO_2 \cdot 2C_5H_5N + 2C_5H_5N = (C_5H_5N)_2H_2SO_4 + 2C_5H_5NHI \quad (1)$$

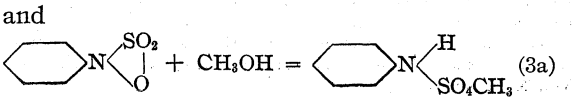
calls for the removal of two moles of water for each mole of iodine introduced, while the writers find that actually about one mole or less of water is removed by the unmodified reagent. In order to shed more light on the mechanism and stoichiometric relations upon which Fischer's method is based, the present paper includes a study of the fundamental molal ratios of the various constituents of the reagent and their relation to water removal. By working with concentrated solutions, crystalline intermediates and products were isolated and identified by optical crystallographic methods. Other bases were substituted for pyridine and other solvents for methanol, and the effect of the various modifications noted.

One of the most interesting results was the discovery that the fundamental reaction occurs in two distinct steps:



(2)

and



(3a)

(1) Smith and Bryant, THIS JOURNAL, **57**, 841 (1935). This reference includes a brief review of earlier work.

(2) Karl Fischer, *Angew. Chem.*, **48**, 394 (1935).

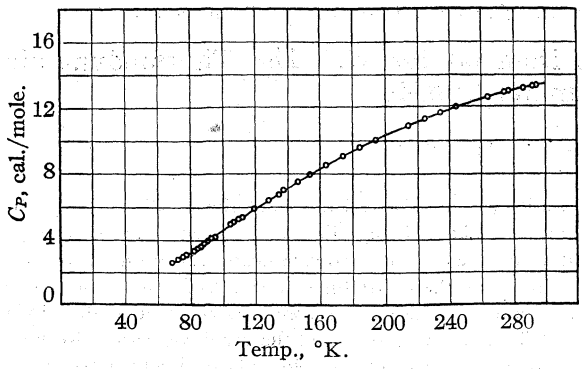


Fig. 1.—Molal heat capacities of TiO_2.

68–175°K. At 68°K., the contribution of the Debye function to the entropy was 1.23 e. u., while that of the two equal Einstein functions was less than the probable experimental error. Between 68–298.1°K., the entropy change was evaluated graphically and amounted to 11.22 e. u. The sum of these values yields 12.45 e. u. for the entropy of titanium dioxide(rutile) at 298.1°K. The accuracy of this figure, with the small extrapolation, is estimated to be within ±0.1 e. u.

Thermodynamic Properties of Titanium Dioxide.—Using accepted[5] values for the entropies of the elements, $\Delta S_{298.1} = -43.18$ e. u. for formation of the oxide. The heat of formation of titanium dioxide has been determined by several investigators, and the latest and apparently most reliable value is that of Neumann, Kroger and Kunz.[6] They find $\Delta H_{298} = -225{,}300 \pm 300$ cal. for formation of the oxide. From this value and the entropy of formation we calculate $\Delta F^\circ_{298.1} = -212{,}430$ cal., for the standard free energy of formation, and thus we can write

$$Ti(s) + O_2(g) = TiO_2(rutile);\quad \Delta S_{298.1} = -43.18 \text{ e. u.};\quad \Delta H_{298.1} = -225{,}300 \text{ cal.};\quad \Delta F_{298.1} = -212{,}430 \text{ cal.}$$

Nasu[7] has studied the equilibrium

$$Ti_2O_3(s) + H_2O(g) = 2TiO_2(s) + H_2(g)$$

and has calculated from these equilibrium measurements, $\Delta H_{298.1} = -4700$ cal.; $\Delta F^\circ_{298.1} = -5280$ cal. Combining these data with those for TiO_2 and $H_2O(g)$ we calculate for the entropy of $Ti_2O_3(s)$; $S_{298.1} = 9.0$ e. u. This value appears much too low for an oxide of this type for which an entropy between 20 and 30 e. u. would be expected. This might indicate some serious error in the equilibrium measurements.

(5) Kelley, Bureau of Mines Bulletin 394, 1935, p. 35.

(6) Neumann, Kroger and Kunz, *Z. anorg. allgem. Chem.*, **218**, 379 (1934).

(7) Nasu, *J. Chem. Soc. Japan*, **56**, 542 (1935).

Deoxidation of Steel by Titanium.—Titanium is used occasionally as a deoxidizer in steel and Chipman[8] has attempted to approximate the free energy equation for the deoxidation reaction

$$2FeO(\%\text{ in Fe}) + Ti(\%\text{ in Fe}) = 2Fe(l) + TiO_2(s)$$

From the data on the formation of titanium dioxide, given above, it should be possible to arrive at a satisfactory free energy equation for this reaction applicable at liquid steel temperatures. From the tables by Kelley[9] we find for the reaction: $Ti(s) + O_2(g) = TiO_2(s)$, $\Delta C_p = -5.37 + 6.14 \times 10^{-3}T + 5.788 \times 10^5 T^{-2}$, and in the usual manner express the standard free energy change of the reaction

$$\Delta F^\circ = -222{,}030 + 5.37T \ln T - 3.07 \times 10^{-3}T^2 - 2.894 \times 10^4 T^{-1} + 5.70T$$

In the temperature range, 1500–1800°C., this can be put in the linear form, approximately

$$\Delta F^\circ = -223{,}800 + 41.2T$$

To convert from Ti(s) to Ti(l), the melting point of titanium is taken as 2273°K. and the ΔH of fusion is estimated on the assumption that, like silicon, the entropy of fusion is 5.5 e. u./gram atom at the melting point, from which it follows

$$Ti(s) = Ti(l);\quad \Delta F^\circ = 12{,}500 - 5.5T$$

Evaluation of ΔF° for the change Ti(l) = Ti(% in Fe) presents some difficulty since a compound Fe_3Ti appears in the iron–titanium system and hence in dilute liquid solutions of titanium in iron marked negative deviations might be expected, and the limiting Henry's law value of the activity coefficient, a/N, for titanium must reach a value considerably less than unity. In the study of liquid metal systems from which intermetallic compounds appear as solid phases, one of the authors[10] has shown that a reasonable estimate of the value of this coefficient is of the order of 0.2. Hence, we can write for low concentrations of titanium

$$Ti(l) = Ti(\%\text{ in Fe})$$
$$\Delta F^\circ = -4.58T \log \frac{100 \times 47.9}{0.2 \times 55.84} = -9.5T$$

Chipman[8] has determined the standard free energy change for the reaction: $Fe(l) + \frac{1}{2}O_2(g) = FeO(\%\text{ in Fe})$, for which in the steel-making temperature range: $\Delta F^\circ = -31{,}780 - 1.16T$. Combining the four equations

$$2FeO(\%\text{ in Fe}) + Ti(\%\text{ in Fe}) = 2Fe(l) + TiO_2(s)$$
$$\Delta F^\circ = -172{,}700 + 58.5T$$

(8) Chipman, *Trans. Am. Soc. Metals*, **22**, 385 (1934).

(9) Kelley, Bureau of Mines Bulletin 371 (1932).

(10) Seltz and DeWitt, THIS JOURNAL, **60**, 1305 (1938).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, CARNEGIE INSTITUTE OF TECHNOLOGY]

The Heat Capacities of Titanium Dioxide from 68–298°K. The Thermodynamic Properties of Titanium Dioxide

BY HUGH J. MCDONALD[1] AND HARRY SELTZ

In an extension of a program of research in these Laboratories on the thermodynamic properties of metal systems, a low temperature calorimeter of the Nernst type has been constructed. In this paper, the results of heat capacity measurements on titanium dioxide from 68–298°K. are described and the entropy of this compound is calculated. From published heats of formation and heat capacities at higher temperatures, the complete thermodynamic properties of the oxide are derived.

Material.—The titanium dioxide used in these measurements was the purest that could be obtained commercially. Spectroscopic analysis showed that the only detectable impurity present was silica. Chemical analysis fixed the amount of this oxide at less than 0.4% and, as the difference between the heat capacity of titanium dioxide and silicon dioxide is small, the error thereby introduced is negligible. There are three allotropic modifications of titanium dioxide, rutile, anatase and brookite, and it was necessary to establish the form of the material used in this investigation from an X-ray powder photograph. Comparison of the X-ray pattern obtained with that of rutile showed perfect agreement for all the characteristic lines.

In order to get the greatest weight of the oxide, which was quite fluffy, into the calorimeter it was pressed into pellets which were ignited in a large platinum crucible for two hours and then broken into small pieces. The X-ray diffraction pattern was not altered by the ignition. The total charge of titanium dioxide used was 87.958 g. (*in vacuo*), or 1.1008 moles.

Apparatus.—The calorimeter used in these measurements was modeled after that described by Gibson and Giauque,[2] and since no significant modifications were made, it will not be described further. The calibrations of the calorimeter and shield windings were made by comparison with copper–constantan couples previously checked against a standardized couple, S-6, which was made available through the kindness of Professor J. G. Aston of Pennsylvania State College. This couple had been calibrated in terms of a helium thermometer.[3] In comparing our couples with S-6 they were soldered with Wood's metal in deep holes in a copper cylinder and electromotive force readings were made with a White double potentiometer over the entire temperature range under conditions comparable to those in the actual measurements. These couples were then soldered in wells in the shield and in the calorimeter and the resistances of the windings were calibrated against them. Frequent checks during specific heat runs have shown no significant variations in the resistances of these windings during the past year. The specific heat measurements were carried out as described by Gibson and Giauque[2] and the usual corrections for heat interchange between the shield and calorimeter were made. The free space in the calorimeter was filled with hydrogen during the measurements and rapid distribution of heat was achieved as indicated by a negligible temperature lag after introduction of the electrical energy. The over-all accuracy of the measurements of the heat capacities of titanium dioxide is believed to be ±0.3%.

Experimental Results

In Table I, the experimental heat capacities for titanium dioxide are given. The conversion from electrical energy to defined calories was made on the basis of 1 calorie = 4.1833 international joules. The results are plotted in Fig. 1.

TABLE I

MOLAL HEAT CAPACITIES OF TiO_2 (RUTILE)

Series I		Series II	
T, °K.	C_p	T, °K.	C_p
85.40	3.58	68.78	2.67
89.15	3.87	73.06	2.85
93.23	4.20	77.80	3.09
106.02	5.04	82.10	3.29
112.09	5.33	86.13	3.60
119.50	5.87	90.05	3.89
128.35	6.40	94.32	4.19
137.52	7.00	105.60	5.01
153.80	7.89	109.69	5.21
163.53	8.49	134.65	6.73
174.28	9.06	146.68	7.53
184.36	9.57	277.09	12.95
194.77	10.07	286.40	13.23
215.08	10.98	291.90	13.36
224.70	11.34		
234.22	11.70		
244.20	12.01		
264.22	12.66		
274.23	12.98		
295.07	13.44		

Calculations

The Entropy of TiO_2.—The method suggested by Kelley[4] was used to extrapolate the heat capacity values from 68–0°K. It was found that

$$C_v = D(306/T) + 2E(670/T)$$

fitted the experimental curve satisfactorily from

(1) Abstracted from a thesis presented by Hugh J. McDonald to the Committee on Graduate Instruction of the Carnegie Institute of Technology, in partial fulfilment of the requirements for the degree of Doctor of Science, June, 1939.

(2) Gibson and Giauque, THIS JOURNAL, **45**, 93 (1923).

(3) Aston, Willihnganz and Messerly, *ibid.*, **57**, 1642 (1935).

(4) Kelley, Bureau of Mines Bulletin 350, (1932), p. 8.

On cooling, a bright orange powder formed. This was washed with alcohol and ether.

Anal. Calcd. for $[Coen_2leu]Cl_2$: Cl, 18.66. Found: Cl, 19.26.

This salt was converted to the *d*-bromo-pi-camphorsulfonate through the action of the silver salt. Attempts to crystallize an active salt from water and water–alcohol solutions met with failure, as only glassy solids were formed.

The Reaction between Racemic Propylenediamine and Optically Active Cobalt Salts.—Racemic propylenediamine was added in 100% excess to solutions of $[Co(l\,pn)_2Cl_2]Cl$, $[Co(l\,pn)_2(NO_2)_2]NO_2$, and $[Co(l\,pn)_2CO_3]_2CO_3$ at various temperatures and concentrations. Complete reaction took place in every case. The excess propylenediamine was recovered (by vacuum distillation or steam distillation) as the racemic base, so the two isomers must have entered the complex at equal rates.

The Preparation and Reactions of the Luteo Chromammines.—Triethylenediamine chromic chloride[12] was resolved and converted to the active iodide as described by Werner.[13] The iodide in 0.5% solution showed $[\alpha]^{25}D$ +67°, somewhat higher than the +60° reported by Werner.

Tri-levo-propylenediamine chromic chloride may be prepared in the same way or by the method of Pfeiffer.[14] The latter method gives a good yield only if concentrated (80% or more) propylenediamine is used. The luteo chloride may be converted readily by metathetical reactions to the less soluble and more stable bromide, iodide, or thiocyanate. The iodide was recrystallized from boiling water.

Anal. Calcd. for $[Cr(l\,NH_2CH(CH_3)CH_2NH_2)_3]I_3\cdot H_2O$, 56.61% iodide. Found, 56.43%. For a 0.55% solution, $[\alpha]^{25}D$ −26.04°.

The two luteo salts react with phenylalanine in the same way, so only one experiment need be described. To 6 g. of phenylalanine in 250 cc. of water was added 5 g. of $[Cren_3]Br_3\cdot 3H_2O$, and the mixture was heated on the steam-bath for six hours. The lavender precipitate which formed was filtered from the pink solution and washed with hot water. The yield is nearly quantitative.

Anal. Calcd. for $(C_6H_5\,ala)_2Cr\langle{}^{OH}_{OH}\rangle Cr(C_6H_5\,ala)_2$: Cr, 13.10; N, 7.05. Found: Cr, 13.41; N, 7.23.

The compound is insoluble in hot or cold water and the usual organic solvents. It is easily soluble in nitric acid, but only slightly soluble in hydrochloric and 50% sulfuric acids. The acid solutions slowly turn green, indicating decomposition. In the attempted resolutions, a 100% excess of phenylalanine was allowed to react with $d[Cren_3]I_3\cdot H_2O$ or $[Cr(l\,pn)_3]I_3\cdot H_2O$. The precipitated tetraphenylalanine-diol-dichromium was examined for optical activity in 50% sulfuric acid. None was observed in any case. The filtrate from the lavender precipitate was made basic, the ethylenediamine or levo-propylenediamine steam distilled out, and the residual phenylalanine examined for optical activity. In every case, it was inactive.

Summary

1. The possibility of using optically active complex ions of cobalt and chromium in the resolution of diamines, dibasic acids and amino acids has been investigated. Positive results have not yet been obtained.

2. An improved method of preparing dichlorodipropylenediaminocobaltic chloride is described.

3. The reaction of luteo chromic salts with phenylalanine has been investigated. This is apparently a new type of reaction, and leads to the formation of tetraphenylalanine-diol-dichromium. The insolubility of this compound suggests the possibility of its use in the separation of phenylalanine from other amino acids.

URBANA, ILLINOIS RECEIVED JUNE 12, 1939

(12) Balthis and Bailar, THIS JOURNAL, **58**, 1474 (1936). A much better method of preparing these salts has been devised since this work was done. It will be described in a forthcoming article.

(13) Werner, *Ber.*, **45**, 866 (1912).

(14) Pfeiffer, *Z. anorg. Chem.*, **24**, 286 (1900).

$[Cr(l\text{-pn})_3]I_3$ and optically active $[Cren_3]I_3$. The complex compounds containing levo-propylenediamine may offer an advantage over those of ethylenediamine because they do not racemize; the optically active diamine forces a definite configuration upon the complex ion.

The reaction of racemic propylenediamine with the cobalt complexes is a simple penetration reaction, both antipodes of the base taking part with equal readiness

$$2[Co(l\text{-pn})_2X_2]X + d,l\text{-pn} \longrightarrow [Co(l\text{-pn})_3]X_3 + [Co(l\text{-pn})_2(d\text{-pn})]X_3$$

The mixed complex ion doubtless rearranges at once, as Smirnoff[4] has shown. The compound formed when alanine reacts with $[Co(l\text{-pn})_2Cl_2]Cl$ is quite stable, and evidently has the formula $[Co(l\text{-pn})_2(ala)]Cl_2$. Both the *d*- and the *l*-alanine react, and several stereoisomers of the product are possible. Their excessive solubility prevented their separation, however. The reaction of $[Coen_2Cl_2]Cl$ with leucine was studied with the thought that each form of the amino acid might react selectively with one form of the complex ion. This would give rise to two mirror-image isomers, $[Coen_2(leu')]^{++}_D$ and $[Coen_2(leu'')]^{++}_L$,[5] which might be separated by resolution. The two forms of the amino acid could then be recovered from these complexes. Unfortunately, however, the salts are so soluble that all attempts at resolution failed.

The reaction of phenylalanine with the luteo chromic salts is more complicated, as the diamine molecules are completely expelled from the complex

$$[CrA_3]I_3 + C_6H_5CH(NH_2)CH_2COOH \longrightarrow [(Phenylala)_2Cr(OH)_2Cr(Phenylala)_2] + 3A\cdot HI$$

The reaction must take place in steps, so at least the first phenylalanine molecules which react are subject to whatever stereochemical influences the complex may exert. The optically active luteochromic salts did not effect a resolution of the phenylalanine, but the reaction is of some interest because of the insolubility of the tetraphenylalanine-diol-dichromium. It might possibly be used in the separation of phenylalanine from other amino acids. Ley and Ficken[6] have prepared the corresponding glycine and alanine compounds, and report them to be somewhat soluble in water.

(4) Smirnoff, *Helv. Chim. Acta*, **3**, 177–195 (1920).

(5) leu' and leu'' represent the two mirror image forms of leu.

(6) Ley and Ficken, *Ber.*, **45**, 380–382 (1912).

Experimental

Preparation of $[Co(l\text{ pn})_2Cl_2]Cl$.—The method of Werner and Frolich[7] was modified as follows: 50 g. of cobalt chloride hexahydrate is dissolved in 1200 cc. of water, containing 25 g. of *l*-propylenediamine. The base is resolved according to the directions of Bauman[8] except that calcium hydroxide is substituted for potassium hydroxide. Air is bubbled through the solution for sixteen hours, slowly at first, so as not to sweep out any of the uncoördinated propylenediamine. Twelve hundred cubic centimeters of concentrated hydrochloric acid is added, and the solution concentrated *in vacuo* (at a temperature not above 70°) to 200 cc. On standing at room temperature for a day, 30 g. of the green *trans*-dichloro salt separate. Evaporation of the filtrate to 150 cc. yields another 3 g. of slightly less pure material. The crystals may be purified by dissolving in alcohol and precipitating with ether. The *trans* salt readily may be changed to the gray-purple *cis* isomer by heating to 100° in an acid-free atmosphere. This was not necessary in these studies, as rearrangement to the *cis* form takes place when an amino acid or propylenediamine is introduced into the molecule. The dichloro salt may be changed to the dinitro or to the carbonato salt by treatment with the appropriate silver salt.

The reaction of alanine with $[Copn_2Cl_2]Cl$ was adapted from the directions of Meisenheimer, Angermann and Holsten.[9] A solution of 1.5 g. of alanine in 20 cc. of water was added slowly and with stirring to a mixture of 5 g. of $[Co(l\text{ pn})_2Cl_2]Cl$ and 2 g. of sodium acetate in 30 cc. of water. The solution became blood red at once, but was heated on the steam-bath for one-half hour to ensure completion of the reaction. The extremely soluble salt was obtained in crystalline form by evaporation to dryness, solution in absolute alcohol, and precipitation with ether. The red crystals were kept over phosphorus pentoxide for several days before analysis.

Anal. Calcd. for $[Co(l\text{ pn})_2ala]Cl_2$: C, 29.51; H, 7.15; N, 19.13. Found: C, 29.38; H, 7.52; N, 19.38.

In another experiment the $[Co(l\text{ pn})_2Cl_2]Cl$ was allowed to react with twice the theoretical amount of racemic alanine. The unused alanine was precipitated as the double mercury salt,[10] freed from the mercury by hydrogen sulfide, and recrystallized from water. Slightly more than half of the alanine was recovered. It showed no optical activity.

The reaction of leucine with $[Coen_2Cl_2]Cl$ was carried out in a similar manner. Five and eight-tenths grams of *trans* $[Coen_2Cl_2]Cl$,[11] 3.49 g. of leucine and 1 g. of sodium carbonate were heated together on the steam-bath in 75 cc. of water. Carbon dioxide was evolved slowly, and the blood red color of the carbonato salt gave way to orange-red. After twelve hours, the reaction was apparently complete, and the mixture was evaporated to about 15 cc.

(7) Werner and Frohlich, *ibid.*, **40**, 2225 (1907).

(8) Bauman, *ibid.*, **28**, 1180 (1895).

(9) Meisenheimer, Angermann and Holsten, *Ann.*, **438**, 266 (1924).

(10) Neuberg and Kerb, *Biochem. Z.*, **40**, 498–513 (1912).

(11) Jörgensen, *J. prakt. Chem.*, **39**, 16 (1889); **41**, 448 (1890).

shown[4] that graphite on oxidation with nitric acid and alkaline permanganate furnishes mellitic and carbonic acids exclusively and studies on the behavior of mellitic acid in the bomb, under the same conditions which were used for the oxidation of graphite, showed that 97% of the carbon of a 25-g. sample was converted to carbon dioxide in twenty-four hours.

The method used for isolation of the individual acids, barium salt fractionation, followed by esterification and vacuum fractionation of the esters, was essentially the same as applied to the acids prepared by the action of alkaline permanganate on the Pittsburgh Seam coal. As in that work, it was found that a significant fraction of the methyl esters will not distil under conditions where the least volatile of the esters of the benzene carboxylic acids, the hexamethyl mellitate, distils rapidly.

Summary

Several types of carbonaceous materials, ranging in rank from an Illinois bituminous coal to artificial graphite, have been oxidized to simple acids by oxygen at elevated pressures, at temperatures of 200 to 250°, in the presence of aqueous alkali. With the lower rank materials a significant fraction of the carbon can be recovered as simple organic acids. From the materials of rank higher than a low temperature coke, decreasing recoveries of organic acids are obtained, and with graphite the soluble products consist almost exclusively of carbonic acid. The effects of temperature, time, oxygen partial pressure, catalysts, surface, and nature of the alkali on the course of the oxidation of a Pittsburgh Seam coal have been studied. Oxalic, trimellitic, pyromellitic, prehnitic, and terephthalic acids have been identified. A significant fraction of the acids forms non-distillable methyl esters, indicating the presence of structures more complex than the benzenecarboxylic acids.

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[CONTRIBUTION FROM THE NOYES LABORATORY OF CHEMISTRY OF THE UNIVERSITY OF ILLINOIS]

The Stereochemistry of Complex Inorganic Compounds. IV. The Introduction of Racemic Organic Molecules into Some Optically Active Complex Ions of Cobalt and Chromium[1]

BY JOHN C. BAILAR, JR., C. A. STIEGMAN, J. H. BALTHIS, JR., AND E. H. HUFFMAN

The penetration of a molecule of an optically active diamine, dibasic acid or amino acid into an optically active complex of the type $[MA_2X_2]$[2] offers several stereochemical possibilities. In some cases, all of the possible stereoisomers of the reaction product are realized. Thus, levo-1,2-*trans*-diaminocyclopentane reacts with racemic dichlorodiethylenediaminocobaltic chloride, $[Coen_2Cl_2]Cl$, to give both the D and the L forms of $[Coen_2$-*l*-Cptdn$]Cl_3$.[3]

Sometimes, however, the entrance of the new group takes place only in certain preferred ways; this gives part, but not all, of the possible stereoisomers. The reaction of racemic diaminocyclopentane with racemic dichlorodiethylenediaminocobaltic chloride gives only two of the four possible isomers; each of the antipodes of the $[Coen_2Cl_2]Cl$ reacts preferentially with one form of the diaminocyclopentane. This effect is certainly not absolute, and may be very slight. It suggests, however, that the reaction between an optically active complex and an *excess* of a racemic coördinating substance might be selective to some extent—that is, that the complex might accept one antipode of the coördinating material preferentially, thus effecting a resolution. Some studies of this possibility are reported here. The results indicate that the preference of the complex for one antipode over the other is slight in these reactions.

The reactions studied were those of propylenediamine and alanine with cobalt complexes containing two molecules of levo-propylenediamine, that of leucine with dichlorodiethylenediaminocobaltic chloride, and that of phenylalanine with

(1) Abstracted from portions of the doctorate theses of C. A. Stiegman, J. H. Balthis, Jr., and E. H. Huffman.

(2) The following symbols are used in this paper: M = metal ion, A = coördinating group occupying two corners of the octahedron, X = an acido group occupying one corner, en = ethylenediamine, pn = propylenediamine, Cptdn = 1,2-*trans*-diaminocyclopentane, Hala = alanine, Hleu = leucine. D and L refer to the dextro and levo configurations of the complex ion, and *d* and *l* to the configurations of the "A" groups.

(3) Jaeger and Blumenthal, *Z. anorg. allgem. Chem.*, **175**, 161–230 (1928).

teristic; those prepared at 200° were deep brown and contained acid precipitable products, "humic acids"; those from the 250° oxidations were pale yellow and no acids precipitated on acidification; while those formed at 225° were intermediate in color and showed variable behavior on acidification.

The data on the effect of oxygen partial pressure at a constant temperature of 225° and an oxidation period of twenty-four hours indicate an increase in rate of formation of carbon dioxide with higher oxygen partial pressures.

Replacement of the potassium hydroxide by sodium hydroxide was found to reduce the rate of oxidation markedly; the fraction of the carbon converted to carbon dioxide was 25% lower at the end of twelve hours. It seems probable that this is due to differences in solubility of the sodium and potassium salts of the organic acids formed in the early stages of the reaction, where the rate of oxidation must be greatly affected by the rate at which fresh coal surfaces are exposed by solution of the initial oxidation products.

Five out of the six equivalents of potassium hydroxide could be replaced by equivalent amounts of calcium hydroxide without adverse effect on the reaction rate. With calcium hydroxide alone only a small fraction of the carbon of the coal, less than 3%, was converted to soluble products, under the same conditions where complete conversion took place with potassium hydroxide.

The distribution of the carbon of a Pittsburgh Seam coal, among the various oxidation products, as a function of time, was studied in detail. The results, which are shown in Fig. 1, are similar to those obtained with oxidizing agents such as nitric acid and alkaline permanganate.

The results of a study of the behavior of several different types of carbonaceous materials, using a standard oxidation procedure, are summarized in Table II. Under these conditions all of the coals investigated and the 500° coke can be oxidized completely to water-soluble products. The 700° coke, the high temperature coke, and the pitch are incompletely oxidized and the soluble products consist largely of carbonic acid. In the case of graphite, carbonic acid is the only soluble acid present in significant amounts. It has been

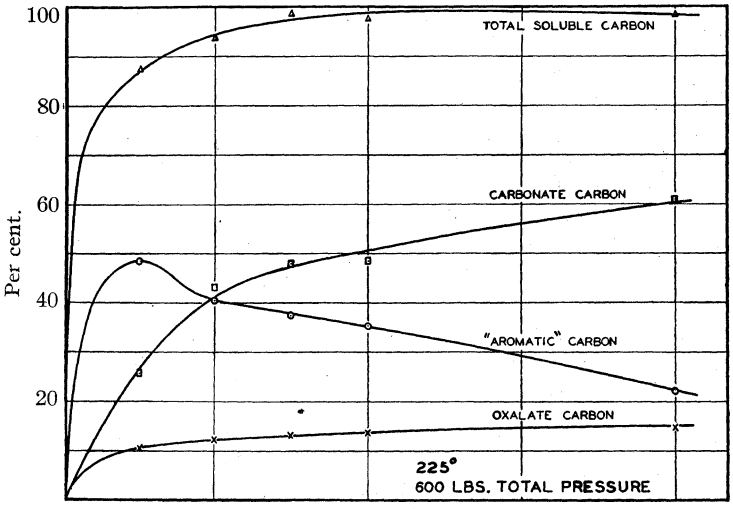

Fig. 1.

TABLE II

OXIDATIONS OF VARIOUS CARBONACEOUS MATERIALS[a]

	Total soluble carbon, %	Carbonate carbon, %	Oxalate carbon, %	"Aromatic" carbon, %	Carbonate / Soluble C	Carbonate carbon, g.	"Aromatic" carbon, g.
Illinois No. 6	100.2	58.1	9.33	32.8	0.58	20.3	11.4
Pittsburgh	98.8	49.7	12.90	36.2	.50	19.2	14.0
High Splint	102.2	57.7	8.03	36.5	.56	22.7	14.3
Pocahontas No. 3	100.6	57.0	4.50	39.1	.52	24.2	16.6
Anthracite	100.5	59.3	3.40	37.8	.59	24.5	15.6
500° coke	99.5	61.3	5.20	33.0	.62	24.5	13.2
700° coke	85.5	59.8	4.15	21.5	.71	24.6	8.2
High temp. coke	72.7	63.1	2.90	6.7	.87	25.6	2.7
Graphite (40 g.)	62.1	57.9	1.90	2.3	.92	28.8	1.1
Pitch (30 g.)	80.5	44.0	6.45	30.0	.55	12.0	8.2

[a] The sources of these materials are given in ref. (4). Oxidized for twenty-four hours at 250°; estimated oxygen partial pressure 137 lb. (9 atm.); −200-mesh, 50-g. sample, except where noted.

The tetramethyl ester of pyromellitic acid (1,2,4,5-benzenetetracarboxylic acid), was isolated from the ester fraction distilling at 125° prepared by the action of diazomethane on the fraction of acids forming barium salts insoluble in water and acetic acid, but soluble in formic acid; m. p. 141°.

Anal. Calcd. for $C_{14}H_{14}O_8$: C, 54.19; H, 4.52. Found: C, 53.90; H, 4.73.

Results and Discussion

Early in the work it was found that the rate of oxidation, measured by the amount of carbon dioxide formed per unit of time, was relatively independent of the weight of coal present. This indicated that the rate was determined by some constant factor, and in view of the rather low oxygen partial pressure employed and the correspondingly low solubility of oxygen, it appeared that the oxidation must be taking place chiefly at the gas–liquid interface and that the area of this interface was the rate controlling factor. Experiments in which the area of this interface was increased by the introduction of packing material confirmed this analysis and showed definitely increased reaction rates, and, as was to be expected, the packing was much more effective at lower oxygen partial pressures (see Table I). The packing consisted of 69 pieces of 2.5 × 20 cm. 6-mesh monel screen twisted into stick form, 6 mm. in diameter.

TABLE I

OXIDATION OF PITTSBURGH SEAM COAL[a]

Temp., °C.	Total pressure, lb.	Estimated oxygen p. p., lb.	% of carbon[b] of coal as CO_2 12 hrs.	24 hrs.	Remarks
250	500	137	23.0	32.5	No packing[c]
250	500	137	34.9	49.5[d]	
225	600	377	40.7	43.6	No packing
225	600	377	43.1[f]	48.5	
225	600	377	53.0	75.8	Copper sulfate
250	500	137	49.0	78.9[e]	Copper sulfate
250	500	137	..	69.5	No packing, copper sulfate
250	500	137	..	66.7	Cobalt sulfate
200	375	250	35.4	38.3	
225	450	227	31.5	44.2	
250	600	237	46.4	64.2	
225	325	102	..	31.5	
225	375	147	..	26.9	
225	450	227	..	44.2	
225	600	377	..	48.5	
225	600	377	32.7	42.3[e]	Sodium hydroxide
225	700	377	..	43.0	Sodium hydroxide

[a] −200 mesh, 50-g. sample; 350 cc. water; 335 g. potassium hydroxide or its equivalent. [b] Values represent single measurements except where otherwise noted. [c] Packing was used in all experiments except where otherwise noted. [d] Mean of 30 oxidations; all values within ±2% of mean. [e] Mean of 2 oxidations. [f] Mean of 3 oxidations.

In a study of the effect of the addition of various anions and cations upon the course of the reaction, 5 g. per 50 g. of coal of the following substances was used: copper sulfate, silver sulfate, zinc sulfate, mercuric chloride, titanium sulfate, cerium sulfate, thorium nitrate, antimony trichloride, chromic sulfate, tungstic acid, uranium nitrate, selenium, manganous sulfate, ferrous sulfate, nickel nitrate, cobalt sulfate, potassium permanganate, potassium chromate, and sodium nitrate. The values for percentage carbon converted to carbonic acid in the oxidations when additions were made did not vary more than a few units from the average of those without additions, run under identical conditions, except in those experiments where copper or cobalt salts were used. Two experiments with addition of copper sulfate gave 79.3 and 78.5% carbon converted to carbonic acid, and one experiment with cobalt sulfate gave 66.7%, as compared with 49.5% for the average of experiments without catalysts. Unfortunately these catalysts appear to have little effect on the rate of initial oxidation of the coal, but accelerate markedly the conversion of the soluble acids to carbon dioxide and water. When an attempt was made to preserve the soluble acids by shortening the oxidation period, considerable coal remained unattacked. The catalytic effect of copper and cobalt also was observed in oxidations of cokes. A 500° coke gave 61.3 and 91% for uncatalyzed and copper-catalyzed reactions, respectively; a 700° coke, 59.8 and 86.8%. No effect was found with graphite.

The oxidations at 200, 225 and 250°, at an approximately constant oxygen partial pressure, showed that the effect of increased temperature was most marked in the later stages of the reaction, after the coal had been largely converted to the alkali-soluble "humic acids." At 200° the amount of soluble carbon and the carbonate carbon both remained nearly constant over the last twelve hours; at 225° there was definite evidence of attack on the "humic acids," over the same period; and at 250°, there was a large increase in the fraction of the carbon appearing as carbon dioxide, with a corresponding marked drop in the carbon in the form of organic acids. The color of the alkaline solutions of the oxidation products obtained at the different temperatures, as well as their behavior on acidification, were very charac-

so that even during oscillation the end of the pressure line was above the liquid level in the bomb. Bomb and pressure tubing were filled with 100–300 pounds (7–21 atm.) of oxygen, depending upon the final pressure to be used, before starting heating or agitation. After the bomb reached the desired temperature the full oxygen pressure was applied and agitation started. The temperature of the bomb was measured by a chromel–alumel couple placed in a well extending from the head to the middle of the bomb. Temperatures were maintained constant to ±2° by a Leeds and Northrup controller.

Total pressures were measured with a Bourdon tube gage placed in the oxygen inlet line near the trap. Oxygen partial pressures were calculated by taking the difference between total gage pressure and the aqueous vapor pressure, at the temperature of the oxidation, of a sodium hydroxide solution of equivalent concentration to the potassium hydroxide actually used, since no data are available for the latter. For this reason the absolute value of the oxygen partial pressure is somewhat uncertain.

In the preliminary experiments the rate of the reaction was followed by oxygen absorption, in the later ones, analytically, through examination of the products formed at the end of definite time intervals.

The analytical procedure was as follows. After cooling, the alkaline solution from the bomb was drained into a 2000-cc. volumetric flask, and bomb, head, and packing material, when used, were washed carefully and the washings and contents of the bomb combined in the volumetric flask, made up to volume and mixed thoroughly. After standing to permit any insoluble matter to settle to the bottom of the flask, which in most cases consisted of inorganic material, aliquot portions were withdrawn from the clear supernatant liquid for determination of total carbon, carbonate carbon, oxalate carbon and, in a few cases, carbon in the form of volatile acids. The volatile acids were never found to constitute more than 1 to 2% of the carbon of the material oxidized and in the later experiments this determination was omitted. The methods used for the determination of the various forms of carbon have been described in a previous publication.[6]

The greater part of the work was done with a Pittsburgh Seam coal, Edenborn Mine, but for comparison oxidations were also carried out on Illinois No. 6, High Splint coal, Pocahontas No. 3, a Pennsylvania anthracite, 500° and 700° cokes, prepared in this Laboratory from the Pittsburgh coal, a commercial high temperature coke, Acheson electrode graphite, and a pitch from a high temperature carbonization process.[7]

In order to obtain sufficient material to examine the aromatic acids in detail, eleven oxidations of Edenborn coal were carried out. Fifty grams of −200 mesh coal was treated at 225° with an oxygen partial pressure of approximately 380 pounds (25 atm.), total pressure 600 pounds (40 atm.), for a period of eighteen hours. The alkaline solution from the bomb was filtered to remove insoluble material, chiefly inorganic, the filtrate was neutralized with sulfuric acid, and excess acid added until the concentration was about 3 *N*. This acid solution was treated with manganese dioxide in an amount about twice the theoretical required to oxidize the oxalic acid present. The excess manganese dioxide was filtered off, the filtrate and washings concentrated to 1500 cc. and the acidity again adjusted to about 3 *N*. A total carbon determination at this point showed, on the average, 85% of the carbon present which was previously calculated to be aromatic from the analytical data, so that presumably this method of removal of oxalate also attacks some aromatic carbon.

This solution was then subjected to ether extraction in a continuous extractor[8] for a period of a week. Of the aromatic carbon which was placed in the extractor an average of 80% was recovered in the seven-day extraction. The greater part of this was recovered in the first twenty-four hours.

The yield of aromatic acids actually obtained in this way, from 50 g. of Edenborn coal, ranged from 15 to 20 g. They were orange to pale yellow in color; slightly hygroscopic; easily soluble in water, except about 1%, which was found to be terephthalic acid; easily soluble in acetone and alcohol; moderately soluble in ether and ethyl acetate, and almost insoluble in benzene.

A sample from a 225°, twenty-four hour oxidation, dried to constant weight at 85°, showed the following average properties: C, 51.91%; H, 2.87%; N, 0.45%; S, 1.03%; residue on ignition, 0.58%; equiv. wt., by titration using phenolphthalein, 73.1; mol. wt. by boiling point elevation in acetone, 230. This average composition, except of course for nitrogen and sulfur, is close to that of a benzenetricarboxylic acid: C, 51.41%; H, 2.85%.

The yellow color was found to be a function of the severity of the oxidation treatment, lighter colored acids resulting from prolonged treatment. Samples of the more deeply colored acids had higher average equivalent and molecular weights ranging up to 76 and 260, respectively.

The methods of barium salt fractionation, esterification and vacuum fractionation of the esters were like those previously described,[6] except that a somewhat more effective design of molecular still was employed and longer time periods were used for distillation of the ester fractions. Terephthalic acid (1,4-benzenedicarboxylic acid), because of its relative insolublity in water, was separated readily before the barium salts were formed. Trimellitic acid (1,2,4-benzenetricarboxylic acid) was found in the water-soluble barium salt fraction and was purified by crystallization from concentrated nitric acid, followed by vacuum distillation. The purified acid melted 215–225°, was converted to the anhydride by heating at 250° and the anhydride vacuum distilled. The m. p. of the anhydride was 166°.

Anal. Calcd. for $C_9H_4O_5$: C, 56.25; H, 2.08. Found: C, 56.02; H, 2.37.

The tetramethyl ester of prehnitic acid (1,2,3,4-benzenetetracarboxylic acid) was isolated from the ester fraction distilling at 125° prepared by the action of diazomethane on the fraction of acids forming barium salts insoluble in water, but soluble in acetic acid; m. p. 130°.

Anal. Calcd. for $C_{14}H_{14}O_8$: C, 54.19; H, 4.52. Found: C, 54.16; H, 4.55.

(6) Juettner, Smith and Howard, THIS JOURNAL, **59**, 236 (1937).

(7) The sources of these materials are given in ref. 4.

(8) Discussed in ref. 6.

If oxygen is present in the fluid, the discharge leads to activation, with formation of hydrogen peroxide or direct chemical reaction of activated oxygen with certain compounds present in solution such as aminophthalichydrazide. Sonic chemiluminescence then results, as shown by Flosdorf, Chambers and Malisoff.[6] Sonoluminescence is remarkably independent of substances dissolved in the water phase but is quenched by high vapor pressure of water (from rise in temperature) or by specific volatile organic compounds.

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[CONTRIBUTION FROM THE COAL RESEARCH LABORATORY, CARNEGIE INSTITUTE OF TECHNOLOGY]

Oxidation of Carbonaceous Materials to Organic Acids by Oxygen at Elevated Pressures[1]

BY R. C. SMITH, R. C. TOMARELLI AND H. C. HOWARD

Coals, cokes, and pitches yield significant amounts of organic acids when subjected to controlled oxidation with oxidizing reagents such as alkaline permanganate and nitric acid,[2] and small amounts of aromatic acids have also been isolated from oxidation products formed by the action of air, at elevated temperatures and pressures, upon suspensions of coal in aqueous alkali.[3]

In the present investigation oxidations were carried out in aqueous alkali at temperatures from 100 to 250° and oxygen partial pressures from approximately 100 to 375 pounds (7–25 atm.). Below 225°, reaction rate was very slow. Bituminous and anthracite coals and low temperature coke can be oxidized completely to carbon dioxide and water or to any desired intermediate stage. High temperature coke and graphite are partially oxidized under the same conditions, 50–60% of the carbon appearing as carbon dioxide, but much smaller amounts of organic acids are recovered. In the case of graphite no significant amount is obtained because mellitic acid is the principal organic acid formed in the oxidation degradation of these higher rank carbonaceous materials,[4] and it has been found to be unstable under the conditions of this oxidation.

Increase in area of gas–liquid interface, by introduction of packing material into the bomb, has been found to increase significantly the reaction rate in the early stages of the degradation.

Of some nineteen different catalysts investigated, only copper and cobalt salts affect reaction rate significantly, and these chiefly in the later stages of the oxidation.

Carbon balances show that under the proper conditions approximately 50% of the carbon of bituminous and anthracite coals can be converted to water soluble organic acids, the rest of the carbon appearing as carbon dioxide. Of the carbon recovered in the form of organic acids about one-fourth is oxalic acid and the balance aromatic acids. The actual amount of the latter recovered by oxidation of a Pittsburgh Seam coal was 30–40 g. per 100 g. of coal.

Experimental.—The oxidations were carried out in an all-nickel bomb of 1-liter capacity of identical design with those supplied for hydrogenation,[5] except that a silver gasket was used. The bomb was heated externally by an electric furnace and agitated in the usual way by oscillation approximately 30° above and below the horizontal, about a transverse axis. Oxygen was introduced through a spiral of high pressure tubing from an oxygen reservoir of constant pressure. Since maintenance of the oxygen partial pressure depended upon absorption of the carbon dioxide formed, the amount of coal oxidized at one time was limited primarily by the amount of alkali which could be introduced. The maximum amount of coal which could be used was 50 g. and with materials of higher carbon content such as graphite it was necessary to reduce the size of the sample. The material to be oxidized was ground to −200 mesh and in most cases was suspended in a solution of 335 g. of potassium hydroxide in 350 cc. of water. In a few oxidations the potassium hydroxide was replaced by equivalent amounts of sodium hydroxide or calcium oxide.

In the early experiments considerable difficulty was encountered with the alkaline solution working back into the pressure tubing which supplied the oxygen. To prevent this a trap was provided in the pressure line just before it entered the head of the bomb and the line was continued inside the bomb and turned upward at the tip,

(1) Presented before the Division of Gas and Fuel Chemistry at the 96th meeting of the American Chemical Society, Milwaukee, Wisconsin, September, 1938.

(2) Bone and co-workers, *Proc. Roy. Soc.* (London), **A110**, 537 (1926), **A127**, 480 (1930); **A148**, 492 (1935); Juettner, Smith, and Howard, THIS JOURNAL, **59**, 236 (1937); **57**, 2322 (1935).

(3) For a review of the work of F. Fischer and co-workers see Horn, *Brennstoff-Chem.*, **10**, 362 (1929).

(4) Juettner, THIS JOURNAL, **59**, 1472 (1937).

(5) American Instrument Company, Silver Spring, Md.

ment shows conclusively that aggregation and coalescence of the gas bubbles cavitated by other means than supersonic does not lead to luminescence.

Duration of Sonoluminescence.—In order to determine whether any substance is produced with which luminescence is associated and which persists for even a short fraction of a second, the flow method of Hartridge and Roughton[28] was adopted. Water from the faucet flowed through a glass tube of 0.78 cm. internal diameter, touched to the oil over the vibrating crystal. With no flow, a faint sonoluminescence of water appeared in the tube. With increasing flow the light became brighter and remained bright up to a certain maximum flow when it began to flicker, first appearing then disappearing over the crystal. A slightly faster flow quenched the light permanently and there was no return of light until the rate of flow had decreased considerably. The fastest rate, just before the light permanently disappeared, corresponded to 100 to 150 ml. per second. For a diameter of 7.8 mm. this means that a column of fluid 200 to 300 cm. long would move past the crystal in one second. *The luminescence never spread even a few mm. beyond the edge of the crystal* so that it could not have persisted over 0.001 second.

By fusing a side-tube connected to a pressure gage to the flow tube it can be shown that the increased luminescence with low rates of flow is due to a slight increase in pressure (0.3 to 1.3 atm.) and the disappearance of the light at a certain rate of flow is due to increase in pressure to above 1.3 atm., which is itself sufficient to prevent cavitation and consequently luminescence (see next section). The disappearance of luminescence is not due to the velocity but to the pressure of water in the tube and we can say that there is no persistence of sonoluminescence with any rate of flow that can be attained by a pressure that allows cavitation. Luminol solution pumped through the glass tube over the crystal also shows no persistence of luminescence with a flow velocity of 130 cm./sec. The luminescence is brighter when the fluid is under slight pressure.

Pressure and Luminescence.—A study of the effect of pressure on sonoluminescence becomes a study of the effect of pressure on cavitation. A pressure chamber was constructed (Fig. 1) which consists of a brass tube with a glass test-tube sealed in one end with picene. At the other end is a cap with stopcock and at the sides a pressure gage and pressure piston are soldered on. The pressure apparatus is completely filled with water and the stopcock closed. By turning the screw thread of the pressure piston any desired pressure can be obtained. It must be emphasized that under these conditions the gas dissolved in the water in the pressure chamber is in equilibrium at atmospheric pressure and not at the pressure indicated by the gage. It was found that the luminescence (and cavitation) becomes intermittent at about 1.3 atm. and disappears at pressures above this figure. The light shifts to the top of the tube just before going out. When the pressure is decreased from above 1.3 atm., light does not again appear until it has reached about 0.8 atm. At slight pressure (0.3 to 1 atm.) the light is brighter than with no pressure. This optimum pressure for sonoluminescence above atmospheric pressure, can be compared with the optimum pressure for supersonic cavitation to produce emulsification, observed by Bondy and Söllner.[29]

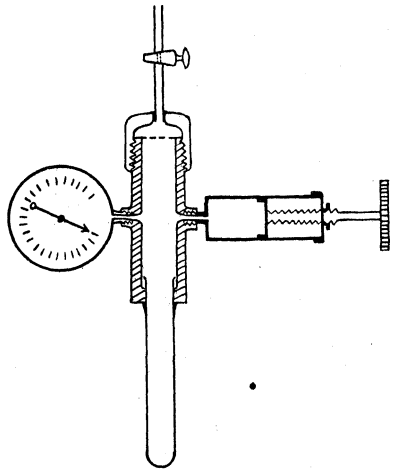

Fig. 1.

Under reduced pressure (in equilibrium with air at the same pressure) sonoluminescence of water is apparent until 31 cm. is reached, when no more luminescence appears and no cavitation is visible.

The sonic chemiluminescence of aminophthalichydrazide behaves under pressure as does the sonoluminescence of water since both are dependent on cavitation. The important fact is the increased luminescence under slight pressures.

Conclusions

The fact that sonoluminescence of pure water and bromine water occur in nitrogen but not in hydrogen is strong evidence for the view that the light is not the result of oxidation but is connected with the development of balloelectric potentials, since these are known to be large in nitrogen and small in hydrogen. The occurrence of luminescence in pure nitrogen shows definitely that activation of dissolved oxygen is not involved. No facts are directly opposed to the balloelectric discharge theory of sonoluminescence. We may therefore picture the minute bubbles of cavitated gas as developing a considerable electrical charge. When they collapse their capacity decreases and their voltage rises until a discharge takes place in the gas of the bubble, giving rise to a weak luminescence. The discharge may be thought of as occurring near the instant of complete collapse. Since velocity of collapse of the bubble would be favored by slightly increased hydrostatic pressures, it is not surprising to find the sonoluminescence intensity increased under slight pressures.

(28) Hartridge and Roughton, *Proc. Roy. Soc.* (London), **B94**, 336–337 (1923).

(29) Bondy and Söllner, *Trans. Faraday Soc.*, **31**, 836–842 (1935).

tetrachloride, chloroform, *o*-xylene, nitrobenzene, benzyl alcohol, paraffin oil, olive oil, *n*-butyl phthalate, bromoform and bromobenzene did not affect the sonoluminescence of water. With carbon disulfide in water the luminescence was brighter than with pure water alone.

When the above compounds are added to luminol solutions which are subjected to the supersonic field, only ethyl butyrate, aniline, benzene and ethyl ether completely quench the chemiluminescence. In chloroform and carbon tetrachloride the sonic chemiluminescence persists. This is due to the liberation of chlorine, as noted by Schmitt, Johnson and Olson[3] in their study of chemical effects of supersound waves.

A survey of the liquids, non-miscible with water, which quench the sonoluminescence of water shows no obvious relation to other properties. The dipole moment may be zero or high and the vapor pressure at 20° may be great or small. Since the development of balloelectric potentials as well as electrical discharges in gases is markedly affected by various conditions, which have been incompletely investigated, it is not surprising to find a quenching of sonoluminescence by certain vapors.

Sonoluminescence of Halogens.—Of the many substances added to water and tested for luminescence at 20° during the present investigation, only bromine water emits a strikingly bright light (comparable to that of luminol) when subjected to supersonic fields. This is true even when saturated bromine water of a deep brown red color is tested. It is especially bright at 0° and faint at 40°. No luminescence was observed in pure bromine. Iodine dissolved in potassium iodide or in water does not luminesce in the supersonic field with any greater brightness than water at the corresponding temperatures, but chlorine water, although about as bright as distilled water at 20°, is decidedly brighter than pure water at 0°. Chlorine water and iodine dissolved in potassium iodide are very very faint at 40°. Just as in the case of pure water, the luminescence of these halogens is brighter the lower the temperature. When salts of these halogens are tested in dilute water solutions (sodium chloride and bromide, potassium iodide), the sonoluminescence intensity is like that of pure water.

The cause of the sonic luminescence of bromine water is of special interest. First it may be noted that bubbling oxygen or ozone through chlorine water, bromine water, or iodine in water does not result in the emission of light either at 20 or at 0°, nor does the addition of hydrogen peroxide to chlorine water, bromine water or iodine water, either with or without a catalyst (platinum black). There is also no visible luminescence at an anode of bright or platinized platinum when bromine water in dilute sulfuric acid is electrolyzed with potentials of 1.5 to 6 v. although the acid bromine water emits a bright sonoluminescence. Therefore the luminescence does not appear to be connected with any source of active oxygen.

A similar conclusion is reached from a study of dissolved gases. When pure hydrogen was bubbled through distilled water and over bromine to flush out the oxygen and the two then mixed in a hydrogen atmosphere and subjected to a supersonic field, the bromine water gave no trace of luminescence. However, if the same experiment is carried out with pure nitrogen, the sonoluminescence in bromine water is just as bright as in air. Luminescence of the bromine cannot therefore be due to any reaction involving oxygen and must be a phenomenon similar to the sonic luminescence of water. Unfortunately no lines can be detected in the spectrum of the bromine water sonoluminescence but only a very faint band in the yellow region.

We now may inquire in more detail into the conditions under which luminescence may accompany cavitation of gas from liquids.

Reynolds Tube Cavitation.—Since water can be made to cavitate by other means than sound waves, it is of interest to look for luminescence in these cases also. A flask of water cavitates dissolved gas and also water vapor just before it boils; a ship's propeller cavitates the water just behind it as it revolves and may become badly corroded from effects of cavitation; water flowing through a constriction in a tube cavitates as a result of the increased velocity of flow and corresponding decrease in pressure, a Reynolds tube.[27] There are no records of luminescence about ship's propellers (apart from the luminescence of disturbed micro-organisms in the sea) and I have not been able to observe a trace of luminescence just before a flask of water boils.

In a Reynolds tube there is also no luminescence. This tube was made of glass 8.5 mm. internal diameter narrowing to 2.5 mm. and then expanding to 8.5 mm. again. It was attached to the water faucet and during flow beautiful cavitation with a hissing sound occurred but no trace of luminescence. A large Venturi meter (with a glass window), 5 in. (12.6 cm.) inside diameter narrowing to 2 in. (10.1 cm.) in the Engineering Building at Princeton University also was observed but no luminescence occurred during the abundant cavitation.

Luminol pumped through a Reynolds tube cavitates abundantly but exhibits no luminescence. Evidently the conditions for building up potentials and for activation of oxygen are very different in the sonic field from those in the Reynolds tube.

Preformed Gas Bubbles.—Although gas bubbles rising through a fluid are electrically charged, it is easy to demonstrate that already formed gas bubbles are not responsible for luminescence in the supersonic field. This experiment is carried out by exhausting the dissolved gas in a weak soap solution with a filter pump. In a tube in the supersonic field this solution does not luminesce, since it cannot cavitate. Then air is forced through a porous diaphragm into the solution while in the supersonic field. The minute bubbles, which are prevented from uniting by the soap film, travel upward, but no luminescence is visible until a certain amount of air has dissolved (after eight seconds). Then the newly air saturated solution cavitates and sonoluminescence appears. The air bubbles show beautiful aggregation as the result of sound wave pressure but not coalescence.

If a Reynolds tube of flowing water was placed over the vibrating crystal, there was no brighter luminescence around the minute bubbles of gas cavitated by the Reynolds effect than from other regions, although the bubbles immediately coalesce in the supersonic field. The experi-

(27) Reynolds, "Papers on Mechanical and Physical Subjects," Cambridge, Vol. II, 1901, p. 578.

that this substance luminesces with relative brightness in the supersonic field even when shielded from all electrostatic influences.

The behavior of luminol solutions when saturated with various gases confirms the chemiluminescent origin of most of the light and in addition shows that the sonoluminescence of pure water has another origin than that of activated oxygen. In carbon dioxide there is no luminescence, since cavitation does not occur with the sound intensities available (and oxygen is absent). In pure hydrogen there is no luminescence since activated oxygen cannot form. In nitrogen (either purified by passing over red hot copper or mixed with 7% of hydrogen and passed over platinized asbestos) there is no bright sonic chemiluminescence of luminol but there still remains the faint sonoluminescence[24] which appears in pure water in absence of oxygen. In neon also the bright sonic chemiluminescence of luminol disappears but a faint luminescence remains similar to that in neon saturated water. Finally, if sodium hydrosulfite is added to luminol in a nitrogen atmosphere, there is no sonic chemiluminescenee but only the sonoluminescence of water.

Therefore, we can conclude definitely that this compound shows a true sonic chemiluminescence when subjected to high frequency sound waves, as the result of the activated oxygen produced.

Temperature.—The sonoluminescence of water and also of solutions is brighter the lower the temperature and is quite marked at 0°. At 30° the intensity is considerably less than at 20° and above 40° there is practically no luminescence, although water at 90° will cavitate. It seems reasonable to suppose that the increased vapor pressure of water at high temperatures suppresses the discharge in the cavitated gas bubbles.

Luminol subjected to supersonics also luminesces more brightly the lower the temperature but the light is easily visible at 60° and does not disappear until a temperature of 85 to 90° is reached.

Hydrogen Peroxide and Luminescence.—Since hydrogen peroxide added to various substances can cause the emission of light and hydrogen peroxide is undoubtedly formed during sonic treatment of water, it seemed important to determine whether substances which combine with hydrogen peroxide or which catalyze the decomposition of hydrogen peroxide affect the sonoluminescence of water or the sonic chemiluminescence of luminol.

First it may be recorded that the mixing of hydrogen peroxide and water does not result in light emission nor does a brighter sonoluminescence appear in the subsequent mixtures than in pure water. I also have never observed luminescence during the decomposition of hydrogen peroxide, whether this is induced by inorganic catalysts (manganese dioxide, platinum black) or by catalase, and whether the decomposition is relatively slow or occurs (with catalase) with explosive violence. Therefore it appears that hydrogen peroxide can play little part in the sonoluminescence of water. Similar evidence is obtained from a study of hydrogen peroxide catalysts which might be expected to decompose hydrogen peroxide before it could react further with possible emission of light.

Since catalase is a hydrogen peroxide catalyst so powerful that solutions of it showing no trace of color decompose hydrogen peroxide explosively, it was prepared[25] from beef liver by the method of Sumner and Dounce,[26] which involves extraction with dioxane. It was washed free of dioxane by half-saturated ammonium sulfate and dissolved in 0.1 *N* phosphate buffer at *p*H 7.4. This solution gave the usual sonoluminescence of water, although it decomposed hydrogen peroxide instantly.

When made slightly more alkaline and luminol added, the relatively bright sonic chemiluminescence of the luminol appeared of the same intensity as in a similar control tube without catalase. The catalase in the more alkaline luminol solution was found to be highly active in decomposing hydrogen peroxide. We are, therefore, led to the conclusion previously reached in sonic experiments by Flosdorf, Chambers and Malisoff[6] that the luminescence of luminol is due chiefly to the activated oxygen rather than the hydrogen peroxide formed by the supersonics.

On the contrary, the oxidation of potassium iodide by supersonics is due largely to the hydrogen peroxide formed. Two tubes of potassium iodide, one containing catalase and the other not, were subjected to a supersonic field for one minute. Then starch solution was added to both. The tube with catalase gave only a trace of blue color while the one without catalase turned blue-black from the abundant liberated iodine and starch.

Ozone and Luminescence.—Although all observers report little if any ozone formed by supersonic treatment of water, it is possible that traces might form that are responsible for luminescence, since ozone passed through many organic substances will emit light. Ozone passed through distilled water or sodium chloride, bromide or iodide solution does not result in luminescence but if a trace of luminol is added, each bubble of ozone rising through the solution luminesces brilliantly. Therefore ozone cannot be concerned with the sonoluminescence of water but might add to the sonic chemiluminescence of luminol.

Inhibition of Sonoluminescence.—Although the sonoluminescence of water is remarkably independent of dissolved substances of various kinds (see a previous section), there are certain compounds which prevent its appearance. This was first noted in a study of sonoluminescence during emulsification by sound waves. It was observed that layers of water and mercury luminesced (somewhat brighter than pure water alone) when emulsified but layers of water and benzene did not. Therefore a systematic study was made of a number of fluids non-miscible with water. One drop of the liquid was added to 10 cc. of water.

It was found that propyl, butyl, amyl and capryl alcohols, ethyl butyrate, amyl acetate, ethyl ether, β,β-dichloroethyl ether, benzene and 1,4-dioxane prevented luminescence; that toluene, thiophene, petroleum ether and aniline allowed a faint luminescence, while carbon

(24) This faint luminescence was probably overlooked by Flosdorf, Chambers and Malisoff,[6] who noticed no luminescence of luminol containing nitrogen in the sonic field.

(25) I am greatly indebted to Mr. R. G. Ballentine for the sample of pure catalase.

(26) Sumner and Dounce, *J. Biol. Chem.*, **121**, 417 (1937).

saturated with neon. When the tube was touched to the supersonic fountain of oil a luminescence appeared of about the same intensity as when water saturated with air at 0° is tested. No trace of red color that might be evidence of excitation of the neon by electrical discharge appeared and no difference in intensity or shade was detected when neon saturated and air saturated sonoluminescence was observed through red, orange or blue-green filters. The neon in the tube gave a bright red luminescence when excited with a leak tester at 0° but none at 20°, due to quenching by water vapor.

Either sonoluminescence in neon (1) is too weak to distinguish color or (2) excitation of the neon does not occur within the cavitated gas bubbles. That the first explanation is correct can be proved easily by a direct experiment. The light from a neon lamp at different distances falling on an opal glass screen is observed by completely dark adapted eyes. All trace of red color disappears from the neon light at intensities considerably greater than those resulting from sonic luminescence of the neon saturated (or air saturated) water. Therefore, the sonoluminescence in pure distilled water cannot be connected with activation of dissolved oxygen and we are probably dealing with electroluminescence from discharge in the cavitated neon, too faint to detect a red color. A similar electroluminescence occurs in nitrogen but it is still less intense.

Hydrogen is of special interest since it is an easily excited gas and one might expect to observe a sonoluminescence in hydrogen saturated water. However both Lenard[17] and Thomson[18] found that the waterfall potentials appearing where water is atomized in a hydrogen atmosphere are much less than in other gases. Therefore sufficient potential is not built up with cavitated hydrogen for a discharge to take place. The gas experiments definitely lead to the view that the sonoluminescence in pure water is balloelectrical in origin.

Effect of Dissolved Substances.—The sonoluminescence of distilled water containing air is remarkably independent of dissolved substances. Thus it is observed of nearly the same intensity[19] whether acid (10% sulfuric acid, 0.1 *N* hydrochloric acid) or alkaline (10% potassium hydroxide, 0.1 *N* ammonium hydroxide, 0.1 sodium hydroxide); whether the salt content (and electrical conductivity) is high [saturated sodium chloride, saturated ammonium sulfate (rather bright), concentrated calcium chloride, "hypo"], medium (sea water) or low (tap water, 0.01 *N* potassium cyanide); in presence of heavy metals (1% copper sulfate, satd. mercuric chloride); of strong oxidants [dilute hypochlorite or hypobromite, potassium bichromate (faint), potassium persulfate, ferric chloride, acid cerium sulfate, potassium ferricyanide, 10% nitric acid, hydrogen peroxide] and strong reductants [sodium hydrosulfite, alkaline stannous chloride, ammonium sulfide (faint), 42% hydrazine hydrate (faint)]; of inert suspensions (zinc stearate, talc, infusorial earth, pumice and kaolin); of emulsions [mercury (rather bright), olive oil in dilute alkali]; of colloidal solutions (ferric hydroxide, starch), of surface active substances (saponin, sodium glycocholate, soap, egg albumin); of peroxide inhibitors and developers (diphenylamine, hydroquinone, resorcinol, phloroglucinol, amidol, elon, pyrogallol) and dilute solutions of many other organic compounds (glucose, α-methyl glucoside, acetanilide, glycerol, ethylene glycol, ethyl and methyl alcohols).

The wide variety of conditions under which the sonoluminescence occurs, especially in either reducing or oxidizing solutions, is additional evidence against the view that the light is chemiluminescent in origin.

Relation to Other Luminescent Compounds.—Conditions which produce luminescence in cavitated water might conceivably excite fluorescence in solution. Very dilute fluorescein, eosin, erythrosin, rose bengale, cyanin, dicyanin A, pinacyanol chloride, rhodamin B, quinine sulfate,[20] uranyl nitrate, lophin and esculin were tested, but the luminescence was not *markedly* brighter than in pure water alone.

When insoluble fluorescent substances such as anthracene, salophen, salicylamide, natural willemite powder and phosphorescent zinc sulfide were suspended in water at 20° and subjected to supersonics, again not markedly greater luminescence appeared than in pure water. The salophen and salicylamide were also treated at 0° since low temperatures favor luminescence, but no *greatly* increased luminescence occurred.

In addition to being fluorescent in ultraviolet light, salophen and salicylamide are also triboluminescent, and lophin and aesculin are chemiluminescent when warmed with alkali in alcohol. Dilute pyrogallol (0.001 *M*) can be excited to luminesce in various ways,[21] most easily by peroxidase and hydrogen peroxide, or by potassium ferricyanide and hydrogen peroxide, or by passage of ozone, but no brighter light appears when high frequency sound waves are conducted through dilute pyrogallol than in distilled water. Crude solutions of luciferin or luciferase from the luminous crustacean, *Cypridina*, also give the same intensity of sonoluminescence as pure water.

One chemiluminescent compound, aminophthalichydrazide, hereafter referred to as *luminol*, responds brilliantly to supersound waves, as first demonstrated for sonic treatment by Flosdorf, Chambers and Malisoff,[6] who used it to detect the presence of active oxygen and of hydrogen peroxide formed from activated oxygen in cavitated gas bubbles reacting with water.

Sonic Chemiluminescence.—Aminophthalichydrazide and related compounds in alkaline solution, as shown by Albrecht[22] and studied by numerous investigators, gives a brilliant bluish luminescence when oxidized in various ways (as by bromine water, ferricyanide or permanganate) and particularly in presence of active oxygen. Luminescence also appears at the anode of solutions containing luminol, electrolyzed with potentials of 0.5 v. or over; with hydrogen peroxide in presence (or absence) of catalysts; by bubbling of ozone (but not molecular oxygen); or even at metallic surfaces (Al, Zn, Cd) which dissolve in water with evolution of hydrogen and formation of hydrogen peroxide.[23] It is not surprising, then, to find

(17) Lenard, *Ann. Physik*, **46**, 584 (1892); **47**, 463–524 (1915).

(18) Thomson, *Phil. Mag.*, **37**, 341–358 (1894).

(19) It must be remembered that the intensity of weak lights cannot be estimated with any accuracy, even by completely dark adapted eyes.

(20) Somewhat brighter than water.

(21) Harvey, *J. Biol. Chem.*, **31**, 311–336 (1917).

(22) Albrecht, *Z. physik. Chem.*, **136**, 321 (1928).

(23) Harvey, *J. Phys. Chem.*, **33**, 1456–1459 (1929).

the hydrogen peroxide arises from frictional electrical discharges (Reibungselektricität) which lead to activation of oxygen in cavitated air bubbles and reaction of the oxygen with water to form hydrogen peroxide. Such discharges themselves easily could give rise to luminescence, with hydrogen peroxide formation a secondary effect.

A more extended investigation of the luminescence is described by Levsin and Kzevkin.[7] They found that four times distilled water will luminesce and conclude that the light is due to electrical discharge in water vapor in cavities within the liquid. All observations, including my own, agree that the luminescence appears when fluids are completely shielded from the electrical field and that it is always connected with cavitation, being brightest where cavitation is most marked.

Electric potentials produced by increase in the surface of a fluid (as when it is atomized) are called balloelectric or Lenard potentials (Wasserfallelektricität) and were first suggested as an explanation of the extraordinary chemical effects of cavitation in hydraulic problems by Föttinger.[8] They have been emphasized by Richards[9] who, in collaboration with G. Hobart, was able to detect random variation in potentials in water in the cavitating region of a Reynolds tube.

If sonoluminescence is due to electrical discharge, it should make little difference what gas is dissolved in the fluid, provided cavitation of the gas occurs. On the other hand, if light emission depends on the activation of oxygen, *i. e.*, if it is a chemiluminescence, there should be no luminescence in hydrogen or nitrogen. Actually both types of luminescence can be observed under different conditions. Experiments to determine these points together with other observations on sonoluminescence are reported herein. The most striking effect is the sonoluminescence of bromine water which emits a light far brighter than that of water alone or of water with any other added substance.

Apparatus.—The oscillator (in a light-tight box) is of the tuned grid tuned plate type with two push-pull 852 tubes and a power input of approximately 300 watts. The quartz crystal is 5.3 cm. in diameter and 0.51 cm. thick, between two thin copper electrodes in transformer oil. Its natural period is 550 kilocycles. At full power, a fountain of oil about 4 cm. high is produced, making possible a demonstration of the well known phenomena associated with supersound waves, including cavitation of gas.[9-14] The oscillator is not strong enough to cavitate vapor from a degassed fluid such as water. Glycerol or nitrobenzene also gave no evidence of cavitation. Black paper screens prevented an occasional sparking at electrodes from disturbing the observation of luminescence in fluids which were placed in test-tubes and touched to the surface of the oil over the crystal. Unless otherwise mentioned the temperature was about 20°.

It gives me great pleasure to thank Mr. Charles Butt, Research Assistant in Physiology, for constructing the oscillator and for faithful assistance during the experiments, and Mr. Alfred L. Loomis, Tuxedo Park, N. Y., for the loan of the quartz crystal and other apparatus.

Effect of Gases.—Pure water cavitates in the supersonic apparatus here described when saturated with air, nitrogen, hydrogen, oxygen and neon but not (or only slightly) if saturated with carbon dioxide or if evacuated with a filter pump or if saturated with air at atmospheric pressure and placed under 1.7 atm. hydrostatic pressure. However, luminescence only appears in air, oxygen, neon and weakly in nitrogen. In hydrogen purified by passing over heated platinized asbestos, there is no trace of luminescence. This might indicate that sonoluminescence depends on oxygen.

However, if nitrogen (purified by passing over freshly reduced copper in the apparatus described by Kendall[15] and led to an all-glass vessel by lead tubing sealed with de Khotinsky cement) is bubbled through distilled water for one and one-half hours, a weak luminescence still appears in the water when exposed to supersonic radiation. There is not enough oxygen present in this nitrogen to allow luminescence of luminous bacteria, which can detect about 0.01 mm. oxygen.[16]

Since luminescences are extraordinarily sensitive tests for oxygen, another method of purifying the nitrogen was used. It was mixed with 2.5% hydrogen in one experiment and with 7% in another. The mixture was then passed over heated platinized asbestos in a quartz tube connected with the vessel by a lead tube. Water saturated with nitrogen purified in this way still showed a faint sonoluminescence in high frequency sound waves and the conclusion is reached that *oxygen is not necessary for sonoluminescence of water.*

The neon gas experiments were undertaken in the hope of observing the characteristic reddish glow from electrical excitation of neon when water saturated with neon is radiated with supersonic waves. Water in a glass test-tube sealed to a 120° stopcock was thoroughly exhausted of gas by boiling at reduced pressure, cooled to 0° and

(7) Levsin and Kzevkin, *C. R. Acad. Sci. U. S. S. R.*, **16**, 399–404 (1937).

(8) Föttinger, "Hydraulische Probleme," V. D. I. Verlag, Berlin, 1936, p. 14.

(9) Richards, *Rev. Modern Phys.*, **11**, 36–64 (1939).

(10) Wood and Loomis, *Phil. Mag.*, **6**, 418 (1927).

(11) Bergman, trans. by Hatfield, "Ultrasonics," Chapman and Hall, London, 1938.

(12) Dognon and Biancani, "Ultra-Sons et Biólogie," Paris, 1937.

(13) Wood, "Supersonics," Brown University Press, Providence, 1939.

(14) Harvey, *Biol. Bull.*, **59**, 306–325 (1930).

(15) Kendall, *Science*, **73**, 394–397 (1931).

(16) Harvey and Morrison, *J. Gen. Physiol.*, **6**, 13–19 (1923).

0.03 to 0.15%. This is the range occurring in the majority of human urines. These concentrations sensitize the Benedict test for the very concentration range of glucose (0.05–0.3%) which yields doubtful results by other methods. A higher creatinine content, such as 0.2%, fortunately not common, in a urine containing 0.1% of glucose, delays the appearance of the opacity beyond the three-minute water-bath time recommended,[22] while the 0.4% creatinine level reported by Folin[24] for a starch and cream diet prevents the precipitation entirely, as it would in any other copper reduction test. On the other hand, creatinine concentrations below the optimum range, which can occur readily after copious water intake, cause the urine to react like an aqueous glucose, so that a 0.1–0.3% glycosuric urine with less than 0.03% creatinine gives in the Benedict test only a barely perceptible red haze, which would be considered negative by its author's instructions. In the Fehling or Trommer tests such a urine would give typical positive results.

It is evident, therefore, that at low glucose levels it is the accompanying content of creatinine which determines the sensitivity of a Benedict test. With this knowledge and the better understanding of the role of the various ingredients of alkaline copper solutions which has accumulated in the years since the appearance of Benedict's method, it may be possible to devise a more nearly infallible test and one sensitive to any significant concentration of glucose in urine. Progress of work on improved methods for the detection of sugar in urine is to be reported in a later paper.

(22) Benedict recommended one to two minutes of boiling over a flame. A three-minute period in a water-bath was shown by Folin and McEllroy (ref. 23) to be equivalent to the two minutes over a flame. The five-minute water-bath time, recommended in many texts, is an unwarranted extension and leads to many doubtful or false positive tests.

(23) Folin and McEllroy, *J. Biol. Chem.*, **33**, 513 (1918).

(24) Folin, *Am. J. Physiol.*, **13**, 66 (1905).

Summary

1. Benedict's test, in distinction to other alkaline copper tests used for the qualitative detection of sugar, is more sensitive to urinary glucose solutions than to aqueous ones.

2. Creatinine is the opacity promoting or sensitizing factor in urine which causes bulky opacity in positive Benedict tests with low concentrations of glucose.

3. The properties of cuprous creatinine account for the interfering effect of creatinine in the precipitation of cuprous oxide in Trommer's and Fehling's tests, and for its opacity promoting effect in the Benedict test.

4. The concentration of creatinine present in the majority of human urine samples has opacity promoting properties in the Benedict test on low glucose urines.

5. Exceptional concentrations of creatinine, higher or lower than the normal proportions, may lead to false results in the Benedict test.

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[CONTRIBUTION FROM THE PHYSIOLOGICAL LABORATORY, PRINCETON UNIVERSITY]

Sonoluminescence and Sonic Chemiluminescence

BY E. NEWTON HARVEY

Introduction

It is customary to designate a luminescence by the method of excitation, as electroluminescence, photoluminescence, triboluminescence, etc. Accordingly the luminescence which appears when sound waves pass through liquids has been called acoustic or sonic luminescence, for short, sonoluminescence. This type of light emission was first observed by Frenzel and Schultes[1] for supersonic and by Chambers[2] for audible frequencies. Using a magnetostriction oscillator of 8900 frequency, Chambers studied 36 pure liquids and found 14 of them to luminesce, the brightness varying inversely as the temperature and directly as the product of viscosity and dipole moment.

Frenzel and Schultes were led to look for luminescence accompanying supersonic waves in water from the formation of hydrogen peroxide which many observers (Schmitt, Johnson and Olson,[3] Beuthe,[4] Liu and Wu,[5] and Flosdorf, Chambers and Malisoff[6]) have found in fluids subjected to sonic treatment. Beuthe[4] believes

(1) Frenzel and Schultes, *Z. physik. Chem.*, **27**, 421–424 (1934).

(2) Chambers, *J. Chem. Phys.*, **5**, 290–292 (1937).

(3) Schmitt, Johnson and Olson, THIS JOURNAL, **51**, 370–375 (1929).

(4) Beuthe, *Z. physik. Chem.*, **163**, 161–171 (1929).

(5) Liu and Wu, THIS JOURNAL, **56**, 1005–1007 (1934).

(6) Flosdorf, Chambers and Malisoff, *ibid.*, **58**, 1069 (1936).

The ratio of copper to creatinine in the complex was determined, using a preparation made from an alkaline copper mixture reduced by fructose instead of glucose, to speed up the reaction and avoid errors due to reducing action of creatinine or its entrainment by precipitation in uncombined form. An aliquot of the complex made in this way was analyzed for copper by the thiosulfate method[13] and for creatinine by the Folin method,[14] preliminary work with the latter having shown no interference by copper in the development of the picramic acid color.

The ratio of copper to creatinine in the aliquot taken was found to be 0.2624 g./0.4444 g., which varies only slightly from the calculated ratio 63.57/113 for one atom of copper to one molecule of creatinine. The complex probably is a simple addition compound, $C_4H_7ON_3 \cdot CuOH$. Such compounds with zinc chloride, silver nitrate or similar salts are well known. More recently it has been shown[15] that creatinine forms addition compounds even with alkali hydroxides.

Previous Work on Cuprous Creatinine.—The existence of this compound was first suggested by Maly,[16] investigating previous observations that Trommer's test is less sensitive to urinary glucose than to aqueous glucose. Maschke[17] prepared such a complex by saturating creatinine solutions with sodium carbonate and adding Fehling solution, but did not analyze it. The work of these investigators appears to have been overlooked in subsequent reports on the influence of creatinine on alkaline copper reactions.[7,18,19] In Merck's "Reagenzien-Verzeichnis"[20] as well as in "Beilstein," Maschke's finding is referred to as a test for creatinine detection, as the author emphasized, rather than as a complex important in copper tests for urinary glucose.

Cuprous Creatinine in Alkaline Copper Tests on Urine.—Aside from its susceptibility to oxidation, cuprous creatinine is a very stable compound, the bond being resistant to alkali, other than a slow conversion of creatinine to creatine which is slight in the time needed for a test. The complex is very soluble in alkali hydroxide, so that in a Trommer or Fehling test on glycosuric urine, containing also sufficient creatinine to combine with all the cuprous oxide formed, no visible precipitate results. In carbonate solution, on the other hand, the cuprous creatinine complex is quite insoluble (Table I), and very voluminous. These properties lead, in effect, to an enormous magnification of the volume of the precipitated cuprous oxide in a positive Benedict test.

The properties of cuprous creatinine, therefore, explain both the sensitivity of Benedict's test for urinary glucose, and the delay in precipitation in alkaline copper reagents employing hydroxide. The explanation of Benedict[10,11] that in the latter creatinine delays precipitation due to the fact that the normal reduction of the solution is inhibited for a period long enough to allow the strong alkali present to decompose the reducing substance formed from the sugar molecule into compounds which have no reducing power is not correct. It may be shown by following the reduction with phosphomolybdic acid as in blood sugar analysis, that any delay by creatinine on the reduction of copper by glucose is negligible. The delay in Trommer and Fehling tests reported by Von Babo and Meissner,[5] Winogradoff,[6] Worm-Müller,[18] Eury,[19] MacLean,[7] and Laird,[21] actually is a delay in the appearance of a precipitate and not a delay in the reduction of copper by glucose.

The Paradoxical Role of Creatinine in the Benedict Test.—It is well known that in addition to creatinine there are other substances either normally present in urine or resulting from pathological conditions or administration of medicaments, which disturb the normal course of alkaline copper reactions. Reduction by creatinine, uric acid, urochrome, etc., has a greater interfering effect in those tests which use a large proportion of urine to reagent (Trommer and most Fehling variations) than in the Benedict test, in which the urine comprises less than 10% of the liquid in the test. It is probable that this low ratio of urine is just as important in the Benedict test as is the use of carbonate as alkali and the stability of the reagent. Even in this restricted urinary proportion, however, creatinine still has interfering properties as well as the desirable sensitizing effect.

The opacity promoting property of creatinine is effective only in a range of concentrations from

(13) "Methods of Analysis," Assocn. Offic. Agr. Chem., 2nd ed., Washington, D. C., 1925, p. 191.
(14) Folin, *Z. physiol. Chem.*, **41**, 223 (1904).
(15) Bolliger, *J. Proc. Roy. Soc. N. S. Wales*, **71**, 40 (1937).
(16) Maly, *Z. anal. Chem.*, **10**, 382 (1871).
(17) Maschke, *ibid.*, **27**, 134 (1878).
(18) Worm-Müller, *Arch. ges. Physiol.*, **27**, 22 (1882).
(19) Eury, *Bull. soc. chim.*, [3] **23**, 41 (1900).
(20) "Merck's Reagenzien-Verzeichnis," 7th ed., Merck and Co., Darmstadt, 1932.
(21) Laird, *J. Path. Bact.*, **16**, 398 (1912).

aqueous glucose solutions which yield typical Trommer or Fehling tests give a barely perceptible red haze by Benedict's method. For urinary work, however, Benedict's reagent is unexcelled, since it gives bulky opacities with glucose concentrations which fail to precipitate with other reagents, and clear tests with urines containing no glucose but which give reductions with the Trommer or Fehling tests. The possibility that the increased delicacy of the Benedict test on urine might be due to a urinary ingredient was the origin of the work reported in this paper.

Creatinine as Opacity Promoter in the Benedict Test.—It is easy to show that an ingredient of urine promotes the typical Benedict test opacity with minimal amounts of glucose. Normal urine if shaken with blood charcoal yields a water-white filtrate which on addition of 0.1% of glucose gives in the Benedict test the barely perceptible red haze of cuprous oxide characteristic of aqueous glucose. A similar concentration of glucose added to the original urine gives the usual opaque test, showing that the urine contains a promoter which is removed by the charcoal. Lloyd's alkaloidal reagent, a type of fuller's earth used by Folin and Berglund,[12] has a similar action. Of the substances known to be removed from urine by Folin and Berglund's method, creatinine alone was found to be an opacity promoter. Solutions made of glucose with a proper amount of creatinine react in the Benedict test exactly as does glucose in urine.

Experimental.—To 37.5 cc. of urine were added 12.5 cc. of 0.1 *N* sulfuric acid and 4 g. of Lloyd's earth. After shaking for two minutes, the mixture was filtered, the filtrate neutralized and glucose added to 0.1%. The solution reacted to the Benedict test like aqueous glucose. The opacity promoter is removed readily from the Lloyd's earth by elution with dilute carbonate solution. The elution plus 0.1% glucose gives an opaque Benedict test.

Cuprous Creatinine.—The knowledge that creatinine is the sensitizer or opacity promoter directs attention to a possible mechanism. Reduction experiments on Benedict solution with glucose and creatinine at lower temperatures than the usual boiling, give at 60° a bulky, slightly yellowish precipitate, at 50° a voluminous white one which agglutinates readily on shaking and filters well. The same reaction goes on at room temperature, slower but complete overnight. Further experiment showed the precipitate to be a compound of creatinine and cuprous oxide, the existence of which has been reported previously, in incomplete form, by several investigators, whose work will be discussed a little later.

(12) Folin and Berglund, *J. Biol. Chem.*, **51**, 209 (1922).

Experimental.—A mixture of 60 cc. of 0.5 *M* creatinine (5.65%) in *N* hydrochloric acid and 25 cc. of 3 *M* glucose was added to 1200 cc. of Benedict reagent and allowed to stand overnight. The bulky white precipitate was filtered off on a Büchner funnel and washed free from cupric ion with 15% sodium carbonate solution. The white solid was removed from the filter and cautiously neutralized with 20% acetic acid, atmospheric oxidation producing some blue color. The heavy neutral suspension was transferred to centrifuge tubes and washed free from cupric ion by repeated settling and resuspension in water. Air oxidation of the moist precipitate may be hindered by storing it in practically full, tightly stoppered tubes. Solubility data for the substance are given in Table I; the aqueous solution shows *p*H 6.5. It is soluble in acids, without effervescence.

TABLE I

SOLUBILITY DATA OF CUPROUS CREATININE, $C_4H_7ON_3 \cdot CuOH$

Solvent	Soly., g./100 cc.
Pure water	1.1
Sodium carbonate, 7.5%	1.0
Sodium carbonate, 8%	0.87
Sodium carbonate, 9%	.14
Sodium carbonate, 10%	.054
Sodium carbonate, 15%	.018
Sodium carbonate, 20%	.016
Sodium carbonate, 30%	.008
Benedict solution at 25°	.019
Benedict solution at 100°	.09

The presence of creatinine in the precipitate may be shown by the picric acid or nitroprusside test, while cuprous copper is proved by oxidation and by precipitation with sulfide, cyanide, ferrocyanide, ferricyanide, or thiocyanate, the last three showing the precipitates characteristic of cuprous ion. Neutral chlorides have no effect but dilute hydrochloric and hydrobromic acids give a white precipitate, soluble in excess.

A saturated aqueous solution of the complex on addition of carbonate gives a bulky and voluminous precipitate rather than the creamy and chalk-like original neutral suspension. High concentrations of citrate and sulfate cause a clouding of the saturated aqueous solution, while tartrate, pyrophosphate, oxalate, acetate, salicylate and sulfite have no visible effect.

Cuprous creatinine may be prepared rapidly in small quantities by heating the mixture to incipient boiling, and then cooling rapidly in running water. Aside from its pure white color, the resulting opacity is similar to that of a positive Benedict test.

lytic activity of the corresponding ammonium salts upon the ammonolysis of esters in liquid ammonia. Like ammonia, butylamine is a strongly basic solvent in which ionization of weak acids is presumably enhanced. On the other hand, however, the low dielectric constant ($\epsilon = 5.4$)[7] of the solvent undoubtedly promotes formation of inactive ion pairs, or even larger aggregates, with the consequence that stoichiometric concentrations give little or no insight into the concentrations of either the butylammonium ions or the negative ions in solution.

It also should be pointed out that the presence of a fairly large mole fraction of ester in the solutions under investigation undoubtedly influences the ionization of the butylammonium salts. Actually, very concentrated solutions of ester in amine were used in all experiments.

It is also apparent from a comparison of the experimental series 4, 9 and 10, that the ratio of amine to ester affects the rate of the reaction very appreciably. In the first eight series the molar ratios of amine, ester and catalyst are given approximately by the numbers 380:200:7. As the mole ratio of amine to ester is increased, the value for the specific reaction rate constant also becomes larger. It is obvious, therefore, that the reaction is not even pseudo-bimolecular in character, except for specified conditions. To obtain more rapid reaction it is advisable to use quantities of amine considerably in excess of those required stoichiometrically.

The tremendous effect of the addition of the relatively small quantity of butylammonium salt is emphasized by a comparison of the half-life times of the first ten series, with that for the uncatalyzed reaction. These findings again emphasize our contention[5] that the mechanism of all solvolytic reactions, whether they be hydrolytic, ammonolytic or aminolytic, is fundamentally the same as illustrated by the reaction

$$\left.\begin{matrix}\mathrm{HOH}\\ \mathrm{HNH_2}\\ \mathrm{R''NH_2}\end{matrix}\right\} + \mathrm{RCOOR'} \xrightarrow{\mathrm{S{\cdot}H^+}} \mathrm{RCO}\left\{\begin{matrix}\mathrm{OH}\\ \mathrm{NH_2}\\ \mathrm{NHR''}\end{matrix}\right. + \mathrm{R'OH}$$

(7) Schlundt, *J. Phys. Chem.*, **5**, 503 (1901).

Summary

1. The aminolysis of ethyl phenylacetate in *n*-butylamine to yield the N-butylamide of phenylacetic acid is catalyzed by butylammonium salts.

2. The catalytic effect of equimolar concentrations of various butylammonium salts decreases with the anion in the following order: $Cl^- > C_2H_3O_2^- > C_6H_5COO^- > Br^- > NO_3^- > CNS^- > I^- > ClO_4^-$.

URBANA, ILLINOIS RECEIVED JUNE 21, 1939

[CONTRIBUTION FROM THE SAMSON LABORATORIES]

The Relation of Cuprous Creatinine to Tests for Sugar in Urine[1]

BY MEYER SAMSON

It is almost a hundred years since Trommer[2] published the first practical directions for a copper reduction test for sugar. Of the hundreds of modifications[3] subsequently proposed, only the methods of Trommer, Fehling[4] and Benedict are largely used today.

Most of the proposed modifications were designed to avoid interference. Creatinine soon was recognized as the principal source of trouble, which arose from its own reducing powers, as well as from its property of holding in solution the cuprous oxide formed in the presence of glucose.[5-7]

Benedict,[8] in reviving the forgotten idea of Possoz[9] of using carbonate in place of hydroxide as alkali, believed he had found a copper solution on which creatinine was without appreciable effect.[10] When he later proposed the copper carbonate–citrate mixture in the solution[11] known by his name, he claimed it to be more sensitive to glucose either in pure solution or in urine than is Fehling's fluid. This is not correct, since

(1) Presented before the Division of Biological Chemistry, 96th meeting, American Chemical Society, Milwaukee, Wis., September 5–9, 1938.

(2) Trommer, *Ann.*, **39**, 360 (1841).

(3) Dehn, Jackson and Ballard, *Ind. Eng. Chem., Anal. Ed.*, **4**, 413 (1932).

(4) Fehling, *Ann.*, **72**, 106 (1849).

(5) Von Babo and Meissner, *Z. Rat. Med.*, **3**, 329 (1858).

(6) Winogradoff, *Arch. Path. Anat.*, **27**, 533 (1863).

(7) MacLean, *Biochem. J.*, **2**, 156 (1907).

(8) Benedict, *J. Biol. Chem.*, **3**, 101 (1907).

(9) Possoz, *Compt. rend.*, **75**, 1836 (1872).

(10) Benedict, *J. Am. Med. Assoc.*, **57**, 1193 (1911).

(11) Benedict, *J. Biol. Chem.*, **5**, 484 (1908).

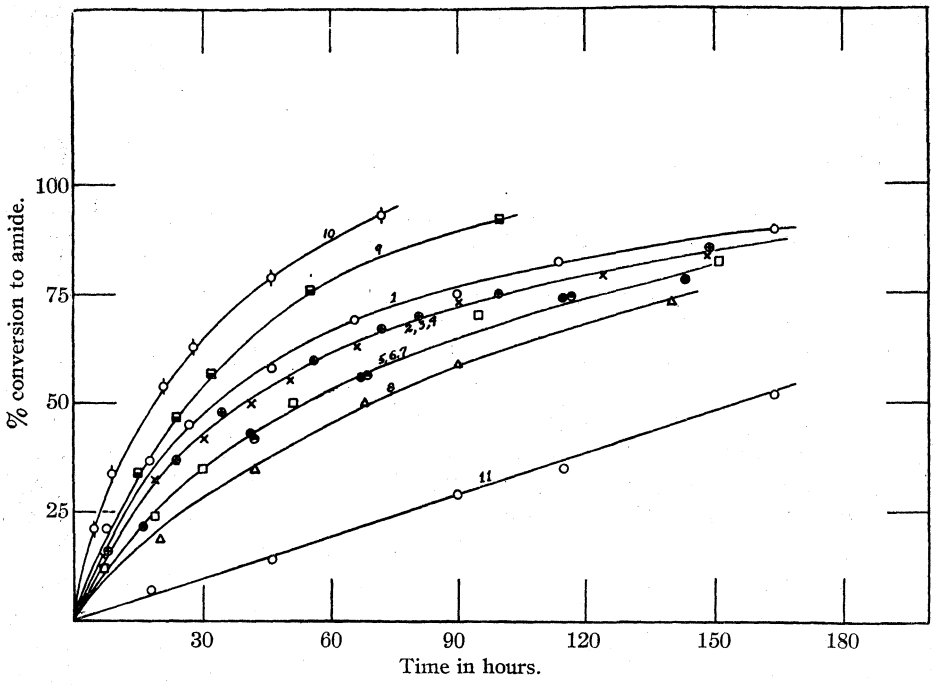

Fig. 1.—Catalytic effect of various butylammonium salts on the reaction between *n*-butylamine and ethyl phenylacetate (see Table I for specific data). Curves represent the use of equimolar quantities of different catalysts (S = $C_4H_9NH_2$): 1, S·HCl; 2, 3, 4, S·HBr, S·$HC_2H_3O_2$, S·$HOOCC_6H_5$; 5, 6, 7, S·HNO_3, S·HSCN, S·HI; 8, S·$HClO_4$; 11, no catalyst. Curves 4, 9, and 10 show the effect of increasing the molar ratio of amine to ester using $C_4H_9NH_2$·HBr as catalyst.

lytic effect is definitely dependent upon the nature of the anion.

A plot of the function log $(a - x)/(b - x)$ against time indicates that these reactions are pseudo-second order, but it is obvious that the butylammonium salt plays a definite part in the reaction, since the values of the specific reaction rate constants as given in Table I vary with the nature of the salt. The data in Table I indicate a specific anion effect which for equimolecular concentrations of added butylammonium salts decreases in the order

$$Cl^- > C_2H_3O_2^- > C_6H_5COO^- > Br^- > NO_3^- > CNS^- > I^- > ClO_4^-$$

No information is available in the literature concerning the physical properties (conductivity, degree of ionization, etc.) of the respective butylammonium salts in butylamine. It is significant, however, that the above order parallels, except for the position of the chloride, the order of cata-

TABLE I

AMINOLYSIS OF ETHYL PHENYLACETATE IN ANHYDROUS *n*-BUTYLAMINE AT 25°

Concentration of catalyst = 0.1 mole per liter; a = concentration of amine in moles per liter; b = concentration of ester in moles per liter.

Curve no. (see Fig. 1)	Catalyst used	a	b	$K \times 10^3$	t 1/2 (calcd.)	t 1/2 (exptl.)
1	$C_4H_9NH_2$·HCl	5.35	2.80	4.65	33	33
2	$C_4H_9NH_2$·$HC_2H_3O_2$	5.36	2.80	3.87	39.5	40
3	$C_4H_9NH_2$·$HOOCC_6H_5$	5.35	2.80	3.85	40	40
4	$C_4H_9NH_2$·HBr	5.37	2.80	3.85	40	40
5	$C_4H_9NH_2$·HNO_3	5.34	2.80	2.93	51	52
6	$C_4H_9NH_2$·HSCN	5.36	2.80	2.81	54	53
7	$C_4H_9NH_2$·HI	5.34	2.80	2.57	59	57
8	$C_4H_9NH_2$·$HClO_4$	5.40	2.80	2.09	73	70
9	$C_4H_9NH_2$·HBr	7.02	1.80	4.04	26	27
10	$C_4H_9NH_2$·HBr	7.78	1.33	5.27	18	18
11	None	5.45	2.80	0.87	171	158

and upon the nature of the functional alcoholic groups and to a smaller extent on the position of the benzene ring in the molecule.

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[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Acid Catalysis in Amines. II. The Catalytic Effect of Various Butylammonium Salts on the Aminolysis of Ethyl Phenylacetate in Anhydrous *n*-Butylamine

BY PAUL K. GLASOE, J. KLEINBERG AND L. F. AUDRIETH

Experimental evidence already has been presented to demonstrate that the ammonolysis of esters in anhydrous liquid ammonia is markedly catalyzed by the presence of ammonium salts.[1-4] The catalytic effect of equimolar concentrations of different ammonium salts has been found to decrease in the following order: $C_2H_3O_2^- > C_6H_5COO^- > Cl^- > Br^- > NO_3^- > I^- > ClO_4^-$.[2,4] This result is quite unexpected, especially if this effect is to be interpreted as an example of acid catalysis in a non-aqueous solvent. This anion order is exactly opposite from what might be expected from a consideration of those physical properties of ammonium salts in liquid ammonia which presumably permit a quantitative estimation of the ammonium ion concentration.

In extending these studies from ammonia to amines it has been shown that aminolytic reactions are also catalyzed by the solvated proton, introduced into the reaction mixture in the form of the amine salt.[5] In view of the anomalous behavior of ammonium salts in accelerating the ammonolysis of esters it became of distinct interest to determine whether the catalytic effect of equimolar concentrations of different amine salts also varied with the nature of the anion, as observed in the case of liquid ammonia. The present investigation was therefore undertaken to study the influence of various butylammonium salts on the rate of the reaction between anhydrous butylamine and ethyl phenylacetate.

Experimental

Procedure.—Due to the excessive solubility of the various butylammonium salts in anhydrous butylamine, and their hygroscopicity, the method used in the actual isolation and preparation of analogous cyclohexylammonium salts[5] could not be employed satisfactorily.[6] Consequently, butylammonium salts were in most instances not isolated, but prepared in butylamine by adding a definite quantity of ammonium salt to an excess of amine. The resulting mixtures were then warmed on the steam-bath under slightly reduced pressure to effect removal of ammonia, yielding solutions of known content of butylammonium salts.

In preparing standard solutions for reaction velocity studies a definite quantity of ester was added to the amine solution of the specific salt and the mixture diluted with amine to exactly 25 cc. Two-cc. samples of this mixture were transferred to small Pyrex test-tubes which were immediately sealed and placed in a thermostat at 25°. At definite intervals of time tubes were removed, broken into an excess of standard hydrochloric acid and back titrated with standard sodium hydroxide using a methylene blue–methyl red indicator. The difference between these titrations and an initial one carried out at the beginning of each series of runs gave a measure of the amount of amine used and therefore a measure of the amount of ester which had reacted to form the N-substituted amide.

Discussion of Results

Ethyl phenylacetate reacts with butylamine in accordance with the equation: $C_6H_5CH_2COOC_2H_5 + C_4H_9NH_2 \longrightarrow C_6H_5CH_2CONHC_4H_9 + C_2H_5OH$. The reaction is very slow, as is evident from Curve 11, Fig. 1, in which the % yield of amide is plotted as a function of time. Addition of butylammonium salts, presumably acting as acids in butylamine because of the presence of the $C_4H_9NH_2.H^+$ ion, accelerates aminolysis markedly. However, the magnitude of the cata-

(1) Slobutsky and Audrieth, *Proc. Natl. Acad. Sci.*, **23**, 611 (1937).
(2) Fellinger and Audrieth, THIS JOURNAL, **60**, 579 (1938).
(3) Audrieth and Kleinberg, *J. Org. Chem.*, **3**, 312 (1938).
(4) Shatenshtein, THIS JOURNAL, **59**, 432 (1937).
(5) Glasoe and Audrieth, *J. Org. Chem.*, **4**, 34 (1939).

(6) It was also observed in the attempted preparation of butylammonium nitrate from butylamine and ammonium nitrate that aminolysis with evolution of ammonia was limited to dilute solutions and that further quantities of ammonium nitrate could be dissolved subsequently in the amine without reaction.

TABLE III

PHYSICAL PROPERTIES OF THE ESTERS

Ester	Recrystn.[a] medium	Crystal form	M. p.,[b] °C.	Analyses (%)[c] Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found
Methyl[d]	C_6H_6–ligroin	Plates	95.5–96.0						
Ethyl[e]	Aq. alc.	Needles	56.0–56.5						
Phenyl	Acetone-alc.	Needles	129–130						
Benzyl	Alc.	Plates	83.5–84.5						
1-Ph-ethyl	Alc.	Needles	42.5–43.5[f]	66.39	66.23	4.83	4.68		
2-Ph-ethyl	Alc.	Plates	61.5–62.0					5.05	4.92
1-Ph-propyl	Alc.	Prisms	56.5–57.5[g]						
2-Ph-propyl	Alc.	Plates	64.5–65.5					4.91	4.82
3-Ph-propyl	Alc.	Needles	46.5–47.5[h]						
1-Ph-isopropyl[i]	Alc.	Long needles	136–137	67.35	67.51	5.30	5.20	4.91	4.82
2-Ph-isopropyl[j]	Alc.	Plates	61–62		67.50		5.35		5.06

[a] Recrystallized to constant m. p. [b] M. p.'s corrected. [c] By Dr. H. Stantial. [d] Calcd.: CH_3O, 17.14; found 17.27. [e] Calcd.: C_2H_5O, 23.09; found 23.25. [f] Ward, *J. Chem. Soc.*, 453 (1927), gives m. p. 47–48°. [g] Meisenheimer, *Ann.*, **442**, 184 (1925), gives m. p. 59–60°. [h] Kirner, THIS JOURNAL, **48**, 1111 (1926), gives m. p. 45–46°. [i] Solubility in methanol and ethanol much less than other esters. [j] Prepared from both alcohols.[11,12] M. p. and mixed m. p. both products identical.

or semi-liquid samples were analyzed by introducing them by a capillary pipet into a tin foil cup of double thickness. An ethanolysis blank on the 1-phenylpropyl ester was similar to those obtained for methanolysis. The experimental values (corrected on the basis of the controls) are shown graphically in Figs. 1 and 2.

Synthesis of the Compounds.—1-Phenylpropanol was prepared in 44% yield according to Klages' method[10]; b. p. 102–104° at 13–14 mm.

2-Phenylpropanol was synthesized in five stages: (1) α,α-phenylmethyl-β-chloroethanol was made by a slight modification of Tiffeneau's procedure[11] from chloroacetone and phenylmagnesium bromide. The reaction mixture was stirred mechanically at −10° during the addition of the Grignard reagent and then allowed to warm slowly to room temperature; a 55% yield of light-yellow liquid, b. p. 129–132° at 21 mm., was obtained. (2) The chlorohydrin was decomposed with sodium ethoxide[12] to give 79% of phenylmethylethylene oxide, a colorless liquid, b. p. 72–75° at 10–11 mm. (3) The oxide was isomerized to hydratropic aldehyde, in 66% yield, by treating with hydrochloric acid.[13] A fraction boiling at 80–87° at 10–11 mm. was collected. (4) Zinc dust–acetic acid reduction of the aldehyde[13] gave 57% of 2-phenylpropyl acetate, b. p. 95–105° at 10–11 mm. Cohen, *et al.*, record a b. p. 125° at 14 mm. while Wohl and Berthold[14] give 103–105° at 11 mm. (5) Saponification of the acetate[13] gave 70% of 2-phenylpropanol, b. p. 110–113° at 11 mm.

2-Phenylisopropyl alcohol was prepared in 58% yield according to Austerweil and Cochin.[15] Carpenter,[16] using phenylmagnesium bromide and propylene oxide, obtained a mixture of this alcohol and 2-phenylpropanol. We obtained by this method only 2-phenylisopropyl alcohol (49% yield, b. p. 105–107° at 22 mm., the same as that for the product of the other reaction). The phenyl urethan, prepared from both products, melted at 87–88°. Emde and Runne[17] give a m. p. of 90°.

1-Phenylisopropyl alcohol resulted in 58% yield when Klages' procedure,[18] with special precautions against too great a rise of temperature during the extraction, was used. Its b. p. was 95–96° at 14–15 mm.

The *p*-nitrobenzoyl esters of the aromatic alcohols, with the exceptions noted, were prepared from the alcohol and the acid chloride (10% excess) in dry pyridine. After standing for several hours at room temperature the ester was extracted with ether, the ether layer was shaken with dilute sulfuric acid, then with dilute sodium carbonate and dried over anhydrous sodium sulfate. The phenyl ester was prepared from the acid chloride and phenol without solvent.[19] The methyl ester was made by dissolving the benzyl ester (2 g.) in methanol (10 ml.), adding about 0.1 equivalent of sodium and allowing the solution to stand one-half hour at room temperature. The ethyl ester was prepared by the action of a dilute sodium ethoxide solution on the ester residues from previous experiments.

Acknowledgments.—The author wishes to acknowledge the assistance given him by the late Dr. F. B. Allan, by Professor W. S. Funnell and Dr. G. F. Wright.

Summary

1. The relative rates of alcoholysis of several aralkyl *p*-nitrobenzoates in methanol, methanol–ether, and ethanol–ether have been studied.

2. Methanolysis takes place more rapidly than ethanolysis.

3. The relative reactivity of eight aralkyl groups has been shown to be dependent largely upon the molecular weight of the aryl alcohol

(10) Klages, *Ber.*, **36**, 621 (1903).
(11) Tiffeneau, *Ann. chim. phys.*, [8] **10**, 352 (1907).
(12) Klages, *Ber.*, **38**, 1969 (1905).
(13) Cohen, Marshall and Woodman, *J. Chem. Soc.*, **107**, 897 (1915).
(14) Wohl and Berthold, *Ber.*, **43**, 2185 (1910).
(15) Austerweil and Cochin, *Compt. rend.*, **150**, 1695 (1910).
(16) Carpenter, *Chem. Zentr.*, **107**, I, 2440 (1936).
(17) Emde and Runne, *Arch. Pharmazie*, **249**, 363 (1911).
(18) Klages, *Ber.*, **35**, 2639 (1902).
(19) Raiford, Taft and Lankelma, THIS JOURNAL, **46**, 2051 (1924).

suitable without modification. The results are shown in Table II.

The efficacy of the method was demonstrated by submitting synthetic ester–alcohol mixtures to the entire procedure. Of the total weight of esters taken, 94–97% could be recovered.

Method II

Reagents.—The methanol (Kahlbaum "zur Analyse") contained 0.35% water, a value that remained constant during four months. The ether was Merck "anhydrous" dried with sodium and redistilled in 5–10 ml. lots just before use. The ethanol was prepared by dehydration of "absolute" alcohol with diethyl phthalate and sodium[8] and was protected from carbon dioxide. Of the sodium methoxide solution the following volumes were used for 0.100 g. of ester: benzyl, 0.47 ml.; phenylethyl, 0.44 ml.; phenylpropyl, 0.41 ml. (0.0110 equivalent sodium per mole ester) and of the sodium ethoxide solution, 0.50 ml., 0.47 ml., and 0.44 ml. (0.0083 equivalent sodium).

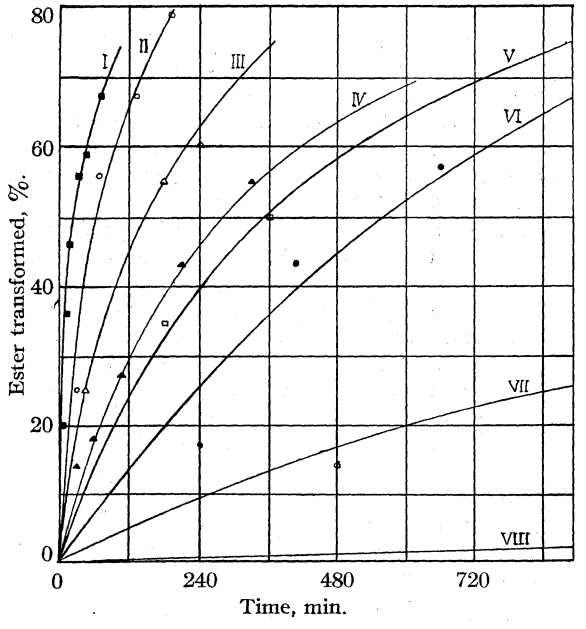

Fig 1.—Rates of methanolysis of aralkyl *p*-nitrobenzoates at 25° in MeOH–ether; 0.0110 equiv. sodium as catalyst; 0.35% water in MeOH: Curve I ■, benzyl; II ○, 2-ph-ethyl; III △, 2-ph-propyl; IV ▲, 3-ph-propyl; V □, 1-ph-propyl; VI ●, 1-ph-ethyl; VII ◪, 2-ph-isopropyl; VIII 1-ph-isopropyl. Additional data: for V, 1080, 75.4%; 1770, 81.8%; VI, 1200, 79.5%; 1800, 89.5%; VII, 1020, 40.6%; 1740, 50.2%; VIII, 3180, 4.4%.

Procedure.—To 0.100 g. of dried ester were added 5.00 ml. of ether, 5.00 ml. of the alcohol, and the catalyst solution, all at 25.0°. The methanolyses were stopped as in Method I while for the ethanolyses a small piece of solid carbon dioxide was used. Both gave consistent results. The solution was transferred to a weighed 15-ml. centrifuge tube provided with a hook of nichrome wire and the solvent was removed *in vacuo* over sulfuric acid; in order to prevent loss by bumping, the tube was provided near the top with a side-arm pulled out to a capillary of 1–2 mm. bore and the top of the tube was closed with a rubber stopper. Methanol could be removed quantitatively in two and one-half to three hours, ethanol in three and one-half to four hours. Control experiments proved that no measurable alcoholysis occurred during the separation. In some of the ethanolyses the intermediate ester–carbinol mixtures obtained were liquid or semi-liquid in which case last traces of solvent were removed in a drying pistol over phosphorus pentoxide. The residue was melted down and, when possible, allowed to crystallize by dipping the tube into ice water. The amount of methyl or ethyl ester present was determined by duplicate analyses.

Synthetic mixtures corresponding to (a) 50% and (b) 100% methanolysis of the original ester, when analyzed by Pregl's procedure, gave inconsistent results, due chiefly to insufficient heating of the sample (twenty minutes). The shorter, volumetric Vieböck method, as adapted by Lieff, Marks and Wright,[9] together with a heating time of forty-five minutes, yielded reproducible values. The blanks were somewhat higher than the theoretical, because of partial codistillation of the aromatic iodide; at half-conversion the error was about 4% and at complete converson, about 11%. Therefore, experimental points above 80% conversion were not considered. Determination of ethoxyl required seventy-five minutes of heating and higher reflux of the vapors in the apparatus. Liquid

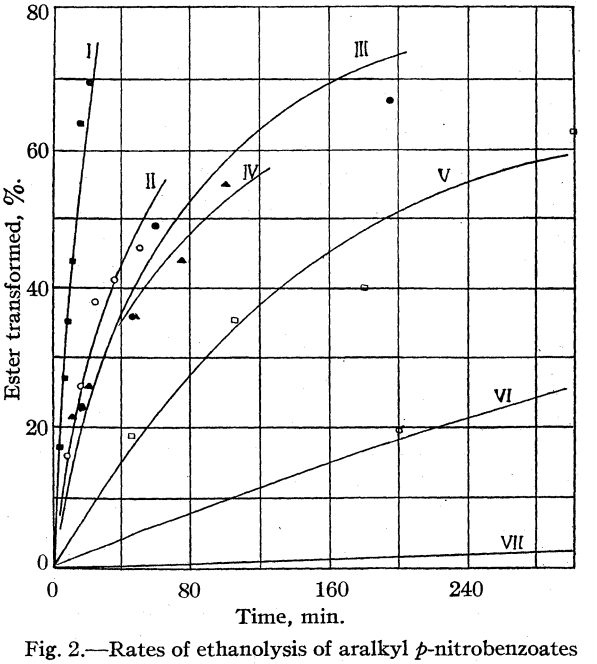

Fig. 2.—Rates of ethanolysis of aralkyl *p*-nitrobenzoates at 25° in EtOH–ether; 0.0083 equiv. sodium as catalyst; 0.0% water in EtOH: Curve I ■, benzyl; II ○, 2-ph-ethyl; III ●, 1-ph-ethyl; IV ▲, 2- and 3-ph-propyl (almost identical); V □, 1-ph-propyl; VI ◪, 2-ph-isopropyl; VII 1-ph-isopropyl. Additional data: for VI, 360, 24.1%; 720, 40.9%; 1380, 56.1%; VII, 1380, 4.6%.

(8) According to Manske, THIS JOURNAL, **53**, 1106 (1931), the water content of alcohol so prepared is too small to be detected.

(9) Lieff, Marks and Wright, *Can. J. Research*, **B15**, 529 (1937).

sults being obtained with peroxide-free solvent and with that giving a strong ferrous chloride test.

Although there is no simple, direct variation between the rate of alcoholysis and the molecular weight of the alcohol combined with the ester, the rate is strongly influenced by the length of the carbon chain. Introduction of one and two methylene groups into the benzyl radical to give 2-phenylethyl and 3-phenylpropyl results in successive, considerable decreases in reactivity. This order is the converse of that obtained by Fehlandt and Adkins[2a] from equilibrium studies of the corresponding acetates in a slightly acid medium. Phenyl *p*-nitrobenzoate reacts with methanol much more rapidly even than the benzyl ester.

The effect of branching of the carbon chain is somewhat more difficult to interpret. As in a large number of other reactions, the substitution of a hydrogen on the α-carbon atom by phenyl or methyl results in lowered reactivity. The tertiary aralkyl (8) is practically inert under the same conditions for which the isomeric primary and secondary radicals react. The secondary propyl and isopropyl groups (5) and (7) are replaced less readily than the primary (3) and (4); and the secondary ethyl (6) is less reactive than the primary (2). The effect of branching at either the β- or the γ-position, such as in (3) and (4)—which of course does not alter the nature of the functional alcoholic group—is not perfectly apparent, although it is reasonable to suppose that any blocking effect will be reduced the farther the substitution occurs from the reactive carbon atom.

Our observation is that methanolysis is a far more rapid reaction than ethanolysis under similar conditions; for instance, reaction in absolute methanol is extremely fast even at low catalyst concentrations while that in absolute ethanol can be very conveniently measured. Fehlandt and Adkins found that methyl alcohol has the highest replacement value of all the alcohols they studied. A possible explanation may be found in a consideration of these alcohols as weak acids in the sense suggested by Brönsted.[5] McEwen[6] has shown that methanol is a stronger acid than ethanol; therefore, it is reasonable to conclude that since more methoxyl ions than ethoxyl ions are available for addition to the ester carbonyl, methanolysis will be the faster reaction. McEwen has found that, in general, the relative acidity of alcohols is in the descending order, primary, secondary, tertiary, which is the same as for the alcoholysis of an ester. With the exception of (6), the order of relative reactivity toward both alcohols is the same. No explanation has been found for the apparently anomalous behavior of this ester.

(5) Brönsted, *J. Phys. Chem.*, **30**, 777 (1926).
(6) McEwen, THIS JOURNAL, **58**, 1124 (1936).

Experimental Part

Two analytical procedures have been adopted: the first is applicable only to esters of alcohols possessing a certain solubility in water, *e. g.*, benzyl and 2-phenylethyl, while the second may be used for the esters of any alcohol provided that the latter has a sufficiently high boiling point. According to Method I the aryl alcohol formed during the reaction is removed prior to analysis; in Method II only the solvent alcohol is separated.

Method I

Reagents.—The methanol was C. A. F. Kahlbaum "zur Analyse," partially dehydrated by distilling from sodium. The fraction of b. p. 64.5–64.8° contained 0.60% water as determined according to Jones and Amstell.[7] It was protected from atmospheric carbon dioxide. The sodium methoxide solution, standardized by Pregl's micro-procedure, showed no variation in concentration on standing for two months.

Procedure.—The ester (0.100 g.), dried several hours *in vacuo*, was dissolved in 7.00 ml. of methanol at the temperature of the thermostat (25.0 ± 0.1° over short reaction periods and ±0.2° over longer intervals). For the benzyl ester 0.55 ml. of catalyst solution was added, and for the 2-phenylethyl ester, 0.52 ml. (0.0230 equivalent of sodium). The alcoholysis was stopped by adding a few drops of a hydrochloric acid–methanol solution. The solution was evaporated just to dryness on the water-bath, the residue was taken up in 5 ml. of ether and transferred to a 15-ml. separating funnel. The ethereal solution was allowed to drop slowly onto a micro filter (prepared according to Pregl for the halogen determination) which was supported in a Pyrex steam jacket attached to the outlet tube of a water-bath. The residual esters and aryl alcohol were separated by extracting the latter with water (5–10 ml.). After dissolving the esters in hot acetone (10 ml.), the solvent was removed, and the residue dried *in vacuo*, powdered fine and analyzed for methoxyl (in duplicate). Pregl's gravimetric method was found to be

TABLE II

METHANOLYSIS OF ARALKYL *p*-NITROBENZOATES

Benzyl		2-Phenylethyl	
Time, min.	Ester transformed, %	Time, min.	Ester transformed, %
5	30	15	25
10.4	52	30	57
20	75	45	73
30	82	60	81
50	95	90	92

(7) Jones and Amstell, *J. Chem. Soc.*, 1316 (1930).

the preliminary reaction. Silver ion adsorption is indicated for both reactions. The reactions were studied over the *p*H range 3.7–8.5.

4. The catalyzed reduction of silver ion by hydroxylamine may be expressed by the equation $Ag^+ + NH_2O^- \longrightarrow Ag + N + H_2O$. The NH_2O radical, if it is formed, decomposes at a rate rapid in comparison with the reduction process.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY, UNIVERSITY OF TORONTO]

The Relative Rates of Alcoholysis of Certain Aralkyl *p*-Nitrobenzoates

BY LAURENCE F. KING

Previous investigations on the alcoholysis of esters, chiefly those of aliphatic alcohols, indicate that the nature of the functional alcoholic groups involved, and the amount of branching of the carbon chain of the alkyl rather than its length, are the chief factors determining both the relative velocity with which replacement of alkyl radicals occurs[1] and the extent to which reaction will proceed until equilibrium is attained.[2] Tertiary alkyls are less reactive than secondary, which in turn are less reactive than primary. The replacement values of straight-chain groups, derived from both types of measurement, are generally of the same order of magnitude no matter what the length of the carbon chain, and are greater than those of more centralized radicals. These generalizations are in disagreement with the observations of Bellet[3] on rates of replacement of certain aromatic alkyls.

The present paper constitutes a method for measuring the velocities with which esters of aromatic alcohols react in a faintly alkaline medium with aliphatic alcohols of low molecular weight. In order to eliminate the necessity for the customary fractional distillation of the reaction mixture, methanol and ethanol were chosen as the solvent alcohols; separation could then be effected quantitatively at room temperature and analysis made by a methoxyl or ethoxyl determination. Rates of reaction of the readily purified solid esters with the sodium alkoxide in a large excess of the alcohol were studied, absolute ether being used as a diluent in most cases.

Pseudo first-order velocity coefficients decrease markedly but regularly with the progress of the reaction; the existence of side reactions is indicated whether the medium is methanol, ethanol or diluted with ether. Kremann[4] has shown that hydrolysis of the ester may be a relatively important factor, and in confirmation of this we observed that the rates of methanolysis of phenyl and benzyl *p*-nitrobenzoates are influenced to an abnormally high degree by slight variations in the concentration of alkali and water in the solvent. Hydrolysis is not the only disturbing side reaction, however, since the K-values in ethanol exhibit no greater constancy than those in methanol; in the latter case the concentrations of alkali and water are much higher than in the former. Assumptions of other than a simple first-order reaction lead to no greater constancy of K. In order to relate, more or less quantitatively, the reactivities of the ester alkyl groups, the first-order coefficients were averaged for the same reaction interval (15–40% ester conversion) and the benzyl radical was assigned a value of 100 (see Table I). The limits of accuracy shown are an indication only of the "fading" of the K-values and not of errors of measurement. The presence of anhydrous ether is apparently of little consequence as far as relative rates are concerned: for groups (1) and (2) the ratio K_1/K_1 is approximately equal to K_2/K_2. The peroxide content of the ether is not a determining factor, identical re-

TABLE I

RELATIVE REACTIVITY OF ARALKYL GROUPS (R) IN ALCOHOLYSIS OF *p*-NITROBENZOATES

R	K_1 (CH_3OH)	K_2 (CH_3OH–ether)	K_3 (C_2H_5OH–ether)
(1) Benzyl	100[a] ± 22	100 ± 16	100 ± 6
(2) 2-Ph-ethyl	37 ± 3	36 ± 6	30 ± 4
(3) 2-Ph-propyl		18 ± 3	16 ± 2
(4) 3-Ph-propyl		10 ± 1	16 ± 1
(5) 1-Ph-propyl		6 ± 1	6.0 ± 0.7
(6) 1-Ph-ethyl		5.0 ± 0.2	16 ± 1
(7) 2-Ph-isopropyl		1.0 ± 0.2	1.0 ± 0.07
(8) 1-Ph-isopropyl		0.0	0.0

[a] K_1 for phenyl considerably >100.

(1) Pfannl, *Monatsh.*, **31**, 301 (1910); **32**, 509 (1911).

(2) (a) Fehlandt and Adkins, THIS JOURNAL, **57**, 193 (1935); (b) Hatch and Adkins, *ibid.*, **59**, 1694 (1937).

(3) Bellet, *Compt. rend.*, **193**, 1020 (1931); **194**, 1655 (1932).

(4) Kremann, *Monatsh.*, **26**, 783 (1905); **29**, 23 (1908).

Similar results were obtained at *p*H 8.54 in the presence of sodium sulfite.

TABLE VI

SALT EFFECT

0.2 *M* Sodium acetate, 25 ml.; 1.0 *M* acetic acid, 10.0 ml.; $AgNO_3$, 0.5 mmole.; hydroxylamine sulfate, 2 mmole.; gum arabic, 0.133%; Au, 2.00 ml.

KNO_3, g.	*p*H	*R*	*R* *p*H 4.16	*T*	100/*T* *p*H 4.16
0.00	4.16	0.170	0.170	6.0	16.7
.50	4.13	.156	.174	9.5	12.0
1.00	4.10	.135	.170	11.4	11.6

An increase in gum arabic concentration resulted in a decrease in the reaction rate, but it was not proportional to the concentration. Thus, at *p*H 4.16, *R* equalled 0.169 for a solution containing 0.133% gum arabic. When the percentage was increased fivefold to 0.665, *R* only dropped to 0.100.

Discussion

The kinetics of the reduction of silver ion by hydroxylamine show some interesting departures from those of the hydroquinone reduction. In the case of hydroquinone, a direct proportionality was observed between the reaction rate and the concentration of the reducing agent. This is approximately true for hydroxylamine at *p*H 3.8 but, as the *p*H increases, the dependence upon the concentration of reducing agent falls off, until at *p*H 8.54 the rate depends upon about the 0.3 power of the concentration. No indication of similar behavior was obtained with hydroquinone. The dependence of the rate upon the solution *p*H follows a similar course and, in the region 3.7–4.4, the dependence upon the power of the hydroxyl-ion concentration is almost exactly double that of the hydroxylamine concentration. These results indicate clearly that the active form of the reducing agent is the ion NH_2O^-. They indicate further that the hydroxylamine *is adsorbed to the silver by means of the amino group*. At low *p*H the hydroxylamine exists chiefly as NH_3OH^+, which presumably is not adsorbed. The concentration of NH_2OH is very small, and this accounts for the power of nearly unity. As the *p*H increases, the concentration of the free amine increases and the power of the concentration in the Freundlich isotherm representing the adsorption decreases. At *p*H 8.54 the hydroxylamine exists almost completely as free amine, and fairly strong adsorption is indicated. Adsorption involving the $-O^-$ end of the molecule is rendered doubtful by the failure of hydroquinone to show any evidence of adsorption.

The dependence of the rate upon the silver-ion concentration almost exactly parallels that found previously in the study of the reaction with hydroquinone. At *p*H 4.16 a power of 0.64 was obtained for hydroxylamine as compared with 0.66 for hydroquinone at *p*H 5.74; and at *p*H 8.54, a power of 0.53 was obtained for hydroxylamine as compared with 0.55 for hydroquinone at *p*H 8.9. Further, the dependence of the rate upon the $SO_3^=$ concentration observed at *p*H 8.54 shows that a reaction between hydroxylamine and the silver sulfite complex does not encroach measurably upon the reaction with silver ion.

In contrast to the hydroquinone–silver-ion reaction, it was possible in the present case to obtain a measure of a preliminary reaction in the gold-nucleated solutions. This preliminary reaction may be either the homogeneous reduction or the gold-catalyzed reduction. Presumably, it is largely the latter, at least in the acid solutions. If we take as a measure of the rate of this preliminary reaction the reciprocal of the *T* values given in Tables I to III, no evidence of adsorption of hydroxylamine is obtained, either in the acid region or at *p*H 8.54. The rate in the *p*H range 3.7–4.4 varied almost exactly as the square of the hydroxyl-ion concentration and as the first power of the hydroxylamine concentration. Once more, however, a dependence upon approximately the two-thirds power of the silver-ion concentration appeared. In addition to the results recorded previously, the real existence of this preliminary reaction received confirmation from the fact that when a freshly prepared nuclear silver sol was employed in place of the gold, only the silver-catalyzed reaction could be detected.

Summary

1. The reaction between silver ion and hydroxylamine is catalyzed by colloidal gold and colloidal silver. The rate of formation of silver was shown to equal the rate of evolution of nitrogen.

2. The reaction in gold-nucleated solution can be resolved into two parts, the silver-catalyzed reaction and a preliminary reaction which is probably gold-catalyzed.

3. Both reactions involve the ion NH_2O^- as the active reducing agent. The kinetics suggest that the ion is adsorbed to silver by way of the amino group in the silver-catalyzed reaction. No adsorption of hydroxylamine is indicated for

TABLE II

$AgNO_3$, 0.50 mmole. Au 2.00 ml.

Hydroxylamine sulfate, mmole.	R	pH	R, corr. pH 4.16	T	Log (100/T)
0.50	0.068	4.22	0.058	21.4	0.56[a]
1.00	.121	4.20	.105	11.0	.88[a]
2.00	.170	4.16	.170	5.4	1.27[a]
4.00	.209	4.09	.275	3.5	1.60[a]
1.00	.021	3.82		55.0	0.26
2.00	.042	3.82		29.0	.54
4.00	.073	3.82		13.0	.89
$AgNO_3$, 0.30 mmole.; Na_2SO_3, 10.0 mmole.					
1.00	0.179	8.54		5.2	1.28
2.00	.228	8.54		2.9	1.54
4.00	.265	8.54		1.4	1.85

[a] Values corrected to pH 4.16.

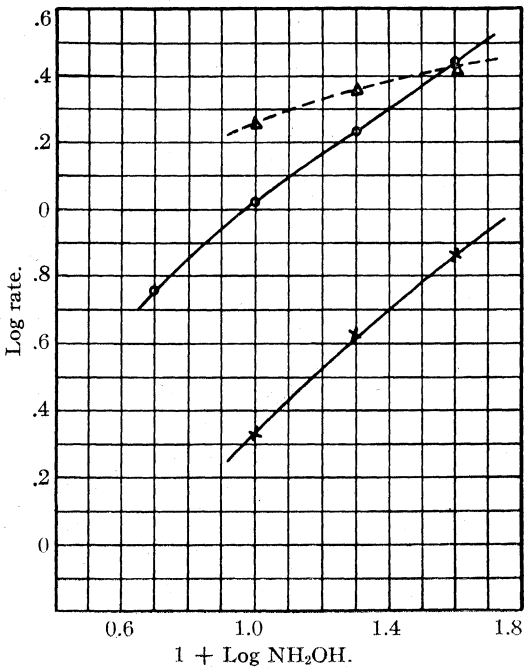


Fig. 3.—Variation of rate with [NH_2OH]: ×, pH 3.82 slope 0.95; ○, pH ~4.16 slope 0.75; △, pH 8.54 slope 0.3.

TABLE III

Hydroxylamine sulfate, 2.00 mmole.; pH 4.16; gum arabic, 0.133%; gold sol, 2.00 ml.

$AgNO_3$, mmole.	R	T
0.20	0.096	11.2
.30	0.123	8.3
.50	1.69	6.0
1.00	0.275	3.9

alkaline region, sodium sulfite was employed to reduce the silver-ion concentration to a sufficiently small value to permit measurement of the reaction rate. Under the conditions employed, no

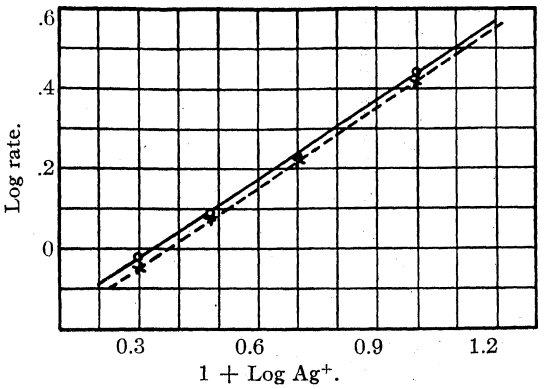


Fig. 4.—Dependence of rate upon silver ion concentration at pH 4.16: ○, R, slope 0.64; ×, 100/T slope 0.66.

evidence was obtained of complications resulting from reduction of silver ion by the sulfite. Once more, nitrogen was evolved in the theoretical amount. In most of the work, sulfite was present in considerable excess, and in calculations of the silver-ion concentration it was assumed that $Ag(SO_3)_2^{\equiv}$ was the only complex ion present. The dissociation constant of this ion was taken as 3×10^{-9}. This rough figure is adequate for calculations of relative concentrations.

The variation of reaction rate with concentration of silver ion and of excess sodium sulfite is given in Tables IV and V. A plot of log R against log C gives an acceptable straight line of slope about 0.53 in the case of silver-ion variation, and of slope about 1.08 in the case of excess sulfite-ion variation.

TABLE IV

VARIATION OF RATE WITH SILVER-ION CONCENTRATION

Hydroxylamine sulfate, 1 mmole.; gum arabic, 0.133%; gold sol, 2.00 ml.; pH 8.54 (borate buffer).

$AgNO_3$	Na_2SO_3	Excess $SO_3^=$	$[Ag^+]$	R	T
0.20	10.0	9.6	4.88×10^{-10}	0.144	6.8
.30	10.0	9.4	7.63	.179	5.2
.50	10.0	9.0	13.7	.245	2.75
1.00	10.0	8.0	35.1	.387	0.90

TABLE V

VARIATION OF RATE WITH SODIUM SULFITE

$AgNO_3$, 0.30 mmole.; hydroxylamine sulfate, 1.0 mmole.; pH 8.54.

Na_2SO_3	Excess $SO_3^=$	R
10.0	9.4	0.179
5.0	4.4	.409
3.0	2.4	.796
2.4	1.8	1.06

The salt effect on the silver-catalyzed reaction is negligible, as shown by the data in Table VI.

data is based upon the rate equation derived in the previous paper.[1] The extension downward of this straight line cuts the t-axis at fairly large values of t when the reaction mixture is nucleated with gold sol. As will appear subsequently, the gold-catalyzed reaction is slower than the silver-catalyzed reaction and involves some difference in mechanism. As the reaction proceeds, however, the gold particles become coated with silver, and the reaction goes over into that of the silver-catalyzed reduction. In the following, the rates of the silver-catalyzed reaction are expressed in terms of the slope of the $V^{1/3}$–t straight-line plots, where the volumes are at 20° and 760 mm. As a measure of the preliminary reaction or reactions, the reciprocal of the time, T, required to yield a nitrogen volume of 0.08 ml. (determined from the straight-line intersection) is employed. Time is expressed in minutes.

Parallel determinations of optical density and nitrogen evolution were made under several sets of conditions, and found to yield identical results within experimental error. This is illustrated for one set of data in Fig. 1. In the construction of this figure, the density and volume units were adjusted to give the same maximum value. These results establish the practical identity of the two methods of following the reaction. Further, they show that, if nitrogen evolution is the result of a subsequent reaction, as suggested by Equations 1 and 2, the reaction must be very rapid in comparison with the reduction of the silver ions.

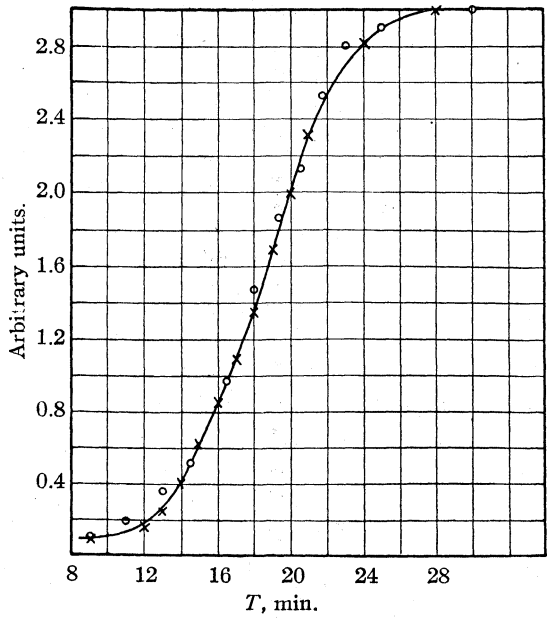


Fig. 1.—Reduction of silver ions by hydroxylamine: ○, silver; ×, N_2 volume.

The variation of reaction rate with *p*H is given in Table I. A plot of log R against pH

TABLE I

VARIATION OF RATE WITH pH

0.2 M sodium acetate, 25 ml.; 1.0 M acetic acid, x ml.; $AgNO_3$, 0.50 mmole.; hydroxylamine sulfate, 2.0 mmole.; gum arabic, 0.133%.

pH	R	2 + log R	T	Log (100/T)
3.70	0.0254	0.405	44.0	0.36
3.89	.0603	.780	19.0	.72
4.16	.170	1.23	5.4	1.27
4.44	.485	1.680	1.5	1.82

(Fig. 2) yields a curve which, at the lower pH values, has a slope of nearly 2.0. At pH 4.4 the slope has dropped to 1.4. On the other hand, a plot of log (100/T) against pH yields a straight line of slope approximately 2.0.

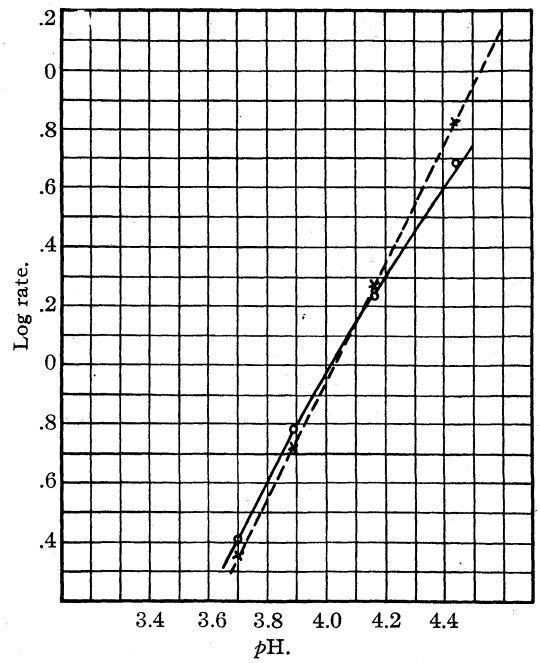


Fig. 2.—Variation of rate with pH; ○, R, silver-catalyzed; ×, 100/T preliminary.

The variation of the rate with hydroxylamine concentration for several pH values is given in Table II. A log–log plot of the data for the silver-catalyzed reaction is given in Fig. 3. The variation of the rate with silver-ion concentration at pH 4.16 is given in Table III. A log–log plot of the data is given in Fig. 4.

The Reaction in the Presence of Sodium Sulfite.—In order to extend the investigation of the hydroxylamine silver-ion reaction into the

determination of the standard potential, E_0.

3. The results indicate a maximum in the ionization constant which occurs at 15°.

4. Log K does not vary linearly with the reciprocal of the dielectric constant.

5. The plot of log K *versus* the mole fraction of dioxane at a given temperature is nearly linear. Numerical equations expressing this linear relationship have been constructed and a table of deviations compiled from which K may be evaluated in all solvents containing 0 to 82% dioxane and at 5° intervals from 0 to 50° with an accuracy comparable to the experimental error.

NEW HAVEN, CONN. RECEIVED JULY 5, 1939

[COMMUNICATION NO. 736 FROM THE KODAK RESEARCH LABORATORIES]

The Reduction of Silver Ions by Hydroxylamine

BY T. H. JAMES

Hydroxylamine appeared to be ideally suited for use in a continuation of the investigation of the reduction of silver ions by developing agents.[1]

The reaction rate can be followed by two independent methods, *i. e.*, optical determination of silver, as previously described, and measurement of nitrogen evolution. The reaction has been subjected to analytical study.[2] Further, it was found that this reaction supplied a transition between the relatively simple kinetics of the hydroquinone reduction and the complicated behavior encountered in a study of the reduction by *p*-phenylenediamine.

Nichols showed that ammoniacal silver nitrate reacts with hydroxylamine to give pure nitrogen. Strongly alkaline silver nitrate–sodium sulfite solution, on the other hand, yields a mixture of nitrogen and nitrous oxide, but the amount of nitrous oxide produced decreases with decreasing alkalinity. For the production of nitrogen, Nichols postulates the alternative mechanisms

$$Ag_2O + 2NH_2OH \longrightarrow 2Ag + H_4N_2O_2 + H_2O$$
$$H_4N_2O_2 \longrightarrow N_2 + 2H_2O \quad (1)$$

or

$$2Ag_2O + 2NH_2OH \longrightarrow 4Ag + H_2N_2O_2 + 2H_2O$$
$$H_2N_2O_2 + 2NH_2OH \longrightarrow 2N_2 + 4H_2O \quad (2)$$

Nitrous oxide, when formed, is considered to arise from the decomposition of hyponitrous acid. Sheppard and Mees showed that the rate of reaction between silver ions and hydroxylamine is accelerated by the addition of alkali, and they concluded that the active species is the ion NH_2O^-. They further observed a catalysis by finely divided silver.

(1) T. H. James, THIS JOURNAL, **61**, 648 (1939).

(2) S. E. Sheppard and C. E. K. Mees, "Investigations of the Theory of the Photographic Process," Longmans, Green and Company, New York, 1907, 141 pp.; M. L. Nichols, THIS JOURNAL, **56**, 841 (1934).

Under the conditions employed in the present investigation, only nitrogen was obtained as reaction product, and this was invariably in the theoretical amount. All measurements were made at 20 ± 0.02°, and a solution volume of 75 ml. was employed. The reactions were carried out in total darkness, or under a no. 1 Wratten safelight.

Materials and Procedure

Hydroxylamine Sulfate.—Eastman Kodak Company preparation recrystallized and dried in vacuum, m. p. 172°.

Colloidal Gold.—Phosphorus reduction[3] failed to show the Tyndall cone.

Salts.—General Chemical Company reagent grade. The reaction mixture was prepared in two parts, one containing the silver nitrate and buffer solution, the other containing the hydroxylamine, 2 ml. of 5% gum arabic solution, and, in general, 2 ml. of gold sol. The solutions were freed from oxygen by means of a stream of pure nitrogen, allowed to attain the temperature of the thermostat, and mixed rapidly at time 0. When nitrogen evolution was employed to follow the reaction course, the apparatus previously employed in the measurement of autoxidation rates[4] was used. The reaction chamber was filled with nitrogen and the buret with water at thermostat temperature. The shaking rate employed was adequate to prevent supersaturation of the reaction mixture with nitrogen. When silver determinations were made, a special apparatus was employed which permitted removal of samples at suitable intervals without allowing air to enter the reaction vessel. The solution was stirred by pure nitrogen throughout the course of reaction.

The reduction of silver ions by hydroxylamine is catalyzed by colloidal gold, and more strongly by colloidal silver. Beyond a nitrogen evolution of 0.08–0.10 ml., a plot of $V^{1/3}$ against t yields a straight line for about one-fourth of the entire reaction. This method of the treatment of the

(3) H. B. Weiser, "Inorganic Colloid Chemistry," J. Wiley and Sons, Inc., New York, N. Y., Vol. I, 1933, p. 38.

(4) T. H. James and A. Weissberger, THIS JOURNAL, **59**, 2040 (1937).

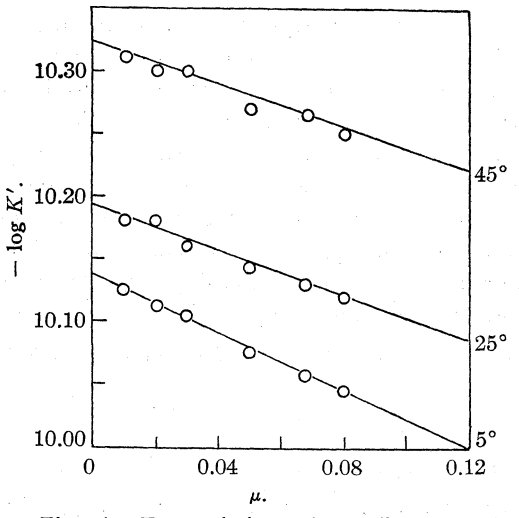


Fig. 1.—Extrapolation plots, diameter of circles equals 0.01 in log K' or approximately 0.4 mv.

may prove important in determining the standard potential in these media of low dielectric constant. It is clear from the nature of the extrapolation plots that an accurate determination of E_0 is possible if the ionization constant is known. A good determination of this quantity by conductance measurements combined with these results would permit the evaluation of E_0 to within ±0.2 mv. Further, there is reason to believe that with an altered technique the accuracy of the present results may be increased.

As previously observed for acetic acid in water and water–organic solvent mixtures of lower dielectric constant, the ionization constant has a maximum value which in this case occurs at about 15°. Owing to the uncertainty of the temperature variation in E_0 and the resulting error in K, we cannot regard the heat data derivable from these results with a high degree of certainty, and have omitted their calculation.

Variation of log K with Mole Fraction of Dioxane–Interpolation Functions.—It has been shown[2] that the plots of log K, or log K_0 − log K, where K_0 is the value of the ionization constant in water, *versus* $1/D$ show considerable curvature both for acetic acid and water. On the other hand, as indicated by Fig. 2, the plot of this quantity against the mole fraction of water or dioxane is nearly linear. This fact can be employed for interpolation by using the equation

$$\log K = -C - C'N_2 \qquad (2)$$

where C and C' are constants and N_2 is the mole fraction of dioxane. The constants were determined from the values of log K in water and 82% dioxane–water mixtures so that the deviations at these solvent compositions are zero. The values of C and C' are given in Table II at all temperatures. The last three columns contain the deviations of the observed results from equation (2) at the concentrations at which K was determined. From these deviations plots can be constructed readily from which log K can be read with an accuracy of the order of 0.002.

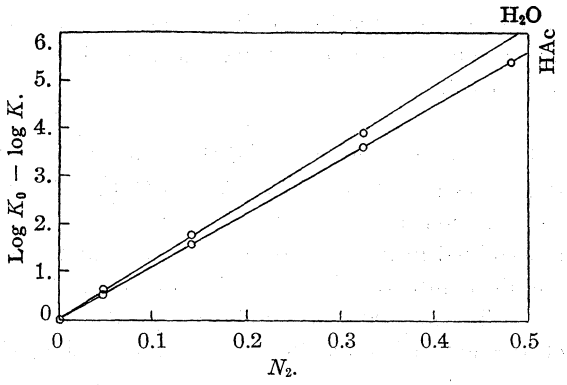


Fig. 2.—Variation of log K of acetic acid and water with mole fraction of dioxane, N_2: upper curve, water, lower curve, acetic acid.

TABLE II

CONSTANTS OF EQUATION (2) AND DEVIATIONS, Δ LOG K, OF OBSERVED VALUES OF LOG K FROM THOSE CALCULATED BY THIS EQUATION

Δ log K to be added to calculated value of log K.
$N_2 = 0$, Δ log $K = 0$; $N_2 = 0.4823$ ($X = 82$), Δ log $K = 0$

	C	C'	Δ log K $N_2 = 0.0486$ ($X = 20$)	Δ log K $N_2 = 0.1433$ ($X = 45$)	Δ log K $N_2 = 0.3231$ ($X = 70$)
0	4.7807	11.1100	−0.001	0.057	0.052
5	4.7695	11.1121	− .001	.053	.045
10	4.7622	11.1148	.000	.045	.040
15	4.7584	11.1231	.003	.0485	.038
20	4.7562	11.1397	.005	.049	.038
25	4.7560	11.1650	.007	.0475	.040
30	4.7570	11.2025	.008	.0480	.044
35	4.7625	11.2407	.012	.050	.051
40	4.7668	11.2898	.014	.052	.060
45	4.7773	11.3468	.016	.055	.071
50	4.7870	11.4150	.018	.059	.084

Summary

1. From measurements of the cells $H_2|HAc$ (m_1), NaAc (m_2), NaCl (m_3), dioxane (X), H_2O (Y)|AgCl–Ag, the ionization constant of acetic acid has been determined from 5 to 45° in a solvent containing 82% by weight of dioxane, the dielectric constant of which is 9.3 at 25°.

2. The principal source of error in this determination is caused by the uncertainty in the

taken to be constant over the temperature range. The accuracy of its determination is of the order of ±5 cal.

Summary

1. From measurements of the cells, $H_2|NaOH$ (m_1), NaCl (m_2), Dioxane (X), H_2O (Y)|AgCl–Ag, the ionization constant of water has been determined in 20, 45 and 70% dioxane mixtures, and at 5° intervals from 0 to 50° inclusive.

2. The heat content and heat capacity changes of the ionization reaction have been evaluated.

3. The uncertainty in the determination of the ionization constant increases with the dioxane content of the solvent. This is caused by the change in relative solubility of silver chloride and hydroxide and cannot be remedied as long as silver–silver chloride electrodes are employed. Cells containing silver–silver bromide or iodide electrodes would probably be more suitable, but, unfortunately, their standard potentials are not known in these media.

NEW HAVEN, CONN. RECEIVED JULY 5, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF YALE UNIVERSITY]

The Properties of Electrolytes in Mixtures of Water and Organic Solvents. III. Ionization Constant of Acetic Acid in an 82% Dioxane–Water Mixture

BY HERBERT S. HARNED AND LESLIE D. FALLON

From the measurements of the electromotive forces of the cells

$H_2|HAC$ (m_1), NaCl (m_2), NaCl (m_3), Dioxane (X), H_2O (Y)|AgCl–Ag

Harned and Kazanjian[1] determined the ionization constant of acetic acid in 20, 45 and 70% dioxane–water mixtures. The first computations depended on standard potentials derived by the Debye–Hückel theory without the use of the extended terms, and have been revised somewhat by Harned.[2] These results have now been extended to 82% dioxane mixtures.

Experimental Results

It was more difficult to obtain high accuracy with these cells than with those containing mixtures of higher dielectric constant. This is caused by the long period of time for equilibrium to be reached, particularly in the cases of cells containing ions at low ionic strengths. However, the average reproducibility of the cells was of the order of ±0.3 mv. The concentrations of acetic acid, sodium acetate and sodium chloride were made equal. These concentrations were known with an accuracy of 0.1% and, consequently, any error from this source was less than that caused by error in the electromotive force measurements. Cells were run in triplicate and the mean values of the electromotive forces taken. These results are compiled in Table I.

TABLE I

ELECTROMOTIVE FORCES OF THE CELLS: $H_2|HAc$ (m_1), NaAc (m_2), NaCl (m_3), DIOXANE (X), H_2O (Y)|AgCl–Ag X = 82% BY WEIGHT IN SOLVENT, $m_1 = m_2 = m_3$ = MOLES PER 1000 G. SOLVENT; $\mu = m_2 + m_3$

t	0.01	0.02	0.03	0.05	0.068	0.08	$K \times 10^{11}$
5	0.6903	0.6715	0.6637	0.6501	0.6404	0.6362	7.4
10	.6911	.6739	.6644	.6508	.6413	.6372	7.6
15	.6929	.6750	.6656	.6519	.6423	.6379	7.6
20	.6945	.6766	.6663	.6532	.6432	.6384	7.6
25	.6962	.6782	.6671	.6540	.6440	.6391	7.2
30	.6978	.6795	.6688	.6549	.6448	.6399	6.9
35	.6994	.6808	.6698	.6559	.6458	.6406	6.6
40	.7011	.6821	.6714	.6568	.6465	.6413	6.0
45	.7028	.6834	.6730	.6577	.6472	.6420	5.4

Ionization Constant

The equation for the cell may be written in the form[3]

$$\frac{F(E - E_0)}{2.303\,RT} + \log \frac{m_1 m_3}{m_2} = -\log \frac{\gamma_H \gamma_{Cl} \gamma_{HAc}}{\gamma_{H} \gamma_{Ac}} - \log K = -\log K' \quad (1)$$

If the left side or $-\log K'$ is plotted against μ, the intercept at zero μ equals $-\log K$. In Fig. 1, plots of $\log K'$ *versus* μ are shown and it is clear that the values of $-\log K$ can be determined to within ±0.005, or about ±0.2 mv. This uncertainty is very much less than that in the values of the standard potentials, E_0. The difficulty of obtaining E_0 in media of as low a dielectric constant as the present one (D_{25} = 9.53) has been discussed carefully by Harned, Walker and Calmon.[4]

This situation suggests that the present cell

(1) Harned and Kazanjian, THIS JOURNAL, **58**, 1912 (1936).
(2) Harned, *J. Phys. Chem.*, **43**, 275 (1939).
(3) Harned and Ehlers, THIS JOURNAL, **54**, 1350 (1932).
(4) Harned, Walker and Calmon, *ibid.*, **61**, 44 (1939).

TABLE II

IONIZATION CONSTANT OF WATER IN 20, 45 AND 70% DIOXANE–WATER MIXTURES

	X = 0		X = 20		X = 45		X = 70	
t	$K \times 10^{14}$	ΔH_i[a]	$K \times 10^{16}$	ΔH_i	$K \times 10^{17}$	ΔH_i	$K \times 10^{19}$	ΔH_i
0	0.1133	14,600	2.702	14,730	2.114	14,530	1.789	13,870
5	.1846	14,390	4.375	14,480	3.409	14,260	2.819	13,630
10	.2920	14,160	6.761	14,240	5.349	13,990	4.348	13,380
15	.4503	13,940	10.67	13,990	8.188	13,720	6.511	13,140
20	.6909	13,720	16.22	13,740	12.34	13,450	9.654	12,900
25	1.008	13,480	23.99	13,500	18.09	13,190	13.95	12,660
30	1.468	13,230	34.77	13,250	25.94	12,920	19.74	12,410
35	2.089	13,000	49.42	13,000	36.55	12,650	27.43	12,170
40	2.917	12,760	69.47	12,760	50.77	12,380	37.79	11,930
45	4.018	12,540	95.31	12,510	69.14	12,110	50.64	11,690
50	5.474	12,300	128.7	12,260	92.77	11,840	67.19	11,430

[a] Evaluated from the combined data of Harned and Hamer,[4] Harned and Donelson,[9] and of Harned and Geary.[10]

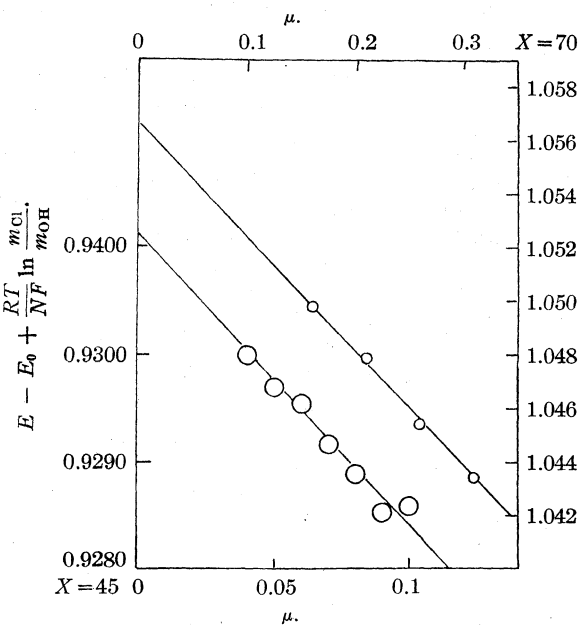


Fig. 2.—Extrapolation of 45 and 70% dioxane–water mixtures at 25°: lower plot ($X = 45$) (diameter of circles equals 0.2 mv.); upper plot ($X = 70$) (diameter of circles equals 0.4 mv.).

in the same manner, the temperature variation of K should be known quite accurately. This is also true of the values of K of the 70% dioxane mixtures in which case the absolute accuracy may not be greater than 0.5 to 1 mv. The values of the standard potentials employed in the case of the 45% dioxane mixtures were those given by Harned and Donelson[7] and for the 70% dioxane mixtures, those obtained by Harned and Calmon.[8] The values of K are given in Table II. For the sake of completeness, values in pure water determined by the same method have been included.[11]

In order to compute the change in heat content and heat capacity of the ionization reaction, we have employed the equation

$$\frac{d \log K}{dT} = \frac{\Delta H_i}{RT^2} \quad (3)$$

and the assumption that ΔH_i varies linearly with temperature. This leads to the equations

$$\log K = (A/T) + B \log T + C \quad (4)$$

$$\Delta H_i = -2.303\,RA + BRT = A' - B'T \quad (5)$$

$$\Delta C_p = BR \quad (6)$$

for K, ΔH_i and ΔC_p, respectively. The constants of these equations derived by the method of least squares are contained in Table III. The

TABLE III

CONSTANTS OF EQUATIONS (4), (5) AND (6)

	X = 20	X = 45	X = 70
A	−6161.329	−6377.395	−5926.389
B	− 24.814	− 27.006	− 24.415
C	67.447	72.472	62.437
A'	28.19	29.18	27.12
B'	49.31	55.66	48.51
ΔC_p	− 49.3	− 53.7	− 48.5

values of the change in heat content, ΔH_i, are given in Table II. Equation (4) with these numerical constants reproduces the observed values of log K with an average accuracy better than ±0.001. It is difficult to estimate the accuracy of this determination of ΔH_i. As previously mentioned, the temperature variation of log K is probably determined fairly accurately even in the case of the 70% dioxane mixtures even though the absolute values of K are somewhat in error. As a tentative estimate, we regard the accuracy of determination of ΔH_i to be of the order of ±50 cal.

ΔC_p according to the method of calculation is

(7) Harned and Donelson, THIS JOURNAL, **60**, 2128 (1938).
(8) Harned and Calmon, *ibid.*, **60**, 2130 (1938).
(9) Harned and Donelson, *ibid.*, **59**, 1280 (1937).
(10) Harned and Geary, *ibid.*, **59**, 2032 (1937).
(11) Harned, *J. Franklin Inst.*, **225**, 623 (1938).

TABLE I

ELECTROMOTIVE FORCES OF THE CELLS:

$H_2|NaOH\ (m_1), NaCl\ (m_2), Dioxane\ (X), Water\ (Y)|AgCl-|Ag$

(1) X = 20% by weight

$m_1 = m_2$ = moles per 1000 g. solvent; $\mu = m_1 + m_2$

t	$m_1 = m_2$..... 0.02426	0.03433	0.04344	0.05301	0.07621
0	1.06352	1.06358	1.06363	1.06371	1.06377
5	1.06438	1.06443	1.06447	1.06454	1.06460
10	1.06524	1.06528	1.06531	1.06537	1.06543
15	1.06610	1.06613	1.06615	1.06620	1.06626
20	1.06696	1.06698	1.06699	1.06703	1.06709
25	1.06782	1.06783	1.06783	1.06786	1.06792
30	1.06868	1.06868	1.06867	1.06869	1.06875
35	1.06954	1.06953	1.06951	1.06952	1.06958
40	1.07040	1.07038	1.07035	1.07035	1.07041
45	1.07126	1.07123	1.07119	1.07118	1.07124
50	1.07212	1.07208	1.07203	1.07201	1.07206

(2) X = 45%. m_1 = 0.01

t	m_2..... 0.03	0.04	0.05	0.06	0.07	0.08	0.09
0	1.06601	1.05877	1.05334	1.04876	1.04477	1.04130	1.03851
5	1.06588	1.05855	1.05303	1.04835	1.04430	1.04086	1.03796
10	1.06575	1.05833	1.05272	1.04794	1.04382	1.04032	1.03741
15	1.06562	1.05811	1.05241	1.04753	1.04335	1.03978	1.03686
20	1.06549	1.05789	1.05210	1.04712	1.04287	1.03924	1.03631
25	1.06536	1.05767	1.05179	1.04671	1.04240	1.03870	1.03576
30	1.06523	1.05745	1.05148	1.04630	1.04192	1.03816	1.03521
35	1.06510	1.05723	1.05117	1.04589	1.04145	1.03762	1.03466
40	1.06497	1.05701	1.05086	1.04548	1.04097	1.03708	1.03411
45	1.06484	1.05679	1.05056	1.04507	1.04050	1.03654	1.03356
50	1.06471	1.05657	1.05024	1.04466	1.04002	1.03600	1.03301

(3) X = 70%. m_1 = 0.01

t	m_2..... 0.15	0.2	0.25	0.3
0	1.05204	1.04346	1.03599	1.02993
5	1.05046	1.04177	1.03412	1.02795
10	1.04888	1.04008	1.03225	1.02597
15	1.04730	1.03839	1.03038	1.02399
20	1.04572	1.03670	1.02851	1.02201
25	1.04414	1.03501	1.02664	1.02003
30	1.04256	1.03332	1.02477	1.01805
35	1.04098	1.03163	1.02290	1.01607
40	1.03940	1.02994	1.02103	1.01409
45	1.03782	1.02825	1.01916	1.01201
50	1.03624	1.02656	1.01729	1.01013

Figure 2 shows the extrapolations in the cases of 45 and 70% mixtures. Although straight lines could be drawn through the points corresponding to the left side of the equation, the extrapolation becomes less certain as the percentage of dioxane increases because the values of μ are so far from the zero axis. As previously explained, it is impossible to remedy this difficulty as long as silver–silver chloride electrodes are employed. The derived values of K in the 45% mixtures are clearly more certain than those for the 70% dioxane mixtures and the absolute values are probably known to within ±0.2 mv. This error in extrapolation is greater than the estimated error of ±0.1 mv. in the evaluation of E_0. However, since extrapolations at all temperatures were made

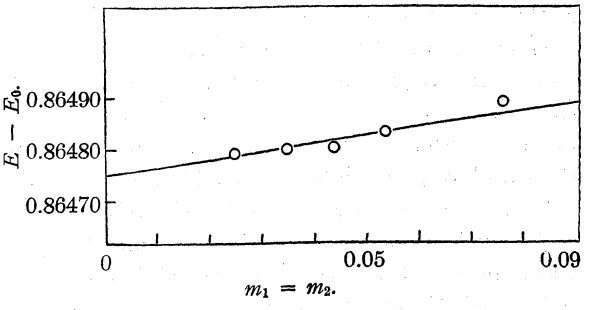


Fig. 1.—Extrapolation of 20% dioxane–water mixtures at 25°. (Diameter of circles equals 0.02 mv.)

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF YALE UNIVERSITY]

The Properties of Electrolytes in Mixtures of Water and Organic Solvents. II. Ionization Constant of Water in 20, 45 and 70% Dioxane–Water Mixtures

BY HERBERT S. HARNED AND LESLIE D. FALLON[1]

Very little is known concerning the ionization constant of water in solvents other than water. In order to determine this quantity in media of lower dielectric constant, the electromotive forces of the cells

$$H_2 \mid NaOH\ (m_1),\ NaCl\ (m_2),\ Dioxane\ (X),\ Water\ (Y) \mid AgCl\text{–}Ag$$

have been measured. The results cover the temperature range from 0 to 50° throughout which results of high accuracy may be obtained. The measurements were made in media containing 20, 45 and 70% dioxane by weight.

Experimental Data

The solutions were prepared with an accuracy greater than that caused by the errors in the measurements of the electromotive forces. In the 20% dioxane mixtures the reproducibility was 0.05 mv. and in the 45 and 70% dioxane solutions it was 0.1 mv. The technique with slight modifications was that employed previously for measurements of this kind.[2]

Unfortunately, an unforeseen circumstance made an accurate determination of the ionization constant impractical in the mixtures containing over 70% dioxane. With the 20% dioxane solutions, one to one ratios of sodium chloride to hydroxide yielded very satisfactory results. In the case of the cells containing 45% dioxane and a one to one ratio of salt to hydroxide, the cell electromotive forces were very erratic. However, when the ratio of salt to hydroxide was three to one or greater, a reproducibility of 0.1 mv. was obtained. With the 70% dioxane–water mixtures, erratic results were obtained until a fifteen to one ratio of chloride to hydroxide or greater was employed. With this latter condition the cell reproducibility was again 0.1 mv.

This behavior is attributed to the change in relative solubility of silver chloride and hydroxide in passing from pure aqueous solutions to those containing the higher percentages of dioxane. Since in the media containing much dioxane, suitable points on the graph used for extrapolation could not be obtained near the zero axis, the determination of ionization constant is somewhat uncertain. Since both silver bromide and iodide are less soluble than the chloride in water, cells containing these electrodes would have been more suitable for the present purpose. Unfortunately, the standard potentials of these electrodes in dioxane–water mixtures have not yet been determined.

In Table I, the observed electromotive forces of the cells have been recorded.

Ionization Constant and Derived Thermodynamic Quantities.—The electromotive force, E, of the cell is given by the equation

$$E - E_0 + \frac{RT}{NF}\ln\frac{m_{Cl}}{m_{OH}} = \frac{RT}{NF}\ln\frac{\gamma_H\gamma_{OH}}{\gamma_H\gamma_{Cl}a_{H_2O}} - \frac{RT}{NF}\ln K^{3,4} \quad (1)$$

where E_0 is the standard potential, m_{Cl} and m_{OH} are the stoichiometrical molalities of the chloride and hydroxide, γ_H, γ_{OH} and γ_{Cl}, the activity coefficients of the species denoted by subscripts, a_{H_2O} the activity of water, and K the ionization constant. In these computations, a_{H_2O} as well as $\gamma_H\gamma_{OH}$ and $\gamma_H\gamma_{Cl}$ have been assigned the value unity at zero electrolyte concentration in each solvent. Since

$$K = \frac{\gamma_H\gamma_{OH}}{a_{H_2O}} m_H m_{OH} \quad (2)$$

it is equal to $m_H m_{OH}$ at zero ionic strength in all solvents.

That the extrapolation in the case of the 20% dioxane mixtures can be carried out with high accuracy is shown in Fig. 1. Here the radii of the circles equal 0.01 mv. and the estimation of log K from the graphs is within ±0.02 mv. The standard potentials employed were those computed by Harned[5] from the data of Harned and Morrison.[6] It is probable that the largest source of error in the absolute magnitude of log K is caused by the error in determining E_0. An error of 0.1 mv. in E_0 causes an error of 0.002 in log K or 0.5% in K.

(1) This communication contains material from a dissertation presented by Leslie D. Fallon to the Graduate School of Yale University in partial fulfilment of the requirements for the Degree of Doctor of Philosophy, June, 1939.

(2) Harned and Morrison, *Am. J. Sci.*, **33**, 161 (1937).

(3) Roberts, THIS JOURNAL, **52**, 3877 (1930).

(4) Harned and Hamer, *ibid.*, **55**, 2194 (1933).

(5) Harned, *ibid.*, **60**, 336 (1938).

(6) Harned and Morrison, *ibid.*, **58**, 1908 (1936).

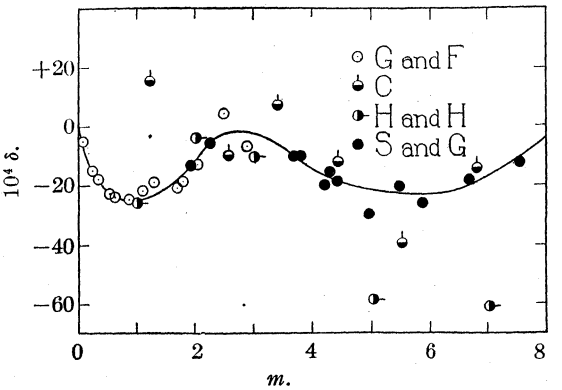


Fig. 1.

striking, and is several times their estimated experimental error. The discrepancy is also apparent if the activity coefficient of the acid be computed from the vapor pressure data (see Table IV) by means of the Gibbs relation[11]

$$d \ln \gamma m = -(55.51/3m) \cdot d \ln a_1 \qquad (5)$$

One is naturally hesitant to assert that the results of such a manifestly careful research as that of

TABLE IV

m	γ V. p.	γ E. m. f.	m	γ V. p.	γ E. m. f.
1	(0.130)	0.130	8	0.385	0.397
2	.125	.124	10	.557	.553
3	.141	.141	12	.763	.743
4	.168	.171	14	1.008	.969
6	.254	.264	16	1.288	1.235

Harned and Hamer are in error. However, when one considers the difficulties encountered in e. m. f. measurements in strong solutions, and the possibility that the cell reaction in such solutions is not that postulated, and then contrasts this with the simplicity and directness of a vapor pressure measurement, it would seem advisable on the whole to place considerable reliance on the vapor pressure data.

Recently, Scatchard, Hamer and Wood[2] have compared isopiestically sodium chloride and sulfuric acid solutions. Up to 3 molal, values of a_1, computed from the osmotic coefficients in their Table IIa, agree with our Table II within a unit or so in the fourth decimal place; for 3.5 and 4 m, their ϕ yield values of a_1 which are 0.0003 and 0.0014 less than the values in Table II. The isopiestic results will be discussed in detail in a forthcoming paper; it is sufficient for the moment to say that their isopiestic ratios of concentration are in satisfactory agreement with the results of similar measurements carried out in this Laboratory, and, moreover, are consistent with the measurements of Gibson and Adams and ourselves for sodium chloride and the results recorded here for sulfuric acid. We feel fairly confident that vapor pressures of sulfuric acid solutions at 25° may be obtained from our Tables II and III accurate to 0.01 mm. or better.

(11) In effecting the integration of Eq. 5, Harned and Hamer's value of γ for $m = 1$ was adopted.

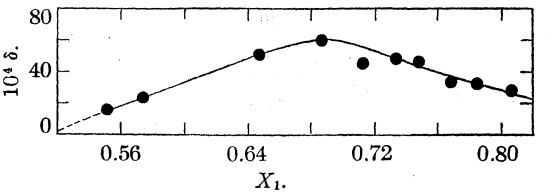


Fig. 2.

Summary

The vapor pressure of sulfuric acid solutions at 25° has been measured by the static method for concentrations ranging from 2 to 23 molal. The results are in good agreement with the vapor pressure measurements of Grollman and Fraser, and are consistent with the vapor pressure measurements of Collins up to 8 molal. They agree with the results of e. m. f. measurements up to 3 molal, but are in definite disagreement at higher concentrations.

Values of the activity of the water and of the activity coefficient of the acid in the solutions have been tabulated at round values of the concentration.

TORONTO, CANADA RECEIVED JUNE 26, 1939

(based on unpublished work of Negus[7]) correspond to $a_1 = 0.1793$ for the 21.53% solution, and, by a slight extrapolation, to $a_1 = 0.2464$ for the solution saturated at 25°, the apparent uncertainty in both cases being ±0.0005.

Table I summarizes the results for sulfuric acid; the first column gives the weight fraction of the acid, the second the molality, and the third the mole fraction of the water defined by

$$X_1 = (x_1/18.016)/(x_1/18.016 + x_2/49.04) \qquad (2)$$

where x_1 is the weight fraction of the water. The fourth column gives the mean observed value of a_1, the activity of the water in the solution (see Eq. 1); as a rule the individual values of a_1 showed a mean absolute deviation from the mean of 0.0002 or less, although in a few cases the deviation was somewhat larger.

TABLE I

25°

x_2	m	X_1	a_1 obsd.	a_1 (II)	a_1 (III)
0.1583_5	1.918	0.9354	0.9174	0.9173	
$.1800_5$	2.239	.9254	.8995	.8994	
$.2641_0$	3.659	.8835	.8048	.8049	
$.2702_5$	3.776	.8802	.7964	.7963	
$.2926_5$	4.218	.8681	.7627	.7630	
$.2956_0$	4.279	.8663	.7586	.7585	
$.2985_0$	4.339	.8648	.7539	.7539	
.3267	4.947	.8487	.7062	.7070	
.3485	5.454	.8357	.6679	.6678	
.3639	5.833	.8263	.6379	.6382	
.3955	6.671	.8062	.5743	.5740	0.5740
.4251	7.540	.7863	.5110	.5112	.5110
.4512	8.383	.7680	.4542		.4545
.4797	9.400	.7470	.3934		.3932
.4985	10.13_5	.7325	.3537		.3533
.5242	11.23_5	.7119	.2993		.3007
.5551	12.72	.6857	.2404		.2406
.5973	15.12	.6473	.1667		.1667
.6695	20.65	.5733	.0720		.0718
.6894	22.63	.5509	.0538		.0538

For convenience in representation, two deviation functions were computed, defined by

$$0 < m < 8 \quad a_1 = 1 - 0.02678m - 0.00922m^2 + 0.000556m^3 + \delta_1 \qquad (3)$$

$$0.52 < X_1 < 0.82 \quad a_1 = f_1X_1 + \delta_2 \qquad (4)$$

where $\log f_1 = -5.5254 + 11.422X_1 - 5.8966X_1^2$. These forms are, of course, entirely empirical, but have the advantage that the resulting δ_1 and δ_2 are everywhere less than 0.01, and consequently can be handled graphically; see Figs. 1 and 2. From our values, and from those computed from the vapor pressure data of Grollman and Fraser[8] and from the electromotive force measurements of Harned and Hamer[9] for concentrations less than 3 molal, the smooth curves in the figures were drawn. From these again, with the aid of Eqs. 3 and 4, values of a_1 at round values of the molality for the dilute range (Table II) and at round values of the mole fraction of the water for the concentrated (Table III) were obtained. The interval in both tables is sufficiently fine to permit interpolation by the method of mean second differences[10] and still obtain results numerically accurate to a unit or so in the fourth decimal place; this is illustrated in the last two columns of Table I, which give the values obtained by interpolation in Tables II and III.

TABLE II

m	a_1	m	a_1	m	a_1	m	a_1
0.5	0.9821	2.5	0.8838	4.5	0.7415	6.5	0.5868
1.0	.9620	3.0	.8514	5.0	.7030	7.0	.5497
1.5	.9389	3.5	.8164	5.5	.6642	7.5	.5140
2.0	.9129	4.0	.7795	6.0	.6252	8.0	.4798

TABLE III

X_1	a_1	X_1	a_1	X_1	a_1	X_1	a_1
0.52	0.0346	0.66	0.1892	0.72	0.3208	0.78	0.4912
.56	.0607	.68	.2285	.74	.3736	.80	.5542
.60	.0996	.70	.2724	.76	.4307	.82	.6183
.64	.1546						

Discussion

A glance at Fig. 1 will show that, where they overlap, our results are consistent with those of Grollman and Fraser, who used a Rayleigh gage, although the scattering of their points from the curve at their highest concentrations would seem somewhat greater than their apparent experimental error. Figure 1 also shows the results of Collins, obtained by an isoteniscope with mercury manometer (his Table II). He records his results only to the nearest 0.1 mm. in the more dilute solutions, so that the smoothed entries in his table might be in error by 0.0040; actually, the agreement with our results is a good deal closer. For solutions between 50 and 65% by weight, however, his results disagree with ours by as much as 0.008 in a_1, and would be entirely off Fig. 2.

The position with respect to Harned and Hamer's electromotive force measurements (their Table II) is a curious one. Up to 3 m, the agreement with the vapor pressure data is excellent, the deviations corresponding to less than 0.05 mv.; at 5 and 7 m, however, the discrepancy is

(7) "International Critical Tables," Vol. III, p. 297.

(8) A. Grollman and J. C. W. Fraser, THIS JOURNAL, **47**, 712 (1925).

(9) H. S. Harned and W. J. Hamer, *ibid.*, **57**, 27 (1935).

(10) H. L. Rice, "Theory and Practice of Interpolation," or any standard text on the calculus of finite differences.

the manometer. The scale had been ruled in millimeters by the dividing engine in the Physics Department of this University, and had been checked by a microscope comparator; interpolation to fractions of a millimeter was accomplished by means of the graticuled scale in the eyepiece of the telescope.

The manometer liquid in the earlier runs was butyl phthalate, which has been recommended by Gibson and Adams; we found it necessary to use the special grade supplied by Distillation Products if satisfactory results were to be obtained. Even when distilled into the manometer under high vacuum and shielded from contact with the air, however, it only could be used for about a week or so before it was necessary to replace it. In some later work, Cenco Hyvac pump oil (density at 25°, 0.895) was employed; this was first out-gassed in the vacuum pump, and was then transferred as quickly as possible to the manometer through a side neck, which was then sealed off; the oil was then refluxed in the manometer under high vacuum for several hours. It proved to be a stable and satisfactory manometer liquid, its principal disadvantages as compared with butyl phthalate being its greater viscosity and its somewhat hazier meniscus. Tests showed that both manometer liquids gave identical results (within the limit of error of the experiments) for the activity of the water in the solutions.

The most serious experimental difficulty in a static vapor pressure measurement is the removal of the residual air from the liquid. This was effected by freezing solution and solvent (as well as the solvent in the auxiliary flask[4] W) while they were boiling under vacuum, the resulting residual pressure being 0.002 mm. or less as determined on the McLeod gage. The flasks were then shut off from the rest of the apparatus, the contents melted, and the whole procedure repeated four or five times. For water, sodium chloride solutions, and for sulfuric acid solutions less than 4 *m*, a mixture of chloroform and dry ice served as freezing mixture, for acid solutions stronger than 4 *m*, liquid air. After out-gassing, the apparatus was allowed to come to temperature equilibrium, and the vapor pressures of water and of solution as well as the differential lowering were followed for a period of from one to three days.

Although the inherent error of a reading is somewhat less than 0.1 mm. of manometer liquid, a fluctuation of bath temperature of 0.01° would cause a change in the vapor pressure of water of nearly twice this amount. However, by having solution and solvent flasks placed symmetrically in the bath, and by always having the contents of the two flasks of approximately the same heat capacity, one would hope that the vapor pressures of both solution and solvent would "hunt" together, and that this error would largely cancel in the ratio. The high reproducibility of the results would seem to show that this is the case. For example, in a series of measurements on a 39.55% by weight solution (6.671 *m*), one result recorded about two hours after the apparatus had been brought on temperature was: $P^0 = 361.1$, $P_1 = 207.4_5$, $\Delta P = 153.7_5$ where P^0, P_1 and ΔP are the vapor pressure of water, the vapor pressure of solution, and the differential vapor pressure lowering, all expressed in mm. of pump oil. The activity of the water, given by

$$a_1 = 2P_1/(P^0 + P_1 + \Delta P) \qquad (1)$$

is thus 0.5744. Twenty-four hours later, a measurement gave $P^0 = 360.1$, $P_1 = 206.7$, $\Delta P = 153.4$, $a_1 = 0.5740$. Thus a_1 only changed by 0.0004, although the individual readings changed by about a part in 300. The mean of all measurements for this run, as recorded in Table I, is $a_1 = 0.5743$ with a mean absolute deviation from the mean of 0.0002.

Chemicals and Analysis.—C. P. sulfuric acid (sp. gr. 1.84) was distilled under vacuum in an all-glass apparatus, the first and last fractions of the distillate being rejected; the final product was free from sulfite. From this acid solutions of desired strength were made up by dilution with a good grade of conductivity water. At the end of each experiment, the acid solutions were analyzed by gravimetric titration with recrystallized sodium bicarbonate which had been fused and cooled in an atmosphere of dry carbon dioxide; after heating to boiling, 0.05 *N* sulfuric acid and carbonate-free sodium hydroxide were used for back titration to obtain the final end-point with methyl red as indicator.[5] Duplicate analyses agreed to 0.03% or better; in calculating the concentration, all weights were reduced to vacuum.

The sodium chloride was British Drug Houses "Analar"; the unsaturated solution used in one experiment was analyzed by evaporating it to dryness on a steam-bath and then heating to 600°.

Experimental Results

As a check on the apparatus and technique, a few preliminary measurements were carried out on sodium chloride solutions. At 25°, a 21.53% by weight solution gave $\Delta P/P^0 = 0.1801$; a saturated solution at 25° gave 0.2468, and at 20.28°, 0.2456. Gibson and Adams[4] have studied sodium chloride solutions at 25° by a dynamic method; interpolation[6] of their results gives for 21.53 weight per cent., 0.1804. By a slight extrapolation of their results to $x_2 = 0.2643$ (6.144 *m*), $\Delta P/P^0$ for the solution saturated at 25° is 0.2469; their result by the static method for the solution saturated at 20.28° is 0.2454. The agreement between our results and theirs in all three cases is satisfactory, and is within the apparent limit of error of either set of experiments. The results recorded in "International Critical Tables"

(5) T. W. Richards and C. R. Hoover, THIS JOURNAL, **37**, 95, 108 (1915).

(6) For the concentrations studied by Gibson and Adams, $\Delta P/x_2P^0$ is practically linear in x_2, the weight fraction of the salt.

deg.$^{-1}$ mole^{-1}. This value does not include the contribution due to nuclear spin.

We thank the Shell Development Company for donating the propylene used for these measurements and Dr. R. A. Ruehrwein for assistance with the experimental work.

Summary

The heat capacity of solid and liquid propylene has been measured from 14 to 226°K.

The melting and boiling points are 87.85 and 225.35°K., respectively. (0°C. = 273.10°K.)

The heats of fusion and vaporization were measured calorimetrically and were found to be 717.6 and 4402 cal./mole, respectively.

The vapor pressure of propylene was measured from 165.8 to 225.9°K. and the results have been represented by the equation

$$\log_{10} P_{(\text{inter. cm. Hg})} = -\frac{1196.9}{T} - 3.92 \times 10^{-3} T + 8.07544$$

The gas density of propylene was determined to be 1.7461 grams per liter at 25.00°C. and 1 atmosphere.

The calorimetric data have been used to calculate the entropy of propylene gas and the value at the boiling point was found to be 59.93 cal. deg.$^{-1}$ mole^{-1}. The value calculated for this temperature from available molecular data is 61.0 ± 0.3 cal. deg.$^{-1}$ mole^{-1}. The entropy discrepancy is interpreted as due to random end for end orientation of $CH_2{=}CH{-}CH_3$ molecules in the crystal lattice.

It is concluded that unsymmetrically placed double bonds in otherwise symmetrical hydrocarbons will lead to a disordered arrangement in the crystal lattice and a suitable entropy correction should be made to the $\int C_p \, d \ln T$.

The most reliable value for the entropy of propylene gas at 298.1°K. and 1 atmosphere is 64.0 cal. deg.$^{-1}$ mole^{-1}, calculated from molecular data.

BERKELEY, CALIF. RECEIVED MAY 29, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF TORONTO]

The Vapor Pressure of Aqueous Solutions of Sulfuric Acid

BY S. SHANKMAN AND A. R. GORDON

The growing importance of the isopiestic method of investigating the thermodynamic properties of aqueous solutions has emphasized the need for reliable standards. In their pioneer work in this field, Sinclair and Robinson[1] adopted potassium chloride as reference substance, but, more recently, Scatchard, Hamer and Wood[2] have selected sodium chloride for their standard curve. While sodium chloride is eminently suitable for the dilute range of concentration, it cannot be employed for solutions in which the activity of the water is less than 0.75; sulfuric acid would seem to be the obvious alternative to serve as standard when studying the more concentrated range. While the vapor pressure and e. m. f. data for sulfuric acid solutions are of high precision and are in satisfactory agreement up to 3 molal, the case is somewhat different for higher concentrations. The vapor pressure measurements of Collins[3] (which are usually quoted in the literature) are not of the highest accuracy, and, moreover, are in disagreement with the e. m. f. measurements. We have therefore measured the vapor pressure of sulfuric acid solutions at 25° for concentrations from 2 molal to 23 molal by the static method.

Experimental

The apparatus was similar to that of Gibson and Adams[4]; we may say at once that we can fully substantiate their claims as to its convenience and accuracy. Since it has been discussed adequately, no lengthy description is needed here; its essential feature is that it is possible to measure the vapor pressure of the solution, the vapor pressure of the pure solvent, and the differential vapor pressure lowering by a suitable manipulation of stopcocks (see Fig. 1 of ref. 4).

In our apparatus, the flasks, containing about 25 cc. of solution or solvent, were of approximately 75 cc. capacity, and were placed symmetrically with respect to regulator, heater and stirrer in a water-bath controlled to 0.01°. The internal diameter of the manometer tubing was 15 mm.; the heights of the manometer liquid were measured by comparing them through a telescope with a vertical plate glass scale, placed immediately in front of the two legs of

(1) D. A. Sinclair, *J. Phys. Chem.*, **37**, 495 (1933); R. A. Robinson and D. A. Sinclair, THIS JOURNAL, **56**, 1830 (1934).

(2) G. Scatchard, W. J. Hamer and S. E. Wood, *ibid.*, **60**, 3061 (1938).

(3) E. M. Collins, *J. Phys. Chem.*, **37**, 1191 (1933).

(4) R. E. Gibson and L. H. Adams, THIS JOURNAL, **55**, 2679 (1933).

TABLE X

SUMMARY OF ENTROPY CALCULATION

0–15°K. Debye function, $hc\nu/k$ = 100	0.482
15–87.85°K., graphical	11.543
Fusion, 717.6/87.85	8.168
87.85–225.35°K., graphical	20.014
Vaporization, 4402/225.35	19.534
Actual gas at boiling point	59.74 ± 0.1
Correction for gas imperfection	0.19
Ideal gas at 225.35°K.	59.93
$\int_{225.35}^{298.1} C_p(\text{gas})\, d\ln T$ from molecular data	3.0
Ideal gas at 298.1°K.	62.9 cal. deg.$^{-1}$ mole^{-1}

The correction for gas imperfection was made by means of an equation of state to be published shortly by Mr. E. E. Roper,[14] who has kindly calculated the value of $S_{\text{ideal}} - S_{\text{actual}}$ for us from his data.

The molecular data on propylene are not known very accurately but Kassel[15] has calculated the translational and rotational entropy by assuming values for interatomic distances which should be reasonably accurate. (Values used were C—C, 1.53×10^{-8} cm.; C=C, 1.35×10^{-8} cm.; C—H, 1.1×10^{-8} cm.; with tetrahedral angles.) From these data and the assumption of free rotation of the methyl group he obtains

$$S_{(\text{Trans. + rot.})} = 11.73 + 9/2\, R \ln T$$

However, Pitzer[16] has predicted that the rotation of the methyl group is hindered and has given tables,[17] based on the assumption of a reasonable type of potential function, which readily allow calculation of the entropy difference of a hindered rotator and a freely rotating group. These tables are expressed as functions of the moments of inertia of the rotating groups and the number and height of the potential barriers.

Kistiakowsky[18] has investigated the heat capacity of propylene gas and has reached the conclusion that the potential barrier lies between 600 and 800 cal. per mole for the rotation of the methyl group. Using 700 cal. per mole and taking the value 4.7×10^{-40} g. cm.^{2} as the moment of inertia for the methyl group, the entropy associated with translation and rotation was calculated. The entropy due to vibration was calculated from levels suggested by E. B. Wilson and used by Kistiakowsky. The values in cm.$^{-1}$ and the statistical weights are: 432, (1); 580 (1); 700, (1); 900, (3); 920, (1); 1100, (1); 1200, (1); 1247, (1); 1300, (1); 1415, (2); 1648, (1); 3000, (6). The entropy calculation is summarized in Table XI.

TABLE XI

THE ENTROPY OF PROPYLENE FROM MOLECULAR DATA

	223.35°K.	298.1°K.
$S_{(\text{Trans. + rot.})}$ assuming free rotation	60.17	62.67
Correction for hindered rotation	−0.23	−1.00
$S_{\text{vib. harmonic}}$	1.08	2.37
S of ideal gas in cal. deg.$^{-1}$ mole^{-1}	61.0 ± 0.3	64.0

The experimental value of the entropy calculated in Table X is 59.90 cal. deg.$^{-1}$ mole^{-1} or 1.1 units less than the calculated value, 61.0 cal. deg.$^{-1}$ mole^{-1}, given in Table XI. The discrepancy is outside the combined limits of error of the theoretical calculation and the experimental determination, and it is believed to be due to random end for end orientation of CH_2=CH—CH_3 in the crystal lattice. Complete lack of discrimination between the CH_2 and CH_3 groups would correspond to a discrepancy of $R \ln 2$ = 1.38 cal. deg.$^{-1}$ mole^{-1}.

This is the first case where false equilibrium due to random orientation of groups of atoms has been demonstrated and it leads to the conclusion that a similar effect is to be expected in all organic molecules where CH_3 and CH_2 groups occupy otherwise equivalent positions in a molecule. In larger molecules, with higher melting points than the 87.85°K. melting point of propylene, random orientation is still more likely to represent thermodynamic equilibrium when the substance solidifies, and the chance of attaining an ordered arrangement as the temperature is lowered is less. Moreover, it seems necessary to conclude that when one or more double bonds are unsymmetrically placed in internal positions in otherwise symmetrical hydrocarbons, a similar disorder will occur and an appropriate correction should be made to the entropy value obtained by the ordinary application of the third law of thermodynamics.

The most reliable value of the entropy for use in the thermodynamic calculations is 64.0 cal.

(14) Personal communication.
(15) Kassel, *J. Chem. Phys.*, **4**, 435 (1936).
(16) Pitzer, *ibid.*, **5**, 473 (1937).
(17) Pitzer, *ibid.*, **5**, 469 (1937).
(18) Kistiakowsky, *ibid.*, **6**, 900 (1938).

(2.5 g.) and zinc chloride (0.5 g.) in acetic acid (25 cc.). The mixture was allowed to stand for thirty minutes, a drop of sulfuric acid was added, and it was then refluxed for thirty minutes. The cooled solution was poured into water and extracted with petroleum ether. The extract was washed with water, and then extracted exhaustively first with aqueous sodium hydroxide (5%) and then with Claisen's alkali. The petroleum ether layer was then washed with water and dried.

From the aqueous alkali extractions, carbon dioxide precipitated a gummy solid (300 mg.), principally unchanged hydroquinone. Acidification and extraction of the Claisen's alkali extract gave 700 mg. of a brown, viscous oil. This was the chroman VI (R = H), possibly containing the chroman VII. The original petroleum ether solution, after extraction, yielded 700 mg. of a viscous oil, the double chroman VIII.

Oxidation of the Non-phenolic Constituent (VIII).—This material (700 mg.) was dissolved in absolute ethanol (35 cc.) and the solution was refluxed with silver nitrate (5 g.) for an hour and forty-five minutes. It was then diluted with water and extracted with ether. Removal of the ether left a red oil which was taken up in petroleum ether. This solution, on cooling, deposited the red quinone IV, m. p. and mixed m. p. 109–110°.

Oxidation of the Phenolic Constituents (VI and VII).—This material (700 mg.) was dissolved in absolute ethanol (500 cc.) and nitric acid (100 cc.) was added. The solution was heated on the steam-bath for fifteen minutes, then diluted with ice water (3000 cc.) and cooled to 0°. The cold solution was extracted exhaustively with ether and the extracts were washed free from acid. Removal of the ether left a red oil (400 mg.) which was taken up in ether–petroleum ether and crystallized. The product was the red quinone IV, m. p. 109.5–110.5°; mixed m. p. 109–110°.

Oxidation of α-Tocopherol; 2,7,8-Trimethyl-2-(4′,8′,12′-trimethyltridecyl-1)-chroman-5,6-quinone (IV, R = $C_{16}H_{31}$).—To a solution of synthetic *dl*-α-tocopherol (1.190 g.) in absolute ethanol (1190 cc.) was added concd. nitric acid (238 cc.). The solution was heated on the steam-bath for twenty-five minutes, then cooled and diluted with a large excess of ice water (3000 cc.). The mixture was extracted with ether, and the extracts were washed with water until free from acid. After drying the ethereal solution, the solvent was distilled off. The residue was a red oil which could not be crystallized.[18]

Phenazine.—The red oil from oxidation of α-tocopherol (0.225 g.) was dissolved in acetic acid (4.5 cc.) and *o*-phenylenediamine (0.159 g.) was added. After standing for three and a half hours, excess water was added and the product was extracted with a mixture of ether and petroleum ether. The extracts were washed with water and dried over sodium sulfate. The dry solution was chromatographed, using a column of Brockman alumina. The bulk of the material appeared in a wide yellow zone which fluoresced strongly in ultraviolet light. This zone was cut out and eluted with ether. The yellow ethereal solution showed a strong greenish fluorescence both in daylight and in ultraviolet light. The solvent was removed, but the residue was an orange oil which could not be crystallized.

Summary

1. When 6-hydroxychromans are oxidized by silver nitrate or by nitric acid, the products are red chroman-5,6-quinones. Any group in the 5-position of the hydroxychroman is eliminated in this reaction. Certain facts having a bearing on the mechanism of this reaction are reported.

2. The structure of the *o*-quinone from 2,2,5,-7,8-pentamethyl-6-hydroxychroman has been proved by synthesizing it from derivatives of *o*-xylohydroquinone.

3. Certain similarities between the absorption spectra of these red compounds and known ortho quinones are discussed.

4. The quantitative aspects of the photometric method of Furter and Meyer are discussed, and the limits of the reaction have been further defined and extended. It is pointed out that catechol derivatives, if present, may interfere.

5. The red chroman-5,6-quinone from α-tocopherol is an uncrystallizable oil. Evidence is presented to show that this substance forms a phenazine, although the latter is also an oil.

MINNEAPOLIS, MINN. RECEIVED JULY 10, 1939

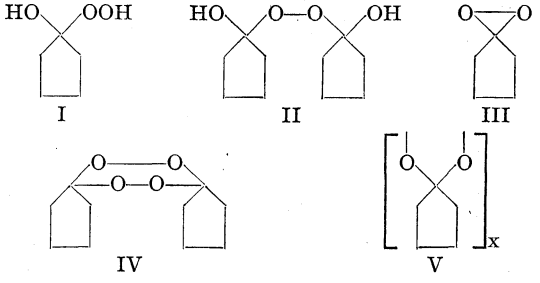
(18) Professor Furter, in a private communication, states that he also was unable to purify this compound.

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, No. 197]

Studies in Organic Peroxides. VI. Cyclane Peroxides[1]

BY NICHOLAS A. MILAS, S. ARTHUR HARRIS[2] AND PAUL C. PANAGIOTAKOS

When cyclic ketones are allowed to react with anhydrous hydrogen peroxide three types of peroxides may form: 1-hydroxycyclanyl hydroperoxide-1 (I), 1,1′-dihydroxydicyclanyl peroxide-1,1′ (II) and cyclanylidene peroxides (III, IV, and V). Using cyclopentyl as the cyclopolymethylene radical these may be illustrated as follows



In certain cases, especially with cyclopentanone and straight chain ketones like acetone, type I reverts spontaneously to type III, IV or V, whereas in other cases this reaction needs a suitable dehydrating agent.

Inasmuch as very little work has been reported in this field[3] and we became interested in exploring it, the present communication describes some of our results in the synthesis of a number of cyclane peroxides. Hydrogen peroxide in aqueous solutions with a suitable catalyst or persulfuric acid have been found convenient reagents for the oxidation of cyclic ketones to the corresponding dicarboxylic acids.[3,4] However, when hydrogen peroxide is used in non-aqueous solvents such as ether or *t*-butyl alcohol, very little or no oxidation occurs but instead peroxides of the type I, II, IV and V are formed.

Experimental Part

1-Hydroxycyclopentyl Hydroperoxide-1 (I).—The cyclopentanone (Eastman Kodak Company) used was purified by fractionation and the fraction boiling at 129–130° collected. A solution of 5 g. of the ketone in 100 cc. of 0.6 molal hydrogen peroxide in anhydrous ether was allowed to stand at room temperature for a few days. The ether was then removed at room temperature under reduced pressure and the viscous residue subjected to a vacuum of about 1 mm. for several hours to remove any unconverted ketone and free hydrogen peroxide. The viscous residue, 6.2 g., was analyzed for active oxygen using an acetone solution of sodium iodide acidified with acetic acid and titrating the liberated iodine against standard sodium thiosulfate.

Anal. Calcd. for $C_5H_{10}O_3$: active (O), 13.6. Found: active (O), 13.9, 14.4.

This experiment was repeated a number of times with both ether and *t*-butyl alcohol as solvents with identical results. It may be mentioned here that the peroxide is highly explosive and on one occasion when the equivalent of 10 g. of cyclopentanone was used with the corresponding amount of hydrogen peroxide in ether, a violent explosion occurred causing a considerable amount of damage, as the ether was being removed under vacuum at the temperature of the water-bath.

1,1′-Dihydroxydicyclopentyl Peroxide-1,1′ (II).—A solution of 5 g. of cyclopentanone in 50 cc. of 0.6 molal hydrogen peroxide in anhydrous ether was allowed to stand at room temperature for a few days, then the ether was removed under reduced pressure and the viscous residue subjected to a vacuum of about 1 mm. for a few hours to remove all volatile products. The residue, 5.5 g., was analyzed for active oxygen.

Anal. Calcd. for $C_{10}H_{18}O_4$: active (O), 7.92. Found: active (O), 8.12, 7.84.

Dicyclopentylidene Peroxide (IV).—When 1-hydroxycyclopentyl hydroperoxide-1 is allowed to stand at room temperature for several days crystals (needles) begin to come out. These were separated and dried on a porous plate. Cooling the viscous residue to 0° for some time enhances crystallization. These crystals melt rather sharply at 73–75° and the melt begins to show evolution of gas at 105°. They explode violently when heated on a steel spatula.

Anal. Calcd. for $C_5H_{10}O_3 \cdot {}^1/_2H_2O_2$: active (O), 17.8. Found: active (O), 18.7, 18.6, 18.64.

This peroxide also has been prepared by allowing cyclopentanone (1 cc.) to react with 30% hydrogen peroxide, "Albone C," (1 cc.) for two days, then cooling the clear solution in an ice–salt mixture whereby a white crystalline solid separated out. This solid was dried on a porous plate and found to have a m. p. of 73–75° and an analysis of 18.6% active oxygen.

In view of these results, we have come to the conclusion that this peroxide is probably 1-hydroxycyclopentyl hydroperoxide-1 with half a mole of hydrogen peroxide of crystallization. Because of its explosiveness we were unable to run combustions for carbon and hydrogen. This also has been the case with all other peroxides obtained from cyclopentanone.

(1) For other papers in this series see THIS JOURNAL, **55**, 349, 352 (1933); **56**, 1219, 1221 (1934); **60**, 2434 (1938).

(2) Fellow of the Massachusetts Pharmaceutical Corporation.

(3) *Cf.* Baeyer and Villiger, *Ber.*, **33**, 863 (1900); Stoll and Scherer, *Helv. Chim. Acta*, **13**, 142 (1930).

(4) Ruzicka and Stoll, *ibid.*, **11**, 1159 (1928).

Whenever the peroxide, m. p. 73–75°, was recrystallized from ether or from a 50–50 mixture of ether and petroleum ether, a new crystalline (needles) peroxide was obtained, m. p. 160° with effervescence. This peroxide is soluble in a number of organic solvents including ether, alcohol, acetone, dioxane, etc. It liberates iodine instantly from a sodium iodide solution in acetone acidified with acetic acid.

Anal. Calcd. for $C_5H_8O_2$: active (O), 16.0. Found: active (O), 16.13, 15.6, 16.5.

Inasmuch as the m. p. of this peroxide is too high for a five carbon substance, it was suspected early that it might be a polymer of cyclopentylidene peroxide. A molecular weight was therefore taken in *t*-butyl alcohol and in camphor and found to be 206 and 202, respectively, as against 200 calculated for dicyclopentylidene peroxide.

Polycyclopentylidene Peroxide.—When 1,1′-dihydroxydicyclopentylidene peroxide-1,1′ (II) is allowed to stand at room temperature for several days a solid peroxide separates out which melts at 166° with effervescence. A mixed m. p. with dicyclopentylidene peroxide showed no depression. However, unlike the latter peroxide this is completely insoluble in ether, alcohol, acetone and other common organic solvents, and, in view of this property, fails to liberate iodine from an acidified acetone–sodium iodide solution even after five days of standing at room temperature. Dioxane was the only suitable solvent, from which it was recrystallized several times with no change in m. p. An attempt to determine its molecular weight was unsuccessful. An analysis for active oxygen in an acidified solution of sodium iodide in dioxane gave highly unsatisfactory results. Finally, when it was refluxed in an acetone–acetic acid–sodium iodide solution for one hour, using appropriate blanks, it yielded only about three-fourths of its active oxygen.

Anal. Calcd. for $(C_5H_8O_2)_x$: active (O), 16.0. Found: active (O), 12.6.

Although this peroxide is very inert, under ordinary conditions, it explodes violently when heated on a steel spatula. A yield of over 50% was obtained as cyclopolypentylidene peroxide from the original reaction product.

This same polymer was also obtained in smaller quantities together with the dimer when the peroxide of m. p. 73–75° was treated with various solvents.

1-Hydroxycyclohexyl Hydroperoxide-1.—Five grams of cyclohexanone (b. p. 155–156°) was mixed with 85 cc. of 0.6 molal hydrogen peroxide solution in anhydrous ether and the mixture allowed to stand at room temperature for one day. The ether was then removed under reduced pressure and the viscous residue allowed to stand at room temperature, whereby it crystallized out after one day. The crystals were dried on a porous plate; yield, 3.8 g.; m. p. 76–78° which did not change appreciably after recrystallization from ether.

Anal. Calcd. for $C_6H_{12}O_3$: active (O), 12.13. Found: active (O), 12.94, 12.96.

This peroxide is rather stable and explodes only mildly when heated on a steel spatula.

1,1′-Dihydroxydicyclohexyl Peroxide-1,1′.—A solution of 8.8 g. of cyclohexanone in 87 cc. of 0.55 molal hydrogen peroxide in anhydrous ether was allowed to stand for two days. The ether was then removed under reduced pressure and the highly viscous residue was allowed to stand at 0° for twenty-four hours, whereby it was converted into a white crystalline mass which was recrystallized from ether; m. p. 68–70°. A yield of 4.1 g. of the pure product was obtained. This peroxide is insoluble in water and fails to liberate iodine from an acidified solution of potassium iodide. It was therefore analyzed by the acetone method used throughout this work.

Anal. Calcd. for $C_{12}H_{22}O_4$: active (O), 6.96. Found: active (O), 6.89.

When heated on a steel spatula this peroxide does not explode but burns with a smoky flame.

Hydroxymethylcyclohexyl Hydroperoxides and Peroxides.—Seven peroxides were obtained from the three methylcyclohexanones. For the hydroperoxides equimolecular proportions of the ketones (Eastman Kodak Company) and 0.6 molal hydrogen peroxide in anhydrous ether were mixed together and the mixtures allowed to stand at room temperature for some time. For the peroxides the molal ratio used of the ketone to peroxide was 2:1. After a number of days, in all cases the ether was removed under reduced pressure and the products obtained separated and analyzed. All peroxides thus obtained with the exception of those obtained from *o*-methylcyclohexanone were highly viscous liquids but failed to crystallize even when cooled to −20°. The viscosity of the peroxides from *o*-methylcyclohexanone was rather low and only increased slightly when cooled to −20°. Analytical and other data of these peroxides are given in Table I.

TABLE I

SUMMARY OF DATA FOR THE HYDROXYMETHYLCYCLOHEXYL HYDROPEROXIDES AND PEROXIDES

Peroxide	Formula	Yield, %	Active (O) Calcd.	Active (O) Found
1-Hydroxy-3-methylcyclohexyl hydroperoxide-1	$C_7H_{14}O_3$	89	10.95	10.25, 10.27
1-Hydroxy-2-methylcyclohexyl hydroperoxide-1	$C_7H_{14}O_3$	90	10.95	10.51
1-Hydroxy-4-methylcyclohexyl hydroperoxide-1	$C_7H_{14}O_3$	86	10.95	11.48, 11.30
1,1′-Dihydroxy-3,3′-dimethyldicyclohexyl peroxide-1,1′	$C_{14}H_{26}O_4$	98	6.21	6.21
1,1′-Dihydroxy-2,2′-dimethyldicyclohexyl peroxide-1,1′	$C_{14}H_{26}O_4$	89	6.21	6.13
1,1′-Dihydroxy-4,4′-dimethyldicyclohexyl peroxide-1,1′	$C_{14}H_{26}O_4$	89	6.21	6.07

When 1-hydroxy-3-methylcyclohexyl hydroperoxide-1 was allowed to stand at room temperature for a number of days, crystals began to separate which, after several recrystallizations from anhydrous ether, melted rather sharply at 120–121°.

Anal. Calcd. for $C_7H_{12}O_2 \cdot {}^1/_2H_2O_2$: active (O), 16.5. Found: active (O), 16.0.

This peroxide is highly explosive when heated on a steel spatula and behaves in all respects like the cyclopentylidene peroxide with hydrogen peroxide of crystallization. However, after several crystallizations we were unable to obtain 3-methylcyclohexylidene peroxide free from hydrogen peroxide.

1-Hydroxycycloheptyl Hydroperoxide-1.—Five grams of cycloheptanone was mixed with 100 cc. of 0.55 molal hydrogen peroxide in anhydrous ether and the mixture

was allowed to stand at room temperature for several days. When the ether was removed under reduced pressure, the highly viscous residue (4.5 g.) partly crystallized out, and the crystals separated and dried on a porous plate; m. p. 92–94°.

Anal. Calcd. for $C_7H_{14}O_3$: active (O), 10.95. Found: active (O), 10.00.

The dihydroxydicycloheptyl peroxide was not prepared.

1-Hydroxycycloöctyl Hydroperoxide-1.—A solution of 4.4 g. of cycloöctanone in 120 cc. of 0.55 molal hydrogen peroxide in anhydrous ether was allowed to stand at room temperature for several days. To remove the excess hydrogen peroxide the mixture was then shaken several times with a saturated ammonium sulfate solution until the aqueous layer gave a negative test for hydrogen peroxide. The ether layer was then dried with anhydrous magnesium sulfate, filtered and the ether removed under reduced pressure. A highly viscous semi-solid product, 4.4 g., was obtained which became curdy on standing for several weeks at room temperature, but failed to crystallize even when cooled to −78°.

Anal. Calcd. for $C_8H_{16}O_3$: active (O), 10.00. Found: active (O), 9.65.

1,1′-Dihydroxydicycloöctyl Peroxide-1,1′.—This peroxide was prepared in the same manner as the monocycloöctyl except that the proportions of reagents used were different. A solution of 2.6 g. (0.0206 mole) of cycloöctanone in 22 cc. of 0.55 molal hydrogen peroxide in anhydrous ether was allowed to stand at room temperature for several days. It was then shaken several times with a saturated solution of ammonium sulfate until the latter showed no test for hydrogen peroxide. Finally, the ethereal solution was dried with anhydrous magnesium sulfate, filtered and the ether removed under reduced pressure. A yield of 2.2 g. of highly viscous product was obtained which failed to crystallize.

Anal. Calcd. for $C_{16}H_{30}O_4$: active (O), 5.59. Found: active (O), 5.53.

We are indebted to Dr. R. B. Woodward of Harvard University for supplying the C_7 and C_8 ketones.

Summary

Seventeen cyclane peroxides have been prepared by the interaction of hydrogen peroxide in anhydrous ether with a number of cyclic ketones.

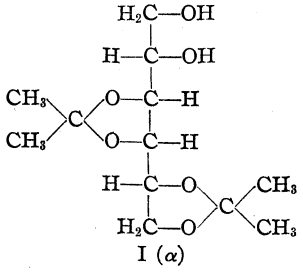
CAMBRIDGE, MASSACHUSETTS RECEIVED JUNE 22, 1939

[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF HEALTH, U. S. PUBLIC HEALTH SERVICE]

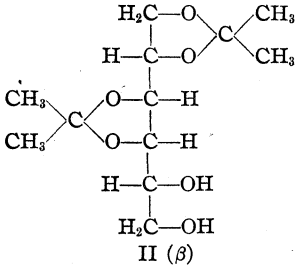
The Structures of the Diacetone Dulcitols[1]

BY RAYMOND M. HANN, W. DAYTON MACLAY AND C. S. HUDSON

Recently Pizzarello and Freudenberg[2] have proposed structures for the two diacetone dulcitols that were originally described by Fischer,[3] assigning to the α-diacetone dulcitol the structure of 3,4:5,6-diacetone dulcitol (I) and to the β-isomer that of 1,2:3,4-diacetone dulcitol (II).



I (α)



II (β)

Pizzarello and Freudenberg point out that the proposed structures are enantiomorphous and they emphasize that the ready separation of the α- and β-diacetone dulcitols by fractional crystallization is thus in conflict with general experience. It also may be added that the substances exhibit very different melting points, solubilities and crystalline forms (as shown by optical crystallographic measurements), all of which facts seem to exclude the idea of enantiomorphism. Neither of them is optically active. The basis of assignment of the enantiomorphous structures was (1) that lead tetraacetate oxidation in benzene solution of both diacetone dulcitols yielded formaldehyde, indicating the presence of contiguous hydroxyl groups, one of which must be primary, in the molecules and (2) that α-diacetone dulcitol could be transformed by alkaline permanganate oxidation to a derivative of D-galactonic acid (potassium diacetone D-galactonate) and (3) that β-diacetone dulcitol under similar oxidative procedure yielded the enantiomorphous derivative of L-galactonic acid (potassium diacetone L-galactonate). A review of the earlier researches of Fischer[3] and of Fischer and Bergmann[4] upon the diacetone dulcitols revealed that these substances undergo several interesting

(1) Publication authorized by the Surgeon General, U. S. Public Health Service.

(2) Pizzarello and Freudenberg, THIS JOURNAL, **61**, 611 (1939).

(3) Fischer, *Ber.*, **48**, 269 (1915).

(4) Fischer and Bergmann, *ibid.*, **49**, 289 (1916).

and unexplained reactions. We have therefore, with the agreement of Dr. Freudenberg, undertaken a further study of the reactions of the isomeric diacetone dulcitols.

The lack of correspondence in physical properties of the α- and β-diacetone dulcitols seems to exclude the possibility of their being enantiomorphous forms, as has been mentioned. Further evidence on this point has now been obtained through the preparation of several of their derivatives. As is apparent from the data recorded in Table I, the melting points of corresponding derivatives are greatly different and the same is true for their crystalline appearances and solubilities; the trityl derivatives have different compositions. None of them exhibits optical activity. It is thus apparent that these derivatives are in no case enantiomorphous forms. One is driven to the conclusion that *the α- and β-diacetone dulcitols are not enantiomorphous substances and hence must be structural isomers.*

TABLE I

MELTING POINTS OF DERIVATIVES OF THE α- AND β-DIACETONE DULCITOLS

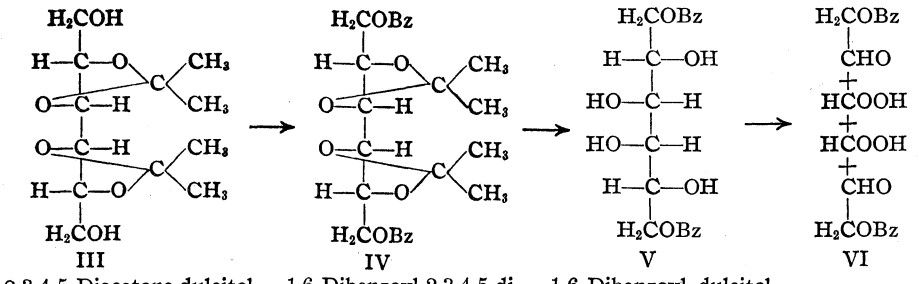
Derivative	From α-diacetone dulcitol	From β-diacetone dulcitol
Diacetate	89°	134°
Ditosylate	101°	165–166°
Trityl	(Monotrityl monoacetyl) 107–108°	(Ditrityl) 233–234°
Dibenzoate	82–83°[a]	183–184°[b]

[a] This is the substance which Fischer and Bergmann (ref. 4) designated empirically β-dibenzoyl-diacetone dulcitol. The proof that it is a derivative of α-diacetone dulcitol is presented later in this article. We change its name to dibenzoyl α-diacetone dulcitol. [b] This is the substance which Fischer (ref. 3) designated empirically α-dibenzoyl-diacetone dulcitol. The proof that it is a derivative of β-diacetone dulcitol is presented later in this article. We change its name to dibenzoyl β-diacetone dulcitol.

Our initial investigation of the action of various oxidizing agents on the diacetone dulcitols indicated that hydrolysis occurred readily in the presence of very dilute mineral acids and slowly even when organic acids were present. Periodic acid of 0.4 normality rapidly removed the acetone groups and attacked the free hydroxyls thus formed. On the other hand, sodium periodate in aqueous solution or lead tetraacetate in glacial acetic acid solution was essentially without effect over a period of twenty-four hours at room temperature and thereafter caused a slow oxidation, which presumably was preceded by some hydrolysis of the acetone groups. Evidently the oxidation that was reported by Pizzarello and Freudenberg, which was partly conducted at steam-bath temperatures, involved some hydrolysis of the acetone groups. The failure of either sodium periodate or lead tetraacetate to oxidize the diacetone dulcitols indicates that *there is no glycol grouping present in either of them and therefore the two hydroxyl groups present in each of them are not attached to adjacent carbon atoms.*

It is evident that if the conclusions that have now been reached are correct, neither of the formulas I and II can apply to the structures of either of the diacetone dulcitols.

The Structure of β-Diacetone Dulcitol.—The ditosyl derivatives of the diacetone dulcitols were of particular interest since it seemed possible that upon iodination by treatment with sodium iodide and acetone under pressure, iodo compounds of importance for structural determination might be obtained. This expectation was fulfilled when it was discovered that the ditosyl derivative of β-diacetone dulcitol gave a diiodo β-diacetone dulcitol in high yield, allowing the inference that the two tosyl groups were attached to two primary hydroxyl groups and that β-diacetone dulcitol therefore possesses two free primary hydroxyl groups. Support for this inference was obtained when it was found that β-diacetone dulcitol readily formed a ditrityl derivative upon treatment with pyridine and triphenylmethyl chloride. Both results are in agreement with the previously mentioned observation that sodium periodate or lead tetraacetate does not oxidize β-diacetone dulcitol. The evidence from these three sources thus makes it highly probable that β-diacetone dulcitol has free hydroxyl groups on carbons one and six. Conclusive proof of this structure was obtained through the following reactions. The β-diacetone dulcitol (III) was converted to dibenzoyl β-diacetone dulcitol (IV) which in turn was transformed to β-dibenzoyl dulcitol (V) by removal of the acetone groups through acid hydrolysis. A 1,6-dibenzoyl dulcitol, upon oxidation by lead tetraacetate, should consume three moles of oxidant and produce two moles of benzoyl glycolic aldehyde (VI) and two moles of formic acid. The oxidation of the dibenzoate prepared from β-diacetone dulcitol with 3.6 moles of lead tetraacetate in glacial acetic acid solution at room temperature for three and one-half hours consumed 3.15 moles of oxidant per mole of diacyl dulcitol.



III — 2,3,4,5-Diacetone dulcitol (β-diacetone dulcitol)

IV — 1,6-Dibenzoyl-2,3,4,5-diacetone dulcitol (dibenzoyl β-diacetone dulcitol)

V — 1,6-Dibenzoyl dulcitol (β-dibenzoyl dulcitol)

VI

From the reaction mixture benzoyl glycolic aldehyde was isolated as its crystalline semicarbazone in a yield of 79%. The fact that this yield is far above 50% proves that both carbons one and six carry benzoyl groups. In a separate experiment the benzoyl glycolic aldehyde was further identified by its oxidation with bromine water to benzoyl glycolic acid, the melting point of which agreed with that reported by Brigl and Grüner,[5] who prepared the substance from 1,6-dibenzoyl mannitol by alkaline permanganate oxidation. The β-dibenzoyl dulcitol is so slightly soluble in water that the oxidation by aqueous sodium periodate could not be studied, but it was possible to obtain analytical data on the periodate oxidation of the similarly prepared β-diacetyl dulcitol, which is moderately soluble in water. If the substance is 1,6-diacetyl dulcitol, 1 mole of it should consume 3 moles of periodate and generate 2 moles of formic acid; it was found to consume 3 moles of oxidant and the increase in acidity corresponded to the production of 2.05 moles of formic acid. The analytical data are thus in agreement with the formulation that *the β-diacyl dulcitols are 1,6-diacyl dulcitols, and the β-diacetone dulcitol is 2,3,4,5-diacetone dulcitol.* The attachment of the two acetone groups is limited to three structures, namely, 2,3:4,5, 2,4:3,5 and 2,5:3,4; decision among them must be deferred at this time. Formulas (III) and (IV) indicate provisionally a 2,3:4,5 arrangement of the acetone groups. In any case, the substances of the β-diacetone dulcitol series that are now known possess meso structures, which accounts for their lack of optical activity.

The Structure of α-Diacetone Dulcitol.—It has been mentioned that β-diacetone dulcitol yields a ditosyl derivative which is convertible to a diiodo derivative through the action of sodium iodide in acetone solution. Under similar experimental conditions α-diacetone dulcitol yields a ditosyl derivative, but iodination of this substance yields a mono-iodo monotosyl α-diacetone dulcitol in nearly quantitative yield. The two diacetone dulcitols also show a dissimilar behavior on treatment with triphenylmethyl chloride. As has been stated, the β-isomer forms a ditrityl derivative, but from similar tritylation reactions involving α-diacetone dulcitol no evidence of ditritylation has been observed, and the isolation of a monotrityl monoacetyl α-diacetone dulcitol in 95% yield indicated that none occurred. These results are good evidence that *α-diacetone dulcitol contains only one free primary hydroxyl group*, and are also inclusive independent proofs of the previous decision that the α- and β-diacetone dulcitols are structural isomers rather than enantiomorphous substances. There remains, then, the problem of determining the position of the secondary hydroxyl group in α-diacetone dulcitol.

Reference to Table II, column 2, shows that the maximum number of diacetone dulcitols which have either one or two free primary hydroxyl groups is fifteen. Three of these structures (nos. 1, 4 and 7) are *meso* forms, one of which must represent β-diacetone dulcitol, as has been proved. The remaining twelve structures are those of potentially optically-active substances for which there must be twelve enantiomorphous forms, not shown in the table. Thus the precise enumeration is three *meso* forms and twelve pairs of enantiomorphs. We digress from the argument at this point in order to explain the convention which we shall use in naming these enantiomorphs. The customary use of the word dulcitol with numbered carbon atoms indicating the places of attachment of substituent groups is unobjectionable in the case of *meso* structures for the reason that the name is the same whether the numbering of the dulcitol chain starts at one end or the other.

(5) Brigl and Grüner, *Ber.*, **65**, 643 (1932).

TABLE II

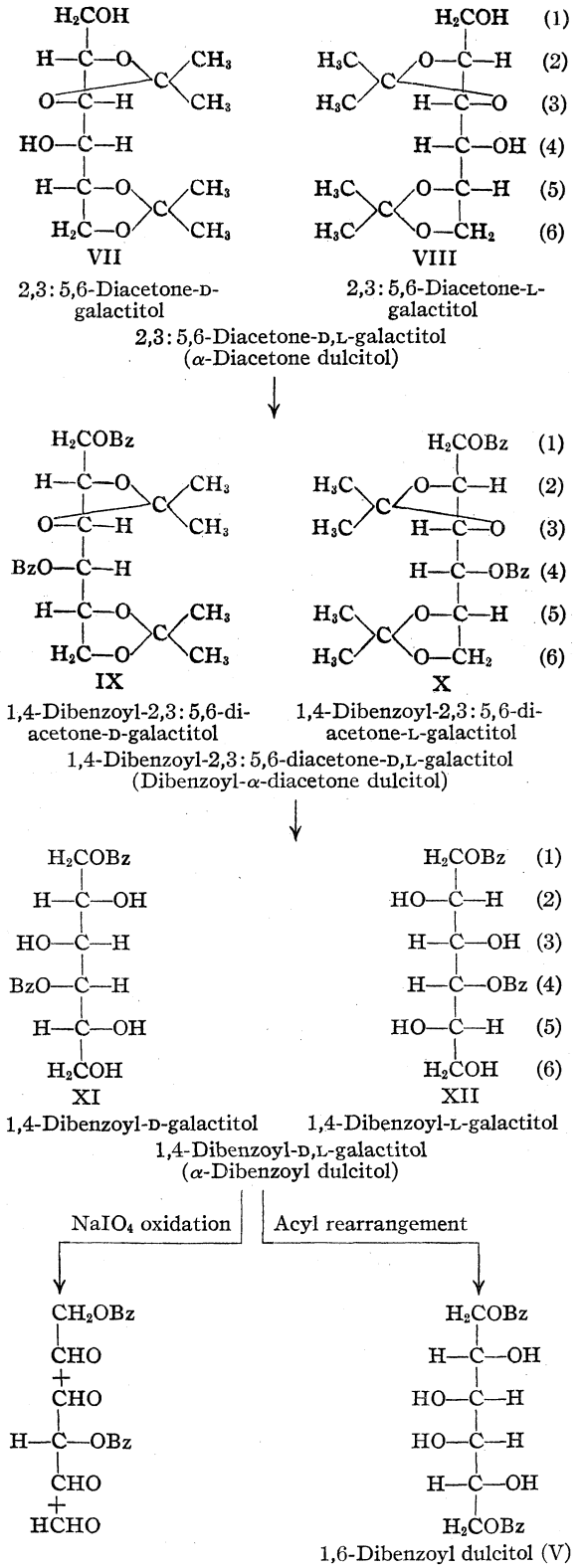
POSSIBLE ARRANGEMENTS OF TWO ISOPROPYLIDENE RESIDUES IN A DIACETONE DULCITOL CONTAINING ONE OR TWO FREE PRIMARY HYDROXYL GROUPS

No.	Acetone attachment	Excluded because of	Corresponding dibenzoyl dulcitol
1	2,3:4,5	Two primary OH's	
2	2,3:4,6	.....	1,5
3	2,3:5,6	.....	1,4
4	2,4:3,5	Two primary OH's	
5	2,4:3,6	.....	1,5
6	2,4:5,6	.....	1,3
7	2,5:3,4	Two primary OH's	
8	2,5:3,6	.....	1,4
9	2,5:4,6	.....	1,3
10	2,6:3,4	.....	1,5
11	2,6:3,5	.....	1,4
12	2,6:4,5	.....	1,3
13	3,4:5,6	Contiguous OH's	
14	3,5:4,6	Contiguous OH's	
15	3,6:4,5	Contiguous OH's	

But such is not the case with respect to the non-*meso* (optically active) structures; the numbering for them is formally different for the two ways of numbering dulcitol. This is illustrated by formulas I and II, with the numbering for their names as given by Pizzarello and Freudenberg; while it is clear after an inspection of the formulas that 3,4:5,6- and 1,2:3,4-diacetone dulcitols are enantiomorphous forms, the fact is not immediately apparent from their names alone because they do not have one and the same name to which the D- and L-symbols, which are customary for enantiomorphs, can be prefixed. We suggest for such cases the convention that the numbering be chosen to conform with that of the appropriate D- or L-galactose, since the numbering of the sugars is precise, and that the use of the convention be indicated by employing the name galactitol in place of dulcitol; thus structures I and II would receive the names, respectively, 3,4:5,6-diacetone D-galactitol and 3,4:5,6-diacetone L-galactitol, or 1,2:3,4-diacetone L-galactitol and 1,2:3,4-diacetone D-galactitol. Formulas VII–XII further illustrate this convention of nomenclature, especially its use for the naming of racemic forms. Returning now to the consideration of Table II, the three *meso* forms (nos. 1, 4 and 7) cannot represent α-diacetone dulcitol because the latter has been shown to possess only one primary hydroxyl group. Nos. 13, 14 and 15 also can be excluded because of the presence in them of contiguous hydroxyl groups. One of the remaining nine structures therefore must apply to α-diacetone dulcitol and, since this substance is optically inactive, as are also its derivatives (Table I), it must be a racemate. Upon dibenzoylation of the nine structures, as racemates, nine different dibenzoyl diacetone D,L-galactitols would result, but upon removing the acetone groups from them only three (1,3, 1,4 and 1,5) dibenzoyl D,L-galactitols can be formed; the problem of assigning the position of the free secondary hydroxyl group in α-diacetone dulcitol thus reduces to that of the establishment of the structure of the α-dibenzoyl dulcitol that results when the isopropylidene residues are removed from dibenzoyl-α-diacetone dulcitol. Fortunately it has proved possible to decide this question through a study of the periodate oxidation of the α-dibenzoyl dulcitol. A 1,5-dibenzoyl dulcitol should consume 2 moles of oxidant and yield 1 mole each of formic acid, 2-benzoylglyceric aldehyde, benzoylglycolic aldehyde and water; 1,4-dibenzoyl dulcitol should consume 2 moles of oxidant and produce 1 mole each of formaldehyde, benzoylglycolic aldehyde and benzoyltartronic dialdehyde, and 2 moles of water, *but no formic acid;* and finally 1,3-dibenzoyldulcitol should require 2 moles of oxidant and form 1 mole each of formic acid, formaldehyde, water and 2,4-dibenzoylthreose. It was found that the oxidation of α-dibenzoyldulcitol with sodium periodate in aqueous alcoholic solution consumed 2 moles of oxidant, but that no acid was produced;[6] it is therefore concluded that *α-dibenzoyl dulcitol is 1,4-dibenzoyl* D,L-*galactitol and α-diacetone dulcitol is accordingly 2,3,5,6-diacetone* D,L-*galactitol.* The question of the arrangement of the acetone groups awaits further study. The observed optical inactivity of the various dulcitol derivatives of the α- and β-series is to be ascribed, according to the structure here shown, to the presence of meso forms in the β-series and of racemic forms in the α-series, as previously mentioned. The reactions through which the structure of α-diacetone dulcitol has been disclosed are illustrated in the structural formulas (VII)–(XII), in which the attachment of the acetone residues at positions 2, 3, 5 and 6 is provisionally assumed to be at 2,3 and 5,6.

Rearrangements in the Dulcitol Series.—Upon melting α-dibenzoyl dulcitol in a capillary tube the substance liquefies completely at 170–

(6) As is described in the experimental part, there was found an apparent titratable acidity corresponding to 0.15 mole of formic acid but it is believed that this acidity is negligibly small and that it probably is due to enolization of benzoyl tartronic dialdehyde.



171° and if maintained at this temperature it rapidly resolidifies and then remelts at 202–203°. The closeness of the latter melting point to that of β-dibenzoyl dulcitol, namely, 209°, suggested that an acyl migration had occurred, the enantiomorphous structures (XI) and (XII) rearranging to the *meso* form (V). This hypothesis was verified by melting a larger amount of α-dibenzoyl dulcitol and crystallizing the melt from acetic acid, whereby pure β-dibenzoyl dulcitol was obtained in nearly quantitative yield. Several such migrations of an acyl group have been observed by others and the postulate has been advanced that they occur through the intermediate formation of dioxolone or meta-dioxane ring compounds.[7] The acyl migration in this case seems to be analogous to that of the benzoyl group in 3-benzoyl monoacetone glucose, which readily migrates to form 6-benzoyl monoacetone glucose.[8] The labile nature of the benzoyl group on carbon four in α-dibenzoyl dulcitol thus furnishes an explanation of the observation by Fischer and Bergmann[4] that β-dibenzoyl dulcitol can be obtained by boiling an aqueous solution of α-dibenzoyl dulcitol; this unusual change is now seen to be due to an acyl migration of the benzoyl group from carbon 4 to carbon 6.

We have confirmed the observation of Fischer[3] that α-diacetone dulcitol upon benzoylation with benzoyl chloride and quinoline at 100° yields a dibenzoate melting at 183–184°, which we designate dibenzoyl β-diacetone dulcitol (Formula IV, see also Table I, footnote b) because its debenzoylation yields β-diacetone dulcitol quantitatively. It is evident from the structures which have been developed for the diacetone dulcitols that *an acetone shift has occurred, the enantiomorphous structures (VII) and (VIII) passing on benzoylation to the meso structure (IV)*. This shift is discussed further in the experimental section ("Rearrangements") where it is shown that the rearrangement is catalyzed by such substances as quinoline hydrochloride and (in less degree) pyridine hydrochloride. Hibbert and his co-workers[9] have shown that the 1,1′ and the 1,2 methylidene, benzylidene, and *p*-nitrobenzylidene cyclic acetals of glycerol are interconvertible in the presence of a trace of hydrochloric acid; the catalysis of the isopropylidene shift in the dulcitol derivatives by quinoline and pyridine hydrochlorides appears to be an analogous reaction.

(7) Fischer, *Ber.*, **53**, 1621 (1920); Hibbert and Carter, THIS JOURNAL, **51**, 1601 (1929).

(8) Ohle, *Ber.*, **57**, 406 (1924).

(9) Hill, Whelan and Hibbert, THIS JOURNAL, **50**, 2235 (1928); Hibbert and Carter, *ibid.*, **50**, 3120, 3376 (1928).

We are indebted to Mr. George L. Keenan of the Food and Drug Administration, U. S. Department of Agriculture, for the determination of optical properties of certain compounds, to Dr. W. T. Haskins for micro-analyses performed in connection with this work, and to the Atlas Powder Company for furnishing a supply of dulcitol.

Experimental

In the preparation of the diacetone dulcitols from dulcitol with acetone and dry hydrochloric acid gas, small variations of conditions markedly affect the yields; indeed Fischer and Bergmann have reported that they obtained at times the β-isomer under conditions which previously had yielded the α-derivative without being able to assign a cause for the difference in result. It seems from present knowledge that these variations may be due to cyclic acetal rearrangement of the sensitive α-diacetone dulcitol. We find that a separable mixture of the two diacetone dulcitols may be obtained readily with good regularity under the following conditions. A suspension of 50 g. of finely powdered dulcitol in 975 cc. of dry acetone containing 24.2 g. of dry hydrochloric acid gas was agitated vigorously for twenty-four hours at 20°; the dulcitol dissolved and pure α-diacetone dulcitol (m. p. 144–145°) crystallized in a yield of 24.3 g. (34%). The mother liquor was stirred with 150 g. of basic lead carbonate for one hour, the lead chloride and carbonate were removed by filtration, and the filtrate was concentrated to 275 cc. in the presence of some basic lead carbonate. Following filtration, the solution was seeded with α-diacetone dulcitol and allowed to stand overnight at 5°; a further crop of 10.5 g. of crude α-diacetone dulcitol (m. p. 138–140°) was obtained (yield of α, 48%). The mother liquor was concentrated to a volume of 90 cc., further crystallization occurring during the process; the magma was refrigerated for twenty-four hours and 31.1 g. of impure β-diacetone dulcitol (m. p. 104–108°) was removed by filtration. A further small amount of the same substance (1.4 g., m. p. 102–104°) was recovered from the final mother liquor upon treatment with petroleum ether (yield of β, 45%).

The α-diacetone dulcitol may be recrystallized from 5 parts of 95% alcohol in yields of 90%, separating in well-formed brilliant prisms. The substance melts at 144–145° (corr.) and is optically inactive in alcohol, acetone or chloroform solution. Optical-crystallographic data on this compound were kindly obtained by Mr. George L. Keenan. The refractive indices (determined by the immersion method in organic liquids) are $n_\alpha = 1.503$, $n_\beta = 1.507$, $n_\gamma = 1.538$, $n_\gamma - n_\alpha = 0.035$, all ± 0.003. In parallel polarized light (crossed nicols), the birefringence is strong, the polarization colors are brilliant, many fragments extinguishing sharply and others remaining bright under the same conditions. In convergent polarized light (crossed nicols), partial biaxial figures are frequently seen, one optic axis being perpendicular to many of the fragments.

The crude β-diacetone dulcitol may be purified by solution in 5 parts of acetone and addition of 10 parts of petroleum ether; it separates in groups of elongated prisms. The substance melts at 111° (corr.) and is optically inactive in alcohol, acetone or chloroform solution. The microscopical examination of the compound was made by Mr. Keenan. Its refractive indices are $n_\alpha = 1.478$, $n_\beta = 1.510$, $n_\gamma = 1.518$, $n_\gamma - n_\alpha = 0.040$, all ± 0.003. In parallel polarized light (crossed nicols), the birefringence is strong, some of the fragments extinguish sharply and others remain bright, the polarization colors being of the first order. In convergent polarized light (crossed nicols) biaxial figures showing the acute bisectrix are common, the optic sign being negative, and $2E = 30°$ (approximately). The optical-crystallographic properties are entirely unlike those of the α-diacetone dulcitol, a fact which precludes the possibility that the substances are enantiomorphous forms.

Periodic Acid Oxidation of α-Diacetone Dulcitol.—Pizzarello and Freudenberg identified formaldehyde qualitatively (as its dinitrophenylhydrazone) as an oxidation product from the action of lead tetraacetate on α-diacetone dulcitol in benzene solution. We have verified this qualitative observation but we doubt its interpretation in terms of structure because of the fact that the oxidation was partly conducted at elevated temperature and there is the possibility that α-diacetone dulcitol may have been hydrolyzed. It was found that at 20° lead tetraacetate in glacial acetic acid solution, or sodium periodate in aqueous solution, oxidized α-diacetone dulcitol to only a slight and negligible extent in twenty hours, but that aqueous periodic acid oxidizes it rapidly at 20°. To a solution of 0.4078 g. of α-diacetone dulcitol in 27 cc. of water, 19.97 cc. of 0.623 *M* periodic acid (8 moles) was added and the volume of the solution adjusted to 50 cc. Analysis of 5-cc. subsamples at fifteen and thirty minutes, one, four and twenty-two hours, indicated that 1.83, 2.77, 3.68, 5.01 and 5.17 moles of oxidant had been consumed at 20°. The results indicate that the acetone groups were hydrolyzed and the dulcitol which was thus liberated was completely oxidized. Such a series of reactions should consume 5.00 moles of periodic acid.

Sodium Periodate Oxidation of α-Diacetone Dulcitol.—To a solution of 0.2838 g. of α-diacetone dulcitol in 30 cc. of water, 12.38 cc. of 0.306 *M* sodium periodate solution (3.5 moles) was added and the volume adjusted to 50 cc. Analysis of 5-cc. subsamples at the expiration of fifteen, thirty and one hundred and forty-five minutes indicated that no oxidation had occurred at 20° and a similar analysis at twenty hours showed that only 0.35 mole of oxidant had been consumed. Evidently the acidity of sodium periodate is so low that hydrolysis is greatly retarded; and the oxidant appears to be without action on unhydrolyzed α-diacetone dulcitol.

Lead Tetraacetate Oxidation of α-Diacetone Dulcitol.—To a solution of 0.1347 g. of α-diacetone dulcitol in 73 cc. of glacial acetic acid, 25 cc. of 0.1282 *N* lead tetraacetate glacial acetic acid solution (3.2 moles) was added and the volume adjusted to 100 cc. with glacial acetic acid. Analysis of 10-cc. subsamples at fifteen, thirty and one hundred and twenty minutes showed that no oxidation had occurred at 20°, and similar analyses at nineteen and forty-five hours indicated that only 0.08 and 0.23 mole of oxidant had been consumed. Lead tetraacetate thus also appears to be without action on unhydrolyzed α-diacetone dulcitol.

Periodic Acid Oxidation of β-Diacetone Dulcitol.—To a solution of 0.3982 g. of β-diacetone dulcitol in 25 cc. of water, 19.44 cc. of 0.625 *M* periodic acid (8 moles) was added and the solution diluted to 50 cc. with water. At the expiration of one hour at 20°, 0.94 mole of oxidant had been utilized and in fifty hours 5.3 moles had been consumed, indicating the conversion of the diacetone dulcitol to free dulcitol and the complete oxidation of the latter compound.

Sodium Periodate Oxidation of β-Diacetone Dulcitol.—To a solution of 0.2692 g. of β-diacetone dulcitol in 25 cc. of water, 11.59 cc. of 0.31 *M* sodium periodate solution (3.5 moles) was added and the solution diluted to 50 cc. with water. Subsamples of 5 cc. were analyzed after the expiration of fifteen and thirty minutes, one and six hours, and at the end of four days, but no sodium periodate was consumed during this period at 20°. Evidently the β-isomer is considerably more resistant than the α-form to hydrolysis.

Lead Tetraacetate Oxidation of β-Diacetone Dulcitol.—To a solution of 0.1067 g. of β-diacetone dulcitol in 73 cc. of glacial acetic acid, 25 cc. of 0.1282 *N* lead tetraacetate acetic acid solution (3.2 moles) was added and the solution diluted to 100 cc. with the same solvent. Subsamples of 10 cc., which were analyzed at the expiration of fifteen, thirty and one hundred and thirty-five minutes, showed no consumption of oxidant at 20°; after twenty hours 0.03 mole of lead tetraacetate had been consumed and after eight days only 0.8 mole.

Summarizing, these oxidation experiments indicate that the diacetone dulcitols are stable toward two oxidizing agents that are known to attack specifically a glycol grouping, provided that the reagent itself is not acidic enough to cause hydrolysis of the isopropylidene residues.

Derivatives of β-Diacetone Dulcitol (2,3,4,5-Diacetone Dulcitol)

Diacetyl-β-diacetone Dulcitol (1,6-Diacetyl-2,3,4,5-diacetone Dulcitol).—To a solution of 1 g. of β-diacetone dulcitol in 5 cc. of pyridine 5 cc. of acetic anhydride was added. A slight warming occurred and within five minutes the formation of a crystalline deposit, which increased rapidly in amount on standing, was noted. After twenty-four hours the solid was removed by filtration, washed with alcohol, and dried; yield 1.3 g. (quantitative). The compound may be recrystallized from 10 parts of alcohol, separating in prisms which melt at 134° (corr.) and show no rotation in chloroform (*c*, 1.28).

Anal. Calcd. for $C_{16}H_{26}O_8$: C, 55.48; H, 7.57. Found: C, 55.62; H, 7.45.

The relative insolubility of diacetyl β-diacetone dulcitol in the acetylating mixture offers an easy procedure for the separation of a mixture of α- and β-diacetone dulcitols.

In a typical experiment, 10 g. of a mixture of m. p. 104–108° was acetylated in 50 cc. of pyridine and 50 cc. of acetic anhydride. Within two hours the β-diacetate began to crystallize and on standing overnight in the refrigerator 8.9 g. of the substance had separated. The diacetyl α-diacetone dulcitol was obtained in a yield of 3.4 g. by pouring the mother liquors into ice and water. The total recovery of acetate was 93%. The respective diacetone dulcitols were obtainable in quantitative yield upon deacetylation with either sodium or barium methylate.

Ditosyl-β-diacetone Dulcitol (1,6-Ditosyl-2,3,4,5-diacetone Dulcitol).—To a solution of 8.3 g. of *p*-toluenesulfonyl chloride (2.2 mols) in 23.6 cc. of pyridine (15 mols) cooled in an ice-bath, 5.1 g. of finely powdered β-diacetone dulcitol was added. Solution occurred readily and was followed by a separation of characteristic crystals of pyridine hydrochloride. The reaction mixture was then held at 40° for seventy-two hours. The solid mass was broken up with addition of 100 cc. of water and the precipitate removed by filtration and washed well with water; yield 10.5 g. (96%). The compound was recrystallized from 7.5 parts of glacial acetic acid, being obtained in small oblique plates which melted at 165–166° (corr.) and showed no rotation in chloroform (*c*, 1.36).

Anal. Calcd. for $C_{26}H_{34}O_{10}S_2$: C, 54.72; H, 6.00. Found: C, 54.75; H, 6.21.

Dityrityl-β-diacetone Dulcitol (1,6-Dityrityl-2,3,4,5-diacetone Dulcitol).—To a solution of 4.7 g. (2.2 mols) of triphenylmethyl chloride in 25 cc. of pyridine, 2.0 g. of finely powdered β-diacetone dulcitol was added. The solution was allowed to stand at room temperature for seventy-two hours and then crystallization of the dityrityl derivative was induced by gradual addition of 100 cc. of water. The precipitate weighed 6.3 g. (theory 5.7 g.) and was contaminated by triphenylcarbinol. The pure dityrityl compound was obtained, after several recrystallizations from 200 parts of acetone, in the form of small elongated glistening prisms which decomposed at 233–234° (corr.) and showed no rotation in chloroform (*c*, 0.39).

Anal. Calcd. for $C_{50}H_{50}O_6$: C, 80.40; H, 6.75. Found: C, 80.39; H, 6.76.

Diiodo-β-diacetone Dulcitol (1,6-Di-iodo-2,3,4,5-diacetone Dulcitol).—A solution of 5.0 g. of ditosyl-β-diacetone dulcitol and 3.9 g. (3 moles) of sodium iodide in 125 cc. of acetone was heated for two hours at 100° in a pressure bottle. The separated sodium salt of *p*-toluenesulfonic acid (2.5 g.; theory for 2 moles, 3.1 g.) was removed by filtration and the acetone mother liquors were concentrated to dryness by an air current. The dry residue was treated with 25 cc. of water and the insoluble portion filtered off and dried: yield, 4.4 g.; m. p., 102–103° (theory, 4.2 g.). By an initial recrystallization from acetone and a second from alcohol the compound was obtained in fine needles which melted at 108–109° (corr.) and showed no optical activity in chloroform solution (*c*, 1.36).

Anal. Calcd. for $C_{12}H_{20}O_4I_2$: C, 29.89; H, 4.18. Found: C, 29.88; H, 4.22.

β-Dibenzoyl Dulcitol (1,6-Dibenzoyl Dulcitol).—Four grams of dibenzoyl-β-diacetone dulcitol, which was prepared from β-diacetone dulcitol, benzoyl chloride and quinoline by the directions of Fischer and Bergmann[4] (see also the later section on "Rearrangements"), was refluxed for half an hour in 100 cc. of 80% acetic acid. On cooling, 2.6 g. of the desired deacetonated product crystallized and a further 0.4 g. was obtained from the reaction mixture upon concentration; yield, 3.0 g. (91%). Upon recrystallization from 25 parts of

glacial acetic acid it separated in shining platelets which melted at 209° (corr.) and showed no optical activity in acetic acid solution. Fischer reported a melting point of 210° and designated the compound α-dibenzoyl dulcitol, because it was the first dibenzoyl dulcitol isolated. It seems advisable, however, to name it a member of the β-series, particularly since we later describe a dibenzoyl dulcitol of the α-series.

Tetraacetyl-β-dibenzoyl Dulcitol (1,6-Dibenzoyl-2,3,4,5-tetraacetyl Dulcitol).—The solution of 2.0 g. of β-dibenzoyl dulcitol in 10 cc. of pyridine and 10 cc. of acetic anhydride was completed by refluxing the mixture for fifteen minutes. The desired acetate separated in a yield of 2.9 g. (quantitative) upon addition of water. The substance may be recrystallized from 10 parts of glacial acetic acid, and separates in diamond-shaped plates which melt at 225–226° (corr.) and show no rotation in chloroform solution (*c*, 1.40).

Anal. Calcd. for $C_{28}H_{30}O_{12}$: C, 60.21; H, 5.41. Found: C, 60.09; H, 5.44.

β-Diacetyl Dulcitol (1,6-Diacetyl Dulcitol).—A suspension of 5 g. of diacetyl β-diacetone dulcitol in 100 cc. of water and 10 cc. of acetic acid was refluxed for one hour, during which time solution gradually occurred. The solution was concentrated *in vacuo* to dryness and the dry residue transferred to a filter funnel with 35 cc. of warm absolute alcohol. The yield of 1.8 g. (m. p. 155–156°) was increased by 0.5 g. (m. p. 154–155°) by further recovery from the mother liquors (60%). The crude material, which apparently contained some dulcitol, was recrystallized from 10 parts of water; it separated in pure condition in large flat plates, melting at 167–168° (corr.) and showing no rotation in chloroform solution (*c*, 0.28).

Anal. Calcd. for $C_{10}H_{18}O_8$: C, 45.11; H, 6.81. Found: C, 45.06; H, 6.95.

Lead Tetraacetate Oxidation of β-Diacetyl Dulcitol.—A sample of 0.1120 g. of β-diacetyl dulcitol was dissolved in 70 cc. of glacial acetic acid, 25 cc. of 0.1267 *N* lead tetraacetate (8 moles) solution in acetic acid was added and the total volume adjusted to 100 cc. Subsamples of 10 cc. were analyzed at the expiration of fifteen and thirty minutes, one, two, eighteen and sixty-seven hours when 2.01, 2.64, 2.82, 2.89, 2.99 and 3.18 moles of lead tetraacetate were found to have been consumed. The expected consumption for 1,6-diacetyl dulcitol would be 3.00 moles.

Sodium Periodate Oxidation of β-Diacetyl Dulcitol.—This experiment was performed to obtain quantitative analytical data on the production of formic acid in the oxidation reaction. A sample of 0.4496 g. of the diacetyl compound was dissolved in 80 cc. of water, 16.51 cc. of 0.307 *M* sodium periodate (3 mols) solution added, and the volume adjusted to 100 cc. After forty-five minutes a 5-cc. subsample was titrated with 0.1 *N* sodium hydroxide, using methyl red as indicator, and found to require 1.72 cc., equivalent to 2.05 mols of formic acid. The expected production from 1,6-diacetyl dulcitol would be 2.00 mols.

Lead Tetraacetate Oxidation of β-Dibenzoyl Dulcitol.—(1) An amount of 0.1017 g. of β-dibenzoyl dulcitol was dissolved in 170 cc. of glacial acetic acid, 24.5 cc. of 0.1275 *N* lead tetraacetate (6 mols) solution in glacial acetic acid added, and the volume adjusted to 200 cc. Subsamples of 20 cc. were analyzed at the end of fifteen and thirty minutes, one, two, four, six and twenty-three hours, and 1.50, 2.21, 2.75, 2.94, 2.98, 3.01 and 3.19 mols of oxidant shown to be utilized progressively. After a further ninety-six hours, 4.32 mols had been consumed and a final analysis at the end of ten days showed 4.90 mols of oxidant had been consumed. The latter figure compares favorably with that expected, namely, 5.00 mols, if the benzoyl groups had been hydrolyzed completely.

(2) A suspension of 0.8062 g. of β-dibenzoyl dulcitol in 127.5 cc. of 0.1167 *N* lead tetraacetate (3.6 mols) acetic acid solution was agitated for three and one-half hours at room temperature whereby solution was completed. Analysis showed that 3.15 mols of oxidant had been consumed. To a subsample of 50 cc. of the oxidized solution, equivalent to 0.266 g. of benzoyl glycolic aldehyde, 0.8 g. of semicarbazide hydrochloride and 2 g. of sodium acetate were added, and on slight warming crystallization of the semicarbazone of benzoyl glycolic aldehyde occurred. After refrigerating overnight the precipitate was separated by filtration and obtained in a yield of 0.284 g. (79%). The fine needles which were thus produced melted at 193–194°, in close agreement with Aoyama's[10] value of 194–195° for benzoyl glycolic aldehyde semicarbazone, and showed the correct analysis.

Anal. Calcd. for $C_{10}H_{11}O_3N_3$: C, 54.29; H, 5.01. Found: C, 54.15; H, 5.04.

(3) To a suspension of 3.01 g. of β-dibenzoyl dulcitol in 50 cc. of glacial acetic acid, 11.3 g. of crystalline lead tetraacetate (3.3 mols) was added and the reaction mixture agitated for five hours, at which time analysis indicated that all the oxidant had been consumed. A small amount (0.2 g.) of unchanged dibenzoyl compound was removed and the residual solution, containing 2.24 g. of benzoyl glycolic aldehyde, was diluted with water and neutralized with sodium carbonate. It was then extracted successively with four 100-cc. portions of ether and the ether extract concentrated to a sirup. The sirup was dissolved in 100 cc. of water and 10 g. of strontium carbonate and 1.8 cc. of bromine added. After the solution had stood for twenty hours the excess bromine was removed by aeration and the strontium carbonate by filtration, and the solution acidified by addition of 10 cc. of *N* sulfuric acid. The benzoyl glycolic acid was extracted by treatment with four 100-cc. portions of ether, and the ether extract concentrated to dryness, crystallization occurring during the process. The dry residue was redissolved in 15 cc. of ether, the solution clarified, and 15 cc. of petroleum ether added. Upon slow evaporation at room temperature 0.84 g. (34%) of benzoyl glycolic acid was obtained in the form of large rhombs which showed a melting point of 110–111° (corr.). Brigl and Grüner[5] report a melting point of 112° for benzoyl glycolic acid isolated from 1,6-dibenzoyl mannitol.

Anal. Calcd. for $C_9H_8O_4$: C, 60.00; H, 4.48. Found: C, 60.20; H, 4.69.

(10) Aoyama, *J. Pharm. Soc. Japan*, **27**, 539 (1927).

Derivatives of α-Diacetone Dulcitol (2,3,5,6-Diacetone-D,L-galactitol)

Diacetyl-α-diacetone Dulcitol (1,4-Diacetyl-2,3,5,6-diacetone-D,L-galactitol).—A solution of 1 g. of α-diacetone dulcitol in a mixture of 5 cc. of pyridine and 5 cc. of acetic anhydride was allowed to stand overnight at room temperature, no crystallization taking place (contrast the behavior of the β-isomer). The reaction mixture was poured into 50 cc. of water, whereupon crystallization readily occurred, the desired diacetate being obtained in a yield of 1.3 g. (quantitative). It was recrystallized from 10 parts of 50% alcohol and obtained in colorless needles which melted at 89° (corr.) and showed no rotation in chloroform solution (*c*, 1.40).

Anal. Calcd. for $C_{16}H_{26}O_8$: C, 55.48; H, 7.57. Found: C, 55.53; H, 7.54.

Ditosyl-α-diacetone Dulcitol (1,4-Ditosyl-2,3,5,6-diacetone-D,L-galactitol).—The tosylation of α-diacetone dulcitol was carried out as described for that of β-diacetone dulcitol, a yield of 9.3 g. (85%) of the ditosyl derivative being obtained. It crystallized from its solution in 5 parts of alcohol in clusters of minute needles which melted at 101° (corr.) and were optically inactive in chloroform solution (*c*, 1.32).

Anal. Calcd. for $C_{26}H_{34}O_{10}S_2$: C, 54.72; H, 6.00. Found: C, 54.89; H, 5.94.

Monotrityl-monoacetyl-α-diacetone Dulcitol (1-Trityl-4-acetyl-2,3,5,6-diacetone-D,L-galactitol).—To a solution of 2.3 g. (1.1 mole) of triphenylmethyl chloride in 25 cc. of pyridine, 2 g. of finely powdered α-diacetone dulcitol was added and the resulting reaction mixture allowed to stand at room temperature for seventy-two hours. It was then cooled in a freezing mixture, 25 cc. of acetic anhydride added, and again allowed to stand for twenty-four hours at room temperature. Upon addition of water, the monoacetate precipitated in a yield of 4.0 g. (95%). The substance was recrystallized several times from 5 parts of alcohol to remove traces of triphenylcarbinol acetate, and was finally obtained in prisms melting at 107–108° (corr.). It is optically inactive in chloroform solution.

Anal. Calcd. for $C_{33}H_{38}O_7$: C, 72.50; H, 7.01. Found: C, 72.33; H, 6.95.

Mono-iodo-monotosyl-α-diacetone Dulcitol (1-Iodo-4-tosyl-2,3,5,6-diacetone-D,L-galactitol).—A solution of 2.9 g. of ditosyl-α-diacetone dulcitol and 2.3 g. of sodium iodide (3 mols) in 75 cc. of acetone was heated for one and one-half hours at 100° in a pressure bottle. The separated sodium *p*-toluenesulfonate (1.0 g., theory for 1 mol, 0.9 g.) was removed by filtration, the filtrate concentrated to dryness by an air current, and the dry residue treated with 50 cc. of water to remove the excess of sodium iodide. The insoluble crude reaction product weighed 2.6 g. (96%) and was recrystallized from 10 parts of methyl alcohol from which it separated in thick quadratic prisms. The pure compound melted at 120–121° and was optically inactive in chloroform solution (*c*, 1.04).

Anal. Calcd. for $C_{19}H_{27}O_7SI$: C, 43.35; H, 5.17. Found: C, 43.52; H, 5.12.

α-Dibenzoyl Dulcitol (1,4-Dibenzoyl-D,L-galactitol).—A solution of 8 g. of dibenzoyl-α-diacetone dulcitol, the preparation of which from α-diacetone dulcitol, benzoyl chloride and pyridine has been described by Fischer and Bergmann[4] (see also the later section on "Rearrangements"), in 100 cc. of 80% acetic acid was refluxed for thirty minutes and allowed to cool; there crystallized 0.6 g. of β-dibenzoyl dulcitol (m. p. 206–207°). The mother liquors were diluted with 500 cc. of water and allowed to stand overnight in the refrigerator, whereupon 2.4 g. of crude α-dibenzoyl dulcitol (m. p. 165–166°) crystallized, and a further yield of 2.4 g. of the same compound was obtained upon concentrating the solution to dryness and crystallizing the residue from 30 cc. of 50% alcohol (yield of the β-isomer, 9.1%; of the α-isomer, 72.7%). The production of some of the β-isomer in this reaction apparently is due to an acyl migration. The crude α-isomer is purified readily by recrystallization from 15 parts of alcohol, separating in clusters of fine needles which show no rotation in chloroform solution (*c*, 1.10). Upon heating in a capillary tube, it melts at 170–171° (corr.), resolidifies, and then remelts at 202–203° (corr.) (see also the later section on "Rearrangements").

Anal. Calcd. for $C_{20}H_{22}O_8$: C, 61.53; H, 5.68. Found: C, 61.35; H, 5.83.

Tetraacetyl-α-dibenzoyl Dulcitol (2,3,5,6-Tetraacetyl-1,4-dibenzoyl-D,L-galactitol).—Acetylation of the α-dibenzoyl dulcitol in pyridine solution by acetic anhydride at room temperature during twenty-four hours produced the tetraacetate in nearly quantitative yield. The compound was recrystallized from 10 parts of alcohol, separating in needles which melted at 113° (corr.) and showed no optical activity in chloroform solution (*c*, 0.82).

Anal. Calcd. for $C_{28}H_{30}O_{12}$: C, 60.21; H, 5.41. Found: C, 60.00; H, 5.57.

Lead Tetraacetate Oxidation of α-Dibenzoyl Dulcitol.—To a solution of 0.2000 g. of α-dibenzoyl dulcitol in 15 cc. of acetic acid, 33.4 cc. of 0.1105 *N* lead tetraacetate (3.6 mols) acetic acid solution was added and the volume adjusted to 50 cc. Subsamples of 5 cc. were analyzed at the end of fifteen and thirty minutes, one, two and nineteen hours and it was found that 1.94, 1.95, 1.95, 1.96 and 2.03 mols of oxidizing agent had been consumed. A 1,4-diacyl dulcitol should consume 2 mols of lead tetraacetate.

Sodium Periodate Oxidation of α-Dibenzoyl Dulcitol.—To a cooled solution of 0.1049 g. of α-dibenzoyl dulcitol in 15 cc. of alcohol, 1.84 cc. of 0.307 *M* sodium periodate (2.1 mols) was added and the solution volume adjusted to 25 cc. with water. Analyses of 5-cc. subsamples at the expiration of fifteen and thirty minutes indicated that 2.05 mols of oxidant had been consumed. Titration of a further 5-cc. subsample with 0.1 *N* sodium hydroxide required 0.08 cc. to obtain a decided alkaline reaction with methyl red indicator. This acidity, equivalent to 0.15 mol of formic acid in the sample, may be due to enolization of benzoyl tartronic dialdehyde; in any event it appears that the observed acidity is negligibly small. The formation of one mol of formic acid would require 0.53 cc. of 0.1 *N* alkali for neutralization of 5 cc. of the oxidized solution.

Rearrangements in the Dulcitol Series

1,6-Dibenzoyl Dulcitol from 1,4-Dibenzoyl-D,L-galactitol.—One gram of 1,4-dibenzoyl-D,L-galactitol

(Fischer and Bergmann's low melting dibenzoyl dulcitol) was heated in a small flask for fifteen minutes at 210° and the melt then recrystallized from 25 cc. of glacial acetic acid. Characteristic glistening platelets of 1,6-dibenzoyl dulcitol melting at 209° (corr.) were obtained in a yield of 90%.

Benzoylation of α-Diacetone Dulcitol (2,3,5,6-Diacetone-D,L-galactitol) in Quinoline.—Following the directions of Fischer, 10 g. of α-diacetone dulcitol was benzoylated with 2.2 mols of quinoline and 2 mols of benzoyl chloride for six hours at 100°. The reaction mixture was then refluxed for a few minutes with 120 cc. of alcohol to complete the solution of quinoline hydrochloride, refrigerated overnight, and the separated solid was removed by filtration: yield 11.8 g.; m. p. 183–184° (corr.); 66%. Fischer reported a melting point of 185–186° and a yield of 60% and called this substance dibenzoyl-α-diacetone dulcitol. The mother liquor was concentrated *in vacuo* to remove the alcohol, 300 cc. of water was added, and the oily suspension extracted four times with 25 cc. of carbon tetrachloride. The extract was washed successively four times with 100 cc. of ice cold 1% hydrochloric acid, twice with dilute sodium carbonate solution, and twice with water, and then concentrated to a dry sirup. The sirupy residue was dissolved in 20 cc. of 85% alcohol and upon standing for several days 2.0 g. (11%) of the isomeric dibenzoyl diacetone dulcitol of melting point 82–83° crystallized from the solution. The latter substance was not reported by Fischer and Bergmann as being obtained by benzoylation of α-diacetone dulcitol in the presence of quinoline, but they did obtain it when pyridine was employed in the diacylation. The isolation of *two* isomeric dibenzoyl diacetone dulcitols upon benzoylation of α-diacetone dulcitol indicated that a rearrangement had occurred in the course of diacylation.

Identification of the Dibenzoate Melting at 183–184° (Fischer and Bergmann's Dibenzoyl-α-diacetone Dulcitol) as a Derivative of β-Diacetone Dulcitol.—The dibenzoate of melting point 183–184° that was obtained from the benzoylation of α-diacetone dulcitol as just described, was recrystallized from 20 parts of carbon tetrachloride. It still melted at 183–184° (corr.) and was optically inactive in chloroform (*c*, 1.60).

Anal. Calcd. for $C_{26}H_{30}O_8$: C, 66.37; H, 6.43. Found: C, 66.28; H, 6.32.

A solution of 5 g. of it in 250 cc. of chloroform was cooled in ice and salt, and 21.9 cc. of 0.972 *N* sodium methylate (2 mols) added dropwise. After standing overnight at 5° the solution was held at 50° for one hour and the separated sodium benzoate removed by filtration. The filtrate was concentrated to dryness and the dry residue dissolved in 30 cc. of acetone. Upon addition of 30 cc. of petroleum ether the typical crystals of β-diacetone dulcitol separated in a yield of 1.0 g. (m. p. 110–111°) and a further amount of 1.0 g. was obtained by working up the mother liquors; yield, quantitative. A similar quantitative debenzoylation to β-diacetone dulcitol occurs if barium methylate be employed as the deacylation agent. Fischer and Bergmann's dibenzoyl-α-diacetone dulcitol (m. p. 183–184°) is therefore a derivative of β-diacetone dulcitol and is 1,6-dibenzoyl-2,3,4,5-diacetone dulcitol; its formation from α-diacetone dulcitol (2,3,5,6-diacetone-D,L-galactitol) results from a molecular rearrangement.

Identification of the Dibenzoate Melting at 82–83° (Fischer and Bergmann's Dibenzoyl-β-diacetone Dulcitol) as a Derivative of α-Diacetone Dulcitol.—This dibenzoate, the preparation of which was described above, is recrystallized conveniently from 6 parts of 85% alcohol, crystallization being rather slow and markedly hindered by presence of impurities. It separates in the form of needles and is optically inactive in chloroform solution (*c*, 1.52). Upon debenzoylation with barium methylate, α-diacetone dulcitol (m. p. 144–145°) was obtained in quantitative yield; the dibenzoate of melting point 82–83° is evidently 1,4-dibenzoyl-2,3,5,6-diacetone-D,L-galactitol.

Anal. Calcd. for $C_{26}H_{30}O_8$: C, 66.37; H, 6.43. Found: C, 66.36; H, 6.36.

Benzoylation of α-Diacetone Dulcitol in Pyridine.—To a solution of 20.8 g. of α-diacetone dulcitol in 18 cc. of pyridine (2.8 mols), 20.4 cc. of benzoyl chloride (2.2 mols) was added, and the reaction mixture heated for three hours at 100°. The reaction products were dissolved in 200 cc. of chloroform and the chloroform solution washed successively with ice cold 0.1% aqueous hydrochloric acid, 2% sodium carbonate solution, and water. The chloroform solution was concentrated *in vacuo* to dryness. Upon attempting to dissolve the dry residue in 180 cc. of 85% alcohol, crystalline dibenzoyl-β-diacetone dulcitol (1.5 g., m. p. 178–180°, 4%) was recovered as an insoluble precipitate. From the alcoholic solution 32 g. (86%) of dibenzoyl-α-diacetone dulcitol (m. p. 82–83°) was recoverable. These results indicate that some rearrangement also occurs upon benzoylation of α-diacetone dulcitol in pyridine at 100°. The failure of Fischer and Bergmann to obtain the β-derivative by the pyridine method of acylation at 100° appears to be due to a far smaller production of it with pyridine than with quinoline.

The Isopropylidene Rearrangement.—From the structural evidence which has been presented it is certain that the α-diacetone dulcitol, which we know to be 2,3,5,6-diacetone-D,L-galactitol, upon benzoylation under the experimental conditions cited, yields both 1,4- and 1,6-dibenzoyl derivatives, namely, 1,4-dibenzoyl-2,3,5,6-diacetone-D,L-galactitol and 1,6-dibenzoyl-2,3,4,5-diacetone dulcitol. The formation of the latter derivative could take place only if there occurred a cyclic acetal shift of an isopropylidene residue, which in terms of the formulas VII, VIII and III is from carbons 5,6 to 4,5 of the galactitol chain. It was found that the shift does not occur after the 1,4-dibenzoyl-2,3,5,6-diacetone-D,L-galactitol is produced. Two grams of the pure substance was heated in quinoline (2.8 moles) and benzoyl chloride (2.2 moles) at 100° for six hours, but no formation of the β-isomer could be demonstrated. In further experiments the pure substance was melted and the melt held at 100° for several hours; neither from this melt nor from a similar one, through which dry hydrochloric acid gas was bubbled, could any β-isomer be isolated. It was sought next to determine whether the isopropylidene shift is caused by a change of α-diacetone dulcitol to its β-isomer through heating at 100° in quinoline alone. Since the isolation of the diacetone dulcitols from quinoline solution did not appear to be feasible, we selected the following experimental test. Five grams of α-diacetone dulcitol was

heated in quinoline (2.5 moles) at 100° for six hours and the solution was then cooled in ice and benzoyl chloride (2.2 mols) was added. After standing for four hours at 0°, followed by twenty-four hours at 25°, the reaction product yielded by customary procedure 0.4 g. (4.4%) of 1,6-dibenzoyl-2,3,4,5-diacetone dulcitol and 6.5 g. (72.5%) of 1,4-dibenzoyl-2,3,5,6-diacetone-D,L-galactitol. The rearrangement in this test is so slight that the cause of the extensive rearrangement which occurs when the benzoylation reaction is carried out at 100°, cannot be attributed to an action of the quinoline alone, particularly if the result of the next experiment be considered. It was carried out with the same quantities of materials but some anhydrous quinoline hydrochloride (1.2 mols) was present during the period of heating at 100°; it yielded 3.8 g. (42.4%) of 1,6-dibenzoyl-2,3,4,5-diacetone dulcitol and 3.5 g. (39%) of 1,4-dibenzoyl-2,3,5,6-diacetone-D,L-galactitol. It appears therefore that the rearrangement is catalyzed by such substances as quinoline hydrochloride and (in less degree) pyridine hydrochloride.

Summary

It is shown that the properties of the α- and β-diacetone dulcitols, as well as those of several new derivatives of these substances, exclude the possibility that they can be enantiomorphous substances and prove that they are structural isomers. Evidence has been obtained from periodate and lead tetraacetate oxidations that neither α- nor β-diacetone dulcitol contains a glycol grouping. The results of a study of the ditosyl, diiodo and ditrityl derivatives of β-diacetone dulcitol indicate that it contains two free primary hydroxyl groups, and a study of the oxidation of the diacyl dulcitols, derivable from it, proves that its structure is that of 2,3,4,5-diacetone dulcitol, a *meso* form. The results of a study of the ditosyl, monotosyl-mono-iodo, and monotrityl-monoacetyl derivatives of α-diacetone dulcitol indicate that it contains one free primary hydroxyl group and one free secondary hydroxyl group, and a study of the oxidation of the dibenzoyl dulcitol derived from it proves that it is 2,3,5,6-diacetone-D,L-galactitol, a racemic form. An acyl migration by which 1,4-dibenzoyl-D,L-galactitol (a racemic form) passes to 1,6-dibenzoyl dulcitol (a *meso* form) has been demonstrated. A cyclic acetal shift has been shown to be the cause of the interesting and unusual changes which Fischer and Bergmann noticed upon acylation of α-diacetone dulcitol. The shift occurs as a stage in the benzoylation of α-diacetone dulcitol with benzoyl chloride and quinoline or pyridine at elevated temperatures and it is catalyzed by quinoline hydrochloride or pyridine hydrochloride. In structural terms it is represented as the passage of 2,3,5,6-diacetone-D,L-galactitol to 1,6-dibenzoyl-2,3,4,5-diacetone dulcitol. Reasons have been given for preferring the name galactitol to dulcitol in designating non-*meso* structures of derivatives of dulcitol which carry in their names a numbering of its carbon atoms.

WASHINGTON, D. C. RECEIVED JUNE 19, 1939

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY OF PRINCETON UNIVERSITY]

Procedure for Preparation of Fully Methylated Carbohydrates and their Derivatives

BY EUGENE PACSU AND S. M. TRISTER[1]

For investigation of certain structural problems in carbohydrate chemistry, it is often necessary to methylate all free hydroxyl groups in the molecule. Methylation usually is carried out either with methyl iodide and silver oxide,[2] dimethyl sulfate and alkali solution,[3] alkali metals in liquid ammonia and methyl iodide,[4] or with the thallium salts of the carbohydrates and methyl iodide.[5]

However, none of these methods, if used alone, gives entirely satisfactory results for various reasons. For complete methylation usually a combination of two of these methods is necessary. In most instances first the dimethyl sulfate–alkali procedure is employed and the products obtained are then repeatedly treated with silver oxide and methyl iodide.

In this Laboratory excellent results were obtained from combination of Haworth's dimethyl sulfate–alkali procedure with a slightly modified process of Freudenberg and Hixon.[6] These

(1) Research Assistant on Special Funds from the Rockefeller Foundation.

(2) Purdie and Irvine, *J. Chem. Soc.*, **83**, 1021 (1903).

(3) (a) Haworth, *ibid.*, **107**, 8 (1915); (b) Haworth and Leitch, *ibid.*, **113**, 188 (1918); (c) West and Holden, THIS JOURNAL, **56**, 930 (1934).

(4) (a) Muskat, *ibid.*, **56**, 693, 2449 (1934); (b) Hendricks and Rundle, *ibid.*, **60**, 2563 (1938).

(5) (a) Fear and Menzies, *J. Chem. Soc.*, 937 (1926); (b) Purves and Hudson, THIS JOURNAL, **59**, 49, 1170 (1937); (c) Hirst and Jones, *J. Chem. Soc.*, 496 (1938); (d) Barker, Hirst and Jones, *ibid.*, 169 (1938).

(6) Freudenberg and Hixon, *Ber.*, **56**, 2119 (1923).

authors' simple but apparently seldom used method is based on the reaction between methyl iodide and the sodium alcoholates of the carbohydrates prepared in ether solution. In many instances we have observed that the incomplete methylation in the dimethyl sulfate–alkali procedure is mainly due to the resistance of the primary hydroxyl group toward the alkylating agent. Since this also holds true but in still higher degree for Purdie's reagent, it seemed to us impractical to attempt the completion of methylation of partially methylated sugars, or to start the methylation of sugar derivatives containing primary hydroxyl groups, by means of methyl iodide and silver oxide. We adopted, therefore, the Freudenberg procedure and found that metallic sodium reacted readily with such products giving sodium alcoholates soluble in ether, toluene and other inert solvents. These sodium alcoholates which can be analyzed easily for sodium, if necessary, would suffer partial decomposition in the presence of moisture, in which case the subsequent treatment with methyl iodide would result in products of low methoxyl content. We have found that this can be avoided if a little methyl iodide is added to the solution of the alcoholate before concentration under diminished pressure. The residue is then shaken vigorously with methyl iodide and the reaction mixture is allowed to stand for several hours. We have successfully applied this comparatively simple and inexpensive procedure to several carbohydrates and their derivatives always obtaining products with correct methoxyl content. Since many of these methyl derivatives represent new compounds to be described in forthcoming publications, in the experimental part of the present article only the methylation of sucrose is given for illustration of the details of the procedure.

Experimental

Preparation of Octamethylsucrose.—Purdie and Irvine[7] methylated sucrose with silver oxide and methyl iodide and after four such methylations isolated a product with a methoxyl content of 50.93% instead of the theoretical value of 54.63%. Haworth[3a] methylated sucrose with dimethyl sulfate and sodium hydroxide and found that after one methylation the isolated product had a methoxyl content of 50.5% which could not be increased after further treatment with the same methylating agent. However, by two subsequent methylations with Purdie's reagent the compound isolated had a methoxyl content of 54.12%. In a later paper[8] he claimed that by modifying the conditions somewhat a fully methylated sucrose was obtained after three operations using dimethyl sulfate and alkali as the only alkylating agent. It is interesting to note, however, that Irvine and Stiller,[9] repeating Haworth's procedure, claimed that the methylation yielded a complex mixture of partially methylated compounds boiling at approximately constant temperature.

In our experiment sucrose was methylated with dimethyl sulfate and potassium hydroxide and worked up in the usual manner. The sirup was non-reducing to Fehling's solution and had a methoxyl content of 45.36%. This upon a single methylation with sodium and methyl iodide gave pure octamethylsucrose with the correct methoxyl content of 54.48%. The methylation was carried out in the following way. A 5-g. sample of the partially methylated product (OCH_3, 45.36%) was dissolved in 50 cc. of absolute ether in a flask fitted with a calcium chloride tube and to the solution 1 g. of clean sodium wire was added. The mixture was gently shaken on an apparatus for several hours and allowed to stand overnight at room temperature. Then the solution was decanted rapidly into a distilling flask containing 10 cc. of methyl iodide. The mixture was evaporated under reduced pressure to a paste, to which 25 cc. of methyl iodide was added. The cloudy solution was shaken vigorously for several hours, then kept standing at room temperature for twelve hours. Throughout the above operation precautions were taken to exclude all atmospheric moisture from the reaction vessel. An equal volume of absolute ether was then added to the reaction mixture and the sodium iodide precipitate was filtered off with activated carbon and washed with absolute ether. The combined filtrate and washings were evaporated *in vacuo* at 30–40° to a sirup which was twice purified by filtration of its petroleum ether (b. p. 30–40°) solution with activated carbon. On evaporation under reduced pressure the clear filtrate gave 3.4 g. of a very pale yellow liquid, octamethylsucrose, with the correct methoxyl content (54.48%) and the following specific rotations for sodium light: 65.5° (chloroform solution; *c*, 1.634; *t*, 26°); 67.6° (methyl alcohol solution; *c*, 5.592; *t*, 25°); 65.6° (acetone solution; *c*, 6.007; *t*, 25°). Haworth[3a] reported 69.3° (methyl alcohol solution; *c*, 7.345) and 66.8° (acetone solution; *c*, 6.782).

In another experiment the partially methylated sample was dissolved in absolute toluene and to the solution sodium wire was added. After the reaction had subsided the mixture was heated on a water-bath at 80° for three hours, then cooled and worked up as described in the previous experiment. A pale yellow liquid with 54.37% methoxyl was isolated.

All the methoxyl estimations were carried out by the method of Vieböck and Schwappach[10] as modified by Clark.[11]

Summary

1. Combination of the Haworth methylation process with a slightly modified method of Freudenberg and Hixon is recommended for prepa-

(7) Purdie and Irvine, *J. Chem. Soc.*, **87**, 1028 (1905).
(8) Haworth and Mitchell, *ibid.*, **123**, 309 (1923).
(9) Irvine and Stiller, THIS JOURNAL, **54**, 1486 (1932).
(10) Vieböck and Schwappach, *Ber.*, **63**, 2818 (1930).
(11) Clark, *J. Assoc. Official Agr. Chem.*, **15**, 136 (1932).

ration of fully methylated carbohydrates or derivatives which contain primary hydroxyl groups.

2. Detailed description of the procedure is given for the exhaustive methylation of sucrose.

PRINCETON, NEW JERSEY RECEIVED JULY 1, 1939

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY OF PRINCETON UNIVERSITY]

The Acetone Derivatives of the Mercaptals of Some Monosaccharides. IV.[1] The 4,5-Monoacetone Derivative of the Dibenzylmercaptal and of the Dimethylacetal of *d*-Galactose

BY EUGENE PACSU, S. M. TRISTER[2] AND JOHN W. GREEN

Fifteen years ago it was shown by Pacsu[1] that new isomers of partially methylated hexoses could be obtained by a series of reactions in which the sugar mercaptals should first be converted into their di- and monoacetone derivatives. Subsequent methylation of the free hydroxyl group or groups would yield compounds which on deacetonylation and removal of the mercaptan residues would give rise to the respective mono- and trimethyl sugars. The exact positions of the methyl groups once determined, the structure of the intermediate acetone derivatives would be known. On the other hand, the knowledge of the positions of the acetone residues would determine the structure of the methylated sugars. At that time it appeared that the elucidation of the structure of the methylated sugars rather than that of the intermediate acetone derivatives was more feasible since methods for removal of the mercaptan residues without simultaneous hydrolysis of the acetone groups were unknown. Direct determination of the positions of the methyl groups in partially methylated sugars fifteen years ago presented almost insurmountable difficulties mainly due to the lack of suitable experimental methods. It was customary, therefore, to assign the structure of newly discovered partially methylated sugars by taking recourse to the method of elimination and to other indirect procedures. However, conclusions based on such negative evidence are usually valid only as long as the accepted structural formulas of the eliminated compounds remain unchanged. In the special field of partially methylated sugars new interpretation of some old experimental results became necessary after Brigl and Schinle discovered[3] that the true 2-methyl glucose[4] was capable of osazone formation with the loss of the methyl group. This striking discovery cast doubt on the structure of those partially methylated sugars the formulas of which previously had been assigned on the assumption, till then unquestioned, that a 2-methyl aldose could not possibly form an osazone. Among those partially methylated sugars affected by this discovery were the assumed 4-methyl sugars and all their mercaptal and acetonylated mercaptal derivatives previously described.[1] As was pointed out by Pacsu,[5] the assignment of position 4 to the methyl group in the new monomethyl glucose was left as the only possibility at the time when the compound was discovered, because a 2-methyl glucose with entirely different properties had been described already both by Pictet[6] and by Irvine.[7] Since Levene and co-workers[8] noticed that this supposed 4-methyl glucose was identical with the true 2-methyl glucose of Brigl, it followed that all the previous conclusions based on an unquestioned existence of the 2-methyl glucose of Pictet and of Irvine became necessarily invalid. In the light of these facts, therefore, a reinvestigation of the entire problem was begun and in the present paper the results concerning the structure of one of the monoacetone galactose mercaptals are presented.

In a preliminary communication[9] it was reported that the formerly described[1c] crystalline "2,3-monoacetone galactose dibenzylmercaptal" with m. p. 102–103° and $[\alpha]^{18}D$ 8.8° in acetylene tetrachloride solution, in spite of its apparent uniformity, is not a chemical individual. By repeated fractional recrystallization from acetone

(1) (a) Part I, Pacsu, *Ber.*, **57**, 849 (1924); (b) Part II, Pacsu and von Kary, *ibid.*, **62**, 2811 (1929); (c) Part III, Pacsu and Löb, *ibid.*, **62**, 3104 (1929); *cf.* (d) Pacsu, *ibid.*, **58**, 1455 (1925).

(2) Research Assistant on Special Funds from the Rockefeller Foundation.

(3) Brigl and Schinle, *Ber.*, **62**, 1716 (1929).

(4) Brigl and Schinle, *ibid.*, **63**, 2884 (1930).

(5) Pacsu, *ibid.*, **65**, 51 (1932).

(6) Pictet and Castan, *Helv. Chim. Acta*, **3**, 645 (1920).

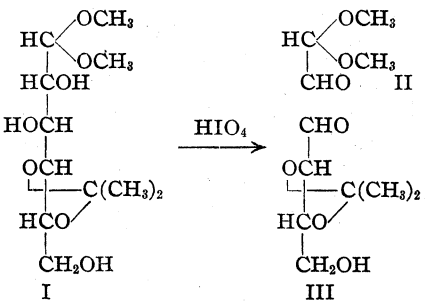
(7) Irvine, *J. Chem. Soc.*, **125**, 1 (1924).

(8) Levene, Meyer and Raymond, *J. Biol. Chem.*, **91**, 497 (1931); *cf. Science*, **73**, 291 (1931).

(9) Pacsu, THIS JOURNAL, **58**, 2076 (1936).

and from ethyl alcohol the substance was separated into two monoacetone mercaptals, one with m. p. 112.5° and $[\alpha]^{20}D$ 17.4° in chloroform solution, and the other with m. p. 103° and $[\alpha]^{20}D$ 31.0° in chloroform solution. Since the latter compound was more easily available in pure form, it was chosen as the first object of our investigation. On removal of the benzyl mercaptan residues in methyl alcoholic solution according to the method of Pacsu and Green,[10] the substance gave rise to a monoacetone galactosedimethylacetal with m. p. 125–126° and $[\alpha]^{20}D$ 37.4° in water solution. Although formation of dimethylacetals by application of this method to *l*-rhamnose- and fructosediethylmercaptal have been reported previously,[11] actually this was the first acetal obtained in this Laboratory, but its structure was unknown when the preliminary communication[9] was published. On the basis of the following experimental results it is now established definitely that the acetone residue is attached to carbon atoms 4 and 5, and, therefore, the starting material represents the 4,5-monoacetone galactosedibenzylmercaptal. Positive reaction of the latter compound with triphenylmethyl chloride in pyridine solution yielding a trityl derivative[12] was the first indication that a free hydroxyl group may be present in position 6. Acetylation of the 4,5-monoacetone dimethylacetal gave readily a triacetate, the 2,3,6-triacetyl 4,5-monoacetone galactose dimethylacetal with m. p. 55° and $[\alpha]^{20}D$ 17.8° in chloroform solution. In the methylation experiments five consecutive methylations of the 4,5-monoacetone dimethylacetal with silver oxide and methyl iodide failed to raise the methoxyl content (43.1%) to the theoretical value (50.3%). This indicated the presence of a primary hydroxyl group resistant to methylation. Finally by application of the modified Freudenberg procedure[13] to this incompletely methylated product, it was possible to obtain the fully methylated compound in one operation. The substance, representing the 2,3,6-trimethyl-4,5-monoacetone galactosedimethylacetal, was then hydrolyzed and the 2,3,6-trimethylgalactose obtained was oxidized with bromine yielding crystalline 2,3,6-trimethyl-γ-galactonolactone with m. p. 97–98° and initial specific rotation of −32.9° in water solution, which value changed after ten days to the constant value of −21.3°.

Application of the periodic acid oxidation method of Jackson and Hudson[14] to the 4,5-monoacetone galactosedimethylacetal (I) showed that one mole equivalent of periodic acid was used up for oxidation.



A survey of the possible structures of monoacetone galactosedimethylacetal indicated that only the 4,6- and 4,5-monoacetone derivatives would require one mole equivalent of periodic acid. If the acetal had its acetone residue at carbon atoms 4 and 6, then the methylated lactone isolated from it would be a 2,3,5-trimethyl derivative, whereas the 4,5-monoacetone derivative would yield a 2,3,-6-trimethyl lactone. On oxidation by periodic acid only the latter lactone should require one mole equivalent of periodic acid, whereas the 2,3,5-trimethyl lactone should not use any. Our experiments showed that the lactone in question required one equivalent of periodic acid for oxidation, therefore it could only be the 2,3,6-trimethyl lactone. In order to isolate and identify the scission products, glyoxal dimethyl acetal (II) and 2,3-monoacetone *d*-threose (III), expected from a 4,5-monoacetone galactosedimethylacetal on oxidation by periodic acid, the sugar acetal was treated with this reagent. The mixture of the scission products formed was separated by distillation of the aqueous solution. Glyoxal was found to be present in the distillate and was isolated as the *bis*-phenylhydrazone. The other component of the mixture, 2,3-monoacetone *d*-threose (III), was hydrolyzed by acetic acid to *d*-threose which was identified by its osazone. The *d*-threose was then oxidized with bromine to *d*-threonic acid which was characterized by its

(10) Pacsu and Green, THIS JOURNAL, **58**, 1823 (1936), *et seq.*

(11) Green and Pacsu, *ibid.*, **60**, 2288 (1938); Pacsu, *ibid.*, **60**, 2277 (1938); **61**, 1671 (1939).

(12) In the preliminary communication[9] it was stated that neither isomer reacted with triphenylmethyl chloride. Subsequently it was found that the triphenylmethyl chloride employed was of a very poor quality since it contained mostly triphenylcarbinol. Reactions carried out with a pure, crystalline preparation gave a positive result for the higher rotating compound but the tests were negative with the low rotating isomer.

(13) Pacsu and Trister, THIS JOURNAL, **61**, 2442 (1939).

(14) Jackson and Hudson, *ibid.*, **59**, 994 (1937).

brucine salt. Subsequent oxidation of *d*-threonic acid with nitric acid gave rise to *l*-tartaric acid which was isolated as the acid potassium salt. From these experimental results it follows that in the original starting material the acetone residue was attached to carbon atoms 4 and 5.

The investigation is being continued.

Experimental

Preparation of 4,5-Monoacetone Galactosedibenzylmercaptal and its 5,6(?)-Isomer.—Monoacetone galactosedibenzylmercaptal was prepared according to the directions of Pacsu and Löb,[1c] and after two crystallizations from chloroform and petroleum ether the fine needles obtained had m. p. 102–104° and $[\alpha]^{20}D$ 8.1° in acetylene tetrachloride solution, which values were in good agreement with those given by the authors for "2,3-monoacetone galactosedibenzylmercaptal." However, a third crystallization, this time from acetone and petroleum ether, gave two fractions with different rotations, which fact indicated that the preparation of Pacsu and Löb was a mixture. Subsequently it was found also that the composition of the preparation varied considerably with minor changes in the conditions of the experiment. In order to secure reproducible results the acetonylation was carried out for four hours at about 25° with copper sulfate monohydrate as dehydrating agent in equal weight of the mercaptal which was suspended in ten times its weight of acetone. Under such conditions the acetone solution at the end of the reaction contained only a little diacetone derivative and unchanged mercaptal. The monoacetone derivative was isolated according to the procedure of Pacsu and Löb and then it was submitted to fractional crystallization by addition of small quantities of petroleum ether to the acetone solution. Several fractions with different rotations were obtained. The fractions which had the highest rotations were united and recrystallized from ethyl alcohol. Finally a product was obtained in the form of long needles showing m. p. 102.5–103° and $[\alpha]^{20}D$ 31.0° in chloroform solution, which values did not change on further recrystallizations. Our investigation centered around the structure of this substance, which was proved to be the 4,5-monoacetone galactosedibenzylmercaptal. The fractions with the lower rotations were purified by recrystallizations from acetone and petroleum ether and finally from acetone alone. This substance crystallized in a jelly-like aggregate of very fine needles. The preparation finally obtained had m. p. 112.5° and $[\alpha]^{20}D$ 17.4° in chloroform solution, which values did not change on further recrystallization. This substance probably represents the 5,6-monoacetone galactosedibenzylmercaptal and its structure is being investigated. The two isomers formed in about equal quantities and the yields were quite satisfactory. When tested with pure[12] triphenylmethyl chloride in pyridine solution, the 4,5-monoacetone derivative gave a trityl derivative which, on account of its amorphous nature, was not investigated further. The other isomer gave negative results and the unchanged material was recovered. The two isomers were analyzed for acetone according to the procedure of Elsner.[15] In order to take out the mercaptan residues, 0.3 g. of mercuric chloride was added to the 0.15-g. samples in these acetone determinations.

Anal. 4,5-Monoacetone galactosedibenzylmercaptal, calcd. for $C_{16}H_{30}O_5S_2$: C, 61.3; H, 6.72; acetone, 12.9. Found: C, 61.45; H, 7.1; acetone, 12.75. 5,6(?)-Monoacetone galactosedibenzylmercaptal: Found: C, 61.2, 61.1; H, 6.64, 6.8; acetone, 12.4, 13.0, 12.8.

Conversion of 4,5-Monoacetone Galactosedibenzylmercaptal into 4,5-Monoacetone Galactosedimethylacetal.—The removal of the mercaptan residues was carried out at room temperature by the method of Pacsu and Green.[10] A solution of 33 g. of mercuric chloride (2 moles) in 75 cc. of absolute methyl alcohol was added in thirty minutes to a mixture of 27 g. of 4,5-monoacetone galactosedibenzylmercaptal, 27 g. of yellow mercuric oxide and a little drierite in 120 cc. of absolute methyl alcohol. After four hours of continuous stirring the mixture was filtered, the filtrate treated with 5 cc. of pyridine and kept at 0° for two hours. The pyridine mercuric chloride was filtered and the solution evaporated to a sirup *in vacuo* at 40°. The residue was dissolved in a little ice-cold water, the solution filtered and neutralized to phenolphthalein with a few drops of sodium hydroxide solution, then evaporated *in vacuo* at 45°. The residue was evaporated successively under reduced pressure from ethyl alcohol solutions and crystallized first from benzene, then from ethyl acetate. The pure substance represented the 4,5-monoacetone galactosedimethylacetal and had m. p. 125–126° and $[\alpha]^{20}D$ 37.4° in water solution; yield, about 70%. It was soluble in cold water and methyl alcohol, in hot acetone, ethyl acetate and dioxane.

Anal. Calcd. for $C_{11}H_{22}O_7$: C, 49.62; H, 8.27; OCH_3, 23.30. Found: C, 49.70; H, 8.22; OCH_3, 23.30.

On acetylation with acetic anhydride and pyridine, 2,3,6-triacetyl 4,5-monoacetone galactosedimethylacetal was obtained in the form of prismatic needles from petroleum ether, or from a mixture of chloroform and petroleum ether at 0°. The substance is very soluble in most of the organic solvents. It had m. p. 55° and $[\alpha]^{20}D$ 17.8° in chloroform solution (*c*, 2.057). In an acetyl estimation 0.2668 g. of the substance required 20.2 cc. of 0.1 *N* sodium hydroxide solution. The value calculated for the hydrolysis of three acetyl groups is 20.4 cc.

Anal. Calcd. for $C_{17}H_{28}O_{10}$: OCH_3, 15.8. Found: OCH_3, 15.4.

Preparation of 2,3,6-Trimethyl γ-Galactonolactone from 4,5-Monoacetone Galactosedimethylacetal.—Ten grams of the acetal was dissolved in 35 cc. of methyl iodide and the solution was treated with 20 g. of silver oxide according to the method of Purdie and Irvine.[16] The methylated material was extracted with chloroform and recovered. After a second methylation with the same amounts of the reagents the isolated sirup had a methoxyl content of 41.2% instead of 50.3% calculated for a fully methylated compound. After a third, fourth (OCH_3, 42.0%) and fifth (OCH_3, 43.1%) methylation, it was concluded that probably the primary hydroxyl group of the substance was resistant to methylation with these reagents. Therefore, the sirup was treated with sodium and methyl iodide

(15) Elsner, *Ber.*, **61**, 2364 (1928).

(16) Purdie and Irvine, *J. Chem. Soc.*, **83**, 1021 (1903).

according to the modified Freudenberg procedure.[13] A pale yellow liquid with 50.1% methoxyl content was obtained. Seven grams of this 2,3,6-trimethyl galactose-dimethylacetal was then dissolved in 50 cc. of 0.05 *N* hydrobromic acid and the solution was heated on a water-bath at 60–70° until constant rotation was observed (three and one-half hours). The solution, which contained 2,3,6-trimethyl galactose, was treated with 20 g. of bromine and kept at 35–40° for sixty-five hours. The non-reducing solution was then worked up in the usual manner (*i. e.*, bromine removed by aeration, acid neutralized with silver carbonate, silver salt decomposed with hydrogen sulfide). The resulting clear solution was concentrated *in vacuo* at 45–50°. A colorless, crystalline compound, the 2,3,6-trimethyl-γ-galactonolactone, separated out; yield, 2.5 g. The substance was recrystallized twice from aqueous methyl alcohol. The fine needles had m. p. 97–98° and an initial specific rotation of −32.9° in water solution (*c*, 1.686), which value after ten days changed to the constant rotation of −21.3°.

Anal. Calcd. for $C_9H_{16}O_6$: OCH_3, 42.3. Found: OCH_3, 41.9.

For the oxidation experiment 10 cc. of a 0.1 molar solution of the lactone was treated first with one equivalent of standard sodium hydroxide solution, and then with 20 cc. of a 0.1 molar periodic acid solution which had been neutralized previously. After thirty minutes 5 cc. of the reaction mixture was titrated for the excess of periodate with standard arsenite solution and it was found that 2.27 cc. of periodic acid was used up for the oxidation of the lactone (calcd. for one mole of periodic acid: 2.30 cc.). Five-cc. samples were again titrated after one hour (found: 2.27 cc.), two and one-half hours (found: 2.27 cc.) and twenty-four hours (found: 2.37 cc.). These results indicated that one mole of periodic acid was required for the scission of the lactone, which fact was considered as evidence that the analyzed product was the 2,3,6-trimethyl derivative.

Oxidation of 4,5-Monoacetone Galactosedimethylacetal with Periodic Acid to Glyoxal and 2,3-Monoacetone *d*-Threose.—It was found in a preliminary experiment that from an excess of a 0.1 molar periodic acid solution only one mole equivalent was used for the oxidation of the monoacetone derivative provided that the acid was previously neutralized with sodium hydroxide. In another experiment, in which the periodic acid was not neutralized, it was found that after one hour one mole equivalent was used up, but if the reaction mixture was allowed to stand for a longer period of time, then further oxidation occurred. This undoubtedly was due to the reaction of the oxidant with adjacent hydroxyl groups liberated by hydrolysis from the acid-sensitive primary oxidation products.

For the isolation of the scission products 3 g. of the 4,5-monoacetone galactosedimethylacetal was dissolved in 1355 cc. of water and to the solution 45 cc. of a 0.2631 molar periodic acid was added (5% excess). After twenty minutes it was found by titration of a sample with arsenite solution that one mole of periodic acid was used up. The solution was then neutralized with barium hydroxide solution to phenolphthalein. Immediately a white, flocculent precipitate separated out. The mixture was kept at 0° for two hours, filtered and the precipitated iodates washed with ice water. To the combined filtrate and washings 3 g. of barium carbonate was added and the mixture was allowed to stand overnight at room temperature. The filtered solution was distilled *in vacuo* at 40–50°. On treatment with phenylhydrazine dissolved in five parts of glacial acetic acid, the distillate gave a yellow precipitate. The residual sirup was dissolved in water and concentrated *in vacuo*, this process being repeated until the distillate gave no more reaction with phenylhydrazine (thirty hours of distillation). The combined precipitates were recrystallized from 85% alcohol; yield, 1.9 g. of pale yellow needles; m. p. 168–169°. The substance represented the *bis*-phenylhydrazone of glyoxal first obtained by Fischer,[17] who gave m. p. 169–170°. The presence of the glyoxal in the distillate probably was due to the hydrolysis of the dimethyl semiacetal during the protracted contact of the latter with water.

The residual sirup, 2,3-monoacetone *d*-threose, was dissolved in absolute ethyl alcohol, the solution filtered with activated carbon and the filtrate evaporated *in vacuo* to a sirup (1.74 g.) which reduced Fehling's solution and had an initial specific rotation of 18.7° in water solution (*c*, 1.065) that changed after two days to 12.5°. The presence of the isopropylidene group was shown by an acetone estimation according to the method of Bell and Harrison.[18]

Conversion of 2,3-Monoacetone *d*-Threose into Potassium Acid *l*-Tartrate.—A solution of 1.7 g. of 2,3-monoacetone *d*-threose in 20 cc. of 10% acetic acid was heated on a water-bath until constant rotation was obtained (one hour). The solution had $[\alpha]^{20}D$ −10.5° which was in good agreement with the values (−10.7 to −12.0°) given by Hockett[19] for the rotation of *d*-threose. The acetic acid was removed by distillation of the solution *in vacuo*. A 70-mg. sample of the sirupy product gave a crystalline osazone with m. p. 159–160° (Hockett[19] reported m. p. 164°). The *d*-threose was then oxidized in 25 cc. of aqueous solution with 4 g. of bromine and the *d*-threonic acid formed was isolated in the usual manner. A clear sirup (0.95 g.) was obtained which had $[\alpha]^{20}D$ −26.1° in water solution (*c*, 1.645).

Anderson[20] gave rotations varying from −20 to −30°. From the threonic acid the brucine salt was obtained in a procedure similar to that of Ruff.[21] The salt crystallized from 85% ethyl alcohol in the form of fine needles which melted at 199° and had $[\alpha]^{20}D$ −37.2° in water solution (*c*, 1.340). Hockett[19] reported m. p. 197–198° and $[\alpha]^{20}D$ −36.8°.

Anal. Calcd. for $C_{27}H_{34}O_9N_4$: OCH_3, 11.69. Found: OCH_3, 11.60.

The *d*-threonic acid (0.7 g.) was oxidized with 3.5 cc. of nitric acid (*d*, 1.2) to *l*-tartaric acid which was converted into the acid potassium salt as described by Reichstein.[22] The crystalline product had $[\alpha]^{20}D$ −28.1° in

(17) Fischer, *Ber.*, **17**, 575 (1884).
(18) Bell and Harrison, *J. Chem. Soc.*, 350 (1939).
(19) Hockett, THIS JOURNAL, **57**, 2260, 2265 (1935).
(20) Anderson, *Am. Chem. J.*, **42**, 423 (1909).
(21) Ruff, *Ber.*, **32**, 3672 (1899).
(22) Reichstein, *Helv. Chim. Acta*, **19**, 1016 (1936).

a 2% potassium hydroxide solution (*c*, 1.425). Hockett[19] recorded $[\alpha]^{24}D$ −29.7 in a 2% sodium hydroxide solution and Reichstein[22] gave $[\alpha]^{22}D$ −32.8° in a 2% potassium solution.

Summary

1. The "2,3-monoacetone galactosedibenzylmercaptal" of Pacsu and Löb was found to be a mixture of two isomeric monoacetone derivatives.

2. The chemical structure of the higher rotating isomer was investigated and it was proved that the isopropylidene group was attached on carbon atoms 4 and 5.

3. This conclusion was drawn from the results of a series of transformations in which the substance was first converted into the 4,5-monoacetone galactosedimethylacetal. On methylation the latter gave rise to the 2,3,6-trimethyl derivative which on hydrolysis and subsequent oxidation yielded crystalline 2,3,6-trimethyl γ-galactonolactone.

4. Oxidation by periodic acid of the monoacetone galactosedimethylacetal gave glyoxal and 2,3-acetone *d*-threose, which scission products could form only if the starting material had the isopropylidene group at carbon atoms 4 and 5.

5. The glyoxal was isolated as *bis*-phenylhydrazone, the 2,3-acetone threose was converted into *d*-threonic acid from which the acid potassium salt of *l*-tartaric acid was prepared.

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[CONTRIBUTION NO. 168 FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, THE UNIVERSITY OF TEXAS]

Acidic Constituents of a California Straight-run Gasoline Distillate

BY KINNEY HANCOCK[1] AND H. L. LOCHTE

The acidic constituents of petroleum from various regions have been a source of rather extensive investigation. The isolation and identification of numerous individuals of the acyclic series have been reported. Among these are: formic and oxalic acids from Grosny distillates by Schidkoff[2]; palmitic, stearic, myristic, and arachidic acids from Ishikari distillates by Tanaka and Kuwata[3]; isoamylacetic and diethylpropionic acids from Baku petroleum by Chichibabin[4]; isovaleric, *n*-heptylic, *n*-octylic, and *n*-nonylic acids and ethyl mercaptan from a West Texas pressure distillate by Williams and Richter[5]; *n*-butyric and *n*-valeric acids and dimethylmaleic anhydride from a Texas distillate by Schutze[6]; and isocaproic acid from Rumanian petroleum by Nenitzescu and co-workers.[7]

As to the phenolic constituents, phenol, the three cresols, and several of the xylenols have been isolated.[5,7,8]

The isolation of numerous naphthenic acids, varying in complexity from cyclopentanecarboxylic acid to pentacosan-naphthenic acid, has been reported. Later investigation has proved that the majority of these acids were mixtures. Von Braun and co-workers[9] are given credit for the isolation of the first homogeneous naphthenic acid. These investigators isolated 3,3,4-trimethylcyclopentanone from the degradation products from mixtures of decanaphthenic acids from various sources. This ketone was then reconverted to 3,3,4-trimethylcyclopentylacetic acid.

Very recently Nenitzescu and co-workers[7] have reported the isolation, through selective amide formation, and identification of cyclopentanecarboxylic, cyclopentylacetic, and 3-methylcyclopentylacetic acids from Rumanian petroleum.

The material investigated in the present study was a complex mixture of crude petroleum acids from the sodium carbonate wash of Signal Hill straight-run gasoline.[10] The objectives of the investigation were: (1) to study and to improve methods of separation of acid mixtures, (2) to attempt to develop new methods of separation, (3) to attempt the isolation and identification of all of the aliphatic acids from formic through the pentanoic acids, and (4) to study the fractions in

(1) This paper represents part of a dissertation submitted to the Graduate School of The University of Texas in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

(2) Schidkoff, *J. Soc. Chem. Ind.*, **18**, 360 (1899).

(3) Tanaka and Kuwata, *J. Faculty Eng. Tokyo Imp. Univ.*, **17**, 293 (1928).

(4) Chichibabin, *et al.*, *Chimie et industrie*, Special No., 306 (March, 1932).

(5) Williams and Richter, THIS JOURNAL, **57**, 1686 (1935).

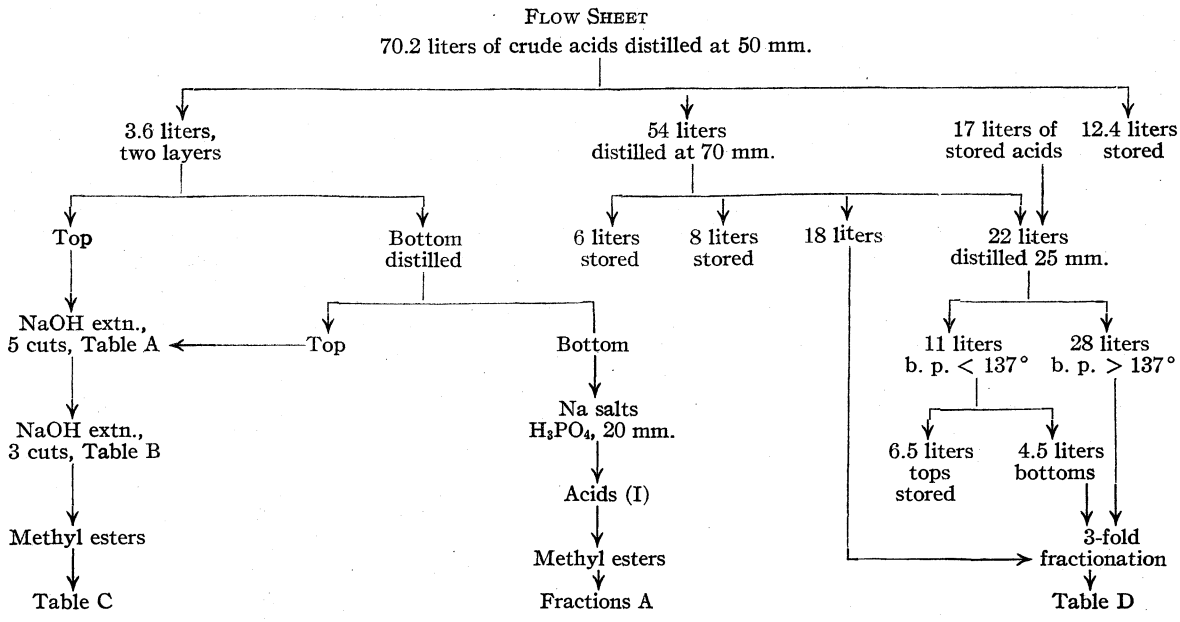
(6) H. G. Schutze, Ph.D. Dissertation, The University of Texas, June, 1938, to be published elsewhere.

(7) Nenitzescu, Isăcescu and Volrap, *Ber.*, **71B**, 2056 (1938).

(8) (a) Tanaka and Kobayashi, *J. Faculty Eng. Tokyo Imp. Univ.*, **17**, 127 (1927); (b) Holzmann and von Pilat, *Brennstoff-Chem.*, **11**, 409 (1930).

(9) Von Braun, Mannes and Reuter, *Ber.*, **66B**, 1499 (1933).

(10) These crude acids were kindly donated by the MacMillan Petroleum Corporation of Long Beach, California.



the region of the nonanoic acids with a view to the isolation and identification of some of the individuals. The fractions in the region of the hexanoic, heptanoic, and octanoic acids are being investigated by another student in this Laboratory. The general procedure for the partial separation of this mixture is shown in the accompanying Flow Sheet.

In two runs, 70 l. of crude acids was distilled under reflux at 50 mm. from a 15-gallon steel still with a 110 cm. × 12 cm. column. Natural gas was used in the capillary in this case and in all subsequent vacuum distillations. The three fractions shown on the Flow Sheet were obtained. The two layers in the first fraction were separated, the top layer amounting to 2840 cc. and the bottom layer 760 cc.

By a series of distillations the 760-cc. portion was separated into 20 cc. of acids and 740 cc. of water solution of acids. The 20-cc. portion was returned to the top layer obtained originally. In this manner, the majority of dissolved acids of higher molecular weight than propionic acid were removed.

The 740-cc. portion was neutralized with 115 cc. of 3 *N* sodium carbonate, and an excess of 25 cc. was added. The basic solution was evaporated to dryness on a steam cone. The residue was pulverized and dried thoroughly at 20 mm. to obtain 29.1 g. of powder. One-half of this powder was distilled at 20 mm. with 25 cc. of phosphoric acid[11] (dried for twenty-four hours at 150–160° and 20 mm. with a capillary leak) to obtain 4.5 g. of acids.

Formic Acid.—Small portions of this mixture (I on Flow Sheet) reduced silver nitrate and mercuric chloride solutions.

The balance of the 4.5-g. portion was distilled with 23 cc. of methyl *n*-caproate[12] and 0.6 cc. of 18 *N* sulfuric acid to obtain 3.0 g. of dry methyl esters. The esters were fractionated under a high reflux ratio through a 70 cm. × 5 mm. column containing a spiral of chromel wire to obtain several fractions with $n^{24}D$ values: A1, 1.3560; A2, 1.3572; A3, 1.3609; A4, 1.3765; A5, 1.3780; residue, not detd.

Acetic Acid.—The $n^{20}D$ value reported for methyl acetate is 1.3619.[13] Fraction A3 yielded, after saponification, Duclaux values of 7.0, 7.5, and 8.0, respectively, for the first three 10% distillates. The Duclaux values for acetic acid given by Kamm[14] are: 6.8, 7.1, and 7.4.

The combined top layers (2860 cc.) amounted to 14.8 equivalents. A consideration of the differences in solubility and in K_a values for the lower acids expected in this mixture indicated the possibility of separation through fractional extraction with sodium hydroxide. The two experimental difficulties recognized were: loss of lower acids as a result of water solubility and solubility of the sodium salts in the free acid layer. The following procedure was designed to lower these factors to a minimum.

The whole portion (2860 cc.) was stirred effectively for six hours with 3 liters of normal sodium hydroxide. The top layer was stirred thoroughly for thirty minutes with three 500-cc. portions of water. The washes were combined with the bottom layer and the combination distilled to small volume. The residue was steam distilled until the distillate became neutral to litmus. All distillates were combined, made slightly basic with sodium hydroxide, evaporated to small volume, and the concentrated solution mixed with the top layer. The residue was concentrated further and an excess of 18 *N* sulfuric acid was added with cooling. The freed acids were separated and the heavy layer extracted three times with petroleum ether (30–60°). The solvent was removed and the acids dried at 100° and 20 mm.

(11) Curtius and Franzen, *Ann.*, **404**, 109 (1914).

(12) Geo. D. Graves (to E. I. du Pont de Nemours and Co.), U. S. 1,882,808, Oct. 18, 1932.

(13) "International Critical Tables," Vol. I, McGraw-Hill Book Co., Inc., New York, N. Y., 1926, p. 276.

(14) Kamm, "Qualitative Organic Analysis," 2d ed., John Wiley and Sons, Inc., New York, N. Y., 1938, p. 153.

This procedure was repeated four times, beginning each time with the mixture of the top layer and the combination of basic distillates which had been concentrated by evaporation. A stubborn emulsion resulted during the fourth extraction. This emulsion was broken through: (1) addition of water and extraction with petroleum ether (30–60°), and (2) steam distillation of the raffinate. This treatment yielded a fraction listed as 4a in Table A. After the fifth extraction, a small portion, insoluble in an excess of sodium hydroxide, was discarded.

TABLE A

	Wt., g.	$n^{20}D$	Equiv. wt.
1	284.0	1.4139	104.5
2	297.3	1.4204	115.6
3	342.7	1.4286	127.9
4	555.5	1.4367	144.3
4a	178.1	1.4410	159.0
5	252.8	1.4407	156.8

Fractions 1 and 2 (Table A) were extracted separately with three equal portions of normal sodium hydroxide as described above. No appreciable emulsion formation occurred in these cases due to the transfer of the weak, emulsifying acids to fractions 4, 4a, and 5 by the previous extraction.

TABLE B

	Wt., g.	$n^{20}D$	Equiv. wt.
1a	67.5	1.4155	90.6
1b	83.1	1.4103	98.0
1c	77.1	1.4147	109.0
2a	79.8	1.4135	107.0
2b	97.4	1.4181	113.1
2c	97.8	1.4273	126.5

Fractions 1a, 1b, 1c, and 2a (Table B) were converted separately to the methyl esters by refluxing for three hours with an equal volume of methanol containing 2% hydrogen chloride. The unchanged acids were recovered and esterified as before. The two portions of esters were combined. This general procedure was followed in all subsequent esterifications, except that in some cases the unchanged acids after the second operation were recovered and esterified as before to yield a third portion of esters. The yields in grams from fractions 1a, 1b, 1c, and 2a were: 57.9, 74.3, 79.8, and 77.8 (one esterification), respectively.

Dimethylmaleic Anhydride.[6]—A solid crystallized out when the unchanged acids recovered after the first esterification of 1a (Table B) were cooled with an ice–salt mixture. This solid melted at 94–95° after two recrystallizations from petroleum ether (60–68°). Treatment with resorcinol and sulfuric acid, followed by neutralization with sodium hydroxide, gave a yellow-green fluorescence.[15] This reaction is given by the anhydride ring group of phthalic anhydride. This same group is present in dimethylmaleic anhydride. The mixed melting point of the isolated acid with synthetic dimethylmaleic anhydride showed no depression. All of this anhydride had been concentrated in the fraction from which it was isolated. Schutze found the same substance in eight different fractions in his investigation of Texas petroleum acids.

(15) Mulliken, "The Identification of Pure Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1st ed., Vol. I, 1905, p. 84.

The methyl esters of fractions 1a, 1b, 1c, and 2a were fractionated separately, under good reflux, from a 200-cc. still with a 130 cm. × 8 mm. (i. d.) column containing a spiral of chromel wire. The fractions obtained were combined on the basis of boiling points and indices of refraction. The combinations were subjected to four-fold refractionation and recombination, the esters with boiling points above that of methyl *n*-valerate being set aside each time. For the smaller combinations a 30-cc. still with a 75 cm. × 5 mm. (i. d.) column containing a spiral of small glass rod was used.

TABLE C

	Wt., g.	$n^{20}D$	B. p., °C.
1	0.35	1.3728	<79
2	2.54	1.3792	79– 80
3	1.2	1.3831	80– 91
4	7.44	1.3843	91– 92
5	5.0	1.3862	92–101
6	3.95	1.3885	101–102
7	8.7	1.3923	102–115
8	57.2	1.3942	115–116
9	11.9	1.3962	116–126
10	12.8	1.3983	126–127
11	165.0	....	>127

Propionic, Isobutyric, *n*-Butyric, Isovaleric, and *n*-Valeric Acids.—Small portions of fractions 2, 4, 6, 8, and 10 (Table C) were saponified and the 2-alkylbenzimidazoles[16] of the recovered acids were prepared.

TABLE C-1

No.	B. p. of acid, °C.	$n^{20}D$ of acid	M. p. of 2-alkylbenzimidazole, °C. Synthetic	Isolated	Mixed
2	141–142	1.3872	174.5	178.5	176
4	153–154	1.3948	234	233.5	234
6	162–163	1.3982	159	158	158
8	175–176	1.4050	190.5	190	190
10	185–186	1.4090	154	153	153

The *p*-phenylphenacyl esters[17] of the acid from fraction 2 (Table C) and of propionic acid were also prepared: m. p., synthetic, 103°; isolated, 100.5°; mixed, 102°.

Attempts to isolate methylethylacetic and trimethylacetic acids were unsuccessful; in fact, there was very little indication, if any, of their presence in the mixture investigated.

In two runs, the 54-liter fraction (Flow Sheet) was distilled under reflux at 70 mm. from the 15-gallon still to obtain the four fractions shown on the Flow Sheet. The top fraction (22 liters) was combined with a similar fraction of 17 liters from an earlier distillation of 30 liters of crude acids. This combination was topped to 137° at 25 mm. from Claisen flasks. The tops were retopped to 137° at 25 mm. in the same manner. This procedure yielded the 11-liter and 28-liter fractions shown on the Flow Sheet.

The 28-liter fraction was combined with the 18-liter fraction (Flow Sheet) and the combination (1500-cc. charges) subjected to two-fold fractionation at 3 mm. under a high reflux ratio from a 2-liter still with a 145 cm. × 3.5 cm. (i. d.) glass marble-(7 mm. diam.)-filled column.

(16) Pool, Harwood and Ralston, THIS JOURNAL, **59**, 178 (1937).

(17) Drake and Bronitsky, *ibid.*, **52**, 3715 (1930).

After each fractionation similar fractions were combined on the basis of boiling points and indices of refraction. The combinations after the second fractionation were combined with similar fractions obtained from the two-fold fractionation (3 mm.) through the 145-cm. column of the 11-liter portion (b. p. < 137° at 25 mm.). These final combinations were then fractionated a third time through the 145-cm. column to obtain the following fractions.

TABLE D

	Vol., cc.	$n^{20}D$		Vol., cc.	$n^{20}D$
Tops	..	....	7	665	1.4415
1	275	1.4349	8	585	1.4426
2	2265	1.4374	9	175	1.4437
3	1865	1.4384	10	1300	1.4450
4	8650	1.4390	11	1250	1.4480
5	1752	1.4398	Bottoms	...	....
6	1005	1.4405			

Menschutkin[18] has shown that primary, secondary, and tertiary aliphatic acids differ greatly in their velocities of esterification. His results suggested the possibility of separation of petroleum acids through fractional esterification.

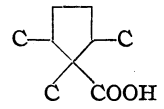
Two liters of fraction 4 (Table D) was fractionated at 3 mm. through the 145-cm. column to obtain a main fraction of 1614 cc.—the tops and bottoms were combined with similar fractions from the previous fractionation. The main fraction was fractionally esterified by refluxing each time for twelve hours with one-fourth of the calculated amount of methanol–2% hydrochloric acid. After each step the mixture of acids and esters was washed, dried and then fractionated at 25 mm. through the 145-cm. column until the distilling temperature rose abruptly. Corresponding fractions from the four series obtained showed very little difference in physical properties. Possibly, interchange between the acids and esters[12] may have occurred during the fractionation, although a detailed study of this type of reaction in this Laboratory with synthetic acids and esters indicated that the reaction would not occur except in the presence of a catalyst.

Fractionation of the unchanged acids remaining after the fourth step yielded a solid acid, m. p. 194–195° from dilute alcohol.

The balance of fraction 4 (Table D) was subjected to three-fold esterification. More of the solid acid was recovered from the unchanged acids remaining after the third esterification. A similar procedure with fraction 5 (Table D) yielded additional solid to total 62.5 g.

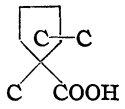
Data Determined on this Solid Acid.—(a) Qualitative analysis: negative for sulfur, nitrogen, and halogen. (b) M. p. 194–195° from dilute alcohol. (c) Equivalent weight: calcd. for $C_9H_{16}O_2$, 156.21; found, 156.33. (d) C and H. Calcd. for $C_9H_{16}O_2$: C, 69.20; H, 10.32. Found: C, 69.41; H, 10.02. (e) Unsaturation tests: negative. (f) 0.1047 g. of acid in 1.0021 g. of camphor melted at 177°, while camphor alone melted at 174°. (g) An electrometric titration proved that the acid is monobasic.

The behavior of the compound in the Rast molecular weight determination and the high melting point led us to suspect a tertiary acid closely related to camphor. A search of the literature on known $C_9H_{16}O_2$ acids and homologs of near the same molecular weight led us to predict that the isolated acid was either



1,2,5-Trimethylcyclopentanecarboxylic acid

or



Camphonanic acid

The former is unknown but Appel[19] in 1933 prepared camphonanic acid. Although his degradation from *d*-camphoric acid yields the dextrorotatory acid while the isolated acid is inactive or slightly levorotatory, his synthesis was repeated since only *d*-camphoric acid was available at the time. The constants of the acid obtained agreed with those of Appel's acid with the exception of the m. p., which was found to be 192–193° instead of 190–191°. In agreement with Appel, esterification by methanol and hydrochloric acid failed. The *p*-bromoanilides and *p*-toluidides of the *d*-camphonanic acid and of the isolated acid were prepared according to Kuehn and McElvain.[20] The melting points of the acids and of their derivatives are tabulated.

	dl-Camphonanic	Isolated	Mixed
Acid	192–193	194–194.5	193–194
p-Bromoanilide	102–103	119–120	111–115
p-Toluidide	114–115	110–111	111–112

Since none of the mixed melting points showed a depression, it appeared that the isolated acid was either pure *dl*-camphonanic acid and the slight rotation due to an error, or that the rotation was due to a small amount of an active acid. The *dl*-acid was then prepared from *dl*-camphor.

dl-Camphoric acid was prepared from *dl*-camphor according to Noyes.[21] The dibasic acid was degraded to *dl*-camphonanic acid by Appel's procedure. The *p*-bromoanilide and the *p*-toluidide were prepared as described above.

	dl-Camphonanic	Isolated	Mixed
Acid	193–194	194–194.5	193.5–194
p-Bromoanilide	119–120	119–120	119–120
p-Toluidide	110–111	110–111	110–111

This proves definitely that the isolated acid is *dl*-camphonanic acid—the first naphthenic acid isolated from American petroleum.

(18) Menschutkin, *Ann. chim. phys.*, [5] **23**, 14 (1881).

(19) Appel, *Z. physiol. Chem.*, **218**, 202 (1933).

(20) Kuehn and McElvain, THIS JOURNAL, **53**, 1173 (1931).

(21) Noyes, *Am. Chem. J.*, **16**, 501 (1894).

Summary

1. A mixture of crude petroleum acids has been partially separated through fractionation as acids, fractional extraction with sodium hydroxide, fractionation as methyl esters, and through differences in tendencies to esterify.

2. The separation of aliphatic acids of low molecular weight through systematic fractional extraction with sodium hydroxide is effective.

3. Fractional esterification of a particular mixture of acids by a batch procedure yielded very little separation.

4. Isolation of peculiar individual substances from the mixture of unchanged acids recovered after esterification has proved to be relatively simple.

5. Formic acid has been identified through qualitative tests. Dimethylmaleic anhydride and acetic, propionic, isobutyric, *n*-butyric, isovaleric, and *n*-valeric acids have been isolated and identified. Of these eight substances, acetic, propionic, and isobutyric acids have not been reported previously.

6. *dl*-Camphonanic acid has been isolated and identified as the first American naphthenic acid.

AUSTIN, TEXAS RECEIVED JUNE 26, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF KENTUCKY]

The Use of *n*-Butyl Chlorosulfonate and *n*-Butyl Chlorosulfite in the Friedel–Crafts Reaction

BY CHAS. BARKENBUS, RALPH L. HOPKINS AND J. FORREST ALLEN

Alkyl halides have been used for many years in the Friedel–Crafts reaction as a means of introducing alkyl groups into aromatic nuclei. More recently efforts to extend the scope of this reaction to permit use of a wider variety of alkylating agents have resulted in the use of many types of esters, both organic and inorganic, with widely varying results. Besides the esters of the fatty acids such inorganic derivatives as alkyl sulfates, orthosilicates, phosphates, hypochlorites,[1] borates,[2] and sulfites[3] have been used.

In a search for a more direct method of making alkyl benzenesulfonates, an investigation was made of the method described by Frèrejacque,[4] who claimed to have prepared the methyl sulfonates of benzene, toluene, naphthalene, and chlorobenzene by the action of methyl chlorosulfonate on the above compound. Using *n*-butyl chlorosulfonate and benzene no butylbenzene sulfonate could be obtained. However, a reaction took place at 60° with evolution of hydrogen chloride, and from the reaction mixture a small hydrocarbon residue was obtained, although most of the product was converted into an unworkable tar. All methods used in attempting to show that some sulfonates were produced failed. The addition of anhydrous aluminum chloride caused the ester to react extremely vigorously even at 0° with copious evolution of hydrogen chloride.

A study of this reaction under the most favorable conditions showed it to be principally one of alkylation with production of *s*-butylbenzene and *m*-di-*s*-butylbenzene. Chlorination also takes place, and chlorobenzene was recovered in quantity. Alkylation of toluene under similar conditions yielded *m*- and *p*-*s*-butyltoluenes and *o*-chlorotoluene along with smaller amounts of *p*-chlorotoluene and various side-chain chlorinated products. In both cases higher boiling hydrocarbon fractions were obtained.

The alkylating action of *n*-butyl chlorosulfite on benzene in the presence of anhydrous aluminum chloride was also investigated. Less high-boiling material is produced by this ester than was observed with the *n*-butyl chlorosulfonate, and chlorination does not take place, but an unstable sulfur compound of undetermined nature is produced, and unfavorably affects the quality of the yield.

Experimental

Reactions of *n*-Butyl Chlorosulfonate

Benzene.—A series of experiments was carried out to determine the most suitable reacting conditions and the proper proportions of reactants necessary for the maximum yield of *s*-butylbenzene. From these it was concluded that the temperature is best maintained between 0 and 5°. The most efficient proportion of aluminum chloride to ester is 2:1. The use of 9 moles of benzene with the

(1) Kane and Lowy, THIS JOURNAL, **58**, 2605 (1936).
(2) Kaufman, German Patent 555,403; French Patent 720,034.
(3) Bowden, THIS JOURNAL, **60**, 645 (1938).
(4) Frèrejacque, *Compt. rend.*, **183**, 607 (1926).

above ratio increases the total yield and greatly facilitates stirring.

From the results of the foregoing conclusions two large-scale runs were made in each of which 3 moles of crude *n*-butyl chlorosulfonate prepared according to Barkenbus and Owen[5] and used without distillation was added slowly to 27 moles (2106 g.) of benzene (dried over sodium) and 6 moles (800 g.) of anhydrous aluminum chloride (technical) with stirring at 0–5°. After the elapse of three hours the mixture was poured onto 5 kg. of cracked ice, washed with concentrated hydrochloric acid and water and allowed to stand overnight with concentrated ammonium hydroxide, which readily removed labile chlorine compounds. The benzene was then washed repeatedly with 80% sulfuric acid until the acid no longer developed a color. This treatment removed unsaturated material, which has a tendency to decompose in distillation. No sulfonates could be isolated from this fraction. After washing with sodium hydroxide, drying over calcium chloride, and distillation of the excess benzene, a total residue of 652 g. remained.

Preliminary fractionation in a short column removed about 60 g. of chlorobenzene which boiled at 128–130° and was identified as *p*-nitrochlorobenzene by nitration. Much chlorine still remained and was removed by heating with sodium. Fractionation of the mixture on a large column similar to that described by Tongberg, Quiggle, and Fenske[6] was performed at 3 mm. and many small fractions were collected. By taking the index of refraction of each fraction and plotting against the amount distilled two main fractions of constant index were obtained. The first main fraction weighing 83 g. was identified as *s*-butylbenzene by the method of Reilly and Hickenbottom:[7] m. p. of acetamino derivative 124–125°; listed m. p. 125–126°; $n^{20}D$ 1.4910. Ipatieff[8] gives 1.4902. The second fraction weighing 165 g. was characterized as *m*-di-*s*-butylbenzene by oxidation to isophthalic acid and conversion of the latter to its methyl ester (m. p. 67–68°); $n^{20}D$ 1.4890; b. p. 88–92° at 3 mm. This fraction contained a trace of the ortho isomer as shown by the fluorescein test: yields, *s*-butylbenzene, 19%; *m*-di-*s*-butylbenzene 26.6%; chlorobenzene 11.2%.

Toluene.—Six moles of *n*-butyl chlorosulfonate was allowed to react with 12 moles of aluminum chloride and 54 moles (4968 g.) of toluene for three hours after addition of the ester at −2°. The product was washed and fractionated in a manner analogous to that used for benzene. The following products were separated and identified: *m*-*s*-butyltoluene 290 g. (32.4%); b. p. 193–197°; $n^{20}D$ 1.4957. This fraction was completely soluble in concd. sulfuric acid; *p*-*s*-butyltoluene 174 g. (19.6%); b. p. 201–202°; $n^{20}D$ 1.4950. Only a trace of this fraction was soluble in cold concd. sulfuric acid; *o*-chlorotoluene 83 g. (21.8%). The *o*-chlorotoluene and *p*-chlorotoluene fractions were not pure but were contaminated slightly with each other, due to the closeness of their boiling points. They were of sufficient purity to obtain readily *o*-chlorobenzoic and *p*-chlorobenzoic acid by oxidation of the respective fractions: *p*-chlorotoluene 23.5 g. (6.2%). A high boiling hydrocarbon residue of 170 g. also was obtained but the components were not identified. Considerable benzoic acid, probably derived from benzotrichloride, resulted from the sodium treatment and smaller amounts of other side-chain chlorinated products were present.

(5) Barkenbus and Owen, THIS JOURNAL, **56**, 1206 (1934).

(6) Tongberg, Quiggle and Fenske, *Ind. Eng. Chem.*, [11] **26**, 1212 (1934).

(7) Reilly and Hickenbottom, *J. Chem. Soc.*, **117**, 120 (1920).

(8) Ipatieff, Corson and Pines, THIS JOURNAL, **58**, 919 (1936).

Summary

The action of *n*-butyl chlorosulfonate on benzene and toluene in the presence of anhydrous aluminum chloride has been investigated. The principal effect is one of alkylation accompanied by nuclear and side-chain chlorination.

n-Butyl chlorosulfite reacts with benzene and aluminum chloride to produce *s*-butylbenzene. The reaction is not accompanied by chlorination, but sulfur derivatives are produced.

LEXINGTON, KENTUCKY RECEIVED MAY 27, 1939

[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY, UNIVERSITY OF CHICAGO]

Fractionation of the Hydrogen Isotopes in the Distillation of Ethyl Alcohol

BY ALEX H. WIDIGER AND WELDON G. BROWN

During the course of some experiments on hydrogen exchange reactions in deutero-alcohol in which it was necessary to recover the alcohol from the mixtures, for deuterium analysis, by careful fractional distillation under reduced pressure, using small laboratory columns, we had occasion to suspect that serious errors were being introduced as a result of fractionation of the hydrogen isotopes during the distillations. In view of the small mass difference between C_2H_5OD and C_2H_5OH, and the difficulty of accomplishing the desired separations (*e. g.*, phenylacetylene and alcohol) with our columns, the possibility of accounting for our results on this basis was not considered seriously until after a number of more obvious possible sources of error had been eliminated. It was nevertheless possible to show, by distillations of alcohol alone, that the degree of isotopic separation is fully capable of accounting for our results.

The first distillations were carried out with a vacuum-jacketed column, 4 mm. i. d., 45 cm. in length, containing a spiral nichrome wire packing. In a typical experiment, a sample of alcohol containing 17.8% C_2H_5OD was distilled at 40 mm. pressure, and the distillate, amounting to one-half of the total, was found to contain 14.8% C_2H_5OD. The boiler residue was correspondingly richer in deuterium and contained 21.1% C_2H_5OD. In order to compare this separation with that to be obtained on the distillation of water, a sample of water containing 3.06% D_2O was distilled under similar conditions and the distillate was found to contain 2.43% D_2O. These results would indicate that the fractionation of the hydroxyl hydrogen in alcohol takes place with very nearly the same efficiency as the fractionation of the isotopic forms of water. However, some allowance would have to be made for the fact that this column could not be made to operate smoothly in distillations of water.

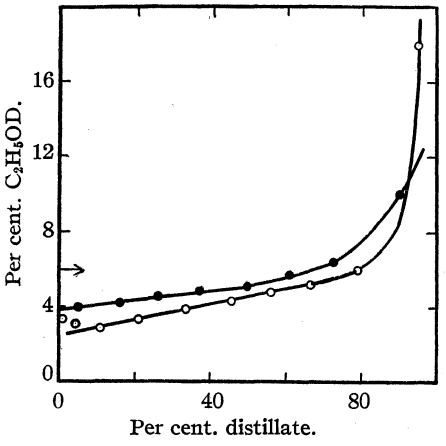


Fig. 1.—The distillation of 6% C_2H_5OD at atmospheric pressure (●) and at 80 mm. (○).

These results immediately suggested that the distillation of alcohol with the aid of high efficiency fractionating columns might prove to be a practicable method for the concentration of deuterium in quantity. The concentration of deuterium by the distillation of water has not thus far been a conspicuous success and it appears to be common experience that the efficiency of fractionating columns in such distillations does not approach that predicted on the basis of performance with organic liquids. The method of distilling alcohol offers a number of advantages from the standpoint of column operation and it was therefore of interest, although there is no intention of pursuing the project further at this time, to determine the degree of isotope separation obtainable with a more efficient column than that described above.

Subsequent distillations were carried out using a column packed with single-turn glass helices, packed length 2.2 m., internal diameter 18 mm. The theoretical plate equivalent of this column was estimated to be in the neighborhood of 25 plates, this estimate being based on its performance in the separation of active amyl and isoamyl alcohols.[1] The results of two distillations, one at atmospheric pressure (750 mm.), the other at 80 mm. pressure, of deutero-alcohol containing 6.0% C_2H_5OD initially are shown in Fig. 1. The isotopic separation obtained corresponds to a fractionation factor 1.6 for the distillation at atmospheric pressure, and a factor 2.4 for the distillation at 80 mm. pressure. Assuming a column efficiency of 25 plates, the enrichment factors for the vaporization process are as follows: at 750 mm. 1.019 and at 80 mm. pressure 1.035.

In a distillation at atmospheric pressure of water containing 0.330% D_2O, the first fraction of the distillate was found to contain 0.195% D_2O. Before this experiment was carried out the column was cleaned thoroughly by distilling nitric acid through it, in order to facilitate uniform wetting of the packing, and no difficulty was experienced in the subsequent operation of the column with pure water. The observed fractionation factor, 1.69, is slightly higher than that found in the distillation of alcohol, and if we again assume a column efficiency of 25 plates we obtain an enrichment factor, 1.021. This is appreciably lower than the value, 1.025, reported by Urey and Teal[2] and our estimate of the column efficiency was therefore, for this distillation at least, too high.

The fact that a partial separation of the hydrogen isotopes can be effected readily by the distillation of water has been known for some time[3] and consequently the possibility of errors arising from this source in work on exchange reactions in heavy water has been recognized almost from the beginning. It is now evident that effects of this type can be equally significant in work on exchange reactions in heavy alcohol and that the necessary precautions will have to be taken to minimize the resulting errors.

Summary

It has been shown, by distillations of alcohol in laboratory fractionating columns, that the isotopic forms, C_2H_5OH and C_2H_5OD, readily undergo a partial separation on distillation, the degree of isotopic separation being comparable with that observed in the distillation of water.

CHICAGO, ILLINOIS RECEIVED JULY 7, 1939

(1) The work on the amyl alcohols was carried out by Mr. W. deAtley.

(2) H. C. Urey and G. K. Teal, *Rev. Modern Phys.*, **7**, 48 (1935).

(3) E. W. Washburn and E. R. Smith, *J. Chem. Phys.*, **1**, 426 (1933); G. N. Lewis and R. E. Cornish, THIS JOURNAL, **55**, 2616 (1933); N. F. Hall and T. O. Jones, *ibid.*, **56**, 749 (1934).

The Salts of Europium

BY HERBERT N. MCCOY

Although nearly forty years have passed since Demarçay[1] characterized europium as a distinct element, its compounds have been studied little. The only systematic study was that made by Sarkar,[2] who made and analyzed a dozen europic salts. Earlier workers[3–7] had made eight or ten other compounds but many of these had not been analyzed. Europous chloride and sulfate have been made and studied by several workers.[8–12]

With the more abundant supply of europium made available through newer methods[11] of separation and purification, it was deemed worth while to make further studies of the salts of this element. The analytical results are shown in Table I.

In a few cases the results of this study were at variance with earlier work. *m*-Nitrobenzenesulfonate, made by James and Robinson,[6] is said to have $3H_2O$; the analysis of my crystalline product, seemingly pure, indicates $6H_2O$. Europium citrate was made and analyzed by Sarkar,[2] whose figures indicate five molecules of water. My analyses lead to but four. That there are other salts of citric acid is indicated by the fact that only by following a definite procedure could this substance be obtained pure. When 4.0 g. of europium acetate in 30 cc. of cold water was mixed with 6.3 g. of citric acid in 15 cc. of cold water (one mole of each) a precipitate formed at once. This dissolved completely when the mixture was well stirred. When the solution was heated to 80° it gave an amorphous precipitate that changed to microscopic crystals. After two hours of stirring these were filtered out, washed, dried and analyzed. Sarkar's iodate is given the formula $Eu(IO_3)_3 \cdot 5^1/_2H_2O$. The results found here indicate four molecules of water.

The methods of preparation varied according to the nature of the acid and of the resulting salt. The formate, acetate, propionate, monochloroacetate, trichloroacetate, furoate, picrate, *p*-toluenesulfonate and *m*-nitrobenzenesulfonate were made by dissolving europium oxide in a hot aqueous solution of acid. These salts were all more soluble in hot than in cold water and crystallized well when their solutions were cooled.

The acetates of the cerium group of rare earths differ from europium acetate in having three molecules of water instead of four and in being less soluble in hot than in cold water.

Solutions of the sodium salts of the acids were treated with a solution of europium acetate or nitrate to prepare the maleate and fumarate. These salts are not much soluble in water. The former is soluble in cold dilute acetic acid. Other salts more or less difficultly soluble in water including the malonate, succinate, lactate, tartrate, pyruvate, citrate, benzoate, salicylate, cinnamate, benzilate, and basic sulfite could be made from a solution of europium acetate and the corresponding acid.

In several cases the salt did not separate at once but came down slowly when its solution was stirred and heated. This was true of the malonate, maleate, pyruvate, salicylate, lactate, citrate, acid tartrate and basic sulfite.

In general the salt, after its precipitation or crystallization, was filtered and washed well with water if it contained any foreign substance and afterward with methanol. It was dried in air or in a desiccator as necessary.

In the analyses when no complication occurred, the salt was simply ignited to the oxide, Eu_2O_3. In other cases europium was precipitated as oxalate and the latter ignited. The bromate and iodate were treated with potassium iodide and the liberated iodine titrated with thiosulfate. The sulfite could be titrated directly with iodine.

Several other euopric salts were made which were not analyzed either because they were extremely deliquescent, as the perchlorate, dichloroacetate, bromide and sulfamate or of doubtful purity or interest as *o*-chlorobenzoate, *p*-bromobenzoate, naphthol-6-sulfonate, fluosilicate, hypophosphate and chromate. In addition there were made a number of very definite and interesting europous salts which have not yet been obtained

(1) Demarçay, *Compt. rend.*, **130**, 1469 (1900); **132**, 1484 (1901).
(2) Sarkar, *Bull. soc. chim.*, [4] **41**, 185 (1927).
(3) Urbain and Lacombe, *Compt. rend.*, **138**, 627 (1904).
(4) Urbain, *J. chim. phys.*, **4**, 31, 105, 232 (1906).
(5) Burion, *Compt. rend.*, **148**, 170 (1909).
(6) James and Robinson, THIS JOURNAL, **35**, 754 (1913).
(7) Katz and James, *ibid.*, **35**, 872 (1913).
(8) Urbain and Burion, *Compt. rend.*, **153**, 1155 (1911).
(9) Jantsch, Alber and Grubitsch, *Monatsh.*, **53–54**, 305 (1929).
(10) Yntema, THIS JOURNAL, **52**, 2782 (1930).
(11) McCoy, *ibid.*, **58**, 1577, 2279 (1936).
(12) Baxter and Tuemmler, *ibid.*, **60**, 602 (1938).

TABLE I

SALTS OF TRIVALENT EUROPIUM: EUROPIC SALTS

Salt	Formula	% Eu_2O_3 Calcd.	Found		
Formate[6]	$Eu(HCO_2)_3$	61.32	60.97		
Acetate[2]	$Eu(C_2H_3O_2)_3 \cdot 4H_2O$	43.89	43.91		
Propionate	$Eu(C_3H_5O_2)_3 \cdot 2H_2O$	43.24	43.19	42.87	
Oxalate[2]	$Eu_2(C_2O_4)_3 \cdot 10H_2O$	47.05	47.15	47.12	
Malonate	$Eu_2(C_3H_2O_4)_3 \cdot 6H_2O$	49.02	48.96		
Succinate	$Eu_2(C_4H_4O_4)_3 \cdot 4H_2O$	48.62	48.13		
Lactate	$Eu(C_3H_5O_3)_3 \cdot 2H_2O$	38.59	38.47	38.56	
Tartrate[2]	$EuH(C_4H_5O_6)_2 \cdot 2H_2O$	36.14	35.81	35.71	
Maleate	$Eu_2(C_4H_2O_4)_3 \cdot 4H_2O$	49.02	49.16		
Fumarate	$Eu_2(C_4H_2O_4)_3 \cdot 4H_2O$	49.02	48.44		
Monochloroacetate	$Eu(C_2H_2ClO_2)_3 \cdot H_2O$	39.04	39.04	39.08	
Trichloroacetate	$Eu(C_2Cl_3O_2)_3 \cdot H_2O$	26.77	26.73	26.63	
Pyruvate	$Eu(C_3H_3O_3)_3 \cdot 7H_2O$	32.65	32.89	32.93	
Citrate	$EuC_6H_5O_7 \cdot 4H_2O$	42.61	42.45	42.45	
Furoate	$Eu(C_5H_3O_3)_3 \cdot 7H_2O$	28.81	28.95	29.00	
Benzoate	$Eu(C_7H_5O_2)_3 \cdot 2H_2O$	31.94	32.05	31.86	
Picrate	$Eu(C_6H_2N_3O_7)_3 \cdot 18H_2O$	15.17	15.12	15.19	
Salicylate	$Eu(C_7H_5O_3)_3 \cdot H_2O$	30.29	30.38	30.26	
Cinnamate	$Eu(C_9H_7O_2)_3$	29.67	29.72	29.75	
Benzilate	$Eu(C_{14}H_{11}O_3)_3 \cdot 4H_2O$	19.50	19.52	19.46	19.36
m-Nitrobenzenesulfonate	$Eu(C_6H_4NSO_5)_3 \cdot 6H_2O$	20.32	20.51	20.19	20.16
p-Toluenesulfonate	$Eu(C_7H_8SO_3)_3 \cdot 8H_2O$	21.75	21.86	21.85	
Basic sulfite	$EuOHSO_3 \cdot 4H_2O$	54.83	54.83		
		SO_2, 19.93	19.86		
Iodate	$Eu(IO_3)_3 \cdot 4H_2O$	23.50	23.37		
		IO_3, 70.10	69.73		
Carbonate	$Eu_2(CO_3)_3 \cdot 3H_2O$	65.42	65.68		

entirely free from europic salts. These include the carbonate, oxalate, succinate, etc.

The fluoride, little soluble in water, oxidizes so fast in air that it sets fire to the filter paper after it has been washed with methanol.

Analysis of Europous Salts.—Soluble europous salts are quickly oxidized in air. The less soluble they are in water, the greater their permanence in air. Europous sulfate, $EuSO_4$, is the most stable so far found. It suffers little change in the course of a year. This very small solubility makes its titration with permanganate very slow and the results uncertain. A completely satisfactory procedure was found in the addition of ferric sulfate prior to the titration. The latter reacts quickly and quantitatively with the europous salt to form soluble europic sulfate and ferrous sulfate. Titration of the latter follows the well-known method with permanganate. Ten cc. of a solution containing 0.5 g. of ferric sulfate and 5 g. of sulfuric acid were used for 0.3 to 0.4 g. of europous sulfate.

This method of analysis was tried with a fresh lot of europous sulfate. Twenty-five cc. of purest europium chloride, of density 1.14, was reduced in a reductor containing 400 g. of ten-mesh amalgamated zinc and run slowly into 150 cc. of a solution containing 25 cc. of 6 *N* hydrochloric acid and 15 cc. of 6 *N* sulfuric acid at 40 to 50°. The β form of europous sulfate resulted. It was filtered, washed with water and methanol, dried at 150° for one hour and titrated. Calcd. for $EuSO_4$: Eu, 61.27. Found: Eu, 61.02, 61.06, corresponding to a purity of 99.54 and 99.62%.

The new volumetric method is also useful in the analysis of other europous compounds.

Summary

A number of europic salts have been made and analyzed. An improved method of titration of europous salts is described.

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RECEIVED JUNE 16, 1939

[CONTRIBUTION NO. 166 FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING OF THE UNIVERSITY OF TEXAS]

The Pressure–Volume–Temperature Relations for Gaseous Monomethylamine[1]

BY CHARLES T. KENNER WITH W. A. FELSING

Introduction

The possible and probable use of monomethylamine as the refrigerating fluid in the absorption type of refrigerating units has led to the determination of its thermodynamic properties in this Laboratory.[2] Since the chemical literature records no systematic investigation of the pressure–volume–temperature relations, such determinations constituted the experimental object of this study.

Leduc[3] has proposed an equation of state for monomethylamine, based *not* upon p–v–T relations, but derived by aid of the theory of corresponding states. Mehl[4] has proposed an equation of state of the Callendar–Mollier type based upon a knowledge of some specific gas volumes and of the heat-capacity ratio.

In this investigation an equation of state will be fitted to the observed p–v–T data.

The Proposed Method.—The method adopted for this investigation is the one that has been in common usage at the Research Laboratory of Physical Chemistry at the Massachusetts Institute of Technology, and which has been described in numerous papers.[5] The method, in essentials, consists of determining the pressures developed by a given mass of substance at different temperatures, the volume being held constant. Thus is obtained a series of pressure–temperature relations at different specific volumes.

From the experimental data thus obtained, an equation of state of the Keyes type[6] was derived; this relation reproduces the experimental values with satisfactory accuracy.

(1) Constructed from a thesis presented to the Graduate Faculty of The University of Texas by Charles T. Kenner in partial fulfilment of the requirements for the degree of Doctor of Philosophy, June, 1939. Present address (C. T. K.): The Citadel, The Military College of South Carolina, Charleston.

(2) (a) Felsing and Thomas, *Ind. Eng. Chem.*, **21**, 1269 (1929); (b) Felsing and Wohlford, THIS JOURNAL, **54**, 1442 (1932); (c) Felsing and Buckley, *J. Phys. Chem.*, **37**, 779 (1932); (d) Felsing and Jessen, THIS JOURNAL, **55**, 447 (1933); (e) Felsing and Ashby, *ibid.*, **56**, 2226 (1934).

(3) Leduc, *Compt. rend.*, **148**, 407, 549 (1909).

(4) Mehl, *Beihefte, Z. für gesamte Kälte-Ind.*, No. 3, p. 27 (1933).

(5) (a) Keyes and Brownlee, "Thermodynamic Properties of Ammonia," John Wiley and Sons, Inc., New York, 1916, p. 11; (b) Keyes and Felsing, THIS JOURNAL, **41**, 589 (1919); (c) Beattie and Edel, *Ann. Physik*, **11**, 633 (1931); (d) Keyes, *Proc. Am. Acad. Arts Sci.*, **68**, 505 (1933).

(6) Keyes, *Proc. Natl. Acad. Sci.*, **3**, 323 (1917).

The Apparatus

The apparatus was a development of the dead-weight piston type pressure gage devised by Amagat and which has been thoroughly described by Keyes and Brownlee,[5a] Keyes and Felsing,[5b] and in its present form by Beattie and Edel[5c] and by Keyes.[5d] No essential differences in design of the pressure measuring device existed. The accuracy attainable in pressure measurements alone is at least 1 part in 3000 at pressures below 10 atmospheres, 1 part in 10,000 or better for pressures 10 to 20 atmospheres, and 1 part in 20,000 for pressures above 20 atmospheres.

Temperatures were measured by a platinum resistance thermometer, calibrated by the National Bureau of Standards, in conjunction with a calibrated Mueller bridge and a high sensitivity galvanometer. The thermometer was calibrated again during the investigation at the ice-point, at the boiling point of water, and at the boiling point of mercury. The true boiling point temperatures of water and of mercury were evaluated from the observed data by means of the relations proposed by Beattie and Blaisdell[7] and by Beattie, Blaisdell and Kaminsky.[8] Temperatures could be measured readily with an accuracy of at least 0.001°.

The thermostat consisted of a large Pyrex dewar flask of about 10 inches (25 cm.) internal diameter and 24 inches (61 cm.) deep. The bath liquids were liquid paraffin, Crisco, or high melting paraffin, depending upon the temperature range. The temperature of the bath could be held constant to ±0.002° for fifteen- to twenty-minute intervals.

All necessary parts of the assembly were calibrated carefully with mercury before use. The piston was calibrated by the method of Bridgeman,[9] employing liquid carbon dioxide at 0°, where its vapor pressure is 26,144.7 mm. The average millimeter equivalent of 1 g. on the piston was 2.00107.

Preparation of Material

The best C. P. Eastman Kodak Co. monomethylamine hydrochloride was dried for several hours at 110°, followed by extended drying over sulfuric acid in a desiccator. This dried hydrochloride was extracted with highly purified, dry chloroform to remove any di- and trimethylamine hydrochlorides. The extracted salt was again dried at 110° and was kept over sulfuric acid.

After evacuation of the generating and drying system,[10] the methylamine gas was generated by treatment of the purified hydrochloride (mixed with a small amount of yellow mercuric oxide to remove any ammonia) with a 40–50% potassium hydroxide solution. The liberated gas passed through several long drying tubes filled with potas-

(7) Beattie and Blaisdell, *Proc. Am. Acad. Arts Sci.*, **71**, 361 (1937).

(8) Beattie, Blaisdell and Kaminsky, *ibid.*, **71**, 375 (1937).

(9) Bridgeman, THIS JOURNAL, **49**, 1174 (1927).

(10) Felsing and Wohlford, *ibid.* **54**, 1442 (1932).

sium hydroxide pellets into a reservoir partially filled with sodium wire and cooled by a dry-ice–acetone mixture. The liquefied amine was allowed to remain in contact with the sodium for at least eight hours until a blue color developed in the solution; this blue color was caused, most probably, by the formation of solvated sodium ions and indicated that the amine was dry. During this period the system was "flushed out" several times by opening the connection to the vacuum system for short intervals, to remove the hydrogen formed. From this reservoir the amine was condensed into an evacuated glass reservoir surrounded by dry-ice; again this system was flushed repeatedly to remove any permanent gas. The amine finally was condensed into a metal reservoir for storage.

From this storage reservoir the amine was distilled in a vacuum into a calibrated three-bulb volumeter of the form described by Keyes and Felsing.[5b] The loading of the piezometer also followed their procedure, except that liquid air was used as the bath surrounding the piezometer during the loading process. This procedure ensured a negligible error in determining the amount of amine left in the volumeter and in the lines of the loading apparatus because of the extremely low vapor pressure of the amine at liquid air temperatures.[2a]

The Experimental Data

The experimental data, calculated to atmospheres, are presented in the table, together with the values of the pressure calculated by the equation of state fitted to the observed data, as shown in the section following.

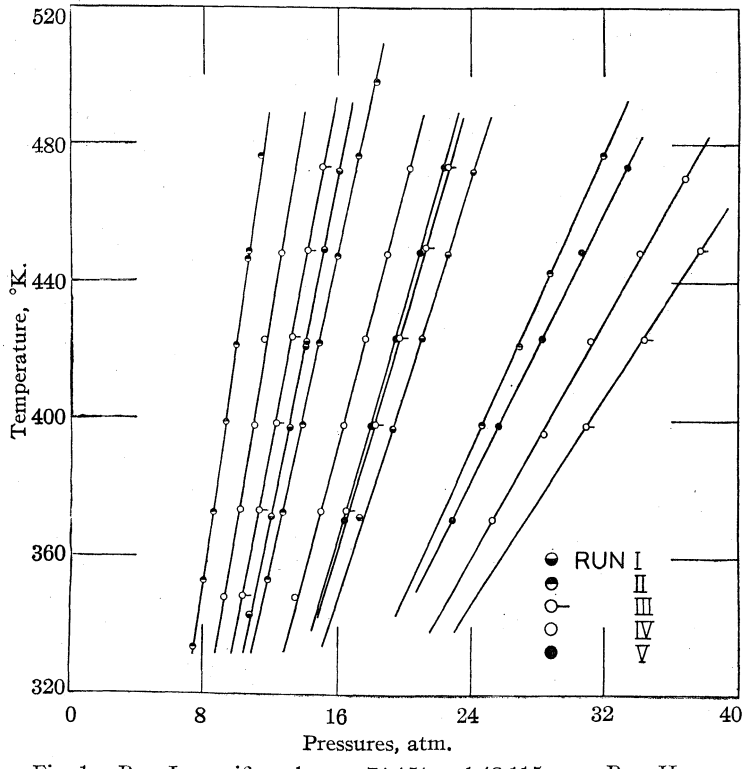


Fig. 1.—Run I, specific volumes, 74.151 and 48.115 cc.; Run II, spec. vol., 107.058, 69.726, and 35.796 cc.; Run III, spec. vol., 79.756, 51.753, and 26.583 cc.; Run IV, spec. vol., 90.253, 58.514, and 30.002 cc.; and Run V, 52.588 and 34.088 cc.

Treatment of Results

The observed pressures were plotted on a large scale as functions of the temperature at the various specific volumes (see figure). The lines were linear over the entire range, though, in several runs, the first and last points seem to indicate a slight curvature. For the purpose of evaluating an equation of state, it was considered sufficiently accurate to consider these isometrics to be linear. Values of $(\partial p/\partial T)_v$ were determined from these linear relations; these values are shown in the table.

It was decided to apply the Keyes equation[6] to the data of this investigation; this equation has the form

$$p = RT/(v - \delta) - A/(v - l)^2$$

where $\delta = f(T)$ and A and l are constants characteristic of the substance. On differentiation, this equation leads to the expression

$$(\partial p/\partial T)_v = R/(v - \delta) \text{ or } \delta = v - R/(\partial p/\partial T)_v$$

The values of $(\partial p/\partial T)_v$, as determined for each isometric, were used to calculate values of δ. A plot of $\log_{10} \delta$ as a function of $1/v$ yielded a linear relation between δ and the volume, v

$$\log_{10} \delta = 1.0548 - 6.120/v$$

which relation reproduces the observed δ values fairly well, except at large specific volumes.

The cohesive pressure term, ϕ, in the Keyes equation is

$$\phi = A/(v - l)^2 = \left(\frac{RT}{v - \delta}\right) - p$$

The values of ϕ are calculated readily from values of δ and of p at any given T. The values of ϕ were calculated for each individual measurement; the average of these closely agreeing values was taken as the correct ϕ for the particular specific volume. Since

$$\phi = A/(v - l)^2 \text{ and } v = (A^{1/2}/\phi^{1/2}) + l$$

a graphical representation of $1/\phi^{1/2}$ as a function of v yielded the linear relation $\phi = 17{,}940/(v + 1.759)^2$.

The Keyes type of equation, hence, for gaseous monomethylamine becomes

$$[p + 17{,}940/(v + 1.759)^2][v - \delta] = RT$$

OBSERVED AND CALCULATED PRESSURES OF GASEOUS MONOMETHYLAMINE

Run	Sp. vol., cc./g.	Temp., °K.	Press., atm. Obsd.	Press., atm. Calcd.	$(\partial p/\partial T)_v$ (calcd.)
I	74.151	343.28	10.771	10.895	0.04081
		371.78	12.071	12.058	
		371.63	12.041	12.052	
		397.08	13.125	13.090	
		420.40	14.039	14.042	
		422.18	14.137	14.115	
		449.15	15.181	15.215	
		472.13	16.108	16.153	
	48.115	371.68	17.410	17.564	.06666
		397.18	19.241	19.261	
		423.18	20.987	20.997	
		449.05	22.561	22.721	
		472.23	24.125	24.267	
II	107.058	333.659	7.492	7.565	.02721
		333.580	7.495	7.563	
		353.081	8.059	8.094	
		353.120	8.058	8.095	
		372.950	8.622	8.635	
		372.981	8.621	8.636	
		398.584	9.324	9.332	
		421.456	9.946	9.954	
		446.354	10.612	10.633	
		448.825	10.678	10.699	
		476.322	11.402	11.448	
	69.726	353.330	11.843	11.936	.04372
		373.000	12.742	12.796	
		373.010	12.741	12.797	
		398.240	13.874	13.899	
		422.049	14.916	14.940	
		447.561	15.999	16.055	
		476.731	17.330	17.331	
		498.288	18.321	18.273	
	35.796	398.426	24.605	24.698	.09391
		421.337	26.873	26.850	
		442.649	28.723	28.851	
		476.655	31.944	32.045	
III	79.756	348.618	10.348	10.416	.03762
		373.564	11.353	11.355	
		398.450	12.308	12.291	
		423.734	13.260	13.243	
		449.059	14.195	14.195	
		473.462	15.090	15.113	
	51.753	373.551	16.518	16.636	.06131
		398.384	18.193	18.159	
		423.755	19.651	19.714	
		448.960	21.249	21.259	
		473.506	22.591	22.764	
	26.583	398.210	30.897	30.539	.13277
		423.662	34.376	33.919	
		449.345	37.314	37.329	
IV(a)	89.812	348.292	9.280	9.351	.03846
		373.096	10.234	10.165	
	58.280	373.179	14.985	15.001	0.05615
		398.327	16.397	16.347	
IV(b)	90.253	348.202	9.310	9.307	.03281
		373.763	10.200	10.145	
		398.072	11.015	10.943	
		423.099	11.837	11.764	
		448.243	12.693	12.589	
		473.224	13.404	13.409	
	58.514	348.167	13.464	13.616	.05329
		373.742	14.970	14.978	
		398.078	16.305	16.276	
		423.147	17.636	17.611	
		448.218	18.938	18.947	
		473.047	20.263	20.271	
	30.002	373.557	25.259	25.314	.11537
		398.059	28.336	28.141	
		423.066	31.147	31.026	
		448.262	34.112	33.933	
		473.002	36.834	36.787	
V	52.588	373.434	16.308	16.404	.06019
		398.191	17.911	17.894	
		423.315	19.442	19.406	
		448.267	20.920	20.909	
		473.440	22.371	22.423	
	34.088	373.593	22.806	23.182	.09942
		398.183	25.105	25.627	
		423.286	28.210	28.123	
		448.371	30.612	30.617	
		473.272	33.020	33.092	

where $\log_{10}\delta = 1.0548 - 6.120/v$. The units here are atmospheres, cc. per gram, and

$$T = 273.16 + t$$
$$R = 2.6421 \text{ cc.-atm.}$$

A comparison of the pressures calculated by this equation with the observed pressures is given in the table.

Summary

1. The pressure–volume–temperature relations for gaseous monomethylamine have been measured over a temperature range of 60 to 225°, a specific volume range of approximately 27 to 107 cc. per gram, and a pressure range of approximately 7.5 to 38 atmospheres.

2. An equation of the Keyes type has been fitted to these data; this equation is

$$p = \frac{RT}{(v-\delta)} - \frac{17{,}940}{(v+1.759)^2}$$

where $\log_{10}\delta = 1.0548 - 6.120/v$. This equation reproduces the observed pressures satisfactorily.

AUSTIN, TEXAS RECEIVED JUNE 12, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF DELAWARE]

Some Properties of the Dioxane–Ethanol System

BY ROBERT N. HOPKINS, EARLE S. YERGER AND CECIL C. LYNCH

In recent years considerable attention has been given to the solvent dioxane, and the dioxane–water system.[1,2] It was believed that a study of the dioxane–ethanol system also should prove interesting. Accordingly some of the properties—densities, refractive indices, viscosities, and boiling points—of the dioxane–ethanol system have been determined.

Preparation of Materials. Dioxane.—Technical 1,4-dioxane from the Eastman Kodak Co. was purified by the method described by Eigenberger.[3] The product was kept over metallic sodium, from which it was distilled when needed.

Ethanol.—Commercial absolute ethanol was refluxed for twenty-four hours over lime and barium oxide, and distilled from the mixture. The product was treated with metallic sodium to remove remaining water and the redistilled product was used. This alcohol had a density at 25° of 0.7852.

Density Measurements.—All solutions were prepared by direct weighing in glass-stoppered flasks, and measurements were made on the freshly prepared mixtures. Two pycnometers of approximately 50 cc. each were employed. The pycnometers with solutions were allowed to reach equilibrium (requiring twenty to thirty minutes) at 25.00 ± 0.05° in a water thermostat. Each value is the result of four independent measurements; the precision ±0.02%. Data are given in Table I.

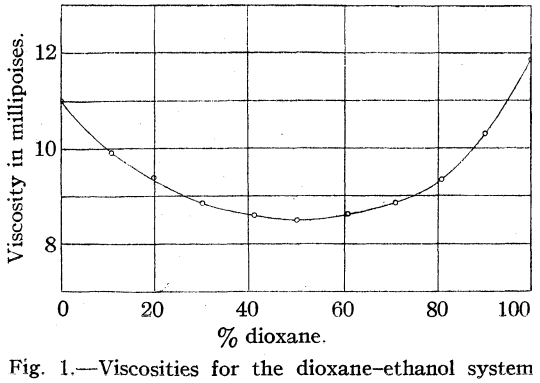


Fig. 1.—Viscosities for the dioxane–ethanol system at 25°.

Refractive Indices.—Solutions used were those prepared for the density measurements. An Abbe refractometer accurate to ±0.0002 unit of refractive index was employed using sodium light as a source of illumination. Each value is the mean of four measurements. Data are included in Table I.

Viscosity Measurements.—The solutions used were those prepared under density measurements. The Ostwald modification of the Poiseuille viscosimeter was used, care being taken to introduce the same volume (7 cc.) of liquid for each measurement. Timing was accurate to ±0.2 second. Each value given is the mean of at least five measurements. Data are given in Table I and in Fig. 1.

TABLE I

DENSITIES, REFRACTIVE INDICES, AND VISCOSITIES FOR THE DIOXANE–ETHANOL SYSTEM AT 25.00 ± 0.05°

% dioxane	Mole fraction dioxane	Refractive index, n_D	Density, d^{25}_4	Viscosity, millipoises
0.00	0.0000	1.3597	0.7852	11.00
5.54	.0298	1.3619	.7960	
10.84	.0584	1.3648	.8067	9.92
15.78	.0893	1.3671	.8166	
20.00	.1156	1.3694	.8252	9.38
25.27	.1503	1.3718	.8361	
30.05	.1834	1.3745	.8463	8.84
35.68	.2250	1.3774	.8584	
41.13	.2678	1.3810	.8706	8.60
45.66	.3052	1.3830	.8808	
50.04	.3438	1.3859	.8912	8.49
54.02	.3809	1.3884	.9008	
60.74	.4473	1.3926	.9172	8.63
70.77	.5589	1.3991	.9429	8.85
80.82	.6890	1.4058	.9700	9.33
90.11	.8264	1.4125	.9966	10.29
95.02	.9088	1.4159	1.0116	
100.00	1.0000	1.4201	1.0276	11.84

A minimum viscosity was observed in the neighborhood of 50% dioxane.

Boiling Points.—Measurements were made using the Othmer apparatus.[4] Mixtures of approximate composi-

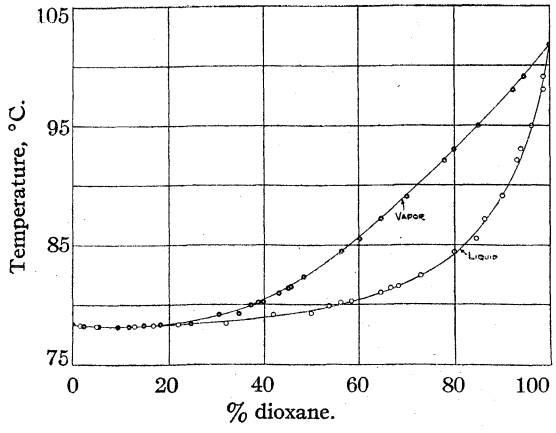


Fig. 2.—Boiling point-composition diagram for the dioxane–ethanol system at 760 mm. pressure.

(1) Åkerlöf and Short, THIS JOURNAL, **58**, 1241 (1936).
(2) Hovorka, Schaefer and Dreisbach, *ibid.*, **58**, 2263 (1936).
(3) Eigenberger, *J. prakt. Chem.*, **130**, 75 (1931).
(4) Othmer, *Ind. Eng. Chem.*, **20**, 743 (1928).

tion were introduced into the apparatus and runs were made until equilibrium had been established between liquid and vapor phases. This required three to four hours for each run. Temperatures were measured with a thermometer (0–110°) with 0.1° divisions, which was checked frequently for accuracy, the precision ±0.03°. Pressure correction to one atmosphere and stem corrections were made for all readings. The equilibrium residue and distillate were analyzed through refractive index. Data are given in Table II, and Fig. 2 shows the boiling point–composition diagram for the system.

TABLE II

BOILING POINT–COMPOSITION DATA FOR THE DIOXANE–ETHANOL SYSTEM AT ONE ATMOSPHERE

B. p., °C.	% dioxane Liquid	Vapor
78.32	Ethanol	
78.22	1.5	2.2
78.19	5.0	5.3
78.13 (min.)	9.3	9.3
78.17	13.0	11.7
78.23	16.8	14.8
78.35	22.0	18.3
78.36	32.0	24.7
79.10	42.0	30.5
79.87	54.0	37.3
80.15	56.5	38.7
80.18	58.5	39.7
80.93	64.7	43.3
81.32	66.7	45.1
81.40	68.5	45.5
82.33	73.0	48.4
84.42	79.9	56.5
85.43	84.8	60.3
87.17	86.4	64.9
89.08	90.2	70.5
92.02	93.3	78.0
93.00	94.0	80.0
94.89	96.3	85.0
97.99	98.7	92.5
99.05	98.8	94.8
101.07	Dioxane	

A minimum boiling point of 78.13° was observed for the composition 9.3% dioxane.

Summary

1. Density, refractive index and viscosity data for the dioxane–ethanol system have been presented. The viscosity curve apparently passes through a minimum in the vicinity of 50% dioxane.

2. Boiling points and the boiling point–composition diagram for the dioxane–ethanol system have been determined. A minimum boiling temperature of 78.13° was observed at 9.3% dioxane.

NEWARK, DELAWARE RECEIVED JULY 8, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF COLUMBIA UNIVERSITY]

The Synthesis of 1,4-Dimethyl-6,7-dihydroxyphenanthrene from *para*-Xylylacetic Acid and 6-Nitroveratraldehyde by the Pschorr Reaction

BY JACK TARKINGTON CASSADAY[1] AND MARSTON TAYLOR BOGERT

Eddy[2] has reported that phenanthrene derivatives carrying a hydroxyl group on carbon no. 3 (no. 6 in our formula) are likely to possess analgesic properties in higher degree than when this group is in other positions on the phenanthrene nucleus.

Small, Eddy, Mosettig and Himmelsbach[3] state that: "No generalizations can be made as to the influence on pharmacological action of the entrance of another substituent in a given monosubstituted phenanthrene. The changes in pharmacological action are very likely dependent to some extent upon changes in chemical or physical properties, among others, differences in acidity or basicity, and in solubility. There was a decided increase in effectiveness from 3-hydroxyphenanthrene to 3,4-dihydroxyphenanthrene, but at the same time also, from 3-hydroxyphenanthrene to 3-hydroxy-4-aminophenanthrene."

So far as our examination of the literature has gone, the hydroxyphenanthrenes reported to date are all insoluble in water, and but few of them are appreciably soluble in cold olive oil.

We have therefore synthesized the 1,4-dimethyl-6,7-dihydroxyphenanthrene (V), in order that its physical, chemical, and pharmacological properties can be studied. It is a white crystalline solid, m. p. 164–164.5° (corr.), appreciably soluble in water, and dissolving in cold olive oil.

In a previous communication[4] from these Laboratories, we reported some unsuccessful attempts to obtain this compound by the hydrolysis of the 1,4-dimethyl-6,7-methylenedioxyphenan-

(1) Ferguson Fellow, Columbia University, 1938–1939.

(2) Eddy, *J. Pharmacol.*, **48**, 183 (1933); **51**, 75 (1934).

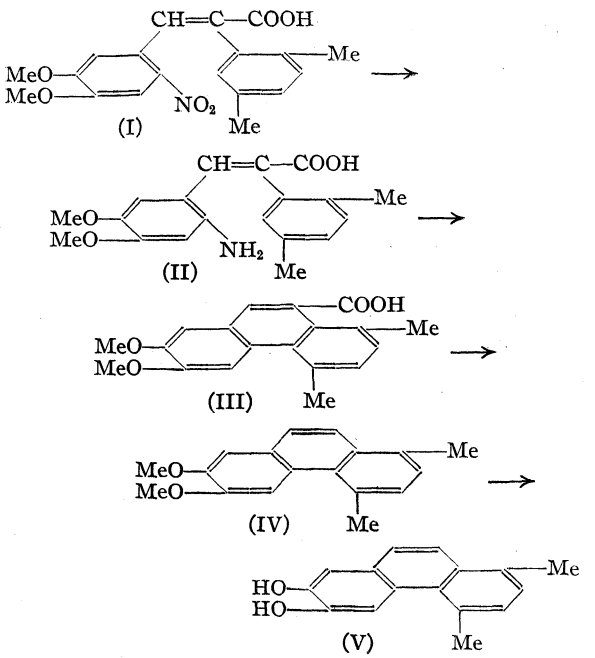
(3) Small, Eddy, Mosettig and Himmelsbach, "Studies on Drug Addiction," *U. S. Pub. Health Repts., Suppl.* No. **138**, 143 pp., 1938, p. 71.

(4) Akin and Bogert, THIS JOURNAL, **59**, 1564 (1937).

threne. Whereas the methylenedioxy group resisted our efforts at hydrolysis, the corresponding dimethoxy compound has been found to be more tractable, and yielded the desired dihydroxy derivative when digested with a mixture of glacial acetic and hydrobromic (48%) acids.

The synthesis followed the classical Pschorr lines, with a few modifications α-(*p*-xylyl)-6-nitrodimethylcaffeic acid (I), from *p*-xylylacetic acid and 6-nitroveratraldehyde, was reduced to the corresponding amine (II) by ferrous sulfate and ammonium hydroxide. Cyclization was accomplished, in dioxane solution containing some sulfuric acid, by the action of isoamyl nitrite, with the subsequent addition of copper powder and sodium hypophosphite. By refluxing the acid (III) with quinaldine and basic copper carbonate, it was decarboxylated, and the dimethoxy compound (IV) then hydrolyzed to the dihydroxy derivative (V). It was found possible also to accomplish a simultaneous decarboxylation and hydrolysis of the dimethoxy acid (III) to the dihydroxy hydrocarbon (V), but the yield of the latter was not very good.

Acknowledgments.—We are happy to have this opportunity of expressing our thanks to the Ella Sachs Plotz Foundation and to the National Academy of Sciences for financial assistance in the purchase of the necessary chemicals and apparatus to carry out this investigation, as well as to Mr. Saul Gottlieb for the analytical work.



Experimental

6-Nitroveratraldehyde was prepared as described by Marr and Bogert,[5] with certain modifications which increased the yield and reduced the time required.

To 300 cc. of concentrated nitric acid (sp. gr., 1.42), there was added in small portions 30 g. of finely pulverized veratraldehyde in thirty minutes, with vigorous mechanical stirring, maintaining the temperature of the mixture at 15–20°. After stirring for an additional half hour at 25–30°, the mixture was poured into about 9 liters of ice water, the precipitate collected, washed with an additional 9 liters of ice water, pressed dry on the filter, and immediately crystallized from ethyl alcohol without further drying; yield 87%, m. p. 132–133° (corr.) (lit.,[4] 133.5–134.5°, corr.). The nitrations and crystallizations can be conducted in artificial light without any appreciable reduction in yield.

α-(*p*-Xylyl)-6-nitrodimethylcaffeic Acid (I).—A solution of *p*-xylylacetic acid (156 g.), prepared according to the procedure of Akin, Stamatoff and Bogert,[6] and 6-nitroveratraldehyde (166.5 g.), in freshly distilled acetic anhydride (1110 cc.), was heated to 105–110° and stirred for eight hours under a reflux condenser carrying a calcium chloride guard tube. Excess of acetic anhydride was hydrolyzed by the addition of hot water, keeping the temperature of the mixture below 120°. It was then poured into a mixture (7 liters) of water, crushed ice, and a little hydrochloric acid. The tarry material which separated became crystalline on standing. It was removed, boiled with water (3–4 liters), to eliminate unchanged initial materials, and crystallized from dilute acetic acid. It separated as a pale tan solid, m. p. 221–224° (corr.), sufficiently pure for use in the next step; yield 61%. After three more crystallizations from the same solvent, it appeared as pale greenish crystals, m. p. 226–227° (corr.); yield 50–55%.

Anal. Calcd. for $C_{19}H_{19}O_6N$: C, 63.9; H, 5.3; N, 3.9. Found: C, 63.8; H, 5.7; N, 4.2.

α-(*p*-Xylyl)-6-aminodimethylcaffeic Acid (II).—A solution of 80 g. of the nitro acid (I) in dilute ammonium hydroxide solution was added, in the course of three to four minutes, to a boiling solution of 440 g. of ferrous sulfate heptahydrate and 100 cc. of ammonium hydroxide solution in 1275 cc. of water. During this addition and for the next half hour, 780 cc. of concentrated ammonium hydroxide solution was slowly run into the boiling mixture, followed by 200 cc. more of the ammonium hydroxide solution for the succeeding forty-five minutes. To prevent foaming, five drops of octyl alcohol was added. When the mixture had cooled, the upper portion was siphoned off through a filter, and the black residues extracted thrice with dilute ammonium hydroxide solution, filtered through Norite, and the combined filtrates poured into a slight excess of dilute acetic acid containing ice. The precipitated amino acid was collected, redissolved in ammonium hydroxide solution and reprecipitated, the mixture heated to boiling, cooled, and the amino acid filtered out; yield 76%, m. p. 185–186° (corr.). Recrystallized twice from benzene, it formed pale yellow crystals, m. p. 191–192° (corr.); yield, 65% or better.

(5) Marr and Bogert, THIS JOURNAL, **57**, 1329 (1935).

(6) Akin, Stamatoff and Bogert, THIS JOURNAL, **59**, 1268 (1937).

Anal. Calcd. for $C_{19}H_{21}O_4N$: C, 69.7; H, 6.4. Found: C, 69.6; H, 6.5.

1,4-Dimethyl-6,7-dimethoxyphenanthrene-10-carboxylic Acid (III).—In our experience with the Pschorr reaction, we have found that, in the cyclization of the *o*-aminocinnamic acids, hydroxy acids are formed often instead of the phenanthrene sought. By carrying out the diazotization in dioxane as the solvent, and using sodium hypophosphite as recommended by Ruggli and Staub,[7] in the second step of the reaction, it has been possible to effect the cyclization without this complication. In this particular series (II), a large excess of dioxane was found requisite to prevent the separation of solid oxonium compounds formed from the sulfuric acid and the dioxane. In other series, this trouble has not been encountered.

To a solution of 44 g. of the amino acid in 850 cc. of dioxane, there was added 10 cc. of concentrated sulfuric acid, followed by 25.2 cc. of isoamyl nitrite when the solution had cooled to room temperature. The nitrite used was washed with dilute sodium bicarbonate solution, followed by a saturated sodium chloride solution, and dried over sodium sulfate. The diazo solution solidified, after about thirty minutes of stirring at 25–30°. To a solution of 139 g. of sodium hypophosphite in 139 cc. of water, there was added some freshly prepared Gattermann copper powder. The mixture was heated to incipient ebullition, cooled to 50°, and the mush of diazo compound added during thirty minutes, while the temperature was kept at 40–50°. After all of the diazo compound had been added, the mixture was heated to 80° for a short time and then poured into six liters of water containing sufficient ammonium hydroxide to assure solution of the acid. The filtered solution was run into 15 liters of very dilute hydrochloric acid containing ice, the precipitated acid removed, and dried, first in the air and then at 105°; yield of crude acid, sufficiently pure for the next step, 83%. By recrystallization from methanol, or from dilute acetic acid, and decolorization with Norite, the acid was obtained in colorless crystals, m. p. 215.5–216.5° (corr.).

Anal. Calcd. for $C_{19}H_{18}O_4$: C, 73.5; H, 5.8. Found: C, 73.2; H, 6.1.

1,4-Dimethyl-6,7-dimethoxyphenanthrene (IV).—A mixture of 1 g. of the crude acid (III), 3 cc. of freshly distilled quinaldine, and 0.2 g. of basic copper carbonate, was refluxed for forty-five minutes, then cooled, extracted with ether, the ether solution washed first with dilute hydrochloric acid, to remove quinaldine, and then with dilute potassium hydroxide solution, to free it from unchanged acid. Glacial acetic acid was added, the ether distilled off, and the residual solution diluted with water. The gummy precipitate which separated, when crystallized from alcohol, yielded 45% of the pure dimethoxy hydrocarbon (IV). Recrystallized from alcohol, in the presence of Norite, it formed glistening white platelets, m. p. 175–176° (corr.).

(7) Ruggli and Staub, *Helv. Chim. Acta*, **20**, 37 (1937).

Anal. Calcd. for $C_{18}H_{18}O_2$: C, 81.2; H, 6.8. Found: C, 80.9; H, 7.0.

1,4-Dimethyl-6,7-dihydroxyphenanthrene (V).—A mixture of 1.6 g. of the dimethoxy derivative (IV), 49 cc. of glacial acetic acid, and 49 cc. of hydrobromic acid (48%), was refluxed for two hours in an all-glass apparatus, and the cold green solution poured into 300–350 cc. of water. After the mixture had stood for fifteen to twenty minutes, the precipitate was collected and crystallized thrice from water, filtering the hot solutions through cotton and filter paper at first, to remove tarry contaminants. It also could be recrystallized from hot alcohol solution by the gradual addition of water. The pure compound formed white crystals, m. p. 164–164.5° (corr.); yield 35%. With ferric chloride solution, it gave an intense green, like catechol, which was changed to a pink or reddish color by the addition of sodium hydroxide or ammonium hydroxide solutions.

Anal. Calcd. for $C_{16}H_{14}O_2$: C, 80.7; H, 5.9. Found: C, 80.8; H, 6.0.

The same compound (mixed m. p., etc.) was secured in one operation from the dimethoxy acid (III), when 0.93 g. of it was refluxed for two hours in a mixture of 31 cc. of glacial acetic acid and 31 cc. of hydrobromic acid (48%), and the crude product purified as above, but the yield was only 10–15% in the different runs.

In 100 cc. of water, the solubility of the pure compound at various temperatures (±2°) was as follows: 100°, 0.038 g.; 37°, 0.007 g.; 0°, 0.003 g. The *p*H of the saturated aqueous solution was 6.4 (±0.2). In alcohol, glycol, or acetone, it was easily soluble, and dissolved also in cold olive oil.

Diacetyl Derivative.—From the dihydroxy derivative (V), acetic anhydride and fused sodium acetate, after repeated crystallization from dilute acetic acid, formed white crystals, m. p. 133–133.5° (corr.).

Anal. Calcd. for $C_{20}H_{18}O_4$: C, 74.5; H, 5.6. Found: C, 74.8; H, 5.9.

Summary

1. 1,4-Dimethyl-6,7-dihydroxyphenanthrene has been synthesized by the Pschorr reaction and found to be slightly soluble in water, and to dissolve also in cold olive oil.

2. In the application of the Pschorr reaction, dioxane has been found preferable to alcohol as a solvent for the diazotization.

3. 1,4-Dimethyl-6,7-dimethoxyphenanthrene-10-carboxylic acid can be hydrolyzed and decarboxylated simultaneously by refluxing with a mixture of glacial acetic and hydrobromic (48%) acids, but the yields are not very good.

NEW YORK, N. Y. RECEIVED JULY 10, 1939

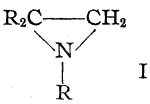
[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Attempts to Prepare Optically Active Ethyleneimine Derivatives Containing an Asymmetric Nitrogen Atom

BY ROGER ADAMS AND T. L. CAIRNS[1]

The fact that many oximes exist in stable *syn-* and *anti*-forms and that the oxime of cyclohexanone-4-carboxylic acid[2] can be resolved has led to the belief that, in these compounds, the nitrogen atom probably exists in a stable tetrahedral form. The work of Meisenheimer[3] has established that many substituted hydroxylamines of the type RR'NOH cannot be resolved and the investigations of many others have failed to find an optically-active compound of the type RR'R''N.

A factor which has been assumed to be responsible for the existence of a stable tetrahedral nitrogen atom thus resulting in stable *syn-* and *anti*-oximes is the strain of the carbon-to-nitrogen double bond. A molecule which reproduces this strain as closely as possible and, at the same time, is constituted so that the nitrogen atom is the only possible source of asymmetry in the molecule is represented by a substituted ethyleneimine of the type I.



I

This report deals with the preliminary work on the synthesis of such a molecule and the determination of whether or not it may exist in optically-active forms.

It was found that the *p*-bromobenzenesulfonyl derivative of 1-amino-2-methyl-2-propanol (II) can be converted into the corresponding chloro compound (III) by means of concentrated hydrochloric acid. The chloro compound, when treated with aqueous alkali, yielded a mixture of the ethyleneimine derivative (IV) and the alcohol (II).

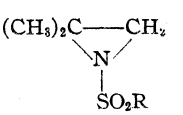
$(CH_3)_2COHCH_2NHSO_2R$

II

R = *p*-bromophenyl

$(CH_3)_2CClCH_2NHSO_2R$

III

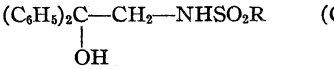


IV

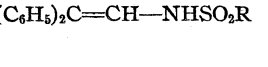
Attempts were made to prepare an optically-active amide analogous to II by the use of camphorsulfonyl chloride or α-bromocamphorsulfonyl chloride. Unfortunately, these derivatives proved to be oils which could not be purified and were consequently unsuitable for further study. The corresponding diphenyl compound, aminomethyldiphenylcarbinol, also gave no crystalline α-bromocamphorsulfonamide.

A comparison of the action of aqueous alkali, under similar conditions, upon the *p*-bromobenzenesulfonyl derivative of β-chloroethylamine and the dimethyl compound (III) was studied. The former gave merely hydrolysis with the formation of 2-*p*-bromobenzenesulfonamidoethanol, whereas the latter gave essentially equivalent amounts of the alcohol (II) and the ethyleneimine derivative (IV). This result might have been anticipated from a consideration of the work of Thorpe.[4] He showed that the *gem*-dimethyl group in place of two hydrogens alters the subtended angle between the valence bonds of carbon in such a manner that the ease of formation of a three-membered ring is increased.

Attempts to convert the *p*-bromobenzenesulfonyl derivative of aminomethyldiphenylcarbinol (V) into an ethyleneimine derivative proved fruitless. The corresponding chloride could not be made by the regular procedure using thionyl chloride or hydrochloric acid. The action of thionyl chloride resulted in the formation of 1-*p*-bromobenzenesulfon-2,2-diphenylvinylamide (VI). This same compound was produced in excellent yields by the action of phosphorus pentoxide on V.



V



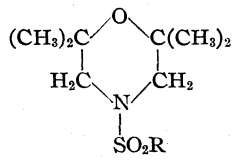
VI

A reaction analogous to this has been reported by Krabbe[5] who found that similar products were formed by the action of certain acid chlorides or of phosphorus pentoxide on N-acyl derivatives of aminomethyldiphenylcarbinol.

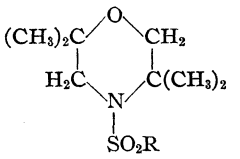
The action of phosphorus pentoxide on 1-*p*-bromobenzene-sulfonamido-2-methyl-2-propanol (II) gave neither the ethyleneimine (IV) nor the

(1) Solvay Process Company Fellow, 1938–1939.
(2) Mills and Bain, *J. Chem. Soc.*, **97**, 1866 (1910).
(3) Meisenheimer, *Ber.*, **65B**, 1799 (1932).
(4) Thorpe, "Annual Reports on the Progress of Chemistry," The Chemical Society, London, **22**, 127 (1925).
(5) Krabbe, *Ber.*, **72B**, 381 (1939).

vinylamine derivative corresponding to VI. Instead, a substance was produced which, by analysis and properties appeared to be a morpholine of structure VII or VIII.



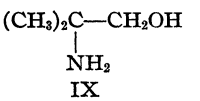
VII



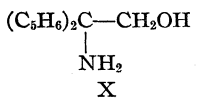
VIII

The action of sulfuric acid followed by alkali on ethanolamine has been reported to give ethyleneimine.[6] Upon treatment of 1-amino-2-methyl-2-propanol in a similar manner the reaction took a different course and β-methylallylamine was formed in good yields. Krabbe[5] found that aminomethyldiphenylcarbinol is converted by cold sulfuric acid into the corresponding vinylamine.

It is quite possible that the complications which have arisen in the formation of ethyleneimine derivatives may be avoided if the compounds IX and X are used. Under these conditions



IX



X

the possibility of dehydration to form an allylamine or a vinylamine derivative is unlikely and the synthesis of an ethyleneimine derivative should be possible.

During the preparation of this manuscript an article by Meisenheimer and Chou[7] has appeared describing attempts to prepare ethyleneimines for resolution studies. They were unsuccessful in obtaining the compounds desired, so that the possibility of resolving properly substituted ethyleneimines is still undetermined.

Experimental

2-*p*-Bromobenzenesulfonamidoethanol.—To a solution of 15 g. of ethanolamine in 150 cc. of water and 125 cc. of aqueous 10% sodium hydroxide solution, maintained at 50–70°, was added slowly 51 g. of *p*-bromobenzenesulfonyl chloride. Upon cooling the reaction mixture and acidification with hydrochloric acid an oil separated that solidified to a white crystalline solid. It was purified by recrystallization from dilute ethanol: white crystals, m. p. 93.5–95° (corr.); yield, 28 g. (59%).

Anal. Calcd. for $C_8H_{10}O_3BrNS$: C, 34.29; H, 3.57. Found: C, 34.59; H, 3.73.

2-*p*-Bromobenzenesulfonamido-1-chloroethane.—To 10 g. of 2-*p*-bromobenzenesulfonamidoethanol was added slowly 30 cc. of thionyl chloride and the mixture was then refluxed for thirty minutes. The solution was poured with rapid stirring into 300 cc. of crushed ice. The product was purified from methanol: white plates, m. p. 150–152.5° (corr.); yield, 3 g. (28%).

Anal. Calcd. for $C_8H_9O_2BrClNS$: C, 32.17; H, 3.01. Found: C, 32.12; H, 3.03.

When 3 g. of this product was shaken for fifteen minutes and then warmed on the steam cone for two hours with 200 cc. of water and 20 cc. of 10% aqueous potassium hydroxide hydrolysis took place. After filtration the filtrate, while still hot, was acidified with hydrochloric acid. White crystals of 2-*p*-bromobenzenesulfonamidoethanol separated.

1-*p*-Bromobenzenesulfonamido-2-methyl-2-propanol.—To a solution of 17.8 g. of 1-amino-2-methyl-2-propanol in 125 cc. of 10% aqueous sodium hydroxide, maintained at 50–80°, was added slowly 51 g. of *p*-bromobenzenesulfonyl chloride. The mixture was then cooled and acidified with dilute hydrochloric acid. After filtering and drying, the product was dissolved in 250–300 cc. of benzene and the solution distilled until a volume of 75–80 cc. remained. White crystals separated which were recrystallized from benzene, m. p. 96.5–98° (corr.); yield, 40 g. (96%).

Anal. Calcd. for $C_{10}H_{14}O_3BrNS$: C, 38.96; H, 4.58; N, 4.54. Found: C, 38.96; H, 4.50; N, 4.79.

When 6 g. of this product was heated under reflux for twenty minutes with 10 cc. of constant-boiling hydrobromic acid, a black oil separated. Steam distillation removed a small amount of a water-insoluble oil which was not identified. The residual solution in the distillation flask, after cooling, gave 4.5 g. (97%) of *p*-bromobenzenesulfonamide.

Action of Phosphorus Pentoxide upon 1-*p*-Bromobenzenesulfonamido-2-methyl-2-propanol, VII or VIII.—A solution of 5 g. of 1-*p*-bromobenzenesulfonyl-2-methyl-2-propanol in 100 cc. of dry benzene was refluxed for an hour with 20 g. of phosphorus pentoxide. The benzene was decanted and then steam distilled. The residual aqueous suspension was made up to a volume of 200 cc., boiled and filtered. A pale yellow solid (2.2 g.) was obtained which on crystallization from methanol gave white needles, m. p. 145–147° (corr.).

Anal. Calcd. for $C_{14}H_{20}O_3BrNS$: C, 46.4; H, 5.54; N, 3.87; S, 8.85. Found: C, 46.92; H, 5.53; N, 4.09; S, 8.95.

The filtrate from this product gave, on cooling, *p*-bromobenzenesulfonamide.

In attempting to prepare 1-*p*-bromobenzenesulfonamido-2-methyl-2-chloropropane from the alcohol by means of thionyl chloride, there was always obtained a small amount of the morpholine derivative as a by-product.

1-*p*-Bromobenzenesulfonamido-2-methyl-2-chloropropane.—A mixture of 24 g. of 1-*p*-bromobenzenesulfonamido-2-methyl-2-propanol was heated with 150 cc. of concentrated hydrochloric acid under reflux for ten minutes. Solution took place with simultaneous separation of a white solid. After dilution with one liter of water, the suspension was cooled and the product filtered and air-dried. It was purified by recrystallization from petroleum ether (b. p. 60–110°): white leaflets, m. p. 123–128° (corr.); yield, 21 g. (71%).

(6) Wenker, THIS JOURNAL, **57**, 2328 (1935).

(7) Meisenheimer and Chou, *Ann.*, **539**, 70 (1939).

Anal. Calcd. for $C_{10}H_{13}O_2BrClNS$: C, 36.70; H, 3.98. Found: C, 36.99; H, 3.97.

1-*p*-Bromobenzenesulfon-2,2-dimethylethyleneimide.—A mixture of 80 cc. of 10% aqueous sodium hydroxide and 18 g. of 1-*p*-bromobenzenesulfonamido-2-methyl-2-chloropropane was shaken vigorously for one hour. It was then warmed on the steam-cone for fifteen minutes during which time the solid present melted and collected as a yellow oil. On cooling, it resolidified and was purified from a mixture of petroleum ether (b. p. 40–60°) and chloroform: white cubic crystals, m. p. 79.5–81.5° (corr.); yield, 7.5 g. (46%).

Anal. Calcd. for $C_{10}H_{12}O_2BrNS$: C, 41.37; H, 4.13; mol. wt., 290. Found: C, 41.50; H, 4.06; mol. wt. (b. p. $CHCl_3$), 274.

This product is insoluble in aqueous alkali, does not react with a chloroform solution of bromine or with aqueous potassium permanganate in the cold.

The filtrate from the preparation of this compound gave, upon acidification, 6 g. of 1-*p*-bromobenzenesulfonamido-2-methyl-2-propanol.

If the chloro compound was refluxed with alcoholic potash instead of aqueous, a yellow oil was obtained, insoluble in aqueous alkali, the constitution of which was not determined. In addition hydrolysis of the chloro compound to the alcohol took place.

β-Methylallylamine.[6]—A solution of 40 cc. of concentrated sulfuric acid in 100 cc. of water, cooled to below 10°, was poured into a cold solution of 70 g. of 1-amino-2-methyl-2-propanol in 100 cc. of water. The mixture was distilled at 30 mm. pressure until the temperature of the solution reached 120°; the distillation was continued at 5 mm. at a temperature of 145° for one hour. A brown viscous liquid remained. After cooling 400 cc. of aqueous 40% sodium hydroxide was added and the mixture distilled rapidly until the distillate became milky. The distillate was dried over solid sodium hydroxide and then distilled through a fractionating column. There was thus obtained 33 g. of β-methylallylamine; b. p., after fractionation, 76.7–77.7° at 746 mm.; $n^{20}D$ 1.4312.

Anal. Calcd. for C_4H_9N: N, 19.76. Found: N, 19.45.

β-Methylallylamine Hydrochloride.—This was prepared in dry ether and purified from a mixture of absolute ethanol and acetone; m. p. 190–191° (corr.).

Anal. Calcd. for $C_4H_{10}NCl$: N, 13.02. Found: N, 12.91.

β-Methylallylamine Picrate.—The picrate formed in ethanol solution and purified from dilute ethanol had a melting point of 202–206° (corr.).

Anal. Calcd. for $C_{10}H_{12}O_7N_4$: N, 18.66. Found: N, 18.48.

N-(β-Methylallyl)-*p*-bromobenzenesulfonamide.—This product was prepared from β-methylallylamine and *p*-bromobenzenesulfonyl chloride and formed white crystals from a mixture of petroleum ether (b. p. 40–60°) and chloroform; m. p. 74–76° (corr.).

Anal. Calcd. for $C_{10}H_{12}O_2BrNS$: C, 41.37; H, 4.13; N, 4.82. Found: C, 41.46; H, 4.13; N, 4.96.

N-Phenyl-N'-(β-methylallyl) Thiourea.—This product was prepared from phenyl isothiocyanate and β-methylallylamine and purified from dilute ethanol; white crystals, m. p. 78–79° (corr.).

Anal. Calcd. for $C_{11}H_{14}N_2S$: N, 13.59. Found: N, 13.34.

N-(β-Methylallyl)-phthalimide.—A mixture of 28 g. of potassium phthalimide and 18 g. of β-methylallyl chloride was heated in a sealed tube at 150° for three hours. The reaction product was transferred to a flask by treatment with benzene, and the benzene and excess β-methylallyl chloride were removed by steam distillation. The brown solid which remained behind was purified by crystallization from methanol with norite; white crystals, m. p. 88.5–90° (corr.).

Anal. Calcd. for $C_{12}H_{11}O_2N$: N, 6.96. Found: N, 6.90.

This product was hydrolyzed to β-methylallylamine as follows. A solution of 4 g. of N-(β-methylallyl)-phthalimide in 15 cc. of ethanol was allowed to stand for twenty-four hours with 2.5 g. of 40% aqueous solution of hydrazine hydrate. The solution was then acidified with hydrochloric acid and concentrated to a small volume. The precipitate of phthalyl hydrazide was filtered and the filtrate made basic with aqueous sodium hydroxide. Upon distillation β-methylallylamine was obtained. The product from the action of sulfuric acid upon 1-amino-2-methyl-2-propanol proved to be identical with it.

1-*p*-Bromobenzenesulfonamido-2,2-diphenyl-2-ethanol.—A solution of 9 g. of *p*-bromobenzenesulfonyl chloride in 75 cc. of boiling benzene was added slowly to a hot solution of 8 g. of aminomethyldiphenylcarbinol[8] in 75 cc. of benzene and 5 cc. of pyridine. The mixture was allowed to stand at room temperature for twelve hours, then 2.2 g. of potassium hydroxide in about 50 cc. of water was added. The benzene and most of the pyridine was removed by steam distillation and the pale yellow residue purified from dilute methanol: white crystals, m. p. 151–153° (corr.); yield, 16 g. (quantitative).

Anal. Calcd. for $C_{20}H_{18}O_3BrNS$: C, 55.55; H, 4.17. Found: C, 55.65; H, 4.16.

1-*p*-Bromobenzenesulfon-2,2-diphenylvinylamide.—A mixture of 50 cc. of thionyl chloride and 5 g. of 1-*p*-bromobenzenesulfonamido-2,2-diphenyl-2-ethanol was refluxed for thirty minutes. The solution was then poured into 400 cc. of ice. The 4.5 g. of brown gummy material was dissolved in acetone and precipitated with water after which it was extracted with petroleum ether (b. p. 60–110°). The petroleum ether insoluble residue was crystallized from dilute acetone; white plates, m. p. 197–198°.

Anal. Calcd. for $C_{20}H_{16}O_2BrNS$: C, 57.97; H, 3.87; S, 7.73; Br, 19.34. Found: C, 58.08; H, 3.93; S, 7.59; Br, 19.04.

The product also could be obtained by refluxing for thirty minutes 2 g. of 1-*p*-bromobenzenesulfonamido-2,2-diphenyl-2-ethanol in 200 cc. of benzene with 10 g. of phosphorus pentoxide.

The product was soluble in hot aqueous alkali.

By heating for one hour a mixture of 1 g. of this compound with 5 g. of chromic anhydride in 30 cc. of glacial acetic acid and then pouring into ice water, benzophenone

(8) Paal and Weidenkaff, *Ber.*, **38**, 1686 (1905).

was obtained. 1-*p*-Bromobenzenesulfon-2,2-diphenylvinylamide dissolved in chloroform reacted rapidly with a chloroform solution of bromine with the evolution of hydrogen bromide.

Summary

1. An investigation has been undertaken to determine whether ethyleneimine derivatives of the type $R_2C\text{—}CH_2\text{—}NR$ can be resolved.

2. Preliminary experiments have indicated that the *p*-bromobenzenesulfonyl derivatives of 1-amino-2-methyl-2-propanol can be converted to the chloride and then to the corresponding ethyleneimine. The replacement of the *p*-bromobenzenesulfonyl group with an optically active sulfonyl group has not yet been successful, since the compounds produced were oils and could not be purified. Corresponding treatment of the *p*-bromobenzenesulfonyl derivative of ethanolamine did not result in the formation of an ethyleneimine.

3. The *p*-bromobenzenesulfonyl derivative of aminomethyldiphenylcarbinol upon treatment with phosphorus pentoxide or thionyl chloride gave 1-*p*-bromobenzenesulfon-2,2-diphenylvinylamide. Similar treatment of 1-*p*-bromobenzenesulfonamido-2-methyl-2-propanol gave what appeared to be a morpholine derivative.

4. Action of sulfuric acid on 1-amino-2-methyl-2-propanol gave β-methylallylamine.

URBANA, ILLINOIS RECEIVED JULY 10, 1939

[CONTRIBUTION FROM THE SQUIBB INSTITUTE FOR MEDICAL RESEARCH, DIVISION OF ORGANIC CHEMISTRY]

The Isolation of α-Spinasterol from Alfalfa

BY ERHARD FERNHOLZ AND MILDRED L. MOORE

In the course of experiments directed toward the isolation of vitamin K from alfalfa, small amounts of a crystalline sterol were obtained regularly. After a number of recrystallizations it melted at 168°. It was characterized as a sterol by the formation of a digitonide, and by positive Liebermann, Salkowski, and Tortelli-Jaffé reactions. The properties of this sterol suggested to us the possibility that it might be identical with α-spinasterol[1] which was first isolated from spinach,[1] and also has been found in senega root.[2] There is little doubt that the sterol isolated by Dam[3] from alfalfa under similar circumstances and called by him medicagosterol II is in fact α-spinasterol.

The constants observed by us, by Dam, and the latest values for α-spinasterol as recorded by Larsen and Heyl[4] are given in Table I.

TABLE I

	Fernholz and Moore alfalfa sterol		Dam, *et al.* medicagosterol II		Larsen and Heyl α-spinasterol	
	M. p., °C.	$[\alpha]_D$	M. p., °C.	$[\alpha]_D$	M. p., °C.	$[\alpha]_{5461}$
Sterol	168	±0	164	−2.4	172.5	−3.7
Acetate	183	−5	173	...	187	−5.8
m-Dinitrobenzoate	195	±0	195	...	...	...

The data agree well enough if one takes into consideration the difficulties of obtaining the sterol in pure form. The melting point reported for α-spinasterol has gone up steadily in successive publications.

Further evidence for the identity of our sterol with α-spinasterol was obtained by studying its catalytic hydrogenation. Our sterol also took up only one mole of hydrogen using Adams catalyst. The compound obtained was still unsaturated and the melting point and rotation of the dihydrosterol and its acetate agreed well with those reported for α-spinasterol and its acetate. Titrations with perbenzoic acid were carried out, and it was found that 3 atoms of oxygen were consumed by the sterol itself and 2 atoms by the hydrogenated sterol. In the literature, on the other hand, it has been reported[4] that 2 or 1 atom, respectively, is used up. We are unable to explain this difference, but have obtained the same result with authentic α-spinasterol,[5] while stigmasterol under the same conditions consumed a little less oxygen than is calculated for two double bonds. It is not rare, however, that sterols use more perbenzoic acid than the number of double bonds would indicate. A pertinent example is dihydro-

(1) M. C. Hart and F. W. Heyl, *J. Biol. Chem.*, **95**, 311 (1932).
(2) J. C. E. Simpson, *J. Chem. Soc.*, 730 (1937).
(3) H. Dam, *et al.*, *Helv. Chim. Acta*, **22**, 313 (1939).
(4) Larsen and Heyl, THIS JOURNAL, **56**, 2663 (1934).
(5) We are greatly indebted to Dr. C. Donald Larsen, University of Rochester, for samples of α-spinasterol and its acetate. Mixed melting points with the corresponding derivatives of our sterol did not show a depression.

ergosterol[6] which contains two double bonds and which consumes 2.7 atoms of oxygen. Like α-spinasterol it also contains a double bond resistant to hydrogenation. We do not believe that our results should be interpreted to indicate the presence of three double bonds in α-spinasterol.

We have obtained 0.8 g. of α-spinasterol, m. p. 165°, from 3.8 kg. of alfalfa. Alfalfa meal is probably the most accessible source for this sterol.

Experimental

Isolation of α-Spinasterol.—By percolation with hexane 140 g. of an extract was obtained from 2.8 kg. of dehydrated alfalfa meal. This material was saponified by boiling for two hours with 50 g. of potassium hydroxide in 1 liter of alcohol. The unsaponifiable matter (28 g.) was isolated by ether extraction. It consisted of a dark brown waxy material. It was dissolved in 200 cc. of hot acetone, and the material coming out on cooling was removed by filtration and discarded. The filtrate was evaporated to dryness (20 g.), the residue dissolved in 200 cc. of hexane and washed five times in succession with 200 cc. of 95% methanol saturated with hexane. The combined methanol extracts left on evaporation a residue weighing 11 g. This residue was dissolved in 50 cc. of alcohol. After two days at room temperature the crystallized sterol was filtered and recrystallized from a mixture of alcohol and benzene; yield 0.8 g., m. p. 165°. It was recrystallized nine times more but the melting point could not be raised above 168°; melting point of a mixture with α-spinasterol (169–171°) 168–169°; $[\alpha]^{25}D \pm 0°$ (21.3 mg. in 2 cc. chloroform, $l = 1$ dm.). *Anal.* Calcd. for $C_{29}H_{48}O \cdot {}^1/_2H_2O$: C, 82.58; H, 11.70. Found: C, 82.70; H, 11.83.

α-Spinasteryl *m*-Dinitrobenzoate.—A sample of 0.1 g. of the above described α-spinasterol was heated on the steam-bath for one hour with 0.3 g. of dinitrobenzoyl chloride and 5 cc. of pyridine. The dinitrobenzoate was then isolated by means of ether and purified by crystallization from benzene by addition of alcohol as small white needles, m. p. 195°, $[\alpha]D \pm 0°$ (27.2 mg. in 2 cc. of chloroform, $l = 1$ dm.). *Anal.* Calcd. for $C_{36}H_{50}O_6N_2$: C, 71.24; H, 8.31. Found: C, 71.11; H, 8.39.

α-Spinasteryl acetate was prepared from the sterol isolated from alfalfa by refluxing with ten times the amount of acetic anhydride for one hour. The acetate crystallized out after cooling and was recrystallized from benzene by addition of alcohol, in which solvent it is but sparingly soluble; m. p. 183°, mixed with authentic material (184.5°) also 183°; $[\alpha]^{23}D - 5.3°$ (33.8 mg. in 2 cc. chloroform, $l = 1$ dm., $\alpha D - 0.09°$). *Anal.* Calcd. for $C_{31}H_{50}O_2$: C, 81.87; H, 11.09. Found: C, 81.74; H, 11.02.

α-Spinastenyl Acetate.—The acetate described above (0.5163 g.) was hydrogenated in acetic acid solution (50 cc.) at room temperature and ordinary pressure with a platinum oxide (0.1643 g.) the hydrogen consumption of which was known from a blank determination. The calculated amount of hydrogen (49.6 cc.) was absorbed within eighty minutes. The hydrogenation product was recrystallized from a benzene–alcohol mixture as large leaflets, m. p. 117°, $[\alpha]^{24}D + 15.3°$ (20.9 mg. in 2 cc. chloroform, $\alpha D + 0.16°$]. *Anal.* Calcd. for $C_{31}H_{52}O_2$: C, 81.58; H, 11.48. Found: C, 81.80; H, 11.74. The literature[4] reports m. p. 119°, $[\alpha]_{5461} + 12°$.

α-Spinastenol was obtained from the acetate by saponification with 5% alcoholic potassium hydroxide. It was purified by crystallization from methanol and obtained in the form of big leaflets. An air-dried sample melted on slow heating at 110°, a value also reported in the literature; immersion into a bath at 100° caused melting at that temperature. The compound thoroughly dried in a high vacuum at 80° melts at 112–114°. At times the compound crystallized in the form of small crystals of this melting point without having been dried at 80°; $[\alpha]^{24}D$ +26° (26.5 mg. in 2 cc. of chloroform, $l = 1$ dm., $\alpha D +$ 0.34). *Anal.* Calcd. for $C_{29}H_{50}O$: C, 83.98; H, 12.16. Found: C, 83.68; H, 12.35.

Titration with Perbenzoic Acid.—The chloroform solution of perbenzoic acid used in these determinations was several months old and contained approximately 3 mg. of active O per cc. The substance was dissolved in 2 cc. of chloroform and 2 cc. of the perbenzoic acid solution added. Blanks were made with the same amount of chloroform and perbenzoic acid. After standing at 0° for three days the samples were titrated and the consumption of oxygen determined by difference. α-Spinasterol from alfalfa: 41.3 mg. consumed 4.57 mg. O = 2.95 atoms; α-spinasterol from spinach: 31.5 mg. consumed 3.6 mg. O = 3.05 atoms; α-spinastenyl acetate: 25.8 mg. consumed 1.97 mg. O = 2.18 atoms; stigmasteryl acetate: 21.2 mg. consumed 1.38 mg. O = 1.81 atoms.

Summary

The isolation of a sterol from alfalfa has been described together with evidence showing its identity with α-spinasterol.

It has been pointed out that Dam's medicagosterol II also obtained from alfalfa is in all probability α-spinasterol.

NEW BRUNSWICK, N. J. RECEIVED JULY 22, 1939

(6) Windaus and Lüttringhaus, *Ann.*, **481**, 120 (1930).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF NORTH CAROLINA]

The Effect of Temperature on the Nitration of *p*-Cymene The Synthesis of 6-Nitrocarvacrylamine and Certain Derivatives

BY GRANVIL C. KYKER[1] AND R. W. BOST

Recently a considerable quantity of 6-nitrocarvacrylamine was needed for certain studies which were in progress in this Laboratory. Much difficulty was experienced in obtaining good yields of pure 2,6-dinitro-*p*-cymene when the methods of Aschan[2] and of Wheeler and Harris[3] were followed.

Since *p*-cymene upon nitration yields 2,6-dinitro-*p*-cymene,[2,4] 2,4-dinitrotoluene,[5] *p*-nitrotoluene,[3] and various oxidation products, it seemed desirable to observe the reaction at carefully controlled, lower temperatures and to employ chemical methods for the separation of the nitrated products.

Early in this study it was noticed that small changes in the reaction temperature resulted in reaction products which were quite different in quality and quantity. The reaction temperature, previously defined as "below 0°C.,"[3] was herein studied at −3 to −5°, −5 to −7°, and −10 to −12°. With decreasing temperature, the quantity of solid product, its melting point, the ratio of 2,6-dinitro-*p*-cymene to nitrated toluene derivatives, and the reaction time were increased. Likewise, the degree of oxidation, color of product, and the quantity of oils decreased. Contrary to previous work,[3] the reaction product yielded no oil but in every case solidified when washed, dried, and refrigerated at 0°. Oils were obtained from the mother liquor when the product was crystallized.

The separation of 2,6-dinitro-*p*-cymene in pure form was improved by crystallization from a pure solvent instead of mixed solvents.[3] In the selection of a solvent, the following were tried: dioxane, ethyl ether, dichlorodiethyl ether, isopropyl ether, petroleum ether, heptane, toluene, carbon disulfide, chloroform, carbon tetrachloride, methyl alcohol, and ethyl alcohol. Methyl alcohol was the superior solvent both for yield and purity of product. After the third crystallization with methyl alcohol the 2,6-dinitro-*p*-cymene melted at 51–53° whereas it melted at 40–42° after the sixth crystallization with ethyl alcohol.[3] For use in this study, the purification of 2,6-dinitro-*p*-cymene by one crystallization from methyl alcohol followed by a chemical separation, as described below, proved to save both time and material. The results of the nitration studies are given in Table I.

TABLE I

THE DINITRATION OF 500 G. OF *p*-CYMENE

Number of runs	2	3	2
Temperature of reaction, °C.	−3 to −5	−5 to −7	−10 to −12
Time of reaction, hrs.	12	20	33
Product, g.	670	750	785
Color, yellow	Brown	Deep	Light
Physical state at 0°	Semi-solid	Solid	Cryst.
Cryst. from MeOH, g.	230	346	420
M. p., °C.	30–32	34–36	38–40
Oil from mother liquor, g.	435	400	360

The reduction of impure 2,6-dinitrocymene with ammonium sulfide gave a reaction product from which 6-nitrocarvacrylamine was separated in pure form after one or two crystallizations. The reduction product was crystallized from dilute hydrochloric acid which yielded 6-nitrocarvacrylamine hydrochloride, m. p., 209°. The free base melted at 52° and the acetyl derivative at 114–115°. These constants confirm those reported by Wheeler and Harris[3] but in the case of the free base and of the acetyl derivative they disagree with those reported by Aschan[2] as 80–82 and 111°, respectively. When an excess of ammonia was added to the mother liquor, 2-nitro-*p*-toluidine separated and after repeated purifications with dilute alcohol it melted at 81°[6]; its benzoyl derivative melted at 174°.[7,8] This formation and identification of 2-nitro-*p*-toluidine confirm the positions of the nitro groups in the dinitrotoluene as proved by Alfthan,[5] who obtained 2,4-toluylenediamine by reduction of both nitro groups. The selective reduction of the para nitro group and not the ortho group agrees

(1) This paper is an abstract of part of the dissertation submitted by Granvil C. Kyker to the Graduate Faculty of the University of North Carolina in partial fulfilment of the requirements for the degree of Doctor of Philosophy, in June, 1938.

(2) Aschan, *Finska Kemistsamfundets Medd.*, **25**, 122 (1916).

(3) Wheeler and Harris, THIS JOURNAL, **49**, 494 (1927).

(4) Kraut, *Ann.*, **92**, 67 (1854).

(5) Alfthan, *Ber.*, **53**, 78 (1920).

(6) Haibach, *J. prakt. Chem.*, [2] **65**, 246 (1902).

(7) Bell, *Ber.*, **7**, 1504 (1874).

(8) Bernthsen, *ibid.*, **15**, 3017 (1882).

with the work of Beilstein and Kuhlberg[9] on 2,4-dinitrotoluene.

By using the nitration product of *p*-cymene obtained at −10 to −12°, 6-nitrocarvacrylamine was prepared from *p*-cymene in a higher yield than that which has been reported previously for the nitration alone. The results of the studies on the reduction of impure 2,6-dinitrocymene with ammonium sulfide are listed in Table II.

TABLE II

THE REDUCTION OF 2,6-DINITRO-*p*-CYMENE

Temp., °C., of nitration	6-Nitrocarvacrylamine HCl From solid, g.	From oil, g.	Yield from cymene, %	2-Nitro-*p*-toluidine From solid, g.	Yield from cymene, %
− 3 to − 5	126	43	19.7	65	11.4
− 5 to − 7	216	40	29.8	56	9.9
−10 to −12	281	36	36.8	51	9.0

Experimental

2,6-Dinitro-*p*-cymene.—One kilogram of fuming nitric acid (sp. gr., 1.52) and 2 kg. of sulfuric acid (sp. gr., 1.84) were placed in a 3-liter three-necked balloon flask equipped with a dropping funnel, thermometer, and an efficient stirrer. After cooling to −15° in a well insulated ice–salt mixture, the addition of 500 g. of *p*-cymene (Eastman, terpene-free, fraction boiling at 176.5°) was regulated so that the temperature did not exceed −10° and was maintained from −12 to −10°. It was necessary to arrange the stirrer so as to prevent the collection of a hydrocarbon layer, since this induced localized heating, oxidation, and a lower yield. The addition of *p*-cymene required thirty-three hours and stirring was continued for an additional hour. The reaction product was poured over 8 liters of cracked ice, stirred vigorously for one hour and washed successively with six to eight 3-liter portions of water by working and removing the aqueous layer by a siphon, once with dilute sodium hydroxide, and again with water. The spongy, lemon yellow product melted at 25°; it was warmed to 35° and separated from the aqueous layer in a separatory funnel. The oil was dried by heating in a distilling flask at 100° and 20–25 mm. The dry oil, when refrigerated at 0°, solidified to a hard crystalline lemon-yellow mass which weighed 785 g. The solid was recrystallized from 750 ml. of methyl alcohol at 0°. Impure 2,6-dinitro-*p*-cymene separated, weighing 420 g., and melted at 38–40°. On evaporation the mother liquor gave 360 g. of heavy, reddish-yellow oil which did not yield a further crop of crystals. Without further purification, the 2,6-dinitro-*p*-cymene was used for the preparation of 6-nitrocarvacrylamine.

6-Nitrocarvacrylamine Hydrochloride.—Two hundred and fifty grams of 2,6-dinitro-*p*-cymene (impure, m. p. 38–40°) in 1 liter of alcohol was placed in a 3-liter flask equipped with an inlet tube and an outlet *via* a reflux condenser. To the flask was added 170 ml. of ammonium hydroxide (28%). Hydrogen sulfide was passed into the flask at a rapid rate until the contents of the flask were saturated and the hydrogen sulfide was continued another five minutes. The reaction mixture was refluxed for fifteen minutes. The process of cooling, saturating, and refluxing for fifteen minutes was carried out three times. After the saturation with hydrogen sulfide the fourth time, the condenser was turned down and the alcohol was removed until the distillate produced a turbidity when allowed to drop in water. The residue was boiled with 3 liters of dilute hydrochloric acid (containing 375 ml. of concd. hydrochloric acid) in three successive portions of 2000, 500, and 500 ml. and filtered after each extraction. The filtrate was boiled, charcoaled, filtered, and cooled slowly to 0°. Straw colored needles separated which weighed 167.5 g.; m. p. 208°; yield 65% (from *p*-cymene, 36.8%).

6-Nitrocarvacrylamine.—Ten grams of the hydrochloride was suspended in 100 ml. of water and ammonia was added in slight excess. The amine which precipitated was recrystallized from dilute alcohol below 45°; yellow needles; m. p. 52°; yield, practically the theoretical.

N-Acetyl-6-nitrocarvacrylamine.—Three grams of the free base was dissolved in 2 ml. of pyridine and treated cautiously with 2 ml. of acetyl chloride. After warming the mixture for ten to fifteen minutes on a steam-bath it was cooled, washed with water until it solidified, and then washed successively with dilute sodium hydroxide, water, dilute hydrochloric acid, and water. After recrystallization from dilute alcohol the melting point was 114–115°.

2-Nitro-*p*-toluidine.—The acid mother liquor from the crystallization of 6-nitrocarvacrylamine hydrochloride was neutralized with concentrated ammonium hydroxide. Fifty-five grams of impure amine separated. After recrystallizing several times with dilute alcohol it melted at 81°.

N-Benzoyl-2-nitro-*p*-toluidine.—Five grams of 2-nitro-*p*-toluidine was dissolved in 3 ml. of pyridine, treated with 5 g. of benzoyl chloride, and warmed on a steam-bath for ten to fifteen minutes. The product was washed with water, dilute alkali, water, dilute acid, and water, respectively. Dilute alcohol was used for crystallization; m. p. 174–175°.

The authors wish to acknowledge the kind counsel of Professor A. S. Wheeler, who directed this problem for several weeks prior to his retirement due to illness.

Summary

1. The dinitration of *p*-cymene has been studied at −3 to −5°, −5 to −7°, and −10 to −12°.

2. The preparation of 6-nitrocarvacrylamine from *p*-cymene has been improved.

3. The chemical method of separation of the nitration products of *p*-cymene is far superior to the methods previously used.

CHAPEL HILL, N. C. RECEIVED JULY 7, 1939

(9) Beilstein and Kuhlberg, *Ann.*, **155**, 14 (1870).

[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY, COLUMBIA UNIVERSITY]

The Synthesis of *dl*-β-Cyclohexylalanine

BY DAVID SHEMIN AND ROBERT M. HERBST

While studying the preparation of *dl*-β-phenylalanine by the reduction of α-acetaminocinnamic acid[1] in the presence of Adams platinum oxide catalyst, the occasional formation of *dl*-β-cyclohexylalanine (hexahydrophenylalanine) was observed. Generally an unsaturated linkage in the side chain of an aromatic compound may be hydrogenated by catalytic methods without reduction of the aromatic nucleus. The rate of hydrogenation of the aromatic nucleus is so much slower than that of the unsaturated side chain that there is a sharp break in the rate of hydrogen uptake when the latter has been completely saturated.

When freshly prepared and still moist Adams catalyst was employed for the reduction of α-acetaminocinnamic acid, the rate of hydrogenation of even the phenyl group was so great that on numerous occasions no break in the rate of hydrogen uptake was apparent until the compound was completely hydrogenated. The reduction of the compound, both of the unsaturated side chain and of the phenyl group, was complete in about an hour and a half. After the same preparation of catalyst had been dried and allowed to stand in a desiccator for a week or longer, it showed the usual differential rate of hydrogenation of the side chain unsaturation and of the aromatic nucleus.

In view of the fact that *dl*-β-cyclohexylalanine has not been described, a brief characterization of the compound may be of value. Waser and Bräuchli[2] have described *l*-β-cyclohexylalanine (*l*-hexahydrophenylalanine), which they obtained by catalytic hydrogenation of *l*-tyrosine. A certain amount of confusion was introduced by their failure in an earlier paper[3] to realize that the hydroxyl group of the tyrosine was at least partially eliminated during the hydrogenation.

Experimental

N-Acetyl-*dl*-β-cyclohexylalanine.—A solution of 10 g. of α-acetaminocinnamic acid[1] (p. 1) in 75 cc. of glacial acetic acid containing about 0.25 g. of freshly prepared Adams platinum oxide catalyst was shaken with hydrogen under two to three atmospheres pressure in a Burgess–Parr hydrogenation apparatus. The theoretical amount of hydrogen (4 mols) was taken up in from one to two hours. After removal of the catalyst the solution was evaporated to dryness *in vacuo*. Recrystallization of the residue from hot water gave 9.5 g. of N-acetyl-*dl*-β-cyclohexylalanine as needles, m. p. 178°.[4,5]

Anal. Calcd. for $C_{11}H_{19}O_3N$: C, 62.0; H, 9.0; N, 6.6. Found: C, 62.0; H, 8.9; N, 6.6.

***dl*-β-Cyclohexylalanine.**—The amino acid was prepared by hydrolysis of the acetyl derivative with twenty parts of boiling normal hydrochloric acid for eight hours. The hydrochloric acid was removed as completely as possible by vacuum distillation. The remainder of the chloride was removed by treatment with silver oxide followed by hydrogen sulfide to remove silver ion. *dl*-β-Cyclohexylalanine was obtained by evaporation of the clear aqueous solution. On recrystallization from hot water it separated in the form of needles that tended to group together in bunches.

Anal. Calcd. for $C_9H_{19}O_2N$: C, 63.1; H, 10.0; N, 8.2. Found: C, 63.0; H, 9.8; N, 8.2.

The compound showed similarity to phenylalanine in its water solubility. It usually was necessary to employ relatively large volumes of boiling water to dissolve the compound completely, and evaporation of some of the solvent was necessary before crystallization took place.

N-Benzoyl-*dl*-β-cyclohexylalanine.—Benzoylation of *dl*-β-cyclohexylalanine was carried out in aqueous solution with benzoyl chloride in the presence of sodium bicarbonate. The benzoyl derivative crystallized from aqueous alcohol as plates, m. p. 182–183.5°.

Anal. Calcd. for $C_{16}H_{21}O_3N$: C, 69.8; H, 7.7; N, 5.1. Found: C, 69.6; H, 7.6; N, 5.1.

α - Phenylureido - β - cyclohexylpropionic Acid.—The phenyl isocyanate derivative of β-cyclohexylalanine was prepared by shaking an aqueous solution of the amino acid with a slight excess of phenyl isocyanate. The derivative crystallized from aqueous alcohol as prisms, m. p. 177.5° with decomposition.

Anal. Calcd. for $C_{16}H_{22}O_3N_2$: C, 66.2; H, 7.6; N, 9.6. Found: C, 66.1; H, 7.5; N, 9.5.

3-Phenyl-5-cyclohexylmethylhydantoin.—The phenylureido derivative was converted into the corresponding hydantoin by boiling in a mixture of equal parts of absolute alcohol and concentrated hydrochloric acid for several hours. After removal of the alcohol by distillation *in vacuo* the product separated from the reaction mixture in the form of needles or long prisms, m. p. 172.5° after recrystallization from aqueous alcohol.

Anal. Calcd. for $C_{16}H_{20}O_2N_2$: C, 70.6; H, 7.4; N, 10.3. Found: C, 70.7; H, 7.4; N, 10.2.

(1) Herbst and Shemin, *Org. Syntheses*, Vol. **19**, 67 (1939).
(2) Waser and Bräuchli, *Helv. Chim. Acta*, **7**, 740 (1924).
(3) Waser and Bräuchli, *ibid.*, **6**, 199 (1923).
(4) All melting points are corrected.
(5) Bernhard [*Z. physiol. Chem.*, **256**, 49 (1938)] reports the melting point of N-acetyl-*l*-β-cyclohexylalanine as 198–199°.

Summary

The preparation of *dl*-β-cyclohexylalanine and several derivatives is described.

NEW YORK, N. Y. RECEIVED JUNE 19, 1939

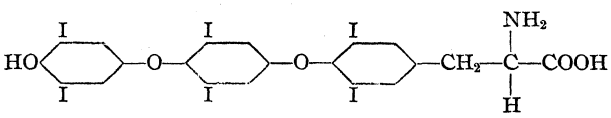
[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY, COLUMBIA UNIVERSITY]

An Analog of Thyroxine

BY M. BOVARNICK, K. BLOCH AND G. L. FOSTER

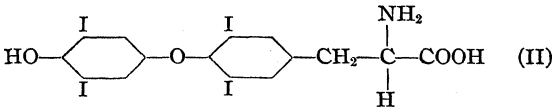
There have been numerous studies on the chemical constitution of thyroxine in relation to its physiological activity. A full discussion of this subject is given by Harington[1] in his monograph on thyroxine. He observes that the presence of certain chemical features in the molecule seems to be responsible for its specific physiological activity, namely, its iodine content, the special orientation of two of the iodine atoms in the ortho position to a phenolic group, the presence of the diphenyl ether linkage, and the α-amino acid residue.

It therefore seemed of some interest to see whether the following compound (I) might possess thyroxine activity.



(I)

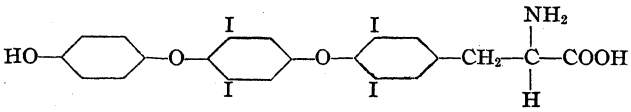
Comparing this with thyroxine (II) the chemical similarities are shown.



(II)

Physiologically, however, the three-ringed amino acid showed no significant activity.

One of the intermediate products in the synthesis is the following



(III)

Because of the parallel relationship between this and our final product (I) on the one hand, and 3,5-diiodothyronine and thyroxine on the other, it was thought worth while to test this physiologically. It showed no more activity than that displayed by the fully iodinated compound (I).

(1) Harington, "The Thyroid Gland," Oxford University Press, London, 1933, Chapter VII.

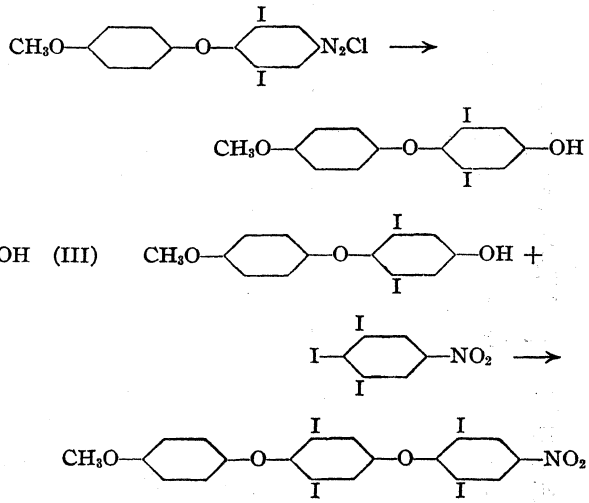
Experimental

Bio-assay.—Since the preliminary estimations, which were done by comparing the weight curves of test animals with thyroxine treated and normal controls, showed so little activity, the more complicated and tedious assay by basal metabolic rates was not undertaken.

Guinea pigs of about 300 g. weight were used. All animals were fed the same adequate diet *ad lib.* The results are shown in Chart I. Each curve represents a group of six animals. Injections and weighings were done daily. The controls received 1 cc. of warm water; the thyroxine and new substances were injected as sodium salts in 1 cc. of warm water. The dosage of thyroxine was 0.05 mg. per animal per day, that of the new compounds 2 mg. per animal per day. The injections were given intraperitoneally.

Since the animals tested with the new substances, although not gaining weight quite as rapidly as the untreated controls, showed no effects comparable to the thyroxine controls, and since the molecular dosage of new substances was about thirty times that of thyroxine, it seems safe to conclude that there is very little, if any, thyroid activity in either of the new compounds.

The synthetic procedure was similar to that followed by Harington and Barger[2] for thyroxine. The only new steps introduced were the following



A 20% solution of 3,5-diiodo-4-(4′-methoxyphenoxy)-benzene diazonium chloride in glacial acetic acid was pre-

(2) Harington and Barger, *Biochem. J.*, **21**, 169 (1927).

pared according to Harington and Barger.[2] This was added to a hot (100–110°), vigorously stirred 50% (by weight) sulfuric acid solution and both temperature and stirring maintained for twenty to thirty minutes, when the β-naphthol test for diazonium salts became negative. The orange mixture turned yellow-gray, and a dark brown sediment separated out. After cooling and standing overnight the solid was filtered off and extracted with 0.5 *N* sodium hydroxide. On addition of an equal volume of 4 *N* sodium hydroxide to the resulting solution the crystalline sodium salt of the phenol separated out. This was centrifuged, washed with 2 *N* sodium hydroxide, dissolved in water, and the solution was made acid to congo with hydrochloric acid. The precipitate was recrystallized from aqueous alcohol or acetic acid. The phenol crystallized as slightly brown, short needles or rods, m. p. 160–163°, yield 48%.

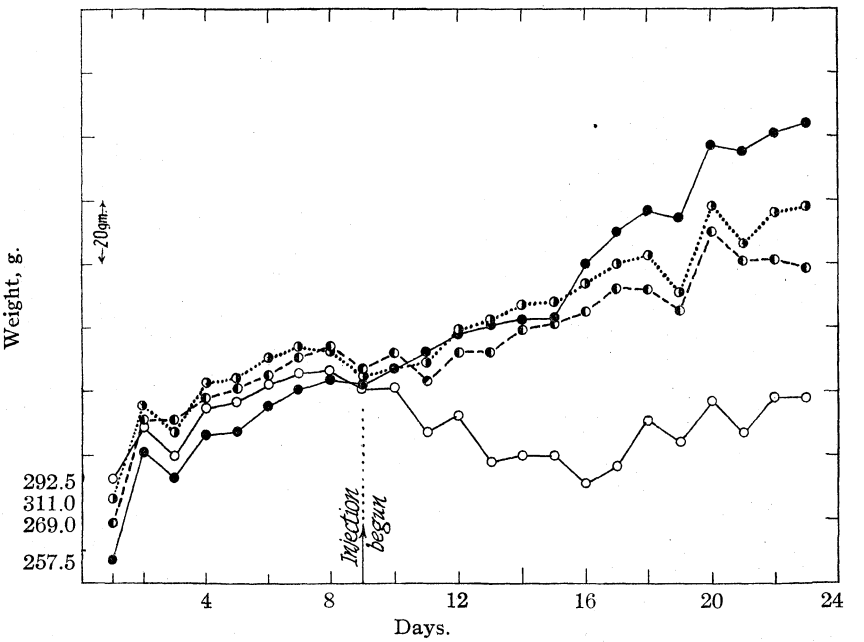


Fig. 1.—●—●, Control; ○—○, thyroxine; ◑···◑, thyroxine *p*-hydroxy phenyl ether; ◐--◐, thyroxine 4-hydroxy-3,5-diiodo phenyl ether.

Anal. Calcd. for $C_{18}H_{10}O_3I_2$: C, 33.3; H, 2.12; I, 54.0. Found: C, 33.2; H, 2.18; I, 53.7.

3,5 - Diiodo - 4 - [3′,5′ - diiodo - 4′ - (4″ - methoxyphenoxy)-phenoxy]-nitrobenzene.—A mixture of 26 g. of the phenol, 8.8 g. of anhydrous potassium carbonate, 31.2 g. of 3,4,5-triiodonitrobenzene, and 125 cc. of dry methyl ethyl ketone was refluxed for fifteen hours on the steam-bath. The hot mixture of salt and yellow product which precipitated out of solution was filtered and washed with the ketone and then with water; 60 g. of almost pure product was left on the filter. The mother liquors on cooling yielded 12 more grams, and still more on dilution with water. The product crystallized in long yellow needles or rods, m. p. 190–192°; yield 87%.

Anal. Calcd. for $C_{19}H_{11}O_5NI_4$: C, 27.0; H, 1.30; I, 60.4; OCH_3, 3.7. Found: C, 27.0; H, 1.35; I, 60.3; OCH_3, 3.6.

3,5 - Diiodo - 4 - [3′,5′ - diiodo - 4′ - (4″ - methoxyphenoxy)-phenoxy]-aminobenzene.—Dry hydrogen chloride was bubbled through a solution of 150 cc. of hot acetic acid containing 15 g. of the trinitro compound and 17 g. of crystallized stannous chloride. The reaction flask was kept hot on the steam-bath. After a while the crystalline stannichloride of the amine began to separate out (one hour). The mixture was cooled and allowed to stand in the icebox overnight. The crystalline precipitate was filtered off and washed with a little cold acetic acid. Then in small portions it was shaken vigorously in a separatory funnel with saturated potassium hydroxide and a large volume of peroxide-free ether containing a little stannous chloride. If no stannous chloride is added, colored products are formed on shaking with alkali, which apparently can be reduced by addition of stannous chloride. The amine is sparingly soluble in ether and large quantities were used, each portion of ether being siphoned off when saturated. The ether solution was filtered and concentrated, whereupon the amine came out as white needles. When hydrochloric acid was passed into the ethereal solution of amine, the hydrochloride separated out as prisms. These were unstable and on being dried lost hydrochloric acid to give the free amine, m. p. 185–187°; yield 87%.

Anal. Calcd. for $C_{19}H_{13}O_3NI_4$: C, 28.1; H, 1.6; I, 62.6. Found: C, 28.0; H, 1.8; I, 62.4.

3,5 - Diiodo - 4 - [3′,5′ - diiodo - 4′ - (4″ - methoxyphenoxy)-phenoxy]-benzonitrile.—Diazotization of the amine was done most conveniently in small lots. To each solution of 1.8 g. (4 *M*) of ethyl nitrite in 40 cc. of glacial acetic acid at room temperature was added slowly and with occasional shaking a 5-g. portion of dry amine. The amine dissolved slowly as the reaction proceeded. The resulting clear orange solutions were combined and added dropwise, at room temperature, and with continuous stirring, to a cuprous cyanide solution prepared by adding, for each 20 g. of amine, 160 g. of potassium cyanide in 280 cc. of water to 120 g. of cupric sulfate in 520 cc. of water. After completion of the reaction as indicated by absence of positive naphthol test for diazonium salt, the mixture was filtered. The light brown solid was dried over phosphorus pentoxide *in vacuo*, and then extracted with benzene solution. The dark brown benzene solution was passed through an aluminum oxide column, losing most of its color and coming out pale yellow. This solution was evaporated to dryness *in vacuo* and redissolved in acetone. On diluting the acetone solution with one-fourth its volume of water and allowing it to stand overnight, a flocculent yellow precipitate came out. This was filtered off and the practically colorless filtrate on further dilution yielded the nitrile as long colorless needles. On purification by crystallization

from acetone–water these melted at 225–226°; yield 64%.

Anal. Calcd. for $C_{20}H_{11}O_3NI_4$: C, 29.2; H, 1.34; N, 1.7; I, 61.8. Found: C, 29.1; H, 1.34; N, 1.8; I, 61.8.

3,5 - Diiodo - 4 - [3′,5′ - diiodo - 4′ - (4″ - methoxyphenoxy)-phenoxy]-benzaldehyde.—To a solution of 6.9 g. of freshly fused, anhydrous stannous chloride in 35 cc. of anhydrous ether saturated with dry hydrogen chloride gas was added 5 g. of nitrile dissolved in 40 cc. of anhydrous chloroform. There was a slight evolution of heat and hydrogen chloride gas, after which the container was tightly stoppered and allowed to stand at room temperature. A yellow, flocculent precipitate soon began to form. After twenty-four hours the heavy yellow precipitate was filtered off, washed with a little cold, dry ether, and suspended in dilute hydrochloric acid. The mixture was brought to boiling and kept there for five minutes. The precipitate became white and granular. It was filtered off and recrystallized from a water–acetone mixture, coming out as clusters of lancets, m. p. 196–198°; yield 70%.

Anal. Calcd. for $C_{20}H_{12}O_4I_4$: C, 29.1; H, 1.54; I, 61.7. Found: C, 28.9; H, 1.50; I, 61.3.

Azlactone of β-3,5-Diiodo-4-[3′,5′-diiodo-4′-(4″-methoxyphenoxy) - phenoxy] - phenyl - α - acetaminoacrylic Acid.—An intimate mixture of 2 g. of aldehyde, 0.28 g. of acetylglycine, 1.2 g. of freshly fused anhydrous sodium acetate, and 4 cc. of acetic anhydride was refluxed on the oil-bath for one hour. After cooling the yellow solid was filtered off, washed with cold acetic anhydride, then with water till the washings came through neutral, dried and recrystallized from acetic anhydride; glistening golden plates, m. p. 264–265°; yield 80%.

Anal. Calcd. for $C_{24}H_{15}O_5NI_4$: C, 31.8; H, 1.76; I, 56.1. Found: C, 31.8; H, 1.65; I, 55.9.

Thyroxine-*p*-hydroxyphenyl Ether.—To a suspension of 2 g. of red phosphorus in a mixture of equal parts (by volume) of acetic anhydride and 57% hydriodic acid was added 2.8 g. of azlactone and the mixture refluxed on the oil-bath for one and one-quarter hours. The phosphorus was removed by filtering the hot mixture through asbestos. Occasionally the hydroiodide of the amino acid separated out of the hot solution during the course of the reaction, but was brought into solution previous to removal of the phosphorus by addition of more hot dilute acetic acid. After removal of the acetic acid and hydriodic acid as completely as possible by repeated addition of small amounts of water and evaporation *in vacuo*, the insoluble light brown solid was filtered off, washed with a little dilute alcohol, suspended in a large volume of hot alcohol, and brought into solution by the addition of a few drops of *N* sodium hydroxide. On acidification with acetic acid and cooling the amino acid came out as clusters of long colorless needles; 1.75 mg. was obtained. This product was very difficult to purify. There was some loss of iodine during the reduction and hydrolysis, the analysis at this point always being 1 to 2% too low. On repeated recrystallization as described above, the product gradually approached analytical purity, but the yield suffered greatly; 200 mg. of pure material was prepared for analysis and bioassay, m. p. 267–268° with decomposition.

Anal. Calcd. for $C_{21}H_{15}O_5NI_4$: C, 29.0; H, 1.7; N, 1.61; I, 58.46. Found: C, 28.9; H, 1.9; N, 1.67; I, 58.30.

Thyroxine-4-hydroxy-3,5-diiodophenyl Ether.—Because of the very slight solubility of the tetraiodo compound in aqueous ammonia, the iodination was carried out in a methyl alcohol–aqueous ammonia mixture.

To a solution of 869 mg. of tetraiodo compound in a mixture of 140 cc. of methyl alcohol and 200 cc. of 25% aqueous ammonia was added dropwise 8 cc. of 0.5 *N* iodine in 0.1 *M* potassium iodide. If more than the calculated amount of iodine was used, there was an increase in destruction, probably due to oxidation. The iodine was taken up rapidly. After addition of the iodine the solution was put in the icebox for several hours. Most of the ammonia was then removed by distillation *in vacuo* at room temperature, and the solution was acidified with acetic acid. The white precipitate obtained weighed 1.1 g. A portion of this, 415 mg., was extracted with hot 95% ethyl alcohol, the solution filtered and diluted to 70% with water. A crop of fine white needles came out. This was filtered off, redissolved in 100 cc. of hot alcohol and diluted with 30 cc. of water; 130 mg. of fine white needles was thus obtained. This compound was rather unstable, coloration and loss of iodine occurring on heating both in solution and in the dry state. It could only be thoroughly dried by heating in high vacuum, and even when kept dry and unexposed to light, there was brown coloration and loss of iodine. Because of these properties it was difficult to purify. Decomposition starts at 210° without melting.

Anal. Calcd. for $C_{21}H_{13}O_5NI_6$: C, 22.48; H, 1.16; N, 1.25; I, 67.9. Found: C, 22.26; H, 1.23; N, 1.34; I, 67.5.

Summary

The synthesis of the 3,5-diiodo-4-hydroxyphenyl ether of thyroxine is described. The product is physiologically inactive.

NEW YORK, N. Y. RECEIVED JULY 6, 1939

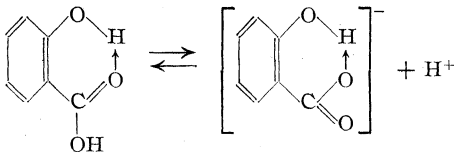
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

Relation between Resonance Stabilized Chelate Rings and Acidity

BY RICHARD T. ARNOLD AND JOSEPH SPRUNG

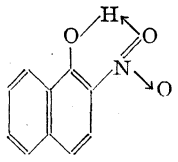
The general effects of chelate rings on the physical properties of organic molecules are well known.[1]

It has been shown recently[2] that the abnormally high acidity of salicylic acid is readily explained by an increased resonance in the anion formed by ionization. Thus



This increased possibility of resonance is brought about by hydrogen bond formation.

It has been assumed[3] that the formation of a chelate ring stabilizes the nuclear double bonds in the aromatic ring to which the chelate ring is attached. We have consistent data which seem to prove the corollary of this idea, *i. e.*, that the amount of hydrogen bond formation is greater around a stabilized double bond. The following molecule will serve as an example



Since resonance of the hydrogen atom among the three oxygen atoms of this chelate ring stabilizes the structure, one could expect a higher degree of resonance and consequently greater stability when the steric factors between the hydroxyl and nitro groups are most favorable. This "locking-up" of the ionizable hydrogen should decidedly decrease the acidity of the molecule.

The inductive effect here however is large and is easily transmitted across the double bond.[4] The decreased acidity predicted above is obvious from the values listed in Table I.

Solvent Effect.—The parallel change in "*pK*" with solvent as shown above indicates that the order of acidity discussed here is not affected by the interaction of solute and solvent.

(1) Lassettre, *Chem. Rev.*, **20**, 259 (1937).
(2) Branch and Yabroff, THIS JOURNAL, **56**, 2568 (1934).
(3) Baker and Lothian, *J. Chem. Soc.*, 628–633 (1935).
(4) Fuson, *Chem. Rev.*, **16**, 1–27 (1935).

TABLE I

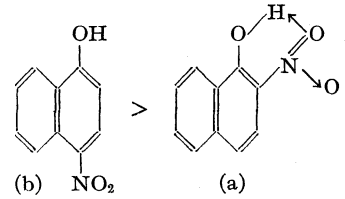
Temperature, 30°

Compound	*pK* 20 cc. (0.05) *M* in ethanol) +10 cc. (0.05 *M*) NaOH	+10 cc. H_2O	+20 cc. H_2O	+30 cc. H_2O	+40 cc. H_2O
1-Hydroxy-2-naphthonitrile	7.05	6.65	6.40	6.20	6.10
4-Hydroxy-1-naphthonitrile	8.62	8.25	8.00	7.80	7.62
3-Hydroxy-2-naphthonitrile	9.10	8.68	8.40	8.15	8.00
1-Hydroxy-2-naphthaldehyde	8.30	7.90	7.62		
4-Hydroxy-1-naphthaldehyde	8.15	7.70	7.42	7.20	7.05
3-Hydroxy-2-naphthaldehyde	10.20	9.88	9.70		
2-Nitro-1-naphthol	7.35[a]	..	..	..	..
4-Nitro-1-naphthol	7.00	6.60	6.32	6.15	6.00
o-Hydroxybenzonitrile	8.78	8.35	8.05	7.82	7.68
Salicylaldehyde	9.60	9.20	8.92	8.75	8.65
o-Nitrophenol	8.55	8.15	7.85	7.68	7.58

[a] $T = 35°$.

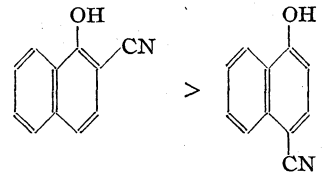
Discussion

It is to be noticed that while the large inductive effect would tend to make (a) more acidic than (b), the reduction caused by chelate ring formation completely overshadows this effect. Thus

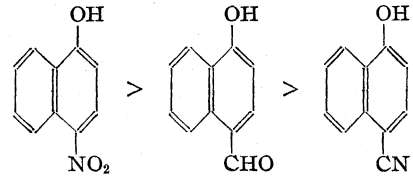


The same situation holds for the corresponding hydroxyaldehydes.

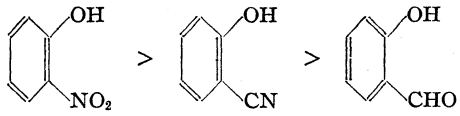
With the cyanonaphthols (no chelate rings) the normal inductive effect becomes important. Thus



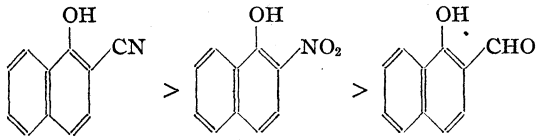
When only the inductive effect is operative the order of acidity is $-NO_2 > -CHO > -C{\equiv}N$. Consequently



When some hydrogen bond comes into play this order changes. Thus



When the hydrogen bond becomes very strong a further change takes place as shown.



All of the above observations are explained readily by assuming stronger hydrogen bond formation around a stabilized double bond. The fact that the order of acidity is not the same in the naphthalene and benzene series as shown above clearly proves this point (since all the other factors involved are constant).

We wish to stress that the low acidity of 2-cyano-3-naphthol is in accord with our ideas concerning the structure of naphthalene.[5]

We have shown that the method considered above will locate stabilized double bonds. We will publish soon our work on the Mills-Nixon[6] problem using the above attack.

Experimental

Apparatus.—The general method was that described in an earlier paper[5] except that the glass electrode was used throughout.

1-Hydroxy-2-naphthonitrile.—Eleven grams of potassium hydroxide was dissolved in 350 cc. of dried glycerol contained in a three-necked flask equipped with a sealed stirrer. Fifty grams of sodium 1-sulfonate-2-naphthonitrile was added and the stirred solution heated for two hours at 140°. The mixture was poured into a liter of water and acidified with hydrochloric acid. The white precipitate was filtered, dried, and refluxed with 25 cc. of acetic anhydride for thirty minutes. The crude 1-acetoxy-2-naphthonitrile was purified by recrystallization, m. p. 87°; yield 7 g. The hydroxy compound was obtained by hydrolysis with dilute sodium hydroxide. After five recrystallizations from ethanol it melted at 178–179°.

Anal. Calcd. for $C_{11}H_7ON$: C, 78.09; H, 4.17. Found: C, 78.18; H, 4.25.

4-Acetoxy-1-naphthaldehyde.—Attempts to follow the literature gave disappointing results.[7] Fifty grams of 4-hydroxy-1-naphthaldehyde was dissolved in a solution of 250 cc. of acetic acid, 50 cc. of acetic anhydride and 20 g. of sodium acetate and refluxed for two hours. The solution was poured into ice water and the precipitate recrystallized from ethanol; yield 4.5 g., m. p. 103–105°. The material was not quite pure.

4-Hydroxy-1-naphthaldehyde Oxime.—Five grams of 4-acetoxy-1-naphthaldehyde was dissolved in 125 cc. methanol and 60 cc. of water. Three and one-half grams of hydroxylamine hydrochloride, 3.5 g. of sodium acetate and 2.0 g. of sodium bicarbonate were added and the mixture refluxed for fifteen minutes. The methanol was removed until crystallization started. Two hundred cubic centimeters of water was added and the temperature raised to 100°. After cooling slightly, the solution was filtered quickly to remove a resinous portion and crystallization completed in an ice-bath; yield 3 g. (68%), decomposition point 150°.

Anal. Calcd. for $C_{11}H_9O_2N$: C, 70.57; H, 4.84. Found: C, 71.03; H, 4.95.

The acetyl group is hydrolyzed in the course of the reaction. An attempt to prepare the oxime directly led to unfavorable results.

4-Hydroxy-N-acetoxy-1-naphthaldehyde Oxime.—Thirteen grams of 4-hydroxy-1-naphthaldehyde oxime was dissolved in 100 cc. of glacial acetic acid and 25 cc. of acetic anhydride added. After one hour the precipitate was filtered and washed with dilute acetic acid; yield 14 g. (88%); decomposition point 155°.

Anal. Calcd. for $C_{13}H_{11}NO_3$: C, 68.11; H, 4.83. Found: C, 67.97; H, 4.86.

4-Hydroxy-1-naphthonitrile.—Fourteen grams of the above compound was heated in 140 cc. of ethanol and 30 cc. of dry pyridine for two hours. The solution was evaporated to one-half volume and poured into dilute hydrochloric acid. The yield of crude nitrile was 9.5 g. (92%); m. p. 173–175°. After recrystallization, m. p. 176–176.5°.

Anal. Calcd. for $C_{11}H_7ON$: C, 78.09; H, 4.17. Found: C, 77.96; H, 4.21.

This compound also was obtained by the decomposition of the diazonium borofluoride[8] of 4-cyano-1-aminonaphthalene.

All of the other compounds measured can be produced easily by methods discussed in the literature.

The authors wish to thank the du Pont Company for generous gifts of isomeric aminonaphthalene sulfonic acids.

Summary

1. It has been shown that chelate rings formed around stabilized double bonds are abnormally strong.

2. A method for finding stabilized double bonds has been developed and its limitations completely recognized.

MINNEAPOLIS, MINNESOTA RECEIVED JUNE 23, 1939

(5) Arnold and Sprung, THIS JOURNAL, **60**, 1163 (1938).

(6) Mills and Nixon, *J. Chem. Soc.*, 2510 (1930).

(7) Kamm, McClugage and Landstrom, THIS JOURNAL, **39**, 1247 (1917).

(8) Smith and Haller, THIS JOURNAL, **61**, 143 (1939).

[CONTRIBUTION FROM THE FURMAN CHEMICAL LABORATORY, VANDERBILT UNIVERSITY]

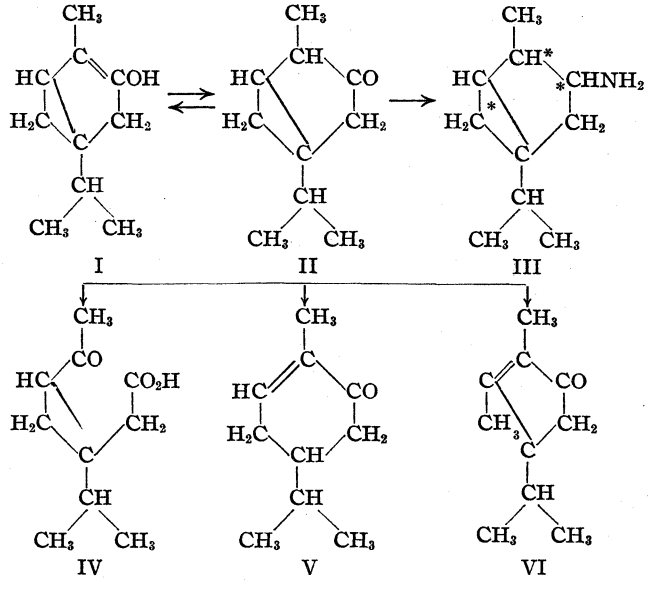
The Terpenoid Amines. I. The Isomeric Thujylamines

BY H. L. DICKISON[1] AND A. W. INGERSOLL

The purpose of this investigation is to characterize the stereoisomeric amines derivable from the five important dicyclic systems represented by thujone, pinocamphone, fenchone, isofenchone and camphor. The various amines are being studied as to their possible value as resolving agents and as to their suitability as derivatives for the analytical determination of the parent terpenoid substances. The present paper is concerned principally with the isomeric thujylamines, the first family that has been fully characterized thus far.

The Isomeric Thujylamines.—Two so-called thujylamines were known when the present work was begun. The more fully characterized amine was first obtained by Semmler[2] by reduction of an oxime, m. p. 51.5°, prepared from dextro-rotatory β-thujone (tanacetone), the principal ketone of tansy oil. The preparation was repeated by Wallach[3] and by Tschugaeff[4] and the amine was reported to have b. p. 195°, $[\alpha]_D$ +101°. It formed a sparingly soluble nitrate and very soluble hydrochloride. The second amine was contained in a mixture which Wallach[5] obtained by heating crude levorotatory α-thujone from thuja oil with ammonium formate and hydrolyzing the resulting formyl derivative. The amine was stated to form a sparingly soluble sulfate but was not completely separated from stereoisomers or from the accompanying fenchylamine.

Wallach[6] later showed that the α- and β-forms of thujone (II) are interconvertible in the presence of either alkaline or acidic reagents, presumably through the common enol (I). The β-form predominates at equilibrium. Both forms yield the same dextrorotatory thujaketonic acid (IV) upon oxidation. Hence the two thujones have the same configuration except for an interchange of H and CH_3 on the upper ring carbon. Wallach also demonstrated the isomerization of both thujones, by heating with strong acids, into *dl*-carvotanacetone (V) and the so-called *dl*-isothujone (VI).



These transformations were of primary importance for the proposed preparation of the thujylamines (III), which it was hoped to accomplish on a large scale by heating the thujone fraction of thuja oil with ammonium formate–formamide reagent. Although this fraction (b. p. 196–200°, α_D −18°) consists largely of α-thujone, together with some levorotatory fenchone, the α–β isomerization undoubtedly would be induced by prolonged heating in the mildly alkaline reaction mixture and could result in the formation of all four of the diastereoisomeric thujylamines—one antipode from each pair. In addition it was possible that amines derived from *l*-fenchone, *dl*-carvotanacetone and *dl*-isothujone might likewise be formed under the conditions used.

Application of this process, followed by alkaline hydrolysis of the crude formyl derivative, actually gave 55–60% yields of mixed amines, b. p. 193–202°, α_D +23°. This material was then converted to salts with a variety of acids and these were gradually and completely separated by prolonged fractional crystallization. In this way there were finally obtained five distinct amines for which the principal properties are given in Table I.

(1) Constructed from a thesis submitted by H. L. Dickison in partial fulfilment of the requirements for the degree of Doctor of Philosophy, Vanderbilt University.

(2) Semmler, *Ber.*, **25**, 3343 (1892).

(3) Wallach, *Ann.*, **286**, 91 (1895).

(4) Tschugaeff, *Ber.*, **34**, 2276 (1901).

(5) Wallach, *Ann.*, **272**, 109 (1893).

(6) Wallach, *ibid.*, **336**, 247 (1904).

TABLE I

PROPERTIES OF THE AMINES

Amine	B. p., °C.	$\alpha^{25}D$[a]	Characteristic salts	M. p., benzoyl deriv., °C.
A	199.6	+27.80°	Sulfate–*p*-Toluene-sulfonate	73.0
B	193.4	+94.94°	Nitrate–Acid oxalate	131.5
C	196.7	−14.15°	Sulfate–Normal oxalate	94.5
D	202.2	−22.07°	*l*-Malate–sulfate	Glassy
E	195.3	+22.19°	*d*-Mandelate–*l*-Malate	90.2

[a] Rotation for 1 dm. without solvent.

The amine E was identified as (+)-fenchylamine, which had been partially characterized previously. The absence of optically inactive amines excluded the presence of amines derived from *dl*-carvotanacetone or *dl*-isothujone. The four remaining amines were therefore probably the theoretically possible thujylamines.

In a supplementary series of experiments, undertaken in an effort to correlate two of these amines with β-thujone, pure crystalline β-thujoneoxime, m. p. 53°, was reduced with sodium and alcohol and the product converted to salts and fractionated. In this way there were obtained 83.7% of an amine identical with B above, 6% identical with A and 4% identical with D. Aside from a trace of C, no other amines were present. These results confirmed the identification of the four thujylamines and indicated with considerable certainty that A and B were derived from β-thujone while the small amounts of C and D were derived from α-thujone, whose oxime must have been formed by an inversion occurring during the reduction.

When this work was practically complete, there appeared a paper by Short and Read[7] dealing in part with two thujylamines. One of these, which these authors named *d*-isothujylamine ($\alpha^{12}D$ +94.82°), likewise was obtained by reduction of β-thujoneoxime, m. p. 53°, and is clearly identical with the less pure amine previously prepared in the same way by Semmler,[2] Wallach[3] and Tschugaeff[4] and with the amine B described above. The other amine, which was named *l*-thujylamine ($\alpha^{13}D$ −24.32°), was obtained by reduction of the crude liquid oxime of α-thujone and purification through the hydrochloride. This amine was probably present in the impure preparation of Wallach and is identical with the amine D described above. Amines corresponding to A and C were not described.

(7) Short and Read, *J. Chem. Soc.*, 2016 (1938).

In view of the constants and relationships that have now been established for the entire group of four amines, it would seem advantageous to systematize their nomenclature. All four amines as well as both thujones have the same configuration at the junctions of the two rings and hence may be regarded as belonging to the same configurational series. It will not be possible to decide whether this is the *d*- or the *l*-series until a suitable derivative can be correlated with some substance of known configuration. However, in order to name the four diastereoisomers in each series it is proposed that the prefixes α- and β-, which have long been used for the two natural thujones, be retained in the names of the derived pair of amines and that the prefix iso- be assigned provisionally to that member of each pair which has the higher numerical rotatory power. With the addition of the sign of rotation, the amines A and B then become (+)-β-thujylamine and (+)-iso-β-thujylamine, respectively, while C and D become (−)-α-thujylamine and (−)-iso-α-thujylamine, respectively. These names are used in the remainder of this paper.

Characterization of the Amines.—The four thujylamines and also fenchylamine have been characterized rather completely as free amines and as salts and other derivatives. The most important data are recorded in the Experimental part. In each instance some six or seven of the most readily crystallizable salts were prepared from each amine and the crystal habit, solubility, rotatory power and other constants were carefully determined. It is expected that, should any of the amines be encountered again in other parts of the present program or by other workers, it should be possible to separate and recognize them readily by reason of their sharply distinctive properties.

Application as Resolving Agents.—This portion of the program has been studied thus far only incidentally to the separation of the isomeric amines, in the course of which *dl*-mandelic acid and *dl*-malic acid were employed. It was found that *dl*-mandelic acid was resolved readily by either (+)-β-thujylamine or (−)-α-thujylamine and that *dl*-malic acid was resolved by (−)-iso-α-thujylamine. Also both of these acids were readily resolved by (+)-fenchylamine. Preliminary experiments have shown further that all of these amines form well crystallized salts with several other types of organic acids and it is ex-

pected that various other resolutions can be carried out. Work is being continued in this direction.

Experimental

α-Thujone.—This was obtained in the crude state by distilling commercial oil of *Thuja occidentalis*, α_D −12.8°, through a jacketed 60-cm. Vigreux column. The fraction b. p. 196–199° (745 mm.), 78–82° (12 mm.), $\alpha^{25}D$ −18° (l = 1), was used for the Leuckart synthesis of amines. This fraction (55% of the oil) contained also considerable levorotatory fenchone. Pure α-thujone is reported[7] to have $\alpha^{18}D$ −19.94°.

β-Thujone.—This was obtained similarly from oil of tansy, $\alpha^{25}D$ +39°. The fraction b. p. 80–82° (12 mm.), $[\alpha]^{25}D$ +59.7° (c = 4, ether) was used to prepare the oxime. This fraction (38% of the oil) contained also some α-thujone and levorotatory camphor. Pure β-thujone is reported to have $\alpha^{15}D$ +72.46°[7] (l = 1), $[\alpha]D$ +76.16 in ether[6] and $[\alpha]D$ +77.45° in hexane.[8]

β-Thujoneoxime.[9]—Crude β-thujone (55 g.), hydroxylamine hydrochloride (28 g.) and sodium acetate trihydrate (60 g.) were dissolved in 85% ethanol (600 cc.) and allowed to remain overnight. It was hoped that mild conditions would minimize the oximation of camphor. The alcohol was evaporated and the liquid oxime extracted with benzene and distilled. The principal fraction (65%), b. p. 117–118° (6 mm.), $[\alpha]^{25}D$ +82° (c = 4, methanol), largely solidified after several days. The liquid portion smelled strongly of camphor. The solid was drained by suction and redistilled with rejection of a small forerun. After solidification this process was repeated on the product. The oxime then had m. p. 53°, $[\alpha]^{25}D$ +105.3° (c = 4, methanol). Short and Read[7] report $[\alpha]^{12}D$ +98.14° (c = 2, ethyl alcohol). The observation of these authors that the crystalline oxime could not be made satisfactorily from fractions containing considerable (liquid) α-thujoneoxime was confirmed. Repeated distillation of material with specific rotation +45° or less produced only slight enrichment of β-thujoneoxime in the higher boiling fractions. In this connection it was found that oximation of β-thujone in the presence of alcoholic pyridine[10] gave a non-crystallizable liquid of low dextrorotation. Partial isomerization of the β- to the α-configuration apparently occurs readily under these conditions.[11]

Leuckart Synthesis of Mixed Thujylamines.—Crude α-thujone (537 g., 3.53 moles) and solid ammonium formate (895 g., 14.2 moles) were heated in a 2-l. flask equipped with an automatic separator arranged to reject the distilled aqueous ammonium carbonate solution and return the ketone. The mixture, which darkened considerably, became homogeneous after two hours and was then heated at 175–185° for seven hours longer. The heating period was purposely made somewhat shorter than usual with the hope that the less reactive fenchone would be incompletely converted. The mixture of crude formyl derivatives, unchanged ketone and condensation products was extracted with benzene and hydrolyzed by refluxing for eight hours with 285 g. of sodium hydroxide in 3 l. of 85% alcohol. A little water was then added to dissolve sodium formate and most of the alcohol distilled through a long column. The crude amine was then distilled with steam, *cautiously* neutralized with cold, dilute hydrochloric acid and extracted with benzene to remove neutral volatile substances. The amine was then liberated with alkali, extracted and dried. The benzene was removed through an efficient column and the amine then distilled through a short column. The mixed amines weighed 314 g. (58% yield) and had b. p. 195–201°, $\alpha^{25}D$ +22.53° (l = 1), d^{25}_4 0.880, $n^{25}D$ 1.4615.

The volatile neutral material (45 g.) was examined briefly. The main fraction, b. p. 69–75° (12 mm.), had $\alpha^{25}D$ −40.2 (l = 1) and smelled strongly of fenchone. The non-volatile condensation products remaining after the steam distillation were not examined.

Several additional runs were made as described above, or by substitution of an equivalent amount of 95% formamide for the ammonium formate, with substantially similar results. In preliminary experiments[12] attempts were made to hydrolyze the formyl derivatives with 20% hydrochloric acid in the usual way. In one experiment brief heating, followed by isolation of the amine as described above, gave a 45% yield of mixed amines having $\alpha^{25}D$ about +15°. With longer heating the yield was much smaller. A somewhat similar result was observed by Short and Read.[7] When purified amine, obtained by alkaline hydrolysis, was neutralized exactly with dilute aqueous hydrochloric acid, the solution at once acquired a violet color. This rapidly deepened and changed to black on long standing or brief heating and much of the amine could not be recovered. No similar coloration or decomposition was noted when other acids were used, but care was always taken in the later work to avoid any excess of strong acid. The amine mixture obtained by acid hydrolysis was not used for the experiments described below.

Fractional Separation of Mixed Amines.—The combined product of several runs (650 g., b. p. 193–200°, $\alpha^{25}D$ +23.0°, $n^{25}D$ 1.4650) was separated eventually by the fractional crystallization of a variety of salts. The principal steps in this long and tedious process are outlined below. Full descriptions of the various salts and amines are reserved for a later section.

The mixture was first subjected to a preliminary fractionation as sulfates. The amine was combined with slightly less than the amount of acid calculated for the normal salt in 2 liters of hot water. The dense crystal mass was filtered after cooling and then heated with 500 cc. of water and again filtered after cooling. The amine (270 g.) recovered from these two filtrates was called Fraction IV. The crystalline portion was then boiled with three successive 1-liter portions of water and the solutions filtered at 60° from undissolved solid. The latter was called Fraction I. The warm filtrates on cooling gave crystalline crops. These were combined into Fraction II and the filtrates into Fraction III.

The sulfate fraction I was found to yield almost com-

(8) Mohler and Lohr, *Helv. Chim. Acta*, **20**, 1183 (1937).

(9) Prepared by Mr. Robert Shirey, M.A. Thesis, Vanderbilt University, 1937.

(10) Bachmann and Boatner, THIS JOURNAL, **58**, 2097 (1936).

(11) Bachmann and Barton, *J. Org. Chem.*, **3**, 300 (1938).

(12) Dickison, M.A. Thesis, Vanderbilt University, 1936.

pletely pure amine A, subsequently called (+)-β-thujylamine. The very sparingly soluble sulfate was recrystallized in portions from large volumes of water. The amine was then recovered and converted to the *p*-toluenesulfonate, which could be recrystallized more conveniently. The pure salt (195 g.) had $[\alpha]^{25}D$ +27.91°. The amine (5.5 g.) recovered from the final mother liquor was combined with that from Fraction II.

Fraction II was converted to the amine (90 g.) and this to the *p*-toluenesulfonate. Brief fractionation gave 20 g. more of the *p*-toluenesulfonate of amine A and mother liquors from which the mixed amines were recovered. Fraction III was also converted to the amine (168 g.) and this to the nitrate. Fractionation gave 24 g. of a characteristic nitrate, $[\alpha]^{25}D$ +70.48°, of the amine B, subsequently called (+)-iso-β-thujylamine. The residual amine was recovered from the mother liquor and combined with that recovered from Fraction II.

The combined amines were then converted to mandelates by the use of *dl*-mandelic acid. Prolonged fractionation of the crystalline portion finally gave two apparently homogeneous fractions, (a) 65 g. having $[\alpha]^{25}D$ +23.4° and (b) 82 g. having $[\alpha]^{25}D$ +1.3°. Actually, neither fraction proved to be uniform. The amine recovered from the portion (a) on fractionation as nitrate gave more of the amine B, and the soluble portion of the nitrate series, on conversion to sulfate, gave a new, rather sparingly soluble sulfate having $[\alpha]^{25}D$ +3.47°. Alternate crystallization as nitrate and sulfate gave exclusively 14.5 g. of amine A and 16.5 g. of the new amine C, subsequently called (−)-α-thujylamine.

The crystalline mandelate fraction (b) yielded an amine which was then converted to the malate by means of *dl*-malic acid. It was found that the principal constituent resolved *dl*-malic acid, giving a sparingly soluble acid *l*-malate, $[\alpha]^{21}D$ −14.73°. In order to obtain the maximum amount of this salt the *dl*-acid was taken in twice the equivalent amount so that at least one equivalent of the *l*-acid was present. The mother liquor gave an amine consisting almost entirely of the amine A. Alternate fractionation as the *p*-toluenesulfonate and malate gave 7 g. of A and 35 g. of the new amine D, subsequently called (−)-iso-α-thujylamine.

The mother liquors of the original mandelate series (containing the unseparated remainder of fractions II and III) gave an amine which was then combined with an excess of *dl*-malic acid. Fractionation gave a small amount of a crystalline malate which was distinctly different from that of the amine D, and a very soluble portion remaining in the mother liquors. A similar behavior had been observed in the meantime with certain parts of Fraction IV (see below). The two malate series were therefore combined and their further fractionation is described later. The crystalline malate proved to be the acid *l*-malate of a fifth amine E, subsequently identified as (+)-fenchylamine.

Since the amines from the sulfate fraction IV distilled over a moderate range, this material was separated into four sub-fractions, (a), (b), (c) and (d), in that order of decreasing volatility. These fractions were examined separately while some of the work described above was still in progress. The fraction (a) (18.3 g.) was combined with *dl*-malic acid and yielded a little of the crystalline malate of E and mother liquors containing very soluble malates. The amine was recovered from the mother liquors and later converted to oxalates. The fraction (b) (76 g.) was combined with *dl*-mandelic acid and yielded a small crystalline crop. The amine recovered from this was further fractionated as nitrate and gave more of the nitrate of amine B already described. The amines in the mother liquors of the mandelate and nitrate were then combined with *dl*-malic acid. Fractionation gave 36 g. more of the *l*-malate of D. The amines in the mother liquors were later converted to oxalates.

The fraction (c) (144.2 g.) was converted to the *d*-tartrate. The crystalline portions of this series could not be obtained uniform. The amine was therefore recovered from it and fractionated alternately as malate and nitrate. This gave more of the pure *l*-malate of D and the nitrate of B. The amines in the tartrate mother liquors were also combined with *dl*-malic acid and the crystals thus obtained were combined with similar material from the foot of fractions II and III and from IV (a). Fractionation gave 60 g. of the pure acid *l*-malate of (+)-fenchylamine. This salt has no observable rotation, apparently because the rotatory effect of each ion is cancelled. The salt was identical with that prepared from the pure amine and pure *l*-malic acid. This acid had therefore been resolved by fenchylamine.

The amines remaining in the mother liquors of the malate series were combined with similar material already mentioned and with IV (d) (32 g.). This material (all that remained of the original mixture) was then fractionated as oxalates. This gave 55 g. of the pure acid oxalate of B and 36 g. of less pure oxalate of D. The latter was purified by conversion to the *l*-malate. The amines in the mother liquors of the oxalate and malate (about 7 g.) were further separated into small additional amounts of the salts already described. No trace of any other amine was discovered.

In summary, there were obtained as pure amines or salts 137.5 g. of A, 54 g. of B, 34.9 g. of C, 54 g. of D, and 53.6 g. of E. The total (334 g.) is slightly over 50% of the original mixture. With the information now in hand concerning the salts it would undoubtedly be possible to separate a similar mixture much more systematically and with very little loss.

Amines from β-Thujoneoxime.—The oxime already described (33.8 g.) was reduced in 550 cc. of absolute alcohol by rapid addition of 47 g. of sodium. This process gave 28.6 g. (92%) of an amine mixture of b. p. 193–195°, $[\alpha]^{25}D$ +75.58° (c = 4, benzene), +93.94° (c = 3.7, ethanol). The entire amount was converted to nitrates and brief fractionation gave 32.4 g. of the characteristic nitrate of amine B. The amine recovered from the mother liquors then gave in succession 1.5 g. of the oxalate of B, 3.6 g. of the *p*-toluenesulfonate of A and 2.5 g. of the *p*-toluenesulfonate of D. The residual amine (1.3 g.) was converted to oxalates. Because of the small amount, pure salts were not obtained from this portion but the rotation data and crystalline appearance of the various fractions indicated a trace of the amine C and small additional amounts of A and D. From the weights of all of the salts it was calculated that the original mixture con-

TABLE II

DERIVATIVES OF THE AMINES

Amine	Derivative	Hydrate[a]	Appearance	M. p., °C.	$[\alpha]^{25}D$[b]	Solubility[d]
A	Benzoyl	...	Prisms	73–75	+91.44	...
	Sulfate	...	Hexag. plates	242 d.	+42.77	0.95
	p-T. S.[e]	...	Thick needles	194.7	+27.91	1.07
	H-Oxalate	Mono	Long needles	d.	+36.10	2.08
	Nitrate	Hemi	Massive plates	105	+35.97[c]	79.30
	d-Mandelate	Di	Thick prisms	80–115	+82.59[c]	3.96
	l-Mandelate	Mono	Fine needles	120–128	−29.52[c]	2.84
B	Benzoyl[h]	...	Needles	131.5	+87.74[g]	...
	H-Sulfate	Mono	Cubes	153 d.	+55.25[c]	23.4
	p-T. S.[e]	...	Long needles	170–171	+41.60	3.24
	H-Oxalate	Mono	Long needles	167	+62.50	1.26
	Nitrate	...	Prisms	176.9	+70.48	3.04
	?-Malate	?	Irregular	160	+49.84	V. s.[i]
	Perchlorate	...	Prisms	168	+55.47	V. s.[i]
C	Benzoyl	...	Plates	94.5	−12.16	...
	Sulfate	Tetra	Dull plates	243 d.	+ 3.47	1.74
	p-T. S.[e]	...	Glass	.....	.....	...
	N-Oxalate	...	Plates	200–201	.....	0.59
	Nitrate	...	Flat needles	150	+ 2.60	8.32
	H-*dl*-Malate	...	Fine needles	148.5	+ 1.73	11.50
	d-Mandelate	Mono	Needles	99.5	+65.23[c]	2.97
D	Benzoyl[h]	...	Glass	.....	.....	...
	p-Nitrobenzoyl[h]	...	Needles	146.5	−51.25[f]	...
	Sulfate	Mono	Scaly plates	263 d.	−16.66	1.67
	p-T. S.[e]	...	Long needles	198.6	−10.40	2.20
	N-Oxalate	...	Plates	235 d.	−12.37	0.80
	Nitrate	...	Long needles	159–160	−15.18	10.33
	H-*l*-Malate	...	Thick plates	186–187	−14.73	2.04
E	Benzoyl[i]	...	Plates	90.2	+24.43	...
	Sulfate	?	.....	.....	.....	V. s.
	p-T. S.[e]	Mono	Thick needles	188–189	+ 2.60	6.68
	H-Oxalate	...	Fine needles	165	+ 3.11	5.64
	Nitrate	Hemi	Rhombic plates	190 d.	+ 3.41	13.80
	H-*l*-Malate	...	Thick prisms	191–193	± 0.0	3.45
	d-Mandelate	...	Thick prisms	190.3	+60.8	2.63

[a] Anhydrous unless otherwise indicated. [b] Values for salts in water; for benzoyl derivatives in methanol. [c] Values taken on the hydrated form. [d] Expressed in grams per 100 g. water at 25 ± 0.5°. [e] *p*-Toluenesulfonate. [f] Rotation value in chloroform. [g] Also $[\alpha]^{21}D$ +90.5° (c = 1, chloroform). [h] Compare Short and Read, Ref. 7. [i] Compare Wallach, Ref. 14. [j] Very soluble.

tained (at least) 6.0% of A, 83.7% of B, 4.0% of D and a trace of C. It may be noted that the previous separation and characterization of the various amine salts enabled the above separation to be carried out rapidly and almost quantitatively. The separation was facilitated considerably by the absence of fenchylamine.

Characterization and Analysis.—Each amine was isolated, in the order already mentioned, as an apparently uniform salt. This was recrystallized to constant properties and decomposed with alkali. The amine was extracted with benzene (sometimes after steam distillation) and distilled and characterized. In each instance the amine was then converted to another salt and the entire process repeated as a check. In no instance did this process or distillation at ordinary or reduced pressures produce any significant change in properties. The distillations under low pressures were made in a flask filled with glass wool with omission of the customary capillary bubbler, and carbon dioxide was excluded as much as possible at all times.

Each pure amine was then converted to various salts and all of these that could be made to crystallize readily were purified and characterized. The properties thus observed were used as guides for the separation of the remaining mixture. The principal data and analyses are recorded in the following sections and in Table II. Additional data and details are recorded in the original thesis.

(+)-β-Thujylamine. (Amine A.)—B. p. 199.6°[13] (750 mm.), 77.0° (12 mm.); $n^{25}D$ 1.4654; $\alpha^{25}D$ +27.8° (l = 1); $[\alpha]^{25}D$ +51.27° (c = 3, ethanol), +35.31° (c = 5.6, benzene). The amine was purified and analyzed as normal sulfate and *p*-toluenesulfonate.

Anal. Calcd. for $(C_{10}H_{19}N)_2 \cdot H_2SO_4$: SO_4, 24.38.

(13) All temperatures in this paper were taken with reliable short range thermometers without further correction.

Found; SO_4, 24.33. Calcd. for $C_{10}H_{19}N \cdot C_7H_8SO_3$: N, 4.31. Found: N, 4.27.

(+)-Iso-β-thujylamine. (Amine B.)—B. p. 193.4° (737 mm.), 76.8° (11 mm.); $n^{25}D$ 1.4564; d^{25}_4 0.860; $\alpha^{25}D$ +94.94° (l = 1); $[\alpha]^{25}D$ +107.9°, +108.4° (c = 1.6, ethanol), +103.6° (c = 3.3, benzene). The amine was purified as nitrate and oxalate; analyzed as oxalate.

Anal. Calcd. for $C_{10}H_{19}N(COOH)_2$: N, 5.76. Found: N, 5.76.

This amine has been partially described previously.[2-4] The constants recorded above agree closely with those given for an amine named *d*-isothujylamine by Short and Read.[7]

(−)-α-Thujylamine. (Amine C.)—B. p. 196.7° (756 mm.), 77.6° (12 mm.); $n.^{26.5}D$ 1.4590; $\alpha^{27.5}D$ −14.15° (l = 1); $[\alpha]^{27}D$ −1.41° (c = 6.3, ethanol), −13.25° (c = 5.8, benzene). The amine was purified as sulfate and normal oxalate; analyzed as sulfate.

Anal. Calcd. for $(C_{10}H_{19}N)_2H_2SO_4$: N, 6.93. Found: N, 6.87.

(−)-Iso-α-thujylamine. (Amine D.)—B. p. 202.2° (748 mm.), 86.2° (15.5 mm.), 81.1° (12 mm.); $n^{26}D$ 1.4640; $\alpha^{27}D$ −22.07° (l = 1); $[\alpha]^{26}D$ −23.29° (c = 2.6, ethanol), −26.92° (c = 2.3, benzene). The amine was purified as *l*-malate and *p*-toluenesulfonate; analyzed as normal oxalate and acid malate.

Anal. Calcd. for $(C_{10}H_{19}N)_2(COOH)_2$: $(COOH)_2$, 22.7. Found: $(COOH)_2$, 22.6. Calcd. for $C_{10}H_{19}N \cdot C_4H_6O_5$: N, 4.88. Found: N, 4.55.

The properties of this amine agree closely with the one named *l*-thujylamine by Short and Read.[7]

(+)-Fenchylamine. (Amine E.)—B. p. 195.3° (730 mm.), 73.4° (11.5 mm.); $\alpha^{27}D$ +22.19 (l = 1); $[\alpha]^{26}D$ +25.89° (c = 5, ethanol), +19.11° (c = 4.6, benzene). This amine was purified as *l*-malate and *d*-mandelate; analyzed as malate.

Anal. Calcd. for $C_{10}H_{19}N \cdot C_4H_6O_5$: N, 4.88. Found: N, 4.85.

This amine and its antipode have been partially characterized by Wallach.[14] Further description of the various isomeric fenchylamines is reserved for a later paper.

Resolution Experiments.—It was observed in the course of the separation of the amines that (+)-β-thujylamine resolved *dl*-mandelic acid. The process was therefore studied on a larger scale with pure amine. Fractionation of the salts with the *dl*-acid gave alternate crops with distinctive rotations and crystalline appearance. Both salts were purified quickly by combining similar crops and recrystallizing systematically. The principal constants of these salts already have been given in Table II.

The resolution of *dl*-mandelic acid with (−)-α-thujylamine was studied similarly. The less soluble salt (−B + A type) was purified readily and had $[\alpha]^{23}D$ +65.23° (c = 1.2, water). The more soluble salt was not purified completely.

Attempted resolution of *dl*-mandelic acid with (+)-iso-β-thujylamine gave three successive crystalline crops having specific rotations +68.9, +61.9 and +48.2°, respectively. Since it appeared that prolonged fractionation would be necessary for the resolution, the attempt was abandoned. Somewhat similar results were obtained with (−)-iso-α-thujylamine, except that the fractions were more distinctly different. This resolution has not been completed.

The resolution of *dl*-malic acid with (−)-iso-α-thujylamine was employed in the original separation of this amine from the mixture. In separate experiments the pure amine was combined with two equivalents of *dl*-malic acid. Fractionation readily gave a good yield of the pure acid *l*-malate, $[\alpha]^{21}D$ −14.78° (c = 4, water). The mother liquor contained principally *d*-malic acid. The identity of this salt was confirmed by its preparation from the amine and pure *l*-malic acid. The much more soluble *d*-malate was not purified. The malates of the other three thujylamines were too soluble for convenient crystallization and the resolutions were not studied.

The use of active fenchylamines as resolving agents has shown that they are probably the most convenient agents yet employed for the resolution of *dl*-malic acid and *dl*-mandelic acid. This work will be described in a later paper.

(14) Wallach, *Ann.*, **263**, 140 (1891).

Summary

The four diastereoisomeric thujylamines derived from the natural thujones have been prepared and their separation from each other and from fenchylamine described. All of these amines have been characterized fully. A preliminary study of the use of these amines as resolving agents is reported.

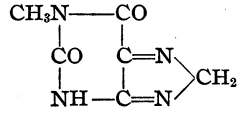
NASHVILLE, TENNESSEE RECEIVED JUNE 19, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

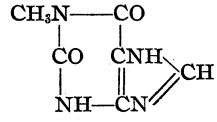
Desmotropism of Xanthine Derivatives[1]

BY TREAT B. JOHNSON AND JOSEPH C. AMBELANG[2]

The conclusion of vanVeen[3] that *toxoflavin*[4] is to be assigned the empirical formula $C_6H_6O_2N_4$ and represented structurally by formula (I), or an isomer of a monomethylxanthine (II) or (III), has stimulated a renewed activity by this Laboratory in the study of new purines, and the relationship of such constructions to the field of chemotherapy for infectious disease.[5] If vanVeen's postulation is correct, then *toxoflavin* (I) assumes a position of immediate scientific interest to workers in the field of purines, and presents the first chemical evidence in support of the desmotropic formulation for purine (IV) to be recorded in the chemical literature.[6]



I



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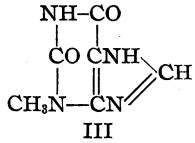

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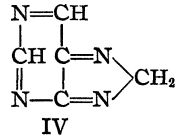
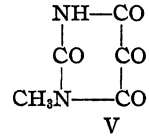


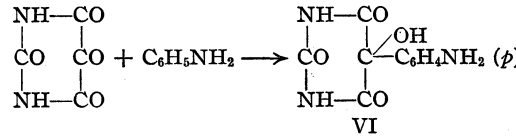
IV



V

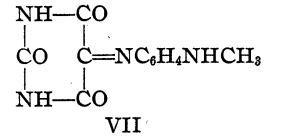
The purpose of this communication is to draw attention to specific reactions which characterize the differences in behavior of the pyrimidine alloxan toward cyclic and acyclic mono- and dibasic amines. The interesting facts that *toxoflavin* gives the murexide reaction, and when oxidized with potassium chlorate and hydrochloric acid yields methylalloxan (V),[5] suggest the possibility of new heterocyclic condensations being brought about by interaction of alloxan with aliphatic diamines. The authors are not aware that the action of such diamines on alloxan has been investigated previously.

The condensation reactions of aromatic amines with alloxan can be divided into two distinct groups as follows: 1, condensations involving addition of alloxan to the nucleus of the aromatic amine used giving derivatives of dialuric acid (VI). This characteristic behavior was first described by Pellizzari[7] and applies to monoamines of the aniline type or its nitrogen substituted derivatives. The same type of reaction applies when phenols are allowed to react with alloxan.

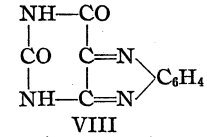


VI

2, Condensations of the anil type which result by interaction of alloxan with diaminobenzene derivatives as illustrated by the formation of the two anils (VII) and (VIII) from *o*-methylphenylenediamine and *o*-phenylenediamine, respectively.[8]



VII



VIII
(Alloxazine)

No anils of either type (VII or VIII) obtained by the action of aliphatic amines on alloxan have been described thus far. This pyrimidine (alloxan) functions as a strong oxidizing agent when allowed to react in aqueous solution with acyclic

(1) Researches on Pyrimidines, CLXIII.

(2) Sterling Professorship of Chemistry Research Assistant, 1938–39.

(3) VanVeen and Mertens, *Proc. Akad. Wetenschappen Amsterdam*, **36**, 666 (1933); *Rec. trav. chim.*, **53**, 257, 398 (1934); vanVeen and Baars, *Proc. Akad. Wetenschappen Amsterdam*, **40**, 1 (1937); *Rec. trav. chim.*, **57**, 248 (1938).

(4) A name given by vanVeen and Mertens to the prosthetic group of a natural pigment formed in the culture of *Bacterium bongkrek*. This substance (toxoflavin) formed by the action of *Bacterium cocovenenans* is the cause of the well-known bongkrek and semaji-poisonings met with in Java.

(5) VanVeen seems to have demonstrated conclusively that *toxoflavin* is a pyrimidine compound closely related structurally to alloxan. It is impossible, however, to conclude from the present experimental evidence whether the methyl group functioning in its formula occupies position 1 or 3 in the supposed purine molecule (I).

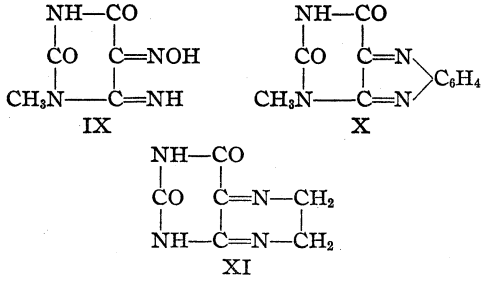
(6) "Harnsäure und Xanthine," H. Biltz, *J. prakt. Chem.*, **145**, 83 (1936). "The 4,5-double bond in xanthines does not exhibit the same unsaturation value as that in the uric acids. Conjugation with the 8,9-double bond in a xanthine, or with the 7,8-double bond in an isoxanthine, bestows on the imidazole ring of the purine an aromatic character [Biltz and Sauer, *Ber.*, **64**, 752 (1931)], thereby destroying the influence of unsaturation exercised by the double bond. This aromatic system exhibits, as might be expected, an influence favorable for substitution in the 8-position of the purine molecule."

(7) Pellizzari, *Gazz. chim. ital.*, **17**, 412 (1887).

(8) (a) Piloty and Finkh, *Ann.*, **333**, 41 (1904); (b) Mohlau and Litter, *J. prakt. Chem.*, **73**, 453 (1907); (c) Kuhling and Kaselitz, *Ber.*, **39**, 1319 (1916); (d) also recent work of Rudy and Cramer, *ibid.*, **72**, 227 (1939).

monoamines leading to complicated molecular changes with formation of the corresponding amine salts of purpuric acid, which finally undergo conversion to murexide.[8a] Strecker[9] first disclosed this remarkable behavior of alloxan in a study of its action on α-amino acids, and observed that such acids are oxidized by alloxan to the corresponding aldehydes with formation of murexide.[10]

The authors are now able to report that the reactivity of alloxan toward methylenediamine and ethylenediamine has been investigated, and that neither diamine was found to be productive of any changes of immediate biochemical interest. Methylenediamine showed no tendency to react with alloxan to form xanthine or any desmotropic modification of a purine (IV) corresponding to the constitution proposed for toxoflavin (I). Also ethylenediamine failed to react with alloxan in a manner corresponding to that of *o*-phenylenediamine with formation of a cyclic anil (XI).



IX

X

XI

A description of the reactions revealed in this study is given in the experimental part of this paper. It is also of especial interest to note here that the imido-oxime derivative of methylalloxan (IX), which is characterized by the same anil type of unsaturation as is expressed in van-Veen's proposed formula for toxoflavin (I), does not react with *o*-phenylenediamine to form *methylalloxazine* (X). VanVeen and Baars[3] report that *toxoflavin* is not methylated further by the action of diazomethane or methyl iodide and undergoes complete destruction by energetic action.

Experimental Part

Attempts at Condensation of Alloxan with Methylenediamine.—The methylenediamine dihydrochloride used in this research was prepared according to the method described by Knudsen.[11]

(9) Strecker, *Ann.*, **123**, 363 (1862).

(10) Leucine = isovaleraldehyde; alanine = acetaldehyde; glycine = formaldehyde. See also Hurtley and Wootten, *J. Chem. Soc.*, **99**, 288 (1911).

(11) Knudsen, *Ber.*, **47**, 2698 (1914).

1. In Glacial Acetic Acid Solution.—One gram (0.009 mole) of pulverized methylenediamine dihydrochloride was added to an acetic acid solution (20 cc.) of 0.8 g. (0.01 mole) of fused sodium acetate. After standing for three hours with occasional shaking, the mixture was refluxed a few minutes and allowed to stand until cold. The acid solution was then filtered to remove undissolved sodium chloride and mixed with a solution of 0.3 g. (0.0028 mole) of alloxan anhydride in 10 cc. of glacial acetic acid. A deep red color developed immediately. After four days of standing the acid solution was heated at 90–100° for one and one-half hours, when the red coloration became somewhat lighter. On cooling, a small amount of crystalline material separated. It was washed carefully with dry ether and dried *in vacuo* over concentrated sulfuric acid; yield 0.12 g. This showed no sharp m. p. and slowly decomposed when heated above 253°. It was identified as alloxan. This experiment was repeated but without securing any evidence of the formation of a purine condensation product. The recovered alloxan was highly discolored, due apparently to admixture of a small amount of murexide.

Anal. Calcd. for $C_4H_2O_4N_2$: N, 20.00. Found: N, 19.73.

2.—No formation of a purine was observed by interaction of methylenediamine dihydrochloride with alloxan in aqueous solution in the presence of sodium acetate. The solution took on a deep red color due to slow formation of murexide, and the odor of formaldehyde was detected easily.

3.—Attempts also were made to bring about a condensation in absolute alcohol solution. In an acidified solution (with hydrochloric acid) ammonium chloride was precipitated, and formaldehyde generated. Alloxan alcoholate was used also for condensation with methylenediamine but without success. Interaction of the diamine with alloxan in pyridine solution led to the production of a black tar. It is of interest to note here that methylenediamine dihydrochloride as well as trioxymethylene reduce Fehling's solution after gentle warming of the alkaline solution.

Condensation of Alloxan with Ethylenediamine. 1. In Acid Solution.—One and six-tenths grams (0.01 mole) of alloxan monohydrate dissolved in 10 cc. of water was added to a solution of 0.75 g. (0.012 mole) of ethylenediamine in 7 cc. of 6 *N* hydrochloric acid (0.042 mole). The characteristic murexide coloration did not develop and a small quantity of colorless crystals finally separated on standing. The yield was only 0.5 g. and this was not increased by warming the solution. This reaction product contained chlorine and was dried for analysis *in vacuo* over concentrated sulfuric acid; m. p. 225–230° with decomposition. The crystals were colored slightly pink, indicating the possible admixture of a trace of murexide. The results of analysis indicated a constitution conforming to that of a hydrochloride of alloxan-[ethylenediamine-anilhydrate]-5.

Anal. Calcd. for $C_6H_{10}O_4N_4 \cdot HCl$: C, 30.1; H, 4.6; N, 23.4. Calcd. for $C_6H_{10}O_4N_4 \cdot HCl \cdot H_2O$: C, 29.1; H, 4.4; N, 22.7. Found: C, 29.7; H, 3.80; N, 22.74.

The filtrate from the preceding experiment was diluted with acetone until no further precipitation of solids took place (1.44 g.). This substance was identified as the di-

hydrochloride of ethylenediamine equivalent to 87% of the diamine originally used.

Anal. Calcd. for $C_2H_{10}N_2Cl_2$: N, 21.1. Found: N, 21.2.

2. In Alcohol Solution.—Alloxan anhydride (0.4 g. or 0.0028 mole) was dissolved in 15 cc. of absolute alcohol, and dry hydrogen chloride gas bubbled into the solution until it was decolorized to a pale yellow. After cooling in a refrigerator (two days) and finally filtering, 0.2 g. (0.0033 mole) of ethylenediamine in 10 cc. of absolute alcohol was added. A colorless, granular precipitate deposited, and took on a pink color on exposure to the air. It was separated, washed with absolute alcohol and ether and then dried *in vacuo* over concentrated sulfuric acid. The yield was only 0.5 g. The compound was free from chlorine. It was very soluble in water and attempts to purify it by precipitation from aqueous solution with acetone or pyridine, or by diluting an acetic acid solution with chloroform, were unsuccessful. A specimen dried to constant weight at 100° over phosphoric anhydride melted at about 214° with decomposition.

Anal. Calcd. for alloxan-[ethylenediamine-anilhydrate]-5, $C_6H_{10}O_4N_4$: C, 35.64; H, 4.9; N, 27.71. Found: C, 35.27, 36.2; H, 4.28, 4.53; N, 26.89, 28.1.

Two-tenths gram of the above condensation product was dissolved in 11 cc. of 0.1 *N* hydrochloric acid and combined with 22 cc. of water containing 0.3 g. of picric acid. After concentrating the solution *in vacuo*, and cooling, the picrate of ethylenediamine separated. This salt was purified by crystallization from water and melted at 227–235° with decomposition. When mixed with pure ethylenediamine picrate, no depression of the melting point was observed.

Anal. Calcd. for $C_{14}H_{14}O_{14}N_8$: N, 21.62. Found: N, 21.82.

Ethylenediamine gives an intense crimson coloration when added to an aqueous solution of alloxan. The dihydrochloride of the amine produces no coloration under the same experimental conditions. Furthermore, the presence of ethylenediamine dihydrochloride did not interfere with the formation of *alloxazine* by interaction of *o*-phenylenediamine dihydrochloride with alloxan in aqueous solution.

Interaction of *o*-Phenylenediamine Dihydrochloride with Methylalloxan-4-imino-5-oxime.—Toxoflavin and methylalloxan[12] react with *o*-phenylenediamine dihydrochloride in aqueous solution on warming to give methylalloxazine $C_{11}H_{18}O_2N_4$ (X). The above oxime derivative (IX)[13] does not interact with the *o*-diamine in a similar manner to form this alloxazine derivative. Combination in boiling water solution leads to the formation of an amorphous, brown substance which is soluble in hot acetic acid, and is reprecipitated in an amorphous condition by addition of water. We were unable to isolate any product of crystalline character from the reaction mixture.

Summary

1. Attention is called to the characteristic differences in chemical behavior of the pyrimidine alloxan toward aromatic and aliphatic amines.

2. Methylenediamine and alloxan do not interact to form xanthine or any tautomeric modification of this purine.

3. Ethylenediamine shows a different behavior toward alloxan than its aromatic analog *o*-phenylenediamine, and does not interact to form the corresponding aliphatic alloxazine analog. A simple addition product is formed without cyclization.

4. The oximido-imide (4,5) derivative of methylalloxan does not interact with *o*-phenylenediamine to form an alloxazine.

(12) VanVeen and Baars, *Rec. trav. chim.*, **57**, 259, 261 (1938).

(13) Traube, *Ber.*, **33**, 3048 (1900).

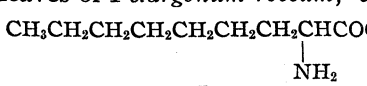
NEW HAVEN, CONN. RECEIVED JUNE 27, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

Synthesis of α-Aminopelargonic Acid

BY TREAT B. JOHNSON

At the urgent request of a group of workers in experimental medicine the author consented to undertake the synthesis of this unknown α-amino acid (I). Polypeptide combinations of this amino acid are believed to occur in the degradation products of the proteins of beet roots and in leaves of *Pelargonum roseum;* and several



I

dipeptide derivatives containing this amino acid have been described previously by Hopwood and Weizmann[1] in 1911.

The fact that pelargonic acid itself is known to influence certain physiological changes of interest to medicine, lends interest in the possible physiological behavior of the unknown amino acid and its derivatives. The fatty acid is characterized, for example, by its physical capacity as a surface-active substance and may act, depending upon the percentage present, as an accelerator or an

(1) Hopwood and Weizmann, *J. Chem. Soc.*, **99**, 1577 (1911).

TABLE I

Oenanthol, g.	Hydantoin, g.	Glac. acetic acid, cc.	Sod. acetate, g.	Time, hrs.	Temp., °C.	M. p., °C.	Hydantoin yield, g.
6	5	30	15	8	140–150	156–158	0.75
6	5	30	30	9	140–150	156–158	0.65
11.4	10	40	50	9	140–150	156–158	2.60
6	5	30	30	9	140–150	156–158	1.8
26	22.8	120	120	9	140–150	156–158	6.3
14	11.6	60	60	10	140–150	156–158	2.4

inhibitor of fermentation.[2] It also has been shown to be bactericidally effective toward certain organisms due to its marked surface-tension depressant action.[3] Addition of pelargonic acid to washed blood cells is known to increase their glucolytic activity to a marked degree. The acid exhibits also a characteristic physiological influence when incorporated into ester constructions of the procaine type (II). In the quantitative comparisons of a series of aliphatic procaine analogs it was shown that the narcotic effect of such esters increases in a normal series until the pelargonate derivative (II) is reached, when toxicity is enhanced to a maximum.[4]

$$CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_2COOCH_2CH_2N(C_2H_5)_2\cdot HCl$$

II

For the preparation of this amino acid (I) the author has applied successfully the aldehyde–hydantoin method of synthesis of α-amino acids originally developed in this Laboratory by Wheeler.[5] The different steps of this method are expressed below (III–VI).

$$\underset{\text{III}}{RCHO} \longrightarrow \underset{\text{IV}}{RCH{=}\overbrace{CCONHCONH}} \longrightarrow \underset{\text{V}}{RCH_2\overbrace{CHCONHCONH}} \longrightarrow \underset{\text{VI}}{RCH_2\underset{\underset{NH_2}{|}}{CH}COOH}$$

While this method of synthesis finds very general application when applied with aromatic aldehydes ($R = C_6H_5$, etc.), it has proved of no practical value, from a synthetic point of view, for the utilization of aliphatic aldehydes in α-amino acid synthesis. It is, therefore, of special interest to report that the author has succeeded in applying this technique of α-amino acid synthesis successfully with the aliphatic aldehyde—*oenanthol*. This aldehyde condenses with hydantoin to form the oenantholal-hydantoin (IV).[6] The latter compound is reduced easily to the saturated hydantoin (V); and this undergoes a normal hydrolysis by digestion with alkali yielding the desired α-aminopelargonic acid I.

(2) Windisch, Henneberg and Dietrich, *Biochem. Z.*, **107**, 172 (1920).
(3) Stanley and Adams, THIS JOURNAL, **54**, 1548 (1932).
(4) Brill and Bulow, *ibid.*, **55**, 2059 (1933).
(5) Wheeler and Hoffman, *Am. Chem. J.*, **45**, 368 (1911).
(6) $R = CH_3(CH_2)_5CH{=}$.

Experimental Part

Oenanthol, $CH_3(CH_2)_5CHO$.—All the oenanthol used in this work, with the exception of 10 g. of a Kahlbaum stock specimen, was manufactured by destructive distillation *in vacuo* of a high grade of castor oil. Heating this oil at an oil-bath temperature of 290–300° a fraction was collected which distilled from 60–68° at a pressure of 23–30 mm. This fraction of crude oenanthol was then purified by distillation at ordinary pressure and a fraction of oenanthol was finally collected boiling at 152–155°. Pure oenanthol boils at 155° at 760 mm. The average yield of oenanthol was 14 g. of the pure aldehyde from 280 g. of castor oil.

Condensation of Oenanthol with Hydantoin

Formation of $\begin{array}{l} \quad\quad\quad\quad CO{-}NH \\ \quad\quad\quad\quad\quad | \\ CH_3(CH_2)_5CH{=}C{-}NH \end{array}\!\!>CO$, **Oenantholal-hydantoin.**—This hydantoin was obtained by digesting molecular proportions of hydantoin and oenanthol in glacial acetic acid solution with anhydrous sodium acetate. The results of the different condensations and the experimental conditions are recorded in Table I.

The yields of hydantoin condensation products were irregular and were not increased by incorporating acetic anhydride with the acetic acid and sodium acetate. After the end of the digestion period the reaction mixture was mixed with water and cooled. The unreacted oenanthol was extracted with ether, leaving behind the insoluble hydantoin derivative. This compound is purified easily by recrystallization from boiling absolute alcohol. It separates on cooling in the form of colorless rosets which melt at 157–159°.

Anal. Calcd. for $C_{10}H_{16}O_2N_2$: C, 61.22; H, 8.16; N, 14.28. Found: C, 61.01; H, 7.98; N, 14.31, 14.50.

The hydantoin dissolves easily in dilute sodium hydroxide solution and is reprecipitated by acidifying the alkaline solution with hydrochloric acid.

Reduction of Oenantholal-hydantoin

Formation of $\begin{array}{l} \quad\quad\quad\quad CO{-}NH \\ \quad\quad\quad\quad\quad | \\ CH_3(CH_2)_6CH{-}NH \end{array}\!\!>CO$, **Hydantoin of α-Aminopelargonic Acid.**—For reduction of the above oenantholal-hydantoin the following reaction mixture was prepared: 5.5 g. of hydantoin, 12.5 g. of $SnCl_2\cdot 2H_2O$, 75 cc. of 20% hydrochloric acid and 50 cc. of alcohol. This mixture was heated at boiling water-bath temperature for one and one-half hours and the excess of alcohol then

evaporated at 100°. The residue left behind was then triturated with water, filtered and the insoluble precipitate saved (see below). The aqueous filtrate was then saturated with hydrogen sulfide gas to precipitate tin as sulfide. After filtering off this tin sulfide precipitate and evaporating the filtrate to dryness no organic residue was recovered.

The insoluble precipitate (above) proved to be the desired reduction product. It was very insoluble in cold water, but separated from boiling water in colorless crystals melting at 142–143°. The total yield of pure crystallized hydantoin was 3.0 g. In a second experiment 8.8 g. of oenantholal-hydantoin was reduced under exactly the same conditions and yielded 8.8 g. of the desired reduced hydantoin.

Anal. Calcd. for $C_{10}H_{18}O_2N_2$: N, 14.14. Found: N, 14.17, 14.09.

Hydrolysis of the Reduced Hydantoin to α-Aminopelargonic Acid, $CH_3(CH_2)_6CH(NH_2)COOH$.—This hydantoin proved to be very resistant to hydrolysis by the action of barium hydroxide. Three grams of the pure reduced hydantoin was suspended in 1000 cc. of a hot, saturated solution of barium hydroxide and the mixture refluxed at its boiling point until the evolution of ammonia gas ceased. This actually required a digestion for fifty-six hours. The barium was then exactly precipitated as barium sulfate by adding the required amount of sulfuric acid, and bringing the solution to an exact neutral point to litmus. After filtering from barium sulfate, the clear aqueous solution was evaporated to dryness when we obtained 2.4 g. of the required α-aminopelargonic acid or 92.3% of the theoretical.

This α-amino acid is very difficultly soluble in hot water, alcohol, benzene and glacial acetic acid. It was purified for analysis by dissolving in hot, dilute hydrochloric acid, and cooling, when the hydrochloride of the amino acid crystallized out as fine colorless needles. This salt showed no definite melting point but slowly underwent decomposition on heating. It was dried for analysis over phosphorus pentoxide in an Abderhalden vacuum drier.

Anal. Calcd. for $C_9H_{20}O_2NCl$: N, 6.68; Cl, 16.94. Found: N, 6.90, 6.52; Cl, 16.81.

In order to obtain the free α-aminopelargonic acid (I) 1 g. of the above hydrochloride was dissolved in hot water and the solution allowed to cool slowly. The amino acid separated in the form of colorless, flaky crystals. This acid did not show a definite melting point and underwent decomposition when heated between 236 and 256°, giving off dense vapors. The yield of free acid was 0.63 g. The crystals gave no test for chlorine, indicating complete dissociation of the hydrochloride in aqueous solution.

Anal. Calcd. for $C_9H_{19}O_2N$: C, 62.42; H, 10.98; N, 8.10. Found: C, 62.23; H, 10.83; N, 8.40, 7.90.

Summary

1. Oenanthol can be utilized with success for the synthesis of α-aminopelargonic acid by application of the aldehyde-hydantoin method of amino acid synthesis.

NEW HAVEN, CONN. RECEIVED JULY 19, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, KWANGSI UNIVERSITY]

Synthesis of 2-*n*-Butyl-α-naphthol

BY YUOH-FONG CHI[1]

In this short paper is described a method of synthesizing 2-*n*-butyl-α-naphthol, which promises to have practical value as an antiseptic. This compound is formed by reducing 2-*n*-butyryl-α-naphthol, which is in turn obtained by condensing α-naphthol with *n*-butyric acid in the presence of fused zinc chloride.

It has long been known that fatty acids react in a characteristic manner with phenols and resorcinol in the presence of fused zinc chloride giving hydroxy-ketones.[2] α-Naphthol also condenses with glacial acetic acid in the presence of acetic anhydride and zinc chloride giving 2-acetyl-α-naphthol.[3] The author finds that α-naphthol reacts likewise with *n*-butyric acid giving 2-*n*-butyryl-α-naphthol, m. p. 85–86°, which is identified by formation of its oxime and semicarbazone. A secondary product of the reaction is α-naphthol *n*-butyrate.

The hydroxy-ketones, such as 2-acetylhydroquinone, 4-acetylresorcinol, 4-propionylresorcinol, 2-propionylhydroquinone, 4-*n*-butyrylresorcinol, 4-acetylanisole, 4-acetylphenetole, 4-propionylphenetole, 2,5-dimethoxypropiophenone, 3,4-dimethoxypropiophenone, etc., which contain the hydroxyl or alkoxyl group in the benzene ring, have been shown to undergo reduction to their corresponding alkyl derivatives by digesting with zinc amalgam and strong hydrochloric acid.[4] In like manneer 2-*n*-butyryl-α-naphthol is reduced

(1) The author desires to express here his appreciation of the help given by Professor Treat B. Johnson of Yale University in organizing this paper for publication.

(2) Nencki and Sieber, *J. prakt. Chem.*, [2] **23**, 147, 537 (1887); Nencki and Schmid, *ibid.*, **23**, 546 (1887); Goldsweig and Kaiser, *ibid.*, [2] **43**, 86 (1891); Crepieux, *Bull. soc. chim.*, [3] **6**, 151 (1891); Nencki, *Ber.*, **26**, R587 (1893); Dzierzgowski, *ibid.*, **26**, R588 (1893); Pauly and Lockemann, *ibid.*, **48**, 30 (1915); Johnson and Lane, THIS JOURNAL, **43**, 348 (1921); Dohme, Cox and Miller, *ibid.*, **48**, 1688 (1926).

(3) Witt and Braun, *Ber.*, **47**, 3219 (1914).

(4) Clemmensen, *ibid.*, **47**, 54 (1914); Johnson and Hodge, THIS JOURNAL, **35**, 1014 (1913); Johnson and Lane, *ibid.*, **43**, 348 (1921); Sonn, *Ber.*, **54**, 773 (1921).

to 2-*n*-butyl-α-naphthol according to the Clemmensen technique.

Experimental Part

2-*n*-Butyryl-α-naphthol.—Fifty-eight and four-tenths grams of α-naphthol was digested with 105.6 g. of *n*-butyric acid in the presence of 108 g. of fused zinc chloride for one minute. The mixture, while still warm, was then poured in a fine stream into 1200 cc. of cold water with stirring, whereupon the oil solidified to a brownish crystalline mass. After being filtered and dried, this reaction product was purified by fractionating in a vacuum. The following three fractions: (a) b. p. 135–150° at 3 mm., (b) b. p. 150–165° at 3 mm., and (c) b. p. 165–170° at 3 mm., were collected. Each fraction was redistilled at 1 mm. pressure, whence two main subfractions: (a) b. p. 125–130°, and (b) b. p. 145–152°, were finally obtained. The yield of the high boiling fraction (b. p. 145–152° at 1 mm.) was 34.3 g. It crystallized from hot petroleum ether in yellow rhombic crystals melting at 85–86°. The ketone also can be recrystallized from ether.

Anal. Calcd. for $C_{14}H_{14}O_2$: C, 78.46; H, 6.59. Found: C, 78.51, 78.39; H, 6.65, 6.73.

The low boiling fraction (b. p. 125–130° at 1 mm.) was proved to be α-naphthol *n*-butyrate. It was purified by recrystallization from a mixture of benzene and petroleum ether, separating in colorless needles, melting at 95.5–96.5°. The yield was 11.6 g. On treatment with hydroxylamine, it was changed into naphthol.

Anal. Calcd. for $C_{14}H_{14}O_2$: C, 78.46; H, 6.59. Found: C, 78.22, 78.35; H, 6.35, 6.50.

Oxime.—One and seven-hundredths grams of 2-*n*-butyryl-α-naphthol dissolved in a small volume of alcohol was treated with 0.7 g. of hydroxylamine hydrochloride and 0.53 g. of sodium carbonate dissolved in a small volume of water, and sufficient alcohol was added to obtain a uniform solution. This was then refluxed for four hours, and finally diluted with a large volume of water, whereupon the impure oxime precipitated. It was filtered, dried, and recrystallized from benzene and petroleum ether in the form of yellow needles, melting at 119° to a clear oil.

Anal. Calcd. for $C_{14}H_{14}O_2N$: N, 6.11. Found: N, 6.26, 6.33.

Semicarbazone.—One and seven-hundredths grams of 2-*n*-butyryl-α-naphthol dissolved in a small volume of alcohol was treated with 1.12 g. of semicarbazide hydrochloride and 0.53 g. of sodium carbonate dissolved in a small volume of water, and sufficient alcohol to obtain a uniform solution. This was heated on a water-bath for four hours, and water added to precipitate the semicarbazone. This was purified by dissolving in a mixture of alcohol, benzene and petroleum ether, and allowing to stand in a vacuum desiccator over sulfuric acid, whereupon the semicarbazone crystallized in microscopic crystals and melted at 201–202° to a clear oil. The yield was 0.3 g.

Anal. Calcd. for $C_{25}H_{17}O_2N_3$: N, 15.50. Found: N, 15.70, 15.61.

2-*n*-Butyryl-α-naphthol Methyl Ether.—Ten and seven-tenths grams of 2-*n*-butyryl-α-naphthol and 2.8 g. of potassium hydroxide were dissolved in 500 cc. of alcohol, and 5 cc. of dimethyl sulfate was added gradually drop by drop, while the solution was shaken vigorously. This was then heated at 50° for four hours to complete the reaction and the solution boiled for five minutes in order to destroy the excess of dimethyl sulfate and remove the excess of alcohol. This solution was then extracted with a large volume of benzene, the benzene solution dried with anhydrous sodium sulfate, filtered, and heated on a water-bath to remove the solvent. The oil left behind solidified on cooling and distilled at 155–157° at 1 mm. pressure. The yield was 6.5 g. After recrystallization from petroleum ether, it melted at 80–81°.

Anal. Calcd. for $C_{15}H_{16}O_2$: C, 78.90; H, 7.07. Found: C, 78.77, 78.83; H, 7.01, 6.94.

2-*n*-Butyryl-α-naphthol Ethyl Ether.—Ten and seven-tenths grams of 2-*n*-butyryl-α-naphthol dissolved in 500 cc. of alcohol was heated for eight hours with 6.5 g. of ethyl bromide and 2.8 g. of potassium hydroxide. After distilling off the alcohol the residue was extracted with a large volume of benzene; the solution was dried with anhydrous sodium sulfate, filtered, and finally heated on a water-bath to remove the solvent. The oil left behind solidified and distilled at 158–159° under 1 mm. pressure. After recrystallization from petroleum ether, it melted at 79–81°.

Anal. Calcd. for $C_{16}H_{18}O_2$: C, 79.29; H, 7.49. Found: C, 79.11; H, 7.57.

2-*n*-Butyl-α-naphthol.—Ten and seven-tenths grams of 2-*n*-butyryl-α-naphthol was digested with 50 g. of zinc amalgam suspended in a mixture of 50 cc. of concentrated hydrochloric acid and 50 cc. of water for seventeen hours. After each hour's boiling, 10 cc. of concentrated hydrochloric acid was added, until a total volume of 150 cc. of hydrochloric acid was used for the reaction. After the acid solution, with a layer of brown oil floating on the surface, was separated from the unreacted zinc amalgam and cooled, the crude 2-*n*-butyl-α-naphthol solidified. It was dried and distilled at 140–149° at 1 mm. pressure. The yield was 6.5 g. After purification by recrystallization from petroleum ether, it separated in colorless needles, melting at 73–74°. On keeping for two months it becomes colored.

Anal. Calcd. for $C_{14}H_{16}O$: C, 83.95; H, 8.06. Found: C, 83.99, 83.84; H, 8.24, 8.19.

Summary

1. α-Naphthol condenses normally with *n*-butyric acid giving 2-*n*-butyryl-α-naphthol.

2. 2-*n*-Butyl-α-naphthol is obtained by reduction of 2-*n*-butyryl-α-naphthol by Clemmensen's method.

3. The bactericidal properties of this new naphthol are under investigation.

WUCHOW, KWANGSI, CHINA RECEIVED JUNE 29, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AT THE OHIO STATE UNIVERSITY]

Fluorinated Derivatives of Propane. III

BY ALBERT L. HENNE AND MARY W. RENOLL

Introduction.—In the preceding paper of this series,[1] the fluorination of C_3Cl_8, of *a*-C_3HCl_7, and of *s*-C_3HCl_7 was described. Formulas for the mono- and the difluorides were demonstrated and plausible formulas were presented for the trifluorides. The present paper proves the correctness of the trifluoride assumptions and describes newly prepared tetrafluorides, for which it offers plausible formulas.

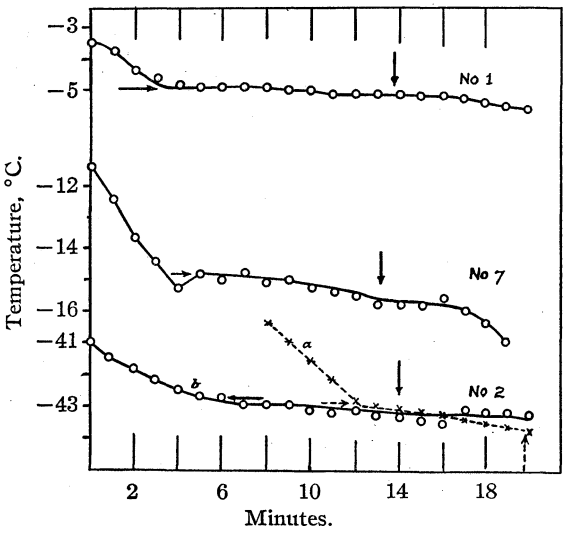


Fig. 1.—Horizontal arrows show the temperature at which crystals were unmistakably seen. Vertical arrows denote end of stirring. a, b and c denote different rates of cooling.

Procedure.—The methods of fluorination and chlorination were the ones used in the preceding papers. So also were the methods of purification and the physical measurements. The analyses for chlorine and fluorine were made after decomposing the organic fluorochlorides over red hot calcium oxide, in a small steel bomb. The freezing curves required a great deal of perseverance because the latent heat of fusion of polyfluorides is small, and because the mushy crystals create a viscous mass, difficult to stir adequately. The rate of cooling must be slow, and the best results were obtained with a cooling bath kept about 5° below the freezing point under measurement. These difficulties are illustrated graphically in Fig. 2.

(1) Henne and Ladd, THIS JOURNAL, **60**, 2491 (1938).

Results.—The actual experimental results appear in the table and diagrams. Figure 1 gives the freezing curve of $CCl_2FCCl_2CClF_2$ (no. 1), of $CCl_3CClFCClF_2$ (no. 7) and of $CClF_2$-CCl_2CClF_2 (no. 2) taken at two different rates of cooling (a and b). Figure 2 refers to CCl_3-$CClFCF_3$ (no. 8), taken at three different rates of cooling (a, b and c); it illustrates the difficulties prevailing when a small sample is used; on both curves b and c, the crystals were seen at −15.8°, and this was adopted as the freezing point, although it is quite probable that the true point may be as much as one degree higher.

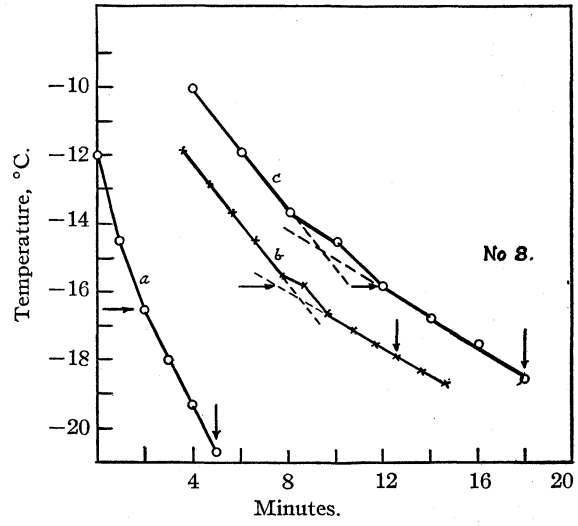


Fig. 2.—Horizontal arrows show the temperature at which crystals were unmistakably seen. Vertical arrows denote end of stirring. a, b and c denote different rates of cooling.

In the table, no comments are required except for no. 4. In this case the analysis result is explained by the presence of trichloroethylene.

Determination of the Formulas.—The procedure used follows that of the preceding paper. Specifically, the trifluorides were obtained from known difluorides, and since no reason exists to expect rearrangements of halogen atoms during fluorination, there are only a limited number of places available for the third fluorine atom. The same reasoning holds true for the fourth fluorine atom of the new tetrafluorides. Reactions with zinc in alcohol gave additional information as

TABLE I

No.	Name	F. p., °C.	B. p., °C.	t	dt_4	nt_D	MRD	ARF	Cl/F Found	Cl/F Calcd.
1	$CCl_2FCCl_2CClF_2$	− 4.9	152.3	20	1.77023	1.43959	40.21	1.04	1.65	1.67
2	$CClF_2CCl_2CClF_2$	−42.9	112.0	20	1.7199	1.39584	35.42	1.07	1.00	1.00
3	$CCl_2FCHClCClF_2$	Glass	128.7	25	1.67471	1.41569	35.32	1.03	1.35	1.33
4	$CClF_2CHClCClF_2$	Glass	88		See text				0.97	0.75
5	$CHCl_2CClFCClF_2$	Glass	129.8	20	1.69124	1.41967	35.27	1.02	1.30	1.33
6	$CHCl_2CClFCF_3$	Liquid	89.8	20	1.6368	1.37613	30.77	1.12	0.76	0.75
7	$CCl_3CClFCClF_2$	−14.8	153.3	20	1.7702	1.43919	40.18	1.03	1.62	1.67
8	$CCl_3CClFCF_3$	−15.8	112.3	20	1.7226	1.39797	35.57	1.10	1.02	1.00
9	$CCl_2{=}CFCF_3$		43.5	10	1.555					
10	$CCl_2BrCFBrCF_3$	35.5–37	154							

to the nature of the halogens attached to adjacent carbon atoms. Finally, the heptahalogenated derivatives (which form glasses at low temperature) were chlorinated in sunlight to crystallizable octahalogenated derivatives and the crystals were compared. The experimental evidence thus obtained was sufficient to establish definitely the formulas of the trifluorides. In the case of the tetrafluorides this did not suffice, as the experimental evidence could only reduce the choice to a limited number of possibilities, and establish a gradation as to their plausibility. The final choice was based on the agreement between predicted and observed melting points, a procedure which can be defended in this particular case on two counts: (a) there is a marked parallelism between the melting points on the one hand, and the number and place of the fluorine atoms on the other hand, which can be seen in the preceding papers on ethane and propane derivatives, and hence it is possible to predict melting points within 2 or 3°. (b) The final choices are to be made between alternates with widely separated melting points, that is, at least 40° apart. This is a consideration of paramount importance and in no case should a choice be made between melting points which can be considered as in the same range.

It should again be emphasized that in the following discussion, a clear cut distinction is always made between demonstrated formulas and plausible formulas, and in the latter case an effort is made to rate the degree of plausibility.

(1) **$CCl_2FCCl_2CClF_2$, m. p. −4.9°.**—This trifluoride was obtained from $CCl_3CCl_2CClF_2$ as well as from $CCl_2FCCl_2CCl_2F$, and in neither case was there another trifluoride formed. Consequently, the proposed formula is experimentally demonstrated.

(2) **$CClF_2CCl_2CClF_2$, m. p. −42.9°.**—This tetrafluoride was easily obtained from the preceding compound. Besides the proposed formulation, it can have only two alternates, namely, $CCl_2FCClFCClF_2$, or $CCl_2FCCl_2CF_3$. The choice results from the following reasons, based on general analogies: (a) the fluorination course and the regularity of the freezing point depression recalls the case of CCl_3CCl_3, whose trifluoride CCl_2FCClF_2 (m. p. −36°) freezes 60° below the difluoride CCl_2FCCl_2F (m. p. 24°) and whose tetrafluoride $CClF_2CClF_2$ (m. p. −94°) freezes 58° lower than the trifluoride. (b) The alternate formulas call for widely different melting points, namely, about −80° for $CCl_2FCClFCClF_2$, and not lower than −5° for $CCl_2FCCl_2CF_3$. The formula adopted is therefore a plausible hypothesis.

(3) **$CCl_2FCHClCClF_2$.**—This compound was obtained from the established $CCl_2FCHClCCl_2F$, with much decomposition. To prove its structure, it was proposed to remove one molecule of hydrogen chloride by means of an alcoholic alkali, then to chlorinate the resulting olefin to obtain a fully halogenated trifluoride. The latter was expected to freeze at −4.9°, thereby proving identical with $CCl_2FCCl_2CClF_2$ (no. 1) and establishing the correctness of the proposed formula. However, the reaction did not follow the expected course, and hydrolysis occurred: the only reaction product that could be isolated boiled at 104–109° at 7 mm., had a density d^{20}_4 1.1794, and a refractive index $n^{20}D$ 1.4320. Its analysis indicated 5.62% H, 42.28% C, 18.87% Cl, and no fluorine. This information, and an experimental determination of the molecular magnitude as about 190, indicated that the compound was the diethyl ester of chloromalonic acid, and this was confirmed by the good agreement between the computed molecular refraction (42.54) and the experimental value (42.80) and by the literature. The chloromalonic ester proves that the central chlorine atom is still unreplaced by fluorine, and demonstrates therefore that the proposed formula of the trifluoride no. 3 is correct.

Efforts to replace the hydrogen atom by chlorine in sunlight, and directly to manufacture $CCl_2FCCl_2CClF_2$ (no. 1) failed completely on account of complete decomposition, an unpredicted behavior.

(4) **$CClF_2CHClCClF_2$.**—This compound, obtained with much decomposition from the preceding trifluoride, proved unstable and never was purified adequately. The best preparations were shown by analysis to be not better than 75% pure. Complete decomposition occurred during chlorination, or during a treatment with alkalies, and it was therefore impractical to link the formula with that of the tetrafluoride no. 2. The formula proposed rests merely on the assumption that fluorination takes place in a symmetrical fashion.

(5) **$CHCl_2CClFCClF_2$.**—This trifluoride was obtained with great ease from the known difluoride $CHCl_2CCl_2$-

$CClF_2$. By chlorination in sunlight it gives a compound $C_3Cl_5F_3$, melting at $-15°$ and different from $CCl_2FCCl_2CClF_2$ (no. 1), a fact which excludes $CHClFCCl_2CClF_2$ as its possible formulation. The choice is thus restricted to the proposed formula, or else to $CHCl_2CCl_2CF_3$. The alternate is not considered plausible, because its chlorination would yield $CCl_3CCl_2CF_3$, a compound which should melt at 20° or higher (CCl_3CF_3 melts at 13°, and a lengthening of the chain by a $-CCl_2-$ group raises the melting point by more than 10°). To conclude, the proposed formula should be regarded as a very plausible hypothesis.

(6) **$CHCl_2CClFCF_3$.**—This compound was obtained from the preceding trifluoride (no. 5) at high temperature and with appreciable decomposition, in sharp contrast with the previous steps. Chlorination in sunlight gave a compound $C_3Cl_4F_4$, which melts at $-15.5°$, and which yields quantitatively an olefin $C_3Cl_2F_4$ and zinc chloride, when treated with zinc in alcohol. This proves that the central carbon atom still bears a chlorine atom. The choice is therefore restricted to $CHClFCClFCClF_2$ and $CHCl_2CClFCF_3$, if the formula of the parent trifluoride (no. 5) is accepted as proposed. The decision to select the second formula is based on the melting point of the compound obtained after chlorination, because the other formula would call for $CCl_2FCClFCClF_2$ after sunlight chlorination, a compound which should freeze at about $-70°$.

For the sake of completeness, it might be added that by starting from the implausible formula of the parent compound, no. 5, *i. e.*, from $CHCl_2CCl_2CF_3$, the tetrafluoride no. 6 could only be $CHClFCCl_2CF_3$ or $CHCl_2CClFCF_3$, and the second formula (identical with that adopted in the preceding paragraph) could not be preferred to the first one because the compounds obtained after sunlight chlorination would have to be written $CCl_2FCCl_2CF_3$ or $CCl_3CClFCF_3$, respectively, and both formulas would call for melting points in the vicinity of $-15°$.

The conclusion is therefore that the proposed formula is acceptable.

(7) **$CCl_3CClFCClF_2$** was synthesized by chlorination of no. 5, and is discussed above, together with the formula of no. 5.

(8) **$CCl_3CClFCF_3$** was obtained from no. 6 and is discussed together with it; its freezing curve was taken on a sample of a few grams only.

(9) **$CCl_2{=}CFCF_3$** was obtained by the action of zinc on no. 8.

(10) **$CCl_2BrCFBrCF_3$** resulted from the bromination of the preceding ethylenic compound. The freezing point was taken on 10 cc. of material obtained by three fractional crystallizations from a batch melting originally at 28°.

Discussion.—The experimental results show, in confirmation of the preceding paper, that $-CCl_3$ groups are by far the most sensitive to fluorination, that $CHCl_2-$ groups are exceedingly resistant, and that —CHCl— groups undergo decomposition before being fluorinated. They show also that $-CCl_2-$ groups are quite resistant to fluorination and require severe conditions to go from the —CClF— to the $-CF_2-$ stage. This last observation applies only to $-CCl_2-$ groups surrounded by halogenated groups and contrasts with the fact that $-CCl_2-$ groups surrounded by hydrogen-bearing carbons are exceedingly easily fluorinated.[2]

The behavior of the compounds containing a —CHCl— group was novel on two counts, the breakage of the molecule at that point and the hydrolysis of the adjacent trihalogenated groups.

The synthesis of a $-CF_3$ group, despite the fact that it was adjacent to a halogen-bearing carbon atom, is a feature which has only one analogous but not identical precedent, namely, the fluorination of $CHCl_2CHF_2$ to CH_2ClCF_3.[3] In other cases where $-CF_3$ groups were obtained, the adjacent group bore hydrogen exclusively.[4] Besides showing the behavior of highly fluorinated compounds, the experimental results fortify the idea that (from the practical standpoint) high molecular polyfluorides should be synthesized by condensation of smaller highly fluorinated molecules, rather than by the fluorination of high molecular compounds obtained by condensation.

Summary

Ten new compounds listed in Table I have been synthesized, and their structural formulas have been discussed.

COLUMBUS, OHIO RECEIVED JUNE 24, 1939

(2) Henne and Renoll, THIS JOURNAL, **59**, 2434 (1937).
(3) Henne and Renoll, *ibid.*, **58**, 887 (1936).
(4) Henne and Renoll, *ibid.*, **58**, 889 (1936).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE UNIVERSITY OF ROCHESTER]

Photochemical Studies. XXIX. The Decomposition of Diethyl Ketone at Short Wave Lengths. A Comparison of Acetone, Ethyl Methyl Ketone and Diethyl Ketone Near 3000 Å.

BY VICTOR R. ELLS[1] AND W. ALBERT NOYES, JR.

The photochemical decompositions of acetone[2] and of ethyl methyl ketone[3] in the wave length region 1850–2000 Å. have been studied. The salient facts of these investigations may be summarized as follows.

(a) The quantum yield of carbon monoxide formation from acetone is about 0.50 at moderate pressures, increases with decreasing pressure, and attains a value of about 0.66 at a pressure of 0.2 mm. In the presence of foreign gases (CO_2, N_2, C_2H_6) this quantum yield is raised.

(b) The quantum yield of carbon monoxide formation from ethyl methyl ketone is about 0.70 at moderate pressures and becomes approximately 0.90 at low pressures.

(c) While for both compounds the ratio of carbon monoxide to hydrocarbons in the products is not far from 1:1, it was shown that diketones are produced upon irradiation of ethyl methyl ketone, both at these short wave lengths and in the near ultraviolet. The quantum yield expressed in terms of molecules of ethyl methyl ketone disappearing was shown to approach a value not far from unity at low pressures.

(d) The yield of methane from ethyl methyl ketone increases with temperature.

The photochemical decomposition of ethyl methyl ketone in the near ultraviolet has been investigated by Norrish and Appleyard,[4] who found the main reaction to give carbon monoxide and a mixture of ethane, propane, and butane. A small amount of decomposition to ethylene and acetaldehyde was also reported.

With ethyl methyl ketone two primary dissociations may be visualized

$$CH_3COC_2H_5 + h\nu = CH_3 + COC_2H_5 \quad (1)$$
$$CH_3COC_2H_5 + h\nu = C_2H_5 + COCH_3 \quad (2)$$

If the primary dissociations of simple ketones have quantum yields of unity, variations in yield are to be associated with the secondary reactions.

Since diethyl ketone can only give propionyl radicals upon rupture of a single carbon–carbon bond adjacent to the carbonyl group, the behavior of this substance upon irradiation may furnish information concerning such radicals.

As shown by Matheson and Zabor,[5] the major portions of the fluorescences of diethyl ketone and of propionaldehyde are identical when excited by near ultraviolet radiation. Thus bipropionyl is probably one of the decomposition products in this region. Unfortunately, no satisfactory method of analyzing for small amounts of this diketone is now available so that quantum yields in the present article are merely those of carbon monoxide formation.

Experimental Procedure and Results

The diethyl ketone (Eastman Kodak Co.) was fractionally distilled several times, both at atmospheric pressure and at reduced pressure. Vapor pressures of this substance have been measured by Rintelen, Saylor and Gross[6] at 10, 30, and 50°, the values being 16.9, 46.1, and 117 mm., respectively. The maximum pressure attainable in the present work (at 27°) is about 38 mm.

The light source has been described,[2] and the method of gas analysis was essentially that of Manning,[7] which has been used with the other ketones.[2,3]

Liquid nitrogen was used first as a refrigerant, the only uncondensed gaseous product being carbon monoxide together with traces of ethane and ethylene. Ethane, butane, and ethylene were pumped off from pentane mush at a temperature between −150 and −155°. A slight hydrocarbon deficiency is again observed in spite of all precautions, indicating that such substances are soluble in the ketone and are difficult to remove.

The hydrogen bromide actinometer was used for measuring the number of quanta absorbed.

Table I shows gas analyses for four runs, two in which radiation from the full aluminum spark was used and two in which the region 1850–2000 Å. obtained through focal isolation was alone present.

(1) Fellow, during 1938–1939, of the Sherman Clarke Fund in Research Chemistry, The University of Rochester.

(2) Howe and Noyes, THIS JOURNAL, **58**, 1404 (1936).

(3) Ells and Noyes, *ibid.*, **60**, 2031 (1938).

(4) Norrish and Appleyard, *J. Chem. Soc.*, 874 (1934).

(5) Matheson and Zabor, *J. Chem. Phys.*, **7**, 536 (1939).

(6) Rintelen, Saylor and Gross, THIS JOURNAL, **59**, 1129 (1937).

(7) Manning, *ibid.*, **56**, 2589 (1934).

TABLE I

ANALYSES FOR HYDROCARBONS AND CARBON MONOXIDE

Pressure $(C_2H_5)_2CO$, mm.	31	28	35	35
Total hydrocarbons, mm.	0.0048	0.0043	0.0236	0.0121
C_4H_{10}, mm.	.0038	.0027	.0161	.0081
C_2H_6, mm.	.0005	.0008	.0038	.0022
C_2H_4, mm.	.0005	.0008	.0037	.0018
CO, mm.	.0045	.0039	.0217	.0108
$CO/[C_4H_{10} + \frac{1}{2}(C_2H_6 + C_2H_4)]$	1.05	1.11	1.09	1.07
% C_2H_5 giving C_4H_{10}	88	77	81	80
Conditions	1850–2000 Å.		Full spark	

From the data in Table I it is evident that most of the ethyl radicals combine to form butane although about 20% disproportionate to give ethane and ethylene. The excess of carbon monoxide is not definite evidence against the formation of bipropionyl because of the difficulty in pumping off the hydrocarbons completely.

Table II shows data for the quantum yield of carbon monoxide formation from diethyl ketone in the wave length region 1850–2000 Å. All runs were made at room temperature (25 ± 2°).

TABLE II

QUANTUM YIELDS OF CARBON MONOXIDE FROM DIETHYL KETONE (1850–2000 Å.)

Press. $(C_2H_5)_2CO$, mm.	Time, min.	Intensity (arbitrary units)	Moles CO × 10^5	Moles H_2 × 10^5 (HBr actinometer)	Quantum yield of CO formation
38	90	35.7	0.01254	0.01534	0.82
36	90	35.3	.00827	.00948	.87
31	120	35.2	.01283	.01340	.96
28	65	37.2	.00570	.00667	.85
22	120	34.3	.01112	.01283	.87
22	30	37.2	.00342	.00389	.88
17	40	38.0	.00228	.00258	.88
6	60	36.9	.00513	.00561	.91
4	60	36.6	.00371	.00389	.95

The figures in the fifth column are corrected for the thermal decomposition of hydrogen bromide and for the transmission of the windows. When multiplied by Avogadro's number these figures would give the number of quanta absorbed.

There seems to be a slight tendency for quantum yields to increase with decreasing pressure. The results scatter so much that an extrapolation has little meaning, but a value of unity at zero pressure would be compatible with the data. At comparable pressures the quantum yield of carbon monoxide formation is definitely higher for diethyl ketone than for ethyl methyl ketone[3] and for acetone.[2] Table III shows a comparison at even pressures of the values for the three ketones.

Since quantum yields of carbon monoxide formation increase with complexity of ketones in the region 1850–2000 Å. and since the quantum yield of carbon monoxide formation from acetone is considerably higher than in the near ultraviolet, it was deemed interesting to make a comparison of the ketones at the longer wave lengths.

TABLE III

COMPARISON OF QUANTUM YIELDS OF CARBON MONOXIDE FORMATION AT SHORT WAVE LENGTHS FOR ACETONE, ETHYL METHYL KETONE AND DIETHYL KETONE 25 ± 2°

Pressure, mm.	$(CH_3)_2CO$	$CH_3COC_2H_5$	$(C_2H_5)_2CO$
20	0.52	0.76	0.88
8	.56	.78	.90
4	.59	.78	.95
1	.62	.82	(.98)
0.3	.64	.86	(.99)

Values in parentheses are obtained by rough graphical extrapolation.

An aluminum spark was used in conjunction with a red-purple corex filter for this comparison. The main lines absorbed by the ketones lie between 3050 and 3100 Å., but the radiation was not strictly monochromatic. At the low pressures used longer wave lengths would not be appreciably absorbed. The fractions of the incident radiations absorbed by the various ketones were determined with the aid of a photoelectric cell and proved to be nearly the same. While too great stress cannot be placed on absolute values, relative values are of interest in the present discussion.

The quantum yields given in Table IV are based on an assumed value of 0.095 ± 0.01 for that of carbon monoxide production from acetone at 25°.[8]

Based on the assumed value of 0.095 for acetone, the average quantum yield of carbon monoxide formation from ethyl methyl ketone is 0.11 and that from diethyl ketone is 0.97. Therefore, while the yields of the first two are low and nearly the same at 3000 Å., that of the latter is about the same at long as at short wave lengths.

(8) This figure is an average of a large number of runs made by one of us (W. A. N., Jr.) during 1931 using an absolute method with a thermopile calibrated by a standard light source. It agrees well with values which will be published in the near future from this Laboratory. The quantum yields obtained by Damon and Daniels [THIS JOURNAL, **55**, 2363 (1933)] and by Norrish, Crone, and Saltmarsh [*J. Chem. Soc.*, 1456 (1934)] are slightly higher but were obtained at higher temperatures. Since Leermakers [THIS JOURNAL, **56**, 1899 (1934)] has shown the yield to be unity at 163°, the value cited at 25° is a reasonable one in comparison with the others. At 3130 Å. and a temperature of 56° Damon and Daniels found a considerable falling off of yield with pressure. In the unpublished work just cited little change with pressure between 5 and 16 cm. could be found. Pressures in Table IV are below 5 cm. so that some doubt exists concerning absolute values.

TABLE IV

COMPARISON OF QUANTUM YIELDS OF CARBON MONOXIDE FORMATION FROM THREE KETONES NEAR 3000 Å.

Assuming yields to be 0.095 for acetone. The values at 10 mm. pressure are least accurate because of the small amount of absorption.

Ketone	Pressure, mm.	Press. CO formed (V = 531 cc.), mm.	Quantum yield of CO formation
CH_3COCH_3	10	0.0007	(0.095)
$CH_3COC_2H_5$	10	.0006	.082
$C_2H_5COC_2H_5$	10	.0049	.67
CH_3COCH_3	10	.0006	(.095)
$CH_3COC_2H_5$	10	.0007	.11
$C_2H_5COC_2H_5$	10	.0062[a]	.98
CH_3COCH_3	21	.0009	(.095)
$CH_3COC_2H_5$	21	.0011	.12
$C_2H_5COC_2H_5$	21	.0092	.97
CH_3COCH_3	36	.0013	(.095)
$CH_3COC_2H_5$	36	.0016	.12
$C_2H_5COC_2H_5$	36	.0142[b]	1.04

[a] Pressure of butane + ethane + ethylene in this experiment is 0.0060. 0.93 of the ethyl groups form butane, and the remainder disproportionate to ethane and ethylene. [b] Total pressure of hydrocarbons 0.0136 mm. in this experiment.

Discussion of Results

The details of the mechanism of photochemical acetone decomposition in the near and far ultraviolet have not yet been elucidated completely. Since the quantum yield of carbon monoxide formation is appreciably greater at 1850–2000 Å. than at longer wave lengths, it is evident either that the acetyl radical separates with enough energy to make it inherently unstable or that secondary reactions leading to carbon monoxide formation are, for some reason, more probable under the conditions under which the short wave experiments were carried out.

From a variety of sources it is quite certain that the quantum yield of the primary process

$$CH_3COCH_3 + h\nu = CH_3 + COCH_3 \qquad (3)$$

is very close to unity in the near ultraviolet.[9] The low yield of carbon monoxide formation may be due to the reactions

$$CH_3CO + CH_3CO = (CH_3CO)_2 \qquad (4)$$

and

$$CH_3CO + CH_3 = CH_3COCH_3 \qquad (5)$$

The mechanism by which carbon monoxide is produced is uncertain, but two possibilities suggest themselves

$$CH_3CO = CH_3 + CO \qquad (6)$$

$$CH_3 + CH_3CO = C_2H_6 + CO \qquad (7)^9$$

Gorin believes that (6) has too high an activation energy to be important at ordinary temperatures and ascribes carbon monoxide production to (7). While no adequate evidence for or against this choice is available as regards the work in the near ultraviolet, a comparison of the yield at 1850–2000 Å. with that at longer wave lengths makes it appear probable that (6) is important in the former region. It should be noted that (3) followed by (6) would be difficult to distinguish clearly from a primary dissociation into two methyls and carbon monoxide.

If the energy required to produce reaction (3) is assumed to be 70 kcal., a wave length of 3130 Å. provides an excess of 21 kcal. per gram molecule. If the excess appears merely as translational energy, the acetyl radicals would possess 5.5 kcal. of energy per gram molecule in that form. Since, however, they have more degrees of freedom than methyl radicals, they might be expected to retain more than half if all were in the form of vibrational energy. Nevertheless, sufficient energy to cause dissociation would scarcely be available if the activation energy (17 kcal.) assumed by Gorin for (6) is correct. At 2536 Å. the acetyl radicals would acquire 10 kcal. if the energy were all translational. This would still be inadequate to evoke (6) except in a few collisions where thermal energy could supply the deficiency. At 1900 Å., however, 20 kcal. would be given to the acetyl radical as kinetic energy. This could cause dissociation at the first impact by reaction (6). The high quantum yield of CO formation at short wave lengths can be explained in this way. In ethyl methyl ketone, the acetyl radical would acquire more kinetic energy of translation than from acetone, assuming no energy in vibrational degrees of freedom. No account is taken of electronic excitation in these simple calculations.

A quantum yield expression derived from (3), (4), (5), (7), and (8)

$$CH_3 + CH_3 = C_2H_6 \qquad (8)$$

shows no variation with either intensity or with pressure as long as all reactions occur in the homogeneous gas phase and third bodies are unimportant. The inclusion of (6) would mean necessarily that the quantum yield of carbon monoxide formation would increase at low intensities although the formal expression is very complex. While no very good evidence exists on this point at present, such as is available favors this sort of variation with intensity.[10]

(9) See Gorin, *J. Chem. Phys.*, **7**, 256 (1939).

(10) Damon and Daniels, THIS JOURNAL, **55**, 2363 (1933).

At short wave lengths the main portion of carbon monoxide must be formed by a spontaneous dissociation of the acetyl radical. All combination reactions of free radicals which would reduce carbon monoxide formation must be relatively unimportant. Only in this way can the lack of intensity effect on the yield be accounted for unless one wishes to admit a peculiar enhancement of the rate of (7) for at present unknown reasons.

When attention is turned to ethyl methyl ketone, the situation becomes very difficult to understand unless some spontaneous dissociation of the radicals CH_3CO and C_2H_5CO is allowed. It is not very satisfactory, although it may prove necessary to postulate nearly all possible types of primary dissociation of this molecule,[9] including a production of propane and carbon monoxide in one step.

In the decomposition of diethyl ketone, either in the near or in the far ultraviolet, the quantum yield of carbon monoxide formation is not far from unity. If the primary process is

$$(C_2H_5)_2CO + h\nu = C_2H_5 + C_2H_5CO \qquad (9)$$

the propionyl radical must either be very unstable, or it must undergo a very probable reaction analogous to (7). The recombination reactions

$$C_2H_5CO + C_2H_5 = C_2H_5COC_2H_5 \qquad (10)$$
$$C_2H_5CO + C_2H_5CO = (C_2H_5CO)_2 \qquad (11)$$

cannot be important. Some evidence for a slight occurrence of (11) is found from a study of the fluorescence of diethyl ketone.[5]

Without considering for the moment the mechanism by which carbon monoxide may be produced from propionyl radicals, let us assume merely that 90% of such radicals yield carbon monoxide. The acetyl radical may be expected to give carbon monoxide (in the near ultraviolet) not more than one-tenth of the time. Therefore if primary processes (1) and (2) are equally probable, the quantum yield of carbon monoxide production from ethyl methyl ketone should be 0.50 in the near ultraviolet. The data in Table IV show that this is not the case, the actual yield being little greater than for acetone.

It seems necessary to conclude, therefore, that primary process (2) predominates.[11] If one assumes that the low yield of carbon monoxide from ethyl methyl ketone is due to the recombination

$$C_2H_5 + COCH_3 = C_2H_5COCH_3 \qquad (12)$$

and that 0.1 of the acetyl radicals and 0.9 of the propionyl radicals yield carbon monoxide, it can be shown that 0.98 of the primary dissociation goes by (2) and 0.02 by (1). A slight combination between methyl and acetyl radicals would alter these figures somewhat, and acetone would be predicted to appear among the products. The amount of diethyl ketone produced should be negligible, but, on the other hand, biacetyl should result from combinations between acetyl radicals. Since the main part of the fluorescence of ethyl methyl ketone is identical with those of acetaldehyde, acetone, and biacetyl, the occurrence of biacetyl among the products is probable.

The fact that approximately equal quantities of ethane, propane, and butane are produced both in the near and far ultraviolet is difficult to explain with any distribution of methyl and ethyl radicals and must be due to peculiarities in the rates of production of these gases from free radicals.[3] With the above mechanism approximately equal numbers of the two free radicals should form hydrocarbons.

In the far ultraviolet if 0.55 of the acetyl radicals yield carbon monoxide, 0.9 of the propionyl radicals yield carbon monoxide, and the over-all yield of carbon monoxide is 0.80, it can be shown that primary process (1) is slightly more probable than (2). However, variations in the ratio are quite sensitive to the quantum yield figures. Since an amount of energy considerably in excess of that necessary to cause dissociation is absorbed at these wave lengths, slight differences in bond strength might be expected to make little difference in the nature of the dissociation.

The fact that butane is the principal hydrocarbon resulting from the photochemical decomposition of diethyl ketone is not surprising. The extents to which ethyl radicals combine to form butane and disproportionate to ethane and ethylene have not been determined satisfactorily. Perhaps one or the other or both of these reactions occurs on the walls. The results of Meinert[12] on the thermal decomposition of tetraethyllead indicate a high probability of butane formation. The 1:1 ratio of ethane to ethylene is evidence, although not proof, against other reactions intervening in the production of ethane and ethylene.

(11) Professor G. B. Kistiakowsky suggested at a symposium held at Stanford University, August 8–11, 1938, that much of the work on photochemistry of ketones could be explained by assuming that the molecules usually split on the side of the carbonyl group toward the heaviest radical.

(12) Meinert, THIS JOURNAL, **55**, 979 (1933).

Summary

1. The quantum yield of carbon monoxide formation from diethyl ketone in the wave length region 1850–2000 Å. is quite high and seems to approach unity as the pressure is lowered.

2. With an assumed quantum yield of 0.095 at 3000 Å. for carbon monoxide formation from acetone it has been shown that the yield from ethyl methyl ketone is only slightly higher and that that of diethyl ketone is about one.

3. These facts indicate either a high intrinsic instability of propionyl radicals or very probable reactions involving them which lead to carbon monoxide.

4. Ethyl methyl ketone probably dissociates almost but not quite solely to give ethyl radicals in the near ultraviolet. At short wave lengths methyl and ethyl radicals are produced in nearly equal amounts from the primary process.

5. Most of the ethyl radicals form butane, but a small fraction yield ethane and ethylene.

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[CONTRIBUTION FROM THE RESEARCH LABORATORY OF PHYSICAL CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, NO. 426]

The Palladium–Deuterium Equilibrium

BY LOUIS J. GILLESPIE AND WILLIAM RICHARD DOWNS

The purpose of this investigation has been to study the absorption of deuterium by palladium black in the region of temperature and pressure in which hydrogen and palladium have been found by Brüning and Sieverts[1] and by Gillespie and Galstaun[2] to exhibit a critical solution temperature, and inclusive of the region at 200° and above in which hydrogen and palladium exhibit a tendency toward compound formation—in short, to obtain part of the phase diagram for deuterium and palladium analogous to that of Gillespie and Galstaun for hydrogen and palladium.

Sieverts and Zapf[3] studied the solubility of hydrogen and of deuterium in a palladium wire. The ratio of the solubility of deuterium to that of hydrogen was 0.67 at 300° and increased to 0.91 at 1000°.

Sieverts and Danz[4] studied the absorption of deuterium by palladium black from 20 to 350° at various low pressures (less than 2 atm.). Isotherms at 80 and 100° gave evidence of two solid phases, but in all cases, even for the corresponding curves for hydrogen, there was considerable hysteresis. Sieverts and Danz[5] have also studied the electrical resistance and magnetic susceptibility of palladium wire charged with deuterium.

Since the early work of Oxley[6] the magnetic susceptibility of palladium charged with hydrogen has also been studied by Aharoni and Simon,[7] Svensson,[8] and Michel and Gallissot.[9] The latter have also studied the variations of the lattice parameter, the Brinell hardness and the electrical resistance as hydrogen is added to the metal.

There are recent X-ray studies of the system palladium–hydrogen by Kruger and Gehm[10] and by Owen and Jones.[11] The latter, as well as Michel and Gallissot, found in agreement with the early experience of Wolf[12] that simple degassing of palladium that has been well charged with hydrogen—to the formation of the second (beta) solid solution—does not entirely restore the original physical constants of the palladium, but that high temperature annealing (*e. g.*, 450° for one-half hour[11]) is necessary and sufficient.

This finding is of two-fold interest in connection with the equilibrium of either hydrogen or deuterium with palladium. In the first place, one need not expect the whole of an isotherm containing a horizontal portion to be reversible, since the palladium would appear not to be the same for the first rising portion when traced upward from zero concentration as when later traced downward after formation of the beta phase and its subsequent decomposition. This effect seems, however, to be rather theoretical than actual. In the second place, one might expect that any reluctance to form the beta phase, if once over-

(1) Brüning and Sieverts, *Z. physik. Chem.*, **163A**, 409 (1933).
(2) Gillespie and Galstaun, THIS JOURNAL, **58**, 2565 (1936).
(3) Sieverts and Zapf, *Z. physik. Chem.*, **174A**, 359 (1935).
(4) Sieverts and Danz, *ibid.*, **38B**, 46 (1937).
(5) Sieverts and Danz, *ibid.*, **38B**, 61 (1937).
(6) Oxley, *Proc. Roy. Soc.* (London), **101A**, 264 (1922).
(7) Aharoni and Simon, *Z. physik. Chem.*, **4B**, 175 (1929).
(8) Svensson, *Ann. Physik*, **18**, 299 (1933).
(9) Michel and Gallissot, *Compt. rend.*, **208**, 434 (1939).
(10) Kruger and Gehm, *Ann. Physik*, **16**, 174 (1933).
(11) Owen and Jones, *Proc. Phys. Soc.*, **49**, 587, 603 (1937).
(12) Wolf, *Z. physik. Chem.*, **87**, 588 (1914).

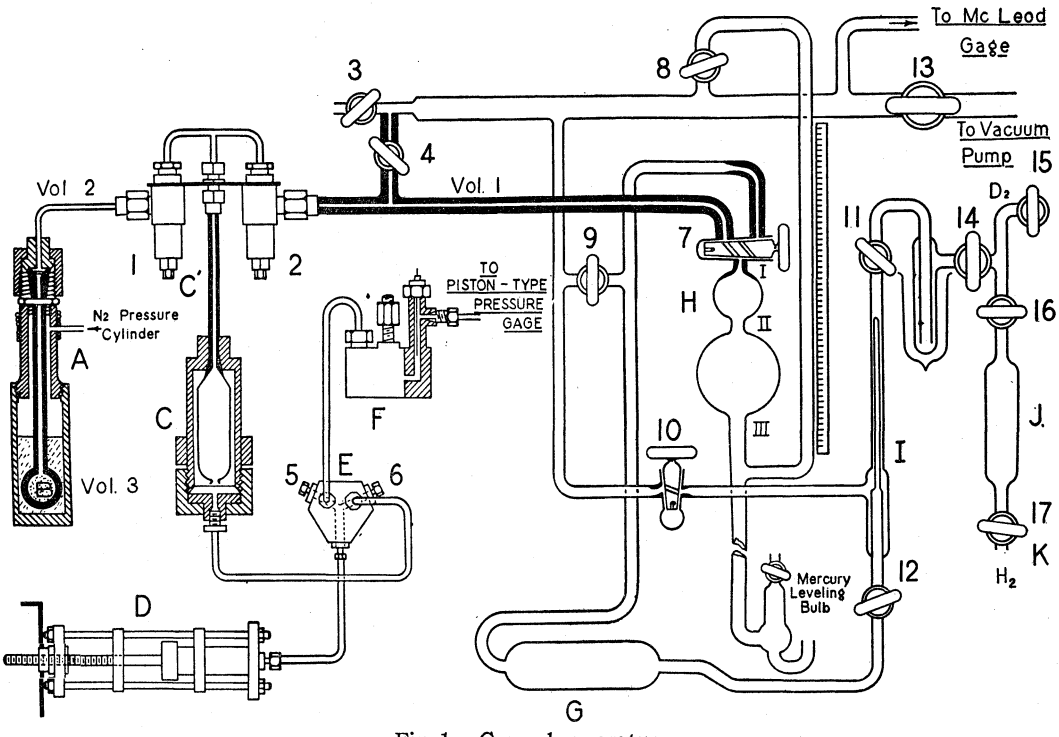

Fig. 1.—General apparatus.

come, might disappear on repetition of the experiment, since the alteration in the physical state of the metal may serve as well as the presence of "nuclei" (or perhaps actually constitute such), about which the new phase may freely form. This expectation has been borne out in the present work with deuterium.

Lacher[13] has derived with the aid of statistical theory an approximate equation to represent the results of Gillespie and Galstaun for palladium and hydrogen. If we remember the arbitrary nature of the fundamental assumption that was made, which did not permit representation of compound formation, we may consider the semi-quantitative success of the representation very gratifying.

Apparatus and Procedure.—The apparatus of Gillespie and Galstaun was used, after redetermination of the dead-space volumes and recalibration of the pressure gage, and the same procedure for the measurements was used. The only modifications were as follows. After we found that the critical solution pressure was to prove much higher than that for hydrogen we installed a steel jacket around the Pyrex reaction bulb and part of its capillary lead, within which jacket a compensating pressure of nitrogen can be maintained. For fear of excessive heat loss along the jacket and consequent unknown stem-correction we have used melted Wood's metal within the jacket to transfer heat to the reaction bulb. Measurements with hydrogen and palladium, with and without the jacket, showed that the stem-correction was zero or the same in both cases. The design is such that without the jacket the stem-correction should be the same as for the platinum thermometer. This jacket and the associated apparatus are shown in Fig. 1. A change was made in the procedure for freeing the palladium black from ammonium chloride, and this will be discussed later.

Deuterium is prepared by electrolysis of a dilute solution of anhydrous potassium sulfate in heavy water in the apparatus shown in Fig. 2. By adjustment of the mercury in the bulb B the volume of bulbs A and B can be made exactly half the volume of the deuterium bulb E, so that electrolysis can take place without attention to the levels in the U-tube at D. Ice was used in a Dewar flask about the U-tube for cooling during electrolysis.

Heavy water guaranteed 99.9% pure was obtained from

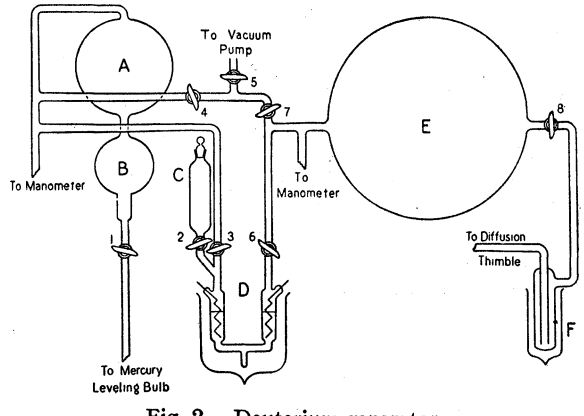

Fig. 2.—Deuterium generator.

(13) Lacher, *Proc. Roy. Soc.* (London), **A161**, 525 (1937).

the California Isotope Company in sealed ampoules. The water was exposed to air only long enough to break off the tip and introduce the liquid into the tube C. The cell was evacuated before introducing any heavy water, and rinsed out before final filling.

Deuterium was not passed over phosphorus pentoxide, but passed through the hot (300°) palladium diffusion thimble (I of Fig. 1) after freezing out the oxide at F with liquid nitrogen.

Precautions were taken at all times to avoid contamination of the deuterium with hydrogen, all parts of the apparatus being well pumped and repeatedly rinsed with deuterium. That this was successful is indicated by the reproducible character of the curves and especially by the horizontal character of the flat portions.

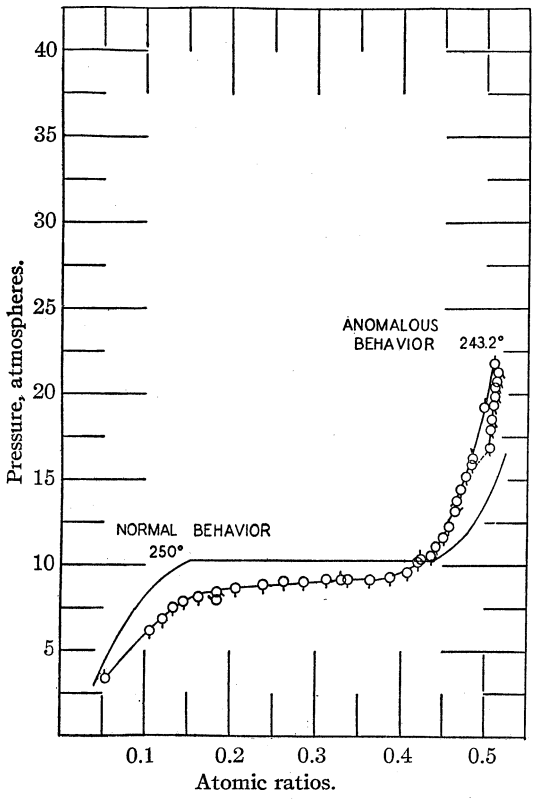

Fig. 3.—Anomalous and normal behavior of hydrogen with palladium black.

The palladium was prepared from ammonium chloropalladate obtained through the kindness of the National Bureau of Standards. This salt was converted into the chloride, then into palladosammine chloride, which was reprecipitated repeatedly from ammoniacal solution, well washed, dried, and converted to metal in a boat in a stream of hydrogen at about 150°. The hydrogen was replaced with carbon dioxide before cooling and then the metal allowed to cool in carbon dioxide. At the temperatures at which 1 atm. of hydrogen was in contact with the metal no beta phase could have been formed, a consideration that proves to be of importance.

For the first experiment the ammonium chloride, formed with the metal upon reduction of the palladosammine chloride, was largely removed by substantially the same procedure used by Gillespie and Galstaun (heating *in vacuo*).

For all the other experiments the ammonium chloride was better removed by thorough washing with hot distilled water until disappearance of chloride ion, after washing for several minutes in boiling 3 *N* ammonium hydroxide to dissolve any unreduced ammine. After being dried at 105°, the metal was then heated between 360 and 380° for an hour or more under vacuum and allowed to cool in a vacuum before weighing. Two portions of metal prepared in this second way were available. After joining the reaction bulb to the apparatus and just before starting an experiment with hydrogen or deuterium, the sample was conditioned by admitting the gas at about 2 atm. at bath temperature and then exhausting, this procedure being repeated several times.

In the calculation of the average compositions of the solid phases, corrections were applied for the deviation of deuterium from the ideal gas law, under the assumption that the equation of state for deuterium is the same as for hydrogen. It should be noted that the sensitiveness of the calculations of composition to small errors of volume, to the allocation of dead space between bath and room temperature along the capillary lead from the reaction bulb, and to uncertainty of the density of the palladium (assumed to be 11.774) increases with the pressure. Therefore the compositions at the highest pressures may not be so exact as those at 20 atm.

Experiments.—Before proceeding to the study of deuterium it was thought well to check with hydrogen some of the results of Gillespie and Galstaun. The first experiment was with palladium prepared substantially as by them, but which stood without exclusion of air for nine months after preparation and before the experiment. The results at 243.2° are shown in Fig. 3, labelled *Anomalous Behavior*, together with the curve of Gillespie and Galstaun at a nearby temperature, 250°, labelled *Normal*. Tails on the circles distinguish points obtained by addition of hydrogen (tails pointing up) from those obtained by withdrawal. It is evident that the hysteresis is slight and the curve within the hysteresis region is lacking in a truly horizontal portion. Gillespie and Galstaun saw such a result but once, and the palladium was then found to be heavily contaminated with mercury (10% or more). Therefore this preparation was examined for mercury by very strong heating in a boat, but none could be detected. The loss of weight on heating, due in part or whole to expulsion of ammonium chloride, was 0.23%, about the same as for the preparation used for the final results of Gillespie and Galstaun. This preparation was not studied further.

Because of the experience of Holt, Edgar and Firth[14] with active and inactive palladium it seems possible that the nine months of storage (and not in an atmosphere of hydrogen) allowed an "inactivation." Our next experiments showed the propriety of the labelling.

For all subsequent experiments the palladium was freed from chloride by washing, as described above, and was recently prepared from the palladosammine chloride.

With such material, hydrogen isotherms were deter-

(14) Holt, Edgar and Firth, *Z. physik. Chem.*, **82**, 513 (1913).

mined at 250 and 280°. The manipulation was isothermal, no "heat treatment" being used at any time in this work. The results are shown by the centers of the circles in Fig. 4. The lines are those by Gillespie and Galstaun. The check is good. The first rising portion of the 250° curve lies underneath the old curve, but a plot of log p against $1/T$ indicates that the new points are more consistent with the earlier results at other temperatures than are the old 250° points. No particular effort was made to fix the exact compositions at the ends of the horizontals, but the confirmation of the earlier results is good so far as it goes; indeed, it seems better for these compositions than for the pressures.

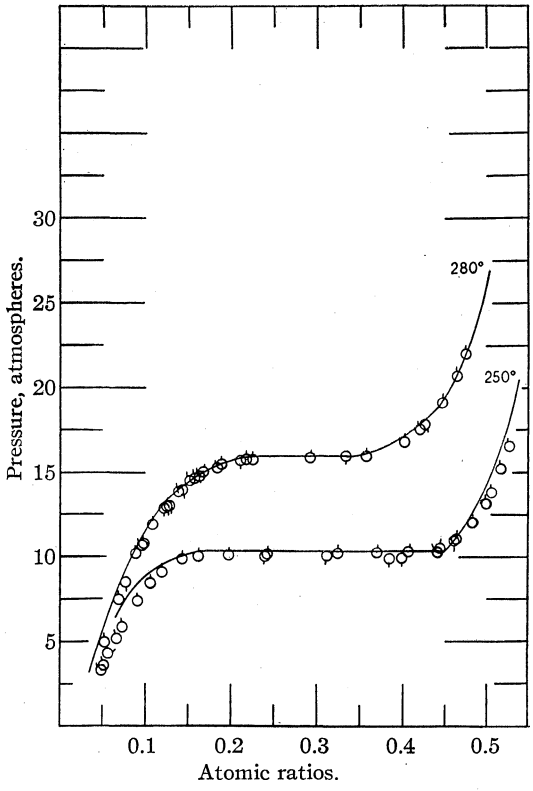

Fig. 4.—Comparison of new hydrogen data (circles) with old (lines).

Figure 4 gives a check of all apparatus constants except the volume of the gas buret and the delta value of the platinum thermometer (the ice-point agreed with the earlier value and also did the settings of the thermostatic control). It proves that the queer result at 243.2° is in fact anomalous.

In the next experiment we determined deuterium isotherms at 200 and 250°. Figure 5 shows by circles the points for deuterium at these temperatures, with the best lines. At 250° circles of two sizes show two experiments. For comparison, the curve for hydrogen of Gillespie and Galstaun is added, as well as their points at 200° (but not at 250°), so that the spread of the points in the horizontal region can be compared. The spread is greater for D_2 at 200° than for H_2. The spread decreases with rising temperature in both cases.

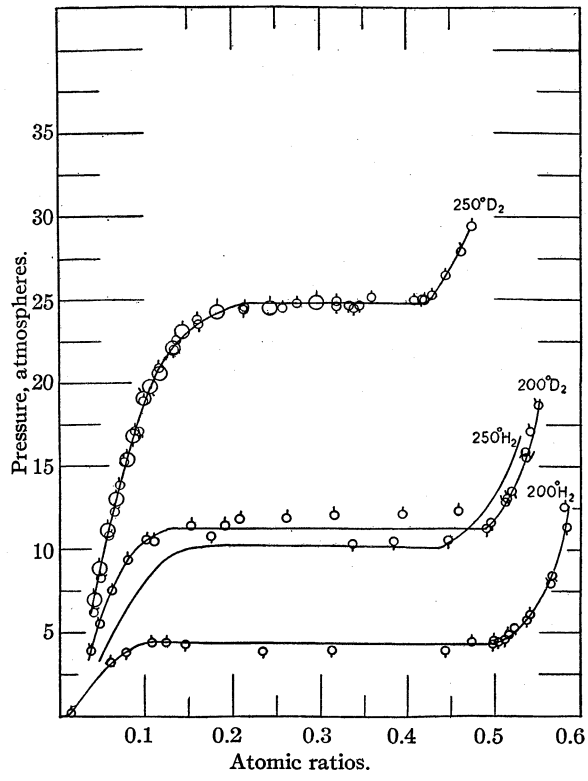

Fig. 5.—H_2:Pd and D_2:Pd at 200 and 250° (normal behavior).

It was at this point that the jacket was installed to protect the reaction bulb and the second portion of the palladium was also placed in the bulb, a portion that had not been exposed to hydrogen so as to form beta phase. The resulting curve is shown at the left of Fig. 6, labelled *Virgin Pd, Sample B*. All the points represent additions. They are so far from the curve previously obtained and here labelled *Normal Curve* that the deuterium was removed, fresh deuterium added to a pressure of about 6 atm. (at 250°) and the system evacuated. This pressure is only one-quarter of that required for beta phase formation under equilibrium conditions, but had some effect on the palladium. This is shown in the same Fig. 6 by the curve labelled *Virgin Pd, Sample B'*. The hysteresis is considerable and the loop does not enclose the normal curve shown without points. If the additions had been extended to high enough pressures the loop might well have enclosed the normal curve or perhaps coincided with it in part.

In the next experiment the deuterium was removed and replaced with hydrogen, and the points of a hydrogen isotherm at 250° determined as shown in Fig. 7 along with the line of the earlier experiment (of Fig. 4). The agreement of the points with the line shows that the metal was like that used before. After removal of hydrogen and flushing with deuterium, the points for a deuterium isotherm were determined as shown in the same Fig. 7 along with the line previously determined (of Fig. 4).

These experiments showed us that there is a reluctance toward formation of the deuterium beta phase, which has

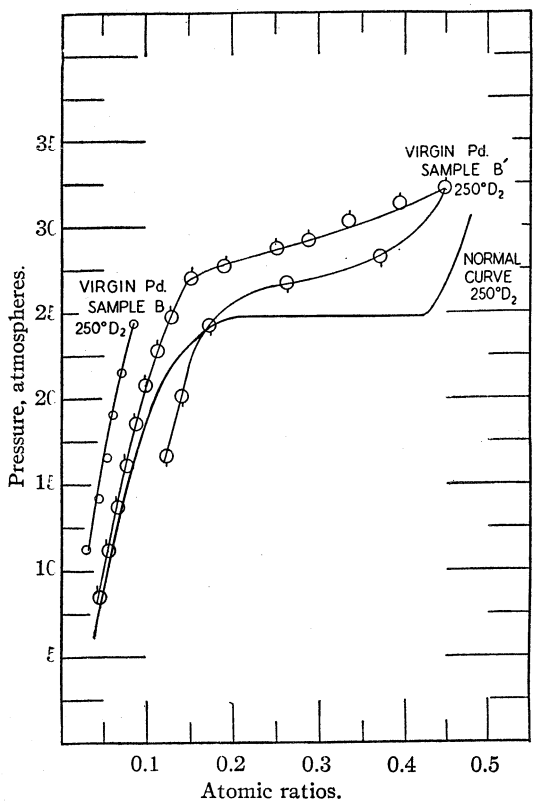

Fig. 6.—Deuterium in virgin Pd and in Pd previously used for hydrogen ("normal curve").

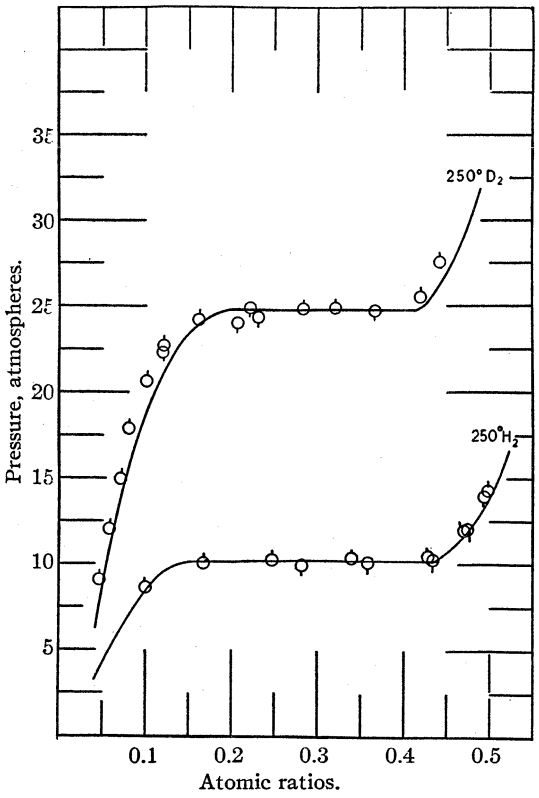

Fig. 7.—Normal H_2 curve followed by normal D_2 curve in the sample of Fig. 6.

seldom been observed by us in the case of hydrogen, but is serious in the case of deuterium. We think that the loop of Fig. 6 indicates the formation of some beta phase at moderate pressures of deuterium (in material within which no beta phase of hydrogen had ever been produced), but that in this case beta phase was not formed in all portions of the metal.

Once beta phase is formed throughout the metal by the use of hydrogen, an effect persists after evacuation. In the X-ray experiments distortion of the diffraction pictures remains and here the material seems to retain enough structure to serve as nuclei for subsequent beta phase formation. We have not hesitated therefore to proceed to extend the study of the deuterium–palladium diagram by the use of palladium thus conditioned with hydrogen.

Our complete phase diagram of the system Pd:D_2 is shown in Fig. 8. The anomalous results quoted above are not included, and no further anomalous results were seen. There is a critical solution temperature at about 276°. The corresponding pressure is 35 atm. to within 0.5 atm., and the composition is about 0.25 atom of D per atom of Pd.

Sieverts and Danz[4] suggested from the course of some low pressure measurements that the critical solution temperature might possibly be lower than for hydrogen, but they did not show that one exists for deuterium.

The pressures along the horizontals for deuterium are given in the following table, as observed directly without regard to temperature consistency, and as calculated from the equation

$$\log_{10} p_{\text{atm.}} = 4.6330 - 1696.11/(t + 273.13) \quad (1)$$

TABLE I

PRESSURES ALONG THE HORIZONTALS FOR D_2 AND Pd IN ATM.

Temp., $t°$	200	250	260	270
Obsd.	11.4	24.5	28.25	32.5
Calcd.	11.7	24.5	28.3	32.4

The calculated pressures agree with the points of each isotherm as well as the directly observed, and should be regarded as the final best values.

From Eq. (1) and the simple Clapeyron equation (with ideal gas assumptions) the heat evolved when 1 mole of deuterium is added to palladium to convert the alpha (first) to the beta (second) solid solution is calculated to be 7760 cal. The corresponding result for hydrogen is 8590 cal. from the previous work.[2] This heat is therefore 10% less for deuterium. Its value is more uncertain, being determined from only four points between 200 and 270°.

As in the case of hydrogen, the fictive heat effect upon adding 1 mole of gas to palladium is least along the first rising portions of the iso-

therms, greater along the horizontals, and greatest along the second rising portions of the isotherms. The fictive heat above the critical point at the critical composition seems to be greater for deuterium than the heat along the horizontals.

Ten weeks after the completion of the isotherms shown in Fig. 8 another isotherm was determined at 260° and also a few points at 280°. These last results did not check exactly with the previous. The pressure of the horizontal at 260° was correct as judged by Eq. (1) and as shown in Table I, but the compositions were lower at both temperatures by about 0.01 in the atomic ratio. This suggests an error in the reading of the gas buret at the beginning of this last experiment, but in any case the check is sufficient to exclude the possibility that the results of Fig. 8 (in which the 260° isotherm is not included) suffer from aging of the palladium, and the results speak definitely against a tendency toward compound formation in the neighborhood of Pd_3D.

The locus of the compositions of the coexistent solid phases, alpha and beta, as shown by the broken line in Fig. 8, discloses no tendency toward compound formation—indeed, seems to exclude the possibility of compound stability. The results shown are not completely convincing as regards a hypothetical Pd_3D, but the 260° isotherm completes our conviction that no compounds are in evidence above 200°, our lowest temperature.

A final analysis was made of the last palladium sample studied, introduced with the jacket as mentioned above, and no mercury could be detected. The loss of weight after very severe heating in a stream of nitrogen was only 0.03%, within the experimental error.

On a large diagram of Fig. 8 new horizontals were drawn at the pressures given by Eq. (1) and with their aid the compositions of the alpha and beta phases determined at the ends of the horizontals. The values are given in Table II.

TABLE II

COMPOSITIONS OF COEXISTENT ALPHA AND BETA PHASES

Temperature, t°	200	250	260[15]	270
Atomic ratio D/Pd, alpha phase	0.130	0.173	0.195	0.215
Atomic ratio D/Pd, beta phase	0.495	0.418	0.365	0.310

The ratio of p_D, the pressure along a horizontal for deuterium at any temperature, to p_H, the pressure along the horizontal for hydrogen at the same temperature, is given by Eq. (2) up to the critical point for deuterium.

$$\log_{10}(p_D/p_H) = 0.0312 + 181.71/(t + 273.13) \quad (2)$$

In our publications we have never presented our reasons (some of which are based on indirect evidence) for believing that our degassing technique has been sufficient to ensure that our compositions really start at zero as is assumed in all our phase diagrams. Mercury diffusion pumps have always been used—the metal was in the finely divided black form—the temperature of degassing in the early work[16] was never less than 360° and in the later work[2] and the present work never less than 200° (the lowest bath temperature). Recent special degassing experiments by Bennett[17] on massive palladium richly charged

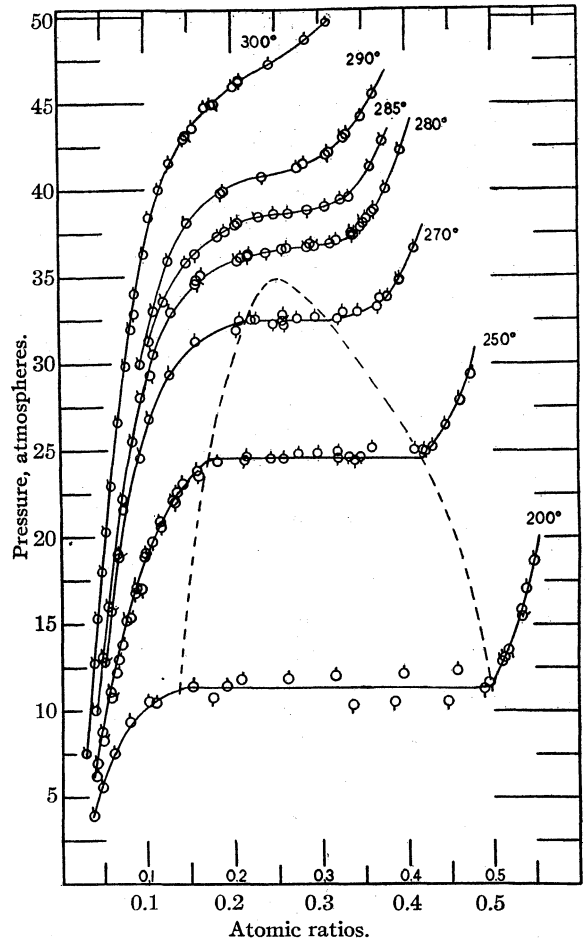

Fig. 8.—Phase diagram of deuterium and palladium.

(15) Estimated by applying the correction of 0.01 to the results of the 260° isotherm.

(16) Gillespie and Hall, THIS JOURNAL, **48**, 1207 (1926).

(17) F. D. Bennett, *ibid.*, to be published. We wish to thank Mr. Bennett and Professor W. R. Ham, through whose courtesy we were able to see the paper in advance of publication.

with hydrogen by electrolysis show no difficulty at 300° (which is above the critical solution temperature) and not too much at 200°. This work seems to close the question and to make it unnecessary to discuss the indirect evidence.

Summary

The isotherms of Gillespie and Galstaun for palladium and hydrogen at 250 and 280° have been confirmed.

A series of isotherms for deuterium and palladium black has been obtained from 200 to 300°, including a critical solution point. A difficulty due to reluctance to formation of the second solid phase was overcome by first forming the beta phase of hydrogen–palladium by pretreatment with hydrogen.

After such pretreatment the isotherms of deuterium are thoroughly reproducible, and after prolonged treatment of palladium with deuterium the hydrogen isotherms are again reproducible.

For a given temperature and pressure, the absorption of deuterium is less than that of hydrogen, but at all the temperatures studied there is not much difference in the maximum absorption of the two gases at the highest practicable pressures after the second solid phase has been formed. Horizontal lines appear in the deuterium isotherms at pressures about 2.3 to 2.5 times the pressures of the corresponding hydrogen horizontals.

The critical solution temperature for deuterium and palladium is found to be 276°, the critical pressure 35 atm., and the critical composition 0.25 atom D per atom Pd.

The heat of solution per mole of deuterium increases regularly with increasing deuterium content and is 7760 cal. per mole for the conversion of the first to the second solid phase.

The phase diagram is given. The locus of the compositions of coexistent solid solutions is smooth and continuous without rising steeply at any simple atomic ratio. This indicates that no palladium deuterides exist in the region above 200°. As the composition of the second solid phase is practically that of Pd_2D at 200° (like the H_2 system), further work at lower temperatures will be required to determine the possible existence of this compound.

The palladium black was prepared by reduction of palladosammine chloride and studied at once.

CAMBRIDGE, MASS. RECEIVED JULY 10, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

The Reduction of Metal Oxides in Liquid Ammonia. I. Preliminary Communication

BY GEORGE W. WATT[1] AND W. CONARD FERNELIUS

Recent studies have shown that bismuth oxyiodide is reduced completely by solutions of sodium and potassium in liquid ammonia.[2] The removal of oxygen from the oxyiodide appears to involve the formation of alkali monoxide and its subsequent ammonolysis to alkali hydroxide and alkali amide. These experiments suggest that some oxides, like almost all halides,[3] may be reduced by liquid ammonia solutions of the alkali metals.

There have been recorded in the chemical literature certain observations which suggest that mercurous oxide,[4] zinc oxide,[5] ferric oxide,[6] and cobaltous-cobaltic oxide[6b] may be reduced under similar conditions. In none of these cases, however, has it been proved that oxygen may be removed *quantitatively* from a heavy metal oxide by means of these reducing agents.

Experimental[7]

Bismuth Trioxide.—One-half gram of bismuth trioxide in the presence of 15 cc. of liquid ammonia[8] was treated with a solution containing 0.25 g. (six equivalents) of potassium in a like volume of ammonia. The characteristic blue color of the potassium solution was discharged immediately and the yellow trioxide was reduced to a gray

(1) Present address: Department of Chemistry, The University of Texas, Austin, Texas.

(2) Watt and Fernelius, THIS JOURNAL, **61**, 1692–4 (1939).

(3) For primary references see Fernelius and Watt, *Chem. Rev.*, **20**, 211–13, 226–32 (1937).

(4) Weyl, *Ann. Physik*, **121**, 601 (1864); **123**, 350 (1864); **131**, 524 (1867).

(5) Weyl, *ibid.*, **123**, 353 (1864).

(6) (a) Bergstrom, THIS JOURNAL, **53**, 3037 (1931); (b) Burgess and Kahler, *ibid.*, **60**, 191 (1938).

(7) The experimental methods employed were those developed by Franklin and co-workers. All reactions were carried out in Faraday tubes at or near room temperature. For details see: Franklin, "The Nitrogen System of Compounds," Reinhold Publishing Corporation, New York, N. Y., 1935, pp. 317–30; Johnson and Fernelius, *J. Chem. Educ.*, **6**, 447–50 (1929).

(8) All of the oxides studied appeared to be insoluble in and unreactive toward liquid ammonia. However, there appears to be some evidence to indicate that cuprous and cupric oxides are slightly soluble; see Franklin and Kraus, *Am. Chem. J.*, **20**, 827 (1898).

metallic solid. At the same time there appeared a small quantity of a white flocculent precipitate (potassium hydroxide). The insoluble reaction product was washed ten times with liquid ammonia. The solvent was vaporized, the tube was evacuated, weighed, opened for analysis, and the insoluble product (0.5795 g.) was washed with water to remove potassium hydroxide.

Anal. Found: Bi, 0.4385 g.

The above weight of bismuth corresponds to 97.7% of the bismuth (as bismuth trioxide) used in the reaction and to 98.4% of the ammonia-insoluble reaction product after allowance is made for the presence of potassium hydroxide.

The aqueous washings were analyzed for potassium hydroxide and nitrogen.

Anal. Found: KOH, 0.1339 g.; N, trace.

The ammonia-soluble product was analyzed for potassium and nitrogen.

Anal. Found: K, 0.1688 g.; N, 0.0415 g.

The weight of nitrogen found in the soluble product is equivalent to 0.16 g. of potassium amide as compared to the 0.18 g. of potassium amide calculated on the assumption that one-half of the potassium used in the reaction should be converted to the amide. The combined analyses for potassium (results from analysis of both soluble and insoluble products), account for a total of 0.26 g. as compared to the 0.25 g. of potassium used in the reaction.

Cuprous Oxide.—One-half gram of cuprous oxide was treated with 0.27 g. (two equivalents) of potassium. After a few minutes a non-adherent copper mirror formed on the walls of the reaction tube. Within one-half hour the blue color was discharged and the liquid ammonia was colored pale yellow (due to dissolved potassium amide). There was no marked change in the color of the oxide. After washing the insoluble material several times with ammonia, the tube was opened and a sample (0.3820 g.) taken for analysis.

Anal. Calcd. for Cu_2O: Cu, 88.8%. Found: KOH, 0.0873 g.; Cu, 0.2628 g. or 89.2% after allowance is made for potassium hydroxide present in the insoluble product.

Cupric Oxide.—One-half gram of cupric oxide was treated with 0.49 g. (two equivalents) of potassium. The black color of the oxide was replaced immediately by the color characteristic of cuprous oxide and after a few minutes a non-adherent copper mirror formed on the walls of the tube. After washing five times with ammonia, a sample (0.1264 g.) was taken for analysis.

Anal. Calcd. for CuO: Cu, 79.9%; for Cu_2O: Cu, 88.8%. Found: KOH, 0.0415 g.; Cu, 0.0732 g. or 86.2% after allowance is made for potassium hydroxide.

Silver Oxide.—One-half gram of silver oxide was treated with 0.17 g. (two equivalents) of potassium. The black oxide was immediately converted to a gray solid. After removal of ammonia- and water-soluble materials, a sample (0.4518 g.) was taken for analysis.

Anal. Found: Ag, 0.4505 g. or 99.7%.

Germanic Oxide.—One-fourth gram of germanic oxide was treated with 0.37 g. (four equivalents) of potassium. The alkali metal was converted to the amide in ten hours. After allowing the apparently unchanged oxide to stand in the presence of the liquid ammonia solution of potassium amide for several hours, the white solid was washed thoroughly with liquid ammonia and analyzed.

Anal. Calcd. for GeO_2: Ge, 69.4. Found: Ge, 68.0.

Other Oxides.—Preliminary studies of the possibility of reduction of the following oxides have also been made: zinc oxide, cadmium oxide, stannous oxide, stannic oxide, lead monoxide, lead dioxide, arsenic trioxide, antimony trioxide. *In every case, reduction has been found to occur.* The reduction products appear to include the elemental metals and (or) soluble or insoluble intermetallic compounds of potassium. These reactions are being investigated further.

Discussion

The results of this investigation show that some metal oxides are reduced by solutions of potassium in liquid ammonia. The primary action involved in such reduction is undoubtedly the removal of oxygen. Subsequently, the resulting alkali monoxide is ammonolyzed to potassium amide and potassium hydroxide.

The formation of potassium hydroxide, which is insoluble in liquid ammonia, prevented the isolation of a single insoluble reduction product. Accordingly it was necessary to correct the analytical data for the heavy metal in the light of results of analyses for potassium hydroxide. This difficulty was obviated in the cases of bismuth trioxide and silver oxide since in these instances the metal formed in the reduction reaction was unreactive toward water and the hydroxide could be removed by washing with water prior to analysis.

When a liquid ammonia solution of an alkali or alkaline earth metal is brought into the presence of a metal oxide, the oxide *may* act as a catalyst[9] for the reaction

$$K \rightleftharpoons K^+ + e^-$$
$$e^- + NH_3 \longrightarrow NH_2^- + {}^1/_2H_2$$

Thus, in the presence of a limited quantity of potassium, an oxide having a marked catalytic activity toward the foregoing reaction might not be reduced to any appreciable extent because of the rapid conversion of potassium to potassium amide; or, more properly, because of the elimination of electrons by virtue of the concomitant formation of molecular hydrogen. The reduction of cupric oxide, for example, appears to be a two-step process. The rate of reduction to cuprous oxide is greater than the rate of interaction between potassium and ammonia. Hence, cupric

(9) For primary references see Fernelius and Watt, *Chem. Rev.*, **20**, 198 (1937).

oxide is reduced to cuprous oxide and it follows that cupric oxide is a relatively poor catalyst for the foregoing reaction. Cuprous oxide, on the other hand, seems to be a very good catalyst and is therefore only slightly reduced when only an equivalent quantity of potassium is used. The ease of reduction of bismuth trioxide and silver oxide precludes the possibility of their exerting any appreciable catalytic effect. Germanic oxide exhibits no marked catalytic effect toward the reaction between potassium and ammonia.

The formation of insoluble or soluble intermetallic compounds of potassium (by the interaction of potassium and the metal liberated from the oxide in the reduction reaction) might have been anticipated, particularly in the case of bismuth.[2] Such reactions were suppressed by the utilization of only that quantity of potassium required for the removal of oxygen, and by the fact that the velocity of the reduction reaction proved to be much greater than that of intermetallic compound formation.

Summary

1. A study of the action of liquid ammonia solutions of potassium on certain metal oxides has shown that: (a) cupric oxide is largely reduced to cuprous oxide; (b) cuprous oxide is reduced to elemental copper to a slight extent; (c) silver oxide and bismuth trioxide are reduced quantitatively to the corresponding elemental metals; and (d) germanic oxide is not reduced.

2. Germanic oxide is not acted upon by a liquid ammonia solution of potassium amide at room temperature.

AUSTIN, TEXAS RECEIVED JUNE 19, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE CREIGHTON UNIVERSITY]

The Partial Pressure of Hydrogen Chloride from its Solutions in Ethylene Glycol and Other Solvents at 25°

BY S. JAMES O'BRIEN, CHRISTOPHER L. KENNY AND ROBERT A. ZUERCHER[1]

It has been pointed out by Rodebush and Ewart[2] that the measurement of the partial pressure of a volatile acid solute provides a means of estimating the extent of the acid–solvent base reaction. More recently, Zellhoefer and co-workers[3] have shown that measurements of the solubility of halogenated hydrocarbons at various pressures in a number of solvents may be interpreted in terms of a solute–solvent reaction, involving the formation of a hydrogen bond, and in terms of the association of the medium. It would seem, then, that a similar study employing a solute like hydrogen chloride, which is at the end opposite to that of the halogenated hydrocarbons, on the scale of hydrogen activity, should be interesting from this point of view. Data of this kind for hydrogen chloride solutions, however, are quite limited. With the exception of a few measurements of the solubility at pressures of about one atmosphere the only direct measurements of the partial pressure of hydrogen chloride from its solutions recorded in the literature are those from water at 25°,[4] glacial acetic acid at the same temperature,[2] and benzene at 30°.[5] Additional information of this kind is also indirectly available for benzene and nitrobenzene solutions at 25° from distribution studies.[6] It is believed that further studies of this kind would be worth while.

Since the work of Zellhoefer and co-workers[3b,3c] shows the solubility of monofluorodichloromethane to be less in ethylene glycol than in nitrobenzene and in acetic acid, while it is to be expected that the solubility of hydrogen chloride in ethylene glycol is greater than that in either of these two solvents, considering the high solubility of hydrogen chloride in alcohols in general, it was decided to make a study of the partial pressure of hydrogen chloride from its ethylene glycol solutions in order to provide concrete evidence concerning this point. It is the purpose of this paper, then, to report the results obtained in this study, and to discuss the available data in terms of the acid–solvent base reaction.

(1) Taken in part from a thesis submitted by R. A. Zuercher to the graduate school of The Creighton University in partial fulfilment of the requirements for the M.S. degree, June, 1939.

(2) Rodebush and Ewart, THIS JOURNAL, **54**, 419 (1932).

(3) (a) Zellhoefer, *Ind. Eng. Chem.*, **29**, 584 (1937); (b) Zellhoefer, Copley and Marvel, THIS JOURNAL, **60**, 1337 (1938); (c) *ibid.*, p. 2666; (d) *ibid.*, p. 2714. See also Copley and Holley, *ibid.*, **61**, 1599 (1939), on similar work with acetylenic compounds.

(4) Randall and Young, *ibid.*, **50**, 1001 (1928).

(5) Saylor, *ibid.*, **59**, 1712 (1937).

(6) Wynne-Jones, *J. Chem. Soc.*, 1064 (1930).

Experimental

Apparatus and Method.—Since the apparatus and method are almost identical with those employed by Saylor,[5] details will not be given here. However, preliminary experiments were performed using solutions of known vapor pressures which showed that the solution–vapor equilibria were established within twenty-four hours. Consequently, the time allowed for the glycol solutions to come to equilibrium with their vapor was approximately two days instead of the longer periods suggested by Saylor.

The constant temperature bath was regulated at 25.00 ± 0.02°.

Materials.—The ethylene glycol used was an Eastman Kodak Co. product of good grade. It was not purified further since the method employed is not of sufficient accuracy to give results that would be seriously affected by the traces of impurities present.

The hydrogen chloride was generated in an all-glass apparatus using C. P. grade potassium chloride and sulfuric acid. It was passed through a drying tower of phosphorus pentoxide before being introduced into the ethylene glycol.

Results

The results obtained are given in Table I in which the first column contains the molalities of the solutions, the second the partial pressure of hydrogen chloride from the solutions and the third, values for the quantity,[7] $k'\gamma$, which will be considered below.

TABLE I

THE PARTIAL VAPOR PRESSURE OF HYDROGEN CHLORIDE FROM ETHYLENE GLYCOL SOLUTIONS AT 25°

m	p, atm.	$k'\gamma$
1.33	0.0008	0.0212
2.27	.0025	.0220
2.45	.0032	.0231
2.72	.0046	.0250
3.02	.0074	.0285
3.07	.0075	.0282
3.11	.0086	.0298
3.13	.0079	.0284
4.66	.0357	.0406
6.57	.135	.0558
6.63	.139	.0562
6.92	.172	.0598
8.78	.424	.0742

A logarithmic plot of the data in Table I, together with those for water, acetic acid, benzene and nitrobenzene solutions, is given in Fig. 1. The data for water solutions were taken from those given by Randall and Young[4]; that for glacial acetic acid solutions from the investigation of Rodebush and Ewart[2]; and those for the benzene and nitrobenzene solutions are direct measurements of the hydrogen chloride pressure above the solutions at 25°, which were taken from unpublished studies made in this Laboratory.[8,9] Since these seem to be the only direct measurements made in these solvents at 25°, some representative data are also given in Tables II and III.

(7) Lewis and Randall, "Thermodynamics and the Free Energy of Chemical Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1923, pp. 329–330, 337.

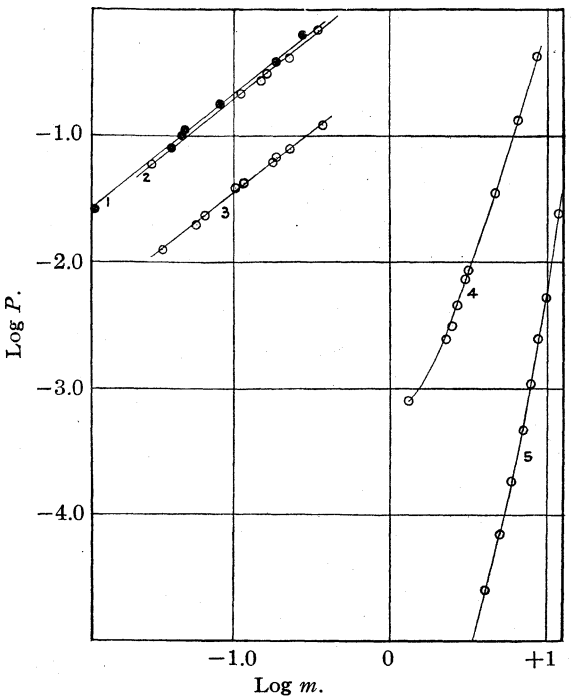

Fig. 1.—The partial pressure of hydrogen chloride from solutions in (1) benzene, (2) nitrobenzene, (3) acetic acid, (4) ethylene glycol, (5) water.

TABLE II

THE PARTIAL PRESSURE OF HYDROGEN CHLORIDE FROM ITS BENZENE SOLUTIONS AT 25°

m	p, atm.	m	p, atm.
0.273	0.601	0.048	0.111
.191	.391	.047	.100
.112	.211	.040	.078
.096	.197	.014	.026

TABLE III

THE PARTIAL PRESSURE OF HYDROGEN CHLORIDE FROM ITS NITROBENZENE SOLUTIONS AT 25°

m	p, atm.	m	p, atm.
0.338	0.689	0.161	0.312
.323	.636	.146	.278
.319	.654	.110	.213
.225	.428	.030	.059

Discussion

From Fig. 1 it is evident that hydrogen chloride solutions in the solvents considered, fall into two groups. In one, which includes benzene, nitro-

(8) Schmelzle, Master's Thesis, The Creighton University, 1938.
(9) Westfall, Master's Thesis, The Creighton University, 1938.

benzene, and acetic acid, its solubility is low, and the law of Henry in the form

$$p = km \quad (1)$$

is followed.[10] In the second, which includes water and ethylene glycol solutions, its solubility is high, and the law of Henry, in the form of equation (1), does not hold, but, as is customary for aqueous solutions, the data can be treated in terms of the law of Henry (or a law similar to it) in the form[7]

$$p^{1/2} = k'\gamma m \quad (2)$$

It seems logical to consider this possible treatment of the data in terms of two forms of the law of Henry, as an indication of two different acid–solvent reactions. Equation (1) corresponds to a reaction which may be represented by

$$HCl + S = S \longrightarrow H—Cl \quad (I)$$

where S represents the solvent and S ⟶ H—Cl is written to indicate the formation of a hydrogen bond with some atom in the solvent. Equation (2) would correspond to the reaction

$$HCl + S = SH^+ + Cl^- \quad (II)$$

where SH^+ represents the solvated proton.

Also, the extent to which these acid–base reactions proceed may be determined, if it can be assumed that the unreacted molecular hydrogen chloride in the solutions corresponds to the law of Raoult[6] (p. 1070)

$$f = f_0 N_u \quad (3)$$

where f is the fugacity of the hydrogen chloride in solution, f_0 is the fugacity of pure liquid hydrogen chloride, and N_u is the mole fraction of unreacted hydrogen chloride. First, however, it should be pointed out that since reaction (I) takes place to some extent, equation (1) should be written

$$p = k(m_u + m_r) \quad (4)$$

where m_u represents the molality of unreacted hydrogen chloride, m_r, reacted hydrogen chloride, and

$$m = m_u + m_r \quad (5)$$

Equation (2), of course, could be written in a similar manner, but since the molality of unreacted solute is negligible in comparison with that which has reacted, in all the cases so far considered which fit into this group, it is only necessary to set

$$m = m_r \quad (6)$$

in order to follow through in equation (2) the notation adopted in equation (4).

(10) Compare Heston and Hall, THIS JOURNAL, **56**, 1462 (1934).

The equilibrium constant of the reaction represented by (I) is given by

$$K_a = a_r/a_u \quad (7)$$

where the a's refer to activities and the subscripts have the same significance as in the previous equations. Using equation (3) and setting $p = f$, it is found that[11]

$$m_u = m_s p/f_0 \quad (8)$$

where m_s is the number of moles of solvent in 1000 g. Assuming that activities are equal to molalities in this case, and making use of equations (4), (5) and (8), equation (7) becomes

$$K_a = (f_0 - km_s)/km_s \quad (9)$$

In like manner, making use of equations (2), (6) and (8), and assuming that the activity coefficients of unreacted hydrogen chloride are equal to unity, the equilibrium constant for reaction (II) becomes

$$K_d = f_0/m_s k'^2 \quad (10)$$

In Table IV are given values of these constants for hydrogen chloride solutions in benzene, nitrobenzene, acetic acid, glycol and water. In obtaining these constants, the value of $f_0 = 30.3$ atm. at 25° was calculated from the vapor pressure of liquid hydrogen chloride, interpolated from the data in "International Critical Tables,"[12] using the approximate method of Lewis and Randall[7] (pp. 197–199), and assuming that the deviation of hydrogen chloride from the perfect gas law at 25° is the same as that indicated by the work of Gray and Burt[13] at 0°; the Henry's law constants given in the second column of this table were obtained from the same data used in constructing Fig. 1, for benzene, nitrobenzene, and acetic acid; that for water is from Lewis and Randall[7]; that for glycol was obtained by extrapolating a plot of m against $k'\gamma$ (Table I) to $m = 0$, where, as in the case of aqueous solutions, it is assumed that $\gamma = 1$. The

TABLE IV

EQUILIBRIUM CONSTANTS FOR THE HYDROGEN CHLORIDE SOLVENT BASE REACTIONS AT 25°

Solvent	k	K_a
Benzene	2.04	0.16
Nitrobenzene	1.98	0.88
Acetic acid	0.347	4.25
	k'	K_d
Ethylene glycol	0.02	4.68×10^3
Water	0.000664	1.23×10^6

(11) The denominator of equation (8) is, of course, $f_0 - p$, but p is neglected since in most cases it is small in comparison with f_0. In the more concentrated solutions of hydrogen chloride, however, this simplification introduces an error of about 3%.

(12) "International Critical Tables," Vol. III, p. 228.

(13) Gray and Burt, *J. Chem. Soc.*, **95**, 1633 (1908).

partial pressure data could not be carried to low enough concentrations by the method employed to make the extrapolation with any great degree of certainty, but the curve was well enough defined so that the value given should be of the correct order of magnitude and may be accepted tentatively until activity data at lower concentrations are available.

The values for K_a and K_d given in this table indicate the relative basicities of the solvents, and the method of their derivation seems to be additional confirmation of the opinion that the basicity of a solvent is determined by the strength of the hydrogen bond formed with some atom in the solvent molecule acting as an electron donor.[14] When the bond formed is weak, the hydrogen chloride remains in the solution in the form of hydrogen bond compound, although the bond distance between the proton and the negative constituent of the acid is increased, as indicated by infrared absorption studies[14d] (p. 224). In solvents forming such bonds, the solubility of hydrogen chloride is low. When the bond formed is relatively strong, the bond between the proton and the negative constituent is so weakened that more or less complete ionization takes place, and when this occurs the solubility of hydrogen chloride is high.

While the formation of a complex between benzene and hydrogen chloride is indicated in Table IV, it should be pointed out that the magnitude of the deviation from the law of Raoult, which leads to the value given for K_a, may be of the same order as the uncertainty involved in the calculation of f_0. In other words, it is not possible to conclude definitely from this work that reaction (I) takes place in this case, although such a process might serve as the explanation for the increased dielectric polarization of hydrogen chloride in benzene solutions,[15] and the apparent slight shift toward longer wave lengths of the vibrational band occurring in the infrared spectra of hydrogen chloride at 3.46 μ.[16] In addition, Hantzsch[17] has considered such a possibility as the explanation for the catalytic action of hydrogen chloride in toluene solutions on the decomposition of diazoacetic acid ester.

The results obtained in this study of ethylene glycol solutions also definitely establish the inverted order of solubility of hydrogen chloride in nitrobenzene, acetic acid and glycol, compared to the solubility of monofluorodichloromethane. This appears to be an indication that the solute itself is an important factor in determining the basicity of the solvent, insofar as it may affect the hydrogen bonding between the molecules of the solvent. The solubility of hydrogen chloride in ethylene glycol is greater than expected from the law of Raoult, while that of monofluorodichloromethane is less. That this is due to a reduction in the amount of association of the glycol in the presence of hydrogen chloride seems quite likely, since the converse case of reduction of hydrogen bonding of solutes in the presence of other solutes that have a strong tendency to form hydrogen bonds, is fairly well established.[18] However, further studies are in progress in this Laboratory and since these may give additional information concerning this point, further discussion will be postponed until the results of these investigations can be given.

Summary

1. The partial vapor pressure of hydrogen chloride from its solutions in ethylene glycol at 25°, over the concentration range, 1.33 to 8.78 *m*, has been measured. Also, data from unpublished studies on the partial pressure of hydrogen chloride from benzene and nitrobenzene solutions at 25° are included.

2. The available data on the partial pressure of hydrogen chloride from solutions in various solvents have been considered in terms of two different acid–base reactions. A method of calculating the equilibrium constants for these reactions has been given.

3. The importance of hydrogen bonding, and the nature of the solute, in determining the basicity of the solvent is indicated.

OMAHA, NEBRASKA RECEIVED JUNE 19, 1939

(14) (a) Gordy, *J. Chem. Phys.*, **7**, 93 (1939); (b) Gordy and Martin, *ibid.*, **7**, 99 (1939); (c) Buswell, Rodebush and Roy, THIS JOURNAL, **60**, 2528 (1938); (d) Rodebush and Buswell, *J. Phys. Chem.*, **43**, 219 (1939).

(15) Fairbrother, *J. Chem. Soc.*, 44 (1932).

(16) Plyler and Williams, *Phys. Rev.*, **49**, 215 (1936); Williams, *ibid.*, **49**, 719 (1936).

(17) Hantzsch, *Ber.*, **58B**, 630 (1925).

(18) Lassettre, *Chem. Rev.*, **20**, 274–278 (1937); Barger, *J. Chem. Soc.*, **87**, 1042 (1905).

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, No. 718]

The Structure of Formaldehyde from Electron Diffraction

BY D. P. STEVENSON,[1] JAMES E. LUVALLE[2] AND VERNER SCHOMAKER

Introduction

The structure of monomeric formaldehyde is of particular interest since it is the simplest molecule containing a carbon–oxygen double bond. Bru[3] found the carbon–oxygen distance to be 1.15 ± 0.05 Å. by electron diffraction. The accuracy, ±0.05 Å., of this determination is very much less than is now obtainable in determining the size of simple molecules.[4] Furthermore, this value for the carbon–oxygen distance is about 0.1 Å. smaller than that predicted by the covalent radius table[5] for the carbon–oxygen double bond, 1.24 Å., and that found for the carbon–oxygen distance of acetaldehyde,[6] 1.22 Å., and glycine,[7] 1.24 Å. Badger's rule[8] applied to the carbon–oxygen frequency gives 1.21 Å.[9] for the distance.

The moments of inertia have been determined very accurately[10] but are insufficient by themselves to determine the structure uniquely. This will be discussed below. Since the carbon–oxygen distance appeared definitely to be shorter than predicted, we were led to redetermining it by the electron diffraction technique.

Experimental

Dieke and Kistiakowsky[10] found it possible to maintain a pressure of 100 mm. of H_2CO by heating paraformaldehyde. For this reason we first attempted to obtain photographs by heating Eastman Kodak Company White Label paraformaldehyde from 150 to 200° in the "high temperature nozzle." Some of the photographs obtained in this fashion had the expected pattern, namely, that of a diatomic molecule, while others showed a much more complicated pattern. The latter were probably due to small polymers (*e. g.*, trimer). In order to eliminate the possibility of polymer in the vapor we prepared 10 cc. of the monomeric liquid according to the method of Spence and Wilde.[11] The liquid was held at −25° in the side-arm of a 200-cc. flask attached to the apparatus. This gave an effective pressure of nearly one atmosphere. Since air was excluded carefully from the preparation, polymerization was delayed long enough to obtain photographs of the monomer. The photographs so obtained were excellent, having a pattern similar to that of a diatomic molecule.

The camera distance was 10.84 cm. and the wave length of the electrons was 0.0611 Å. based on transmission pictures of gold, the structure of which is known (a = 4.070 Å.).

Interpretation.—Only the photographs obtained by the second technique will be considered since polymers may have been present in the gas in the high temperature photographs. The photographs showed five minima and five maxima of gradually decreasing intensity. The measured values of $s\left(s_0 = \frac{4\pi}{\lambda}\sin\frac{\vartheta}{2}\right)$ are given in the third column of Table I. Comparison with a simple $\sin x/x$ curve indicated the carbon–oxygen distance to be about 1.20 Å. This distance and the moments of inertia (see below) give a carbon–hydrogen distance of 1.09 Å. and a hydrogen–carbon–hydrogen angle of 120°. A theoretical intensity curve was then calculated for the corresponding model. In place of the commonly used coefficients Z_iZ_j, $\overline{(Z_i - f_i)(Z_j - f_j)}e^{-A_{ij}}$ was used in the expression

$$I(s) = \sum_i\sum_j \overline{(Z_i - f_i)(Z_j - f_j)}e^{-A_{ij}}\frac{\sin l_{ij}s}{l_{ij}s}$$

The use of the "temperature factor," "$e^{-A_{ij}}$," will be discussed by one of us.[12] The atomic scattering factors "f" were obtained from Pauling and Sherman.[13] The curve so obtained is shown in Fig. 1, curve C, along with a common visual curve calculated for the same molecular dimension and the curve $\sin 1.20x/1.20x$. The vertical lines indicate the position of the measured maxima and minima. Quantitative comparison with the curve calculated with temperature fac-

(1) National Research Fellow.
(2) Julius Rosenwald Foundation Fellow.
(3) L. Bru, *Ann. soc. españ. fis. quim.*, **30**, 483 (1932).
(4) *Cf.* V. Schomaker and D. P. Stevenson, THIS JOURNAL, to be published.
(5) L. Pauling and M. L. Huggins, *Z. Krist.*, **87**, 205 (1934); L. Pauling and L. O. Brockway, THIS JOURNAL, **59**, 1223 (1937).
(6) D. P. Stevenson and H. Burnham, *ibid.*, to be published.
(7) G. Albrecht and R. B. Corey, *ibid.*, **61**, 1087 (1939).
(8) R. M. Badger, *J. Chem. Phys.*, **2**, 128 (1934), and **3**, 710 (1935).
(9) H. W. Thompson and J. W. Linnett, *J. Chem. Soc.*, 1391 (1937).
(10) G. H. Dieke and G. B. Kistiakowsky, *Phys. Rev.*, **45**, 4 (1934).
(11) R. Spence and W. Wild, *J. Chem. Soc.*, 338 (1935).
(12) V. Schomaker, to be published.
(13) L. Pauling and J. Sherman, *Z. Krist.*, **81**, 1 (1932).

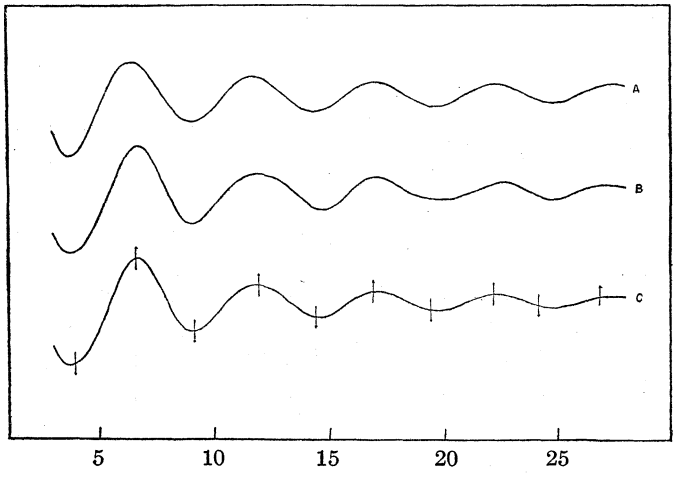

Fig. 1.—Theoretical intensity curves for formaldehyde: A, sin $1.20s/1.20s$; B, ordinary intensity curve for C–O = 1.20 Å., C–H = 1.09 Å., ∠H–C–H = 120°; C, like B with coefficients including the atomic scattering factors and a "temperature factor."

tor is given in Table I. It leads to a carbon–oxygen distance of 1.213 ± 0.008 Å.

TABLE I

Max.	Min.	s_2	$s_{calcd.}$[a]	s_c/s_0
	1	3.95	3.73	(0.944)[b]
1		6.62	6.71	1.014
	2	9.15	9.12	0.997
2		11.95	11.89	0.995
	3	14.40	14.59	1.013
3		16.90	17.10	1.012
	4	19.40	19.61	1.011
4		22.15	22.21	1.003
	5	24.16	24.81	1.027
5		26.86	27.50	1.024

Average of 9 features 1.011 ± 0.008

Carbon–oxygen distance = 1.20 × 1.011 = 1.213 ± 0.008 Å.

[a] From curve calculated with C–O = 1.20, C–H = 1.09, ∠H–C–H = 120°, with temperature factor. [b] Omitted from average.

Discussion

Dieke and Kistiakowsky[10] have determined values for the moments of inertia of formaldehyde from the analysis of the rotational structure of six ultraviolet bands. Since the molecule is planar, there are only two independent moments of inertia while there are three parameters which determine the structure of the molecule, namely, the carbon–oxygen and carbon–hydrogen distances and the hydrogen–carbon–hydrogen angle. An independent determination of any one of these structural parameters along with the moments of inertia suffice to determine the other two structural parameters. In Fig. 2 we have plotted the values of the carbon–oxygen and carbon–hydrogen distances which are consistent with the moments of inertia as a function of the hydrogen–carbon–hydrogen angle. Our value of 1.213 Å. for the carbon–oxygen distance (marked by a circle on the graph) corresponds to an angle of 120° and a hydrogen–carbon distance of 1.086 Å. Ebers and Nielsen[14] from an incompletely resolved infrared band at 4.5 μ have determined rough values for the moments of inertia of deuteroformaldehyde. Although their value for the small moment of inertia is in good agreement with that of Dieke and Kistiakowsky[10] for light formaldehyde, their value for the large moment is not sufficiently accurate to be used in determining the structure of formaldehyde.

Thompson and Linnett[9] using the frequencies of Nielsen[15] and a five constant potential function have found $k_{C-O} = 12.3 \times 10^5$ dynes/cm. and $k_{C-H} = 4.3 \times 10^5$ dynes/cm. With these values Badger's rule[8] leads to a carbon–oxygen distance of 1.21 Å. and a carbon–hydrogen distance of 1.09 Å. in good agreement with our determination. Very little significance can be assigned to the agreement in the case of the carbon–oxygen bond distance since Thompson and Linnett[9] find the

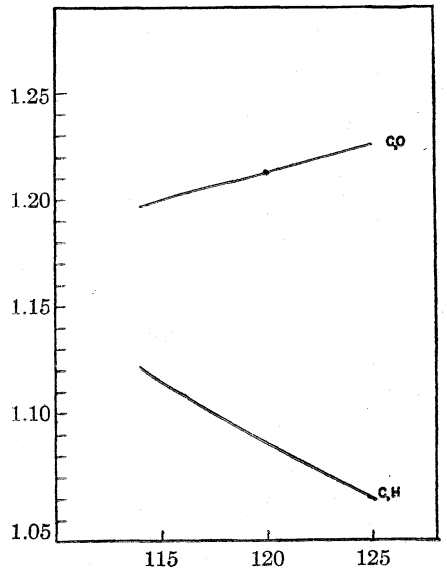

Fig. 2.—Graph of distances and angles consistent with the moments of inertia of formaldehyde: $I_1 = 2.941 \times 10^{-40}$ g. cm.²; $I_2 = 21.39 \times 10^{-40}$ g. cm.²

(14) E. S. Ebers and H. H. Nielsen, *J. Chem. Phys.*, **6**, 311 (1938).
(15) H. H. Nielsen, *Phys. Rev.*, **46**, 117 (1934).

same distance for ketene, which has been found by electron diffraction to have a carbon–oxygen distance equal to 1.17 Å.[16]

The large value of the hydrogen–carbon–hydrogen angle, 120°, may be interpreted as indicating that the bonding in formaldehyde is primarily of the sp^2, π type which gives three coplanar bonds at 120°. It has been found that in acetaldehyde[6] a similar situation obtains, the carbon–carbon–oxygen angle being 122 ± 2°. The carbon–oxygen distance in formaldehyde is definitely shorter than that predicted by the covalent radius table for a carbon–oxygen double bond.

(16) J. Y. Beach and D. P. Stevenson, *J. Chem. Phys.*, **6**, 75 (1938).

Summary

Electron diffraction photographs of monomeric formaldehyde have been obtained using fast electrons. Their interpretation leads directly to a carbon–oxygen distance equal to 1.21 ± 0.01 Å. Using this distance and the accurately known moments of inertia one finds the carbon–hydrogen distance to be 1.09 ± 0.01 Å. and the hydrogen–carbon–hydrogen angle to be 120 ± 1°.

PASADENA, CALIFORNIA RECEIVED JULY 10, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING OF THE UNIVERSITY OF PENNSYLVANIA]

The Hydrolysis of Ethylal[1]

BY PAUL M. LEININGER[2] AND MARTIN KILPATRICK

In a study of the inversion of sucrose[3] it was shown that the parameters of the Arrhenius equation

$$\ln k = B - (E_A/RT) \qquad (1)$$

depended upon electrolyte concentration and temperature. The present paper extends the study to the hydrolysis of ethylal. This reaction was chosen because the velocity constant can be determined conveniently over similar ranges of hydrochloric acid concentration and temperature.

Skrabal and Schiffrer[4] measured the rate of hydrolysis of ethylal in aqueous hydrochloric acid solutions by indirectly determining the amount of formaldehyde present at suitable intervals. The formaldehyde was oxidized to formic acid and titrated. In 1926 Skrabal and Eger[5] continued the work at 25°, using a modification of the sulfite method of Lemme[6] to determine the quantity of formaldehyde.

Subsequently the hydrolysis of ethylal was studied at 25 and 35° by Salmi[7] and by Palomaa and Aalto[8] using analytical methods. In 1934 Palomaa and Salonen[9] measured the reaction rate dilatometrically. Löbering and Fleischmann[10] investigated the hydrolysis at 10, 20 and 30° in sulfuric acid solutions.

If the claim of an accuracy of ±4% in the measurement of the rate constant, made by one of the authors,[8] can be regarded as typical, it is apparent that for this reaction the data in the literature are insufficiently accurate for a study of the parameters of the Arrhenius equation. In addition, both the temperature and concentration ranges investigated are too limited to enable one to observe possible variations in the parameters, E_A and B.

The present investigation extends over a range of hydrochloric acid concentration from 0.5 to 3.0 molar, at 0, 10, 15, 20, 25, 30, 35 and 40° (concentrations resulting in too rapid reaction being omitted at the higher temperatures).

Experimental

Ethylal.—Ethylal from the Eastman Kodak Company was purified by fractional distillation, the fraction boiling between 87.0 and 88.0° (760 mm.) being used. That the preparation was free of acidic impurities was established by titration of an aqueous solution in an atmosphere of nitrogen using brom thymol blue as indicator. A further check upon the purity of the product was made by determining the refractive index by means of a Zeiss dipping refractometer. At 17.5° different preparations gave values of n_D varying from 1.3736 to 1.3745 as compared with

(1) Abstracted from the dissertation of Paul M. Leininger presented to the Faculty of the Graduate School of the University of Pennsylvania in partial fulfilment of the requirement for the degree of Doctor of Philosophy, April, 1939. Paper presented before the Baltimore Meeting of the American Chemical Society, April, 1939.

(2) E. I. du Pont de Nemours and Company Fellow, 1938–1939.

(3) Leininger and Kilpatrick, THIS JOURNAL, **60**, 2891 (1938).

(4) Skrabal and Schiffrer, *Z. physik. Chem.*, **99**, 290 (1921).

(5) Skrabal and Eger, *ibid.*, **122**, 349 (1926).

(6) Lemme, *Chem. Ztg.*, **27**, 896 (1903).

(7) Salmi, *Annal. Univ. Aboensis*, **A3**, no. 3 (1932).

(8) Palomaa and Aalto, *Ber.*, **66**, 468 (1933).

(9) Palomaa and Salonen, *ibid.*, **67**, 424 (1934).

(10) Löbering and Fleischmann, *ibid.*, **70B**, 1713 (1937).

1.3760 in the literature.[11] An examination of the experimental results reveals no difference in the velocity constants for the various preparations.

Hydrochloric Acid.—Baker C. P. analyzed hydrochloric acid was used. Experiments made with solutions prepared from constant-boiling acid checked the others within the experimental error.

Apparatus.—The dilatometers and thermostats were the same as in the study of the inversion of sucrose.[3]

Determination of Temperature.—Temperature regulation was slightly better than in the previous work,[3] the determination of temperature being carried out as previously described.

Determination of Concentrations.—The weight of ethylal used in an experiment was calculated from its density[12] and volume at the temperature of the experiment. The molarity of the ethylal was obtained from the weight of ethylal, the density of the reacted mixture, and the weight of hydrochloric acid solution. This procedure permits the calculation of molalities as well as molarities. The molarity of the hydrochloric acid was determined directly for each solution at the temperature at which the experiment had been performed by titration of the reacted mixture. The validity of the method was established by titrating a blank in the absence of ethylal. The concentration of acid was known to 0.1%.

Determination of the Rate.—A definite volume (150 cc.) of a hydrochloric acid solution of known concentration was introduced into the mixing chamber of the dilatometer and subjected to reduced pressure to prevent subsequent bubble formation. To this solution, at the temperature of the thermostat, 5 cc. of ethylal was added. The mixture was stirred until the solution became homogeneous, sealed off in the dilatometer and the rate of contraction noted. Velocity constants were evaluated by the Guggenheim method.[13]

Results

The hydrolysis of ethylal is represented conventionally as taking place in two steps: first hydrolysis, then the decomposition of the hemi-acetal.

$$CH_2(OC_2H_5)_2 + H_2O = CH_2(OC_2H_5)(OH) + C_2H_5OH$$
$$CH_2(OC_2H_5)(OH) = CH_2O + C_2H_5OH$$

The results of the present work indicate that the reaction is of the first order over the entire range of temperature and concentration investigated. Because of the great difficulty, if not impossibility, of preparing hemi-acetals, Skrabal[4] has concluded that the first of the above steps involves the rate determining process. The actual existence of hemi-acetals seems to be indicated, however, by some work of Adkins and Broderick.[14]

The validity of the dilatometric method is based upon the agreement of the results obtained in the present investigation with the values of other workers at 25° using analytical methods (see Fig. 1). As in the case of the other formals,[9] the reaction is accompanied by a contraction.

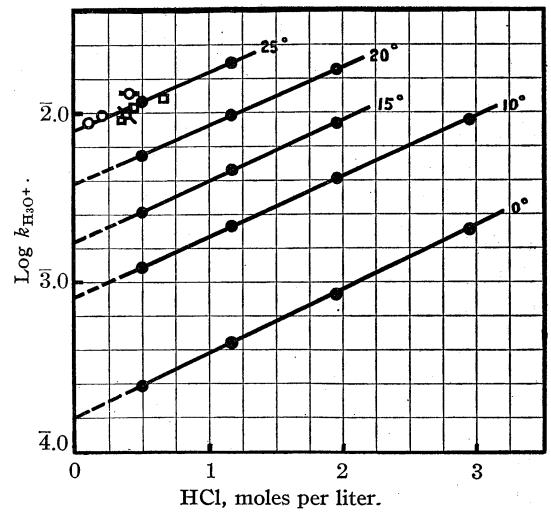

Fig. 1.—Electrolyte effect at various temperatures: ●, this investigation, 0.26 molar ethylal; ○, Skrabal and Schiffrer,[4] 0.2 molar ethylal; -○-, Skrabal and Eger,[5] 0.022 molar ethylal; □, Palomaa and Salonen,[9] 0.22 molar ethylal; -◇-, Salmi,[7] 0.21 molar ethylal.

In Table I are listed the values of $k_{H_3O^+}(k_{obsd.}/C_{H_3O^+})$ obtained. The molarity of the ethylal is 0.260 ± 0.004 unless otherwise indicated. The

TABLE I

SUMMARY OF $k_{H_3O^+}$ VALUES

Temp., °C.	No. of expts.	HCl, moles/liter	$10^3 k_{H_3O^+}$
−0.01	3	0.4941	0.2430
−0.01	3	1.165	.4370
−0.01	1	1.945	.8473
−0.01	1	2.940	2.028
10.00	2	0.4959	1.214
10.00	2	1.164	2.151
10.00	2	1.959	4.053
10.00	2	2.945	9.387
15.00	2	0.4963	2.625
15.00	2	1.172	4.602
15.00	2	1.953	8.577
20.00	4	0.4950	5.595
20.00	2	1.164	9.613
20.00	4	1.951	17.76
25.00	2	0.4994	11.63
25.00	2	1.165	19.78
30.00	2	0.4956	23.19
35.00	2	.4998	46.47
35.00	4	.5011	46.37[a]
40.00	3	.4940	91.64
40.00	1	.4751	84.68[b]

[a] 0.234 molar ethylal. [b] 0.362 molar in ethylal; 0.246 molar in reacted ethylal.

(11) Ghysels, *Bull. soc. chim. Belg.*, **33**, 57 (1924).

(12) Timmermans and Hennaut-Roland, *J. chim. phys.*, **27**, 401 (1930).

(13) Guggenheim, *Phil. Mag.*, [7] **2**, 538 (1926).

(14) Adkins and Broderick, THIS JOURNAL, **50**, 499 (1928).

average of the average deviations for these experiments has been calculated and is 0.7%.

An examination of Table I shows that the bimolecular constant increases with concentration of hydrochloric acid. In Fig. 1 values of log $k_{H_3O^+}$ have been plotted against the molarity of the hydrochloric acid. The curves reading from top to bottom are for 25, 20, 15, 10 and 0°, respectively. The straight lines obtained indicate that the effect obeys the equation

$$\log k_{H_3O^+} = \log k^0_{H_3O^+} + \beta C \qquad (2)$$

at each temperature for the concentration range considered. The following equations were obtained from the above data.

$$\log k_{H_3O^+} = \bar{4}.2001 + 0.3760\ C \text{ (at } -0.01°) \qquad (2A)$$
$$\log k_{H_3O^+} = \bar{4}.9066 + 0.3612\ C \text{ (at } 10.00°) \qquad (2B)$$
$$\log k_{H_3O^+} = \bar{3}.2458 + 0.3529\ C \text{ (at } 15.00°) \qquad (2C)$$
$$\log k_{H_3O^+} = \bar{3}.5790 + 0.3444\ C \text{ (at } 20.00°) \qquad (2D)$$
$$\log k_{H_3O^+} = \bar{3}.8914 + 0.3478\ C \text{ (at } 25.00°) \qquad (2E)$$

The effect of ethylal concentration upon $k_{H_3O^+}$ is small, as evidenced by the value in Table I with superscript "*a*". A further examination of Fig. 1, however, shows that the value of $k_{H_3O^+}$ reported by Skrabal and Eger[5] is considerably higher (*ca* 20%) than one would expect for that concentration of hydrochloric acid. Since the only difference between this experiment and all the others is the fact that the molarity of ethylal was about 0.02 instead of 0.2, one would conclude that the bimolecular constant increased with decreasing ethylal concentration. This conclusion is further substantiated by the experiment reported in Table I with a superscript "*b*". In this case another portion of ethylal was added to the reacted mixture from a previous run (which might be considered equivalent to increasing the concentration of ethylal). Here a marked decrease in $k_{H_3O^+}$ was noted.

In Table II are recorded the values of E_A calculated from the data of Table I by the equation

$$E_A = \frac{RT_1T_2}{(T_1 - T_2)} \ln \frac{k_{T_1}}{k_{T_2}} \qquad (3)$$

The maximum error, ΔE_M, in E_A is calculated from the relation

$$\Delta E_M = \Sigma(\delta E_x) \qquad (4)$$

where δE_x represents the change in E_A due to the variation, δ_x, in the quantity x (x representing in turn T_1, T_2, ΔT, $k_{H_3O^+(T_1)}$ and $k_{H_3O^+(T_2)}$). The values assigned to δT_1 and δT_2 are 0.01°, to $\delta(\Delta T)$ 0.01° and to δk_1 and δk_2 = 0.7%. ΔE_M is approximately ±300 cal. A calculation of the

$$\Delta E_{PM} = \sqrt{\Sigma(\delta E_x)^2} \qquad (5)$$

precision measure, ΔE_{PM}, yields ±200 cal. Two things become apparent: E_A increases with increase in temperature, and decreases with increase in hydrochloric acid concentration. The concentration effect is also indicated by the decrease in the slope of the equations (2A) to (2D) as the temperature increases.

TABLE II

SUMMARY OF ACTIVATION ENERGIES

Temp. range, °C.	HCl, moles/liter	k_{T_1}/k_{T_2}	E_A, cal.
−0.01 to 10.00	0.4950	4.996	24,690
− .01 to 10.00	1.165	4.922	24,460
− .01 to 10.00	1.952	4.783	24,020
− .01 to 10.00	2.943	4.629	23,520
− .01 to 20.00	0.4946	23.02	24,940
− .01 to 20.00	1.165	22.00	24,570
− .01 to 20.00	1.948	20.96	24,190
10.00 to 20.00	0.4955	4.609	25,200
10.00 to 20.00	1.164	4.469	24,690
10.00 to 20.00	1.955	4.382	24,370
15.00 to 25.00	0.4979	4.430	25,410
15.00 to 25.00	1.169	4.298	24,890
20.00 to 30.00	0.4953	4.145	25,110
25.00 to 35.00	.4997	3.996	25,290
30.00 to 40.00	.4948	3.952	25,920

There are only three values of E_A available in the literature for the hydrolysis of ethylal by hydrochloric acid. From the work of Salmi[7] one calculates an activation energy of 25,760 cal., from that of Palomaa and Aalto[8] 24,620 cal., and from that of Palomaa and Salonen[9] 25,910 cal. An average value of 25,430 cal. is thus obtained for solutions approximately 0.4 molar with respect to hydrochloric acid and 0.2 molar with respect to ethylal. In this investigation the value of E_A at 30° for solutions 0.5 molar with hydrochloric acid was found to be 25,290 cal.

The effect of hydrochloric acid concentration is illustrated by a plot of values of E_A (taken from Table II) against molarity of acid.

In similar fashion, one can show the effect of temperature by plotting E_A against the midpoint of the temperature interval. This is done in Fig. 3, using values from Table II for 0.5 molar solutions of hydrochloric acid. The position of the line in Fig. 3 was determined by least squares.

Values of E_A for 0, 1 and 2 molar solutions of acid (read from Fig. 2) and for 0.5 molar acid (read from Fig. 3) are summarized in Table III. Values of E_A for zero molarity were likewise checked by calculation from the intercepts of equations (2A) to (2E).

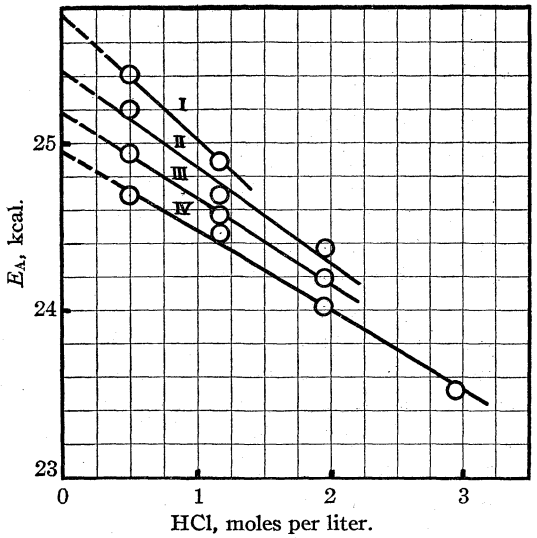

Fig. 2.—Electrolyte effect on energy of activation: I, 15.00 to 25.00°; II, 10.00 to 20.00°; III, −0.01 to 20.00°; IV, −0.01 to 10.00°.

TABLE III

VARIATION OF THE ENERGY OF ACTIVATION WITH TEMPERATURE AND ACID CONCENTRATION

	E_A, cal.			
Temp. range, °C.	0 molar HCl	0.5 molar HCl	1 molar HCl	2 molar HCl
−0.01 to 10.00	24,960	24,760	24,480	24,010
−0.01 to 20.00	25,180	24,920	24,670	24,160
10.00 to 20.00	25,440	25,070	24,860	24,280
15.00 to 25.00	25,760	25,220	25,020	....
20.00 to 30.00	....	25,370	....	....
25.00 to 35.00	....	25,530	....	....
30.00 to 40.00	....	25,680	....	....

Values of B calculated by equation (1), $k_{H_3O^+}$ being expressed in reciprocal seconds, are summarized in Table IV.

TABLE IV

VARIATION OF B WITH TEMPERATURE AND ACID CONCENTRATION

	B			
Temp. range, °C.	0 molar HCl	0.5 molar HCl	1 molar HCl	2 molar HCl
−0.01 to 20.00	33.54	33.50	33.47	33.39
10.00 to 20.00	34.00	33.76	33.80	33.60
15.00 to 25.00	34.56	34.04	34.08	...
20.00 to 30.00	...	34.28	...	...
25.00 to 35.00	...	34.53	...	...
30.00 to 40.00	...	34.79	...	...

From Table IV it appears that B increases with increasing temperature. The variation of B with concentration is within the experimental error, which is calculated to be ±0.3 of a B unit.

Discussion

From the results it is evident that the energy of activation decreases with increasing hydrochloric acid concentration, as in the case of the inversion of sucrose, but that the effect of temperature on E_A is in the opposite direction to that for the inversion of sucrose, dE_A/dT being positive and equal to 31 cal. per degree. The effect appears to be linear with temperature.

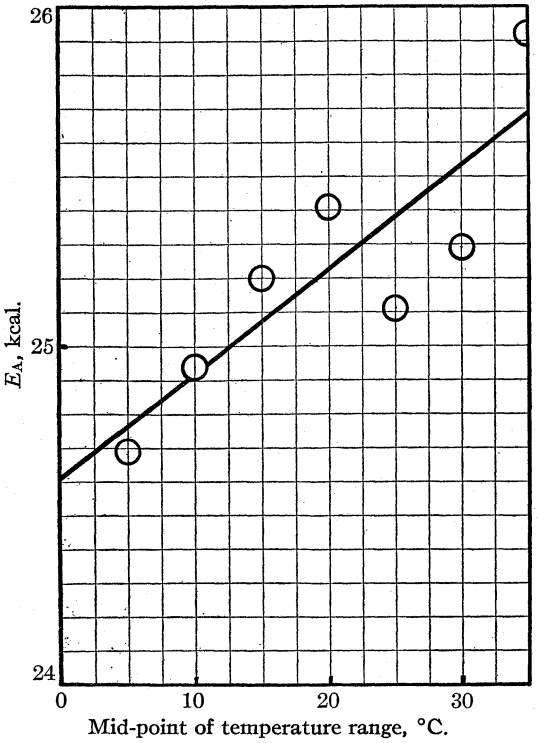

Fig. 3.—Effect of temperature on energy of activation (0.5 molar HCl).

In a recent paper Moelwyn-Hughes[15] reviews the examples of the change of E_A with temperature and reports experiments on the hydrolysis of methyl halides. He finds that the temperature coefficient of the apparent activation energy is always negative in the region explored. This is not the case for the hydrolysis of ethylal.

Even though the variation of E_A and B with temperature has been established definitely, it is still possible to write an expression of the form of equation (1) which holds for the data in 0.5 molar hydrochloric acid solution. In fact it is possible to calculate values of $k_{H_3O^+}$ from the following equation, over the range of temperature studied, which on the average agree with the observed values to ±1.2%, the maximum deviation being 3.8%. The equation

$$\ln k_{H_3O^+} = 34.175 - (25{,}304/RT) \qquad (6)$$

(15) Moelwyn-Hughes, *Proc. Roy. Soc.* (London), **A164**, 295 (1938).

was determined by considering ln $k_{H_3O^+}$ as a linear function of $1/T$ and determining the intercept and slope of the line by least squares. The constancy of E_A and B cannot be judged from the conventional plot of log k *vs.* $1/T$.

In similar fashion the data for the inversion of sucrose[3] at zero hydrochloric acid concentration can be represented by the equation

$$\ln k_{H_3O^+} = 35.33 - (26{,}250/RT) \quad (0\text{–}40°) \qquad (7)$$

The average deviation of the values of $k_{H_3O^+}$ from this equation is 3%, the maximum deviation 6%. Moelwyn-Hughes[16] reports equations of this type for 0.2 molar hydrochloric acid for three temperature ranges.

$$\ln k_{H_3O^+} = 34.19 - (25{,}430/RT) \quad (15.45\text{–}27.26°) \qquad (8A)$$
$$\ln k_{H_3O^+} = 32.55 - (24{,}470/RT) \quad (27.26\text{–}41.00°) \qquad (8B)$$
$$\ln k_{H_3O^+} = 30.12 - (22{,}950/RT) \quad (41.00\text{–}57.10°) \qquad (8C)$$

As already pointed out, the values for E_A and B are lower than the values of Leininger and Kilpatrick.[3] Jackson and Gillis,[17] in a study of the Clerget method, measured the velocity of inversion of sucrose at temperatures from 20 to 90° and conclude that the results are in agreement with the exponential law first proposed by Arrhenius. The exponential equation for 0.01 normal hydrochloric acid may be put in the form

$$\ln k_{H_3O^+} = 34.61 - (25{,}705/RT) \quad (30\text{–}90°) \qquad (9)$$

where B is calculated at 49.85°, E_A calculated by equation (3) for each interval shows no trend with increasing temperature, the average deviation being 330 cal. These results, however, are not in disagreement with those of Leininger and Kilpatrick,[3] who found dE_A/dT to approach zero in the range 30–40°. Moelwyn-Hughes, on the other hand, observed no decrease in dE_A/dT at higher temperatures.

In considering a possible theoretical explanation of the variation of E_A with electrolyte concentration, it becomes necessary to decide whether the rate determining step is bimolecular or unimolecular. Unfortunately the kinetic measurements of this investigation permit no decision. In the following discussion the rate determining mechanism is to be considered unimolecular. This latter view seems the more probable in the light of recent investigations of reaction rates in heavy water.[18]

Hornel and Butler[19] noted that the hydrolysis of acetal proceeded more rapidly in heavy water than in ordinary water. One would logically expect that the substitution of deuterium for hydrogen would slow down the process if the rate determining mechanism involved a proton transfer. The only possible explanation of the effect observed, therefore, seems to be in the consideration of a preëquilibrium.

In a previous discussion[3] the change in E_A with electrolyte concentration was related to a corresponding change in the difference in heat content between the collision complex and the reactants. A comparison of the observed variation of E_A with electrolyte concentration, and the corresponding value of ΔH_2, is given in Table V. ΔH_2 is the heat of dilution of the hydrogen ion between the two solutions. For comparison, the results for the inversion of sucrose are included.

TABLE V

COMPARISON OF ΔH_2 AND ΔE_A

C_2 (moles per liter)	C_1	ΔH_2	(Calories per mole) ΔE_A, 20° Sucrose	ΔE_A, 15° Ethylal
4	3	300	610	...
3	2	300	620	...
2	1	300	630	580
1	0.5	200	...	210
0.5	0	300	...	370
1	0	500	630	580

From these calculations it appears that the change in energy of activation is understandable on the basis of a preëquilibrium.

Summary

1. The velocity constant, $k_{H_3O^+}$, for the hydrolysis of ethylal has been measured from 0 to 40° over a range of hydrochloric acid concentration.

2. Equations for the effect of the electrolyte, hydrochloric acid, on $k_{H_3O^+}$ are given at −0.01, 10.00, 15.00, 20.00, and 25.00°. The effect of electrolyte decreases with increasing temperature.

3. The energy of activation calculated from the Arrhenius equation shows that E_A and B increase with increasing temperature.

4. A decrease in the energy of activation with increasing concentration of the electrolyte, hydrochloric acid, has been noted.

5. A plausible explanation of the effect of electrolyte concentration upon E_A has been given on the basis of a preëquilibrium.

PHILADELPHIA, PENNA. RECEIVED JUNE 15, 1939

(16) Moelwyn-Hughes, *Z. physik. Chem.*, **B26**, 281 (1934).
(17) Jackson and Gillis, *Bur. Standards J. Research*, **16**, 125 (1920).
(18) Bonhoeffer, *Trans. Faraday Soc.*, **34**, 252 (1938).
(19) Hornel and Butler, *J. Chem. Soc.*, 1361 (1936).

[CONTRIBUTION FROM THE GEOPHYSICAL LABORATORY, CARNEGIE INSTITUTION OF WASHINGTON]

Pressure–Volume–Temperature Relations in Solutions. II. The Energy–Volume Coefficients of Aniline, Nitrobenzene, Bromobenzene and Chlorobenzene

BY R. E. GIBSON AND O. H. LOEFFLER

Recent measurements have shown[1] that the compressions of benzene and a number of its monosubstituted derivatives over considerable ranges of pressure may be well represented by the Tait equation[2]

$$k = C \log [(B + P)/(B + P_0)] \qquad (1)$$

where k is the decrease in volume per unit volume when the pressure is raised from P_0 to P kilobars. B, a function of the temperature, is a constant characteristic of the liquid or liquid mixture, and C is a constant independent of temperature and the same for all the derivatives of benzene we have examined. In this paper we shall give data on the thermal expansions of the liquids mentioned in the title, give more complete compressibility data, and discuss some of the thermodynamic quantities derivable from these measurements, including the pressure–temperature coefficient $(\partial P/\partial T)_V$ which, following Hildebrand,[3] we shall denote as γ, and especially the energy–volume coefficient $(\partial E/\partial V)_T$.

Experimental

The compressions of the liquids to various pressures up to 1000 bars were measured at 25, 45, 65 and 85° in vitreous silica piezometers in our latest pressure apparatus,[4] and depend on the same constants for vitreous silica and mercury that were employed in the investigation of benzene.[5]

The specific volumes of the liquids at atmospheric pressure were measured at intervals of 10° between 25 and 85° in a weight dilatometer of the type used by Burlew[6] and by Pesce and Hölemann.[7] The dilatometer, made of vitreous silica, is shown diagrammatically in Fig. 1. Its chief merits are simplicity and ease of manipulation. By following Burlew's design of having the open end of the capillary above the dilatometer, we were able to avoid the complicated thermostat used by Pesce and Hölemann, and by having an opening at the top of the dilatometer bulb we were able to fill it readily with solutions whose composition would have changed if evacuation had been necessary. The opening in the dilatometer was closed by a silica glass plate. The faces of this plate and of the supporting flange were ground flat and polished to an optical quality. No trouble from leakage occurred after we had acquired the technique of bringing the optically flat surfaces together. During an experiment the dilatometer was immersed in a well-stirred oil-bath and the tip of the capillary dipped into mercury contained in a small glass cup. The temperature was controlled "by hand" to ±0.01° and measured with the help of a 5-junction copper–constantan thermoelement[8] calibrated at the inversion point of sodium sulfate decahydrate (32.384°)[9] and at the steam point. The departures from L. H. Adams' table[10] were, respectively, +1 and −1 microvolt on the 5-junction element.

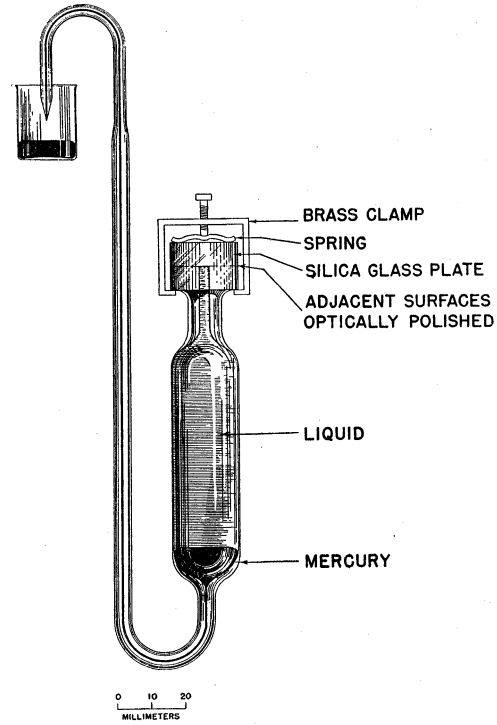

Fig. 1.—Diagrammatic sketch of weight-dilatometer made of vitreous silica for the determination of the thermal expansions of solutions over considerable temperature ranges.

After the temperature had been held constant (within 0.01°) for an adequate time, the small glass cup was

(1) R. E. Gibson and O. H. Loeffler, *J. phys. Chem.*, **43**, 207 (1939).

(2) This equation in the differential form was proposed by Tait in 1881 to fit the compressibility data for water. It was rederived by A. Wohl [*Z. physik. Chem.*, **99**, 234 (1921)], who applied it to some organic liquids, and it was later applied successfully to the existing data on a large number of liquids by H. Carl [*ibid.*, **101**, 238 (1922)], who showed that the constant C did not depend on the temperature.

(3) W. Westwater, H. W. Frantz, and J. H. Hildebrand, *Phys. Rev.*, **31**, 135 (1928).

(4) R. E. Gibson, THIS JOURNAL, **59**, 1521 (1937).

(5) R. E. Gibson and John F. Kincaid, *ibid.*, **60**, 511 (1938).

(6) J. S. Burlew, *ibid.*, to be published.

(7) G. Pesce and P. Hölemann, *Z. Elektrochem.*, **40**, 1–5 (1934).

(8) R. E. Gibson and John F. Kincaid, THIS JOURNAL, **59**, 25 (1937).

(9) H. C. Dickinson and E. F. Mueller, *Bull. Bur. Standards*, **3**, 656 (1907).

(10) "International Critical Tables," Vol. I, p. 58.

removed and weighed. From the mass of mercury deposited in or taken from the cup during a given change of temperature, the thermal expansion was computed. Readings made with rising and with falling temperature indicated no hysteresis in the thermal expansion of the dilatometer itself. Over 10° intervals the thermal expansions were reproducible within 0.05%.

The volume of the dilatometer at different temperatures was determined from experiments with water and mercury confined in it, the volume–temperature data for these substances being taken from the "International Critical Tables."[11] After approximate corrections had been made for the volume of mercury in the emergent stem of the dilatometer, we computed the mean cubic expansion coefficients of vitreous silica in the form $(v_t - v_{25})/v_{25}(t - t_{25})$. At 45, 65, 85 and 95° this expression multiplied by 10^6 had the values: 1.43 (1.34), 1.46 (1.43), 1.57 (1.49), 1.63 (1.51). The figures in parentheses represent values of the same expression interpolated linearly from the mean coefficients of cubic expansion of vitreous silica given by Sosman.[12] The agreement is satisfactory.

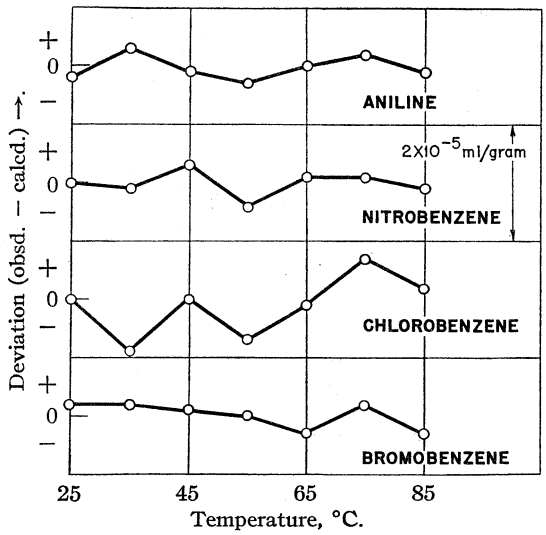

Fig. 2.—Differences between the observed thermal expansions of different liquids and those computed by cubic equations of the type of equation (2).

Aniline, nitrobenzene, chlorobenzene and bromobenzene were obtained from the Eastman Kodak Company. The three first-named were distilled under reduced pressure and the middle fractions were used. The original sample of bromobenzene was fractionated in a small column packed with glass beads. The second and third fractions were used. In Table I the specific volumes at 25° of the samples of liquid[13] we used are compared with apparently reliable ones found by other investigators. We concluded that the agreement indicated that our samples were sufficiently pure for the work in hand.

(11) "International Critical Tables," Vol. II, p. 548; Vol. III, p. 24.

(12) R. B. Sosman, "The Properties of Silica," Chemical Catalog Co., New York, 1927, p. 363.

(13) These specific volumes were determined in the usual way with U-tube pycnometers.

TABLE I

A COMPARISON OF THE SPECIFIC VOLUMES AT 25.00° OF THE LIQUIDS USED IN THIS WORK WITH DATA OF PREVIOUS INVESTIGATORS. THE FIGURES IN PARENTHESES ARE SPECIFIC VOLUMES AT 0°

Authors	Specific volumes (v) Chloro-benzene	Bromo-benzene	Nitro-benzene	Aniline
Gibson and Loeffler	0.90818	0.67162	0.83451	0.98290
	(.88642)	(.65673)	(.81759)	(.96240)
Martin and Collie[a]	.90816	.67158		.98281
Martin and George[b]			.83438	
Timmermans and Martin[c]	.90834	.67193		
	(.88659)	(.65703)		
Albright[d]				.9828
Timmermans and Hennaut-Roland[e]			.83449	.98284
			(.81763)	(.96242)

[a] A. R. Martin and B. Collie, *J. Chem. Soc.*, 2662 (1932). [b] A. R. Martin and C. M. George, *ibid.*, 1413 (1933). [c] J. Timmermans and F. Martin, *J. chim. phys.*, **23**, 733 (1926). [d] P. S. Albright, THIS JOURNAL, **59**, 2099 (1937). [e] J. Timmermans and Mme. Hennaut-Roland, *J. chim. phys.*, **32**, 589 (1935).

It was possible to use the dilatometer for direct measurements of the specific volumes of the liquids at 25°. Weighed amounts of mercury and solutions were introduced into the dilatometer and the whole warmed until the mercury completely filled the capillary. Mercury was then allowed to flow in from one of the weighed cups until the dilatometer and its contents were in equilibrium at 25.00°. From a knowledge of the total amount of mercury in the dilatometer, the mass of the solution—the total volume (determined from similar experiments with water)—it was easily possible to measure the specific volume to 1 in the fifth decimal place. At the end of each run all the mercury in the dilatometer was removed, cleaned and weighed. Such a method possesses distinct advantages when one is dealing with volatile liquids.

Results

The specific volumes were represented as functions of the temperature by cubic equations written for convenience in the form

$$v = v_{55} + a(t - 55) + b(t - 55)^2 + c(t - 55)^3 \quad (2)$$

TABLE II

COEFFICIENTS IN EQUATION 2 REPRESENTING THE SPECIFIC VOLUMES OF DIFFERENT LIQUIDS AS FUNCTIONS OF THE TEMPERATURE AT 1 ATMOSPHERE. THE CONSTANT v_{55} REFERS TO OUR SAMPLE (SEE TABLE I)

Substance	v_{55}	10^4a	10^7b	10^9c
Chlorobenzene	0.935873	9.589	13.229	4.38
Bromobenzene	.690481	6.498	7.602	1.875
Nitrobenzene	.855751	7.274	6.931	1.528
Aniline	1.008746	8.874	9.292	2.083

Our results are presented, therefore, in Table II, which gives the values of v_{55}, and the other coefficients in the equations for the four liquids. The excellent way in which these equations fit our data is shown in Fig. 2 where the differences between the observed specific volumes and those

calculated by equation (2) are plotted at different temperatures. It should be noted that the values of v_{55} refer to the samples we used. The expansion equations may be adapted to give the specific volumes of purer samples merely by adjusting the value of v_{55}. By differentiation of equation (2) we were able to compute the expansion coefficient $(\partial v/\partial T)_P$ at any temperature, and these computed values were used in any subsequent calculations without any reference to the deviations.

To test the validity of these equations for extrapolation beyond the observed range, we computed the specific volumes at 0°, which are given in parentheses in Table I. These were compared with the measured values obtained by Timmermans and his colleagues, also in parentheses.

The results of the compressibility experiments are summarized in Table III, which gives the

TABLE III

CONSTANTS IN THE TAIT EQUATION FOR BENZENE AND SOME OF ITS DERIVATIVES AT DIFFERENT TEMPERATURES. FOR ALL THE LIQUIDS AT ALL THE TEMPERATURES C = 0.2159$_1$

Substance	B in kilobars 25°	45°	65°	85°
Benzene	0.970	0.829	0.701	
Chlorobenzene	1.2491	1.0978	0.9609	0.8350
Bromobenzene	1.4044	1.2473	1.1033	0.9720
Nitrobenzene	1.8652	1.6788	1.5045	1.3416
Aniline	2.0066	1.7983	1.6056	1.4294

values of B in the Tait equation for the different liquids at different temperatures, and in Fig. 3 where the deviations are plotted. It should be noted that although the chlorobenzene results at 500 bars deviated most widely, the values of the compressibilities at 1 atmosphere calculated from the Tait equation agreed within 1% with those obtained from sound velocities by Freyer, Hubbard and Andrews.[14] We already have commented[1] on the fact that the constant C has the value 0.2159$_1$ for all the liquids discussed in this paper and apparently it does not change with temperature.

The Pressure–Temperature Coefficient $(\partial P/\partial T)_V$.—To compute the coefficient $(\partial P/\partial T)_V$ at atmospheric pressure we used the relation

$$\gamma \equiv \left(\frac{\partial P}{\partial T}\right)_V = -\left(\frac{\partial v}{\partial T}\right)_P \Big/ \left(\frac{\partial v}{\partial P}\right)_T = \frac{1}{v_t}\left(\frac{\partial v}{\partial T}\right)_P \times \frac{(B+P)}{0.4343C} \quad (3)$$

where v_t is the specific volume of the liquid at temperature t and one bar pressure,[15] with the values of $(\partial v/\partial T)_P$ at 1 bar computed from equation (2). Two methods were used to compute $(\partial v/\partial T)_P$ at higher pressures. (a) The specific volumes at a given pressure were calculated from the compressions at each temperature, *i. e.*, 25, 45, 65 and 85°, and then expressed as a function of temperature by empirical cubic or quadratic equations—the latter being quite adequate at the higher pressures. From these empirical equations $(\partial v/\partial T)_P$ was computed at each pressure. (b) From a consideration of the Tait equation it readily may be seen that

$$\left(\frac{\partial v}{\partial T}\right)_{P=P} = \left(\frac{\partial v}{\partial T}\right)_{P=P_0}(1-k) + 0.4343Cv_t\frac{P}{B+P}\frac{1}{B}\left(\frac{dB}{dT}\right) \quad (4)$$

This equation enables us to compute the expansion coefficient at any pressure, $(\partial v/\partial T)_{P=P}$, if we know its value at 1 atmosphere (P_0), the constants

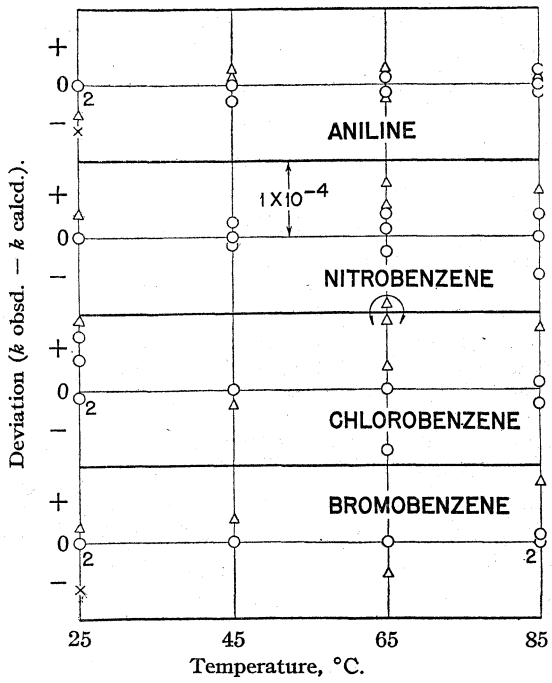

Fig. 3.—Differences between the observed compressions of different liquids and those calculated from the appropriate Tait equation (coefficients in Table III). The open circles ○, triangles △ and crosses × refer to compressions at 1000, 500 and 750 bars, respectively. All the experimental results except those of the compressions to 250 bars are included in the diagram.

(14) E. B. Freyer, J. C. Hubbard and D. H. Andrews, THIS JOURNAL, 51, 759 (1929).

(15) The symbols generally used in this paper are summarized as follows. The specific volume is denoted by v, the molal volume by V, t is the temperature in °C., T the absolute temperature, E is the internal energy, P is the pressure in bars, 10^6 dynes/sq. cm., or kilobars, 10^9 dynes/sq. cm.

in the Tait equation and the change of B with temperature. This last quantity, which was obtained from empirical equations of the form

$$B = B_{25} + a_1(t - 25) + b_1(t - 25)^2 \quad (5)$$

values of a_1 and b_1 being given in Table IV for B

TABLE IV

COEFFICIENTS IN EQUATION 5 REPRESENTING B AS A FUNCTION OF TEMPERATURE

Substance	B_{25}	10^3a_1	10^5b_1
Chlorobenzene	1.2491	− 7.897	1.66
Bromobenzene	1.4044	− 8.179	1.62
Nitrobenzene	1.8652	− 9.616	1.48
Aniline	2.0066	−10.813	1.99

expressed in kilobars, is the weakest part of the whole calculation.[16] We used method (*a*) to compute $(\partial v/\partial T)_{P=P}$ at 1 bar and at 1000 bars, and method (*b*) at 250, 500, 750 and 1000 bars. Except in the case of chlorobenzene both methods gave essentially the same results.

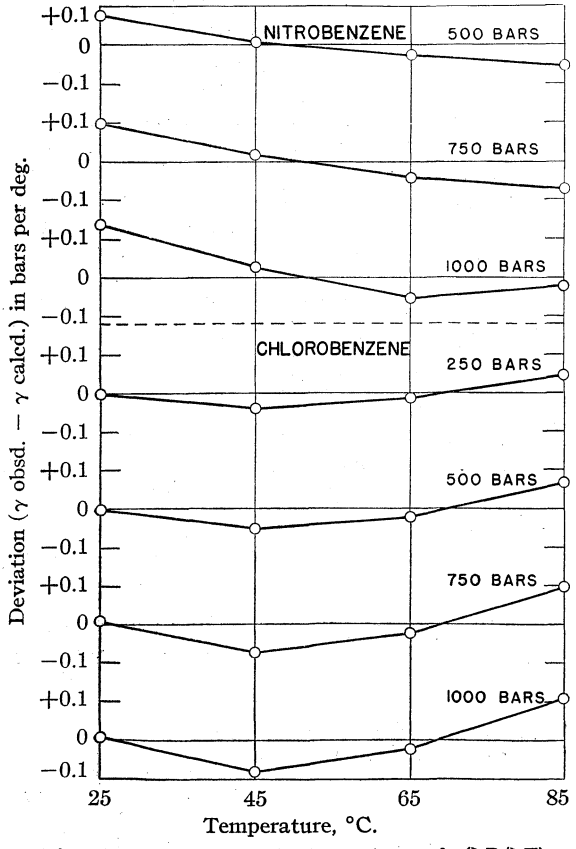

Fig. 4.—Deviations of the values of $(\partial P/\partial T)_V$ computed by the empirical equation (6) from the "observed" values.

(16) Carl[2] proposed the simple equation $B = T_c/T - constant$, where T_c is the critical temperature, to represent B as a function of T. This equation does not fit our data, and even if T_c is taken as an adjustable constant, it does not represent the data over the observed range as well as equation (5).

The coefficient γ increases with pressure at constant temperature, decreases with temperature at constant pressure, and decreases with temperature at constant volume. This last change is not large but is undoubtedly real and very significant. It is in accordance with Bridgman's general conclusions.[17]

We found empirically that the variation of γ over the temperature range at any pressure could be represented most simply by making γ a linear function of $(B + P)$, and, moreover, that the coefficient of $(B + P)$ is independent of pressure. At present no significance is attached to this relation, but to summarize our results in a concise and readily available form we give in Table V the constants l and m in the equation

$$\gamma = l + m(B + P) \quad (6)$$

TABLE V

CONSTANTS IN EQUATION 6 REPRESENTING THE PRESSURE–TEMPERATURE COEFFICIENTS AS FUNCTIONS OF $(B + P)$ (SEE TABLE III)

		The coefficient l				
Substance	m	1 bar	250 bars	500 bars	750 bars	1000 bars
Chlorobenzene	8.17	2.85	1.59	0.28	−1.08	−2.47
Bromobenzene	7.79	2.65	1.42	.16	−1.14	−2.47
Nitrobenzene	7.35	2.73	1.56	.36	−0.86	−2.11
Aniline	7.37	3.43	2.29	1.12	− .75	−1.29

for the different liquids and a deviation curve in Fig. 4 for those cases where the difference between the observed and calculated values is greater than ±0.04 bar/degree. The fact that equation (6) holds so well is interesting because it means that the expansion coefficient is simply related to B by equation (7)

$$\frac{1}{v_t}\left(\frac{\partial v}{\partial T}\right)_P = 0.4343C\left\{\frac{l}{(B + P)} + m\right\} \quad (7)$$

and, as the compressibility of the liquid is given by $0.4343C/(B + P)$, it means further that over a range of temperature at a given pressure the expansion coefficient $(\partial v/\partial T)_P/v_t$ varies approximately linearly with the compressibility. The coefficient l as a function of the pressure decreases somewhat less rapidly than linearly as P increases. It is of interest to note that at constant volume the expansion coefficients $(\partial v/\partial T)_P$ and the compressibilities of all these liquids decrease as the temperature is raised.

The Energy–Volume Coefficient $(\partial E/\partial V)_T$

From the thermodynamic relation $(\partial E/\partial V)_T = T\gamma - P$ we computed the energy–volume coefficients for the various liquids at different temperatures and pressures. The results are given in

(17) P. W. Bridgman, *Rev. Modern Phys.*, **1**, 12 (1935).

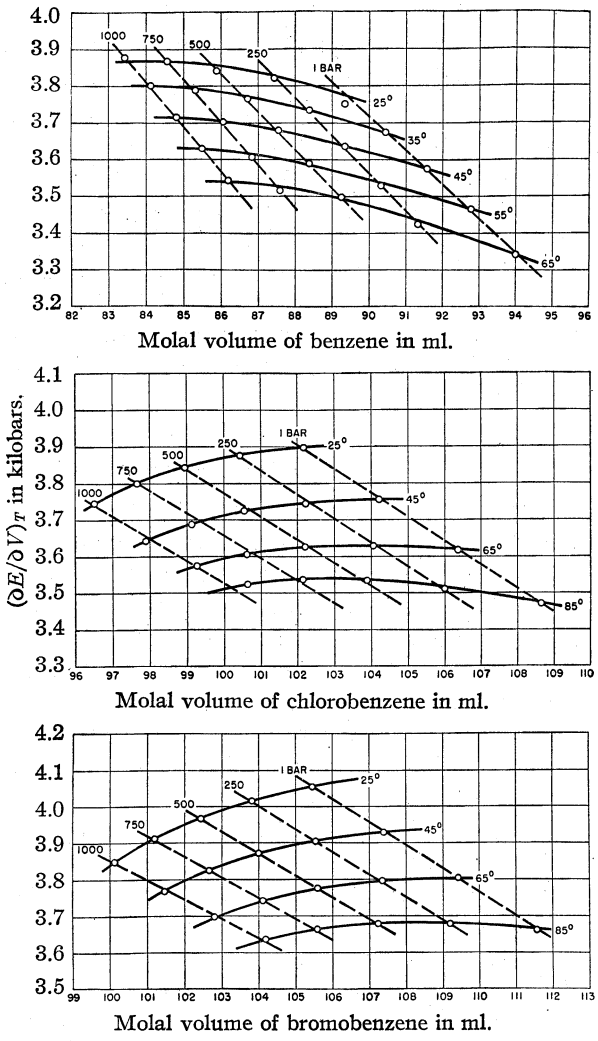

Fig. 5.—The internal pressures $(\partial E/\partial V)_T$ of benzene, chlorobenzene and bromobenzene as functions of the molal volumes at different temperatures.

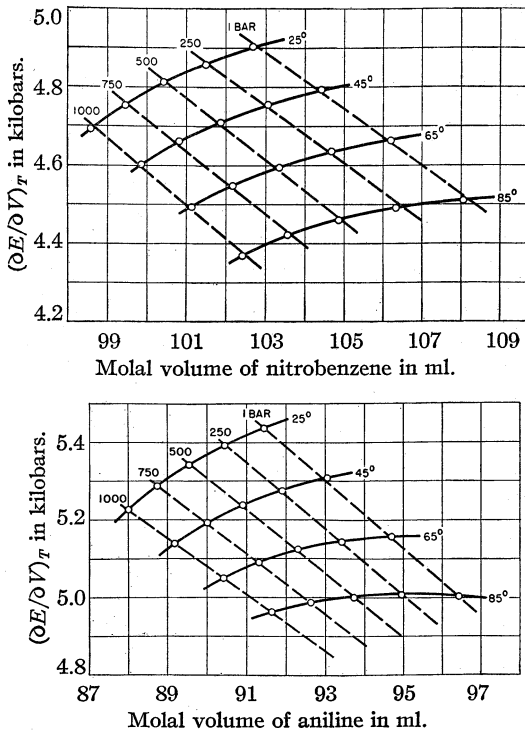

Fig. 6.—The internal pressures $(\partial E/\partial V)_T$ of aniline and nitrobenzene as functions of the molal volumes at different temperatures.

Figs. 5 and 6, where $(\partial E/\partial V)_T$ is plotted against the molal volume of the liquid, the isotherms and isobars being drawn. No special significance is attached to the apparent rectilinearity of the isobars. The results for benzene were computed from the data of Gibson and Kincaid.[5] We wish to call attention to two significant features of the curves in Figs. 5 and 6. (1) Our results cover the interesting but not much studied region in the neighborhood of the pressure and temperature where $(\partial^2 E/\partial V^2) = 0$, a region where such simple formulas as $(\partial E/\partial V)_T = constant/V^n$ certainly do not apply.[18] (2) At constant volume $(\partial E/\partial V)_T$ diminishes as the temperature rises. The coefficient $(\partial E/\partial V)_T$ is positive and quite large for these liquids, ranging from 3.5 to 5.5 kilobars (84 to 131 cal. per cc.) and the changes of $(\partial E/\partial V)_T$ at constant volume illustrated in the diagrams are relatively small, being only about 10% of the total value. We believe, however, that these changes are real. At a given temperature $(\partial E/\partial V)_T$ increases from liquid to liquid in the order benzene, chlorobenzene, bromobenzene, nitrobenzene, aniline. The introduction of the polar group increases $(\partial E/\partial V)_T$ and at the same time makes $(\partial^2 E/\partial V^2)_T$ more positive.

Where classical mechanics are applicable, the total energy of a fluid may be regarded as the sum of a term dependent only on the temperature, $E(T)$, the mean kinetic energy of the molecules at their equilibrium positions together with energy associated with rotation or internal degrees of freedom, and terms giving the potential energy due to intermolecular forces of attraction and repulsion,[19] E_A and E_R. Thus $E = E_R + E_A +$

(18) (a) J. H. Hildebrand, "The Solubility of Non-Electrolytes," Reinhold Publishing Corp., New York, 1936, p. 98; (b) *J. Phys. Chem.*, **43**, 481 (1939); (c) *Phys. Rev.*, **34**, 984 (1929); (d) P. W. Bridgman, ref. 17, p. 11; (e) O. K. Rice, *J. Chem. Phys.*, **5**, 492 (1937).

(19) For expressions giving the energies of fluids containing spherical molecules see J. O. Hirschfelder and W. E. Roseveare, *J. Phys. Chem.*, **43**, 15 (1939), or J. H. Hildebrand, ref. 18a, Chap. V. The authors express the total potential energy in terms of the potential energies of pairs of molecules and the distribution function for the molecules in the liquid. A fundamental treatment of the subject

$E(T)$ and $(\partial E/\partial V)_T = (\partial E_R/\partial V)_T + (\partial E_A/\partial V)_T$. If, following common usage,[20] we call $(\partial E/\partial V)_T$ the internal pressure P_i, we may call $(\partial E_R/\partial V)_T$ and $(\partial E_A/\partial V)_T$ the repulsive and attractive pressures P_R and P_A, respectively. It will be noted that P_R is negative and P_A is positive. In the region we are studying $-(\partial P_R/\partial V)_T$ increases more rapidly than $(\partial P_A/\partial V)_T$ as the volume is diminished along an isotherm and at the maximum where the observed $(\partial P_i/\partial V)_T = 0$, $(\partial P_A/\partial V)_T = -(\partial P_R/\partial V)_T$; at lower volumes further increase of repulsive pressure causes P_i to fall as the volume decreases.[21]

Our second observation that $(\partial E/\partial V)_T$ diminishes with temperature at constant volume is equivalent to the statement (which is obvious from Figs. 5 and 6) that $(\partial E/\partial V)_T$ increases more rapidly as the volume is diminished along an isobar than along an isotherm. We may explain this result by the hypothesis that increase of temperature increases the randomness of the distribution of the molecules in the liquid and that this increase of randomness increases the repulsive internal pressure. Lennard-Jones and Devonshire[22] have developed quantitatively the idea that when a solid melts the disorder introduced increases the free energy and causes an excess repulsive pressure. It is now generally assumed that the molecules are not distributed at random in a liquid, especially near its melting point, but that there persists an order (short range at least) in the arrangement of the molecules,[23] which is a function of pressure and temperature. As the temperature is raised the arrangement of the molecules in the liquid becomes more random.[23] If this happens when the volume of the liquid is kept constant, an additional disorder term is added to the repulsive pressure as in the melting phenomenon discussed by Lennard-Jones and Devonshire. The forces which determine the attractive pressure vary much less rapidly with distance than do those determining the repulsive pressures. It seems plausible to assume, therefore, that at constant volume the attractive pressure is unchanged by changes in the molecular distribution function[24] and that it is the increase in repulsive pressure which lowers the observed value of $(\partial E/\partial V)_T$. In other words, a simple consequence of the decrease of $(\partial E/\partial V)_T$ with temperature at constant volume is that $(\partial^2 P/\partial T^2)_V$ is negative or that the P–T curves at constant volume are concave to the temperature axis and that $T(\partial P/\partial T)_V$ rises less rapidly with temperature at constant volume than does the external pressure. This abnormal increase in the external pressure is a result of the increase in repulsive pressure due to increase of randomness.[25]

The Attractive Internal Pressure

From our previous work with the Tait equation[1,5] we have adopted the working hypothesis that $(B + P)$ at any pressure represents the difference between the thermal and attractive pressures or is equal to the repulsive pressure. It might be expected, then, that the increase of $(B + P)_V$ with temperature should just be equal to the decrease of $(\partial E/\partial V)_T$ with temperature at constant volume, and calculations show that this is approximately true in all the liquids we have studied. It will be seen at once that this result is expressed by the statement that $(T\gamma + B)$, which represents the attractive pressure P_A, is the same function of the volume for all temperatures, and, indeed, we have found that we may express $(T\gamma + B)$ in the form $a'V^{-n}$ over the whole range of pressures and temperatures we have investigated. In Fig. 7 we have plotted log $(T\gamma + B)$ against log V, the slopes of the curves give $-n$ and the intercepts on the ordinates give log a'. It will be seen that the

has been given by J. G. Kirkwood [*J. Chem. Phys.*, **3**, 300 (1935)]. A complete formula for a mixed fluid in which the relative orientations of the molecules are taken into account is given by G. Scatchard, *Trans. Faraday Soc.*, **33**, 160 (1937).

(20) T. W. Richards, THIS JOURNAL, **46**, 1419 (1924).

(21) For discussions of the complete $(\partial E/\partial V)_T$–$V$–curves for liquids, see J. H. Hildebrand, ref. 18a, Chap. V; O. K. Rice, *J. Chem. Phys.*, **5**, 492 (1937).

(22) J. E. Lennard-Jones and A. F. Devonshire, *Proc. Roy. Soc.* (London), **A169**, 317 (1939).

(23) J. D. Bernal, *Trans. Faraday Soc.*, **33**, 27 (1937).

(24) Changes in the relative orientation of the molecules may produce changes in the attractive potential energy at constant volume. This will be discussed later.

(25) That the repulsive potential energy of a liquid increases with temperature at constant volume may also be seen from the following considerations. It has been found convenient and, indeed, necessary in the explanation of many phenomena in fluids to assume that the repulsive energy of a pair of molecules rises rapidly as the molecules approach one another but that the slopes of the repulsive energy–distance curves are not infinite as would be the case for hard spheres [P. W. Bridgman, ref. 17, p. 10; J. Hirschfelder, D. Stevenson and H. Eyring, *J. Chem. Phys.*, **5**, 896 (1937)]. This is all that is implied by the brief but loose statement that it is assumed that the molecules are compressible. Hence, as their kinetic energy increases, the distance of closest approach of the molecules decreases. Curves giving the distribution functions of the atoms in liquid potassium [C. D. Thomas and N. S. Gingrich, *J. Chem. Phys.*, **6**, 411 (1938)] and sodium [F. H. Trimble and N. S. Gingrich, *Phys. Rev.*, **53**, 278 (1938)] show that the probability of finding atoms at very short distances from a given atom increases as the temperature increases. As the repulsive potential energy varies exponentially with the distance between molecules, it must rise considerably as the probability of finding molecules at short distances increases. It is not yet clear, however, how this temperature effect is modified by volume changes.

points for all temperatures lie substantially on the same straight line.[26]

It will be seen that n is approximately the same for aniline, nitrobenzene, bromobenzene and chlorobenzene, the slopes of the curves being -2.70, -2.69, -2.78 and -2.78, respectively. These give an average of -2.74 so that we may write

$$P_A = (T\gamma + B) = a'V^{-2.74} \qquad (8)$$

The values of $10^{-6}\ a'$ for P in kilobars and V in cc. per mole are as follows: chlorobenzene, 1.621; bromobenzene, 1.870; nitrobenzene, 2.163; aniline, 1.730. The curve for benzene, which is not a straight line, indicates that n diminishes as the volume increases. Over most of the range we have studied, however, P_A for benzene is given by $3.38 \times 10^6/V^3$, indicating that at low volumes the attractive potential energy is proportional to V^{-2}, which is in qualitative agreement with the theory of van der Waals forces.[27] In the polar derivatives the longer-range forces may be responsible for making the exponent of V less than that of benzene. It is certain that the linear relation between log $(T\gamma + B)$ and log V does not hold over a large range of volume for any of these liquids. At high volumes the attractive pressure in fluids is proportional to $1/V^2$ no matter what the law of force is.[28] The quantity $E_A = -V(T\gamma + B)/1.74$ should be larger than the heat of evaporation of the liquid, as it neglects entirely the repulsive potential energy. Actually E_A so computed is lower than the values of the heat of evaporation given in the literature, although these are not concordant,[29] indicating that P_A decreases less rapidly at the higher volumes than it would if equation (8) held over the whole range.

In the study of benzene[5] it was pointed out that $(B + P)_V$ was a linear function of the temperature

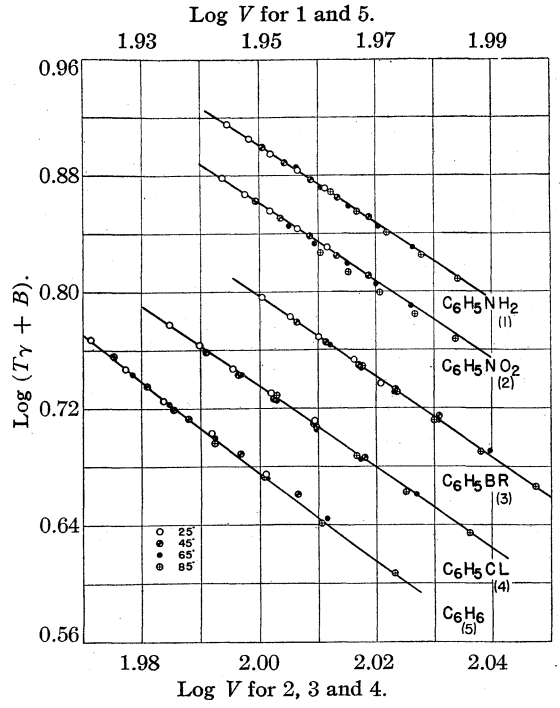

Fig. 7.—The logarithm of the attractive internal pressures of different liquids as functions of the logarithm of the molal volume. Note the points at different temperatures all lie on one curve for each liquid.

and that the extrapolated values of $(B + P)_V$ at 0°K. were approximately inversely proportional to the square of the volume. Over the range we have investigated, $(B + P)_V$ is also a linear function of T for nitrobenzene, but the extrapolated values at 0°K. increase as the volume increases. It will be noticed that the slopes of the $(\partial E/\partial V)_T - V$ curves for these two substances are opposite in sign. For the other liquids $(B + P)_V$ is not a linear function of the temperature, the slope decreasing as the temperature is raised. From the foregoing argument it will be seen that where $(B + P)_V$ increases linearly with T, $(\partial E/\partial V)_T$ decreases linearly with T at constant volume. The linear relation we found holds because over a relatively short range of temperature the "disorder" part of the repulsive pressure is proportional to the thermal energy of the molecules.

A consideration of Figs. 5 and 6 suggests that, for a given change in volume, variation of temperature at constant pressure produces a larger change in the distribution of molecules in a liquid than does the corresponding variation of pressure at constant temperature. The coefficient $(\partial P/\partial T)$ along the melting curve might be regarded as

(26) In this work we are dealing with molecules that are not spherically symmetrical and are also polar. Doubtless changes in the orientation of the molecules occur as the temperature is changed, but our results indicate that changes in P_A arising from changes in orientation make a contribution to the change of $(\partial E/\partial V)_T$ with temperature at constant volume which is small compared with the contribution due to the distribution of the molecules. We find, however, that at constant volume $(T\gamma + B)$ decreases slightly with temperature, indicating a possible decrease of P_A due to change in the distribution function, but the difference is so close to the over-all uncertainty of our calculations that further discussion of it is undesirable. For instance, in the extreme case of nitrobenzene $(\partial E/\partial V)_T$ for $v = 0.8345$ decreases by 525 bars from 25 to 85°, whereas under the same conditions $(T\gamma + B)_V$ decreases by 104 bars. With other liquids the total change in $(T\gamma + B)_V$ over the same temperature range was less than 50 bars.

(27) See F. London, *Trans. Faraday Soc.*, **33**, 8 (1937).

(28) See J. A. Beattie and Oscar C. Bridgeman, *Proc. Am. Acad. Arts Sci.*, **63**, 239 (1928).

(29) See table by J. H. Hildebrand, ref. 18a, p. 104; G. Scatchard, *Chem. Rev.*, **8**, 329 (1931).

a measure of the change in pressure which must be applied to counteract the change in randomness produced by a given rise of temperature. Here we may suppose that the distribution of the molecules is constant, being that existing in the crystal. We have recently measured $(\partial P/\partial T)_V$ for solid benzene; it is approximately 23 bars per degree. The coefficient $(\partial P/\partial T)$ along the melting curve is approximately 36 bars per degree.[30] For a given rise of temperature, the pressure change necessary to keep constant the distribution in the solid is, according to this argument, more than 1.5 times the pressure change required to keep constant the volume of the solid.

Summary

From measurements of the specific volumes at 25°, the thermal expansions and the compressions of aniline, nitrobenzene, chlorobenzene and bromobenzene, we have been able to compile a table of the volumes of these liquids at any temperature and pressure in the region 25 to 85° and 1 to 1000 bars. Suitable equations for computing the first and second derivatives also are given. From these data the coefficients $(\partial P/\partial T)_V$ and $(\partial E/\partial V)_T$ were computed. Our data enable us to discuss the variation of these and other thermodynamic functions with temperature at constant volume. Both $(\partial P/\partial T)_V$ and $(\partial E/\partial V)_T$ decrease as the temperature increases at constant volume. It is suggested that this effect is due to an increase in the repulsive internal pressure which follows from an increased randomness in the distribution of the molecules in the liquids at higher temperatures. The quantity $(B + P)$ in the Tait equation for the compressibility of the liquids is identified empirically as the repulsive internal pressure. It increases with temperature at constant volume and, when it is combined with the total internal pressure, an estimate of the attractive pressure is made. The attractive pressure so computed is expressible as $P_A = a'V^{-n}$ and is dependent only on the volume within the limits of our experimental error. The exponent n has the value 3 for benzene and 2.74 for the polar liquids.

A weight dilatometer of vitreous silica suitable for the rapid and precise measurements of the thermal expansions of solutions is described.

(30) R. E. Gibson, THIS JOURNAL, **56**, 5 (1934); L. Deffet, *Bull. soc. chim. Belg.*, **44**, 71 (1935).

WASHINGTON, D. C. RECEIVED JUNE 15, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF DUKE UNIVERSITY]

A Lead–Iodine Voltaic Cell

BY W. C. VOSBURGH AND VERNON H. DIBELER

Among the cells made by Gerke[1] the cell

$$Pb(Hg)/PbI_2, Pb(ClO_4)_2/Pb(ClO_4)_2, PbI_2, I_2/(Pt)$$

is outstanding in that its temperature coefficient $(\Delta E/\Delta T)$ is as small as that of the saturated Weston cell and the two cells that he made agreed unusually well. These results suggested that the cell might have some value as a standard cell. A number of cells were made and they agreed unusually well with Gerke's cells. They were constant in electromotive force as long as observed and were superior to the Weston cell with respect to recovery from polarization.

The cells were set up in vessels of the type used by Vosburgh and Craig.[2] Lead amalgam, about 5% lead, was prepared electrolytically. In some of the cells a more dilute amalgam was used by mistake. The iodine was resublimed. Lead iodide and lead chloride were precipitated from dilute solutions. Lead nitrate was recrystallized. Lead perchlorate solution was prepared by the addition of an excess of lead oxide to a perchloric acid solution, followed by filtration and the addition of enough perchloric acid to give a clear solution.

In the construction of the iodine electrodes, equal quantities of dry lead iodide and iodine were ground, mixed thoroughly and placed in one leg of the cell vessel. Lead perchlorate solution was then introduced to a depth of several centimeters and then lead iodide was allowed to fall through the solution to form a layer about one centimeter thick above the iodine–iodide mixture. A platinum electrode sealed into the end of a glass tube was then introduced carefully into the mixture. In some of the cells a platinum wire in the form of a helix was used for the electrode, but usually the electrode was of platinum foil about 1 sq. cm. in total surface area. The area of the amalgam electrode was about 1 sq. cm. also.

The cells may be divided into three groups. In the first group, Cells 3–16, the materials were not free from oxygen, and air was not excluded. Six of these cells agreed well with each other. Four others were rejected

(1) Gerke, THIS JOURNAL, **44**, 1684 (1922).
(2) Vosburgh and Craig, *ibid.*, **51**, 2012 (1929).

because of accidents and four because of disagreement. The disagreement of the last group may be ascribed at least partly to inexperience. In the second group, Cells 17–24, there were no cells rejected. In the construction of these cells the solution was freed from dissolved air and vacuum-nitrogen technique was used for the exclusion of oxygen from the vessel and other materials. In Cells 21 and 22 a saturated lead nitrate solution with excess of solid lead nitrate was used for the electrolyte instead of a lead perchlorate solution, and in Cells 23 and 24 saturated lead chloride solution with excess of solid was used. No significant dependence of the electromotive force on the nature or concentration of the electrolyte was observed. Cells 21–22 and 23–24 became variable when it was attempted to change their temperatures, but they were constant at 25° for over a week and during that time agreed with the perchlorate cells.

Most of the above cells had amalgams that were more dilute than intended. While satisfactory at temperatures below 30°, measurements at higher temperatures showed that the amalgams became unsaturated. Therefore Cells 25–31 were made, and more care was taken that the amalgam was 5% lead. Vacuum technique was not used in their construction, but no cells were rejected. The electromotive forces of the six cells agreed within 0.1 mv. The electromotive forces of all of the satisfactory cells over a period of time are shown in Table I. The average electromotive force agrees well with the value of 0.89363 at 25° found by Gerke.

TABLE I

CONSTANCY OF ELECTROMOTIVE FORCE

Cells	Electrolyte M	E − 893.00 mv., 25° 1–2 wks.	1 mo.	3	5–6	10
3	0.2	0.54	0.58	0.60	0.59	0.60
6, 7, 13	0.5	.58	.60	.59	.57	.58
15, 16	1.0	.41	.59	.59	.58	.59
17–20	0.5	.58	.58	..	.59	
21, 22	Satd.[a]	.61	..	..	..	
23, 24	Satd.[b]	.51	..	..	..	
25–31	1.0	.60	..	.65	.61[c]	

[a] Lead nitrate solution. [b] Lead chloride solution. [c] Calculated from measurement at 28.5°.

Two series of measurements were made at temperatures other than 25°. Cells 3, 14–16 and 18–20 were measured at 20, 10, 15, 20 and again at 25°, but some of the cells disagreed at 30° and others at higher temperatures, presumably because the amalgams became unsaturated. Cells 25–31 were later measured at 40, 35, 30, 25, 20 and again at 25°. The results are given in Table II. The average change in electromotive force with temperature was 0.000042 v. per degree, which is the value found by Gerke.

TABLE II

CHANGE IN ELECTROMOTIVE FORCE WITH TEMPERATURE

Cells	$E_{25} - E_t$, mv. 10°	15°	20°	30°	35°	40°
3–20	−0.65	−0.43	−0.22	..	..	..
25–31	....	....	− .20	0.20	0.42	0.65

It was found by Niederhauser and Hulett[3] that practically all of the polarization of the Weston cell takes place in the mercury limb. Since no mercury salt is present in the lead–iodine cell, it was of interest to test its polarization.

Cell no. 7 was discharged through a resistance of about 150,000 ohms (current 5.3 microamperes) for thirty minutes and the potential drop across the resistance was measured periodically. After fifteen minutes a steady potential difference of 0.89100 v. was attained, which was 2.58 mv. less than the electromotive force of the cell. On breaking the circuit, the electromotive force returned to its original value in twenty minutes. This is typical of the results for several cells discharged through various resistances from 0.1 to 2.5 megohms. Cell 3, discharged for thirty minutes through 9000 ohms, recovered to within 0.01 mv. of its original electromotive force in thirty minutes.

After charging one of the lead–iodine cells for forty-five minutes with a current of 5 microamperes, the cell recovered its original electromotive force in twenty minutes. Measured immediately after the charging was stopped, the electromotive force was 0.3 mv. too high. A normal Weston cell containing a small concentration of acid in the electrolyte when treated in the same manner was still 0.34 mv. too high in electromotive force at the end of thirty minutes. These experiments were repeated on other cells and are believed to be typical.

One cell of larger capacity with electrode areas of about 54 sq. cm. was constructed. The electrode systems were separated by a porous cup. It came to good agreement in electromotive force with the other cells, but later disagreed, presumably because of unequal evaporation of the electrolyte. On discharging through 4000 ohms a constant potential drop across the resistance was attained in twenty minutes and was maintained until measurements were discontinued ten minutes later.

Summary

The cell $Pb(Hg)/PbI_2$, $PbClO_4(m)$,/$PbClO_4(m)$, PbI_2, I_2/(Pt) has been found to be easily reproducible and to remain constant in electromotive force over periods of at least several months. It recovers its original electromotive force after charge or discharge more quickly than the Weston cell.

DURHAM, N. C. RECEIVED JULY 21, 1939

(3) Niederhauser and Hulett, THIS JOURNAL, **51**, 2332 (1929).

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF THE UNIVERSAL OIL PRODUCTS COMPANY AT ARMOUR INSTITUTE OF TECHNOLOGY]

Aromatization of *n*-Octane and *n*-Decane in the Presence of Nickel–Alumina Catalyst

BY V. I. KOMAREWSKY AND C. H. RIESZ

In a previous article[1] the alkylation of aromatic and naphthenic hydrocarbons with olefin in the presence of nickel–alumina catalyst was described. In the attempt to perform the same reaction with paraffin hydrocarbons it was necessary to study first the behavior of paraffins alone toward the same catalyst. It was found that the paraffin hydrocarbons *n*-octane and *n*-decane undergo dehydrogenation, accompanied by cyclization, the final products being aromatic hydrocarbons. Thus, *n*-octane at 300° yielded a liquid stable toward permanganate. From this liquid, 10% (by weight of *n*-octane charged) of toluene was isolated. The gases from the reaction contained hydrogen and methane (no olefins). These facts show that *n*-octane undergoes dehydrogenation and aromatization to ethylbenzene and the latter decomposes to toluene and methane, as it was shown in another paper.[2] Similarly *n*-decane at 350° over the same catalyst gave a liquid from which 2% toluene was isolated, together with a higher boiling fraction which was not identified. In the reaction gases hydrogen and methane were found. These facts show that *n*-decane also undergoes dehydrogenation and cyclization with splitting of the aromatic formed to toluene and methane. In addition iso-paraffins (1.6%) were found in the aromatic-free product by the antimony pentachloride method.[3]

Comparing these results with the work of Kazansky and Plate[4] and Moldavsky and Kamusher,[5] a definite difference in the action of nickel–alumina catalyst must be noticed. Thus, the platinum charcoal used by Kazansky and Plate produced from *n*-octane at 300° a mixture of ethylbenzene and *m*-xylene. Chromium oxide catalyst used by Moldavsky and Kamusher produced at 460° the same aromatic hydrocarbons and olefins. Nickel–alumina produced toluene.

Only traces of aromatization were observed with isoöctane and diisoamyl over nickel–alumina catalyst at 300–350° and, in addition, olefins were formed.

(1) Komarewsky, THIS JOURNAL, **59**, 2715 (1937).
(2) Ipatieff and Komarewsky, *ibid.*, **58**, 922 (1936).
(3) Moldavsky, *Compt. rend.* (U. S. S. R.), **1**, 507 (1935).
(4) Kazansky and Plate, *Ber.*, **69**, 1862 (1936).
(5) Moldavsky and Kamusher, *Compt. rend. Acad. Sci. U. S. S. R.*, **1**, 9 (1936).

Experimental Part

Apparatus and Procedure.—The paraffin hydrocarbons were passed at the rate of 3–4 cc. per hour through a glass tube of 14 mm. inside diameter filled with 40 g. of 8–10 mesh catalyst. The slow stream of nitrogen simultaneously was passed through the tube. The tube was placed in a horizontal electric furnace. The liquid products were fractionated by a micro-Podbielniak column The gases were analyzed by the Göckel method.

Material.—*n*-Octane, *n*-decane, and diisoamyl were synthesized by the Wurtz method from *n*-butyl bromide and *n*-amyl bromide, respectively. *n*-Octane, b. p. 124.5–125°, $n^{25}D$ 1.3950; *n*-decane, b. p. 169–170.5°, $n^{25}D$ 1.4098, diisoamyl, b. p. 156–158°, $n^{25}D$ 1.4067. Isoöctane was Röhm and Haas Co. product, b. p. 99–100°, $n^{25}D$ 1.3866. Nickel–alumina catalyst was prepared according to the procedure of Zelinsky and Komarewsky.[6]

Aromatization

***n*-Octane.**—At 300°, 50.0 g. of *n*-octane yielded 48.5 g. of liquid, $n^{25}D$ 1.4130, stable toward permanganate. Distillation gave fractions of the following weight, boiling point and refractive index: (1) 5 g., 110–115°, $n^{25}D$ 1.4750; (2) 2.2 g., 115–123°, $n^{25}D$ 1.4050; (3) 37.0 g., 123–126°, $n^{25}D$ 1.3950; (bottoms) 1.0 g., no boiling point, $n^{25}D$ 1.4120. Nitration of the first fraction gave crystals of 2,4-dinitrotoluene, m. p. 70°.

Anal. Calcd. for $C_6H_5 \cdot CH_3$: C, 91.3; H, 8.7. Found: C, 91.1; H, 8.9.

***n*-Decane.**—At 350°, 39.9 g. of *n*-decane yielded after two passages 25.6 g. of a liquid, $n^{25}D$ 1.4122, stable toward permanganate. Distillation of 22.9 g. gave fractions of the following weight, boiling point and refractive index: (1) 0.5 g., 105–120°, $n^{25}D$ 1.4790; (2) 0.5 g., 120–165°, $n^{25}D$ 1.4150; (3) 2.2 g., 165–169°, $n^{25}D$ 1.4105; (4) 14.5 g., 169–170.5°, $n^{25}D$ 1.4108; (5) 3.2 g., 170.5–172°, $n^{25}D$ 1.4125; (bottoms) 2.0 g., no boiling point, $n^{25}D$ 1.4590. Nitration of the first fraction gave crystals of 2,4-dinitrotoluene, m. p. 70°. The gas from the reaction contained 25% hydrogen and 75% paraffin (index 1.0). 9.4% of aromatics were found on the total product with fuming sulfuric acid. Distillation of 16.9 g. of the aromatic-free product gave fractions of the following weight, boiling point and refractive index: (1) 3.7 g., 165–169°, $n^{25}D$ 1.4085; (2) 12.8 g., 169–170.5°, $n^{25}D$ 1.4098; (bottoms) 0.4 g., no boiling point, $n^{25}D$ 1.4100. The boiling range of fraction (1) is lower than that of the original material. Since this fraction does not contain any olefins or aromatics, iso-paraffins must be present. By the antimony pentachloride method[3] 11.6% of isoparaffins was found in fraction (1).

(6) Zelinsky and Komarewsky, *Ber.*, **57**, 667 (1924).

Isoöctane produced at 350° a liquid with $n^{25}D$ 1.3880, traces of reaction with nitrating mixture.

Diisoamyl produced at 300, 325 and 350° a liquid with $n^{25}D$ 1.4080, 1.4090 and 1.4090, respectively. The combined product contained 9.7% of olefins and traces of aromatics.

Summary

In the presence of nickel–alumina catalyst, the normal paraffins *n*-octane and *n*-decane undergo dehydrogenation accompanied by cyclization to aromatic hydrocarbons. A splitting forming toluene and methane also takes place which is not observed with catalysts of platinum charcoal or chromium oxide. Isomerization of the normal paraffins also was noted.

CHICAGO, ILLINOIS RECEIVED JUNE 24, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF THE UNIVERSAL OIL PRODUCTS COMPANY AT ARMOUR INSTITUTE OF TECHNOLOGY]

Aromatization of Fatty Alcohols

BY V. I. KOMAREWSKY, C. H. RIESZ AND GEORGE THODOS

The role of various substituents of mixed catalysts in heterogeneous catalysis such as promoter and carrier (support) action has assumed prime importance in our present knowledge of the subject. While in many cases it may be difficult to distinguish between catalyst, promoter, and carrier phenomena, the fact remains that only one reaction is catalyzed in one specific direction. There are, however, mixed catalysts which accomplish two or more different reactions, due to the action of each component of the mixed catalyst working in its own specific direction. It is proposed to call such catalysts "complex-action" catalysts.

In such cases the resulting reaction is a series of parallel or consecutive steps leading to the formation of desired product.

Thus, by combining nickel oxide and alumina, it was possible to obtain directly from camphor, isocamphane by simultaneous reduction, dehydration and hydrogenation.[1,2] By combining a polymerizing and hydrogenating catalyst, isooctane was obtained in one step from isobutylene and hydrogen (hydropolymerization).[3,4] The dehydropolymerization of ethylene[5] represents another example of these types of reactions.

In the development of these ideas a simultaneous combined reaction of dehydration and dehydrogenation of aliphatic alcohols was carried out. The dehydration of fatty alcohols results in the formation of olefin hydrocarbons which by further dehydrogenation can produce more unsaturated material such as diolefins and acetylenes. It was of particular interest to perform this type of simultaneous reaction with the fatty alcohols containing a chain of six or more carbon atoms in order to see whether a more complete dehydrogenation of this chain could take place causing cyclization and formation of aromatic hydrocarbons. For these reactions a mixed dehydrating–dehydrocyclizing catalyst was required.

In this work an alumina-chromium oxide catalyst was used; alumina was the dehydrating and chromium oxide the dehydrogenating and cyclizing catalyst. The simultaneous dehydration and dehydrocyclization of *n*-hexyl, *n*-heptyl and *n*-octyl alcohols, and di-*n*-propylcarbinol was performed. As expected it was found that the simultaneous reaction took place with the production of aromatic hydrocarbons according to the scheme

$$C_nH_{(2n+1)}OH \longrightarrow C_nH_{2n} + H_2O \longrightarrow C_nH_{2n-6} + 3H_2$$

In addition to this reaction, dehydrogenation of the alcohols to aldehydes also took place as shown by the presence of carbon dioxide and carbon monoxide in the reaction gases.

For the fatty alcohols containing six and seven carbon atoms, cyclization of the olefin produced gave the corresponding aromatic hydrocarbon. When *n*-octyl alcohol was subjected to this reaction, a more complex reaction product was obtained. As expected, the eight-carbon chain cyclized to *o*-xylene and ethylbenzene. In addition, however, *m*- and *p*-xylene and toluene were identified. Thus, with this alcohol it is evident that isomerization occurs and *m*- and *p*-xylene are produced by the migration of a methyl

(1) Ipatieff, *Ber.*, **45**, 3205 (1912).
(2) Ipatieff and Matov, *J. Russ. Phys.-Chem. Soc.*, **44**, 1695 (1912).
(3) Ipatieff and Komarewsky, THIS JOURNAL, **59**, 720 (1937).
(4) Ipatieff and Komarewsky, *Ind. Eng. Chem.*, **29**, 958 (1937).
(5) Komarewsky and Balai, *ibid.*, **30**, 1051 (1938).

TABLE I

Expt.	Alcohol charged	G.	Temp., °C.	Recov., g.	$n^{25}D$	Liquid product: $n^{25}D$ without bottoms	Aromatics % by weight By $n^{25}D$	Aromatics % by weight By H	Aromatics found	Aromatics identified as	M. p., °C.	Reaction gases: Total evolved, cc.	Gas analysis H_2	Gas analysis CO	Gas analysis CO_2	Total olefins	Paraffins	Paraffin index
1	*n*-Heptyl	16.3	450	11.4	1.4065	1.4035	7.8	..	Toluene	2,4-Dinitrotoluene	70	....	..	...	..	..	..	...
2	*n*-Heptyl	30.2	500	14.6	1.4660	1.4554	58.1	66.0	Toluene	2,4-Dinitrotoluene	70	14,420	67.0	3.8	7.1	5.0	17.1	1.8
3	Di-*n*-propyl carbinol	30.9	468	21.85	1.4143	1.4068	7.2	6.7	Toluene	2,4-Dinitrotoluene	70	4,580	48.8	2.6	11.1	22.0	15.5	1.7
4	Di-*n*-propyl carbinol	26.0	480	16.3	1.4192	1.4136	12.5	13.0	Toluene	2,4-Dinitrotoluene	70	5,520	51.1	2.9	10.0	20.6	15.4	1.8
5	*n*-Hexyl	26.1	467	18.3	1.4065	1.4022	7.5	7.6	Benzene	*m*-Dinitrobenzene	89	3,480	62.1	2.1	9.2	15.3	11.3	1.8
6	*n*-Hexyl	17.8	500	10.4	1.4405	1.4377	38.0	37.7	Benzene	*m*-Dinitrobenzene	89	7,140	58.2	2.2	5.4	18.3	15.9	1.7
7	*n*-Octyl	39.0	475	17.5	1.4533	....	..	47.2	Toluene—3%	2,4-Dinitrotoluene	70	12,000	63.5	6.4	6.8	11.8	11.5	3.2
									Ethylbenzene—4.5%	Benzoic acid	121							
									*o-Xylene } —7%	o-Phthalic acid anhydride	127							
									m-Xylene }	Dimethyl ester of meta-phthalic acid	64							
									p-Xylene }									
									Higher boiling aromatics—32.7%	Dimethyl ester of terephthalic acid	137–138							

* Traces of *m*-xylene.

group. Toluene probably is formed by splitting off of a methyl group. Besides, higher boiling unidentified aromatics were found in the reaction product.

The dehydration of alcohols over alumina catalyst takes place with measurable velocities even at 200–300°; however, the dehydrogenation of the olefin produced requires higher temperatures. Therefore the experiments were conducted at 450° and higher. At these temperatures the dehydration takes place with non-measurable speed so that the total reaction might be considered kinetically as being a simple monomolecular (found experimentally) dehydrogenation of olefin hydrocarbons. Due to excellent constancy and reproducibility of the reaction speed an attempt was made to evaluate the energy of activation.

Experimental Part

Apparatus and Procedure.—The alcohols were passed at a rate of 7–10 cc. per hour through a 14-mm. inside diameter glass tube filled with 50 g. of 8–10 mesh catalyst, in a slow stream of nitrogen. The tube was contained in a horizontal electric furnace. The liquid products were condensed by means of a water condenser and an ice trap.

Alcohols.—*n*-Hexyl alcohol, b. p. 153–156°, $n^{25}D$ 1.4170; *n*-heptyl alcohol, b. p. 172–176°, $n^{25}D$ 1.4222; *n*-octyl alcohol, b. p. 196.0–197.0°, $n^{25}D$ 1.4295; di-*n*-propylcarbinol, b. p. 151–154°, $n^{25}D$ 1.4159.

Catalyst.—The catalyst was prepared by the simultaneous precipitation of chromium and aluminum hydroxides from an alkaline solution of aluminate and chromite by nitric acid. The precipitate was washed anion free, dried and reduced at 450° in a stream of hydrogen. The chromium oxide content was 25%.

Analysis of the Products.—The first exploratory experiment indicated that:

1. A complete decomposition of the alcohols took place, since no traces of alcohols could be detected in the product.

2. The formation of carbon monoxide and dioxide in the gases showed that a certain amount of the alcohol charged underwent a dehydrogenation to aldehyde with a consecutive decomposition of the latter. The decomposition of the aldehyde formed is complete since no undecomposed aldehyde was detected in the liquid reaction product by the sodium bisulfite method. Thus the amount of the aldehyde formed can be calculated from the amount of oxygen evolved in the gas in the form of carbon monoxide and dioxide. Consequently, the amount of hydrogen formed in the reaction gas belongs to two reactions: (a) alcohol dehydrogenation to aldehyde; and (b) olefin cyclization to aromatics.

3. The boiling points of the liquid reaction products are always lower than those of the charged alcohol and usually correspond to the boiling points of the mixture of corresponding olefin and aromatic hydrocarbons. Small

TABLE II

Expt.	Alcohol charged	Temp., °C.	% by weight of alcohol charged Dehydrated	Dehydrogenated	Cyclized	Cyclization of dehydrated alc., % by weight
2	*n*-Heptyl	500	55.5	44.5	32.0	57.7
3	Di-*n*-propylcarbinol	468	80.5	19.5	4.7	5.9
4	Di-*n*-propylcarbinol	480	74.8	25.2	8.2	11.0
5	*n*-Hexyl	467	83.3	16.7	5.3	6.3
6	*n*-Hexyl	500	76.1	23.9	12.0	15.8
7	*n*-Octyl	475	64.3	35.7	21.2	33.0

(about 5%) higher boiling bottoms probably are formed due to polymerization of unsaturated and hydrocarbon fragments from aldehyde decomposition. These bottoms have a very high refractive index (incomparably higher than the corresponding aldehyde or alcohols) which indicates that unreacted alcohol, or undecomposed aldehyde, is absent in the liquid reaction product.

Taking these facts into consideration, the following analytical procedure was applied.

Gas Analysis.—The gas was analyzed by the Göckel method. The amount of alcohol dehydrogenated to aldehyde (or ketone) and the amount of aromatic hydrocarbon formed was calculated, as follows.

Total gas evolved, 5520 cc.; carbon dioxide content, 10.0%; carbon monoxide content, 2.90%. Oxygen, as calculated from carbon dioxide and carbon monoxide, 0.903 g. This oxygen corresponds to 6.55 g. of alcohol dehydrogenated to ketone, producing 1265 cc. of hydrogen. Total hydrogen evolved, 2820 cc. (N. T. P.). Hydrogen evolved from toluene formation 2820 − 1265 = 1555 cc. This corresponds to 2.12 g. of toluene or 13.0% in the product, or 8.2% on alcohol charged.[6]

Liquid Analysis.—The liquid products of the reaction were separated from water (formed on dehydration), dried with calcium chloride (since no undecomposed alcohol was found in the product) and fractionated by means of a 36-inch (91-cm.) distilling column of the Podbielniak type. As mentioned previously, the boiling point of the product was typical of a mixture of corresponding unsaturated and aromatic hydrocarbons. The combined fractions were analyzed for olefins by sulfuric acid. The amount of aromatics formed was checked also by the refractive indices of the product (without the bottoms) using refractive index curves. In the case of octyl alcohol the product was hydrogenated selectively before fractionation in order to eliminate the olefins. The results of the experiments are given in Tables I and II.

Kinetics of the Reaction

Experiments 3, 4, 5, and 6 were carried out under carefully controlled conditions, each time with a freshly regenerated catalyst. The reaction took place with a constant speed during a sufficiently long time (two to four hours). Thus it was possible to evaluate the kinetic constants and calculate the energy of activation.

(6) Data from Experiment 4.

Calculations from the experimental data showed that the reaction of aromatization is of the first order and the formula $K = \frac{2.303}{t} \log \frac{a}{a - x}$ (t, time, a, the amount taken into the reaction; and x, the amount of product in per cent.) can be applied. The energies of activation, Q, were calculated using the formula

$$2.303 \log \frac{K_2}{K_1} = \frac{Q}{R}\left(\frac{1}{T_1} - \frac{1}{T_2}\right)$$

where K_1 and K_2 were the velocity constants, and T_1 and T_2 the corresponding absolute temperature. The constants were determined for two reactions: (1) alcohol aromatization, and (2) alcohol dehydrogenation to aldehyde (or ketone).

Table III presents the results of these calculations.

TABLE III

Alcohol	Cal./mole, Q for aromatization	Q for aldehyde (or ketone) formation
n-Heptyl alcohol	59,700	
Di-*n*-propylcarbinol	57,600	31,100
n-Hexyl alcohol	62,000	14,200

Summary

1. Under the action of a mixed, chromic oxide–alumina catalyst, the fatty alcohols undergo a complex reaction involving dehydration, dehydrogenation, and cyclization producing aromatic hydrocarbons.

2. The reaction was accomplished with alcohols containing six, seven, and eight carbon atoms.

3. Each component of the chromic oxide–alumina catalyst influenced the reaction in its own specific direction, alumina acting as dehydration and chromium oxide as a dehydrogenation and cyclization catalyst.

4. It is proposed to name this type of mixed catalysts "complex-action catalysts."

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Hydroxyl and Amino Derivatives of Dehydroabietic Acid and Dehydroabietinol

BY LOUIS F. FIESER AND WILLIAM P. CAMPBELL[1]

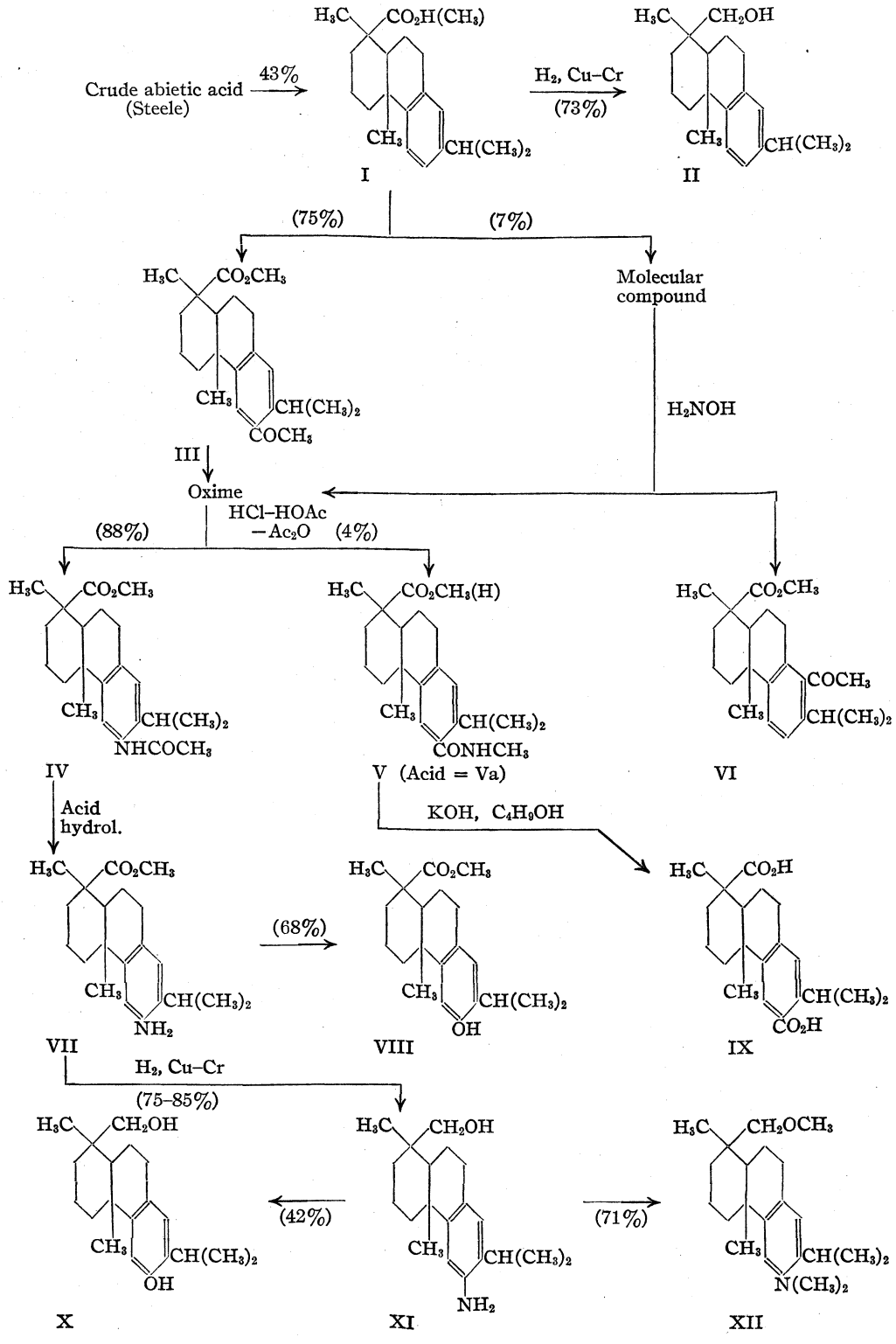
The objective of our work in the resin acid field has been to utilize abietic acid as a starting material for the synthesis of hydrophenanthrene derivatives having a sufficient structural similarity to certain other important natural products of this group to offer promise of exhibiting some of their physiological actions. A foundation for this project was laid in the first investigation[2] by the isolation and characterization of the partially aromatized dehydroabietic acid, and later a practical method was found for the preparation of the pure acid in quantity.[3] On investigating methods for the introduction of the hydroxyl and amino groups into the aromatic ring, it was found that nitration proceeds too readily to the stage of disubstitution and that the readily prepared sulfodehydroabietic acid on alkali fusion gives an intractable mixture containing products of degradation and dehydrogenation. An analogous dehydrogenation has been observed by Mosettig and Stuart[4] who found that 9,10-dihydrophenanthrene-2-sulfonic acid gives 2-phenanthrol on fusion with alkali.

The Friedel and Crafts reaction of methyl dehydroabietate was observed to proceed smoothly in nitrobenzene solution to give as the chief product a substance characterized as the 6-acetyl derivative[3] (III), and this has now proved a suitable intermediate for the preparation of the compounds desired. In the preparation of large quantities of the substance there accumulated an adequate amount of the previously observed by-product for further characterization. This sharply melting substance formerly was thought to be a different crystalline modification of the 6-acetyl derivative, for it has the same composition and gives an identical oxime, but it is now recognized as a molecular compound of the 6- and 8-isomers. No separation could be accomplished by crystallization, but it was found that the more hindered 8-acetyl compound (VI) is unattacked by hydroxylamine even under rather drastic conditions and may be separated from the oxime of the 6-derivative by mechanical segregation of the crystals. The structure VI was established by oxidation with nitric acid and identification of the product as prehnitic acid (1,2,3,4-acid).

On treatment with hydrogen chloride in acetic acid–anhydride in the cold the oxime of methyl 6-acetyldehydroabietate rearranges very smoothly to give a mixture consisting largely of the desired acetyl amine ester IV but containing an appreciable quantity of the methyl amide ester V. A separation is not practical at this stage but can be accomplished after partial hydrolysis. Short boiling with hydrochloric–acetic acid results in complete hydrolysis of the ester group of V without attacking the methyl amide substituent, giving the alkali-soluble methyl amide acid Va. The acetyl amine ester IV under these conditions is converted largely into the corresponding amine ester VII, which is found in the neutral fraction along with a small amount of the unchanged acetyl compound. With this isomer (IV) there is but little hydrolysis of the ester group, and as this apparently occurs after elimination of the acetyl group the material carried into the alkaline extract can be separated from Va by precipitation of the hydrochloride from ether. To obtain pure methyl 6-aminodehydroabietate the partially hydrolyzed neutral fraction is submitted to further treatment with hydrochloric–acetic acid to destroy the remaining acetyl compound. After separation of a quantity of the free amino acid with alkali, the amino ester is obtained easily in a pure, crystalline condition.

The separations indicated were all sharp, and the total yields of pure end-products based upon the oxime used were as follows: methyl 6-aminodehydroabietate (VII), 62%; 6-aminodehydroabietic acid, 26%; 6-methylamidodehydroabietic acid (Va), 4%. The last-named substance was characterized by saponification to 6-carboxydehydroabietic acid, the 1-methyl ester of which was described previously.[3] Various derivatives of the amino acid and ester of the other series were prepared, and the amine VII was converted by diazotization with nitrosylsulfuric acid in pyridine[5] and by hydrolysis into methyl 6-hydroxydehydroabietate. There is a possibility that this phenolic

(1) Squibb Research Fellow.
(2) Fieser and Campbell, THIS JOURNAL, **60**, 159 (1938).
(3) Fieser and Campbell, *ibid.*, **60**, 2631 (1938).
(4) Mosettig and Stuart, *ibid.*, **61**, 1 (1939).
(5) De Milt and Van Zandt, *ibid.*, **58**, 2044 (1936).



substance is structurally related to podocarpic acid, for on the basis of the evidence adduced by Sherwood and Short[6] it is conceivable that the phenolic acid isolated from resins of Java and New Zealand differs from the acid corresponding to VIII only in the absence of the isopropyl group in the 7-position.

(6) Sherwood and Short, *J. Chem. Soc.*, 1006 (1938).

Having developed satisfactory methods for the introduction of the amino and hydroxyl group into the aromatic nucleus, we next sought to modify the functional group in the alicyclic part of the molecule, and the way was paved in model experiments using methyl dehydroabietate. Bouveault reduction of the ester with sodium and amyl alcohol was tried briefly but found to result chiefly in hydrolysis. Satisfactory results were obtained, however, by high pressure hydrogenation over copper chromite catalyst,[7] dehydroabietinol (II) being obtained in 73% yield. The carbinol is a liquid giving a crystalline dinitrobenzoate. The hydrogenation of methyl 6-aminodehydroabietate presented the further complication that ammonia was liberated if the temperature was raised too high, but under carefully controlled conditions the amino alcohol XI was obtained in excellent yield as a crystalline solid. The reduction of methyl 6-hydroxydehydroabietate gave unpromising results in the first trials, but the desired carbinol X was obtained easily from the amino alcohol XI by the diazo reaction.

6-Hydroxydehydroabietinol (X) is one end-product envisioned in the original plan of our research,[2] for it is a hydrophenanthrene derivative with one aromatic ring having a phenolic hydroxyl group at one end of the molecule and an alcoholic hydroxyl group at the other. The substance therefore possesses some of the structural features of oestradiol and it is being tested for oestrogenic activity.[7a]

It also seems possible that in the resin acid series suitable amino derivatives may be found to have a morphine-like action. As a start in this direction one such compound has been prepared in consultation with Dr. L. F. Small, who has kindly agreed to submit the substance for pharmacological tests. Like morphine, 6-aminodehydroabietinol (XI) is an amino alcohol derivative of a hydrophenanthrene having one benzenoid nucleus, and in analogy with the extensive observations of Small, Eddy, and associates[8] it was thought that the substance might have some activity but that the quality would be improved by methylation, preferably of both the amino and the hydroxyl groups. Methylation was accomplished moderately well in some experiments with dimethyl sulfate and ammonium hydroxide, but the results were erratic. A better method was found in exhaustive treatment with methyl iodide and silver oxide in ether, which gives a water soluble product apparently consisting of the methohydroxide of XII. The aqueous extract on treatment with ammonium iodide gave a precipitate of the methiodide and this decomposed smoothly on heating in vacuum, giving the amine XII as a viscous oil. The substance was isolated as the crystalline hydrochloride and the presence of the ether group established by a methoxyl determination. Both functional groups are thus covered by methylation and the substance is of the type sought.

(7) Compare the hydrogenation of abietic acid esters, Hercules Powder Co., U. S. Patent 1,901,630 (1933).

(7a) Assays of X kindly conducted at the Squibb Institute for Medical Research are reported as follows by Dr. G. A. Harrop. When given at a dose level of 20 γ to 45 castrated rats, 23% of the animals showed a completely cornified smear, while at a level of 5 γ 60% of 40 rats gave a full oestrous response. The difference suggests that the substance may be rather toxic at the higher dosage. In another series a 2.5-γ dose produced full oestrus in 24% of 100 rats and and at a level of 5 γ the response in 40 rats was 55%. Under the conditions of these experiments oestrone produces a high oestrous response at a level of 7.5 γ. The resin acid derivative thus appears to possess marked oestrogenic activity.

(8) Small, Eddy, Mosettig and Himmelsbach, Studies on Drug Addiction, Supplement No. 138 to the Public Health Reports, 1938.

Experimental Part[9]

Preparation of Dehydroabietic Acid.—In preparing further quantities of this substance by the previously described procedure[3] it was found that purification of the starting material by the Palkin process can be dispensed with an entirely satisfactory material obtained from crude Steele's abietic acid, once crystallized as the acid sodium salt. The hydrolysis of sulfodehydroabietic acid is conveniently modified by using 60% sulfuric acid (480 cc. of concentrated acid and 500 cc. of water) and stirring the mixture at 135° with a Hershberg tantalum stirrer. The yield in this step (with 80-g. batches) was better, averaging 80%, and the over-all yield of pure dehydroabietic acid from the crude acid sodium salt was the same as that previously reported using pure salt (43%).

Acetylation of Methyl Dehydroabietate.—By the previous method,[3] 46.7 g. of the ester gave 33.0 g. of **methyl 6-acetyldehydroabietate** (m. p. 133.5–134°) in the first crop of crystals (prisms) from ether, and the mother liquor afforded 5.3 g. more of this substance, m. p. 132–134° (total yield 75%) and 3.8 g. (7%) of the substance, m. p. 119.5–120° (needles), which is now recognized as a complex.

Isolation of Methyl 8-Acetyldehydroabietate.—One gram of the complex, m. p. 119.5–120°, was refluxed for four hours with 0.5 g. of hydroxylamine hydrochloride in 2.5 cc. of pyridine and 5 cc. of alcohol and the mixture was poured into water and extracted with ether. After washing with dilute acid and with sodium bicarbonate solution and drying the solvent was evaporated and the product crystallized from ether–petroleum ether. Two kinds of crystals were deposited simultaneously and a mechanical separation could be accomplished rather easily. There was obtained in all 0.35 g. of fine needles of the oxime of methyl 6-acetylabietate, m. p. 151.5–152°, identified by

(9) All melting points are corrected. Microanalyses by Lyon Southworth, with the exceptions noted.

mixed melting point determination, and 0.28 g. of methyl 8-acetyldehydroabietate. This substance crystallizes in clusters of diamond-shaped tablets and melts on rapid heating at about 133°, resolidifies above this temperature, and remelts sharply at 153–153.5°; $[\alpha]^{25}D$ + 40° (1.0% in alcohol). The substance contains no nitrogen.

Anal. Calcd. for $C_{23}H_{32}O_3$: C, 77.47; H, 9.03. Found: C, 77.69; H, 9.02.

The substance exists in two forms which are easily interconvertible. When the above low-melting tablet form was heated in a test-tube at 140° it melted and resolidified; on immersing this material in a capillary tube in a bath at 140° it showed no change and melted sharply at 153–153.5°. This high-melting form was then melted on a watch glass and cooled rapidly to room temperature, giving a glass. When seeded with the low-melting form and warmed slightly, crystals were formed which melted when immersed in a bath at 137°, or sintered at 132° when heated slowly, and then showed the higher m. p.

For proof of structure 0.1 g. of the 8-acetyl compound was heated with 1 cc. of concentrated nitric acid and 2 cc. of water at 190° for twenty hours and the resulting clear yellow solution evaporated to dryness. The residue was dissolved in hot water and caused to crystallize by adding concentrated nitric acid, giving a product, m. p. 236–238° with gas evolution. This was identified as **prehnitic acid** (1,2,3,4-acid) by conversion with excess diazomethane to the tetramethyl ester, which crystallized from methanol as colorless needles, m. p. 130–130.5°, giving no depression when mixed with an authentic sample.[10] We can confirm Smith and Carlson's[11] observation concerning the purple color which this ester acquires on exposure to light and the recovery of colorless material on recrystallization.

The **oxime of methyl 6-acetyldehydroabietate** exhibits an interesting property in forming what appears to be a molecular compound with glacial acetic acid. On shaking 0.55 g. of the oxime with 2 cc. of this solvent at room temperature the substance dissolved completely in a few seconds and the complex then promptly separated. After bringing this into solution by heating and then allowing crystallization to proceed slowly, there was obtained 0.45 g. of product, m. p. 121.5–122.5°, $[\alpha]^{25}D$ + 76° (1.4% in alcohol). The m. p. is not changed by recrystallization.

Anal. Calcd. for $C_{23}H_{33}O_3N \cdot CH_3CO_2H$: C, 69.58; H, 8.64; neut. equiv., 431.5. Found: C, 69.70; H, 8.83; neut. equiv., 431.

The free oxime is recovered on neutralization or on heating the complex for some time at 125°.

Beckmann Rearrangement of the Oxime of Methyl 6-Acetyldehydroabietate and Hydrolysis.—A solution of 0.5 g. of the oxime in 2 cc. of warm glacial acetic acid was cooled, treated with 1 cc. of acetic anhydride, and saturated with dry hydrogen chloride. The reaction product soon began to separate in the form of colorless plates, and after twenty-four hours this was collected, washed with acetic acid and dried; yield 0.5 g., m. p. 179–183°. This apparently is a mixture of the $ArNHCOCH_3$ and $ArCONHCH_3$ compounds in which the former predominates, but separation at this point by crystallization is not practical. The yield and character of the mixture was the same in larger runs (40 g.) and on using three times the specified quantities of acetic acid and anhydride.

For partial hydrolysis facilitating a separation of products, the crude, undried material from 37.1 g. of oxime was refluxed for one hour with 250 cc. of acetic acid and 125 cc. of 6 *N* hydrochloric acid; the solution was poured into 1.5 liters of cold water and the colorless precipitate was collected and combined with that obtained by neutralizing the acid liquor with alkali. The total moist solid was stirred with excess alkali and extracted with ether, and after separation of the ether layer the alkaline liquor was acidified with acetic acid, giving 3.0 g. of an **acid mixture B,** which subsequently was worked up as described below. The ethereal solution (800 cc.) was dried, concentrated to a volume of about 200 cc., and saturated with dry hydrogen chloride. The precipitated material, washed with ether and air dried at 50°, weighed 35 g. and will be referred to as **mixture A.** This consists largely of the hydrochloride of methyl 6-aminodehydroabietate but contains a sufficient amount of the unhydrolyzed acetate of this amine to interfere with the isolation of the amine in a pure, crystalline condition unless removed by further hydrolysis. The presence of the acetate was ascertained on submitting mixture A to diazotization. On dissolving the diazonuim salt in water an insoluble residue remained, and when purified by distillation and crystallization from methanol this formed flat needles, m. p. about 90°, having the characteristics of the 6-acetylamino ester described below. It is odd that this acetate should be carried down from an ethereal solution by hydrogen chloride, but this behavior was noted with an analytical sample prepared from the pure amine as described below.

Methyl 6-Aminodehydroabietate (VII).—A solution of 5 g. of the partially hydrolyzed mixture A in 40 cc. of acetic acid and 20 cc. of 6 *N* hydrochloric acid was refluxed for four hours, cooled, and poured into a solution of 36 g. of sodium hydroxide in 400 cc. of water. The liberated amine was extracted with ether (saving the **alkaline liquor C,** see below) and after drying and concentrating the solution it was obtained crystalline; the yield of satisfactory material was 2.9 g. (62%, based upon the oxime). Crystallized from ether–petroleum ether, it formed diamond-shaped plates, m. p. (evacuated capillary) 137–137.5°, $[\alpha]^{25}D$ +81° (1% in alcohol).

Anal. Calcd. for $C_{21}H_{31}O_2N$: C, 76.54; H, 9.48. Found: C, 76.36; H, 9.33.

The **hydrochloride** was prepared by saturation of an ethereal solution of the amino ester with dry hydrogen chloride. For crystallization 0.25 g. of the salt was warmed with 2–3 cc. of 6 *N* hydrochloric acid and enough alcohol to bring the material into solution at the boiling point. The substance separated as colorless leaves which sintered at about 160° and melted at about 250°, dec.; $[\alpha]^{25}D$ +61° (1% in alcohol). Immersed in a bath at 245°, the sample melted with loss of water, resolidified and melted at 250–260°, dec. The substance, dried at 80° and 9 mm., appears to be a monohydrate; after heating at 245° and evacuating the capillary the product remained unmelted at 290°.

(10) Fieser and Peters, THIS JOURNAL, **54**, 4347 (1932).

(11) L. I. Smith and Carlson, *ibid.*, **61**, 288 (1939).

Anal. Calcd. for $C_{21}H_{32}O_2NCl \cdot H_2O$: C, 65.69; H, 8.93. Found: C, 65.47, 66.06; H, 8.77, 8.70.

The salt was also isolated from mixture A by crystallization from acid-alcohol and showed the same characteristics on heating.

6-Aminodehydroabietic Acid.—The alkaline liquor C mentioned above on acidification with acetic acid gave 1.1 g. (24% from the oxime) of this acid as a white solid. Crystallization from alcohol gave pure material separating in laths, m. p. (vacuum) 214.5–215°; $[\alpha]^{25}D$ + 82° (1% in alcohol).

Anal. Calcd. for $C_{20}H_{29}O_2N$: C, 76.15; H, 9.27. Found: C, 76.29; H, 9.09.

The **hydrochloride** was prepared by passing dry hydrogen chloride into an ethereal solution of the amino acid and crystallized from a mixture of alcohol and 6 *N* hydrochloric acid. It is unmelted at 295°.

Anal. Calcd. for $C_{20}H_{30}O_2NCl$: C, 68.26; H, 8.59. Found: C, 68.06; H, 8.63.

6-Methylamidodehydroabietic Acid (Va).—The 3 g. of the acid mixture B separated after partial hydrolysis of the rearrangement product on crystallization from aqueous alcohol afforded 2.7 g. of material melting in the range 210–240°. About one-third of this was found to consist of 6-aminodehydroabietic acid, which was dissolved by extraction of the solid with 150 cc. of boiling ether in two portions, precipitated from the ethereal extract with hydrogen chloride, reconverted to the amino acid (0.8 g.), crystallized from alcohol, giving 0.7 g. of pure material (2% yield from the oxime).

A little of the amide-acid (0.2 g.) was recovered from the remaining ether solution by extraction with alkali and precipitation with acid, and this was combined with the material which did not dissolve in the ether (1.5 g.). Crystallization of the total V from aqueous alcohol gave 1.5 g. (4% from the oxime) of shiny leaves, m. p. 253–254°, and the fully purified substance melted at 254–255°; $[\alpha]^{25}D$ +82° (0.9% in alcohol).

Anal. Calcd. for $C_{22}H_{31}O_3N$: C, 73.90; H, 8.74; N, 3.93; neut. equiv., 358. Found: C, 74.30, 73.77; H, 8.78, 8.38; N (Kjeldahl), 4.12; neut. equiv., 359.

6-Carboxydehydroabietic Acid (IX).—A solution of 0.2 g. of the amide-acid V in 5 cc. of *n*-butyl alcohol containing 0.5 g. of potassium hydroxide was refluxed for four hours, the solvent was removed by steam distillation, and the clear aqueous solution remaining was acidified with hydrochloric acid, giving 0.2 g. of an amorphous white solid which did not melt at 280°. This remained undissolved when boiled with 15 cc. of alcohol, but on adding a few cc. of water it dissolved readily. After adding more water at the boiling point the solution became turbid and on cooling the dibasic acid separated as the monohydrate in the form of colorless needles (0.18 g.). The sample was further purified by crystallization from aqueous acetone and gave $[\alpha]^{25}D$ +71° (0.9% in 80% alcohol).

Anal. Calcd. for $C_{21}H_{28}O_4 \cdot H_2O$: C, 69.59; H, 8.33; neut. equiv., 181. Found: C, 69.41; H, 8.54; neut. equiv., 181.

Acetylation of Methyl 6-Aminodehydroabietate.—The **diacetyl derivative** was obtained by heating the amine recovered from 0.5 g. of the hydrochloride with 5 cc. of acetic anhydride at the boiling point for a few minutes Water was added and the mixture warmed to hydrolyze the excess reagent, cooled, and the product extracted with ether. Crystallization from ether–hexane and then from methanol yielded 0.25 g. of the pure derivative in the form of thick prisms, m. p. 150–151°; $[\alpha]^{25}D$ +75° (1.7% in alcohol).

Anal. Calcd. for $C_{25}H_{35}O_4N$: C, 72.60; H, 8.53. Found: C, 72.78, 72.40; H, 8.47, 8.82.

The **monoacetyl compound** (IV) was made by allowing a solution of 0.3 g. of the free amine in 5 cc. of pyridine and 2 cc. of acetic anhydride to stand at 35–40° for two days and pouring the mixture into 30 cc. of water containing excess hydrochloric acid. The oily product soon solidified and was crystallized twice from methanol. The substance forms characteristic flat needles but does not melt normally or sharply. At 93–95° it changes gradually to a transparent but very viscous liquid which does not flow to the bottom of the capillary. The rotation was $[\alpha]^{25}D$ +79° (1.0% in alcohol).

Anal. Calcd. for $C_{25}H_{33}O_3N$: N, 3.77. Found (Kjeldahl): N, 3.87.

6-Acetylaminodehydroabietic acid was prepared from the amino acid (0.4 g.), pyridine (5 cc.) and acetic anhydride (2 cc.). After twenty-four hours at 35°, 100 cc. of water was added and the product slowly crystallized (0.4 g.). One crystallization from methanol gave 0.32 g. of thick hexagonal plates, m. p. 255–256°, $[\alpha]^{25}D$ +80° (1.2% in alcohol).

Anal.[12] Calcd. for $C_{22}H_{31}O_3N$: C, 73.90; H, 8.74; N, 3.93. Found: C, 74.00; H, 8.65; N (Kjeldahl), 3.97.

Methyl 6-Hydroxydehydroabietate (VIII).—One gram of powdered sodium nitrite was added to a stirred mixture of 10 cc. of concentrated sulfuric acid and 5 cc. of water at 0°; the mixture was warmed gradually to 35–40° with stirring until a nearly clear solution resulted. This was cooled to −5° and a solution of 2 g. of methyl 6-aminodehydroabietate in 6 cc. of pyridine was added dropwise with stirring, keeping the temperature below 0°. Sufficient ice and water was added to the thick cream-colored paste to permit good stirring, and after forty-five minutes the volume was made up to about 200 cc., 0.6 g. of urea was added, and stirring was continued for one-half hour. The suspension of the diazonium salt was then poured rapidly into 300 cc. of boiling water and boiling was continued for a few minutes. The phenol separated as a granular precipitate and was collected after cooling. Crystallization from ether–hexane yielded 1.0 g. of diamond-shaped plates, m. p. 157–157.5° and a second crop of 0.5 g., m. p. 156–157°; total yield 68%. Further crystallization did not change the m. p. of the first crop; the rotation was $[\alpha]^{25}D$ +71° (1.2% in alcohol).

Anal. Calcd. for $C_{21}H_{30}O_3$: C, 76.63; H, 9.15. Found: C, 76.32; H, 9.15.

Dehydroabietinol (II).—Methyl dehydroabietate (5 g.) was reduced to the carbinol in dioxane (5 cc.) using copper chromite catalyst (0.5 g.) with hydrogen at 1310–1070 lb. (87–71 atm.) pressure at 250°. After forty-eight hours

(12) Analysis by the Arlington Laboratories.

there was no further absorption of gas. After dilution with water the product was extracted and dried in ether and obtained as a stiff resin consisting largely of the carbinol but containing some unreduced ester. It was refluxed for four hours with 1.5 g. of potassium hydroxide in 15 cc. of *n*-butyl alcohol, the solvent was removed with steam, and the neutral fraction extracted and dried in ether. On distillation the carbinol fraction boiled almost completely at 177° at 1 mm.; yield 3.3 g. (73%). The rotation was $[\alpha]^{25}D$ +53° (2.4% in alcohol).

Anal. Calcd. for $C_{20}H_{30}O$: C, 83.87; H, 10.55. Found: C, 84.25; H, 10.91.

Acidification of the alkaline liquor gave 0.6 g. (12.5%) of dehydroabietic acid.

For characterization the carbinol was converted into the 3,5-dinitrobenzoate by warming it with the corresponding acid chloride in benzene–pyridine at 35–40° for seventeen hours. The substance crystallized from ether–hexane in clusters of prisms, m. p. 123–124°.

Anal. Calcd. for $C_{27}H_{32}O_6N_2$: C, 67.49; H, 6.71. Found: C, 67.58; H, 6.87.

6-Aminodehydroabietinol (XI).—A mixture of 3.3 g. of methyl 6-aminodehydroabietate, 1 g. of copper chromite catalyst, and 25 cc. of dioxane was shaken at 200° with hydrogen at 2400–2100 lb. for seventeen hours, when approximately two moles of gas had been absorbed and the reaction was stopped. The solution was filtered through a thin layer of Norite, washed through with methanol, and the colorless solution concentrated to 40–50 cc., and diluted with water while hot. On cooling, the amino alcohol crystallized in long, shining laths, m. p. 135–137°; yield 2.2 g. (73%). From the mother liquor 0.2 g. more of the product (total yield 80%) was obtained after removing the solvent with steam and removing unchanged ester by saponification of the resin (0.78 g.) with potassium hydroxide (1 g.)–*n*-butyl alcohol (10 cc.) by boiling for four hours. The amine was extracted with ether, converted with aqueous acid to the hydrochloride (0.3 g.), recovered, and crystallized from ether–petroleum ether.

On thorough purification from ether–petroleum ether the amine separated both as flat needles and as leaves of the same m. p. (and mixed m. p.) 139.5–140°; $[\alpha]^{25}D$ +72° (1% in alcohol).

Anal. Calcd. for $C_{20}H_{31}ON$: C, 79.68; H, 10.37. Found: C, 79.97; H, 10.39.

The **hydrochloride** can be purified by crystallization from aqueous hydrochloric acid, forming fine white needles; $[\alpha]^{25}D$ +63° (1.0% in alcohol).

Anal.[12] Calcd. for $C_{20}H_{32}ONCl$: C, 71.08; H, 9.55; Cl, 10.49. Found: C, 71.16; H, 9.49; Cl, 10.35.

The yield in several hydrogenations conducted as above varied from 75 to 85% using pressures from 1000 to 2500 lb. (67 to 167 atm.). The yield was lower at higher temperatures; in one run at 250° ammonia was formed (green color, test with litmus), while in another, using crude starting material, no ammonia was produced but in four and one-half hours the yield of amine was only 45 and 41% of acid was recovered on saponification. A longer reaction time at 200° (forty-eight hours) gave a lower yield (68%).

6-Dimethylaminodehydroabietinol Methyl Ether (XII) Hydrochloride.—A solution of 0.3 g. of 6-aminodehydroabietinol in 10 cc. of dry ether was treated with 5 cc. of methyl iodide and 0.3 g. of silver oxide and refluxed for forty-four hours in a Soxhlet apparatus containing anhydrous sodium sulfate in the thimble to absorb the water formed. During the refluxing two 5-cc. portions of methyl iodide and five 0.3-g. portions of silver oxide were added. The solvent was evaporated and the residue was digested with three 10 to 15-cc. portions of water on the steam-bath. Each aqueous extract was treated while hot with 1 g. of solid ammonium iodide and the resulting gel converted to the crystalline methiodide by heating and shaking. This gave in all 0.45 g. of colorless needles, m. p. 152–152.5° with evolution of gas. For decomposition to the tertiary amine the methiodide was placed in a tube with a constriction providing two compartments and heated in a furnace at 140° and 1–2 mm. pressure, when the amine slowly distilled as a very viscous, clear oil. This was dissolved in ether and treated with dry hydrogen chloride, giving 0.3 g. of the hydrochloride, m. p. (vacuum) 226–227°, with gas evolution. The salt crystallized from a mixture of about equal parts of methanol and 6 *N* hydrochloric acid in the form of colorless laths of the same m. p. (which is somewhat dependent on the rate of heating), yield, 2.7 g. (71%), $[\alpha]^{25}D$ +78° (0.8% in alcohol).

Anal. Calcd. for $C_{23}H_{38}ONCl$: C, 72.70; H, 10.08; OCH_3, 8.17. Found: C, 72.97; H, 10.07; OCH_3, 8.22.[12]

In methylating a 3-g. portion of the amine (eighty hours) it was found expedient during the extraction with water to add 2 g. of silver oxide with each 50-cc. portions of water in order to complete conversion to the water soluble methohydroxide. In this case the methiodide contained a small amount of infusible solid but this did not alter the m. p. of the methiodide or interfere with its decomposition, being left as a white, non-volatile residue. The yield of pure hydrochloride was 68%.

6-Hydroxydehydroabietinol (X).—Attempted preparation of this substance by high pressure hydrogenation of methyl 6-hydroxydehydroabietate gave a product which could be obtained only as a gel or an amorphous solid.

A solution of 1 g. of crude 6-aminodehydroabietinol, m. p. 136–137°, in 100 cc. of hot water containing 0.9 cc. of 6 *N* hydrochloric acid was filtered, cooled to 0–5°, and the hydrochloride precipitated as a fine suspension by adding 10 cc. of 6 *N* acid. A solution of 0.24 g. of sodium nitrite in a little water was added all at once. The salt rapidly dissolved and a flocculent, light yellow precipitate separated. After thirty minutes 0.5 g. of urea was added, and in ten minutes more the precipitate (0.3 g.) was removed by filtration and washed with cold water. The cloudy filtrate and wash water (250 cc. in all) was poured into a solution of 400 cc. of 3 *N* sulfuric acid at 85° and heating was continued for twenty minutes. After cooling, the crude phenol was collected as a light yellow resin (0.65 g., 65%). Crystallization from ether–hexane yielded in all 0.42 g. (42%) of faintly yellow prisms, m. p. 180–181.5°, $[\alpha]^{25}D$ +72° (1.1% in alcohol). The behavior on melting is like that of camphor, liquid appearing at the lower temperature indicated and the crystal skeleton disappearing at the higher temperature.

Anal. Calcd. for $C_{20}H_{30}O_2$: C, 79.42; H, 9.99. Found: C, 79.52; H, 10.25.

Summary

Pure dehydroabietic acid can be prepared very conveniently by the previous process but starting with Steele's abietic acid. The Friedel and Crafts reaction of the ester with acetyl chloride gives chiefly the 6-acetyl derivative, but this is accompanied by a small amount of the 8-isomer with which it forms a stable molecular compound resolvable by preferential reaction with hydroxylamine.

The oxime of methyl 6-aminodehydroabietate rearranges smoothly on treatment with hydrogen chloride in acetic acid–anhydride and gives chiefly the acetylamine derivative, along with a small amount of the isomeric methyl amide. After suitable hydrolysis, derivatives of these substances can be separated efficiently and pure 6-aminodehydroabietic acid and its ester can be obtained by this route in good yield.

By hydrogenation over copper chromite catalyst methyl dehydroabietate and its 6-amino derivative can be converted smoothly to the carbinols. The amino alcohol on methylation with methyl iodide–silver oxide gives 6-dimethylaminodehydroabietinol methyl ether, which is being tested for possible morphine-like actions. The phenols methyl 6-hydroxydehydroabietate and 6-hydroxydehydroabietinol were prepared from the amines by the diazo reaction; the latter substance has some of the structural features of oestradiol.

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CAMBRIDGE, MASSACHUSETTS RECEIVED JULY 17, 1939

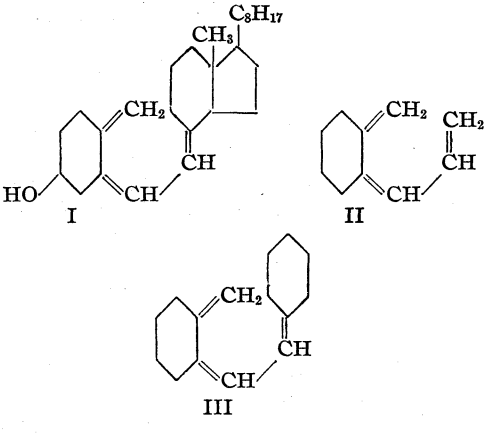
[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, NO. 198]

Studies in the Synthesis of the Antirachitic Vitamins. I. The Synthesis of 3-[2′-Methylenecyclohexylidene-1′]-propene-1

BY NICHOLAS A. MILAS AND W. LYSLE ALDERSON, JR.

Although the structure of the antirachitic vitamins has been fairly well elucidated, ultimate proof is lacking because they have not yet been synthesized from simple substances. Some time ago we undertook the problem of synthesis, but in view of its complexity we decided first to synthesize the most unstable portion of the vitamin molecule, then to build the other parts together with the necessary functional groups around this portion. The most unstable portion of an antirachitic vitamin, represented by structure I, is that which includes the three conjugated double bonds. This is known to be responsible for the characteristic spectrum of the vitamin and, together with the hydroxyl group and the side chain,[1] contributes to its antirachitic action.

Two of the simplest configurations which represent this portion of the antirachitic molecule are indicated by structures II and III. After a number of attempts on various reactions which would lead to the synthesis of II and III, we have found that in the case of II the reactions outlined by the equations below led to the expected product in fairly good yields. In view of similar work



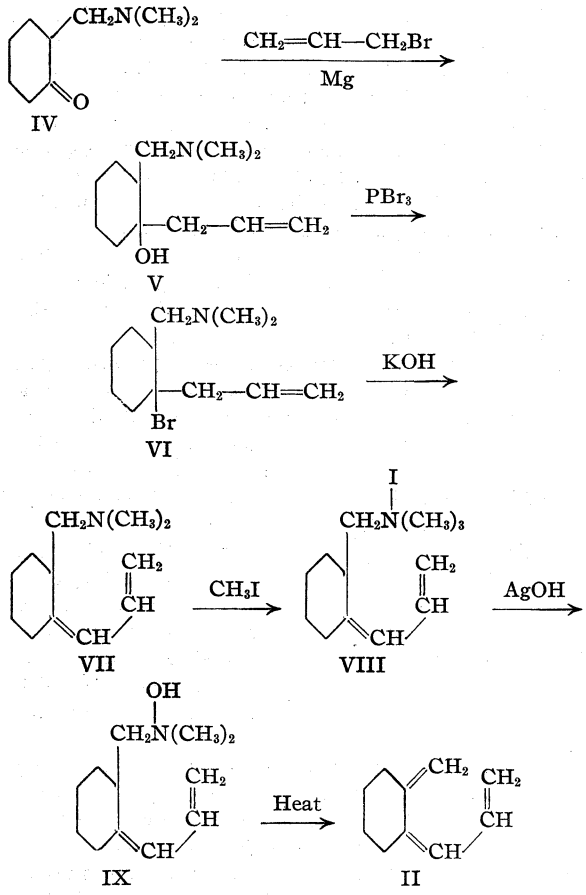
undertaken in other laboratories,[2,3] we are publishing at present the synthesis of II which will be followed shortly by that of III and other portions of the antirachitic molecule.

The ultraviolet absorption spectra of II and VII have been plotted side by side in Fig. 1. It may be seen readily that the amine VII absorbs rather strongly in the region of 236 mμ. Its extinction coefficient has been calculated to be 10,500, which is of the right order of magnitude

(1) Milas and Milone, unpublished work which indicates that the side chain of the antirachitic vitamins plays an important role.

(2) Aldersley and Burkhart, *J. Chem. Soc.*, 545 (1938).

(3) Dimroth, *Ber.*, **71**, 1333, 1346 (1938); Dimroth and Jonsson, *ibid.*, **71**, 2658 (1938).



for substances of this type having two conjugated double bonds. The triene II has a very prominent band with a maximum at 255 mμ which is slightly displaced toward the short ultraviolet as compared with the important maximum of calciferol at 265 mμ. However, its molecular extinction coefficient agrees remarkably well with that of calciferol, vitamin D_3 and vitamin D_4 as shown in Table I.

TABLE I

THE MOLECULAR EXTINCTION COEFFICIENT, ε, OF THE ANTIRACHITIC VITAMINS

	ε
Calciferol[4] (Vitamin D_2)[5]	19,200 (18,200)
Vitamin D_3[5]	19,200
Vitamin $_4$[5]	18,700
Triene II	19,000

Experimental Part

2-Dimethylaminomethyl Cyclohexanone-1 (IV).—In the preparation of this ketone the procedure of Mannich and Braun[6] was followed. A mixture of 49 g. of cyclohexanone (b. p. 155–156°), 9 g. of 39% formaldehyde solution (Merck) and 9 g. of dimethylamine hydrochloride was heated slowly over a free flame until refluxing commenced. The flame was then removed as the heat evolved by the reaction was sufficient to cause vigorous refluxing which subsided after about two minutes. After the reaction product was allowed to cool to room temperature, it was shaken with 50 cc. of water, the aqueous layer extracted several times with ether to remove any unconverted cyclohexanone, made alkaline with potassium hydroxide and the liberated amine extracted with ether, the ethereal solution dried over anhydrous sodium sulfate, filtered and the ether removed under reduced pressure. Finally, the amine was fractionally distilled and the fraction, 10 g., boiling at 91–92° (7 mm.) collected. The b. p. of this was redetermined at 13 mm. and found to be 97–100°. Mannich and Braun[6] report the b. p. of 2-dimethylaminomethylcyclohexanone-1 to be about 100° (13 mm.).

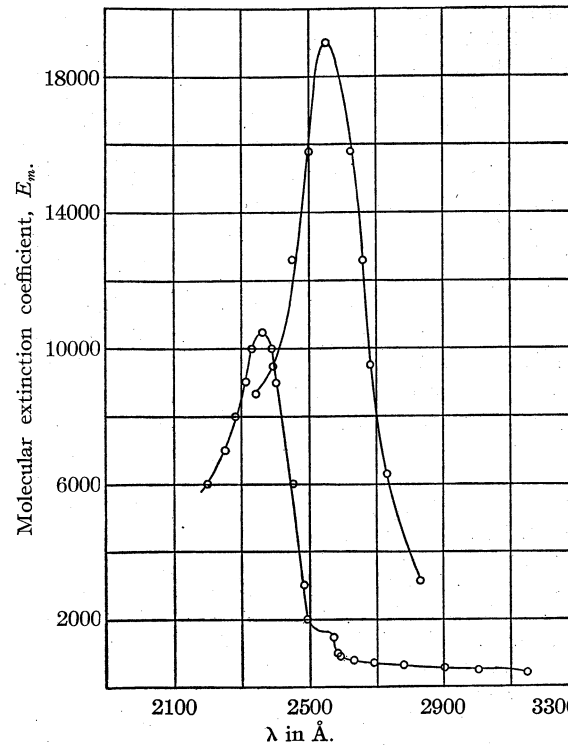


Fig. 1.—The absorption spectra of II and VII.

2-Dimethylaminomethyl 1-Allylcyclohexanol-1 (V).—A solution of 41.5 g. of 2-dimethylaminomethyl-cyclohexanone-1 in 100 cc. of anhydrous ether was added over a period of four hours to an efficiently stirred solution of allylmagnesium bromide[7] in 500 cc. of dry ether. A white precipitate was formed which remained insoluble in ether. After all the ketone had been added, stirring was continued for twelve hours, then the mixture was poured on ice which was mixed with ammonium chloride to decompose the addition product. The ether layer was separated, dried over anhydrous sodium sulfate, filtered, the ether removed under reduced pressure, the residue fractionated,

(4) Morton, "Absorption Spectra of Vitamins and Hormones," Adam Hilger, Ltd., London, 1935, p. 11.

(5) Brockmann and Busse, *Naturwissenschaften*, **26**, 122 (1938); *Z. physiol. Chem.*, **256**, 252 (1938).

(6) Mannich and Braun, *Ber.*, **53**, 1875 (1920).

(7) (a) Gilman and McGlumphy, *Bull. soc. chim.*, **43**, 1325 (1928); (b) Milas and McAlevy, THIS JOURNAL, **57**, 581 (1935).

and the fraction boiling at 112–117° (5 mm.) collected; yield 34.3 g. This substance was a colorless oil with a rather unpleasant odor.

Inasmuch as it was nearly impossible to obtain this alcohol free from the diene, the dehydrated alcohol, and in order to identify it definitely, it was decided to prepare the acetate. Three grams of the dimethylamino alcohol was refluxed with 6 g. of acetic anhydride for one and a half hours. The product was then poured on cracked ice, neutralized with dilute potassium hydroxide, the resulting mixture extracted several times with ether and the ether extracts dried over anhydrous sodium sulfate, filtered and the ether removed in vacuum. The residue was then fractionated and the fraction, 1.8 g., boiling at 129–130° (9 mm.) collected and analyzed.

Anal. Calcd. for $C_{14}H_{25}O_2N$: N, 5.85. Found: N, 5.8, 5.9.

The acetate is a colorless viscous oil of a sharp, rather pleasant odor, having the physical constants: d^{25}_4 0.9596; $n^{25}D$ 1.4740. When exposed to air for long periods of time, it turns brown.

3 - [2′ - Dimethylaminomethylcyclohexylidene - 1′]-propene-1 (VII).—Potassium acid sulfate, phenyl isocyanate, oxalic acid, phthalic anhydride, methylmagnesium iodide and the xanthate method of Tschugaeff were used for the dehydration of 2-dimethylaminomethyl-1-allylcyclohexanol-1. All gave varying yields of the dehydrated amine, but it was found that a purer product could be obtained in higher yields by first converting the alcohol into the bromide and eliminating hydrogen bromide with solid potassium hydroxide.[7b] Although the use of potassium acid sulfate led to satisfactory yields of a dehydrated product, its b. p. of 100–103° (9 mm.) was considerably lower than that produced by the use of the other reagents. This was probably the undesirable product in which the double bond migrated into the ring, a reaction which Wallach[8] has shown to take place readily with similar compounds under the influence of acid reagents.

2-Dimethylaminomethyl-1-allylcyclohexyl Bromide-1 (VI).—In view of its high instability this bromide was not isolated but was prepared as follows. Two grams of freshly distilled phosphorus tribromide dissolved in 5 cc. of anhydrous benzene was added slowly to a vigorously stirred and well cooled solution of 3 g. of the dimethylaminocarbinol dissolved in 10 cc. of dry benzene. The temperature of the reaction mixture while the bromide was added was never allowed to exceed +5°. After all of the bromide had been added, the reaction mixture was stirred at room temperature for six hours longer, whereby the phosphorous acid salt of the amine began to crystallize. To this mixture was then added 6 g. of finely powdered solid potassium hydroxide and the mixture distilled under reduced pressure using an oil-bath. After the benzene distilled over, the oil-bath was heated rapidly to 175°, whereupon the salt of the dimethylamino bromide began to decompose and 2 g. of the crude dimethylaminodiene distilled over at 116–126°. When 2 g. of this amine was fractionated from finely divided sodium, 1.8 g. of pure product was obtained boiling at 126.5–128° (10 mm.).

Anal. Calcd. for $C_{12}H_{21}N$: N, 7 Found: N, 7.6, 7.5.

This amine is a colorless liquid, with a sharp but not unpleasant odor, having the following physical constants: d^{26}_{26} 0.8776; $n^{26}D$ 1.4909, $n^{25}D$ 1.4910; *MR*, calcd. for $C_{12}H_{21}N$, 2F, 58.43, found, 59.03; exaltation, 0.6. That the two double bonds in this amine are conjugated is shown by the presence of an exaltation and also by its absorption spectrum shown in Fig. 1 (VII). This was determined in pure ethyl alcohol and found to have a prominent band in the ultraviolet region with a maximum at 236 mμ. The molecular extinction coefficient was calculated to be 10,500, a value which is of the same order of magnitude as that calculated for substances of this type having two conjugated double bonds.

3 - [2′ - Methylene - cyclohexylidene-1′]- propene - 1 (II).—Three grams of the dimethylaminodiene was converted into the methylammonium iodide by allowing it to react for twenty-four hours at room temperature with excess methyl iodide. The white solid formed was dissolved in water and converted into the methylammonium hydroxide by shaking the aqueous solution for three hours with twice the theoretical amount of freshly precipitated silver oxide. The mixture was then filtered and the filtrate concentrated under reduced pressure in an atmosphere of nitrogen using an oil-bath. After most of the water had been removed, the pressure was reduced to 5 mm. and the temperature of the oil-bath slowly raised to 60° at which temperature the ammonium base began to decompose with considerable foaming. One gram of a pleasant smelling product distilled over. This was taken up in ether and the ethereal solution washed several times with a solution of 50% acetic acid followed by a concentrated solution of sodium bicarbonate, dried over anhydrous sodium sulfate, filtered, the filtrate fractionated under reduced pressure in an atmosphere of nitrogen and the fraction, 0.8 g., boiling at 62–63° (7 mm.) collected and analyzed.

Anal. Calcd. for $C_{10}H_{14}$: C, 89.5; H, 10.5. Found: C, 89.5, 89.4; H, 10.9, 10.5.

The triene is a colorless liquid, with a very characteristic terpene-like odor, having the physical constants: d^{27}_{27} 0.8744; $n^{15}D$ 1.5281, $n^{20}D$ 1.5255, $n^{27}D$ 1.5224; *MR*, calcd. for $C_{10}H_{14}$, 3F, 43.57, found, 46.82; exaltation, 3.24. It is highly reactive and when allowed to remain in contact with oxygen it polymerizes rapidly into a white solid. When hydrogenated in ethyl alcohol using platinum oxide as the catalyst, it was found to absorb 2.98 and 3.3 moles of hydrogen as against the theoretical value of 3 showing the presence of three double bonds.

The ultraviolet absorption spectrum of the triene was then determined in pure ethyl alcohol and the results plotted in Fig. 1 (II). This shows a prominent band with a maximum at 255 mμ and a molecular extinction coefficient of 19,000, a value which is of the right order of magnitude for systems containing three conjugated double bonds one of which is joined to an exomethylene group.

That this triene had not cyclized to form one of the hexahydronaphthalenes is further shown by the work of Morton and de Gouveia[9] and of Huber.[10] These investigators have found that the hexahydronaphthalenes absorb in the region 234–239 mμ and show practically no exaltation.

(8) Wallach, *Ann.*, **360**, 29 (190).

(9) Morton and de Gouveia, *J. Chem. Soc.*, 916 (1934).

(10) Huber, *Ber.*, **71**, 729 (1938).

The authors are indebted to Dr. Robert Heggie for valuable suggestions and aid in the spectroscopic measurements. This is the first article of a program of research on the synthesis of vitamins A and D, support of which is derived through contributions from Abbott Laboratories, Eli Lilly and Company, Merck and Co., Inc., Parke, Davis and Company, and the United Drug Company, such contributions being made through the Research Corporation of New York.

Summary

1. A successful synthesis has been accomplished for the triene, 3-[2′-methylenecyclohexylidene-1′]-propene-1, which possesses a conjugated system identical with that present in all antirachitic vitamins.

2. The molecular extinction coefficient of this triene is nearly identical with that reported for the antirachitic vitamins.

3. Work is being continued with the ultimate goal of synthesizing an antirachitic vitamin.

CAMBRIDGE, MASS. RECEIVED JULY 1, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. LXX.* The Steroid Content of Mares Pregnancy Urine

BY RUSSELL E. MARKER AND EWALD ROHRMANN

In a previous paper[1] from this Laboratory it was pointed out that the ratios of pregnanediol-3(α)-20(α), *allo*-pregnanediol-3(α)-20(α) and *allo*-pregnanediol-3(β)-20(α) which occurred in human and cows pregnancy urine and in bulls urine appeared to be constant. The figures reported for mares pregnancy urine were arbitrarily based upon the amount of *allo*-pregnanedione[2] obtained from the oxidation of the total carbinol fraction and from this it was assumed that the observed ratio of the occurrence of the various pregnanediols held for all pregnancy urines. Both pregnanediol-3(α),20(α)[2] and *allo*-pregnanediol-3(β)-20(α)[3] have been isolated while *allo*-pregnanediol-3(α),20(α) was assumed to be present from the amount of *allo*-pregnanedione obtained by oxidation of the total carbinol fraction.

Because of the large amount of tar present in mares pregnancy urine the isolation of the pregnanediols by the methods used to work up other urines is extremely difficult and this fact has greatly delayed a quantitative investigation of this urine. Recently we have obtained indications that mares pregnancy urine differs considerably from the other urines studied, especially in regard to the ratio of pregnanediols present. In order to obtain more quantitative information concerning these substances we have undertaken the present investigation of the carbinol fraction from 10,000 gallons of mares pregnancy urine.

The results obtained show a remarkable difference between mares pregnancy urine and other urines as is shown in the following table.

APPROXIMATE AMOUNTS INDICATED IN MG. PER GALLON OF URINE

	Pregnanediol-3(α), 20(α)	*allo*-Pregnanediol-3(α), 20(α)	*allo*-Pregnanediol-3(β), 20(α)
Human pregnancy	50	25	6
Cow pregnancy	25	15	3
Bull	100	50	12
Mare pregnancy	3	2	25

The crude carbinols from 10,000 gallons of hydrolyzed mares pregnancy urine from which the ketones were previously removed with Girard's reagent were separated from the hydrocarbons by means of the half phthalates and the entire carbinol fraction precipitated with an excess of digitonin to separate the steroids epimeric at C-3. The material precipitated by digitonin consisted largely of uranediol-3(β),11[4] and *allo*-preganediol-3(β),20(α) together with a new substance of the composition $C_{48}H_{82}O_3$. This latter substance appears to be a molecular compound of cholesterol and uranediol-3(β),11 since oxidation of the product yielded uranedione while treatment with acetic anhydride yielded cholesteryl acetate.

The carbinol fraction which did not precipitate with digitonin was oxidized under mild conditions with chromic anhydride and the ketones separated with Girard's reagent. The ketonic material yielded some pregnanedione and *allo*-pregnane-

(*) Paper LXIX, Marker and Rohrmann, THIS JOURNAL, **61**, 2072 (1939).

(1) Marker, Wittle and Lawson, *ibid.*, **60**, 2931 (1938).

(2) Marker, *et al.*, *ibid.*, **59**, 2297 (1937).

(3) Marker and Rohrmann, *ibid.*, **60**, 1565 (1938).

(4) Marker, Rohrmann and Wittle, THIS JOURNAL, **60**, 1561 (1938).

dione in addition to a new compound of the composition $C_{18}H_{16}O_2$, m. p. 214°. This substance which is evidently an unsaturated diketone formed only a monosemicarbazone, which suggests that the substance may be 3-desoxy-11-keto-equilenin. We are planning to investigate the nature of this compound and its possible origin more fully when more of the substance becomes available.

We have also obtained evidence of the presence of urenetriol and of a new *allo*-pregnanetriol in the digitonin precipitable fraction (*cf.* flow sheet, ref. 4, p. 1563). The bromination and mild oxidation with chromic anhydride of two fractions of non-sublimable carbinols[4] gave in one case urenetrione identical with that prepared from uranetrione[5] while the other fraction yielded a new trione, m. p. 129°. This trione upon Clemmensen reduction gave *allo*-pregnane.

Examination of the ligroin soluble fraction referred to in a previous paper (*cf.* flow sheet, ref. 4, p. 1563) yielded the characteristic urinary hydrocarbon of the composition $C_{28}H_{58}$ identical with that previously reported from other urines,[6,7] together with cholesterol and equistanol.[1,3,8]

It seems strange that cow pregnancy urine and bull urine should resemble human pregnancy urine so closely in regard to the ratio of the various pregnanediols present, while mares pregnancy urine, which one might expect to resemble cow pregnancy urine in composition, is so widely different from all the urines so far studied. Mares pregnancy urine differs from the other urines studied not only in regard to the ratio of the pregnanediols present but also by its extreme complexity, as is shown by the large number of substances which have been isolated from it and from the large amount of tarry products of unknown nature which are present. In view of these facts we feel that the investigation of the urines of a number of animal species may give highly interesting results. The fact that equistanol appears to be present in most animal urines but not in human urine may be of great importance and a further investigation of the occurrence and nature of this substance seems highly desirable.

This investigation was supported by a grant from the Committee for Research in Problems of Sex, National Research Council. We wish to thank Parke, Davis and Company for the supply of urine concentrate used and their coöperation in various phases of this work.

(5) Marker, *et al.*, THIS JOURNAL, **60**, 1061 (1938).
(6) Marker, *ibid.*, **60**, 2442 (1938).
(7) Marker, *ibid.*, **61**, 1287 (1939).
(8) Marker, Lawson, Rohrmann and Wittle, *ibid.*, **60**, 1555 (1938).

Experimental Part

Digitonin Precipitation.—The neutral extract of 10,000 gallons of mares pregnancy urine after hydrolysis with hydrochloric acid, followed by steam distillation with an excess of sodium hydroxide and removal of the ketones by Girard's reagent, weighed 5.2 kg. The pregnanetriol and uranetriol were removed as previously described.[9]

The residue was dissolved in 2 liters of hot acetic acid and poured into 50 liters of ether. The ethereal solution was washed well with water and then stirred with an excess of aqueous sodium hydroxide solution. A large amount of tar, which upon burning left a large inorganic residue, separated out and was discarded. The ethereal solution was washed well with water and the ether removed. The residue was dried by distilling benzene from it. This was then heated on a steam-bath with 1500 cc. of pyridine and 1500 g. of phthalic anhydride for one hour. Ether and ice were added, and the pyridine removed by shaking with hydrochloric acid. The ethereal solution was shaken with an excess of potassium carbonate solution to remove the phthalic esters. These were hydrolyzed by refluxing with alcoholic potassium hydroxide. The carbinol fraction weighed 2.3 kg.

This was dissolved in alcohol and a 2% solution of alcoholic digitonin added until no more digitonide separated. This required a total of 2100 g. of digitonin for the complete precipitation. The digitonides were washed well, dried and decomposed by heating on a steam-bath with 10 liters of dry pyridine until dissolved. This was poured into an excess of ether and filtered from the precipitated digitonin. The pyridine was removed by washing with dilute hydrochloric acid and the ether was evaporated. The residue consisting of digitonin precipitable sterols was dissolved in 500 cc. of benzene.

The Carbinol Fraction Non-Precipitable by Digitonin.—The filtrate from the digitonide precipitation was evaporated, but due to the large amounts of aliphatic carbinols present resisted separation. The concentrate was dissolved in acetic acid and vacuum evaporated several times to remove any alcohol. The residue was then dissolved in 20 liters of acetic acid, cooled to 20° and 3 kg. of chromic anhydride dissolved in 3 liters of water and 5 liters of acetic acid slowly run in with stirring over a period of two hours, keeping the temperature at 20°. It was stirred for an additional hour. Ether and water were added and the ethereal solution washed with water and dilute alkali. The ether was removed and the ketones separated by means of Girard's reagent to give 215 g. of material. Upon steam distillation 75 g. of volatile ketones was removed. The ketones which did not steam distil were extracted with ether and upon concentration to 300 cc. and cooling 5.2 g. of material was obtained. This was sublimed in high vacuum at 140° and the sublimate was crystallized from acetone, methyl alcohol and ethyl alcohol to give a product of m. p. 212–214°. It

(9) Marker, *et al.*, *ibid.*, **60**, 210 (1938).

gave a depression in melting point when mixed with uranetrione and *allo*-pregnanedione.

Anal. Calcd. for $C_{18}H_{16}O_2$: C, 81.8; H, 6.1; mol. wt., 264. Found: C, 82.0, 81.6; H, 6.1, 6.0; mol. wt., (Rast), 248.

Upon heating with semicarbazide hydrochloride and sodium acetate in alcohol for two hours, it gave a semicarbazone which was crystallized from 80% ethanol to give a product, m. p. 255–260° dec. It analyzed for a monosemicarbazone.

Anal. Calcd. for $C_{19}H_{19}N_3O_2$: C, 71.0; H, 5.9. Found: C, 71.4; H, 5.9.

The ketones from the mother liquors of the above product were sublimed in high vacuum, collecting the fraction from 100–220°. These were dissolved in two liters of alcohol and refluxed for two hours with 100 g. of semicarbazide hydrochloride and 120 g. of sodium acetate. The extremely insoluble semicarbazone decomposed at about 320°. This product (21 g.) was hydrolyzed with sulfuric acid and the product crystallized from methanol, ethanol and acetone to give white crystals, m. p. 200–201°; yield 12 g. It gave no depression in melting point when mixed with *allo*-pregnanedione.

The filtrates from the above semicarbazone were combined and recrystallized. The first fraction upon acid hydrolysis gave a further quantity of 1.4 g. of *allo*-pregnanedione. The next fraction of semicarbazones gave only oily products which could not be separated. The following fraction, after hydrolysis of the semicarbazone and sublimation, was crystallized from dilute ethyl alcohol after seeding with a crystal of pregnanedione. It was recrystallized to give 21 g. of pregnanedione, m. p. 117–119.5°, which gave no depression in melting point when mixed with an authentic sample of pregnanedione.

The Digitonin Precipitable Sterols.—This fraction was dissolved in an equal quantity of benzene and allowed to stand at room temperature for one week. The precipitate which formed was filtered and crystallized from acetone. After treatment with Norite this product was crystallized from methanol to give 25 g. of compact white crystals, m. p. 210–212°. This gave no depression with a sample of uranediol obtained previously from mares urine.

The filtrate remaining after the separation of the crude uranediol was evaporated and the semicrystalline product crystallized repeatedly from ethyl acetate to give white flaky needles, m. p. 191–192.5°. The mixture with uranediol melted from 189 to 205°. The product sublimed unchanged in high vacuum at 120–160°.

Anal. Calcd. for $C_{21}H_{36}O_2 \cdot C_{27}H_{46}O$: C, 81.5; H, 11.7; mol. wt., 706. Found: C, 81.6, 81.5, 81.5, 81.4; H, 11.8, 11.5, 12.0, 11.9; mol. wt. (Rast), 363.

When refluxed for thirty minutes with acetic anhydride the product yielded an **acetate** which crystallized from aqueous acetone as white plates, m. p. 111–113°. This gave no depression with an authentic specimen of cholesteryl acetate.

Anal. Calcd. for $C_{29}H_{48}O_2$: C, 81.2; H, 11.3. Found: C, 81.2, 81.5, 81.2; H, 11.6, 11.3, 11.4.

When oxidized with chromic anhydride in acetic acid at room temperature for one hour the substance yielded a product which after treatment with Norite crystallized from ether–pentane as white crystals, m. p. 177–178°. This gave no depression with a sample of uranedione.

Anal. Calcd. for $C_{21}H_{32}O_2$: C, 79.7; H, 10.2. Found: C, 79.4; H, 10.0.

The total sterol fraction remaining after removal of the uranediol and most of the uranediol–cholesterol compound was sublimed in high vacuum, the material distilling at 100–220° being collected. The sublimate was dissolved in 5 liters of acetic acid and the solution oxidized with 200 g. of chromic anhydride at 20° for three hours. The mixture was diluted with water and the precipitated solid taken up in ether and washed with sodium carbonate solution. Partial evaporation of the ether gave 205 g. of solid which after crystallization from methanol and acetone gave 165 g. of white crystals, m. p. 197–200°. This gave no depression in melting point with *allo*-pregnanedione.

The combined filtrates from the above yielded an additional 44 g. of *allo*-pregnanedione as well as a small amount of material which was crystallized from ethanol, acetic acid, methanol and acetone to give white crystals, m. p. 245–248°. Upon heating to 255° gas was evolved. The product, which analyzes for a hydroxy ketone, was recovered unchanged after refluxing with acetic anhydride.

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.2; H, 10.8. Found: C, 79.2, 79.2; H, 11.1, 11.2.

Oxidation of Residue from Carbinol Mixture C. (*Cf.* flow sheet, ref. 4, p. 1563.)—The portion of carbinol mixture C which would not sublime at 200° was dissolved in acetic acid and a slight excess of bromine added to prevent oxidation of unsaturated compounds. To this solution was added an excess of chromic anhydride in 90% acetic acid and the mixture was allowed to stand at room temperature for ninety minutes, after which 10 cc. of methanol and 5 g. of zinc dust was added. After heating for thirty minutes on the steam-bath the mixture was filtered and the filtrate diluted with water. The precipitated solid was taken up in ether and the product sublimed in high vacuum, the product distilling at 140–160° being collected and crystallized from methanol to give short thick needles, m. p. 127–129°.

Anal. Calcd. for $C_{21}H_{30}O_3$: C, 76.3; H, 9.2. Found: C, 76.2; H, 9.1.

When treated with semicarbazide acetate under the usual conditions, the substance yielded a **semicarbazone** melting above 300°.

Anal. Calcd. for $C_{23}H_{36}O_3N_6 \cdot {}^1/_2H_2O$: C, 60.9; H, 8.3; N, 18.6. Found: C, 60.9, 60.8; H, 8.4, 8.3; N, 19.3.

A solution of 75 mg. of the ketone in 25 cc. of acetic acid was treated with 10 g. of amalgamated zinc and 25 cc. of concentrated hydrochloric acid and the mixture refluxed for three hours. The mixture was extracted with ether and the product crystallized from acetone–methanol to give white crystals, m. p. 80–82°. This gave no depression with an authentic sample of *allo*-pregnane.

Urenetrione from Residues of Carbinol Mixture A. (*Cf.* flow sheet, ref. 4, p. 1563).—The residue remaining after the high vacuum sublimation of carbinol mixture A at 200° was dissolved in 50 cc. of glacial acetic acid. A slight excess of bromine was added and the solution was oxidized with 3 g. of chromic anhydride as described in the

previous experiments. The oxidation product was sublimed in high vacuum at 130° and the sublimate crystallized from methanol as pale yellow plates, m. p. 192°. This gave no depression with a sample of urenetrione (m. p. 195°).

Anal. Calcd. for $C_{21}H_{28}O_3$: C, 76.8; H, 8.6. Found: C, 76.7; H, 8.5.

Ligroin Soluble Fraction.—The ligroin soluble material corresponding to 1000 gallons (3700 liters) (*cf.* flow sheet, ref. 4, p. 1563) was used. The ligroin was evaporated *in vacuo* and the residual tar taken up in 350 cc. of hot 95% ethanol. The solution was cooled at 0° and the white crystals collected, washed with ethanol and crystallized from ethyl acetate after treatment with Norite to give greasy white plates, m. p. 64°. This gave no depression with samples previously reported from human and cows pregnancy urine.

Anal. Calcd. for $C_{28}H_{58}$: C, 85.3; H, 14.8. Found: C, 85.1; H, 14.8.

The filtrate from the above containing the ethanol soluble material was made up to a volume of 500 cc. with 95% ethanol and the solution was precipitated with digitonin (13 g.) to yield 12 g. of dried digitonide. This was decomposed with pyridine in the usual manner and the product was crystallized from ethyl acetate to give white plates, m. p. 146°, which gave no depression with a sample of cholesterol.

The filtrate remaining after removal of part of the cholesterol was made up to a volume of 50 cc. with 95% ethanol and treated with a slight excess of bromine in ethanol solution. To the resulting solution at 25° was added a solution of 2 g. of digitonin in 40 cc. of ethanol and 8 cc. of water at 25°. The mixture was kept at 3° for twelve hours. The digitonide was collected, washed, dried and decomposed with pyridine. The product was crystallized from acetone to give white plates, m. p. 132°. This gave no depression with a sample of β-equistanol.

Summary

Mares pregnancy urine has been found to differ from other urines in the proportion of the three pregnanediols present, *allo*-pregnanediol-3(β),20-(α) being present in considerable amounts while only small amounts of pregnanediol-3(α),20(α) and *allo*-pregnanediol-3(α),20(α) are present.

State College, Penna. Received July 7, 1939

[Contribution from the Department of Chemistry, Stanford University]

The Sorption of Methylene Blue by Curd Fibers of Sodium Palmitate

By J. W. McBain, Josephine M. McDowell and Margaret E. Worden

Soap curd fibers account for the whiteness and much of the opacity of many commercial soaps. They are formed in characteristic manner when a solution of pure sodium palmitate is cooled and sets to a solid white mass, or curd, consisting of a fine mesh of these fibers of hydrated neutral soap enmeshing any excess of liquid or solution. They possess some remarkable properties. X-Ray examination clearly shows them to be crystalline, with rows of double molecules placed at right angles to the long axis of the fiber. However, although they may grow to be as much as several centimeters long, microscopic and ultramicroscopic examination shows them to be made up of bundles of very much finer fibers.

It is the purpose of the present study to obtain information as to the actual size of these curd fibers by measuring the superficial area available for the sorption of methylene blue from solution. It is also of interest to find whether such a dye is incorporated within the fibers or, as seems to be the case, lies upon their external surface. Furthermore, this method of study yields information as to changes, such as aging, that take place in curd fibers. Some progress also has been made toward characterizing the differences between curd fibers separating from concentrated and from dilute solution.

Materials.—The sodium palmitate was the special preparation by Kahlbaum, found by analysis to be exactly neutral, that was used by McBain, Vold and Jameson[1] in their recent phase rule study. It was dried at 105° and all solutions were made up by weight. The methylene blue chloride was from the Eastman Kodak Company. Its concentration in the aqueous liquid was determined colorimetrically.

Sodium palmitate although highly soluble at temperatures above 60 to 70° is almost completely insoluble at room temperature, the mother liquor containing only the slightest trace of palmitate in addition to a few thousandths or a few hundredths normal sodium hydroxide as will be described later. Its hydration although large and variable does not appreciably affect the calculation of the amount of sorption. The mother liquor enmeshed in the curd is readily released by mechanical means when the concentration is 0.025 *N* or less. In higher concentrations it is generally possible to cause the apparently hard curd to soften and syneresе by merely rotating the bottle to and fro for a short time, a striking (as yet unnamed)[2] phenomenon which is the opposite of "rheopexy."

(1) J. W. McBain, R. D. Vold and W. T. Jameson, This Journal, **61**, 30 (1939).

(2) *Cf.* ultrasonic effects on sodium stearate curds; Freundlich and Gillings, *Trans. Faraday Soc.*, **34**, 657 (1938).

Method.—Two general types of experiment were employed. In the first or "*in situ*" experiments the dye is added to the hot solution so that the fibers form on cooling to 25° in the presence of the dye. In the more usual type of experiment with "preformed" fibers the curd is first made and only then is the dye presented to the already formed curd. The solution of the dye is mixed as well as possible with the white curd. Both procedures could be varied because in the *in situ* experiments the curd fibers could be formed either from concentrated solution in the presence of the methylene blue and subsequently diluted for observation and analysis, or all of the three constituents could be added initially in one homogeneous solution. Similarly with preformed fibers, these can be kept to any desired age before adding methylene blue and may be diluted either before or afterward. The final dilution was generally $N/20$, $N/24$ or $N/40$. Seventy-three experiments were set up (mostly by J. M. M.) and the observations then extended from the period of initial mixing up to an age of as much as a year.

A standard solution of methylene blue did not fade on prolonged standing; but all experiments were made up from solid dye. A blank experiment showed that addition of sodium hydroxide to make the *p*H equal to 10 does not affect the color of methylene blue. As will be seen later, however, it does affect the amount of sorption.

The Experimental Results

In the first few experiments only 0.086 g. of methylene blue was added to 0.695 g. of sodium palmitate, the initial concentration for the preformed soap being $N/20$, being diluted with the methylene blue solution to $N/24$, the concentration of the *in situ* solutions from the beginning. Practically all (99.6%) of the methylene blue was sorbed in all cases, the final value of x/m being 0.123 g. of methylene blue per gram of sodium palmitate, leaving a concentration of 0.0006 g. of methylene blue per 100 g. of water in solution, but at least four months were required for the final value to be obtained. When the amount of methylene blue was raised to 0.43 g., again the sorption was almost complete ($x/m = 0.617$) with but little difference between *in situ* and preformed experiments, except that the former reached equilibrium more quickly. After the first few weeks noticeable desorption set in again in both cases.

In most of the experiments subsequent to the first four groups just summarized, 1.25 to 2.5 g. of methylene blue was used with 0.695 g. of sodium palmitate, and the methylene blue was found to be fairly divided between the curd fibers and the solution. All these experiments were carried out at 25.0°.

In Situ Experiments.—It is very interesting that sorption by the *in situ* fibers is not completed as soon as the fibers are fully formed in the presence of the methylene blue. Instead, it required a period of hours or days for maximum sorption which afterward fell off again during the next few months.

It may therefore be concluded that sorption in *in situ* fibers does not consist of incorporation of methylene blue within the interior or as an integral part of the fiber. It must be upon the external surfaces of the fiber. This is borne out by the fact that there is little difference between the results with *in situ* and with preformed curds. This is in contrast with the finding of Brocklesby and Kuchel[3] that the oil-soluble vitamin A is sorbed to the extent of 39% by soaps formed *in situ* as compared with only 6% by preformed soaps. Finally, it is clear that the *in situ* curds first formed are unstable in respect either to composition or to size or to both, and that they then recrystallize with less surface.

A typical *in situ* experiment (no. 28) gave the following results: 2.5 g. of methylene blue in 25 g. of water with the *p*H adjusted to 10 by addition of solid sodium hydroxide was added to 0.695 g. of sodium palmitate in 25 g. of water, the $N/20$ solution after cooling to room temperature being diluted to $N/40$. The *p*H of the diluted mixture was also found to be 10. The values of x/m in grams of methylene blue sorbed per gram of sodium palmitate were

15 min.	4.5 hrs.	1 day	3 days	5 days
1.5	1.8	2.0	2.0	1.8
7 days	14 days	23 days	31 days	159 days
1.7	1.4	1.5	1.4	0.8

The maximum value averaged from three series with $N/20$ curd was 2.2 attained after several days, the concentration of equilibrium liquid being 1.01 g./100 g. of water, and the total methylene blue sorbed being 60%. In another experiment x/m had fallen to the value 1.2 in eighty-five days and to 0.4 in one hundred and eighty-one days; but in yet another it was still 1.2 at two hundred and one days.

Without alkali the maximum value of x/m is much less; namely, for solutions originally $N/20$ then diluted as above to $N/40$, it is 1.5. With the solution originally $N/4$ diluted to $N/40$, it is 2.1, and if originally N it is 2.8. In all cases the maximum value is attained after a few days, experiments being quicker than those with preformed curds, partly because in the latter experiments the

(3) H. N. Brocklesby and C. C. Kuchel, *J. Biol. Chem.*, **123**, xvi, May (1938).

methylene blue had to diffuse into the interstices of the solid mass.

The value finally attained after several months with $N/20$ and $N/4$ diluted to $N/40$ is 1.3 in equilibrium with a concentration of 1.6 g. of methylene blue per 100 g. of water, only 36% of the total dye being sorbed. Thus 7 and 24%, respectively, has been desorbed, since the middle of the first week. On the other hand, the solution that was originally normal desorbs the same amount in three months, but x/m is still at the high value of 2.1. Bennett[4] has proved that the curd that separates from a normal solution of sodium palmitate is for some time definitely different from that separating from the more dilute solutions (*cf.* final section of this paper).

Preformed Curd.—All the remaining experiments were carried out with preformed curd. Sorption reaches a maximum in seven days and falls off again for several months.

With 0.43 g. of methylene blue practically the whole of the dye is sorbed, making x/m 0.62. The initial stages are slower when the curd is more concentrated or when more alkali is added. It is significant that desorption is inappreciable, x/m retaining 99.6% of its maximum value even after one hundred and fourteen days, and 99% after two hundred and forty-five days, showing that there is not more than enough dye to saturate the new curd formed by recrystallization. The same result is observed with *in situ* experiments.

With 1.25 g. of methylene blue and solutions originally $N/20$, $N/4$ and N diluted to $N/40$ typical results for x/m were:

Original	15 min.	19 hrs.	1 day	7 days
$N/20$	0.4	1.0	1.0	1.1
$N/4$	.15	0.9	0.9	1.1
N	.05	1.0	1.0	1.1
Original	14 days	84 days	197 days	382 days
$N/20$	1.0	0.76	0.72	0.55
$N/4$	1.0	.76	.70	.57
N	1.0	.76	.66	.56

With 1.8 g. of methylene blue the values of x/m were:

Original	10 min.	2 hrs.	1 day	
$N/20$	0.75	0.99	1.0	
$N/4$	.16	.74	1.1	
N	.002	.28	0.8	
Original	7 days	21 days	140 days	216 days
$N/20$	1.1	0.8	0.75	0.25
$N/4$	1.1	.7	.70	.56
N	1.1	.8	.58	.23

(4) H. B. Bennett, *J. Chem. Soc.*, **125**, 1971 (1924); see also M. Laing McBain, *ibid.*, **117**, 1524 (1920).

Solutions with 2.5 g. of methylene blue were studied more thoroughly with and without added alkali, again using N, $N/4$ and $N/20$ curds diluted to $N/40$. Without alkali, the maximum reached in seven days was $x/m = 1.2$, in every case, falling to a value of 0.4 after six or seven months. At twenty-four days the *p*H was 7.56. With added alkali the maximum value is increasingly larger, being 1.4 for addition of 0.12 N sodium hydroxide, 1.6 with 0.024 sodium hydroxide (*p*H of the mixture being 7.83 at two hundred days), 1.8 for *p*H maintained at 10, and 2.2 for *p*H of the added methylene blue being 11.5. The final value, however, with alkali, is not so increased, but again tends to 0.4 or less.

For $x/m = 1.2$ the concentration of the equilibrium solution is 1.66 and only 34% of the methylene blue is sorbed.

Discussion

It appears that the sorption of dye by sodium palmitate curd fibers is largely or wholly external, as is evident from the time required for sorption even with curds formed *in situ* in presence of the dye, and the similarity of the maximum sorption with preformed and *in situ* curds. Acid soap formed by interaction with the methylene blue hydrochloride sorbs less than soap that has been preserved by keeping the *p*H sufficiently high. The effect of added alkali is to increase the sorption even when no acid soap is present. Most of the excess dye is sorbed until the surface is nearly saturated and thereafter any excess added accumulates in the solution.

Some idea of the extent of the surface may be derived from the numerical results for the saturation value of x/m. Methylene blue has been used since the experiments of Paneth and collaborators to measure approximately the extent of accessible surface on the assumption that 1 mg. of methylene blue indicates 1 square meter. although Bancroft and Barnett[5] have shown that at least over a certain range the results are much affected by the value of *p*H. Gorter[6] found at *p*H 1 and again at the isoelectric point 1 mg. of various proteins cover 1 square meter. Voet[7] found 1.25 mg. of Night Blue to be sorbed per square meter.

The exterior surface of fibrous colloids is of special significance. For example, when 70%

(5) "Colloid Symposium Monograph," **6**, 73 (1928).

(6) Gorter, van Ormandt and Meijer, *Biochem. J.*, **38**, 29 (1935); see also Seaston, *J. Gen. Physiol.*, **21**, 621 (1938).

(7) Voet and Van Elteren, *Rec. trav. chim.*, **56**, 923 (1937).

of a cellulose fiber is acetylated, it has been calculated[8] that all of the triacetate would be on the micellar surface as a monomolecular layer.

Similarly, Dr. F. Olsen (private communication) has found that the solubility of nitrocellulose depends solely upon the adjustment of the nitrogen on the exterior.

Size and Shape of Palmitate Curd Fibers.—The data here obtained enable us to reach rather definite conclusions as to the size and shape of the sorbing solid in sodium palmitate curd.

It appears that we must conclude that if x/m can be as great as 1.5, it would require sheets of sodium palmitate to be only 13 Å. thick, an impossibly low value when it is remembered that to satisfy the X-ray data the molecules would have to be laid end to end almost normal to the surface. However, if the fibers are square rods, the indicated area corresponds to breadth and thickness each of 27 Å. It is clear therefore that the fibers are not more than two molecular lengths thick and they must be rod-like or even narrower and lath-like. Even if the methylene blue molecules lay parallel to the exposed sodium palmitate molecules, this would indicate that the cross section of the rod would consist of not over twenty-two sodium palmitate molecules. The subdivision of the curd into fibers is thus carried to an excessive extent, which is still so great even after very many months of standing that one must conclude that sorption occurs on the primary ultramicroscopic fibers.

A similar result follows from the assumption (Dr. M. J. Vold) that the methylene blue molecules are attached in a continuous coating in vertical orientation to the exposed carboxylate ends of the soap molecules; one methylene blue (mol. wt. 319) to each soap molecule (mol. wt. 278). However, as has been noted, especially in the presence of alkali, the amount of methylene blue may sometimes be twice even this value.

Similarly, Mrs. McBain[9] found that 7% of the molecules in insoluble curd fibers from 1 N_W sodium palmitate are ionized and conducting; this would appear to set a minimum value for the exposed molecules unless the conduction could occur through the lattice also.[10]

The reduction of available area of a crystalline precipitate of colloidal dimensions has been ascribed to one or all of three causes: (a) perfection of an originally imperfect surface of a primary particle, improbable in the present case, (b) cementing of the primary fibers to ultramicroscopic bundles, and (c) actual recrystallization to coarser particles.

The Solubility and Hydrolysis-Alkalinity of Sodium Palmitate Curds of Different Concentrations and Ages.—Since Bennett[4] had shown that solubility and hydration of sodium palmitate curd fibers initially obtained from 1.0 and 0.25 N solution differed greatly, a few further determinations of solubility were made. First it was shown that the mother liquors differed in refractive index, but they contained sodium hydroxide as well as soap. Hence the method adopted was to isolate a known quantity of mother liquor by filtration using suction or a Carver press as necessary. This mother liquor was then analyzed by treating with a known amount of standard hydrochloric acid, filtered and the filtrate treated to give total sodium and the residue titrated in neutralized 80% alcohol with sodium hydroxide to measure total fatty acid. The results are given in Table I. It may be noted that the fibers began to form at about 67° from the 1.0 N_W solution, 58° from 0.25 N_W and 50° from 0.05 N_W.

TABLE I

THE COMPOSITION OF THE MOTHER LIQUORS OF SODIUM PALMITATE CURDS AT 25°

Expressed in molalities × 10^4 of total sodium, total palmitate and therefore excess of free sodium hydroxide.

Concn.,	1 day			4–8 days			40–44 days		
N	Na	NaP	NaOH	Na	NaP	NaOH	Na	NaP	NaOH
0.05	35	18	17	30	13	17	29	9.8	19
.05	36	16	20	31	14	17	30	9.6	20
.1	..	..	..	19	12	7	..	..	..
.1	37	26	11	16	11	5	..	..	..
.1	40	19	21	..	..	..	53	12	41
.1	41	..	..	..	..	..	50	13	37
.25	63	18	45	63[a]	15[a]	48[a]	76	11	65
.25	57	23	34	..	..	..	..	..	..
.25	47	15	32	69	20	49	..	..	..
.25	62	22	40	..	..	..	94	15	79
.25	66	23	43	..	..	..	84	14	70
1.0	229	22	207	264	19	245	..	..	..
1.0	166	15	151	250	11	239	..	..	..
1.0	236	19	217	272	14	258	..	..	..

[a] 2 days.

The analytical data in Table I serve to emphasize that curd fibers separating from higher concentrations of pure sodium palmitate in water may be slightly more soluble but are very much more alkaline than those which come out from

(8) Centold, *Gazz. chim. ital.*, **65**, 1021 (1935).

(9) M. E. Laing McBain, *Trans. Faraday Soc.*, **31**, 164 (1935).

(10) Carnegie Inst. Wash., Geophysical Laboratory, publication No. 990, pp. 15–16.

more dilute solution. However, the solubility of all the curds definitely decreases with time, being on an average 0.0020, 0.00145 and 0.0012 N for one day, one week and one and one-half months, respectively, all four curds being then 0.0012 N with respect to total palmitate in solution.

The solubilities recorded by Bennett[4] were the mean of total palmitate and total sodium, but it is now clear that these two quantities should have been kept separate since alkalinity and solubility change independently, and are very different for different curds.

The alkalinity is most striking. Since 1910 we have had occasional indications that the formation of curd is accompanied by the development of alkali. The mother liquors of the stronger curds are now found to be more alkaline than any actual solution of soap is ever found to be, and the alkalinity is maintained. The alkalinity of a 1 N curd is ten times and that of a $N/4$ curd twice that of a dilute curd. Furthermore, the alkalinity increases with time for all the stronger curds. The sodium palmitate from which the curds were derived was exactly neutral in composition. Hence curding is accompanied by definite and appreciable hydrolysis, possibly an example of membrane equilibrium or ion exchange on the exposed surface of the fibers. The pH of a fifteen-year old specimen of $N/20$ sodium palmitate was 9.2.

Summary

Curd fibers of sodium palmitate sorb methylene blue to about the same extent when dye is added to fibers already formed and to those which form in presence of the dye. Since in both cases time is required to complete the sorption, it is evident that sorption is largely external upon the surface of the excessively fine primary ultramicroscopic crystalline fibers. After a week the weight and number of dye molecules sorbed exceeds the weight and number of sodium palmitate molecules. Thereafter the sorption distinctly diminishes and after a year may be only one-third, without any indication that a final value is yet attained, although the fibers must still be less than 100 Å. in diameter.

The solubility of curd fibers formed from concentrated solution is at first only slightly greater than those from dilute solutions, but all diminish to about the same extent with time.

The alkalinity of the stronger curds is far greater than that of any soap solution and it is ten times larger for a 1 N curd than for a 0.05 N curd, although the latter falls in the course of years to pH 9.2.

STANFORD UNIV., CALIF. RECEIVED JUNE 26, 1939

[CONTRIBUTION FROM THE DIVISION OF CHEMISTRY, NEW YORK STATE AGRICULTURAL EXPERIMENT STATION]

Pectic Enzymes. IV. Structural Considerations in Connection with the Enzymic Hydrolysis of Pectins[1]

BY Z. I. KERTESZ

The high viscosity of aqueous solutions of pectins attracted attention over a hundred years ago but no satisfactory theory has been proposed as yet to explain the physical properties of pectins in the light of our present knowledge of their chemical composition. The final disproval of Ehrlich's tetragalacturonic acid theory[2] paved the way for renewed activity in this field. By the use of various concentrations of ethanol,[3] arabans and galactans[4] may be removed from the crude pectin preparations. The resulting compound (a true pectin composed almost exclusively of galacturonic acid anhydride residues with CH_3O present as ester in most carboxyl groups) lends itself well for investigations of the relation between physical and chemical properties.

Without having conclusive evidence on hand and reasoning mostly by analogy, the chains of galacturonic acids have been regarded by most investigators as being responsible for the viscosity of pectins. Accordingly the loss of viscosity under certain conditions has been attributed to the decomposition of the polygalacturonic acid chains.

(1) Approved by the Director of the New York State Agricultural Experiment Station as Journal Paper No. 327, April 1, 1939. Presented at the Baltimore meeting of the American Chemical Society, April, 1939.

(2) Ehrlich, *et al.*, *Biochem. Z.*, **168**, 263 (1926); **169**, 13 (1926); **212**, 162 (1929); etc.

(3) Henglein and Schneider, *Ber.*, **69**, 309 (1936); Schneider, *et al.*, *ibid.*, **69**, 2530 (1936); **69**, 2537 (1936); **70**, 1611 (1937); **70**, 1617 (1937); **71**, 1553 (1938).

(4) Hirst and Jones, *J. Chem. Soc.*, 454–460 (1939).

Based upon such reasoning Mehlitz and Scheuer[5] proposed a method for the determination of the enzymic hydrolysis of pectins by the changes which occur in the viscosity.

A study of the enzymic decomposition of pectins has been in progress at this Laboratory for several years.[6] The results obtained here never indicated a close relationship between changes in the viscosity and the decomposition as measured chemically. A systematic study of this problem was therefore undertaken to explain this discrepancy. The results obtained are presented herewith.

Experimental Methods

The viscosity determinations were performed at 30.0°, using Ostwald viscosity pipets. In the experiments yielding the data presented in Fig. 1 and Fig. 3 the viscosity determinations were made as follows. When the

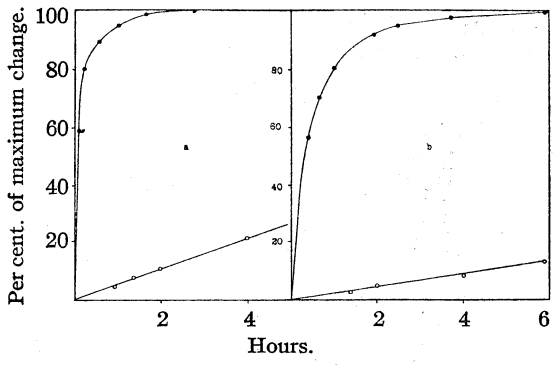


Fig. 1.—Changes in the viscosity (●), and reducing power (○), of pectin solutions during hydrolysis by 0.10% enzyme (a) and 0.05% enzyme (b).

reaction mixtures were made up from the prewarmed components and mixed, 3 cc. was pipetted immediately into the Ostwald pipet, which had been placed in the bath more than half an hour earlier. The determinations were started about three minutes later. The values obtained for the relative viscosity represent the average value for the period required for the outflow. In constructing the viscosity curves in Fig. 1 and Fig. 3 the viscosity values were taken as representing this average viscosity at the time of starting of the viscosity determination plus half of the time needed for the outflow.

In the case of the experiments demonstrated in Figs. 2 and 3 the pectin solution was heated in a bath of boiling water. To obtain the viscosity values for Fig. 2 the volumetric flasks holding the pectin solution were cooled at the end of the heating period and the contents made up to the original volume.

The reaction mixtures were composed of 100 cc. of pectin solution of *p*H 3.2 plus 10 cc. of 1% (filtered) commercial pectinase.[7] Only 10 cc. of 0.5% enzyme was used in obtaining Fig. 1b. Experiments reported in this paper have been repeated with different pectins giving essentially the same results. The data presented herein have been obtained on purified citrus pectin. The concentrations of the solutions used in Figs. 1, 2, and 3 were 0.854, 0.686, and 0.849%, respectively.

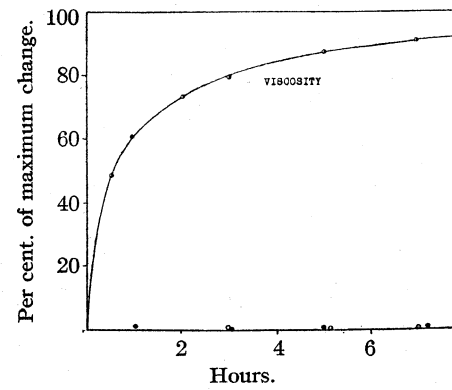


Fig. 2.—Changes in the viscosity (◑), reducing power (○), and methoxyl content (●), of a pectin solution upon heating.

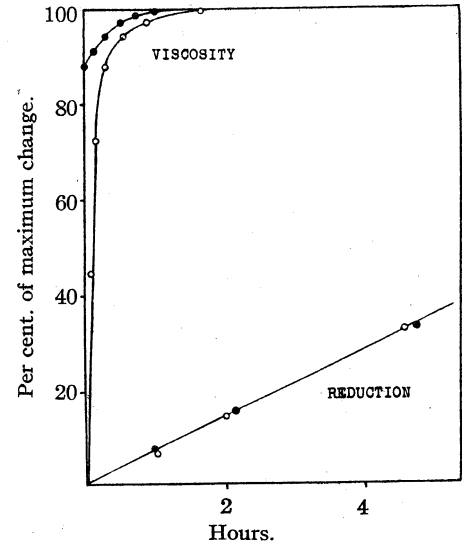


Fig. 3.—Changes in the viscosity and reducing power of unheated (○), and heated (●), pectin solutions upon enzymic hydrolysis.

The Willstätter–Schudel hypoiodide method[8] was used for the determination of the increase in the reducing power resulting from the activity of the pectin-polygalacturonase. It is essential to keep the limitations of this method in mind[9] in order to obtain dependable results. The enzymic demethoxylation was followed by titrating 10-cc. samples

(5) Mehlitz and Scheuer, *Biochem. Z.*, **268**, 355 (1934).

(6) Kertesz, *Ergebnisse Enzymforschung*, **5**, 233 (1936).

(7) For the commercial pectinase used in these experiments the author is indebted to the Röhm and Haas Company of Bristol, Penna. It was produced by precipitation with ethanol from a water extract from *Aspergillus sp.* grown on special media.

(8) Willstätter and Schudel, *Ber.*, **51**, 780 (1918).

(9) Myrbäck and Örtenblad, *Svensk Kem. Tidskrift*, **50**, 72 (1938).

of the reaction mixture with 0.1 *N* sodium hydroxide, using phenolphthalein indicator and adding 5 cc. more alkali. The excess of the alkali was titrated after one hour's standing at room temperature. One cc. of alkali consumed for the saponification equals 3.1 mg. of CH_3O split off.

The pectic enzymes available at this time are mostly mixtures of several enzymes acting upon pectin. In spite of the attempts made in this Laboratory and elsewhere,[10] no method is available as yet for the quantitative separation of the enzymes present in commercial pectinases. As a result, the action of several enzymes upon pectins is proceeding simultaneously in the reaction mixtures. The most important known chemical change occurring during the enzymic decomposition of pectins is the hydrolysis of the polygalacturonic acid chains by the pectin-polygalacturonase. Another enzyme which is present and may influence the viscosity as well as the velocity of the hydrolysis is pectin-methoxylase,[11] an esterase responsible for the splitting off of the CH_3O groups attached to most COOH groupings of pectins. It is not held likely that at the *p*H of the reaction mixtures the demethoxylation would have had a significant effect on the changes in viscosity. Furthermore, the changes which may have been caused by this enzyme would be negligible as compared with those caused by the pectin-polygalacturonase. As will be discussed later in this paper, a 1% hydrolysis of the polygalacturonic acid chains would cause approximately 33% reduction in the viscosity. A 1% demethoxylation on the other hand will cause only about 1% loss of the viscosity caused by the presence of the methyl esters.

Results and Discussion

To study the relation between the changes which occur in the viscosity and reducing power during enzymic hydrolysis, pectin solutions were exposed to the action of a commercial pectinase in two different concentrations. The results presented in Fig. 1 are expressed as percentages of the maximum possible changes. Complete hydrolysis of the structure into galacturonic acid would cause a reduction of 100, while the low initial reduction was taken as 0. Similarly the difference between the time of outflow of the original reaction mixtures and those completely decomposed was taken as 100 and the decrease observed as a fraction thereof. There is an abrupt change in the viscosity of the mixtures in the first few minutes of the reaction. The reducing power is increasing slowly and (up to the extent of decomposition shown in the figure) at a constant rate.

It is necessary at this time to consider briefly the interrelation of the changes followed by the determination of the viscosity on the one hand and by the increase in the reducing power on the other. In pectin as well as in the case of other polysaccharides some heterogeneity must be assumed with regard to the size of the molecules present (in whatever sense the word molecule may be understood). This heterogeneity is even more increased upon a limited degree of cleavage of the chains and the "average" values calculated will depend on the method of measurement as well as on the method of calculation. Determinations of the increase in the reduction (as well as all other end-group methods and also freezing point and osmotic pressure determinations) give averages defined by the expression[12]

$$M_n = \frac{1}{\Sigma f_i/M_i}$$

where f_i is the fractional weight of the constituent of molecular weight M_i and the summation is to be applied to all constituents present. This is the "number average." On the other hand, viscosity measurements give an average value for the size of the molecule according to the expression

$$M_w = \Sigma f_i M_i$$

This is a "weight average." Calculations with the possible degradation products of homogeneous polymers (as pectin is thought of, for instance) indicate that upon hydrolysis the "weight average" molecular weight or chain length as measured by the viscosity will decrease slower than the "number average" measured by reduction. A mathematical consideration of this problem will be presented elsewhere, but it may be cited here that a 1% increase in the reduction in the case of pectin should result in a halving of the "number average" molecular size while the "weight average" (and thus according to Staudinger the viscosity) should decrease only about 33%. As stated before, the experimentally observed decrease in the viscosity is more rapid than the corresponding change in the reducing power would allow according to the calculations.

If the observed changes in the viscosity are actually caused by the changes in the size of the polygalacturonic acid chains, then any decrease in the viscosity should be accompanied by a corresponding increase in the reducing power. It is known that the viscosity of pectin solutions decreases upon heating.[13] To obtain information on this matter pectin solutions were heated (at *p*H 3.2) to 100° and the changes in the viscos-

(10) Rothschild, *Enzymologia*, **5**, 359 (1938).
(11) Kertesz, *J. Biol. Chem.*, **121**, 589 (1937).
(12) Kraemer and Lansing, *J. Phys. Chem.*, **39**, 153 (1935).
(13) Myers and Baker, Univ. of Delaware Expt. Sta. Bull. No. 149 (1927).

ity (as determined at 30.0°) and reducing power and methoxyl content followed. The results, shown in Fig. 2, prove conclusively that there is no correlation between the changes in the viscosity and reducing power. There is no indication that polygalacturonic acid chains were split during the heating of the pectin solution.

There also appeared some possibility that the decrease of the viscosity may be caused by progressive demethoxylation of the pectin. It has been shown by von Fellenberg,[14] and more recently by the author,[15] that the viscosity of pectin solutions will decrease upon extensive demethoxylation. Tests conducted during the heating and shown in Fig. 2 proved that there was no demethoxylation whatsoever during the period of heating used in this experiment.

If the viscosity is not a property of the chemical polygalacturonic acid chains, the velocity of the enzymic hydrolysis of a pectin solution in which the viscosity has been lowered by heat should be identical with the velocity of hydrolysis of the original unheated pectin solution. That this indeed is the case is shown in Fig. 3 where "reduction" represents the hydrolysis of both the original pectin solution and that heated for five hours to 100° before the enzyme was added. The viscosity changes are also indicated in the figure, showing that there was some additional decrease in the viscosity of the heated solution "b" during the hydrolysis. Determinations of the progress of changes in the reducing power of the heated and unheated solutions showed that the changes were identical in both mixtures. The progress of demethoxylation, not shown in the figure, was also identical. These observations make it even more probable that no chemical changes are induced by the heating of the pectin solution. In other words, the viscosity is not directly associated with the chemical structure of pectin.

It is obvious, therefore, that changes in the viscosity may not be used as a measure of enzymic decomposition.[16] The changes occur only in the early part of the hydrolysis. In the case of many pectins of "low quality" or of those which are degenerated by heat treatment, there would be but little change at all in the viscosity upon enzymic decomposition.

(14) Von Fellenberg, *Biochem. Z.*, **85**, 118 (1918).

(15) Kertesz, *Food Research*, **3**, 481 (1938).

(16) The measurement of the viscosity of a pectin solution may nevertheless give valuable information concerning its usefulness for various practical purposes where its colloidal properties are important [Baker, *Food Ind.*, **6**, 305 (1934)].

Assuming for the present that all aldehyde groups which are set free during the enzymic hydrolysis show the reduction characteristic of galacturonic acid, the conclusion must be drawn that the viscosity is not directly caused by the polygalacturonic acid molecules. The formula $[(G)_m]_n$ presents a possible explanation of this observation. The polygalacturonic acids $(G)_m$ containing m galacturonic acid anhydride residues form a secondary aggregate or polymer by the association of n polygalacturonic acid chains. The viscosity of pectins is mostly caused by the aggregate $[(G)_m]_n$ which is destroyed by heating. The units of $(G)_m$ show no additional reducing power when n is lowered to approach 1. On the other hand, if the galacturonic acid chains $(G)_m$ are attacked by the enzyme, the secondary structure falls apart. It is reasonable to assume that the formation of aggregates from the $(G)_m$ units is a property of polygalacturonic acid chains of certain minimum length. With the disturbance of this primary structure by reducing the size of the chemical unit, the secondary polymer is automatically destroyed.

This hypothesis explains why the viscosity in enzyme hydrolyzed pectin solutions decreases more rapidly than one would expect from the molecular size and the viscosity calculated therefrom by Staudinger's method. It also accounts for the observed decrease in the viscosity of heated pectin solutions without an increase in the reducing power, *i. e.*, without splitting of the polygalacturonic acid chains $(G)_m$.

From the trend of the viscosity curves obtained during this work one may draw the conclusion that the polygalacturonic acid structure $(G)_m$ also possesses some viscosity higher than that corresponding to a solution of galacturonic acid of equal concentration (see Fig. 2). This is indicated also when pectin is hydrolyzed by low concentrations of pectin-polygalacturonase, but its viscosity is relatively low when compared to that of the complete structure $[(G)_m]_n$.

It is of interest to note that a similar double structure has been found to exist in the case of starches. Baird, Haworth and Hirst[17] reported the disaggregation of starch without decomposing the chemical unit. Later Hassid and Dore[18] isolated a natural starch which showed low viscosity and appeared to be composed of unaggre-

(17) Baird, Haworth and Hirst, *J. Chem. Soc.*, 1201 (1935).

(18) Hassid and Dore, THIS JOURNAL, **59**, 1503 (1937).

gated starch molecules. From the work reported in this paper it seems likely that the structure of the large pectin molecule is similar to that of certain starches. On the other hand, Schneider and Fritschi[19] claim that pectin has a "macro molecule" bound with main valences only and is not an aggregate of the chemical units. The observations made at this Laboratory are not in favor of their contention.

There is no information available on the relative reducing power of polygalacturonic acids containing different numbers of galacturonic acid anhydride residues. The formula proposed for polygalacturonic acid by Morell, Baur and Link[20] is generally accepted and if true would indicate a direct proportionality between the number of molecules in the polymer and its reducing power. In case of starch the presence of non-reducing aldehyde groups has been assumed[21] but without conclusive evidence to that effect. The low reducing power observed in purified pectins is believed by the author to be a characteristic property of the pectin molecule. In spite of many attempts made at this Laboratory, no pectin preparation entirely free of reducing power has been obtained as yet. The significance of the natural reducing power of pectins will be the subject of a later contribution.

Assuming that the aldehydic reducing groups are tied up or masked in some manner in higher polymers of galacturonic acid, this would only modify and not eliminate the postulated secondary structure. Until evidence of this fact is presented, it seems more likely that the aggregates of polygalacturonic acid molecules are held together by means of secondary valence attractions not affecting the reducing power of the terminal aldehydic groups of the chemical polygalacturonic acid units.

(19) Schneider and Fritschi, *Ber.*, **69**, 2540 (1936).
(20) Morell, Baur and Link, *J. Biol. Chem.*, **105**, 1 (1934).
(21) See a discussion of this matter in Hanes, *The New Phytologist*, **36**, 101 (1937).

Summary

1. When pectin solutions are enzymatically decomposed the viscosity decreases more rapidly than corresponds to the increase in reducing power.

2. The viscosity of pectin solutions can be reduced by heat without any increase in the reducing power. This heat-degenerated pectin is decomposed by enzymes at the same velocity as the original unheated pectin solution.

3. These results are explained by postulating a structure $[(G)_m]_n$ for pectin in which $(G)_m$ is a polygalacturonic acid. The n units of polygalacturonic acids form a secondary aggregate which is mostly responsible for the viscosity of pectin.

GENEVA, NEW YORK RECEIVED MAY 17, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

The Action of Chlorine on Thiocyanates

BY TREAT B. JOHNSON AND IRWIN B. DOUGLASS[1]

This paper is contributed as a report of an investigation carried out recently in this Laboratory on the development of new methods for synthesis of sulfonyl chlorides. The recent interest in the chemotherapy of sulfanilamide and related compounds has stimulated a demand for new and improved methods of synthesizing sulfonyl chlorides. We have reported previously on a method of formation of chlorides of this type by interaction of chlorine with isothioureas,[2] and also the action of chlorine on other types of sulfur combinations.[3]

Observations on the chemical action of anhydrous chlorine on the lower alkyl thiocyanates have been made by Cahours,[4] Riche,[5] and James,[6] but none of the workers identified a sulfonyl chloride among the various reaction products described. Cahours mentioned obtaining by the chlorination of methyl thiocyanate a heavy yellow oil which solidified in contact with ammonia. If the experimental conditions employed by him

(1) Sterling Professorship of Chemistry Research Assistant, 1937–1938.
(2) Johnson and Sprague, THIS JOURNAL, **58**, 1348 (1936); *Science*, **83**, 528 (1936); Sprague and Johnson, THIS JOURNAL, **59**, 1837 (1937); **59**, 2439 (1937).
(3) Johnson and Douglass, THIS JOURNAL, **60**, 1486 (1938).
(4) Cahours, *Ann.*, **61**, 96 (1847).
(5) Riche, *ibid.*, **92**, 357 (1854).
(6) James, *J. Chem. Soc.*, **51**, 268 (1887).

were not strictly anhydrous, this oil may have contained some methyl sulfonyl chloride, but it was undoubtedly a mixture of reaction products. A careful search of the literature has failed to disclose other instances in which a sulfonyl halide may have been produced directly from a thiocyanate by treatment with a halogen.

We have found that aliphatic thiocyanates can be transformed readily into sulfonyl chlorides in excellent yields by the action of aqueous chlorine at low temperatures. The reaction has proved to be one of very practical technique in most of the applications made of the chlorination process. In addition to the sulfonyl chlorides, cyanogen chloride (CNCl) is also a product of the chlorination reaction. Cahours,[4] Riche,[5] and James,[6] all reported obtaining crystals of the trimolecular form of this chloride $(CNCl)_3$.

The behavior of benzyl thiocyanate (I) on chlorination was very puzzling until it was discovered that there was an intermediate formation of benzylsulfinic acid (II), which was only slightly soluble in water and comparatively unreactive toward chlorine at the low temperature of the reaction. This formation of benzylsulfinic acid is very interesting because it affords probably the easiest method yet available for the preparation of this unstable compound, and also because of the light it throws on the mechanism of the reaction leading to the formation of the sulfonyl chloride (III). Benzyl sulfinyl chloride, $C_6H_5CH_2SOCl$, is a possible intermediate of this reaction, and could be the precursor of either benzylsulfinic acid, II, or benzylsulfonyl chloride, III. This will be discussed more fully in a future paper from this Laboratory. In none of our chlorination experiments with thiocyanates have we obtained any evidence of the formation of intermediate sulfur compounds of the *sulfenic* acid type (—SOH or —S(OH)).[7]

$C_6H_5CH_2SCN$	$C_6H_5CH_2SOOH$	$C_6H_5CH_2SO_2Cl$
I	II	III

In a patent application now pending,[8] based partially on this work, examples are given of the preparation of fifteen different sulfonyl chlorides by the action of aqueous chlorine on thiocyanates, and of *n*-butoxyethoxyethyl sulfonyl bromide by the action of aqueous bromine on the corresponding thiocyanate. The reaction is of general application whether the nucleus linked to the —SCN group is substituted or unsubstituted, and whether it is alkyl, aralkyl, aryl, alicyclic or heterocyclic in nature.

(7) Tonnies, *J. Biol. Chem.*, **122**, 27 (1937).

(8) Serial No. 201728, "Sulfonyl Chlorides," Filed in U. S. Patent Office April 13, 1938; Application allowed March 7, 1939.

Experimental Part

Methylsulfonyl Chloride, CH_3SO_2Cl.[9]—Twelve and one-half parts of methyl thiocyanate (CH_3SCN) and 100 parts of water are mixed in a vessel immersed in an ice-bath. The mixture is agitated thoroughly while chlorine gas is bubbled into the solution at a rate such that the temperature is kept at 5° or lower. The passage of the chlorine is continued until the yellow color of the reaction mixture shows that an excess of chlorine is present. This takes about two to two and one-half hours. The oil which separates is extracted with ether, the resulting ether solution washed first with sodium bisulfite solution and then with sodium bicarbonate solution, and finally dried over anhydrous calcium chloride. The methylsulfonyl chloride is distilled at reduced pressure and boils at 55° under 11 mm. This chloride is converted easily to methyl sulfonic acid (CH_3SO_2OH) by acid hydrolysis, and to the corresponding sulfonamide ($CH_3SO_2NH_2$) by the action of ammonia;[10] yield 75%.

Ethylsulfonyl Chloride[11] ($C_2H_5SO_2Cl$).—Twenty grams of ethyl thiocyanate (C_2H_5SCN) suspended in 200 cc. of water is stirred vigorously at a temperature of 0–5° during the addition of chlorine gas at a rate of 2–3 liters per hour. Treatment with chlorine is continued until a permanent greenish-yellow color is produced, indicating an excess of the halogen. Air is then blown gently through the mixture to remove the excess of chlorine, after which an oil separates and is extracted with ether. After washing with sodium bisulfite and sodium bicarbonate solutions, and drying the ether extract over calcium chloride, the ethylsulfonyl chloride was obtained in a yield of 79%. It was identified by its boiling point (71–72° at 20 mm.) and refractive index.

Cyanogen chloride (CNCl) was identified in the water layer after the removal of the sulfonyl chloride by extraction with ether. The solution was heated and a gentle stream of air was blown through it and into 5 cc. of aniline oil. The aniline was then washed with dilute sodium hydroxide to remove the phenylcyanamide formed and the alkaline solution, after neutralization of the excess of sodium hydroxide, was shaken with a few drops of benzoyl chloride. Benzoyl phenylcyanamide precipitated and after recrystallization from alcohol melted at 124–125°. The melting point of this product mixed with an authentic sample was not lowered.

Benzylsulfinic Acid ($C_6H_5CH_2SOOH$), and Benzylsulfonyl Chloride from Benzyl Thiocyanate ($C_6H_5CH_2SCN$).—

(9) Billeter, *Ber.*, **38**, 2019 (1905).

(10) Helferich and Gnüchtel [*ibid.*, **71**, 712 (1938)] and Helferich and Mittag [*ibid.*, **71**, 1480 (1938)] have found this sulfonyl chloride (CH_3SO_2Cl) is of practical use in preparing characteristic derivatives for identifying certain carbohydrates and α-amino acids. They write, however, as follows regarding the experimental difficulties in preparing pure methanesulfonyl chloride: "In the preparation of methanesulfonyl chloride from the sodium salt of methanesulfonic acid by the action of phosphorus pentachloride, it is very difficult to separate the sulfonyl chloride from the phosphorus oxychloride. Only by repeated fractional distillation can this be accomplished, and then with great losses."

(11) Gerhardt and Chancel, *Jahresberichte*, 434 (1852); Spring and Winssinger, *Ber.*, **15**, 447 (1882).

Benzyl thiocyanate (10 g.), freshly crystallized and finely pulverized, was suspended in 200 cc. of water and chlorinated as described above at a temperature of 0–2°. In two to three hours the contents of the flask consisted of a yellow pasty mixture which was filtered through an ice cold Büchner funnel. The solid was washed with ice water to remove chlorine hydrate and sucked as dry as possible. The filtrate gave a heavy precipitate with barium chloride and smelled strongly of cyanogen chloride. The latter was identified by the formation of benzoylphenylcyanamide as described above.

The solid product of reaction was spread on filter paper to dry in the air, but after three to four hours of exposure it had decomposed with the evolution of sulfur dioxide and had absorbed into the filter paper. From the paper were extracted unchanged starting material, and a white solid which contained sulfur but no halogen or nitrogen. This was insoluble in acid or alkali, evolved sulfur dioxide on heating and melted at 108–109°. Since these properties are those that might be expected of a disulfone or a disulfoxide, and since the melting point corresponded to that recorded for $C_6H_5CH_2SOSOCH_2C_6H_5$,[12] the original reaction product that spontaneously decomposed was suspected of being benzyl sulfinic acid, $C_6H_5CH_2SOOH$.

To establish this conclusion the chlorination experiment was repeated and the white solid formed was treated immediately with sodium bicarbonate solution, in which most of it dissolved. The residue, consisting chiefly of unchanged benzyl thiocyanate, was removed by washing with ether. The alkaline solution was then treated with 1 cc. of benzyl chloride and heated on the steam-bath for one hour. On cooling, colorless crystals separated having a melting point of 151–152°, which corresponds with the melting point recorded for dibenzylsulfone.

Anal. Calcd. for $C_{14}H_{14}O_2S$: S, 13.02. Found: S, 13.22.

In another experiment 10 g. of benzyl thiocyanate was chlorinated at 0–2° to apparent saturation, then the temperature was raised to 15–20° and the chlorination continued. The products of the reaction were $C_6H_5CH_2SO_2Cl$ in 45% yield, benzyl chloride, cyanogen chloride, and positive evidence of the formation of sulfate ion by interaction with barium chloride to form barium sulfate. Again when chlorination of 10 g. of pure benzyl thiocyanate was carried out at 20–30°, 9.33 g. of impure benzylsulfonyl chloride melting at 84–88° was obtained. This smelled distinctly of benzyl chloride and the aqueous filtrate gave a heavy sulfate ion test.

To determine whether the benzyl chloride and sulfate ion resulted from the action of chlorine water on the benzyl thiocyanate or on the benzylsulfinic acid, 10 g. of benzyl thiocyanate was chlorinated at 0–2° and the white solid product was treated quickly with sodium bicarbonate solution. After extracting with ether to remove all undissolved material from which was recovered unchanged thiocyanate and a few milligrams of benzylsulfonyl chloride, the solution was acidified with an excess of hydrochloric acid and immediately chlorinated at 20–25° to saturation. The product consisted of 5.75 g. of benzylsulfonyl chloride which melted at 92° without further purification. Although the water in which the original chlorination was carried out reacted strongly for sulfate ion, the final filtrate after removing the sulfonyl chloride gave only a slight cloudiness with barium chloride.

The amount of benzyl chloride and sulfate formed seemed to be increased if the benzyl thiocyanate was impure or if the temperature during chlorination was not kept under rigid control. A chlorination experiment carried out in 80% acetic acid solution resulted in the formation of benzyl chloride almost to the complete exclusion of benzylsulfonyl chloride.

The Formation of Benzylsulfonyl Chloride by Chlorination of Benzyl Isothiourea Hydrochloride.—This hydrochloride was chlorinated under conditions identical to those employed in the treatment of benzyl thiocyanate. There was no evidence of the formation of benzylsulfinic acid and benzylsulfonyl chloride which melted at 92° without purification was obtained in 76% yield. Barium chloride solution formed only a slight precipitate in the aqueous filtrate.

Chlorination of Phenyl Thiocyanate (C_6H_5SCN).—This aromatic thiocyanate is much more resistant to the action of chlorine than the aliphatic compounds. Chlorination for eight hours under the usual experimental conditions gave a product that contained less than half the calculated amount of chlorine required for benzenesulfonyl chloride. Chlorination for even sixty hours at room temperature failed to yield a product free of the starting material. Some benzenesulfonyl chloride was formed, however, for when the product was treated with aniline and the reaction mixture extracted with sodium hydroxide, benzenesulfonyl anilide was obtained by acidifying the alkaline solution.

Summary

1. Organic thiocyanates can be employed with success for the synthesis of sulfonyl chlorides.

2. Chlorination of such thiocyanates in aqueous suspension and at low temperatures leads to a transformation of —SCN to —SO_2Cl.

3. Benzyl thiocyanate can be changed by chlorination at low temperatures into benzylsulfinic acid. On chlorination in aqueous suspension at higher temperature, benzylsulfonyl chloride is formed in excellent yield.

4. The question of the mechansim of the different chlorination reactions thus far reported from this Laboratory will be discussed in a future paper.

(12) Fromm and de Seixas Palma, *Ber.*, **39**, 3315 (1906).

NEW HAVEN, CONNECTICUT RECEIVED JULY 3, 1939

NOTES

Optical Properties of Sulfamic Acid

By W. M. D. Bryant

Sulfamic acid, $NH_2 \cdot SO_3H$, has been the subject of crystallographic studies at widely different times by at least two experimenters.[1,2] Only very meager optical data incidental to goniometric observations were reported, and these were inadequate for purposes of identification. Recently M. E. Cupery[3] described a new process for industrial scale preparation of pure sulfamic acid and kindly placed some of this substance at the writer's disposal for optical crystallographic examination.

The methods employed in this study were those described in an earlier paper.[4] The refractive indices and optic axial angles were measured in green monochromatic light (5461 Å.) from the mercury arc. Due to the weak dispersion optic axial angles in white light were not appreciably different. The observed optical data are tabulated.

Refractive indices at 25 ± 3°: $\alpha = 1.553$; $\beta = 1.563$; $\gamma = 1.568$ all ±0.003.

Optic axial angle: $2H_a = 65 \pm 1°$; $2H_0 = 120 \pm 5°$; $2V = 64°$ (calculated from $2H_a$ and $2H_0$ by the tangent relation); $2V = 63°$ (calculated from $2H_a$ and β).

Dispersion: weak, indeterminate.

Optical character: negative.

Crystal system: orthorhombic bipyramidal, according to both Fock and Jaeger. However, these investigators each used a different setting, so that the crystallographic *b*- and *c*-axes are transposed in their respective treatments.

Crystal habit: tablets and compact prisms from cold aqueous solution; large lozenge-shaped plates on cooling hot aqueous solution; the fused material is glassy.[5]

Optical orientation: the optic axial plane coincides with the principal pinacoid, which is 001 according to Jaeger or 010 according to Fock. The obtuse bisectrix apparently coincides with the *a*-axis for both settings.

The only numerical optical constant found in the earlier literature is the optic axial angle reported by Fock[1] as $2E$ = *circa* 85°. $2E$ calculated from the present $2H_a$ value is about 109 ± 2°. Since no indications of a second crystal modification of sulfamic acid have been obtained to date, it is believed that Fock's $2E$ value is erroneous.

Ammonia Department
E. I. du Pont de Nemours and Co., Inc.
Wilmington, Delaware Received June 28, 1939

(1) A. Fock, *Z. Krist.*, **14**, 531 (1888); E. Raschig, *Ann.*, **241**, 177 (1887).

(2) F. M. Jaeger, *Verslag Akad. Wetenschappen, Amsterdam*, [1] **35**, 68 (1926).

(3) M. E. Cupery, *Ind. Eng. Chem.*, **30**, 627 (1938).

(4) W. M. D. Bryant, This Journal, **60**, 1394 (1938).

(5) The writer is indebted to Dr. Cutler D. West (private communication) for a measurement of the refractive index of the amorphous phase obtained on cooling molten sulfamic acid. The value reported, $n^{27.5}D$ 1.5048, was measured on an Abbe refractometer using the pure Lamotte product.

A Method of Coupling Organic Radicals by Means of the Grignard Reagent: A Correction

By John H. Gardner and Lionel Joseph

In a paper of this title published in 1929[1] the statement was made that when iso- and *s*-butylmagnesium bromides were allowed to react with silver bromide, there is formed a mixture from which no pure compound could be isolated. In connection with some other work in progress in this Laboratory, some results were obtained which led us to doubt the correctness of this statement. Consequently, the experiments were repeated using more effective distilling apparatus than was available at the time the earlier work was done. In this way, we obtained the dimethylhexanes which would be expected from the coupling of the radicals in high purity but in rather poor yield. The other products were gases, very likely the corresponding butanes and butenes, although definite proof of their identity has not as yet been obtained. It is thus definitely established that in all cases so far studied of the action of Grignard reagents on silver bromide, there is no rearrangement.

Experimental

Reaction of Iso- and *s*-Butylmagnesium Bromides with Silver Bromide.—To an ethereal solution of 1 mol of the Grignard reagent in a flask provided with a mechanical stirrer and two reflux condensers, and cooled in an ice–salt bath, there was added a slight excess of silver bromide, with continual stirring. The mixture was stirred in the cooling bath for a half hour and then for an hour at the boiling point. After the addition of very dilute hydrochloric acid, the organic products were separated by steam distillation, dried over calcium chloride and distilled through a 70-cm. Vigreux column. In both cases, after

(1) J. H. Gardner and P. Borgstrom, This Journal, **51**, 3375 (1929).

the ether had distilled, the distillation curve rose sharply and the hydrocarbon fraction was collected over an approximately 5° range. The products were boiled for an hour over metallic sodium to remove any alkyl halide and redistilled. There was thus obtained from isobutylmagnesium bromide, 20 g. (37.5%) of 2,5-dimethylhexane, b. p. (755 mm.) 107–108.5°, d^{20}_4 0.6911, $n^{21}D$ 1.3922. Egloff[2] gives b. p. (760 mm.) 109.3°, d^{20}_4 0.6949, $n^{20}D$ 1.39295 as the preferred values. Similarly, from *s*-butylmagnesium bromide, there was obtained 7.5 g. (13%) of 3,4-dimethylhexane, b. p. (757 mm.) 116–117°, d^{22}_4 0.7199, $n^{26}D$ 1.4040. Egloff[2] (p. 54) gives as the preferred values, b. p. (760 mm.) 117.8°, d^{20}_4 0.7195, $n^{20}D$ 1.4045.

(2) G. Egloff, "Physical Constants of Hydrocarbons," Vol. I, Reinhold Publishing Company, New York, 1939, p. 53.

DEPARTMENT OF CHEMISTRY
WASHINGTON UNIVERSITY
ST. LOUIS, MISSOURI

RECEIVED JULY 3, 1939

Morpholine Condensations

BY CHESTER B. KREMER, M. MELTSNER AND L. GREENSTEIN

In the course of researches dealing with the condensation of secondary amino alcohols with *o*- and *p*-chloronitrobenzenes, we also investigated the condensing ability of the secondary amine, morpholine. The products obtained have been described by others in a recent article,[1] but were prepared in a manner somewhat different from ours. We are therefore recording our procedures and at the same time including data for one compound as yet unreported.

The general method of procedure was to reflux molar quantities of morpholine and the chloronitrobenzene in the presence of anhydrous sodium carbonate for approximately four hours. The reaction mixture was then steam distilled to rid it of unreacted material. A dark oil, slowly solidifying, remained in the distillation flask in the run with *o*-chloronitrobenzene, an orange-red solid remaining in the case of the para compound. These were recrystallized from benzene: N-(*o*-nitrophenyl)-morpholine, light orange product, m. p. 40–41°; N-(*p*-nitrophenyl)-morpholine, yellow in color, m. p. 149–150°.

Another method used in preparing N-(*p*-nitrophenyl)-morpholine was as follows: 1.0 g. of phenylmorpholine was added to 4 cc. of concentrated sulfuric acid and 4 cc. of concentrated nitric acid added dropwise. The reaction mixture turned red and foamed violently. When the reaction was complete, the mixture was poured onto ice and finally filtered. The filtrate yielded orange crystals of the desired product.

Reduction of the nitro compounds with tin and hydrochloric acid yielded the previously reported N-(*p*-aminophenyl)-morpholine[2] and the new compound, N-(*o*-aminophenyl)-morpholine, m. p. 98–98.5°; calculated N, 15.73; found, 15.87.

N-(*o*-Aminophenyl)-morpholine can be purified by sublimation, yielding beautiful white platelets. In the pure state the compound is quite stable, but when somewhat impure discolors fairly rapidly on standing.

The present work proves that the compound formed in treating *o*-chloronitrobenzene with diethanolamine is not N-(*o*-aminophenyl)-morpholine as had been tentatively advanced[3] in a previous publication.

(1) R. H. Harradence and F. Lions, *J. Proc. Roy. Soc. N. S. Wales*, **70**, 406–412 (1937).

(2) H. A. Lubs, U. S. Patent 2,004,763 (1935).

(3) Meltsner, *et al.*, THIS JOURNAL, **59**, 2660 (1937).

LABORATORIES OF ORGANIC CHEMISTRY
THE CITY COLLEGE
COLLEGE OF THE CITY OF NEW YORK
NEW YORK, N. Y.

RECEIVED JUNE 27, 1939

Hydrogen and Deuterium Exchange between Nitramide and Water

BY V. K. LA MER AND SEYMORE HOCHBERG

On the basis of measurements of the decomposition rate of proto-nitramide dissolved in mixtures of H_2O and D_2O, La Mer and Greenspan[1] suggested two mechanisms for the decomposition. The first assumed that only one H of nitramide exchanges promptly on being dissolved in D_2O; the second that both H atoms of nitramide exchange promptly.

On the basis of the data then available it was impossible to decide whether the decomposing substrate was HDN_2O_2 or $D_2N_2O_2$ when proto-nitramide is dissolved in D_2O.

We now present evidence based upon two independent procedures that both H atoms are exchanged promptly for D atoms in a solvent of high deuterium content, and that the rate-determining step in D_2O involves $D_2N_2O_2$.

I. Decomposition Rate of $D_2N_2O_2$.—Deutero-nitramide was prepared by the reaction of potassium nitrocarbamate with 99% D_2O and SO_3. On reaction of this nitramide with water (0.01 *N* hydrochloric acid) the observed rate constant, based upon manometric measurement[2] of

(1) La Mer and Greenspan, *Trans. Faraday Soc.*, **197**, XXXIII, Part 9, 1266 (1937).

(2) Greenspan, La Mer and Liotta, THIS JOURNAL, **59**, 1606 (1937).

the nitrous oxide formed, is $k^* = 387 \times 10^{-5}$ min.$^{-1}$ (decadic logs) at 35°, in excellent agreement with Baughan and Bell's[3] $k^* = 386 \times 10^{-5}$ min.$^{-1}$ obtained for proto-nitramide in H_2O.

Partially deuterized nitramide prepared from 48% D_2O and sulfur trioxide yielded $k^* = 125.5 \times 10^{-5}$ min.$^{-1}$ at 24.84° in 0.01 *N* hydrochloric acid in H_2O. La Mer and Greenspan[1] obtained $k^* = 126.6 \times 10^{-5}$ min.$^{-1}$ under the same conditions for proto-nitramide in H_2O.

II. Direct Exchange.—Proto-nitramide was dissolved in D_2O (temp., approx. 5°). The nitramide produced by exchange was extracted with ether (dried over sodium) by the freezing method of Marlies and La Mer.[4,5] The exchange and extraction required less than one hour.

To ensure the complete removal of possible traces of deutero-solvent, the nitramide was kept over phosphorus pentoxide for one week. It was then decomposed by gentle heating in the presence of a trace of anhydrous sodium carbonate. The liberated water was redistilled and the density determined by the falling drop method.[6]

The following results show that the deuterium content of the nitramide approximated the deuterium content of the water from which it had been extracted.

Mole fraction of D in the solvent water in which exchange takes place	0.28	0.87	0.97
Mole fraction of D in the water from the decompn. of the extracted nitramide	.25	.65	.94

There is no point in calculating an exchange constant because, due to the method of extraction, the equilibrium temperature and the equilibrium concentration of D_2O cannot be held constant. Since deutero-nitramide decomposes in water at the same rate as proto-nitramide and since deutero-nitramide containing more than one atom of D per molecule may be extracted from a solution of proto-nitramide in D_2O, it is evident that both atoms of hydrogen in nitramide exchange with D_2O before decomposition occurs.

DEPARTMENT OF CHEMISTRY
COLUMBIA UNIVERSITY
NEW YORK, N. Y. RECEIVED JUNE 13, 1939

(3) Baughan and Bell, *Proc. Roy. Soc.* (London), **A894**, 158, 464–478 (1937).
(4) Marlies and La Mer, THIS JOURNAL, **57**, 2008 (1935).
(5) Marlies, La Mer, and Greenspan, "Inorganic Syntheses," McGraw-Hill Book Co., Inc., New York, N. Y., Vol. I, p. 72.
(6) Hochberg and La Mer, *Ind. Eng. Chem., Anal. Ed.*, **9**, 291 (1937).

Ferric Chloride as a Condensing Agent

BY W. M. POTTS AND R. J. DODSON

A further investigation[1] of anhydrous ferric chloride as a condensing agent in the alkylation of benzene has been carried out using butyl alcohols.

1. Condensation products were not formed with *n*-butyl alcohol and benzene. This agrees with the results reported by Huston and Hsieh[2] using aluminum chloride and primary alcohols up to and including *n*-hexyl alcohol.

2. *s*-Butyl alcohol gave evidence of a reaction but no product was identified. With aluminum chloride under the same conditions, a 69% yield of *s*-butylbenzene was obtained. Huston and Hsieh[2] reported a 25–28% yield, while Tzukervanik and Tokareva[3] reported a 70% yield. The *s*-butylbenzene was identified by its physical constants and the diacetamino derivative, m. p. 193°.[4]

3. At room temperature, one mole of *t*-butyl alcohol, one mole of ferric chloride and five moles of benzene gave an 82% yield of *t*-butylbenzene. With aluminum chloride under the same conditions a 50% yield of *t*-butylbenzene was obtained. Using two moles of *t*-butyl alcohol, one mole of benzene and one mole of ferric chloride, a 24% yield of mono-*t*-butylbenzene and 64% of 1,4-di-*t*-butylbenzene was obtained. The acetamino derivative of the former melted at 168°.[4] The latter was identified by the method reported by Potts and Carpenter.[1]

Better yields of *t*-butylbenzene were obtained with ferric chloride than with aluminum chloride, but ferric chloride does not effect the condensation of primary and secondary alcohols with benzene. Higher temperatures and larger quantities of ferric chloride lower the yields of *t*-butylbenzene.

(1) Potts and Carpenter, THIS JOURNAL, **61**, 663 (1939).
(2) Huston and Hsieh, *ibid.*, **58**, 439 (1936).
(3) Tzukervanik and Tokareva, *J. Gen. Chem.* (U. S. S. R.), **5**, 764 (1935); *C. A.*, 442 (1936).
(4) Ipatieff and Schmerling, THIS JOURNAL, **59**, 1056 (1937).

DEPARTMENT OF CHEMISTRY AND
CHEMICAL ENGINEERING
A & M COLLEGE OF TEXAS
COLLEGE STATION, TEXAS RECEIVED JUNE 21, 1939

α-Hydrindone

BY CHARLES C. PRICE AND FREDERICK M. LEWIS

Although ring closures of many β- and γ-aryl butyric acids to the corresponding cyclic ketones have been accomplished successfully by the ac-

tion of sulfuric acid, it has been reported[1] that this reagent will not effect such a ring closure for the simplest β-arylpropionic acid, hydrocinnamic acid, to yield α-hydrindone.

By varying the conditions for the reaction of hydrocinnamic acid in sulfuric acid it has been found possible to obtain a very pure product rapidly and conveniently although in only moderate yield.

The concentration of acid was varied from 15% fuming to 85% sulfuric acid, the time of heating from one minute to three hours and the reaction temperature from 100 to 160°. Optimum conversion was obtained by using 5% fuming sulfuric acid at 140° for five minutes. In each case the sulfuric acid (20 cc.) was heated to the desired temperature in an oil-bath, the hydrocinnamic acid (5 g., m. p. 49–50°) added with stirring and, at the end of the specified time, the reaction mixture poured over cracked ice (100–150 g.). The α-hydrindone was extracted with two 25-cc. portions of benzene. After drying over sodium sulfate, the benzene was removed by evaporation on a steam plate, leaving a pale yellow oil which crystallized on cooling to room temperature, maximum yield 1.2 g. (27%), m. p. 40–41°. A mixture of these crystals with the starting material was liquid at room temperature. The identity of the product was established further by preparation of the 2,4-dinitrophenylhydrazone, m. p. 254–255°. No starting material was isolated in any case.

The addition of boron fluoride or aluminum chloride to the sulfuric acid lowered the yield considerably.

(1) Von Miller and Rohde, *Ber.*, **23**, 1887 (1890).

NOYES CHEMICAL LABORATORY
UNIVERSITY OF ILLINOIS
URBANA, ILLINOIS

RECEIVED JUNE 16, 1939

Some Schiff Base Hydrochlorides. A Test for Arylamines[1]

BY J. V. SCUDI, H. D. RATISH AND J. G. M. BULLOWA[2]

In the course of certain studies,[3] a very simple color test was devised for the estimation of sulfanilamide and other arylamines. The test is not as sensitive (1 part in 200,000) as diazotization procedures,[4,5] but its simplicity has made it useful in following various concentrates in a semi-quantative way. Recently the Ehrlich reagent has been more rigorously standardized[6] for the determination of sulfanilamide, although the reaction mechanism was left in doubt. It was therefore decided to record our observations.

The test consists in adding 1 cc. of 10% hydrochloric acid to 5 cc. of a 1% solution of cinnamaldehyde in alcohol followed by 5 cc. of a 2–4 mg. % solution of the arylamine. A yellow color is instantly formed. This is stable for several days, but unstable to alkali. Other aldehydes may be used, but not benzaldehyde. Toluenesulfonamide does not give the test. The sensitivity is increased ten-fold by performing the test in absolute alcohol in the presence of concentrated sulfuric acid.

The color producing substances were shown to be the somewhat labile hydrochlorides of the Schiff bases of sulfanilamide and sulfapyridine. These were converted to the free bases. In accord with the finding of Dimroth and Zoeppritz[7] and Moore and Gale,[8] the color appears to be produced by the halochromic effect of the acid upon the Schiff base. The compounds reported are not submitted as crystalline derivatives for the characterization of the arylamine, but as evidence of the mechanism of the color development.

Experimental

Schiff Base Hydrochlorides.—These were prepared essentially by the method of Dimroth and Zoeppritz[7] with the exception that one mole of cinnamaldehyde was dissolved in alcohol prior to addition to the arylamine in dilute hydrochloric acid. Yields of 85–95% of the products were precipitated instantly as golden-orange plates. The cinnamylidene sulfanilamide hydrochloride, melting at 203–205° dec., was recrystallized with some hydrolysis from dilute hydrochloric acid. Calculated for $C_{15}H_{14}O_2N_2S\cdot HCl$: Cl, 11.01. Found: Cl, 11.35.

The cinnamylidene sulfapyridine hydrochloride was too labile to be crystallized. Washed with a minimal amount of alcohol and ether, the product melted at 178–180° dec. Calculated for $C_{20}H_{17}O_2N_3S\cdot HCl$: N, 10.52; Cl, 8.90. Found: N, 10.15; Cl, 9.65.

Free Bases.—Crystallization of cinnamylidene sulfanilamide hydrochloride from water gave 70–80% yields of the base, m. p. 213–215° dec. The melting point was unchanged when mixed with an authentic sample,[9] although

(1) Presented at the Baltimore meeting of the American Chemical Society, April, 1939.

(2) These studies received financial support from the Littauer Pneumonia Research Fund, from the Metropolitan Life Insurance Company, and from Mr. Bernard M. Baruch, Mr. Bernard M. Baruch, Jr., Miss Belle N. Baruch, and Mrs. H. Robert Samstag.

(3) H. D. Ratish, J. G. M. Bullowa, J. B. Ames and J. V. Scudi, *J. Biol. Chem.*, **128**, 297 (1939).

(4) E. K. Marshall, Jr., *J. Biol. Chem.*, **122**, 263 (1938).

(5) J. V. Scudi, *ibid.*, **122**, 539 (1939).

(6) A. E. A. Werner, *Lancet*, **1**, 1095 (1938).

(7) O. Dimroth and R. Zoeppritz, *Ber.*, **35**, 984 (1902).

(8) F. J. Moore and R. D. Gale, THIS JOURNAL, **30**, 394 (1908).

(9) W. H. Gray, G. A. H. Buttle and D. Stephenson, *Biochem. J.*, **31**, 724 (1937).

it was depressed when mixed with a sample of the hydrochloride. Recrystallized from dilute hydrochloric acid, the free base gave the hydrochloride along with hydrolysis products. The cinnamylidene sulfapyridine hydrochloride was dissolved in cold 2% sodium hydroxide, and precipitated by neutralizing with acetic acid; pale yellow needles, m. p. 208–210° dec. The melting point was depressed by mixing with the hydrochloride. Calculated for $C_{20}H_{17}O_2N_3S$: N, 11.57. Found: N, 11.32.

FROM THE MEDICAL SERVICE AND THE
DEPARTMENT OF PATHOLOGY
HARLEM HOSPITAL, DEPARTMENT OF HOSPITALS
NEW YORK, N. Y. RECEIVED MAY 18, 1939

The Directive Influence of the Electric Moment on Substitution in the Benzene Ring

BY W. J. SVIRBELY

A few years ago[1] a comparison of the electric moments of the monosubstituted benzene derivatives which direct substitution to the ortho and para positions with those which direct substitution to the meta position resulted in the following rule: *in general, if the electric moment of a monosubstituted benzene derivative is greater than ~2.07D, the next substituted group will be directed to the meta position; if the moment is less than ~2.07D, the next group will be directed to the ortho and para positions.*

In Table I there are listed the monosubstituted benzene derivatives whose moments have been determined since 1935. The compounds are divided into two groups depending upon whether the second substituted group is directed to the ortho and para or to the meta position. An examination of the data shows that in all of these compounds the rule is obeyed. Compounds which contained unsaturated bonds in the monosubstituted group such as the styrenes, diazoaminobenzenes, cinnamyl derivatives, etc., where the side chain is first attacked, have not been included in the table although their moments are listed in the literature.

TABLE I

ELECTRIC MOMENTS AND THE OBSERVED ORIENTING INFLUENCE

Ortho–para substitution compound, phenyl	$\mu \times 10^{18}$ e. s. u.	Meta substitution compound, phenyl	$\mu \times 10^{18}$ e. s. u.
$-CH_2-C_6H_5$	0.33	$-CONHNHCOC_6H_5$	2.63
$-(CH_2)_2C_6H_5$	.45	$-CONHNH_2$	2.70
$-(CH_2)_3C_6H_5$	.48	$-CON{=}N-COC_6H_5$	2.85
$-(CH_2)_8C_6H_5$	.50	$-COCl$	3.33
$-(CH_2)_6C_6H_5$	.52	$-CONHNHCOC_6H_4CH_3$	3.38
$-(CH_2)_4C_6H_5$	.52	$-C(=N-O-N=)C-C_6H_5$	3.45
$-(CH_2)_5C_6H_5$	.55		
$-(CH_2)_4CHC_6H_5(CH_2)_4-C_6H_5$	.85	$-CONHNHCOC_6H_4Cl$	3.82
$-(CH_2)_2CHC_6H_5(CH_2)_2-C_6H_5$	.98	$-S(=O)-C_6H_5$	4.08
$-(CH_2)_2CHC_6H_5(CH_2)_2-CHC_6H_5(CH_2)_2C_6H_5$	1.51	$-SO_2Cl$	4.47
$-CHOHCH_3$	1.55	$-CONHNHCOC_6H_4NO_2$	5.57
$-(CH_2)_2CH_2OH$	1.71		
$-CH_2COOH$	1.75		
$-CH_2CH_2CH_2Cl$	1.76		
$-CH{=}CHCOOH$	1.78		
$-CH_2CH_2CH_2Br$	1.78		
$-OOCC_6H_5$	1.92		
$-CH{=}CHCOOCH_3$	1.93		
1-$C_{10}H_7Cl$	1.51		
2-$C_{10}H_7Cl$	1.65		

(1) Svirbely and Warner, THIS JOURNAL, **57**, 655 (1935).

In a search for practical solvents for silicon tetrafluoride, its solubility in a number of organic solvents at room temperature (27–33°) has been determined. Saturated solutions were prepared by circulating the purified gas through the various solvents, contained in an absorption tower or an Orsat pipet, in a closed system at atmospheric pressure until saturation appeared to be attained. The non-aqueous solvents, except absolute ethyl alcohol, were used as purchased without additional purification. The rate at which the gas dissolved seemed to depend largely on the fluidity of the solvent. The concentration of silicon tetrafluoride in the solutions was calculated from the determination of fluorine in weighed samples. The saturated solutions remained clear, showing no precipitation of silica, when allowed to stand overnight out of direct contact with air. The results obtained are given in the table below. Owing to lack of temperature control and the possibility that the more viscous solutions may have been incompletely saturated, the results are regarded as approximate, but of practical value.

The data show that the solubility of silicon tetrafluoride in the homologous series of monohydroxy alcohols decreases definitely and quite regularly with an increase in the number of carbon atoms and for the same number of carbon atoms with an increase in the number of hydroxyl groups. Compounds containing ether groups (diethylene glycol), carbonyl groups (acetone and pyruvic acid), and carboxyl groups (acetic and pyruvic acids) were found not to be very good solvents for silicon tetrafluoride.

CHEMISTRY LABORATORY
THE UNIVERSITY OF MARYLAND
COLLEGE PARK, MD. RECEIVED JULY 24, 1939

The Solubility of Silicon Tetrafluoride in Organic Solvents. Behavior of Such Solutions

BY GRADY TARBUTTON, E. P. EGAN, JR., AND S. G. FRARY

TABLE I

SOLUBILITY OF SILICON TETRAFLUORIDE AT ROOM TEMPERATURE (27–33°) AND TOTAL PRESSURE OF 750–760 MM.

Solvent	G. SiF_4/100 cc. solvent	Wt. % of SiF_4 in soln.
Methyl alcohol, absolute	..	32.8
Methyl alcohol, 94% by wt.	..	39.0
Ethyl alcohol, absolute	57.2	36.4
Ethyl alcohol, 96.1% by wt.	60.8	37.8
Ethyl alcohol, 95% (U. S. P.)	61.4	38.1
Ethyl alcohol, 94.3% by wt.	61.5	38.1
Ethyl alcohol, 92.6% by wt.	63.4	38.8
Ethyl alcohol, 91.0% by wt.	63.9	39.0
Isopropyl alcohol, 98%	39.4	28.2
n-Butyl alcohol, 98% (U. S. P.)	30.4	23.4
Amyl alcohols (fusel oil)	20.9	17.3
Glycol, C. P.	..	26.2
Diethylene glycol, C. P.	..	17.6
Glycerol, C. P.	..	5.7
Acetone, C. P. anhyd.	3.2	3.1
Acetic acid (glacial)	1.1	1.1
Pyruvic acid, tech. (38–45%)	..	4.4

In addition to these quantitative data, it was found that silicon tetrafluoride is sparingly soluble in benzene and trichloroethylene, and insoluble in carbon tetrachloride at room temperature.

On the addition of 9% by weight of water to the saturated solution in 95% alcohol (U. S. P.), a gelatinous precipitate of hydrated silica was formed. However, when the original solution was subjected to vacuum distillation at room temperature, silicon tetrafluoride was evolved until a solution containing approximately 26.5% of the gas remained, which corresponds to a mole ratio of alcohol to silicon tetrafluoride of approximately 6:1. On adding an equal volume of water to the residual solution from the vacuum distillation, no precipitate formed, possibly because the silicon tetrafluoride had combined chemically with the ethyl alcohol. Subsequent addition of a soluble barium salt precipitated 95% of the fluorine as pure barium fluosilicate. This reaction offers a convenient method for preparing barium fluosilicate of high purity.

When saturated solutions in glycol were distilled in a vacuum at room temperature, 50 and 100°, the residual solutions contained fluorine equivalent to 26.2, 24.5, and 2.8% silicon tetrafluoride, respectively; on addition of water to them, a precipitate was formed in each case.

The above information is of interest in that such solutions in organic solvents may furnish the basis for the synthesis of organic fluorine compounds as well as a means of preparing pure fluorine salts. However, the authors do not plan to pursue the investigation further and, therefore, wish to relinquish the problem to others who may be interested in it.

TENNESSEE VALLEY AUTHORITY
DEPARTMENT OF CHEMICAL ENGINEERING
WILSON DAM, ALABAMA RECEIVED MAY 8, 1939

Occurrence of the Syringyl Radical in Plant Products

BY EINAR WEST, A. S. MACINNES, JOSEPH L. MCCARTHY AND HAROLD HIBBERT

It has now been shown that treatment of jute fiber, rye straw and corn stalks with a 2% solution of hydrogen chloride in anhydrous ethanol, according to the method described for the ethanolysis of spruce and maple woods,[1] gives rise to typical ethanolysis products, namely, ethanol lignin and a mixture of volatile oils. The yields of ethanol lignin and volatile oils are of the same order of magnitude as those obtained from spruce and maple woods. The presence of the syringyl radical has been established in the volatile oils from each of these fibers. Thus, following the procedures previously described,[2] α-ethoxypropiosyringone as the *p*-nitrobenzoate (m. p. 141–142°), syringoylacetaldehyde as the monosemicarbazone (m. p. 207–208°), and syringaldehyde as the 2,4-dinitrophenylhydrazone (m. p. 235–235.5°), were isolated. Mixed melting points with authentic specimens showed no depression.

These, and previous results with hard woods,[1,2] would seem to point to the presence of syringyl derivatives in the lignin constituents of all angiosperms, for example as indicated in corn and rye (monocotyledons) and in jute and maple (dicotyledons).

(1) Brickman, Pyle, McCarthy and Hibbert, THIS JOURNAL, **61**, 868 (1939).

(2) Hunter, Cramer and Hibbert, *ibid.*, **61**, 516 (1939); Pyle, Brickman and Hibbert, *ibid.*, **61**, 2198 (1939).

DIVISION OF INDUSTRIAL AND CELLULOSE CHEMISTRY
MCGILL UNIVERSITY
MONTREAL, CANADA RECEIVED JUNE 30, 1939

Reaction of *p*-Fluorophenol with Benzene and Aluminum Chloride

BY ARTHUR W. WESTON[1] AND C. M. SUTER

Recently it was found[2] that in the deëthylation of *p*-fluorophenetole with aluminum chloride in benzene solution a by-product was obtained in

(1) Sharp and Dohme Post-Doctorate Fellow 1938–1939.

(2) Suter, Lawson and Smith, THIS JOURNAL, **61**, 163 (1939).

considerable amount. This was phenolic in nature and in an impure condition melted at 153–156°. It has now been determined that the same substance results from heating *p*-fluorophenol with benzene and aluminum chloride. When purified it melted at 163.5–164° and upon oxidation gave a high yield of benzoic acid. No depression of the melting point occurred when a sample of the unknown was mixed with *p*-hydroxybiphenyl. Hence

$$C_6H_6 + FC_6H_4OH \xrightarrow{AlCl_3} C_6H_5C_6H_4OH\ [+ HF]$$

p-fluorophenol must react as shown and the *p*-hydroxybiphenyl obtained in the deëthylation of *p*-fluorophenetole also results from this reaction.

Attempts to extend the reaction in various directions have been without success. Because aromatic fluorine may be under some conditions replaced by chlorine,[3] it seemed possible that *p*-chlorophenol was an intermediate in the reaction. However, *p*-chlorophenol showed no activity toward benzene in the presence of aluminum chloride. None of the corresponding hydroxybiphenyl was isolated when *p*-fluorophenol and aluminum chloride were heated with toluene or chlorobenzene.

By heating a mixture of 3 g. of *p*-fluorophenol, 7 ml. of benzene and 7 g. of aluminum chloride under reflux for two and one-half hours there was obtained about 1 g. of *p*-hydroxybiphenyl, m. p. 164°. The 51 g. obtained in the deëthylation of *p*-fluorophenetole[2] corresponds to 13% of the *p*-fluorophenol reacting with the benzene.

(3) Bacon and Gardiner, *J. Org. Chem.*, **3**, 281 (1938).

CHEMICAL LABORATORY
NORTHWESTERN UNIVERSITY
EVANSTON, ILLINOIS

RECEIVED APRIL 24, 1939

COMMUNICATIONS TO THE EDITOR

SYNTHETIC AND NATURAL ANTIHEMORRHAGIC COMPOUNDS

Sir:

In our last communication [THIS JOURNAL, **61,** 1923 (1939)] the reported antihemorrhagic activity of 2-methyl-1,4-naphthoquinone was a minimum assay result. The total comparative activity of this compound is given in Table I. It is by no means as active as vitamin K [Ansbacher and Fernholz, *ibid.*, **61,** 1924 (1939)] or as low in activity as reported by Thayer, *et al.*, [*ibid.*, **61,** 1932 (1939)] and would seem to provide an effective, cheap, synthetic substitute for vitamin K. This compound, like phthiocol and others, is capable of maintaining the prothrombin level of chick blood at a normal value when sufficient is given.

We have purified or synthesized and tested a number of naphthoquinones and related compounds (Table I). Assays were conducted and results expressed as noted previously [*ibid.*, **61,** 1923 (1939)]. Entirely negative results were obtained with 1,4-benzoquinone, naphthalene, 1,4-naphthoquinone, anthraquinone, 1,2-dihydroxyanthraquinone, and hydrolapachol at levels of 100 mg. or more per kg. of diet. Thayer, *et al.*, [*ibid.*, **61,** 1932 (1939)] have reported some activity in 1,4-naphthoquinone. Fieser, *et al.*, [*ibid.*, **61,** 1925 (1939)] have indicated activity in lomatiol, lapachol and hydrolapachol. We have previously found lomatiol and lapachol to be inactive [*ibid.*, **61,** 1923 (1939)]. These other workers employ assay methods which require only twenty-four hours or less but which are, in our experience, likely to give misleading results.

TABLE I

ANTIHEMORRHAGIC ACTIVITY OF NAPTHOQUINONES

Substance	Level fed per kg. of diet, mg.	Activity in terms of cc. of ref. standard per g.[a]
2-Methyl-1,4-naphthoquinone	10	> 2400
2-Methyl-1,4-naphthoquinone	2.5	5150
2-Hydroxy-1,4-naphthoquinone	75	139
Phthiocol	20	287
Phthiocol ethyl ether	15	100
Phthiocol octadecyl ether	20	95
Phthiocol phytyl ether	20	< 50
Phthiocol monoacetate	15	420
Phthiocol triacetate	15	192
Alfalfa concentrate	0.5	>53600
Alfalfa concentrates[b]	0.2 to 0.3	63000

[a] Standard hexane extract of dried alfalfa representing 1 g. per cc. [b] From preliminary assays of alfalfa preparations (E. A. Doisy, P. Karrer).

We have made the observation that solutions of the vitamin, the purified pigment derived from the vitamin by alkaline hydrolysis, the low temperature distillate from the molecular still (contains no vitamin K), and pure phytol all exhibit a characteristic white fluorescence when exposed to the light from an argon lamp. The same fluorescence was noted in samples of vitamin K obtained from Professor E. A. Doisy and Professor P. Karrer. The active nucleus, 2-methyl-1,4-naphthoquinone, does not show this fluorescence.

We prepared 2-methyl-3(?)-phytyl-1,4-naphthoquinone by condensation of 2-methyl-1,4-naphthoquinone with phytol. Purification was effected by repeated molecular distillation. *Anal.* Calcd. for $C_{31}H_{46}O_2$: C, 82.6; H, 10.3. Found: C, 82.5; H, 10.6. The product has the color, oily form and solubilities similar to those of vitamin K from alfalfa and sublimes in the molecular still under the same temperature and pressure. It shows the characteristic white fluorescence previously mentioned and gives the color changes of the natural vitamin in sodium methylate [*ibid.*, **61,** 1610 (1939)], although the transient purple is rather weak. When administered orally to vitamin K deficient chicks three weeks old at a level of 0.2 mg. per chick the compound restored blood clotting power to normal within a few hours. Quantitative assays have not been completed [see *Biochem. J.*, **33,** 1055 (1939)].

DIVISION OF POULTRY HUSBANDRY
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H. J. ALMQUIST
A. A. KLOSE

RECEIVED JULY 21, 1939

THE CONSTITUTION AND SYNTHESIS OF VITAMIN K_1

Sir:

In a previous communication [THIS JOURNAL, **61,** 1928 (1939)] we reported some experiments on the oxidation of vitamin K_1, in which we obtained phthalic acid, a quinone acid, and a ketone $C_{18}H_{36}O$. The ketone was identified as 2,6,10-trimethylpentadecanone-14 by means of the semicarbazone, melting point 66–67°. An authentic specimen of this semicarbazone was not available at the time but we have subsequently prepared it from the ketone which we obtained by the oxidation of phytol [F. G. Fischer and K. Löwenberg, *Ann.*, **464,** 69 (1929)]. The melting point was 64–66° and the mixed melting point 64–66°.

The amount of quinone acid obtained was so small (3.5 mg.) that only one analysis was possible, and the results indicated the formula $C_{14}H_{12}O_4$. On the basis of this, it was tentatively suggested that the acid was 2-ethyl-1,4-naphthoquinone-3-acetic acid. When this acid was synthesized and found to be different, we prepared an additional amount of the quinone acid from the vitamin and converted it to the methyl ester (melting point 121–122°). This was found to be identical with a synthetic specimen of the methyl ester of 2-methyl-1,4-naphthoquinone-3-acetic acid. *Anal.* Calcd. for $C_{14}H_{12}O_4$: C, 68.84; H, 4.95. Found: C, 68.55; H, 5.22. The synthetic ester melted at 121.5–122.5° and the mixture showed no depression.

These results have been confirmed by further experiments with the diacetate of dihydro vitamin K_1 [THIS JOURNAL, **61,** 1612 (1939)]. Oxidation of this with chromic acid gave a good yield of a colorless diacetate acid melting without decomposition at 205°. *Anal.* Calcd. for $C_{17}H_{16}O_6$: C, 64.55; H, 5.10. Found: C, 64.40, 64.56; H, 5.09, 5.16. Treatment with diazomethane gave the methyl ester which melted at 127.5–128.5°. *Anal.* Calcd. for $C_{18}H_{18}O_6$: C, 65.45; H, 5.49. Found: C, 65.12; H, 5.36. This was found to be identical with a synthetic specimen of the methyl ester of 1,4-diacetoxy-2-methylnaphthalene-3-acetic acid (melting point 125–126°). The mixed melting point was 126–127°. Chromic acid oxidation of the diacetate acid from the vitamin converted it to the quinone acid which gave a methyl ester identical with the methyl ester of 2-methyl-1,4-naphthoquinone-3-acetic acid. These experiments demonstrate conclusively that the structure of vitamin K_1 is correctly represented by the formula 2-methyl-3-phytyl-1,4-naphthoquinone.

Confirmation of this structural formula for vitamin K_1 has been obtained through synthesis which was easily accomplished through direct alkylation by the method of Claisen [*Ann.*, **442,** 210 (1925)] for direct carbon alkylation of phenols. The reaction of phytyl bromide with a benzene suspension of the monosodium salt of 2-methyl-1,4-naphthohydroquinone produced the hydroquinone of the vitamin which was oxidized by the air to the quinone. This was purified by chromatographic adsorption and by high-vacuum distillation and was then subjected to reductive acetylation. The diacetate obtained in this man-

ner was crystallized from methyl alcohol. *Anal.* Calcd. for $C_{35}H_{52}O_4$: C, 78.33; H, 9.77. Found: C, 78.06; H, 9.81. The mixed melting point with an authentic specimen of diacetate from the natural vitamin showed no depression.

BIOCHEMISTRY DEPARTMENT
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E. A. DOISY

RECEIVED AUGUST 21, 1939

SYNTHETIC APPROACH TO VITAMIN K1

Sir:

In seeking a method for the introduction of the phytyl group into the 3-position of 2-alkyl-1,4-naphthoquinones we have investigated various procedures for condensing 2-methyl-1,4-naphthohydroquinone with phytol, geraniol and simpler β-unsaturated alcohols, and with dienes. In the work on vitamin E such condensations have been brought about in the presence of mineral acids (either added or liberated in the reaction) or zinc chloride and have been attended with cyclization to compounds of the tocopherol type. Since cyclization introduces a complication in the case at hand, trial was made of less powerful agents and it was found that, with anhydrous oxalic acid in dioxane solution, methylnaphthohydroquinone can be condensed with simple β-unsaturated alcohols and dienes to give considerable amounts of the uncyclized substituted hydroquinones. With 2,3-dimethylbutadiene, after refluxing for twenty-four hours, there was obtained 29% of the substituted hydroquinone, characterized as the diacetate (m. p. 119–120°, found: C, 74.04; H, 7.23), and 13% of a stable substance, m. p. 73–73.5°, which appears to be of the tocopherol type (found: C, 79.95; H, 7.63). The crude hydroquinone was converted quantitatively on oxidation to 2-methyl-3-(β,γ,γ-trimethylallyl)-1,4-naphthoquinone, m. p. 95–95.5° (found: C, 80.33; H, 7.25); this gives the above diacetate on treatment with pyridine, acetic anhydride, and zinc dust. Condensation with cinnamyl alcohol gave a hydroquinone (extracted with 10% sodium hydroxide) which formed a diacetate, m. p. 167.5–168° (found: C, 77.17; H, 6.09) and a quinone, m. p. 127–127.5° (found: C, 83.63; H, 5.71).

The reaction is being extended to other examples, including the isoprenoid alcohols, and the use of esters and ethers of the hydroquinone is being investigated. We have ascertained that phytol enters into the condensation under the above conditions or at 140°, and viscous oils have been obtained of the composition of the substituted hydroquinone or tocopherol. One preparation, purified by rather drastic treatment with alkali and by high vacuum distillation, gave C, 82.62; H, 10.52 ($C_{31}H_{48}O_2$ requires C, 82.24; H, 10.69); another after distillation gave C, 82.36; H, 10.71. The general character of the distilled material suggests that it is the tocopherol. In the geranyl series a similar product was oxidized with lead tetraacetate to a substance having the composition of the acetoxyquinone (found: C, 74.92; H, 8.15; $C_{23}H_{28}O_4$ requires C, 74.93; H, 7.69), and this route is under investigation.

Synthesis by the addition of a Grignard reagent to a 2-alkyl-1,4-naphthoquinone oxide does not appear promising. Such oxides (2-methyl, 2,6- and 2,7-dimethyl) are conveniently prepared by adding aqueous sodium carbonate to an alcoholic solution of the quinone and excess hydrogen peroxide. The 2,6-dimethyl compound, m. p. 97–98° (found: C, 71.23; H, 5.07), with either allylmagnesium bromide or magnesium bromide in ether gave a considerable amount of the bromohydrin, m. p. 146–148° (found: C, 51.05; H, 4.18; Br, 28.33), characterized by conversion to the bromodimethylnaphthoquinone, m. p. 114–114.7° (found: C, 54.64; H, 3.61).

CONVERSE MEMORIAL LABORATORY
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LOUIS F. FIESER
WILLIAM P. CAMPBELL
EDWARD M. FRY
MARSHALL D. GATES, JR.

RECEIVED JULY 25, 1939

SYNTHESIS OF 2-METHYL-3-PHYTYL-1,4-NAPHTHOQUINONE

Sir:

When equivalent amounts of phytol and 2-methyl-1,4-naphthohydroquinone are heated in dioxane solution in the presence of anhydrous oxalic acid at the reflux temperature, condensation occurs readily but the methylphytylnaphthohydroquinone produced is cyclized about as rapidly as formed and the chief reaction product appears to be the naphthotocopherol. By using a large excess of methylnaphthohydroquinone to accelerate the bimolecular condensation reaction and by operating at a temperature (75°) where cyclization is slow, it is possible to produce a considerable amount of the substituted hydroquinone.

The unchanged hydroquinone is removed by extraction from ether with dilute alkaline hydrosulfite and the phytyl-substituted hydroquinone is separated from the ether residue as a waxy, white solid by digestion with petroleum ether and centrifugation. The white sludge is oxidized in dry ether with silver oxide, and evaporation gives 2-methyl-3-phytyl-1,4-naphthoquinone as a pure yellow, rather mobile oil (Calcd. for $C_{31}H_{46}O_2$: C, 82.61; H, 10.29. Found: C, 82.76; H, 10.53). The preparation has been completed successfully ten times under slight variation of the conditions and the pure quinone obtained in yields up to half the weight of the phytol employed. Trichloroacetic acid has been used satisfactorily in place of oxalic acid and the procedure has been applied to the preparation of 2,6-dimethyl-3-phytyl-1,4-naphthoquinone (M. D. Gates, Jr.) and 2-methyl-3-geranyl-1,4-naphthoquinone (yellow oils).

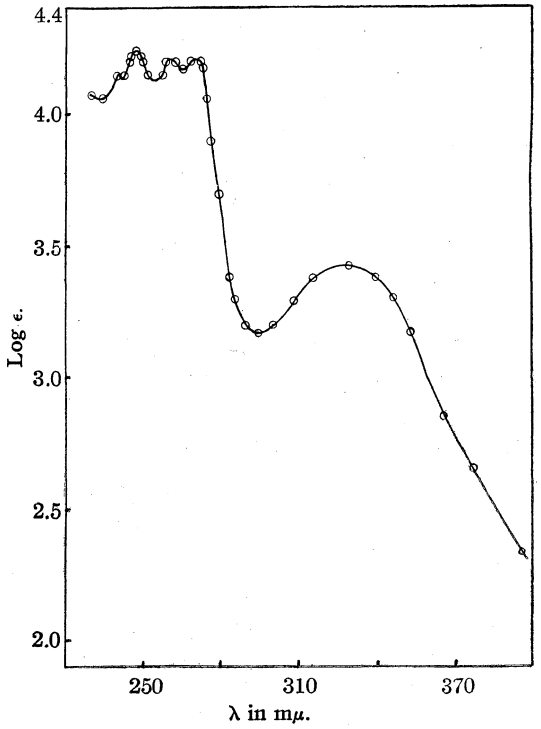

Fig. 1.—2-Methyl-3-phytyl-1,4-naphthoquinone in absolute alcohol. Maxima in mμ (with log ε values in parentheses): 241 (4.15), 248 (4.24), 260.5 (4.20), 270.5 (4.20), 328 (2.42).

In the Dam–Karrer test with alcoholic alkali, 2-methyl-3-phytyl-1,4-naphthoquinone gives striking purple or deep blue colors, depending upon the concentrations. The absorption spectrum, kindly determined by D. M. Bowen, closely resembles that reported for vitamin K_1, the curve being practically identical in form with that given by Dam, Karrer, *et al.* [*Helv. Chim. Acta*, **21**, 310 (1939)]. The positions of the maxima correspond closely with the values given for the vitamin by Dam, Karrer, *et al.*, and by Doisy, *et al.*, THIS JOURNAL, **61**, 1295, 1612 (1939), although the high extinction coefficient reported by Doisy has not been observed.

Dr. W. L. Sampson has found synthetic 2-methyl-3-phytyl-1,4-naphthoquinone to have marked antihemorrhagic activity. The substance was administered in 0.1 cc. of peanut oil to chicks which had been on a vitamin K deficient diet for two weeks and the blood clotting time determined eighteen hours after administration. The control birds all showed a clotting time of more than two hours and the following assays were made on the same day with the same group of chicks. With the Walker–Gordon standard alfalfa 75 mg. reduced the clotting time of 90% of the birds below ten minutes (av. 6.1 min.). With 2-methyl-3-phytyl-1,4-naphthoquinone a dose of 4 γ reduced the c. t. below ten minutes in 90% of the birds (av. 5 min.), while 2 γ was effective in 50%; thus 2–4 γ of the quinone is equivalent to approximately 75 mg. of alfalfa. Doses of 1 γ and 0.5 γ of 2-methyl-1,4-naphthoquinone were effective in 90% (av. c. t. 5 min.) and 30%, respectively, indicating an activity definitely greater than that of the phytyl derivative.

That the phytyl group very probably is linked through the terminal carbon atom is inferred from (1) analogy to the synthetic compounds of the vitamin E group, (2) analogy to similar condensations observed with cinnamyl alcohol and benzyl alcohol, and (3) the color reaction, which is interpreted as requiring an enolizable hydrogen on the α-carbon of the unsaturated side chain. Reductive acetylation gave the hydroquinone diacetate as a nearly colorless oil (Calcd. for $C_{35}H_{52}O_4$: C, 78.31; H, 9.77. Found: C, 78.43; H, 10.01), which resisted first attempts to effect crystallization but which eventually separated in part from methanol as colorless nodules after exposure of the solution in a Pyrex flask to sunlight, although it is not yet established that this treatment is essential. Recrystallized from methanol, the diacetate melted at 57–59° (Found: C, 78.34; H, 9.87). The hydroquinone dibenzoate, obtained as a solid after exposure to sunlight, melted at 85–86° (Calcd. for $C_{45}H_{56}O_4$: C, 81.77; H, 8.54.

Found: C, 81.63; H, 8.59). For the corresponding diacetyl derivative of natural vitamin K_1 Doisy (*loc. cit.*) found the m. p. 59°.

CONVERSE MEMORIAL LABORATORY LOUIS F. FIESER
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RECEIVED AUGUST 12, 1939

IDENTITY OF SYNTHETIC 2-METHYL-3-PHYTYL-1,4-NAPHTHOQUINONE AND VITAMIN K_1

Sir:

A comparison of the synthetic product described earlier with the natural vitamin was made possible by Dr. Byron Riegel, who generously supplied me with a highly purified 3–5% alfalfa concentrate [Riegel, Schweitzer and Smith, *J. Biol. Chem.*, **129**, 495 (1939)]. An alcoholic suspension of 5.3 g. of this oil was shaken with aqueous hydrosulfite and the vitamin hydroquinone taken into petroleum ether, extracted with Claisen's alkali containing hydrosulfite, and recovered from the yellow liquor by dilution with water and extraction with ether. Digestion with petroleum ether and centrifugation, following the procedure of the synthesis, gave a white solid yielding on oxidation 60 mg. of vitamin K_1 as a yellow oil (Found: C, 82.64; H, 10.20). The substance gives the characteristic Dam–Karrer color test, the spectrum agrees very closely with that of the synthetic quinone (T. J. Webb), and in antihemorrhagic activity the two substances appear identical within the limit of error (W. L. Sampson). Reductive acetylation gave a diacetate, m. p. 58.5–60° (Found: C, 78.13; H, 10.11) showing no depression when mixed with synthetic 2-methyl-3-phytyl-1,4-naphthohydroquinone diacetate (purified sample, m. p. 60–61.5°, remelting at 60–60.5°). Subsequent to my comparison, this finding has been confirmed by Dr. E. A. Doisy, who kindly examined my synthetic diacetate and found that it did not depress the m. p. of a purified sample of his diacetate from natural vitamin K_1. The sample was sent, at Dr. Doisy's stipulation, at the conclusion of his own work (sample received August 21, examined August 22). In contrast to the behavior noted with the synthetic compound of the methyl series and with the natural vitamin, synthetic 2-ethyl-3-phytyl-1,4-naphthohydroquinone did not separate from petroleum ether even after considerable purification had been effected by extraction with Claisen's alkali, and a sample of the quinone showing a strong color test was found inactive in fairly high dosage. The conclusion from this work is indicated by the title. A further observation, made with a sample of the synthetic material, is that the Dam–Karrer reaction results in the formation of phthiocol, m. p. 171–172°, mixed m. p. 171.5–172.5°.

In a clinical trial Drs. H. A. Frank and A. M. Seligman of the Beth Israel Hospital, Boston, found that 10 mg. of the synthetic vitamin given by mouth with 3 g. of ox bile to a patient with a complete malignant biliary obstruction reduced the prothrombin clotting time (method of Quick) from 37.5 to 17 seconds on one occasion and from 55 to 28 seconds on another. Intravenous injection of the quinone (10 mg.) in dispersion in 10% glucose solution (1 liter) was also successful and the patient was carried through operation without abnormal bleeding.

CONVERSE MEMORIAL LABORATORY LOUIS F. FIESER
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RECEIVED AUGUST 25, 1939

NEW THERMODYNAMIC DATA FOR THE CYCLOHEXANE–METHYLCYCLOPENTANE ISOMERIZATION

Sir:

The equilibria at several temperatures in the isomerization reaction Cyclohexane (liq.) $\rightleftarrows$ Methylcyclopentane (liq.) have been studied carefully by Glasebrook and Lovell [THIS JOURNAL, **61**, 1717 (1939)]. From their measurements on this reaction they have calculated the thermodynamic data at 25° which appear in the second column of Table I and then have compared these results with similar ones (Column 3) derived from the free energy studies of Parks and Huffman ["The Free Energies of Some Organic Compounds," The Chemical Catalog Co., New York, 1932, p. 90]. Here the Parks–Huffman value for ΔS, which should be quite reliable, is in fairly good agreement with the value derived indirectly by Glasebrook and Lovell but the ΔH and $\Delta F°$ values differ even in sign. These discrepancies are undoubtedly due to the fact that the Parks–Huffman ΔH value (and therefore also their $\Delta F°$) is based on early and somewhat uncertain combustion data for these two hydrocarbons. Indeed an error of only 0.25% in the two heats of combustion might conceivably account for this difference.

TABLE I

THERMODYNAMIC DATA FOR THE REACTION: CYCLOHEXANE (liq., 25°) ⟶ METHYLCYCLOPENTANE (liq., 25°)

	Calcd. from equil. meas.	Calcd. from Parks and Huffman	Calcd. by Moore and Parks
ΔH, cal.	3510	−1100	3930
ΔS, e. u.	7.9	10.0	10.0
$\Delta F°$, cal.	1150	−4100	950

In view of this situation we recently included these two substances in an extensive and very precise investigation of the heats of combustion of organic compounds which is in progress in this Laboratory. We have now obtained the following values, in terms of the "defined" calorie, for the heats of combustion of the liquid hydrocarbons per gram (*in vacuo*) at 25° and 1 atm. constant pressure: cyclohexane, 11,126.7 (±2.1) cal.; methylcyclopentane, 11,173.4 (±3.6) cal. From these data we find for the cyclohexane–methylcyclopentane isomerization $\Delta H_{298.16} = 46.7$ (±4.2) cal. per gram or 3930 (±350) cal. per mole. Taking $\Delta S = 10.0$ (±0.8) e. u. and using the relation $\Delta F = \Delta H - T\Delta S$, we next obtain $\Delta F°_{298.16} = 950$ (±420) cal. per mole. This new third law value for the free energy of isomerization is thus in good agreement with that derived from the equilibrium study of Glasebrook and Lovell.

The new thermodynamic data are now recorded in Column 4 of the table. They serve to emphasize the necessity of very precise combustion data in any accurate free energy calculations based on the third law.

Before concluding, we wish to thank the Shell Development Company for the preparation of extremely pure samples of these hydrocarbons and for the financial support which made this study possible.

DEPARTMENT OF CHEMISTRY
STANFORD UNIVERSITY
STANFORD UNIVERSITY, CALIF.
GEORGE E. MOORE
GEORGE S. PARKS

RECEIVED JULY 31, 1939

SYNTHESIS OF 2-METHYL-3-β-HYDROXY-ETHYL-N-[(2-METHYL-6-AMINOPYRIMIDYL-(5))-METHYL]-PYRIDINIUM BROMIDE HYDROBROMIDE

Sir:

In view of the marked specificity of thiamin with respect to the loading of the heterocyclic rings, it seemed of interest to synthesize the isosteric 2-methyl-3-β-hydroxy-ethyl-N-[(2-methyl-6-aminopyrimidyl-(5))-methyl]-pyridinium bromide hydrobromide. This has been accomplished in ten steps, starting with 6-amino-3-nitro-2-picoline [Seide, *J. Russ. Phys.-Chem. Soc.*, **50,** 542 (1920)]. This was converted into the 6-hydroxy-3-nitro-2-picoline according to the method of Seide (*ibid.*, p. 540). From the hydroxy compound the 6-chloro-3-nitro-2-picoline was obtained by treatment with phosphorus pentachloride. Chlorine was eliminated and the nitro group simultaneously reduced to the amino group with hydrogen and a palladium catalyst [Binz and von Schickh, *Ber.*, **68,** 320 (1935)]. The 3-amino-2-picoline (m. p. 113°) was converted into the corresponding nitrile (m. p. 58°) by a Sandmeyer reaction at *p*H 4.5. The nitrile was converted into the 2-picolyl methyl ketone (b. p. 75–78°, 2 mm.) by a modified LaForge procedure [THIS JOURNAL, **50,** 2480 (1928)]. The ketone was brominated, the reaction product without isolation being converted into the acetyl derivative by treatment with potassium acetate in alcohol. The acetylated ketol was reduced without isolating it to 2-methyl-3-β-hydroxyethylpyridine (b. p. 125°, 3 mm.), picrate (m. p. 125°). (*Anal.* Calcd. for $C_{14}H_{14}O_8N_4$: C, 45.95; H, 3.81; N, 15.3. Found: C, 46.04; H, 3.66; N, 15.37). This compound was acetylated using the method described by Kuhn [*Z. physiol. Chem.*, **259,** 50–51 (1939)] (b. p. 90–92°, 3 mm.). (*Anal.* Calcd. for $C_{10}H_{13}O_2N$: N, 7.82; CH_3CO, 24.02. Found: N, 7.9; CH_3CO, 24.4, 24.2.) The β-hydroxyethyl derivative was condensed with 2-methyl-5-bromomethyl-6-aminopyrimidine hydrobromide [THIS JOURNAL, **59,** 1052 (1937)] and the 2-methyl-3-β-hydroxyethyl-N-[(2-methyl-6-aminopyrimidyl-(5))-methyl]-pyridinium bromide hydrobromide (m. p. 247°) was obtained. (*Anal.* Calcd. for $C_{14}H_{20}ON_4Br$: C, 40.00; H, 4.76; N, 13.33; Br, 38.09. Found: C, 39.72; H, 4.97; N, 13.83; Br, 37.75.)

Owing to the difference between the pyridine and thiazole rings, the new derivative permits synthesis of isomers not possible for a thiazole and, therefore, the corresponding 2-methyl-5-β-hydroxyethyl-N-[(2-methyl-6-aminopyrimidyl-(5))-methyl]-pyridinium bromide hydrobromide (m. p. 245°?) was synthesized in a similar manner starting from the corresponding ketone [*Ber.*, **57,** 832 (1924)]. The 2-methyl-5-β-hydroxyethylpyridine is a low melting solid (b.p. 103°, 2 mm.). (*Anal.* Calcd. for $C_8H_{11}ON$: C, 70.00; H, 8.03; N, 10.21. Found: C, 69.60; H, 7.77; N, 10.08.)

A detailed report of our work will be presented in the future.

We acknowledge gratefully valuable suggestions of Dr. H. Gilman and Dr. F. B. LaForge. We are also indebted to Merck & Co., Inc., for generously furnishing us with a supply of the pyrimidine derivative used in this work. The analytical work was carried out by Dr. Carl Tiedcke of New York City.

RESEARCH LABORATORY FRANZ C. SCHMELKES
WALLACE & TIERNAN PRODUCTS, INC. ROBERT R. JOINER
BELLEVILLE, NEW JERSEY

RECEIVED JULY 3, 1939

VITAMIN K POTENCIES OF SYNTHETIC COMPOUNDS

Sir:

In view of the failure of the absorption of many patients in which vitamin K therapy is highly desirable, we have been examining various compounds which could be administered intravenously in aqueous solution. The most active compound found is 1,4-dihydroxy-2-methylnaphthalene which has a potency of approximately 1000 Thayer–Doisy units per milligram. It can be prepared readily by the reduction of the highly potent 2-methyl-1,4-naphthoquinone. Since this preparation is soluble in dilute alkali and has a high degree of potency (approximately equal to the potency of 2-methyl-1,4-naphthoquinone), it seems that this compound may prove very important for intravenous vitamin K therapy.

Supplementing our previous preliminary report [THIS JOURNAL, **61**, 1932 (1939)], we have reassayed several quinones to determine their optimum potency values. Except for 2-methyl-1,4-naphthoquinone, these more recent data agree with our previous findings. The assay of this compound was carried out by the Thayer–Doisy method, making a concurrent test, at six, eighteen and seventy-two hours. The standard was also run at varying levels at the same time for each series. The data are given in Table I. The details as to the method of feeding, care of the chicks, length of test period, manner of bleeding, etc., were essentially the same as described previously.

TABLE I

Assay period	Thayer–Doisy units per mg.
6 hours	1110
18 hours	970
72 hours	1070
Average	1050

The potency of 2-methyl-1,4-naphthoquinone (Thayer–Doisy units) agrees with the value previously assigned to the natural K_1, namely, 1000 units per milligram [*Proc. Soc. Exp. Biol. Med.*, **41**, 194 (1939)]. These results also confirm the findings of Ansbacher and Fernholz [THIS JOURNAL, **61**, 1932 (1939)].

Incidentally, in view of these observations and the lack at this time of a suitable standard, it is suggested that 2-methyl-1,4-naphthoquinone should be adopted as a basic standard for the assay of vitamin K. This compound has the desirable qualities of a standard in that it can be obtained readily in a satisfactory state of purity, has a definite melting point for characterization, and when protected from excessive exposure to light is relatively stable. The unit could then be defined in the terms used by the League of Nations committee as the specific vitamin K activity of one microgram of pure 2-methyl-1,4-naphthoquinone.

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DETROIT, MICHIGAN ORSON D. BIRD

RECEIVED AUGUST 21, 1939

ANTIHEMORRHAGIC ACTIVITY OF SIMPLE COMPOUNDS

Sir:

In connection with our investigation of vitamin K, we have tested recently a large number of derivatives of α-naphthoquinone, many of which have been prepared and reported by Professor Fieser and his collaborators[1] and some of which were synthesized in this Laboratory. At this time we wish to report our findings of the antihemorrhagic activity of 2-methyl-1,4-naphthoquinone and of some other related substances of significance.

One of the first quinones we assayed was 2-methylnaphthoquinone and, because it did not appear at that time to be as active as 2,3-dimethyl-1,4-naphthoquinone,[1] we did not determine its minimum dose.

Following the appearance of the extremely interesting report of Ansbacher and Fernholz,[2] we reinvestigated the activity of 2-methyl-1,4-naphthoquinone, and we are now in complete agreement with them.

(1) Fieser, *et al.*, THIS JOURNAL, **61**, 1925, 1926, 2206 (1939).
(2) Ansbacher and Fernholz, *ibid.*, **61**, 1924 (1939).

The assay method we employed was as follows: Day old chicks were placed on a vitamin K free diet and kept on this diet for fourteen to seventeen days. When a preliminary determination of clotting time showed that at least 90% of the chicks had clotting times above thirty minutes, the samples, dissolved in 0.1 cc. of peanut oil, were administered orally. Eighteen hours later, the clotting times on the dosed birds were determined. Usually ten chicks were used at each dose level.

In the course of six weeks, nine assays were run on 2-methylnaphthoquinone. Following is a typical protocol of our results:

Substance	Dose	No. birds	Clotting time in min. 0–5	6–10	11–30	>30	Per cent. under 10 min.
2-Methyl-naphtho-quinone	1 γ	10	5	4	1	0	90
2-Methyl-naphtho-quinone	0.75 γ	9	4	3	1	1	77
2-Methyl-naphtho-quinone	0.5 γ	9	3	1	3	2	44
Alfalfa extract	≏75 mg.	9	3	3	2	1	67
Negative controls	0	10	0	0	0	10	0

In all over 120 chicks were used in testing 2-methyl-1,4-naphthoquinone at levels of 0.5 to 1.0 γ and the results in every case were essentially the same as above.

From the results of Ansbacher and Fernholz and from ours, it would appear that, in the chick at least, 2-methylnaphthoquinone possesses antihemorrhagic activity of the same order of magnitude as the vitamin K_1 reported by Thayer, *et al.*[3] These results are particularly striking inasmuch as hitherto no simple compounds corresponding in chemical structure to the chemically identified vitamins exhibit the same order of activity as the vitamins themselves. It is also noteworthy that 2-ethylnaphthoquinone (activity above 200 γ) and 2-*n*-propylnaphthoquinone[4] (inactive at 400 γ) are decidedly less effective than the methyl homolog. While 2,3-dimethylnaphthoquinone has some antihemorrhagic activity (effective at 50 γ), 2,6- and 2,7-dimethyl-1,4-naphthoquinone[1] exhibit little, if any (inactive at 400 γ), notwithstanding the fact that the substituents about the quinone systems of the latter two compounds are similar to 2-methylnaphthoquinone.

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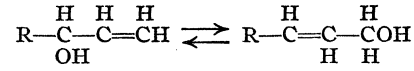
RECEIVED AUGUST 18, 1939

(3) Thayer, *et al.*, *Proc. Soc. Exp. Biol. Med.*, **41**, 194 (1939).
(4) Prepared by Professor Fieser and his collaborators.

THE INTERCONVERSION OF CROTYL ALCOHOL AND METHYLVINYLCARBINOL IN AQUEOUS SULFURIC ACID

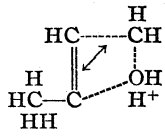
Sir:

According to the generally accepted ideas [Burton and Ingold, *J. Chem. Soc.*, 1907 (1928); J. W. Baker, "Tautomerism," pages 241–7, Routledge, London, 1934], carbinol systems of the type



are the least mobile of the allylic systems, exhibiting little or no tendency to isomerize. Although the system has been reported to be mobile when R = phenyl [Valeur and Luce, *Bull. soc. chim.*, **27,** 611 (1920)], Burton and Ingold [*loc. cit.*] were unable to verify the observation. Another example of isomerization was reported by Prévost [*Ann. chim.*, [10] **10,** 147 (1928)], who found that crotyl alcohol was formed during the dehydration of methylvinylcarbinol over alumina at high temperatures.

However, work on the mechanism of the reaction of the butenols with solutions of hydrogen bromide [Young and Lane, THIS JOURNAL, **60,** 847 (1938)] convinced us that crotyl alcohol and methylvinylcarbinol should be interconvertible in the presence of acids to form equilibrium mixtures even at room temperatures. This predicted interconversion was based on a postulate that activation of the oxonium ion of either crotyl alcohol or methylvinylcarbinol might lead to the same resonating molecule



in which the oxygen is bonded weakly to both carbons 1 and 3 [Young and Nozaki, paper in process of publication]. Consequently 50-ml. portions of crotyl alcohol and methylvinylcarbinol are being treated with mixtures of water and sulfuric acid adjusted so that the normality of acid in 228 ml. of reaction mixture is 7.4, 3.7, and 1.9. With methylvinylcarbinol after one week at room temperature the 7.4 *N* acid had caused the production of 4.5 g. of crotyl alcohol and 5 g. of a fraction which appears to be a mixture of crotyl and methylvinylcarbinyl ethers. With crotyl alcohol after two weeks the 7.4 *N* acid had produced 22 g. of the ether fraction and equal quantities, 4 g., of methylvinylcarbinol and

crotyl alcohol, while the 3.7 *N* acid had produced less ether and more alcohol, 7 g. of each. Since the problem requires a careful study of the effect of the acid concentration on the proportion of hydration, ether formation and alcohol rearrangement, we wish to record the fact that mobility may be induced in this supposedly stable allylic system even at low temperatures. The possibility that butenyl sulfates are involved in the rearrangement is being investigated.

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RECEIVED JULY 31, 1939

NEW BOOKS

Lehrbuch der organischen Chemie. (Textbook of Organic Chemistry.) By PAUL KARRER, Professor in the University of Zurich. Sixth, revised and enlarged edition. Georg Thieme Verlag, Rossplatz 12, Leipzig C 1, Germany, 1939. xxiii + 689 pp. 6 figs. 17.5 × 24 cm. Price, RM. 34; bound, RM. 36.

The sixth German edition is practically identical with the English edition recently reviewed in these pages [THIS JOURNAL, **61**, 756 (1939)]. The new subject matter in the sixth edition (which is also incorporated in the English translation) includes only the section on organic deuterium compounds (five pages), a page on ergot alkaloids and half a page on phthalocyanins. Other topics have been brought up to date, especially in the active fields of natural products. In the preface the author calls attention to a greater inquiry into reaction mechanisms than in previous editions. The change in this regard seems slight, the text retaining its almost purely descriptive character.

PAUL D. BARTLETT

The Oxidation States of the Elements and their Potentials in Aqueous Solutions. By WENDELL M. LATIMER, Ph.D., Professor of Chemistry, University of California. Prentice-Hall, Inc., 70 Fifth Avenue, New York, N. Y., 1938. xiv + 352 pp. 16 × 24 cm. Price, $3.00.

The usefullness of thermodynamic data is determined by the carefullness with which they have been obtained, the clearness with which they are presented and the convenience with which they may be used. Judged by these criteria Latimer has achieved a remarkably successful volume. The author has endeavored to include references to all works published up to 1938. The results of these investigations are presented concisely in a series of tables in the appendix. The first two give E^0 values for several hundred half cell reactions, one for acid solutions and one for alkaline solutions. Then follows a table of free energies of formation and one giving equilibrium constants, arranged alphabetically by the elements. The next table gives values for the activity coefficients of strong electrolytes and the last gives values for the entropy of elements, compounds and ions. If the volume contained only these thirty pages of tables it would be invaluable.

For the convenience of students who are not working in the field of physical chemistry, the first two chapters give an introduction to the use of the tables. These chapters discuss the subject of units, conventions, general methods employed in the determination of oxidation–reduction potentials, ionization potentials, electron affinities, lattice energies, and their relation to standard oxidation–reduction potentials. A section of the appendix serves as a guide in the use of activity coefficients and the concept of the ionic strength. Although these chapters of a general nature are designed to make the remainder of the volume useful they will also serve as a convenient review of the most often used portions of thermodynamics for students of organic and inorganic chemistry.

Nineteen chapters follow these first two general sections, taking up in detail the chemistry of the elements arranged by families. Here an investigator interested in any particular element will find gathered together the available thermodynamic data and references to the literature. These data are interpreted and applied to the chemical behavior of the element. Where no data are available the author frequently has given estimates, which will be useful guides to those without a background of long experience in this field.

This volume will not only constitute an essential part of every chemist's reference library but will also introduce students who wish to use physico-chemical data to the elements of thermodynamics.

HENRY E. BENT

Inorganic Quantitative Analysis. By HAROLD A. FALES, Ph.D., Columbia University, and FREDERIC KENNY, Ph.D., St. Francis College. Second edition. D. Appleton-Century Company, Inc., 35 West 32nd Street, New York, N. Y., 1939. xiii + 713 pp. 132 figs. 15 × 22.5 cm. Price, $4.00.

The educational philosophy of this excellent book is contained in the following sentences from the preface: "It has been the aim of the authors, in preparing this work, to apply the principles of Physical Chemistry to the theory of Quantitative Analysis in a detailed and thorough manner. In stressing this point of view, it has not been forgotten, however, that the two other

aspects of the subject, namely, technique and methods, play an equally important part in the education of the analyst." This is the pattern of nearly all the recent books in Analytical Chemistry and therefore such a book must be judged by the ratio of theory to techniques and methods. No one, however, knows what the correct ratio is, and therefore authors should not be criticized for using a given ratio. In this book there is a full measure of theory and as far as possible the techniques and method of analysis are presented from the standpoint of theory. This is also followed in the arrangement of the subject matter, as is shown by the departure from the traditional division into gravimetric and volumetric analysis.

The general techniques and the detailed procedures for carrying out the laboratory exercises are well done. At the end of each chapter is a list of problems, and there is a long appendix with a table of five-place logarithms, specific gravity tables and tables of equivalent units of the metric and English systems of weights and measures. The appendix also contains such mathematical derivations as are deemed too advanced for the text.

The chapters on precision, weighing and calibration of weights are particularly good in the wealth of information they contain. The use of organic reagents and solvents is presented in a chapter of 22 pages, and 38 pages are given to a chapter on Photometry. So much space to these subjects is unusual in a book of this kind, and, to the reviewer at least, the chapter on Photometry seems out of balance. It is nearly all theory with only one laboratory exercise, the determination of free ammonia in water. There are no exercises in turbidimetric or nephelometric methods. In the excellent chapter on electrometric methods there is no mention of the simple and accurate differential and dead-stop end-point systems of titration which require scarcely more electrical equipment than a galvanometer. The old method of determining sodium by difference is given but there is merely a literature reference to one of the triple acetate methods. These points, however, are but differences of opinion between the reviewer and the authors. Perhaps the authors are right. At any rate the reviewer likes the book and commends it heartily to students of analytical chemistry.

C. W. FOULK

Kinetik der Phasenbildung. (Kinetics of Phase Formation.) By Dr. MAX VOLMER, Professor and Director of the Division of Physical and Electrochemistry of the Institute of Technology of Berlin. Verlag von Theodor Steinkopff, Residenzstrasse 32, Dresden-Blasewitz, Germany, 1939. xii + 220 pp. 61 figs. 15.5 × 22.5 cm. Price, RM. 14.25; bound, RM. 15.

This book presents a new case—older ones are the phase rule, the Donnan equilibrium, the galvanic cell, the correlation between adsorption and surface tension—where a seed sown by Willard Gibbs and fallen, as it were, on barren land, begins to grow after many years, when touched by the moisture of true understanding. An equation given by Gibbs for the formation of a first droplet of a second liquid phase in the interior of an infinite mass of another one, which was independently re-derived by Volmer, is one fundament on which the book is based. Some others are: a molecular kinetic formulation of the continuous formation and growth of liquid nuclei and of the discontinuous formation and growth—already preconceived by Gibbs—of crystalline nuclei.

As important results of this theoretical treatment may be mentioned: a quantitative agreement as to the rate of nuclei formation in vapors of different liquids on adiabatic expansion and as to the influence of pressure upon the temperature to which a liquid may be overheated; Wilhelm Ostwald's "metastable limit" and his frequently observed rule, that the newly formed phase is generally an instable one, may be understood; the production of nuclei is enormously favored at interfaces;—this explains that "cavitation," *i. e.*, the disrupture of a liquid under the influence of supersonic waves, also occurs mainly at interfaces (reviewer's remark).

It may be hoped that many puzzling phenomena in meteorology and, particularly, in the formation of Liesegang's rings (*e. g.*, the influence of light, the similarity of complicated ring systems with wave patterns) will soon become clearer, when attacked by these new methods.

Volmer's most interesting book is very lucidly arranged: 1, a historic survey; 2, the transport of molecules from one phase to another; 3, general theory of supersaturation and of nuclei formation; 4, special kinetic treatment and comparison with experimental results (droplets in gases, bubbles in liquids, formation of crystalline nuclei in the interior of phases and at interfaces, etc.); 5, nature of new phase (primary formation of instable phases); 6, structure of new phase (growth of nuclei, etc.). Nevertheless, this book is no easy reading, because exactness of theoretical conception and derivation is the author's first law and because his "thermodynamical dialect," mainly based on Gibbs' thermodynamical potential μ, is somewhat unusual.

H. FREUNDLICH

Lehrbuch der anorganischen Chemie. (Textbook of Inorganic Chemistry.) By Prof. Dr. ERNST H. RIESENFELD. Second, revised edition. Verlag von Franz Deuticke, Helferstorferstrasse 4, Wien, Germany, 1939. xxvii + 706 pp. 90 figs. 17.5 × 25.5 cm. Price, M. 14; bound, M. 16.

The reviewer found this textbook most useful when looking up recent developments of general and inorganic chemistry. Chapters which have been treated with particular thoroughness are those on the structure of atoms (isotopes, natural and artificial radioactivity, etc.), on metals and their compounds, on crystal structure, and on complex salts. The author frequently refers to the biochemical importance of the elements. Many recent technical applications are described.—The age in which the book has been published has left a rather curious mark: gas masks are mentioned no less than five times in different chapters.

The book is well arranged and well written; an abundance of facts has been collected. There were only very few, where the reviewer did not find the information he looked for: the polarographic method, now used more and more in analytical chemistry, is not mentioned; Brönsted's conception of acids and bases has been treated rather too briefly.

H. FREUNDLICH

The Chemistry of Organic Compounds. A Year's Course in Organic Chemistry. By JAMES BRYANT CONANT, President of Harvard University, Revised with the Assistance of MAX TISHLER, Ph.D., Merck and Co. The Macmillan Company, 60 Fifth Avenue, New York, N. Y., 1939. x + 658 pp. 35 figs. 15 × 22 cm. Price, $4.00.

This admirable text, the first edition of which appeared six years ago, has now been revised with due consideration, not only to the useful newer chemical reactions, but also to the trends of organic chemistry in the direction of industry, and of biological chemistry and physical chemistry. Actually there have been added but thirty-five additional pages, yet this fact does not in any sense indicate the extent of revision, as the book has been modernized in a very effective and pleasing manner. There is a commendable choice of industrial applications. The electron theory of valence has been extended. The concept of resonance has been interestingly introduced in connection with the guanidinium ion, and elaborated further in the treatment of aromatic compounds. Indeed, wherever appropriate, there has been shown the importance of physical chemistry to organic chemistry. New and interesting information has been given on topics of biochemical significance including hormones, vitamins, sugars and proteins. The chapter on heterocyclic compounds has been enlarged. The last two chapters dealing with "Plant Pigments" and with "Advanced Topics in Stereochemistry" should certainly be provocative of interest and thought to students looking forward to advanced courses.

This is a scholarly, well-written book, which should take a front rank position among the newer organic chemistries. It is refreshing to read a text which, like the present one, departs from the stereotyped.

ARTHUR J. HILL

Photochemistry and the Mechanism of Chemical Reactions. By GERHARD K. ROLLEFSON, Ph.D., Associate Professor of Chemistry, University of California, and MILTON BURTON, Ph.D., Instructor in Chemistry, New York University. Prentice-Hall, Inc., 70 Fifth Avenue, New York, N. Y., 1939. xiv + 445 pp. 58 figs. 16 × 23.5 cm. Price, $5.75.

An excellent comprehensive survey of modern photochemistry. Following a brief introductory chapter, the authors summarize those portions of the quantum theory of atomic and molecular spectra which are necessary for an empirical understanding of spectral notation, selection rules, and potential energy curves. Fluorescence and photodissociation are discussed in two well-written chapters on the physical and chemical effects following the absorption of light. A chapter on photochemical kinetics summarizes the principles and methods used in the determination of secondary reaction mechanisms, and gives particular attention to the reactions of free atoms and radicals. In the next chapter, on photolysis in the solid state, the authors assume the de Boer "perforated lattice" model and interpret existing data, chiefly on the alkali and silver halides, on the basis of this model. The remaining two-thirds of the book is devoted to a critical summary and discussion of existing data on a large number of photochemical reactions. Most of the cases discussed involve reactions in gases, but chapters on reactions in solution and on heterogeneous reactions are included. Photography and photosynthesis, considered as photochemical processes, are interestingly discussed in the chapter on heterogeneous reactions. Useful appendices on spectral notation, bond and dissociation energies, and activation energies are included.

The experimental technique of photochemistry is not systematically discussed, although certain specialized techniques are referred to at various places in the book. Owing to the order of discussion which the authors have adopted, certain reactions will be found treated in part in one chapter and in part in another. Thus, the mercury sensitized dissociation of hydrogen is discussed in chapter 3 and again in chapter 10, the photolysis of hydrogen bromide is taken up in chapter 7, its synthesis in chapter 11, and the discussion of the photographic latent image is divided between chapters 6 and 15.

The book reflects very clearly the extent to which modern photochemistry is interrelated with spectroscopy on the one hand, and the elementary reactions of free atoms and radicals on the other, and the change in emphasis in the subject during recent years is illustrated by the fact that the law of photochemical equivalence is mentioned at only two places, while these interrelations receive much attention throughout. The book is authoritatively and clearly written and the reviewer agrees with the contention of the authors that it is possible for a person using it to "find himself with a working understanding of what has been done and an appreciation of what is still needed" in photochemistry.

PHILIP A. LEIGHTON

Calculations of Quantitative Chemical Analysis. By LEICESTER F. HAMILTON and STEPHEN G. SIMPSON. Third edition. McGraw-Hill Book Company, Inc., 330 West 42d Street, New York, N. Y., 1939. 293 pp. Price, $2.50.

Among the more difficult parts of chemistry for the elementary student to grasp thoroughly are the calculations involved in analytical work. Hamilton and Simpson have attempted to remedy this by presenting all the types of calculation concerned in a clear and concise manner under one cover, with such success that the previous editions of this book achieved wide popularity. Almost every imaginable type of problem is covered, both in explanation and in the many problems which accompany the text.

The present third edition retains the good features of the old with many improvements. The chapter on oxidation and reduction has been considerably modernized, and the sections dealing with electrolytic processes and with indicators have undergone a needed expansion. A discussion of methods of weighing also has been added, which omits, however, the method of single swing weighing. The calibration of weights also has been left out. One might also have wished for some consideration of the relative concentration of ions in solution at the end-point in oxidation–reduction titrations. The rules for balancing equations seem needlessly complicated and do not appeal to me.

On the whole, however, the book is excellently written, and should continue to be a standard text for teaching and student reference in this field.

J. C. MORRIS

Experimental Methods in Gas Reactions. By A. FARKAS and H. W. MELVILLE. The Macmillan Co., 60 Fifth Ave., New York, N. Y., St. Martin's Street, London, 1939. 389 pp. Price $7.50.

Until now the graduate student and research worker in the field of gaseous reaction kinetics have had to depend largely upon verbal exchange and chance gleanings from the literature for their information as to the techniques available in the field. Too often valuable methods have been confined to individual laboratories or have suffered untimely burial in the back files of magazines. It is true that there have been monographs on special phases such as the technique of achieving and measuring vacua, but before this there has been no attempt to provide a volume on technique in this entire field in which technique plays such an important role.

Because of this the present book by A. Farkas and Melville is an important and noteworthy one, the more especially so when the general excellence of the work is considered. Hardly a stone has been left unturned to make it a complete compendium. All the common problems of experimental method in connection with homogeneous, photochemical, and catalytic gas reactions, and many of an unusual nature have been covered. The chapter headings, Kinetical Gas Theory, Apparatus for Control of Pressure and Temperature, Preparation and Analysis of Gases, Photochemical Technique, and Experimental Methods for the Investigation of Chemical Reactions, do not give an adequate picture of the wealth and variety of material contained in the book. For example, the last chapter covers such widely varied and important topics as the construction of reaction vessels, measurement of the progress of the reaction, the theory and operation of flow systems, production and reactions of free radicals, preparation of catalysts and operation of catalytic systems, electrical activation, and the investigation of explosions and flames. Other chapters are as rich in the material considered. The procedure of the book is to present some of the major methods in considerable detail and to give many others in concise, though generally adequate form, with appropriate literature references in case further information is wanted. This allows a greater coverage than would be otherwise possible. The value of the book is further increased by the inclusion of many tables of properties of gases and gaseous systems, arranged in convenient form for the kineticist.

It is naturally difficult in a book of wide scope to maintain the same high plane throughout, particularly in one which is a pioneer. In the present instance the discussions on the construction of furnaces for high temperature work, and the automatic control of high temperatures is rather inadequate. For example, the use of solid metallic blocks for attaining even temperature distribution at elevated temperatures is not considered, nor are photoelectric devices for the regulation of temperature, of which at least one excellent type is on the market. In some instances the methods given for the preparation of gases seem not the best available, or are rather incomplete. There are other less important omissions. All these, however, are minor flaws.

One's guess is that graduate students should welcome this book with open arms, and that more mature research workers should find it of considerable inspiration and assistance. Although by its nature it will serve chiefly as a reference work for the solution of specific problems, nevertheless a straight through reading gives a fine conception of general possibilities, and may, as in the case of the reviewer, furnish suggestions for improvement of technique in unexpected places.

The book is quite free from typographical errors in the text itself, but it should be noted that in several instances the labelling on diagrams does not agree with the text explanation of them.

J. C. MORRIS

Respiratory Enzymes. Compiled under the direction of C. A. ELVEHJEM and P. W. WILSON, University of Wisconsin. Burgess Publishing Company, Mimeoprint and Photo Offset Publishers, 426 South Sixth Street, Minneapolis, Minn., 1939. x + 236 pp. 21.5 × 27.5 cm. Price, $3.28.

Different individuals in several Departments at the University of Wisconsin, interested in respiratory enzymes, were assigned, for seminar purposes, topics such as, the oxidases, dehydrogenases, hydrogen-carriers, coenzymes, etc. Their reports make up the different chapters in the book.

In gathering together the material from the current literature sufficient background from older work has been included so as to furnish an appropriate perspective for setting forth that which seems most significant in recent contributions. The presentation is well done and quite complete bibliographies are given. The authors have rendered a valuable service in bringing together in one volume a convenient survey of the current knowledge in this field of research.

J. M. NELSON

Textbook of Organic Chemistry. By E. WERTHEIM, Professor of Organic Chemistry in the University of Arkansas. P. Blakiston's Son and Company, 1012 Walnut Street, Philadelphia, Pennsylvania, 1939. xiv + 830 pp. Illustrated. 16.5 × 24 cm. Price, $4.00.

There is need for a variety of textbooks of different kinds so that the teacher may select the one adapted to his particular needs. At one end we have an outline which is to be filled in and supplemented by the teacher as he wishes; at the other end a book which comprises a large amount of information from which the teacher may select. The present text is an example of the latter kind. Comprehensiveness is its outstanding characteristic. In its 800 well-printed pages there is a deal of information, much more than can possibly be assimilated by any one student in his first year. This gives the teacher the opportunity for selection and provides the exceptional student with additional information which will interest him and

lead him on. The book is succinctly but clearly written; its size is due to the amount of material included.

The first 374 pages deal with aliphatic compounds, the next 230 with aromatic. Then come terpenes, dyes (36 pp.), alicyclic, heterocyclic, alkaloids, proteins, chemistry of the human body (12 pp.) and identification of organic compounds (14 pp.). There are a number of features not usually found in textbooks. Scattered throughout the book, without any relation to the context, are pictures with biographical sketches of 46 chemists besides Emil Fischer as a frontispiece. These are mostly moderns. The U. S. is represented by Remsen, Franklin, Baekeland, Gomberg, Stieglitz, Bogert, G. N. Lewis, Nieuwland, Whitmore, Adams, Adkins, Conant, Gilman and Kharasch.

At the back of the book there are flow sheets of a number of industrial processes, a list of books on organic chemistry, a glossary of chemical terms and a table of physical properties of some 600 organic compounds. At the end of each chapter there are a number of review questions and also literature references.

The book will make a useful text for teachers who like an abundance of material and will be useful to students and others as a compendium of information on organic chemistry. It includes many new developments such as vitamins and sex hormones.

E. EMMET REID

Fortschritte der Chemie organischer Naturstoffe. Eine Sammlung von Zusammenfassenden Berichten. (The Chemistry of Natural Products. A Collection of Review Papers.) Edited by L. ZECHMEISTER. Vol. I. Verlag von Julius Springer, Linkstrasse 22–24, Berlin W 9, Germany, 1938. vi + 371 pp. 41 figs. 16 × 24 cm. Price, RM. 28.

This timely collection contains comprehensive surveys to the middle of 1938 of the following subjects: Neuere Richtungen der Glykosidsynthese, by G. Zemplén, The Component Glycerides of Vegetable Fats, by T. P. Hilditch, Recent Advances in the Chemistry of Sterols, by I. M. Heilbron and F. S. Spring, Cozymase, by F. Schlenk and H. v. Euler, Nucleinsäure, by H. Bredereck, Chlorophyll, by H. Stoll and E. Wiedemann, and Anwendung physikalischer Methoden zur Erforschung von Naturstoffen, by O. Kratky and H. Mark.

It fills a real need for an organ for the presentation of current advances in that field of organic chemistry closely related to physiological processes. Although the chemistry of such investigations gradually finds its way into advanced organic texts, this normally occurs after the topic has been fully developed. For the presentation of subjects still in a fluid and developing state this medium is well suited.

The reviewer feels that more emphasis might be placed on the biological functions of the compounds considered, the few pages devoted to this phase of cozymase or coenzyme I being quite inadequate for the proper presentation. But he might well turn to the more biological publications, as the Ergebnisse der Enzymforschung, for their detailed treatment, and leave this publication for their chemical consideration. Thus have the editors, perhaps wisely, decided.

The fortunate choice of authors to discuss each of the fields selected for the first volume, supported by the good workmanship of the publisher, makes certain the scientific success of this volume, and it is sincerely hoped by the reviewer that it may be feasible to continue the series.

WILLIAM F. ROSS

Handbuch der Lebensmittelchemie. A. BÖMER, A. JUCKENACK and J. TILLMANS. Fünfter Band. **Getreidemehle, Honig, Zucker, Früchte, Gemüse.** (Handbook of Food Chemistry. Vol. V. Flour, Honey, Sugar, Fruits, Vegetables.) Edited by A. JUCKENACK, F. BAMES, B. BLEYER AND J. GROSSFELD. Verlag von Julius Springer, Linkstrasse 22–24, Berlin W 9, Germany, 1938. 1048 pp. 332 figs. 17.5 × 26 cm. Price: RM. 135; bound, RM. 138.60.

This volume represents the collaborative efforts of ten authors, all of them well known as contributors to *Zeitschrift für Untersuchung der Lebensmittel.* Eight chapters are devoted to the five foods which form the subject matter of this member of the *Handbuch.* Four are unique in that there is appended to each a sub-chapter on the microscopy of the food, or food product, in question. This feature is the work of one author, C. Griebel, who has written also the separate chapter (29 pages) on the microscopical examination of vegetables, potherbs and edible mushrooms.

The chapter headings and the authors responsible for the contents of each are: cereals, legumes and flour (116 p.) and bakery products (42 p.) by K. Täufel; alimentary pastes (37 p.) by R. Strohecker and R. Vauble; fruits and fruit products (198 p.) by A. Beythien; honey and imitation honey (63 p.) by W. Bartels; sugar and sugar products (121 p.) by J. Grossfeld; vegetables and vegetable products (78 p.), and fungi and mushrooms (15 p.) by O. Windhausen. Griebel, besides his contribution already noticed, treats in a masterly manner the microscopy of the starches and flours (93 p.), honey (18 p.), bakery products and baker's yeast (9 p.), and fruits, fruit products and the diseases of fruits (35 p.). The book closes with digests, written by F. Bames, of the foreign (31 p.) and Austrian food laws (7 p.). At greater length are presented the pertinent German laws (108 p.) by H. Holthöfer.

Space does not permit of a critical review of each chapter; all constitute in themselves a literary accomplishment and an authoritative presentation of the subject with a liberal use of literature citations and illustrations. Comment on a typical one, however, will suffice to illustrate the general excellence of this work.

Bartels has done food chemistry, and the honey industry in particular, a grateful service by bringing together the scattered and often times not readily accessible, newer information on the composition of honey. Griebel's use here of his original microphotographs of pollen grains adds greatly to the value of the whole chapter. The analytical aspects of the subject are given full treatment to the end that the whole constitutes an invaluable aid to the analyst.

This volume, also, rightfully deserves a place among its six predecessors in the series, for by collecting and collating the vast amount of authoritative scientific and technical matter on the several subjects in question it has performed a service not only for food chemistry in

particular, but for its allied fields of botany, biology, physiology, and agriculture as well.

H. A. SCHUETTE

Annual Review of Biochemistry. Vol. VIII. Edited by JAMES MURRAY LUCK and JAMES H. C. SMITH. Annual Reviews, Inc., Stanford University P. O., California, 1939. ix + 676 pp. 16 x 23 cm. Price, $5.00.

Volume VIII of this very useful publication continues the high standard that has been set by the previous volumes. The editor and editorial committee have shown excellent judgment in their choice of topics and have been unusually successful in their efforts to keep the size of the individual articles within reasonable bounds without sacrificing clarity of presentation or omitting mention of papers of real importance. Several of the contributors point out that exhaustive review is quite impossible within the space available, but add lists of papers not otherwise mentioned which serve to extend the ground actually covered. In spite of their deprecatory statements, little that is of moment to the average biochemist has been overlooked.

The excellent policy of frequent change in the authorship of the reviews has been continued. Owing to the appearance of a companion volume, Annual Review of Physiology, reviews of purely physiological topics are this year restricted in number while the field of biochemical topics is extended. Thus the present volume contains articles on Polysaccharides and Lignin, by K. Freudenberg; Ruminant Nutrition, by H. R. Marston; X-Ray Studies of the Structure of Compounds of Biological Interest, by W. T. Astbury; Growth Hormones in the Higher Plants, by F. W. Went; The Biochemistry of Yeast, by E. I. Fulmer; and Animal Poisons, by C. H. Kellaway; none of which has been dealt with recently if at all. The field of enzymes is divided, K. Linderstrøm-Lang having prepared the review of the Proteolytic Enzymes and K. Myrbäck that on Nonproteolytic Enzymes.

It is interesting to note the increase in space occupied by the proteins. Whereas in Volume III, in 1934, two articles were sufficient, in the present volume there are five if the two enzyme reviews may be included in this field with Astbury's paper already mentioned, A. Tiselius' article on The Chemistry of Proteins and Amino Acids, and R. W. Jackson and J. P. Chandler's on the Metabolism of Proteins and Amino Acids.

Several subjects receive attention every two years. In Volume VIII, these are The Chemistry and Metabolism of the Compounds of Sulfur, by G. Medes; Metabolism of Brain and Nerve, by J. H. Quastel; The Alkaloids, by L. Small; Chemical Aspects of Photosynthesis, by H. Gaffron; Mineral Nutrition of Plants, by J. W. Shive and W. R. Robbins; and Immunochemistry, by M. W. Chase and K. Landsteiner. Mineral Metabolism, by D. M. Greenberg has not been reviewed since 1936 and is restricted to Calcium, Magnesium, and Phosphorus, and choline has not been dealt with since 1935: the present review by C. H. Best and J. H. Ridout of Choline as a Dietary Factor is of particular interest since most of the work on this aspect of choline chemistry has been accomplished since that date.

The lipids are discussed in two sections, that on Lipid Metabolism by W. M. Sperry and that on The Chemistry of the Acyclic Constituents of Natural Fats and Oils, by R. J. Anderson and L. F. Salisbury. Carbohydrate Metabolism is reviewed by I. L. Chaikoff and A. Kaplan, Hormones by J. Freud, E. Lacqueur and O. Muhlbock, The Water-Soluble Vitamins by C. G. King, and the Fat-Soluble Vitamins by E. M. Nelson and C. D. Tolle. The review of Biological Oxidations and Reductions was prepared by M. Dixon.

A subject and an author index are included, and an errata sheet for several previous volumes is prefixed. The Editors regret that a review of Nucleic Acids, Purines and Pyrimidines failed to arrive in time for inclusion. The international aspect of this publication is emphasized by the fact that only 13 of the 25 contributions are from American laboratories; three are from English, two from Australian, and one from a Canadian source, while Germany and Sweden each provide two, Denmark and Holland each one.

H. B. VICKERY

An Introduction to Crystal Chemistry. By R. C. EVANS, M.A., Ph.D., B.Sc., Demonstrator in the Department of Mineralogy and Petrology, University of Cambridge. Cambridge University Press: The Macmillan Company, 60 Fifth Avenue, New York, N. Y., 1939. xi + 388 pp. 113 figs. 14.5 × 22.5 cm.

Since von Laue's discovery of the diffraction of X-rays by crystals in 1912, the study of atomic arrangement in solids has gone through three stages. In the first stage the laws of X-ray diffraction were developed and methods of structure analysis established. Next, the structures of an enormous number of crystalline materials were worked out, and the most important features of each structure tabulated in reference works such as Wyckoff's "Structure of Crystals" and the "Strukturbericht." In the third stage, an attempt is made to find correlations in these results, to seek out the fundamental principles which determine the structures, to relate the structures to fundamental properties of the atom and theories of chemical bonding, and to find the relationship between crystalline structure and physical properties. It is this third stage of the work which is called crystal chemistry.

The present book is an excellent introduction to this field. The author has carefully avoided making it a Strukturbericht, that is, describing structures, and as a secondary matter pointing out principles. Instead he has written the book around fundamental principles, and described only those structures which are well adapted to illustrate the principles. It is very evident that the author has put in a great deal of care and thought in the organization of the material. In a book on crystal chemistry, which is to remain of reasonable size, it is obviously impossible to include everything which various readers might desire. The Pauling–Slater theory of directed valence bonding could have been given in more detail, and a number of examples, which are here treated from the purely ionic point of view, could be shown to be equally amenable to treatment as homopolar bonding with the bond directions given by the theory. The intricate arrangement of the hydrogens in ice proposed by Bernal and Fowler is presented, but no mention is made of Paul-

ing's result that a randomness in the arrangement gives the correct entropy discrepancy.

The book is very readable, and the figures and printing are clear. It can be highly recommended as a textbook or for reading by anyone interested in the present status of the structural chemistry of solids.

B. E. WARREN

Crystalline Enzymes. The Chemistry of Pepsin, Trypsin and Bacteriophage. By JOHN H. NORTHROP, Rockefeller Institute for Medical Research. Columbia University Press, 2960 Broadway, New York, N. Y., 1939. xv + 176 pp. Illustrated. 16 × 23.5 cm. Price, $3.00.

Dr. Northrop's book is an elaboration of his Jesup Lectures, delivered at Columbia University in 1938. It brings together for the first time the studies by which he and his associates have fundamentally clarified the nature and kinetics of enzyme action. The book should be reviewed by a chemist as well as by a biologist, since the latter must take much for granted which his experimental experience is not adequate to appraise with precision. However, in the case of an investigator of Dr. Northrop's distinction, such blind acceptance is not a risk.

The part of Northrop's work which has aroused the greatest interest among biologists is that which deals with the isolation and crystallization of enzymes. After Willstätter's preparations of highly purified enzymes in 1928, it was generally believed that, since his active solutions did not give protein or carbohydrate reactions, neither of these substances was concerned with enzyme activity. But since that time, much evidence has been presented which indicates that Sumner's crystallized urease, Northrop's crystallized pepsin, trypsin and chymo-trypsin, and Anson's carboxypeptidase, as well as the amylase, papain and lysozyme preparations of other investigators, are simple proteins. Warburg's respiratory ferment is a conjugated protein and, unlike the others, has been shown to contain a prosthetic group.

Northrop is, of course, more than others less experienced in protein chemistry, aware of the fact that constant composition after repeated crystallization is not alone proof of purity in the case of proteins, and that the usual criterion of purity—melting point determination—is not applicable, since proteins decompose before melting. He has, therefore, added to his crystallization studies solubility measurements, based on Willard Gibbs' phase rule (for the conclusiveness of which this bacteriologist is unfortunately compelled to take Dr. Northrop's word); rate of sedimentation in the ultracentrifuge; quantitative relation between protein and proteolytic activity; parallelism between alkali-denaturization and loss of activity; proportionate recovery of activity with reversal of alkali-denaturization on standing near neutrality (Anson and Mirsky); constancy of activity per milligram of protein as pepsin solution is slowly inactivated at 50° and *p*H 1.8, conditions under which protein is rapidly hydrolyzed; and parallelism between inactivation and loss of native protein under ultraviolet light. He has thus followed Pasteur's historic advice and neglected no available methods to prove himself wrong—that is, to disprove the identity of his crystallized enzymes and the protein molecules comprising them. To the present reviewer it appears that there is no question of the truth of his conclusions and, indeed, their validity is no longer disputed except by isolated critics who must assume the "burden of disproof" against a mass of affirmative evidence adduced with precise experimentation and authoritative knowledge of protein chemistry.

Among the most significant of Northrop's results are his experiments on the reactivation of purified enzymes after inactivation by simple chemical and physical procedures. The most interesting of these are the acetylation experiments with pepsin. Purified pepsin was acetylated by treatment with ketene and the activity observed to decrease as the acetylation proceeded. An acetylated preparation was obtained in crystalline form which had only 60% of the original activity. When such material was subjected to treatment with $N/1$ sulfuric acid under suitable conditions the specific activity increased to the value of pure pepsin while the acetyl contents decreased from nine to four acetyl groups per molecule. The experiments, which cannot be dealt with in detail, appear to indicate that acetylation of the primary amino groups changes the activity by 10% or less, whereas addition of acetyl groups in other places causes marked decrease.

The demonstration that enzyme activity—which, in the last analysis, is the fundamental factor of metabolic activity and therefore of life processes—depends upon molecular alterations of apparently pure proteins (of molecular weights ranging from 35,000 to 70,000), is obviously a matter of fundamental importance to science in general. To the bacteriologist, however, who is dealing with problems of parasitism and with infections by ultramicroscopic virus agents, these studies are of particular importance. There can, of course, be no question that these "active" enzyme proteins are products of synthetic cell metabolism. And considering the specific nature of the enzymes produced by cells in various locations of the animal body, one must assume a chemical "director" which in each cell type determines the nature of the synthesis which leads to the building up of each particular enzyme. From this, considering the crystallization of at least one type of virus agent ("mosaic," by Stanley), it is not an intellectual trapeze act to postulate the possibility that virus agents, which have been shown experimentally to depend for multiplication on the metabolism of the living susceptible cell, may be products of abnormal autocatalytic action initiated by seeding an active enzyme system (a living cell) with small amounts of the end-product. The conception of such a "directed" synthesis is actually demonstrable in the study of bacterial dissociation; the best example being that observed with pneumococci. It has been possible in this group, for instance, to suppress by suitable manipulation the synthesis of the type specific carbohydrate of the virulent organisms, producing thereby a relatively non-virulent "rough" organism. By subjecting this rough culture to contact with dead virulent organisms containing its own or another type carbohydrate, these organisms can be made to resume the synthesis and grow out as virulent cultures of the original type or of some other, according to that of the dead organisms added. In other words,

carbohydrate synthesis is re-established and chemically directed by the addition of the respective "type" polysaccharide under suitable conditions. There is much that points in the same direction for virus agents, which play such an increasingly important role in medicine and which exhibit many of the properties of enzymes—except that they are immensely larger (10,000,000 molecular weight and above) and have not so far been observed to increase except by "seeding" living cells with pre-existing virus. Northrop has worked along these lines with bacteriophage, the formation of which—probably a nucleoprotein—from the bacterial cell he compares to the rapid increase of pepsin when small amounts of pepsin are inoculated into pepsinogen solutions. The analogy is an apt one, though as far as virus agents are concerned, the crucial experiments are still lacking. Moreover, among the virus agents, where the variation of size and chemical complexity ranges from the crystallizable probably pure protein of Stanley to the visible elementary bodies of vaccinia (mμ 200+) which appear to contain protein, carbohydrate and lipin, it is by no means clear whether we are confronted with synthetic or polymerized cell products, or with parasites that have degenerated to the extent of losing their own enzyme systems. However, until decisive experiments can be devised, it is wise to discourage speculative garrulousness which, in this zone between the "animate" and "inanimate" too often spreads from the legitimate ground of the biochemical or biophysical into what we may call the bio-metaphysical.

In pursuit of the analogy between enzymes and virus agents, immunological phenomena are of considerable importance, since there is no longer any doubt about the fact—whether one favors the intrinsic autocatalytic origin of virus or conceives them as extraneous parasites degenerated to the point of "borrowing" their metabolic enzymes, that these agents are "antigenic"—that is, sufficiently alien to the body chemistry as a whole to stimulate antibody response. Enzymes have long been regarded as possessing such "antigenicity," resembling in this sense "organ specific" proteins such as those of the lens of the eye, spermatozoa, etc. For Kunitz and Northrop's trypsin, Ten Broeck has shown such antigenic activity, as has Seastone for crystallized pepsin. These experiments, while not entirely satisfactory, still indicate adequately that, in producing enzymes, the cells are capable of building up within themselves a protein antigenically foreign to the general species antigen.

A review of this book by anyone except an experienced protein chemist must necessarily be incomplete. To the biologist it represents an achievement that cannot help making him happy to be living in an era in which biochemistry and biophysics are carrying biology out of its vagueness into the precision of chemical definition and quantitative methods.

HANS ZINSSER

BOOKS RECEIVED

July 15, 1939, to August 15, 1939

ARTHUR K. ANDERSON. "Essentials of Physiological Chemistry." Second edition. John Wiley and Sons, Inc., 440 Fourth Ave., New York, N. Y. 323 pp. $2.75.

WALLACE R. BRODE. "Chemical Spectroscopy." John Wiley and Sons, Inc., 440 Fourth Ave., New York, N. Y. 494 pp. $6.00.

NEIL CAMPBELL. "Qualitative Organic Chemistry." D. Van Nostrand Co., Inc., 250 Fourth Ave., New York, N. Y. 213 pp. $2.60.

JAMES ARNOLD CROWTHER. "Ions, Electrons and Ionizing Radiations." Seventh edition. Longmans, Green and Co., Inc., 114 Fifth Ave., New York, N. Y. 348 pp. $4.00.

LOUIS DE VRIES. "German-English Dictionary." McGraw-Hill Book Co., Inc., 330 West 42d St., New York, N. Y. 473 pp. $3.00.

RALPH E. DUNBAR. "Visual Outline of General Chemistry." Longmans, Green and Co., Inc., 114 Fifth Ave., New York, N. Y. 348 pp. $0.75.

THOMAS C. GREGORY, Editor. "Uses and Applications of Chemicals and Raw Materials." Reinhold Publishing Corp., 330 West 42d St., New York, N. Y. 665 pp. $10.00.

FRANCIS CLINT GUTHRIE AND JOHN TRENGOVE NANCE. "Cumming-Kay: A Textbook of Quantitative Chemical Analysis." Seventh edition. D. Van Nostrand Co., Inc., 250 Fourth Ave., New York, N. Y. 496 pp. $5.00.

ROZELLE PARKER JOHNSON. "Compositiones Variae. From Codex 490, Biblioteca Capitolare, Lucca, Italy. An Introductory Study." University of Illinois Press, Urbana, Ill. 116 pp. $1.50.

H. R. MAUERSBERGER AND E. W. K. SCHWARZ. "Rayon and Staple Fiber Handbook." Third edition. Rayon Handbook Co., 303-305 Fifth Ave., New York, N. Y. 832 pp. $4.50.

PERCY MAY AND G. M. DYSON. "Chemistry of Synthetic Drugs." Fourth edition. Longmans, Green and Co., 114 Fifth Ave., New York, N. Y. 370 pp. $6.00.

HARIDAS T. MAZUMDAR. "Gandhi Triumphant." Universal Publishing Co., 20 Vesey St., New York, N. Y. 103 pp. $1.00.

CARL OPPENHEIMER, KURT G. STERN AND W. ROMAN. "Biological Oxidation." Nordemann Publishing Co., Inc., 215 Fourth Ave., New York, N. Y. 317 pp. $8.25.

LINUS PAULING. "The Nature of the Chemical Bond and the Structure of Molecules and Crystals." Cornell University Press, 124 Roberts Place, Ithaca, N. Y. 429 pp. $4.50.

J. F. THORPE AND M. A. WHITELEY. "Thorpe's Dictionary of Applied Chemistry. Vol. III. Chemical Calculations-Diffusion." Fourth edition. Longmans, Green and Co., Inc., 114 Fifth Ave., New York, N. Y. 608 pp. $25.00.

RAYMOND FRANCIS YATES AND S. A. PELLERANO. "How to Make and Use a Small Chemical Laboratory." Norman W. Henley Publishing Co., 2 West 45th St., New York, N. Y. 140 pp. $1.00.

Søren Peter Lauritz Sørensen

Honorary Member of the American Chemical Society

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SØREN PETER LAURITZ SØRENSEN

1868–1939

Denmark has contributed many great figures to the world of Science since the time of Ørsted but few have left their impress on the fields in which they labored to a greater extent than Søren Peter Lauritz Sørensen, who died in Copenhagen on the twelfth of February, 1939. His seventieth birthday had been celebrated by a jubilee just over a year before his death. On that occasion a Jubilee Volume had been published to which contributions had been made by more than seventy-five students and friends working in the fields which Sørensen had influenced in Denmark and in twelve other countries of Europe and Asia, Africa and America.

Born on January 9, 1868, at Havreberg, Slagelse, the son of a farmer, Hans Sørensen, he left high school at Sorø in 1886 and went to the University of Copenhagen. Three years later, in 1889, he received the Gold Medal of the University for a paper on the conception of the chemical radical. His experimental work, however, was largely in the field of analytical chemistry and included studies on pure strontium compounds, for which he again received the Gold Medal of the University in 1896, and "Studies on Cobaltic Oxalates," which was the subject of his doctor's dissertation in 1899. Meanwhile, from the time he received the degree of Master of Science, in 1891, he was assistant at the chemical laboratory of the Danish Polytechnical Institute under Professor S. M. Jørgensen (1892–1901) and chemical consultant at the Royal Naval Dock Yard (1892–1901).[1]

In 1901, at the age of thirty-three, Sørensen was appointed Director of the Chemical Department of the Carlsberg Laboratory in Copenhagen in succession to Johann Kjeldahl. From this time on, his interest never veered from the study of amino acids and peptides, proteins and enzymes. Sørensen never doubted that the chemistry of these nitrogenous molecules was interdependent and concerned with one fundamental problem.

Sørensen began his studies of this complex field by investigations for which he was completely prepared by his earlier training. On the one hand he explored methods for the synthesis of amino acids, on the other methods for the more accurate determination of nitrogen and other analytical procedures. Then came the "Studies on Enzymes." The first of these in 1907, "Om Kvantitativ Maaling af Proteolytiske Spaltninger" was concerned with following enzyme action with the formal titration method, the second with the electromotive force method of

(1) I am indebted to Dr. K. Linderstrøm-Lang, the present Director of the Chemical Department of the Carlsberg Laboratory, for some of the information regarding Sørensen's early studies.

measuring hydrogen ion concentration. Both represent exhaustive, painstaking standardizations of procedures of such value in the study of changes in biochemical systems that the methods are still in general use and these classical papers are still constantly consulted.

The advantages of an acidimetry in terms of the negative logarithm of the hydrogen ion concentration, a quantity linear in the electromotive force, were clearly stated by Sørensen and the symbol, pH, defined in this second paper. Chemical and medical students, zoölogists, physiologists, bacteriologists, public health workers, agricultural and industrial chemists have by now become familiar with the symbol pH. In the more than thirty years since Sørensen's great paper appeared, but very few workers have seen the field more clearly in all its ramifications. In this first paper he considered the electromotive force and colorimetric methods, the choice of indicators and of standard buffer solutions, and, finally, the use of these methods in the study of enzyme action.

The methods having been developed to this point Sørensen's next great contribution was the characterization as a chemical individual of a member of the class of large nitrogenous compounds, the proteins. In 1917, there was published from the Carlsberg Laboratory a description of the crystallization of egg albumin, of its dialysis, its purification and standardization, of the estimation of its molecular weight by osmotic pressure measurements, of its acid and base combining capacity by electromotive force measurements and of the influence of neutral salts upon this and upon its solubility. A classicist by temperament and training, he began the study of proteins with a consideration of Henry's law and of the phase rule and ended it by demonstrating that even such complex molecules as the proteins could be prepared and studied with such care as had previously not been lavished upon them.

Beccari and Denis, Bence-Jones and Scherer, Ritthausen, Hofmeister, Hardy, Hopkins, Pauli, Mellanby, T. B. Osborne and a host of others had prepared and studied proteins. Conditions for the crystallization of certain of them had been described. With Sørensen the physical chemistry of the proteins passed from the stage of qualitative observation and the description of phenomena to accurate quantitative characterization in terms of laws and constants.

Sørensen subsequently studied many proteins other than egg albumin. In 1924 when he visited the United States he described in various lectures and in the *Journal of the American Chemical Society* the investigations on serum proteins on which he spent many years. On that occasion, too, he was elected an honorary member of the American Chemical Society, the first of many honors conferred upon him by American institutions. Indeed, following the war, during which his magnificent study on egg albumin appeared, Sørensen's connections with America became far closer than they had previously been. He learned English and had numerous American followers. His influence upon the approach to the study of biochemical systems by means of physico-chemical methods can scarcely be exaggerated.

The great contributions of Sørensen to science, the revolutions that he brought about, depended in the last analysis on his faith that the classical methods of chemistry could be applied to the most complex biochemical systems without sacrifice of accuracy, provided patience and understanding were constantly employed in the slow, orderly development of methods and the unfolding of problems.

During the last years of his life although his interest in the laboratory did not diminish, his concern with the role of science in industry, agriculture and the state occupied much of his time. He was a president of the Danish Scientific Society and an honored member of learned societies in Norway, Sweden, Belgium, England, France, the United States, Germany, Finland, Poland and Spain. His counsel was widely sought and his influence as a scientist upon the affairs of Denmark and of the other Scandinavian countries will be missed. His influence upon the men that he trained and upon the fields of science to which he contributed will, however, continue, for he sought the enduring qualities of precision and perfection.

EDWIN J. COHN

[CONTRIBUTION FROM THE BELL TELEPHONE LABORATORIES]

X-Ray Investigation of the Decamethylene Series of Polyesters

BY C. S. FULLER AND C. J. FROSCH

In two previous papers[1,2] results of X-ray studies on several members of the ethylene series of polyesters have been reported. The present investigation deals with the decamethylene series of polyesters and is a continuation of this work, the general aim of which is to clarify the structures of substances composed of chain molecules of high molecular weight.

The previous work has shown that polyesters of sufficiently high average molecular weight are capable of producing sharp X-ray fiber patterns when oriented specimens[3] are employed. An analysis of the fiber patterns obtained from the ethylene esters and the self ester of ω-hydroxydecanoic acid[2] has shown that in general two types of fiber patterns are present. One type found in the case of polyethylene succinate gives a much shorter fiber period than that calculated for this ester on the assumption of a planar zigzag model[1] and agrees best with a helical or coiled form of the long-chain molecules present. The other type of pattern, the one usually observed, gives fiber periods which are only slightly less (0.3 to 0.4 Å.) than the values calculated for a planar zigzag model.

In the ethylene polyesters showing the zigzag type of pattern the ester groups apparently play a part in the alignment of the chain molecules with respect to one another. The previous work on the ethylene polyesters indicated that in the odd esters studied, *i. e.*, those containing an odd number of chain atoms in the repeating unit, the chains were arranged so that the carbonyl groups of adjacent chains fell in planes perpendicular to the fiber axis. In the even esters, however, evidence favored an arrangement whereby these groups fell in planes inclined to the fiber axis. For the three even esters studied the inclination of this plane to the fiber axis was calculated to be approximately 65°.

All the members of the decamethylene series of polyesters examined in the present work show the zigzag type of fiber pattern. These patterns differ from those obtained on the ethylene series in several respects, however, and indicate that the laws determining the manner in which the chains associate are perhaps not as simple as heretofore expected. As will be shown later, however, most of the present results can be explained, qualitatively at least, by a theory proposed recently by T. Schoon.[4]

Compounds Examined.—The preparation of the polyesters and the X-ray technique employed already have been described.[1] In the present experiments decamethylene glycol reacted with the successive members of the aliphatic dicarboxylic acid series up to and including sebacic with the exception of pimelic. Polyesters suitable for X-ray investigation were obtained in all cases except that of malonic acid. The average molecular weight in each case was above 10,000 as determined by viscosity measurements. The purity of the final polyesters in view of the small amount of cyclic ester theoretically produced was considered sufficient without fractionation. Table I lists the compounds studied and their melting points.

TABLE I

SOFTENING POINTS OF DECAMETHYLENE POLYESTERS

	Compound	Softening point, °C.
1	Oxalate	77
2	Succinate	69
3	Glutarate	60
4	Adipate	74
5	Suberate	75
6	Azelate	66
7	Sebacate	73

X-Ray Results.—Highly oriented specimens of the various esters were employed in order to secure sharp X-ray fiber patterns. Characteristic copper X-radiation filtered free of beta was employed. The interplanar spacings were calculated on the basis of the known spacings in sodium chloride, which was applied as a powder directly to the specimens. The patterns corresponding to the compounds listed in Table I are shown in Fig. 1, A to G inclusive. Figure 1H illustrates the type of picture obtained when sodium chloride powder is applied to the sample of Fig. 1G. The results of the measurement of these fiber patterns are shown in Tables II and III. Table II

(1) Fuller and Erickson, THIS JOURNAL, **59**, 344 (1937).
(2) Fuller and Frosch, *J. Phys. Chem.*, **43**, 323 (1939).
(3) Carothers and Hill, THIS JOURNAL, **54**, 1579 (1932).
(4) T. Schoon, *Z. physik. Chem.*, **39B**, 385 (1938).

TABLE II

INTERPLANAR SPACINGS OF DECAMETHYLENE POLYESTERS

Reflection	Oxalate d, Å.	Oxalate Int.	Succinate d, Å.	Succinate Int.	Glutarate d, Å.	Glutarate Int.	Adipate d, Å.	Adipate Int.	Suberate d, Å.	Suberate Int.	Azelate d, Å.	Azelate Int.	Sebacate d, Å.	Sebacate Int.
A_1			4.75	W.	4.61	W.	4.64	W.	4.67	W.	4.63	W.	4.64	W.
A_2	4.23	V.S.	4.20	V.S.	4.17	V.S.	4.22	V.S.	4.20	V.S.	4.19	V.S.	4.18	V.S.
A_3	3.50	V.S.	3.67	V.S.	3.70	V.S.	3.70	V.S.	3.70	V.S.	3.70	V.S.	3.69	V.S.
A_4	2.92	S.	2.99	M.	2.98	S.	2.99	S.	2.99	S.	2.99	S.	3.00	S.
A_5	2.64	S.	2.53	M.	2.49	M.	2.51	M.	2.51	S.	2.49	M.S.	2.50	M.S.
A_6	2.47[a]	V.W.	2.38	W.	2.35	W.	2.40	V.W.	2.37	W.	2.37	M.W.	2.38	W.
A_7	2.12	S.	2.21	S.	2.22	S.	2.23	S.	2.22	S.	2.22	S.	2.23	S.
A_8			2.08	M.	2.08	M.	2.09	M.	2.08	M.	2.07	M.	2.08	M.
I_1	13.2	V.S.	13.1	S.			15.2	M.						
II_0					19.9	S.	11.0	M.	12.4	V.S.	25.0	S.		
II_1	6.62	S.	6.62	W.	13.4	M.			4.65	W.			12.0	S.
III_1	4.38[a]	W.	4.43	V.W.			6.64	M.	5.77	W.			8.50	M.
III_2	3.77	W.							3.67	W.				
III_3	3.39	W.												
IV_1	3.66	W.	4.31	V.W.			5.33	M.	3.87[a]	V.W.	9.80	M.	4.17	V.W.
IV_2	3.36	W.												
V_1	3.07	M.			5.25	W.	4.24	W.	4.03	V.W.	6.10	W.	4.98	W.
VI_0			3.20[c]	W.	6.88	W.			4.11	S.	8.49[c]	M.		
VI_1					5.03	W.	3.55	W.	3.19		7.58	M.	4.42	W.
VII_0							3.09[c]	W.						
VII_1	2.22	S.			5.58	M.			3.16	V.W.			3.73	V.W.
VII_2	2.05[b]	S.			4.59	M.								
VIII_0					5.20	M.	2.67[c]	W.	3.03[c]	W.				
VIII_1			2.22	V.S.	3.23	W.							3.29	V.W.
VIII_2			2.08[b]	M.										
VIII_3			1.89	M.										
IX_0									2.69[c]	W.				
IX_1					3.93	M.	2.22	V.S.	2.41	W.			2.94	V.W.
X_1					2.94	W.			2.21	S.			2.66	V.W.
X_2									2.13[b]	M.				
X_3									1.98	M.				
XI_0													2.39[c]	W.
XI_1													2.22	V.S.
XI_2													2.13	M.
XI_3													2.07	S.
XI_4													1.90	M.
XI_5													1.71	M.
XIV_0					2.95[c]	W.								
XVI_0					2.61	W.					3.16[c]	W.		
XVI_1					1.97	W.								
XVII_0					2.37[c]	W.								
XVII_1					2.21	V.S.								
XVII_2					2.11	M.								
XVIII_1					1.95	W.								
XX_1											1.97	W.		
XXI_1											2.22	S.		
XXI_2											2.13	M.		
XXI_3											2.06	M.		
XXI_4											1.90	W.		
XXI_5											1.85	W.		
XXI_6											1.70	S.		
XXII_1											1.99	W.		

[a] Doubtful reflection. [b] Probably a multiple reflection. [c] This may be a pseudo meridian reflection due to overlapping of layer-line arcs.

gives the interplanar spacings and Table III gives the observed fiber periods and the fiber periods calculated on the basis of a planar zigzag chain for comparison.

Several reflections not reported in Table II have also been found. At least four inner equatorial spots have been observed in the various decamethylene compounds which were not observed in the ethylene compounds. Some of these, however, may be caused by the Ag or Br

TABLE III

COMPARISON OF OBSERVED AND CALCULATED FIBER PERIODS OF DECAMETHYLENE POLYESTERS (ÅNGSTRÖM UNITS)

Polyester	Fiber period Obsd.	Calcd.
Oxalate	17.0	17.24
Succinate	19.6	19.76
Glutarate	41.6	42.04
Adipate	22.1	22.27
Suberate	24.6	24.79
Azelate	51.7	52.10
Sebacate	27.1	27.30

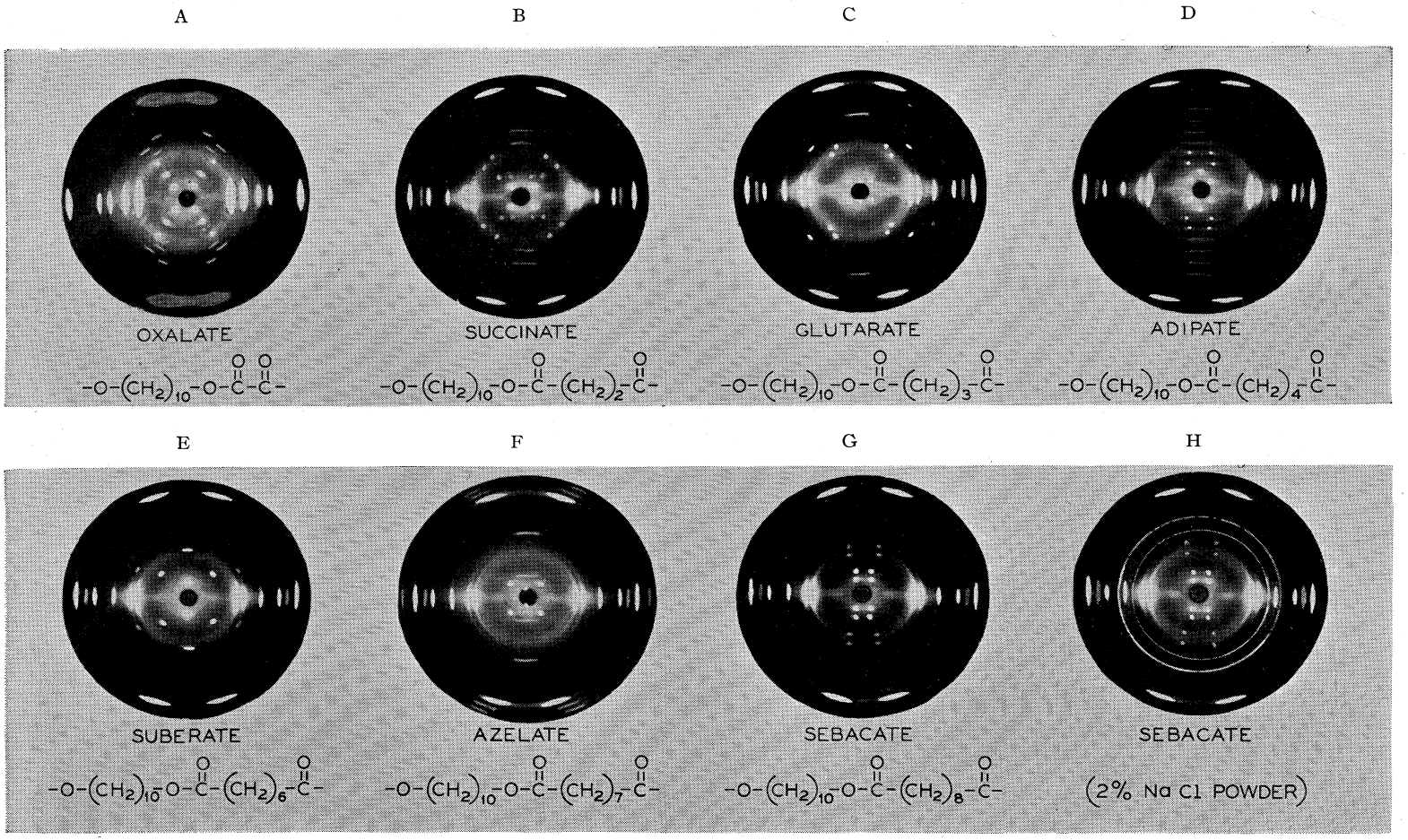


Fig. 1.—X-Ray fiber patterns of decamethylene polyesters. Fiber axis vertical.

absorption edges or by copper beta radiation. Further work is necessary before their presence can be considered proved.

Discussion of Results

(1) **The Fiber Periods.**—Examination of Table III shows that in the case of all the decamethylene polyesters studied, the observed fiber periods and the fiber periods calculated on the basis of a planar zigzag chain agree within 0.2 Å. The chains in these compounds therefore conform very closely indeed to the planar zigzag model. A somewhat greater deviation (0.4 Å.) has been reported previously[1] for the higher members of the ethylene series of polyesters. This is in support of the view advanced at the time that the ethylene glycol portion of these esters may vary somewhat from the planar configuration. The closeness of these differences to the experimental error, however, makes further investigation of this point desirable. It is entirely possible that a slight shortening of the identity periods can occur as a result of atomic vibrations in the plane perpendicular to the chains as Huggins[5] has suggested. A value of 1.51 Å. for the C–C distance would likewise bring about agreement between the calculated and observed results.

In view of the possibility of resonance in the oxalate ester a shortening of the fiber period due to a shortening of the C–C bond between the two carbonyl groups is to be expected.[6] Table III shows, however, that the oxalate fiber period deviates no more than the other esters. This is probably explained by the small magnitude of the shortening and by the fact that the increased angle between the C–C and C–O bonds partially compensates for the smaller C–C distance.

(2) **The Equatorial Reflections.**—As pointed out in a previous paper[2] the equatorial reflections for the modification of the ethylene polyesters possessing the zigzag type of chain configuration agree well in spacing with those corresponding to the (*hk*0) planes reported for the lower molecular long-chain paraffins[7,8] and esters.[9,10] This is in general true of the decamethylene polyesters also and indicates that the chain molecules pack together in the plane perpendicular to the chain axes in the same fashion in all of these cases. There are, however, certain deviations from this rule for the oxalate, as can be seen from Table II. This indicates that the distribution of polar groups along the chains influences to some extent the effective cross-section of the chains. With the exception of the oxalate, however, the interchain spacings are constant for all the esters within the experimental error and practically the same as have been found for aliphatic hydrocarbon chains ($ab \sin \beta = 37.0$ Å.^{2}).

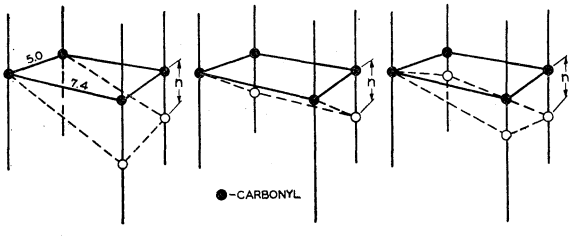
(3) **Layer-Line Reflections.**—In the decamethylene series as in the ethylene series strong second-order meridian reflections are observed in the case of the odd esters (Fig. 1C and F). These in the case of decamethylene azelate fall very close to the primary beam and are barely visible in the reproduction. These reflections agree with the twofold screw axis present in the structure and constitute further proof of the zigzag chain configuration. Unlike polyethylene azelate, however, polydecamethylene azelate shows, in addition to the second-order meridian reflections, reflections of large spacing which arise from planes inclined to the fiber axis (IV_1 Table II). Since the presence of the strong second-order meridian reflection requires an alignment of the carbonyl groups of neighboring chains in planes perpendicular to the fiber axis, these strong layer-line reflections indicate that in the case of some of the chains the carbonyl groups fall in planes inclined to the fiber axis. This also is true of decamethylene glutarate in which pyramidal spacings (II_1 Table II) occur on the same layer-line as the meridian reflections. The best interpretation of these patterns at present is that the chain molecules fit two forms of lattice. In one of these the C=O groups are aligned in planes perpendicular to the fiber axis, whereas in the other they lie in planes which form an angle with this axis.

In the case of the even decamethylene esters (Fig. 1 A, B, D, E and G) certain differences as compared with the ethylene esters are also evident. The oxalate, succinate, and sebacate behave normally in that no low-order meridian reflections are present. The adipate and suberate esters, however, show second-order reflections on the meridian. These reflections are weak in the case of the adipate and are accompanied by pyramidal reflections on the first layer-line. The suberate is unique in possessing very strong meridian reflections on the second layer-line together with weak pyramidal reflections on the third layer-line.

(5) M. L. Huggins, private communication.
(6) Robertson and Woodward, *J. Chem. Soc.*, 1817 (1936).
(7) A. Müller, *Proc. Roy. Soc.* (London), **120A**, 437 (1928), *et seq.*
(8) Kohlhaas and Soremba, *Z. Krist.*, **100**, 47 (1938).
(9) G. Shearer, *J. Chem. Soc.*, **123**, 3152 (1923), *et seq.*
(10) R. Kohlhaas, *Z. Krist.*, **98**, 419 (1938).

In view of the fact that the zigzag structure of the chain holds in the case of the suberate, as shown by the agreement of the observed and calculated fiber periods, we are forced to assume that in this ester a twofold screw axis or a glide plane exists but that it does not coincide with the chain axis. In other words, a displacement of one-half the fiber period parallel to the chain direction must occur in the case of some of the chains. Because of the high intensity of this reflection it is probable that half of the chains are shifted this amount. An analogous situation exists in the adipate. The much lower intensity of the corresponding meridian reflection in this case suggests that the halving of the fiber period may not occur as often. However, the general fuzziness of the pattern indicates that the chain arrangement is less perfect than in the case of the suberic ester.

As in the case of the odd esters the best interpretation of the fiber patterns produced by the adipate and suberate esters is that more than one form of crystalline arrangement is present. It is possible that the sebacate ester also is complicated by more than one form. The patterns of the oxalate and succinate on the other hand can be explained on the basis of one form of crystal (monoclinic). In the case of these patterns the strong pyramidal planes arise from the fact that all of the carbonyl groups fall in inclined planes. As will be seen in the next paragraph, these findings are capable of a general interpretation.



(a) (b) (c)

Fig. 2.—Possible types of gliding in polyesters.

The patterns of the even esters other than the adipate and suberate agree with the behavior of the even ethylene polyesters in showing no low order meridian reflections.[11] The pyramidal planes observed in these compounds are best interpreted as arising from the fact that a predominance of carbonyl oxygen atoms fall together with chain carbon atoms in these planes.

General Theory of the Crystalline Structure of Polyesters.—The determination of the positions of the atoms in the crystals composing the polyesters is too complex an undertaking to be solved by means of the present X-ray data. Because of the known chemical structure and the zigzag nature of the chains, however, the problem is simplified considerably. The X-ray results show that the polyester chains having the zigzag type of structure assume the same relative positions in the plane perpendicular to their long axes as do the lower molecular long-chain compounds.[12] As mentioned previously, this is strong evidence that the long chains in the polyesters have the same cross-sectional area and shape as in these lower molecular chain structures and that they behave like rigid rods in so far as packing in the crystal is concerned. Because of the great length of the chains in the polyesters and therefore the negligible influence of the end-groups on the structure, we may consider the repeating unit as the unit of packing, and attempt to work out the crystal structure on this basis.

In a bundle of chain molecules all having a common repeating unit it is evident that various crystal structures will arise depending on the relative displacement of the repeating units in the direction of the chain axis. Thus, corresponding atoms in adjacent parallel chains will assume various positions in the structure depending on the amount of gliding these chains undergo with respect to one another in the direction of their lengths. In this manner orthorhombic, monoclinic and triclinic lattices may arise. If no gliding occurs in the case of identical chains, an orthorhombic cell is possible. If, on the other hand, a glide parallel to the *ac* plane takes place as shown in Fig. 2a, a monoclinic cell may be formed. An alternative monoclinic cell may be produced by a glide parallel to the *bc* plane (Fig. 2b). Finally, a glide parallel to the diagonal plane as illustrated in Fig. 2c may result in a triclinic cell. It is possible, therefore, that all of these lattices will be observed in crystals composed of chain structures of this nature.[13]

In order to show that the crystalline polyesters

(11) Compare K. H. Storks, THIS JOURNAL, **60**, 1753 (1938). As pointed out in ref. 2, most of the polyesters undoubtedly possess meridian reflections on the layer-line corresponding to the number of chain atoms in the repeating unit. Because of the comparatively long wave length employed, however, these reflections are not observed in this work.

(12) As pointed out, in the oxalate ester the interchain spacings are somewhat different from the higher decamethylene esters.

(13) It is possible to draw up unit cells in which the chain axis is always perpendicular to one face. These large cells, however, turn out to be multiples of the smaller cells considered in the present treatment. The latter are, therefore, to be regarded as the true unit cells.

so far examined can be explained on the basis of the theory briefly outlined above, let us consider those chain structures which are essentially zigzag in form and in which the chains fall on a Müller net ($a = 5.0$, $b = 7.4$). The assumption is made that when gliding occurs, its magnitude is always an integral multiple of the distance between chain atoms as measured parallel to the chain. In the case of the esters this distance is obtained by dividing the observed identity period along the fiber axis by the number of bonds composing the repeating unit. For the ethylene polyesters[14] the distance averages 1.19 Å., whereas for the decamethylene polyesters the average distance is 1.23 Å. Decamethylene oxalate[15] has a slightly lower value, 1.21 Å. By multiplying this distance by n the total displacement in the chain direction is obtained.

TABLE IV

Ester	Reflection	Obsd.	Calcd. for Glide n	
Decamethylene oxalate	I_1	49	49.2	5(ac)[a]
			47.5	4(bc)
Succinate	I_1	42	40.7	7(ac)
			39.1	5(bc)
Glutarate	II_0	90	90.0	Zero
	II_1	40	40.7	7(ac)
			39.1	5(bc)
Adipate	I_1	43	45.1	6(ac)
			45.5	4(bc)
	II_0	90	90.0	Zero[b]
Suberate	II_0	90	90.0	Zero[b]
	III_1	45	45.1	6(ac)
			45.5	4(bc)
Azelate	II_0	90	90.0	Zero
	IV_1	49	50.3	5(ac)
			47.5	4(bc)
Sebacate	II_1	62	63.8	2(bc)
			63.5	3(ac)
Ethylene adipate	I_1	65	64.3	3(ac)
			64.7	2(bc)
Suberate	I_1	65	64.3	3(ac)
			64.7	2(bc)
Azelate	II_0	90	90.0	Zero
Sebacate	I_1	65	64.3	3(ac)
			64.7	2(bc)
ω-Hydroxy-decanoic ester	II_0	90	90.0	Zero

[a] (ac) designates glide parallel to *ac*-plane. [b] In these cases as noted in the text a screw axis non-coincident with the chain is supposed to be present.

Table IV shows the agreement obtained between the observed angles and angles calculated on the basis of the above glides. In the second column are given important low order reflections for each of the esters employing the designations of Table II. Reflections for the ethylene polyester and ω-hydroxydecanoic ester taken from previous publications are also included. The angles which the planes causing these reflections make with the fiber axis are given in the third column. These angles have been calculated from the observed fiber periods and the *d*-values corresponding to the planes in question. In column 4 are listed the angles calculated on the basis of the glides in column 5. Only values of n which agree best with the observations are recorded. Glides parallel to the diagonal planes as shown in Fig. 2c have not been considered since the angles corresponding to these cannot be calculated on the basis of the available data. The possible solutions in column 5 therefore are not to be considered as inclusive. The agreement between the observed and calculated angles is, however, confirmatory of the gliding theory. The choice of the proper lattice and unit cell from among the various possibilities must await more complete experimental results. It is planned to present a more detailed analysis in the case of some of the structures in a later publication.

The general theory given above to account for the various polyester structures is essentially that given by T. Schoon[4] to explain the various polymorphic forms of the lower molecular weight chain compounds. In this way Schoon accounts nicely for the various monoclinic and orthorhombic forms shown by these compounds. On this same basis one might expect that the polyesters would also exhibit a variety of stable modifications in the case of each compound. From the results presented above on the decamethylene polyesters this appears to be the case.

The authors wish to thank Mr. N. R. Pape for his assistance in the X-ray work.

Summary

1. Decamethylene polyesters of average molecular weight above 10,000 have been prepared from the following acids: oxalic, succinic, glutaric, adipic, suberic, azelaic and sebacic.

2. X-Ray fiber patterns have been obtained on oriented fibers of these compounds. Complete measurements of the patterns are given and it is shown that in all cases the molecules conform closely to the planar zigzag model. Except in the

(14) The present argument applies only to zigzag chain configurations.

(15) For the oxalate $a = 5.28$ Å., $b = 7.00$ Å. have been employed.

case of the oxalate ester, all of the structures conform to the same lateral packing as is shown by the lower molecular chain compounds.

3. A discussion of the origin of the various fiber patterns is given. It is shown that in the case of certain esters the presence of different crystal forms is indicated. A general interpretation of these forms on the basis of the theory of Schoon is presented.

NEW YORK, N. Y. RECEIVED MAY 17, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

Kinetics of the Exchange of Oxygen between Benzoic Acid and Water[1]

BY IRVING ROBERTS AND HAROLD C. UREY

The organic compounds which thus far have been found to exchange their oxygen with that of water are aldehydes, ketones, carboxylic acids, and a few very reactive alcohols.[2] A kinetic study of the exchange of oxygen between acetone and water in the medium 90% acetone-10% water was made by Cohn and Urey,[3] who demonstrated a general acid catalysis which is significant for the mechanisms of both the hydration and the enolization of acetone. The obvious structural similarity of the acid catalyzed esterification and ester hydrolysis reactions to the oxygen exchange reactions of carboxylic acids indicates that a kinetic study of the latter should yield results at least as interesting as those obtained in the acetone exchange.

Benzoic acid exchanged both its oxygen atoms with that of water, the reaction being catalyzed by acids, as is the case for the exchange of carboxylic acids in general.[4-6] The usual method for following exchange, that of mixing comparable amounts of the reacting substances, cannot be used at ordinary temperatures in the case of benzoic acid since the compound is not sufficiently soluble in water to cause an appreciable change in the heavy oxygen content of the water. Rather than introduce the complication of a mutual solvent, we have devised a method of determining the heavy oxygen content of benzoic acid and have carried out the kinetic experiments in dilute aqueous solution.

(1) Presented at the Baltimore meeting of the American Chemical Society, April, 1939.

(2) For a summary of the literature on this subject, see Reitz, *Z. Elektrochem.*, **45**, 100 (1939).

(3) Cohn and Urey, THIS JOURNAL, **60**, 679 (1938).

(4) Roberts, *J. Chem. Phys.*, **6**, 294 (1938).

(5) Senkins and Brown, *J. Org. Chem.*, **2**, 569 (1938).

(6) The present work shows that the statement of Koizumi and Titani [*Bull. Chem. Soc. Japan*, **13**, 607 (1938)] that only one oxygen atom of benzoic acid is readily exchangeable cannot be correct. Such a statement is quite unreasonable in the light of our present knowledge of the rapid dissociation of the hydrogen ion from a carboxylic acid and of the symmetrical structure of a carboxylate ion.

Experimental

Decarboxylation Apparatus.—The determination of the O^{18} content of benzoic acid depends upon the observation of Sabatier and Mailhe[7] that benzoic acid will be converted almost quantitatively into benzene and carbon dioxide when passed over reduced copper at 500°. For the present work, it was necessary to construct an apparatus which would perform the decarboxylation of a few milligrams of benzoic acid in a stream of nitrogen gas, and which would be free of traces of oxygen, carbon dioxide, water, or copper oxide. In addition, after each conversion, the apparatus should be easily made ready for the succeeding one, since many samples must be converted for each kinetic experiment.

The apparatus finally used is shown in Fig. 1. Tank nitrogen was admitted at the left through a flowmeter (A) and successively through a tube of copper at 350° (B), a bubbler containing sulfuric acid (C), and tubes D and E, filled with potassium hydroxide and anhydrous calcium sulfate, respectively. At this point the nitrogen can be made to take one of two paths; if stopcock K is closed, it can pass through J into the decarboxylation tube (I) containing copper at 500° and into the air through stopcock F. On the other hand, with stopcock J closed, the nitrogen could enter tube I through stopcock F and pass successively through K, a trap (L), and into the air through stopcock O. Tube I was made of temperature-resistant glass (Corning 172), and sealed directly to the Pyrex tubing at either side. Tube H was 1.5 cm. in diameter and contained a ring seal with an opening of about 2 mm. diameter. The apparatus also contained a safety seal (G), a manometer (M), a sample tube fitted with a break seal (N), and a trap (P) surrounded with solid carbon dioxide to protect a Hyvac pump connected at the right.

After sweeping out with hydrogen gas to reduce the oxides of copper, the entire apparatus was evacuated and filled with nitrogen. Trap L was surrounded with liquid nitrogen. The nitrogen stream was then adjusted to 30 cc./min., and directed through J, through tubes I and H and into the air through F (stopcocks K and O being closed). The plug in tube H was removed, the tube containing the benzoic acid inserted around the ring seal and the plug replaced. The benzoic acid sample tubes, which were 10 mm. in diameter and of the shape shown in the upper left of Fig. 1, were first wiped with chamois to

(7) Sabatier and Mailhe, *Compt. rend.*, **159**, 219 (1914).

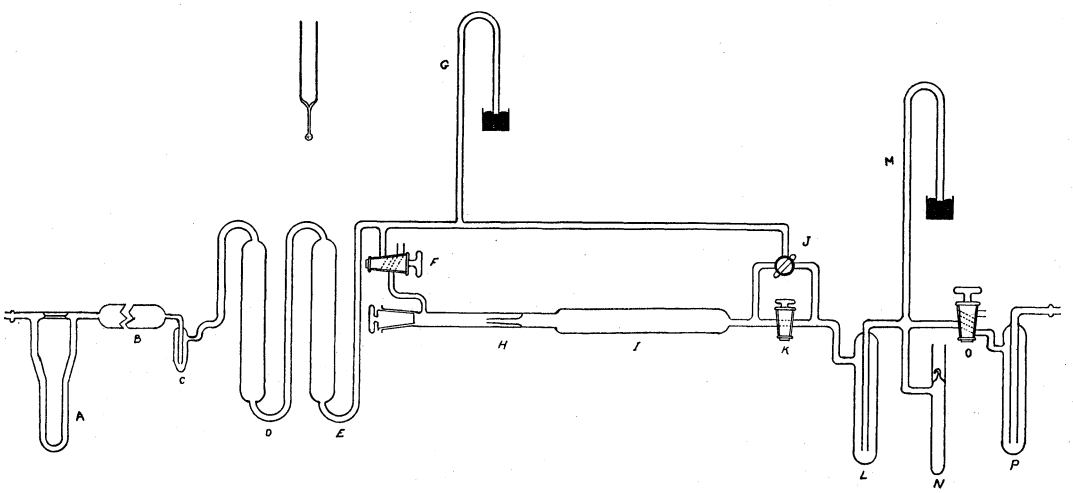


Fig. 1.

remove any organic material which would produce carbon dioxide on being heated. The purpose of the inner seal of tube H was to direct the stream of nitrogen into the benzoic acid sample tube when it was put into place.

After sweeping out the air introduced with the tube for four minutes, the nitrogen stream was reversed by turning stopcock F, closing stopcock J, opening stopcock K, and opening stopcock O to the air. The benzoic acid was then sublimed into I with an ordinary Bunsen flame, both the benzene and the carbon dioxide produced being caught in trap L. After allowing the nitrogen stream to continue for fifteen minutes, stopcocks O and K were closed, and the gas was again directed through J, I, H, and F, into the air. The nitrogen gas remaining in the portion of the apparatus to the right of stopcocks J and K was then pumped out through O and P. Stopcock O was turned off and the liquid nitrogen around trap L was removed and replaced with solid carbon dioxide–acetone mixture, thus keeping the benzene frozen while allowing the carbon dioxide to vaporize. After observing the pressure on the manometer (M), the carbon dioxide was distilled into the sample tube (N) by cooling it to liquid nitrogen temperature, the sample tube being then sealed off at the side-arm and set aside for mass spectrometer analysis.

To prepare the apparatus for the next conversion, the first benzoic acid sample, stopcock O was opened to the air and a new carbon dioxide sample tube sealed on. The air was then pumped out, liquid nitrogen placed around trap L, and the evacuated space filled with nitrogen through stopcock J (stopcock F having been closed). In this way no air was admitted to tube I at any time. The nitrogen stream was again directed from left to right through tube I and the process carried out as before. The time elapsed between the beginning of one conversion to the beginning of the next was about fifty-five minutes.

Materials and Solutions.—Benzoic acid, recrystallized twice from alcohol and water and once from water, was dried over phosphorus pentoxide. Hydrochloric acid solutions were prepared from the C. P. concentrated reagent and standardized against standard 0.1 *N* sodium hydroxide, the primary standard being Bureau of Standards potassium acid phthalate. C. P. potassium chloride was used directly.

Heavy oxygen water, prepared by fractional distillation,[8] was refluxed with alkaline permanganate for one hour, fractionated, and distilled from chromic acid. Analysis by the method of Cohn and Urey[8] showed that this water was 0.515% H_2O^{18}. Heavy oxygen benzoic acid was prepared as follows. A solution of 1.7 g. of benzoic acid in 65 cc. of heavy oxygen water which was also 0.1 *N* in hydrochloric acid was allowed to stand in the thermostat at 80° for forty-eight hours. The heavy oxygen water and the hydrochloric acid were completely distilled away *in vacuo*, and the remaining solid was powdered and dried over phosphorus pentoxide. Conversion of a sample to carbon dioxide by the above procedure and analysis in the mass spectrometer showed that this benzoic acid contained 0.465% O^{18}. Ordinary benzoic acid was found to contain 0.204% O^{18}.

Kinetics.—Kinetic measurements were made in an oil thermostat set at 80.00 ± 0.03° with a Bureau of Standards platinum resistance thermometer. In general, 10 cc. of hydrochloric acid solution (ordinary H_2O or H_2O^{18}) was pipetted into a 20-cc. long-necked flask fitted with a ground-glass joint and stopper. After allowing the flask to stand in the thermostat for at least thirty minutes, a glass bucket containing about 120 mg. of benzoic acid (heavy) was lowered into it by means of a platinum wire. The flask was shaken vigorously and the time recorded; the benzoic acid was completely dissolved within one minute. In calculating velocity constants, concentrations were corrected for expansion of the solution from room temperature to 80°; evaporation error was found to be negligible.

At known intervals, approximately 1-cc. portions were withdrawn by means of a long medicine dropper and delivered into the benzoic acid sample tubes of the type mentioned above and shown in the upper left of Fig. 1. The tubes were chilled immediately to room temperature, causing most of the benzoic acid to crystallize and effectively stopping the reaction. Most of the solution was then drawn off by means of a fine capillary pipet, the benzoic acid crystals being large enough to remain behind. Before decarboxylation, the last traces of water were

(8) Huffman and Urey, *Ind. Eng. Chem.*, **29**, 531 (1937).

pumped away from each sample by inserting the tube into a larger tube fitted with a ground cap and connected to a Hyvac pump.

The efficiency of this drying process was tested by crystallizing ordinary benzoic acid from heavy oxygen water in the absence of hydrochloric acid catalyst, drawing off the water, and pumping for various lengths of time. The benzoic acid was then decarboxylated and the carbon dioxide analyzed in the mass spectrometer. It was found that four hours of pumping were necessary to remove the water completely within the precision of analysis. About one-fourth of the benzoic acid was also lost during the pumping process.

Mass Spectrometer Analysis.—The carbon dioxide samples from the benzoic acid decarboxylations were analyzed for the ratio of mass 44 to mass 46, corresponding to the species CO_2^{16} and $CO^{16}O^{18}$, respectively. The relation of the heavy oxygen content of the carbon dioxide to this ratio can be seen from the following. If α is the atom fraction of O^{18} in the carbon dioxide, the amounts of the three species CO_2^{18}, $CO^{16}O^{18}$ and CO_2^{16} will be in the ratio $\alpha^2 : 2\alpha(1-\alpha) : (1-\alpha)^2$, assuming the gas to be in statistical equilibrium. The ratio of mass 44 to mass 46 will then be

$$R = (1-\alpha)^2/2\alpha(1-\alpha)$$

Solving for α, we have

$$\alpha = 1/(2R+1)$$

as the formula for calculating the mole fraction of O^{18} from the experimentally determined ratio. Only small amounts of gas are necessary for a mass spectrometer determination; the precision of these analyses was in general better than 1%.

Kinetics of the Reaction

In the exchange of O^{18} between benzoic acid and water, the three species of benzoic acid and two species of water react as follows

$$C_6H_5CO_2{}^{18}H + H_2O^{16} \underset{k^{-1}}{\overset{k_1}{\rightleftharpoons}} C_6H_5CO^{16}O^{18}H + H_2O^{18}$$

$$C_6H_5CO^{16}O^{18}H + H_2O^{16} \underset{k^{-2}}{\overset{k_2}{\rightleftharpoons}} C_6H_5CO_2{}^{16}H + H_2O^{18}$$

Assuming that there are no specific differences in reactivity between O^{16} and O^{18} species of the same compound, and that both oxygens of benzoic acid exchange with equal ease, the relations of the various rate constants to each other may be determined by inspection. For example, at equal concentrations, reaction 1 will be twice as successful as reaction 2, since only half the reactions of $C_6H_5CO^{16}O^{18}H$ with H_2O^{16} will result in exchange; that is, $k_2 = k_1/2$. In like manner, it will be seen that $k_{-1} = k_1/2$ and that $k_{-2} = k_1$.

If the three forms of benzoic acid are statistically distributed, their concentrations may be represented

$$[C_6H_5CO_2{}^{18}H] = \alpha^2[C_6H_5CO_2H]$$
$$[C_6H_5CO^{16}OH^{18}] = 2\alpha(1-\alpha)\,[C_6H_5CO_2H]$$
$$[C_6H_5CO_2{}^{16}H] = (1-\alpha)^2\,[C_6H_5CO_2H]$$

where α is the atom fraction of O^{18} in the benzoic acid and $[C_6H_5CO_2H]$ is the (constant) total concentration of the benzoic acid in moles/liter. Similarly, we may write

$$[H_2O^{18}] = \beta[H_2O]$$
$$[H_2O^{16}] = (1-\beta)[H_2O]$$

where $[H_2O]$ is the total concentration of water and β is the atom fraction of O^{18} or the mole fraction of H_2O^{18} in the water.

Considering the initial condition in which the benzoic acid contains the excess of O^{18}, the rate of the reaction will be

$$\frac{-d}{dt}\{[O^{18}] \text{ in benzoic acid}\} = \frac{-d}{dt}\{[C_6H_5CO^{16}O^{18}H] + 2[C_6H_5CO_2{}^{18}H]\}$$
$$= k_1[C_6H_5CO_2{}^{18}H][H_2O^{16}] + k_2\,[C_6H_5CO^{16}O^{18}H][H_2O^{16}]$$
$$-k_{-1}[C_6H_5CO^{16}O^{18}H][H_2O^{18}] - k_{-2}[C_6H_5CO_2{}^{16}H][H_2O^{18}]$$

Substituting for the various rate constants their equivalents in terms of k_1 and for the concentrations of reactants the values given above, we obtain, after cancelling terms

$$-2[C_6H_5CO_2H]\frac{d\alpha}{dt} = k_1[C_6H_5CO_2H]\,[H_2O]\,(\alpha-\beta)$$

$$\frac{d\alpha}{dt} = k(\beta-\alpha), \text{ where } k = k_1[H_2O]/2.$$

Therefore the change of the O^{18} content of the benzoic acid with time should be independent of the concentration of benzoic acid and first order in the difference of O^{18} content of the reactants. Integrating, holding β constant[9]

$$k = \frac{2.303}{t}\log\frac{\alpha-\beta}{\alpha_0-\beta}$$

By an entirely similar derivation, it can be shown that when the water contains the excess of O^{18} initially

$$k = \frac{2.303}{t}\log\frac{\beta-\alpha_0}{\beta-\alpha}$$

(9) Under the conditions of these experiments, the water is in large excess over the benzoic acid so that the heavy oxygen content of the water does not change measurably. If the water were not in large excess, one would proceed by noting that the total O^{18} concentration is a constant, *i. e.*

$$[O^{18}] = 2\alpha[C_6H_5CO_2H] + \beta[H_2O] = \text{constant}$$

Substituting for β in the above rate expression

$$\frac{d\alpha}{dt} = \frac{k_1}{2}\{[O^{18}] - \alpha([H_2O] + 2[C_6H_5CO_2H])\}$$

an equation which is symmetrical in the water and the benzoic acid and which is easily integrated.

Results and Discussion

A typical set of data is shown in Table I and plotted in Fig. 2. The second column of Table I gives the amount of carbon dioxide at atmospheric pressure obtained from each benzoic acid sample; this was calculated from the volume of the apparatus and the pressure observed. The best straight line which is drawn through the points of Fig. 2, was calculated by the method of least squares. The length of the lines represents the probable error. Velocity constants were calculated from the slope of the least squares straight line, the time being in minutes.

TABLE I

KINETIC EXPERIMENT 4

$[HCl] = 0.478\ N$; $[C_6H_5CO_2H] = 0.0564\ M$; $\beta = 0.00200$; $\alpha_0 = 0.00465$

t, min.	Cc. CO_2 at atm. P	R	α	$-\text{Log}\ (\alpha - \beta)$
0	4.4	107.1	0.00465	2.5767
30	0.6	121.0	.00412	2.6737
45	.8	120.3	.00414	2.6696
60	.8	129.2	.00386	2.7305
75	.8	137.0	.00364	2.7852
90	1.0	150.8	.00330	2.8861
120	1.0	159.4	.00313	2.9469
150	0.8	172.9	.00288	3.0555
180	1.6	180.1	.00277	3.1135
210	0.5	189.4	.00263	3.2007

The results of the five experiments performed are shown in Table II. A comparison of Experiments 1 and 2 will show that the rate of the reaction is independent of which reactant contains the excess of O^{18} initially. In Experiment 3, the hydrochloric acid concentration was increased five-fold, causing a five-fold increase in the rate. Decreasing the concentration of benzoic acid by a factor of two in Expt. 4 had no effect on the reaction velocity, as predicted by our derivation above. Finally, addition of potassium chloride in Expt. 5 had no effect on the rate, demonstrating the absence of any salt effect. The variation of k_H is within the precision of about 4% for the determination of a rate constant.

TABLE II

RATES OF EXCHANGE AT 80°

Expt.	α_0	β	[HCl]	$[C_6H_5CO_2H]$	k	k_H[b]
1	0.00204	0.00515	0.0932 M	0.1088 M	0.00129	0.0138
2	.00465	.00200	.0936	.1058	.00129	.0138
3	.00465	.00200	.478	.1082	.00693	.0145
4	.00465	.00200	.478	.0564	.00711	.0149
5[a]	.00465	.00200	.0936	.1009	.00131	.0141

[a] This reaction mixture was also 0.0937 N in potassium chloride. [b] k_H is the rate constant for 1 N hydrochloric acid. Mean $k_H = 0.0142 \pm 0.0004$.

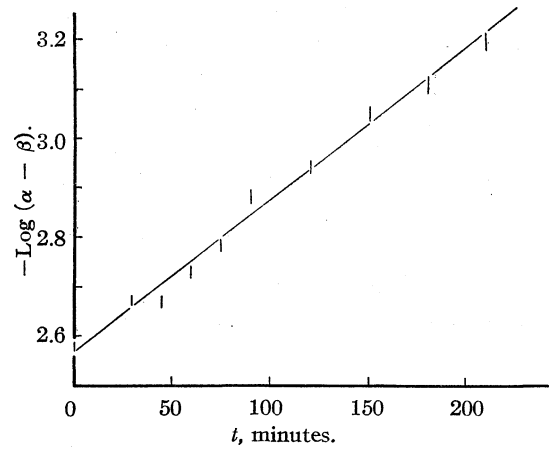


Fig. 2.—Expt. 4.

The fact that the exchange reaction is first order in hydrogen ion serves to further demonstrate the similarity of the nature of this reaction to the acid catalyzed esterification and ester hydrolysis reactions. The agreement of the rates of these three reactions with each other offers further evidence toward this conclusion. We already have demonstrated that in methyl alcohol as a medium the rates of esterification and exchange of benzoic acid are comparable.[10,11] In addition, the rate of hydrolysis of methyl benzoate at 80° is of the same order of magnitude as the rate of exchange determined in the present work,[12] the exchange being about ten times faster.[13] Discussion of the mechanisms of the three reactions on the basis of oxygen exchange work and the existing kinetic data is left for a succeeding paper.

From the point of view of reaction kinetics in general, further work on the exchange of oxygen between benzoic acid and water should include the temperature coefficient, the rate in H_2O–D_2O mixtures, and the effect of substituents in the benzene ring on the rate. It should be emphasized that oxygen exchange reactions proceed at convenient rates with no change in the medium and are of a simple first order dependence.

Summary

The rate of exchange of oxygen between benzoic

(10) Roberts and Urey, THIS JOURNAL, **60**, 2391 (1938).

(11) Herbert and Lander, *Trans. Faraday Soc.*, **34**, 1219 (1938); *Nature*, **142**, 954 (1938), have predicted this result on the basis of our previous experiments.[8]

(12) Bolin, *Z. anorg. Chem.*, **177**, 227 (1938).

(13) The observed k_H for the exchange was multiplied by 2 to obtain $k_1[H_2O] = 0.0284$ as compared to $k[H_2O] = 0.0028$ calculated from the data of Bolin for the hydrolysis. k_1 as defined in the derivation above is the constant which should be used for this comparison since it represents the rate constant for the exchange which is effective at every reaction.

acid and water has been measured at 80° in dilute aqueous solution using hydrochloric acid as a catalyst. The reaction was followed by decomposing into benzene and carbon dioxide samples of benzoic acid crystallized from the reaction mixture and analyzing the carbon dioxide in the mass spectrometer. The rate is first order in the difference of O^{18} content of the reactants, first order in hydrogen ion, independent of the concentration of benzoic acid, and free of salt effects.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

The Mechanisms of Acid Catalyzed Ester Hydrolysis, Esterification and Oxygen Exchange of Carboxylic Acids

BY IRVING ROBERTS AND HAROLD C. UREY

In addition to the known kinetic data on the acid hydrolysis of esters and on the esterification of carboxylic acids, we now have available the results of heavy oxygen studies of both the esterification[1] and the exchange[2] of carboxylic acids. The purpose of this paper is to show that by combining these data it is possible to eliminate all but a few of the large number of mechanisms which may be proposed for all three reactions.

The three reactions show a number of striking similarities. Besides the structural similarity of reactants and products, the reactions are all catalyzed by acids. In addition, there seems to be little doubt that both the hydrolysis and esterification are general acid catalyzed. Dawson[3] has shown that the hydrolysis of ethyl acetate is catalyzed by acetic acid molecules, chloroacetic acid molecules and bisulfate ions. Hinshelwood[4] has demonstrated catalysis of the esterification by a number of fatty acid molecules and Goldschmidt[5] has done the same for such acids as trichlorobutyric acid. On the basis of this general acid catalysis the retardation of esterification in alcoholic media by the addition of water discovered by Goldschmidt[6] is explained by the fact that ROH_2^+ is a stronger acid than H_3O^+ in the Brönsted sense. The exchange of oxygen between benzoic acid and water is first order in hydrogen ion[2]; as yet there are no data to determine whether the reaction is general acid catalyzed.

A further correlation lies in the fact that the rates of the three reactions are of the same order of magnitude. The nearness of the rates of hydrolysis and esterification is well known; one of the problems in studying the kinetics of either reaction has been the elimination of the reverse one. Furthermore, in a methyl alcoholic medium containing about 5% water, the rate of esterification is about twice the rate of exchange of benzoic acid[1]; when these rates are corrected to the same concentrations of methanol and water, the latter is about four times as fast as the former. Finally, in water as a medium, the rate of exchange of benzoic acid is about ten times the rate of hydrolysis of methyl benzoate at the same temperature.[2]

A similarity in the linkages broken on esterification and exchange is also known. In the esterification of benzoic acid a carbon–oxygen bond of the benzoic acid is broken rather than that of the methyl alcohol.[1] The same must of course be true for the exchange of oxygen between benzoic acid and water. A recent heavy oxygen study of acid catalyzed ester hydrolysis has shown that the same linkage is broken in this reaction.[7]

Because of the above evidence, we are assuming that the mechanisms of all three reactions are entirely similar. This would presuppose a symmetrical mechanism for esterification and hydrolysis, since it is reasonable to assume that the reverse of one would be the mechanism of the other. The term "symmetrical mechanism" is used here in the sense that the reverse of such a mechanism for esterification will be a mechanism for hydrolysis which is structurally similar to it. A symmetrical mechanism must obviously be the case for the oxygen exchange reaction, where for example the mechanism of the reaction of $RCO^{16}O^{18}H$

(1) Roberts and Urey, THIS JOURNAL, **60**, 2391 (1938).
(2) Roberts and Urey, *ibid.*, **61**, 2580 (1939).
(3) Dawson and Lowson, *J. Chem. Soc.*, 2444 (1927); 393 (1929); Dawson, Pycock and Spivey, *ibid.*, 291 (1933).
(4) Rolfe and Hinshelwood, *Trans. Faraday Soc.*, **30**, 935 (1934); Newling and Hinshelwood, *J. Chem. Soc.*, 1357 (1936); Fairclough and Hinshelwood, *ibid.*, 593 (1939).
(5) Goldschmidt, *Trans. Faraday Soc.*, **24**, 662 (1928).
(6) Goldschmidt, *Ber.*, **28**, 3224 (1895); Goldschmidt and Udby, *Z. physik. Chem.*, **60**, 728 (1907).
(7) Dalla, Day and Ingold, *J. Chem. Soc.*, 838 (1938).

with H_2O^{16}, would be similar to its reverse, the reaction of $RCO^{16}{}_2H$ with H_2O^{18}. Finally, as a further simplification, we are making the usual assumption that each mechanism will contain only one rate controlling step, *i. e.*, that there is only one activated complex whose disappearance controls the rate of the reaction.

An important consideration which does not seem to have been emphasized previously is that the esterification and hydrolysis reactions are very probably first order in alcohol and water, respectively. The existence of the relationship

$$\frac{\text{moles ester} \times \text{moles water}}{\text{moles alcohol} \times \text{moles acid}} = K$$

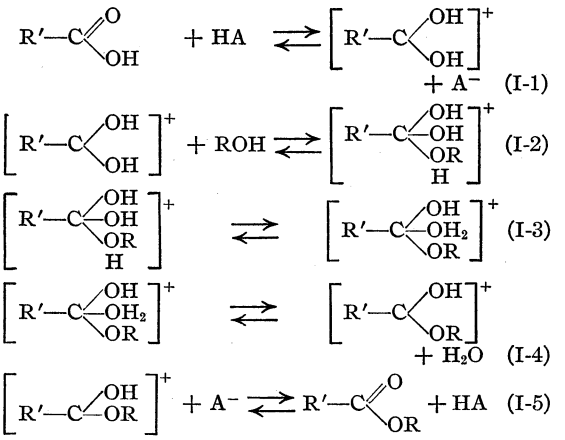
which is so universal as to be largely independent of medium as well as temperature,[8] would argue at least at equilibrium for a first order dependence of esterification rate on the alcohol concentration and of hydrolysis rate on the water concentration. While some reactions are known to change in mechanism while approaching equilibrium, this would not be expected to take place for these comparatively simple reactions. This is especially true for the exchange reaction, where the equilibrium constant is undoubtedly very close to unity. It is therefore difficult to see how the first order dependence on the alcohol and water concentration would apply to the condition of equilibrium and not to other conditions.

In addition, a first order dependence of the rate of esterification on the alcohol concentration is known in formic and acetic acid as media from the cryoscopic measurements of Kailan and co-workers,[9] who have also demonstrated different esterification rates for different alcohols.

The Reactive Complex

It is possible to eliminate immediately a large number of mechanisms by a consideration of the reactive complex for each of the three reactions under discussion. As Wynne-Jones and Eyring[10] have emphasized, kinetics of a reaction alone can only determine the compounds entering into the rate controlling step, *i. e.*, the composition of the reactive complex. Granting that the exchange, esterification, and hydrolysis reactions are general acid catalyzed and first order in alcohol or water, their reactive complexes must be, respectively, R'COOH·H_2O·HA, R'COOH·ROH·HA, and R'COOR·H_2O·HA. Of course, the last two are identical since the reactive complex must be the same for forward and reverse reactions.

Having determined the composition of the critical complex, we can state that all mechanisms which do not form this complex are incorrect. Under this classification falls a group of bimolecular mechanisms (*i. e.*, mechanisms consisting of a series of bimolecular steps) several of which have been widely supported. For example, the esterification mechanism of Watson,[11] although not given as a symmetrical one, may be written



The reverse of this mechanism will be seen to be a similar mechanism for ester hydrolysis.

None of these steps produces the critical complex required by the kinetic data for step (I-1) lacks a molecule of alcohol, steps (I-2), (I-3), and (I-4) lack an A^- ion, and step (I-5) lacks a water molecule. Or, from another point of view, one may state that step (I-1) cannot be rate controlling, since the reaction would then be independent of the alcohol concentration, and that step (I-2) cannot be rate controlling, for then the reaction would be specific hydrogen ion catalyzed. This last may be seen from the rate expressions

$$V = k_2[\text{ROH}]\left[\text{R}'\text{—C}(\text{OH})_2\right]^+ = k_2K_1\frac{[\text{ROH}][\text{RCOOH}][\text{HA}]}{[\text{A}^-]}$$

$$= \frac{k_2K_1}{K_a}[\text{ROH}][\text{RCOOH}][\text{H}^+]$$

where k_2 is the rate constant for step (I-2), K_1 is the equilibrium constant for step (I-1), and K_a is the dissociation constant of the acid HA.

(8) Berthelot and Pean de St. Gilles, *Ann. chim. phys.*, [3] **65**, 385 (1862); **66**, 5 (1862); **68**, 225 (1863); Schultz, THIS JOURNAL, **61**, 1443 (1939).

(9) Kailan and co-workers, *Monatsh.*, **51**, 334 (1929); **60**, 386 (1932); **61**, 116 (1932); **62**, 284 (1933); **63**, 52 (1933); **63**, 155 (1933).

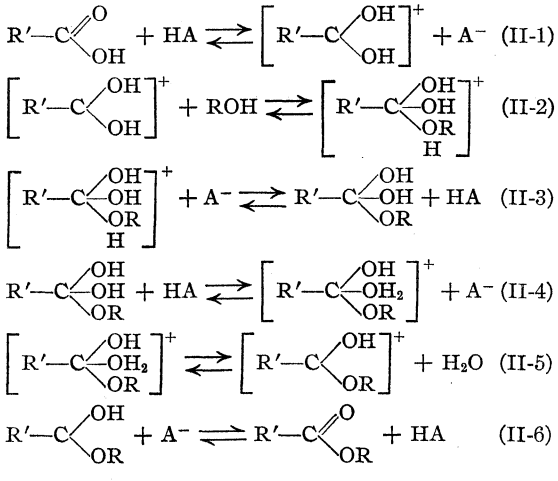
(10) Wynne-Jones and Eyring, *J. Chem. Phys.*, **3**, 492 (1935).

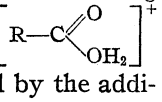
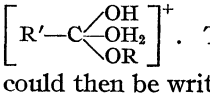
(11) Evans, Morgan, and Watson, *J. Chem. Soc.*, 1168 (1935); Watson, "Modern Theories of Organic Chemistry," Oxford University Press, 1937, pp. 130, 211.

Similar reasoning would apply to the other steps, but this is sufficient to demonstrate that the much simpler consideration of the critical complex involved would eliminate these steps as possibilities.

The mechanism proposed by Ingold[7,12] for ester hydrolysis involving the intermediate ion RCO^+ is eliminated similarly since none of its steps contains the correct reactive complex. In fact, on this basis we have eliminated eight other such bimolecular mechanisms, any of which are as reasonable as the two mentioned above.

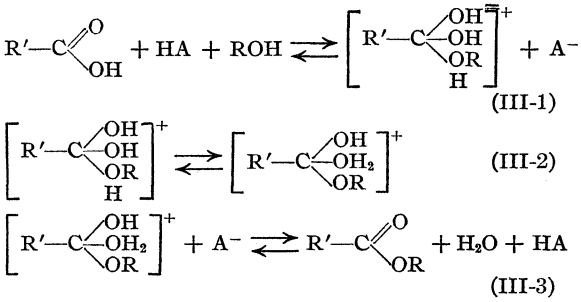
There are three possible mechanisms, however, which do lead to the reactive complex required by the kinetics. One of these is a bimolecular mechanism



Reaction (II-1) cannot be rate controlling since it does not contain the alcohol. If (II-2) or (II-5) were rate controlling the reaction would be specific hydrogen ion catalyzed. (II-6) cannot be rate controlling since it does not contain the water. Only (II-3) or (II-4) contain the required reactive complex and hence can be rate controlling. Modifications of this reaction mechanism may be made. Thus instead of (II-1) a reaction donating the proton to the OH group giving  is possible. This might be followed by the addition of the ROH to the double bond giving  . The remainder of the mechanism could then be written in a symmetrical way.

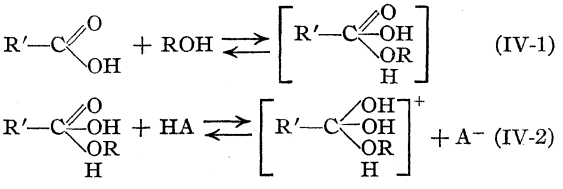
This mechanism II, or its modification discussed above, is in line with current mechanisms of similar reactions. From this point of view, the formation of an acid or ester ion by the addition of a proton seems probable. Only after the formation of such an ion or when HA is in the neighborhood of the acid or ester could water or alcohol take part in the reaction since otherwise the reaction would not be catalyzed. The addition and subtraction of protons represented by steps (II-3) and (II-4) are commonly assumed mechanisms.

Lowry[13] has proposed a termolecular mechanism for esterification of the following nature

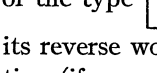


where either step (III-1) or (III-3) may be rate controlling. This mechanism is entirely possible, since it would yield both general acid catalysis and a first order dependence on the alcohol concentration or on the water concentration in the case of the hydrolysis reaction.

An alternative mechanism would be obtained by separating step (III-1) into the equivalent reactions



in which step (IV-2) would be rate controlling. This differs from mechanism (III) merely in that it supposes a time interval between addition of alcohol and catalyst molecules, rather than a simultaneous addition of the two to the carboxylic acid. In the case of ester hydrolysis this mechanism is lent some support by cryoscopic studies which demonstrate the existence of ester–water compounds in aqueous solution.[14]

The complex formed in step (IV-1) cannot be of the type  since this reaction and its reverse would result in uncatalyzed esterification (if a water molecule were removed) as well as rapid uncatalyzed exchange of carboxylic

(12) Ingold and Ingold, *J. Chem. Soc.*, 756 (1932).

(13) Lowry, *ibid.*, 1381 (1925); *ibid.*, *Trans. Faraday Soc.*, **24**, 545 (1928); Waters and Lowry, "Physical Aspects of Organic Chemistry," Van Nostrand, New York, 1936, pp. 270–272.

(14) Kendall and Harrison, *Trans. Faraday Soc.*, **24**, 588 (1928).

acids. Step (IV-3) could be divided into two steps in an entirely similar manner.

The reactive complex method also proves to be more than a method of simplification; it may, in addition, bring out mechanisms which might otherwise have been missed. For example, in the exchange of oxygen between acetone and water, not only is the bimolecular mechanism of Cohn and Urey[15] a possibility, but several other mechanisms, including a termolecular one, will yield the same reactive complex. At the present time there seems to be no method of distinguishing among these mechanisms for acetone exchange, and also of distinguishing among the mechanisms proposed for the three reactions discussed in this paper. However, the elimination process which we have presented above does lead to a criticism of current theory of the relative rates of acid catalyzed reactions in light and heavy water.

The criterion of pre-equilibrium proposed by Bonhoeffer and Reitz[16] is based on a two step mechanism similar to the first two steps of mechanism I. The criterion may be stated as follows. If the rate of an acid catalyzed reaction is increased on going from H_2O to D_2O, then a pre-equilibrium exists and the reaction is specific hydrogen ion catalyzed. If, however, the rate is decreased on going from H_2O to D_2O, the first step is not an equilibrium but is rate controlling, and the reaction is general acid catalyzed.

It has been demonstrated that the rate of ester hydrolysis is greater in D_2O than in H_2O for both methyl acetate[17] and ethyl acetate.[18] Thus, by the above criterion, we would expect the reaction to be specific hydrogen ion catalyzed. Actually, the data of Dawson quoted above show that ester hydrolysis is general acid catalyzed. A similar contradiction exists for the esterification reaction. Since the equilibrium constant for the equilibrium ester + water $\rightleftarrows$ alcohol + acid does not change on going from H_2O to D_2O,[19,20] and since the rate of hydrolysis is known to be greater in D_2O than in H_2O, the rate of esterification must also increase on going from H_2O to D_2O. Here again the data quoted above show general acid catalysis, whereas the Bonhoeffer criterion would predict a pre-equilibrium.

The source of these difficulties lies in the assumption of a simple two step mechanism, a mechanism which, as we have shown in the discussion given previously, is very improbable for ester hydrolysis and esterification since neither of these steps contains the correct reactive complex.

Summary

1. By combining recent heavy oxygen studies with the available kinetic data for acid catalyzed ester hydrolysis, esterification and oxygen exchange of carboxylic acids, it has been shown to be very probable that all three reactions are similar in mechanism.

2. On the basis that these reactions are general acid catalyzed and first order in alcohol or water, it is possible to write the composition of the reactive complexes whose disappearance will control the reaction rates.

3. Of the large number of mechanisms which have been proposed for these reactions, only three yield the critical complex required by the kinetics.

4. The Bonhoeffer criterion of pre-equilibrium in light and heavy water has been criticized on the ground that the mechanism assumed is incorrect for the reactions discussed here.

NEW YORK, N. Y. RECEIVED JULY 14, 1939

(15) Cohn and Urey, THIS JOURNAL, **60**, 679 (1938).

(16) Bonhoeffer and Reitz, *Z. physik. Chem.*, **A179**, 135 (1937); Bonhoeffer, *Trans. Faraday Soc.*, **34**, 252 (1938); Reitz, *Z. Elektrochem.*, **44**, 72 (1938).

(17) Hornel and Butler, *J. Chem. Soc.*, 1361 (1936).

(18) Schwarz, *Z. Elektrochem.*, **40**, 474 (1934).

(19) Nachod, *ibid.*, **44**, 72 (1938).

(20) Kailan and Ebeneder, *Z. physik. Chem.*, **A180**, 157 (1937).

[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY AND PHARMACOLOGY, SCHOOL OF MEDICINE AND DENTISTRY, THE UNIVERSITY OF ROCHESTER]

Adsorption Studies on Enamel, Dentine and Bone[1]

BY MARIAN LEFEVRE MANLY AND SYLVIA R. LEVY

The adsorption of radioactive phosphorus by calcified tissues is possible both during the preparation of samples using the glycol-extraction procedure[2] and during calcification of these tissues in the animal body.

In previous work from this Laboratory using rats fed radioactive phosphorus, tooth and bone samples were freed from organic material by extraction with a 3% potassium hydroxide–ethylene glycol solution. If adsorption occurred during the extraction procedure, phosphate from the organic portions would be added to the inorganic material, thereby giving high results. Adsorption might be expected for tooth and bone apatites if their behavior is analogous to that of precipitated hydroxyl-apatite. Hodge, LeFevre and Bale[3] postulated that "commercial tertiary calcium phosphates are probably hydroxyl-apatite with more or less adsorbed phosphate ions to give empirical formulas approaching the theoretical."

Adsorption may also have a role in calcification *in vivo*, since the mineral salts have an apatite structure[4] yet contain greater than the theoretical amounts of phosphorus. A demonstration that phosphate ions in contact with the mineral phase of tooth or bone substance yield solutions which are described by the Freundlich adsorption isotherm would constitute an important confirmation of the adsorption hypothesis.

Procedure

Radioactive sodium acid phosphate was prepared by dissolving radioactive red phosphorus in *aqua regia* and neutralizing with sodium carbonate to *p*H 6–7.

Samples.—The samples used were powdered, size-graded dentine, powdered enamel and bone, all of which had been extracted with 3% potassium hydroxide in ethylene glycol to remove the organic material.[5] The enamel and dentine had been separated according to the flotation method of Manly and Hodge.[6] Samples of approximately 100 mg. of the dried powders were placed in 50-cc. centrifuge tubes, 10 cc. of 3% potassium hydroxide in ethylene glycol added and amounts of the radioactive sodium acid phosphate (not greater than 1 cc. volume) added to give various concentrations of phosphate. The mixtures were boiled for one and one-half hours, centrifuged and the glycol decanted according to the procedure already published.[5] The powder was then washed in boiling distilled water, centrifuged, and the water decanted and the powder washed with hot water into a porcelain filter set in a suction flask. After a second washing with hot distilled water, the powder was dissolved in hydrochloric acid, the solution evaporated down to 2 cc. and the activity determined with a Geiger–Müller counter.[7]

Results

To ascertain the relation of the phosphate adsorbed to that remaining in the glycol, all the data have been plotted to test the agreement with the Freundlich adsorption equation.

$$\log_{10}\frac{x}{m} = \log_{10} k + \frac{1}{n}\log_{10} C$$

The curves for enamel, size-graded dentine and bone are found in Figs. 1 and 2. Regardless of the particle size or the amount of phosphate used for each tissue, when the logarithm of the amount of phosphate adsorbed per unit weight of adsorbent is plotted against the logarithm of the concentration remaining in the solution, a straight line is obtained.

Discussion

Appreciable adsorption of phosphate takes place *in vitro* on enamel, dentine and bone. However, significant amounts of phosphate would be adsorbed during the preparation of samples for analysis only if the concentration of phosphate in the extraction medium is high. The calcified part of tooth tissues contains much larger amounts of marked phosphorus than the associated soft tissues, for example, the average percentage of the dose in incisor pulps is 0.007%, while that in the incisors from the same animals is 0.38%.[8] Therefore, even with a 95% adsorption of the phosphate from the pulp, the error would not exceed 2%, which is less than the error of the radioactivity measurement.[7]

According to Freundlich, the constant k is the

(1) The data in this paper were submitted by one of us (M. L. M.) in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

(2) Crowell, Hodge and Line, *J. Dent. Research*, **14**, 251 (1934).

(3) Hodge, LeFevre and Bale, *J. Ind. Eng. Chem.*, **10**, 156 (1938).

(4) Bale, LeFevre and Hodge, *Naturwissenschaften*, **40**, 636 (1936).

(5) LeFevre and Manly, *J. Am. Dent. Assoc. Dental Cosmos*, **25**, 233 (1938).

(6) Manly and Hodge, *J. Dent. Research*, **18**, 2 (1939).

(7) Bale, Haven and LeFevre, *Rev. Sci. Instruments*, **10**, 193 (1939).

(8) Manly and Bale, *J. Biol. Chem.*, **129**, 125 (1939).

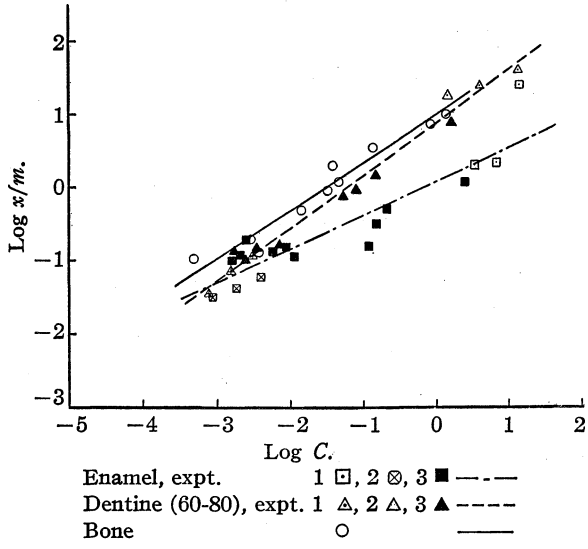


Fig. 1.—Showing the adsorption of radioactive phosphate by powdered enamel, dentine and bone. Note the adsorption in each case obeys the Freundlich equation.

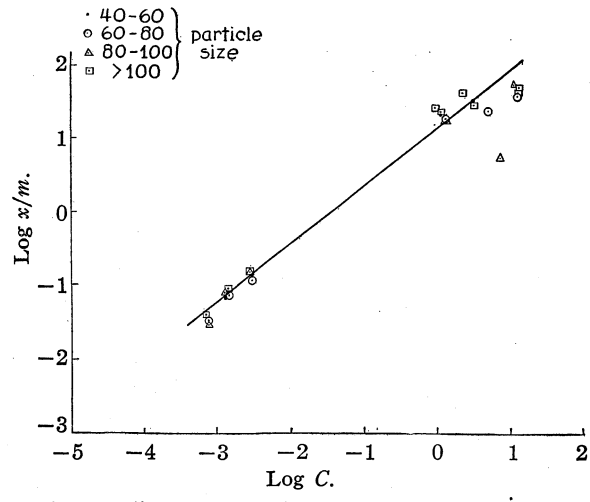


Fig. 2.—Showing the adsorption of radioactive phosphate by powdered size-graded dentine of different sizes. Note that there is no relation between adsorption and particle size.

adsorbent value; and, for any specified adsorbed substance, is characteristic of the adsorbent. The adsorption exponent $1/n$ at a given temperature and for adsorbents of identical chemical composition is characteristic of the adsorbed substance. Although the mineral phase of dentine is known to have slightly more magnesium and carbonate than that of enamel, the principal constituents (calcium and phosphorus) are present in equal amounts in the two tissues[9] and the principal molecular lattices apparently are identical.[10] Therefore, $1/n$ can be assumed to be independent of the adsorbent. From the curves for enamel, dentine and bone (Fig. 1) the calculated constants are as follows.

	Enamel	Dentine	Bone
Adsorption exponent (n)	2.3	1.4	1.6
Adsorbent value (k)	1.4	7.3	8.8

Since the adsorbed substance is the same for these experiments, the adsorption exponents should be the same. The values found for enamel, dentine and bone, 2.3, 1.4 and 1.6, respectively, are regarded as agreeing satisfactorily. However, the k values, which characterize the adsorbent, are not the same for the three tissues. Although the values for dentine and bone are nearly alike (7.3 and 8.8) the enamel value (1.4) is about one-sixth as large. This means a much greater adsorptive power for dentine and bone than for enamel. The greater adsorption is consistent with the fact that the ultimate crystals of dentine and of bone are smaller than those of enamel (of the order of 10^{-6}, 10^{-6} and 10^{-5}, respectively).[11] The effect must be attributed to the ultimate crystal size, for differences in particle size do not affect the amount of phosphate adsorbed (Fig. 2).

Furthermore, the concept of Hodge[12] that tooth and bone crystals are hydroxyl-apatite with varying amounts of adsorbed phosphate is supported by these findings.

One point should be emphasized: these studies demonstrate true adsorption and not the establishment of a chemical equilibrium between the tooth or bone powder and the phosphate in the surrounding medium. At the beginning of the experiment, there is a certain ratio of marked to total phosphorus in the extraction medium. If there were a chemical exchange of phosphorus, a constant ratio between marked phosphorus in the tissue and in the extraction medium would be observed and there would be no change in the total phosphorus in either phase. The data presented here show no such linear relationship; they satisfy exactly the criteria for adsorption according to Freundlich's adsorption isotherm.

Acknowledgments.—The authors acknowledge the assistance of Dr. Harold C. Hodge and Dr. Richard S. Manly in supplying some of the samples and for aid in preparing the manuscript.

(9) Armstrong and Brekhus, *J. Biol. Chem.*, **120**, 677 (1937).
(10) Bale and Hodge, *Naturwissenschaften*, **24**, 141 (1936).
(11) Bale, Hodge and Warren, *Am. J. Roent. Rad. Therap.*, **33**, 369 (1934).
(12) French, Welch, Simmons, LeFevre and Hodge, *J. Dent. Research*, **17**, 401 (1938).

We are indebted for the radioactive phosphorus to the Physics Department of The University of Rochester and to the Radiation Laboratory of the University of California. This work was supported by a grant from the Rockefeller Foundation.

Summary

Quantitative measurements on the adsorption of phosphate ion by powdered enamel, dentine and bone have been made. From varying concentrations of radioactive phosphorus as sodium acid phosphate in ethylene glycol, the tissues adsorb phosphate according to the Freundlich adsorption isotherm. The adsorptive power of dentine and bone are about the same and seven times greater than that of enamel.

ROCHESTER, NEW YORK RECEIVED JULY 3, 1939

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, NO. 715]

A Redetermination of the Fluorine–Fluorine Distance in Potassium Bifluoride

BY L. HELMHOLZ AND M. T. ROGERS

Introduction

In an electron diffraction investigation of gaseous hydrogen fluoride, Bauer, Beach and Simons[1] obtained the value 2.55 ± 0.03 Å. for the F–H–F distance and confirmed the existence of polymers $(HF)_n$. The reported values for the F–H–F distance in crystals are:

NH_4HF_2 = 2.37 ± 0.1 Å.[2]
$NaHF_2$ = 2.50 ± 0.2 Å.[3]
KHF_2 = 2.25 ± 0.2 Å.[4]

The assumption that the mean value 2.25 Å. reported for potassium bifluoride is correct leads to the conclusion that the F–H–F bond is weakened and the distance correspondingly increased when additional hydrogen bonds are formed as in $(HF)_n$. Also the distance is not accurately enough known to judge whether the two additional hydrogen bonds from fluorine to nitrogen in ammonium bifluoride cause a lengthening of the F–H–F distance over that in alkali bifluorides. In view of the large limits of error ascribed to the F–H–F distance, a redetermination of the parameter in potassium bifluoride has been carried out in order to test this conclusion.

In this work the value 2.26 ± 0.01 Å. has been found for the F–H–F distance in close agreement with the mean value reported by Bozorth.[4]

Experimental

Potassium hydrogen fluoride crystallizes in the tetragonal system forming plates with {001} developed and sides parallel to {110}. The structure was determined by Bozorth,[4] who gives it the space group D_{4h}^{18}, four molecules in the unit cell, with the atoms in the following positions

4H in $0\frac{1}{2}0$; $\frac{1}{2}00$; $\frac{1}{2}0\frac{1}{2}$; $0\frac{1}{2}\frac{1}{2}$
4K in $00\frac{1}{4}$; $00\frac{3}{4}$; $\frac{1}{2}\frac{1}{2}\frac{1}{4}$; $\frac{1}{2}\frac{1}{2}\frac{3}{4}$
8F in $u,\frac{1}{2}+u,0$; $\bar{u},\frac{1}{2}-u,0$; $\frac{1}{2}-u,u,0$; $\frac{1}{2}+u,\bar{u},0$; $\frac{1}{2}+u,u,\frac{1}{2}$; $\frac{1}{2}-u,\bar{u},\frac{1}{2}$; $u,\frac{1}{2}-u,\frac{1}{2}$; $\bar{u},\frac{1}{2}+u,\frac{1}{2}$
a = 5.67 Å. c = 6.81 Å. u = 0.14 + 0.01 F–H–F = 2.25 ± 0.02 Å.

Symmetric and asymmetric Laue photographs were taken with the beam normal to (001). The parameter was narrowed down to a small range by the use of qualitative Laue data.

Theoretical curves for the dependence of intensity on the parameter u were calculated from the equation

$$I = C \left| S \right|^2 e^{-3.0(\sin\theta/\lambda)^2}$$

using f values from the Pauling–Sherman tables.

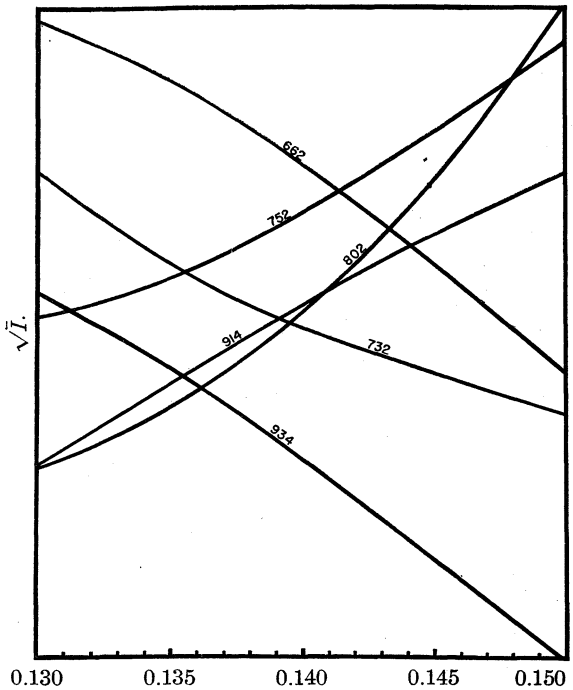
Comparing observed intensity ratios with the theoretical curves of Fig. 1, the upper and lower limits shown in Table I were placed on the value

TABLE I

PARAMETER DETERMINATION FOR POTASSIUM BIFLUORIDE USING INTENSITIES OF LAUE REFLECTIONS

Reflecting planes	$\frac{\sin\theta}{\lambda}$	λ	Observed intensity ratio	Parameter
(802)	0.720	0.349	(802) < (732)	$u > 0.1393$
(732)	.687	.350		
(6$\bar{6}$2)	.762	.333	(7$\bar{5}$2) > (6$\bar{6}$2)	$u <$ .1413
(7$\bar{5}$2)	.773	.328		
(914)	.851	.361	($\bar{1}$94) > (7$\bar{3}$2)	$u >$ .1390
(732)	.687	.367		
(8$\bar{6}$4)	.924	.406	(8$\bar{6}$4) > (934)	$u >$ .1381
(934)	.884	.408		

(1) S. H. Bauer, J. Y. Beach and J. H. Simons, THIS JOURNAL, **61**, 19 (1939).
(2) L. Pauling, *Z. Krist.*, **85**, 380 (1933).
(3) C. Anderson and O. Hassel, *Z. physik. Chem.*, **123**, 151 (1926).
(4) R. M. Bozorth, THIS JOURNAL, **45**, 2128 (1923).



802-732 →.
← 752-662.
194-732 →.
864-934 →.
u →.

Fig. 1.

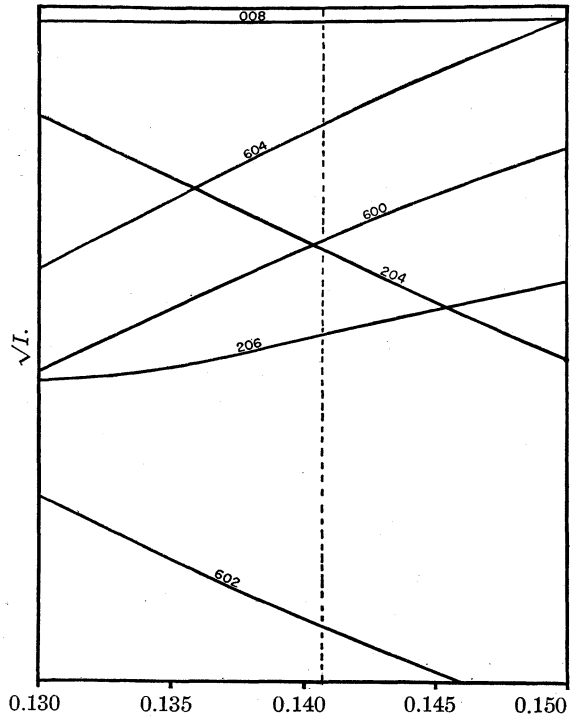


Fig. 2.

of u. This gives $0.1394 \leqq u \leqq 0.1413$ and $2.235 \leqq$ F–H–F distance $\leqq 2.265$ Å.

A more exact value of the parameter was then found by visually comparing intensities of reflections on oscillation photographs. Theoretical curves for the dependence of intensity on parameter were drawn (Fig. 2) using

$$I = \text{Const.}\ \frac{1 + \cos^2 2\theta}{\sin^2 2\theta} \left| S \right|^2 e^{-3.0(\sin\theta/\lambda)^2}$$

From a visual estimate of the ratio of the intensities of two reflections, estimates of the parameter value probably good to ±5% were made using the theoretical curves. Comparisons were made between reflections in the same layer line and not too widely separated values of sin θ. The mean value for the twenty-seven independent estimates made was weighted by multiplying each value by the angle between the intensity curves for the planes involved. The weighted mean for the parameter u is 0.1408, the average deviation is 0.0015 and the most probable deviation is $0.0015/27^{1/2}$ or 0.0003. The value $u = 0.1408 \pm 0.0003$ corresponds to the distance F–H–F = 2.258 ± 0.005 Å. This is in good agreement with the

TABLE II

PARAMETER DETERMINATION FOR POTASSIUM BIFLUORIDE USING INTENSITIES OF OSCILLATION REFLECTIONS

No.	(*hkl*)	Angle between F curves	Intensity ratio	Parameter
1	(400) (006)	22.5	0.5	0.1432
2	(600) (204)	55	1.10	.1417
3	(204) (206)	35	1.25	.1408
4	(008) (604)	20	1.20	.1423
5	(602) (604)	6	0.20	.1409
6	(026) (024)	24	0.91	.1410
7	(026) (422)	20	1.3	.1400
8	(321) (125)	27	1.1	.1420
9	(224) (024)	20	1.25	.1408
10	(323) (523)	20.5	0.83	.1417
11	(600) (206)	15	1.25	.1408
12	(512) (215)	16	1.33	.1416
13	(420) (024)	30	1.1	.1368
14	(424) (024)	24.5	0.91	.1420
15	(521) (323)	23	.74	.1411
16	(321) (226)	22	.57	.1423
17	(321) (422)	13	.67	.1396
18	(125) (323)	19	1.75	.1390
19	(424) (321)	31	2.3	.1419
20	(026) (321)	31	2	.1400
21	(611) (411)	37	1.75	.1370
22	(611) (413)	32	2	.1402
23	(316) (411)	31	3.3	.1389
24	(510) (514)	34	0.91	.1418
25	(512) (514)	24	0.74	.1442
26	(510) ($\bar{2}$15)	20	2	.1445
27	(413) (316)	23	0.22	.1422

Laue data, and, considering both, the value of the F–H–F distance may be given as 2.26 Å. with a probable error of not more than 0.01 Å.

Discussion

In going from the HF_2^- ion in crystalline potassium bifluoride to the $(HF)_n$ polymers in gaseous hydrogen fluoride there is a lengthening of 0.29 ± 0.06 Å. in the F–H–F distance. This shows that formation of additional hydrogen bonds lengthens the F–H–F distance. While the value 2.37 ± 0.1 Å. for the F–H–F distance in ammonium bifluoride leaves some doubt as to a lengthening, it is strongly indicated that the formation of two additional N–H . . . F bonds causes a weakening of the F–H–F bond and a probable lengthening of about 0.1 Å. The theoretical value calculated by Pauling[5] for this distance is 2.32 Å. with a symmetrical linear configuration for F–H–F.

Summary

A redetermination of the parameter in potassium bifluoride has been carried out using Laue and oscillation photographs. The value $u = 0.1408 \pm 0.003$ leads to the fluorine–fluorine distance 2.26 ± 0.01 Å. in $\{F\text{–}H\text{–}F\}^-$. A comparison is made with other reported values.

(5) L. Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 1939, p. 277.

PASADENA, CALIFORNIA RECEIVED JUNE 26, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF DUKE UNIVERSITY AND THE STERLING CHEMISTRY LABORATORY OF YALE UNIVERSITY]

Silver and Mercurous Iodide Electrodes

BY WARREN C. VOSBURGH, PAUL F. DERR, GERALD R. COOPER AND ROGER G. BATES[1]

The silver and mercurous iodide electrodes have both been shown to be reproducible under favorable conditions,[2] and it seemed desirable to attempt a direct comparison of the two. This was found surprisingly difficult, and the result can be considered only approximate. Some of the observations made in the course of the study are of value, however.

Silver Iodide Electrode.—All of the silver iodide electrodes were prepared by the thermal method; some from silver oxide and iodate[2a] and some from oxide and iodide.[2b] In the preparation of some, the platinum wire was electroplated with silver before application of the paste, but this was found unnecessary and was omitted in the later electrodes.

Silver iodide electrodes agreed within 0.02 mv. when compared in the same vessel with oxygen-free potassium iodide solution (about 0.02 *m*) as the electrolyte. The agreement was better on the second day than on the first, and continued good indefinitely. The agreement was not as good when the electrolyte was saturated with lead iodide or when 0.01 *m* cadmium iodide was used as the electrolyte. When air was admitted to a cell consisting of two silver iodide electrodes in the same vessel, it caused disagreement of the electrodes.[3] A trace of mercurous iodide also caused disagreement.

Mercurous Iodide Electrodes.—While the mercurous iodide electrode is highly reproducible when the electrolyte is a saturated cadmium iodide solution,[2c,d] it was found much less reproducible when the electrolyte was a potassium iodide solution. Two mercurous iodide electrode systems in a single H-vessel prepared with nitrogen-vacuum technique gave a cell with an electromotive force anywhere from zero to well over a millivolt in spite of considerable care to avoid errors. When one electrode had a thick (1 to 2 cm.) layer of mercurous iodide paste covering the mercury and the other a thin (0.5 cm.) layer, the thick-layer electrode was always positive, and the electromotive force varied from 0.3 mv. to nearly 2 mv. in different cells and at different times. When both layers of mercurous iodide were thin, the electromotive force varied from zero to 0.3 mv. When the electrolyte was a 0.01 or 0.02 *m* cadmium iodide solution, the effect of thick and thin layers was not as pronounced. Solid lead iodide at both electrodes, with a potassium iodide electrolyte, reduced the effect of thick and thin layers, also.

(1) Sterling Fellow at Yale University, 1937–39.

(2) (a) Owen, THIS JOURNAL, **57**, 1526 (1935); (b) Bates, *ibid.*, **60**, 2984 (1938); (c) Vosburgh, *ibid.*, **50**, 2391 (1928); (d) Bates and Vosburgh, *ibid.*, **59**, 1584 (1937).

(3) (a) Smith and Taylor, *Roczniki Chem.*, **18**, 762 (1938); (b) Taylor and Smith, *J. Research Natl. Bur. Standards*, **22**, 307 (1939).

The effect of thick and thin layers may possibly be explained on the basis of the reaction

$$Hg_2I_2 + 2I^- \rightleftarrows Hg + HgI_4^=$$

This reaction takes place when mercurous iodide and sufficient iodide ion come together, and therefore the iodide ion concentration at a mercurous iodide electrode is not the same as in the main body of the electrolyte. If the reaction is slow, diffusion would be able to keep the iodide ion concentration at the thin-layer electrode larger than at the thick-layer electrode. A larger iodide ion concentration means a smaller mercurous ion concentration and consequently a more negative electrode. Mercurous iodide electrodes are reproducible in saturated cadmium iodide solutions because the small iodide ion concentration[4] is held practically constant by the various equilibria in the solution. If this theory is correct, the value assigned to the normal potential of the mercurous iodide electrode[4] must be considered less certain than the precision of the measurements would indicate.

Cells.—A large number of cells were made, each with one silver iodide and one mercurous iodide electrode. When made in ordinary H-shaped vessels the constancy was not satisfactory. Diffusion of the mercurous iodide to the silver iodide electrode was probably responsible. A plug of glass wool to retard diffusion helped, but did not overcome the trouble, and the special cell vessel illustrated in Fig. 1 was designed. The electrode systems were placed in parts A and B, with the use of nitrogen-vacuum technique. The tube C was not filled with electrolyte until a measurement was to be made. It was then filled through tube D with air-free solution from a flask like that described by Brown and MacInnes.[5] After a measurement, the solution in C was expelled through F by nitrogen pressure. Some of the vessels used had interchangeable ground-glass joints at C. This allowed an interchange of electrodes between cells. A few vessels had two legs at A and two at B, allowing the preparation of duplicate electrodes of each kind. Cells made in the vessels having the joints at C were maintained at constant temperature in an air-bath and the others in an oil-bath.

Of a large number of cells made with 0.02 *m* potassium iodide solution as the electrolyte, 48 were selected as the most satisfactory. The electromotive forces of these on the first day varied between 0.1119 and 0.1141 v. at 30°, the silver iodide electrode being negative.

The highest cells decreased during the next few days and most of the lower ones increased. For 18 cells that varied less than 0.2 mv. during the first four days the range was 0.1127 to 0.1136 v. This is within the range of variability of mercurous iodide electrodes with different thicknesses of the mercurous iodide layer. Three of the cells were measured over a period of twenty-four to forty days. One of these started at 0.1141 v. and decreased to 0.1131 v. On shaking the mercurous iodide electrode, the value dropped to 0.1128 v. and remained constant thereafter for twenty-five days. Another cell started at 0.1130 v., decreased in four days to 0.1128 v. and remained constant for thirty-six days. Its electromotive force was not affected by shaking. The third was like the first, except that its initial electromotive force was not as high. All three cells gave the value 0.1128 v. after shaking.

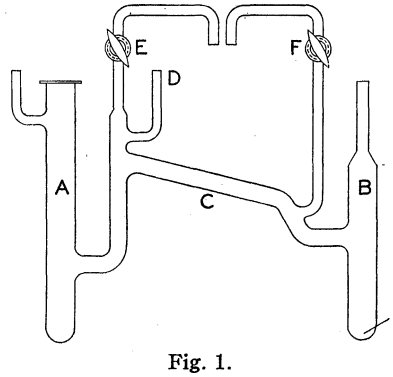


Fig. 1.

If the differences between cells is ascribed in part to differences in thickness (or denseness of packing) of the mercurous iodide layer, the lower electromotive forces should correspond to cells in which the layer is thin. The effect of shaking is probably to aid diffusion, and this lowers the electromotive force to the thin-layer value of 0.1128 v.

A group of cells made with 0.01 *m* potassium iodide solution was less satisfactory, but the best ten varied between 0.1124 and 0.1130 v. between the second and fourth days, with an average of 0.1127 v. A number of cells made with an electrolyte of 0.02 *m* potassium iodide solution saturated with lead iodide were variable and unsatisfactory, except for one cell that was constant at 0.1128 v. The use of a dilute cadmium iodide

(4) Bates and Vosburgh, THIS JOURNAL, **59**, 1189 (1937).
(5) Brown and MacInnes, *ibid.*, **57**, 1358 (1935).

solution as the electrolyte gave cells that were rather variable and lower than 0.1128 v. Saturated cadmium iodide gave cells that started very high and decreased continuously. The bad effect of cadmium iodide is undoubtedly on the silver iodide electrode.

In connection with a study of the thermodynamics of zinc iodide in aqueous solution by means of zinc–silver iodide cells,[2b] some cells with mercurous iodide electrodes were made from which the electromotive force of the silver–mercurous iodide cell could be calculated. The calculated values are given in Table I. The results are in

TABLE I

CALCULATED ELECTROMOTIVE FORCE OF THE CELL Ag/AgI, $ZnI_2(m)/ZnI_2(m)$, Hg_2I_2/Hg

ZnI_2, m	E_{15}	E_{20}	E_{25}	E_{30}	E_{35}
0.01075	0.1076	0.1091	0.1106	0.1122	0.1139
.01474	.1081	.1096	.1112	.1127	.1144
.01801	.1086	.1102	.1117	.1134	.1150
.03373	...	...	.1125	.1141	...
.06068	.1117	.1132	.1147	.1163	.1179

approximate agreement with those described above. They show that the electromotive force depends on the electrolyte concentration, which is in agreement with the theory proposed above for the variability of the mercurous iodide electrode. Table I and also some measurements of the previously described cells show that the temperature coefficient is about 0.00030 v. per degree; 0.1127 v. at 30° corresponds to 0.1112 v. at 25°.

Bates and Vosburgh[4] found for the normal potential of the mercurous iodide electrode the value 0.0405 v. at 25°. They used rather thin layers of mercurous iodide and a molality of potassium iodide of about 0.01 and their value can be combined with 0.1112 v. to give the approximate value 0.1517 v. at 25° for the normal potential of the silver iodide electrode. Owen[2a] found 0.1522 v. and Cann and Taylor[6] found 0.1510 v. In view of the uncertainty of the value 0.1517 v., it cannot be considered to be in serious disagreement with either of these. Some recent measurements by Gould and Vosburgh of the silver iodide electrode against a hydrogen electrode are in as good agreement with 0.1517 v. as could be expected.

Summary

The cell Ag/AgI, I^-/I^-, Hg_2I_2/Hg was found to be not as reproducible or constant as experience with the two electrode systems in other cells would lead one to expect, but the most probable value based on a large number of cells leads to an approximate value for the silver iodide electrode.

The trouble with the silver–mercurous iodide cell may be summarized by saying that while each of the electrode systems is highly reproducible under favorable conditions, no single electrolyte was found that did not affect one or the other of the electrodes unfavorably.

(6) Cann and Taylor, THIS JOURNAL, **59**, 1484 (1937).

DURHAM, N. C. RECEIVED JULY 19, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, CARNEGIE INSTITUTE OF TECHNOLOGY]

A Thermodynamic Study of the Lead–Antimony System

BY HARRY SELTZ AND BERNARD J. DEWITT

In the hope that the accumulation of data on the thermodynamic properties of binary liquid metal solutions may lead eventually to a better understanding of the nature of such systems, investigations along these lines are being continued in this Laboratory. In this paper the results of a study of the lead–antimony system are described. The electromotive force values of cells of the type

$$Pb(l)/PbCl_2 \text{ in } KCl\text{–}LiCl(l)/Pb\text{–}Sb(l)$$

were measured, using the purified metals and technique described in previous publications.[1,2]

(1) Strickler and Seltz, THIS JOURNAL, **58**, 2084 (1936).

(2) Seltz and DeWitt, *ibid.*, **60**, 1305 (1938).

In this work it was found possible to extend the e. m. f. readings in rather thick-walled Pyrex H-cells under vacuum up to 630° without collapse of the cells. This permitted measurements to a mole fraction of lead of 0.1 and eliminated any difficulty in the extrapolation of the activity and partial molal relative heat content curves.

Experimental Data

In Table I, the experimental results are tabulated, along with the calculated activities and relative heat contents for lead at the various mole fractions. (The subscript 1 will be used to designate values for the lead component.) At the

highest mole fraction of antimony the readings, due to separation of the solid phase, could be made over a range of only 30°; but, as in previous measurements with fused salt electrolytes, this permitted a sufficiently accurate determination of the slope of the curve to evaluate $\bar{L}_1$ within ±15 cal.

TABLE I

Average number of readings per run, 20; maximum deviations, ±0.04 mv.

N_1	E. m. f. at 748.1°K., mv.	a_1 748.1°K.	$dE/dT \times 10^5$ volts/°C.	$\bar{L}_1$	Temp. range of meas., °C.
0.1095	79.56	0.0621	9.70	−321	600–630
.1992	58.48	.1629	7.11	−243	560–610
.3057	40.68	.2657	5.54	2	550–605
.4012	32.25	.3676	4.34	10	480–520
.4997	24.52	.4673	3.44	56	420–470
.6145	16.82	.5934	2.34	34	390–490
.7024	11.94	.6904	1.725	46	385–475
.7926	7.67	.7882	1.122	34	390–490
.8710	4.63	.8662	0.689	27	370–460

In Table II the activities and relative heat contents for both components are tabulated at round number mole fractions; the values for antimony were determined by the usual graphical methods. In the last column, the integral heat of formation, ΔH, of one mole of solution from the liquid metals is given. The activity curves at 748.1°K. are shown in Fig. 1 and the $\bar{L}_1$, $\bar{L}_2$ and ΔH curves in Fig. 2.

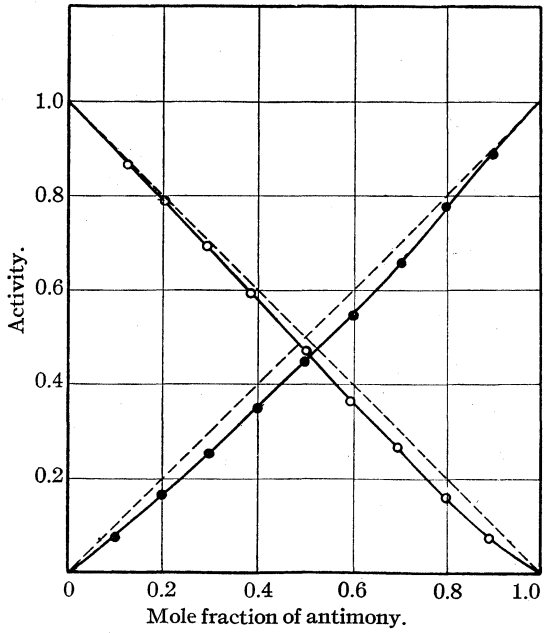


Fig. 1.—Activity curves for Pb and Sb: ○, experimental; ●, calculated.

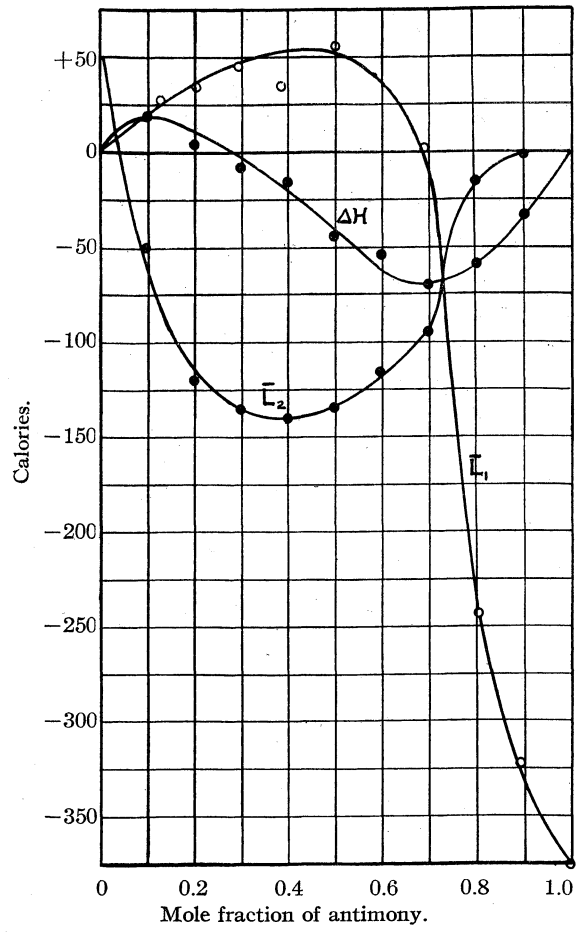


Fig. 2.—Relative heat contents and heats of formation of solutions: ○, experimental; ●, calculated.

TABLE II

N_1	at 748.1°K. a_1	a_1/N_1	a_2	a_2/N_2	$\bar{L}_1$	$\bar{L}_2$	ΔH
0.0	0.000	0.748	1.000	1.000	−380	0	0
.1	.078	.780	0.894	0.993	−330	0	−33
.2	.162	.810	.777	.971	−235	− 15	−59
.3	.259	.863	.660	.943	− 10	− 95	−70
.4	.362	.905	.549	.915	+ 35	−115	−55
.5	.470	.940	.450	.900	+ 45	−135	−45
.6	.576	.960	.348	.870	+ 50	−140	−16
.7	.686	.980	.251	.847	+ 45	−135	− 9
.8	.790	.988	.162	.810	+ 35	−125	+ 4
.9	.892	.991	.078	.780	+ 25	− 50	+18
1.0	1.000	1.000	.000	.750	0	+ 50	0

Discussion of Results

The forms of the activity and $\bar{L}$ curves for this system are surprising when compared with those of the previously studied lead–bismuth solutions. Here, the negative deviations of the activities are comparatively slight, with the extrapolated Henry's law value for the activity coefficient, a_1/N_1, reaching a value of only 0.740, while for

the lead–bismuth system this value is 0.480. Furthermore, the lead–bismuth solution followed "regular" solution behavior closely, with a "b" value of -1200. A plot of log a_1/N_1 *vs.* N_2^2 for this system, Fig. 3, indicates clearly the deviations from such behavior, and this is demonstrated further by the forms of the $\overline{L}$ and ΔH curves, which are not compatible with the regular solution concepts. In fact, it would seem that two

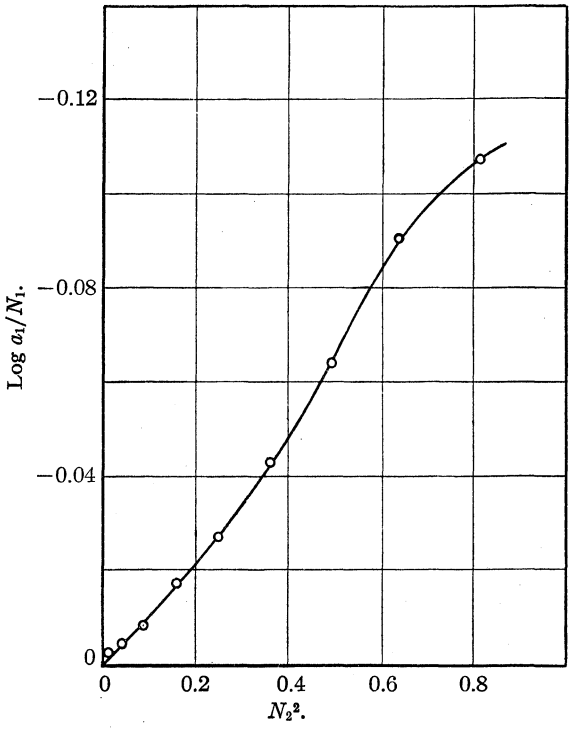


Fig. 3.—Deviations from "regular" behavior.

opposing factors contribute to the deviations from Raoult's law, one tending to produce positive and the other negative deviations. This is not apparent in the activity curves which show negative deviations over the entire range at this temperature. However, with positive values of $\overline{L}_1$ at higher mole fractions, the activity coefficients would tend to become greater than one at lower temperatures. At lower concentrations of lead, on the other hand, the negative $\overline{L}_1$ values would decrease the activity coefficients to yet smaller values. For the cadmium–antimony system,[2] in which intermetallic compounds separate in the solid state, these opposing influences are more pronounced; the activity curve for cadmium shows both positive and negative deviations at 753.1°K. Similar results, not yet published, have been obtained for the zinc–antimony system.

Calculation of Solid–Liquid Equilibria

Solid–liquid equilibria in the lead–antimony system have been studied by several investigators and the data have been reviewed critically by Hansen.[3] It has been established that the system shows a simple eutectic with α- and β-solid solutions of antimony in lead and lead in antimony respectively as the solid phases. The eutectic temperatures and compositions reported range between 245–252° and 12.1–13% antimony. From the activity data for the two components in the liquid state, it should be possible to calculate these conditions more accurately and also to establish the solid solubility limits of the α- and β-phases at the eutectic. For these calculations the free energies of fusion of the two components are needed, and the heats of fusion and the heat capacity data recommended by Kelley[4] lead to the equations:

$$\mathrm{Sb(s)} = \mathrm{Sb(l)};\quad \Delta F^\circ = 4015 - 1.64T \ln T + 0.89 \times 10^{-3}T^2 + 5.914\,T \quad (1)$$

$$\mathrm{Pb(s)} = \mathrm{Pb(l)};\quad \Delta F^\circ = 969 - 1.03\,T \ln T + 1.01 \times 10^{-3}T^2 + 4.371\,T \quad (2)$$

Hansen[3] has accepted 247° for the eutectic temperature and 13% antimony, corresponding to a mole fraction $N_2 = 0.2027$, for the composition of the eutectic liquid. From the experimental activity and $\overline{L}$ values, we calculate at this temperature and composition $a_2 = 0.1556$. From equation (1) the activity of pure solid antimony, a_2(s), relative to pure liquid as the standard state, is calculated to be 0.1451. At this temperature, it is obvious that a liquid containing 13% antimony cannot exist in equilibrium with even pure solid antimony. Taking the lower limit of the reported values of 12.1% ($N_2 = 0.1898$), we calculate $a_2 = 0.1457$, which likewise is greater than a_2(s) at this temperature. Since the β-solid solution has been shown to contain at least 4% of lead, it would seem that 247° is too low for the eutectic temperature. To confirm this conclusion, cooling curves were taken on 12 and 13% melts using the calibrated chromel–alumel couples employed in the e. m. f. studies. In both runs, complete solidification took place when the temperature reached 250°. At this temperature a_2(s) is calculated to be 0.1487 and a_2 for a 13% solution is 0.1557, which indicates that even at this temperature the eutectic must be richer in

(3) M. Hansen, "Der Aufbau der Zweistofflegierungen," Verlag von Julius Springer, Berlin, Germany, 1936, p. 984.

(4) K. K. Kelley, Bureau of Mines Bulletins 383 (1935) and 393 (1936).

lead for equilibrium. Taking the lower limit of 12.1%, we calculate that $a_2 = 0.1458$, which is now less than the value $a_2(s) = 0.1487$. Assuming Raoult's law to be obeyed in the dilute β-solid solutions, as has been shown to be true for lead–bismuth solid solutions,[1] we calculate for the solid solubility of lead in antimony at the eutectic temperature, $N_\beta = 0.1458/0.1487 = 0.973$, which corresponds to a solubility of 4.51% of lead. In a similar manner, the composition of the α-solid solution at the eutectic can be determined. The activity of solid lead, relative to liquid, from equation (2) is 0.8694, and a_1 for the 12.1% solution is 0.8132, which gives for the solid solubility $N_\alpha = 0.936$, corresponding to a solubility of 3.86% of antimony.

Summary

1. The activities and relative heat contents of lead and antimony in their liquid alloys have been determined.

2. The eutectic temperature for the system has been shown to be 250° and the eutectic composition 12.1% antimony. The eutectic solids have been calculated to have the compositions 3.86% antimony for the α-phase and 4.51% lead for the β-phase.

PITTSBURGH, PENNA. RECEIVED JULY 10, 1939

[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY, UNIVERSITY OF CHICAGO]

Proof of the Steric Nature of the Ortho Effect in the Hydrogen Exchange Reactions of Aromatic Tertiary Amines

BY WELDON G. BROWN, ALEX H. WIDIGER AND NICHOLAS J. LETANG

It has been postulated previously[1] that the acid catalyzed hydrogen exchange reactions of dimethylaniline and its derivatives take place through a direct addition of deuterons at the ortho or para positions, giving rise to tautomeric forms of the amine salt with a quinoid type of structure. In view of the requirement in classical structural theory that the dialkylamino group should be coplanar with the quinonoid ring in these forms, it was possible to interpret the inhibiting effect of an ortho nitro group, which had been observed in a study of the exchange reactions of the nitrodimethylanilines in deuteroalcohol, as a steric effect having to do with the obstruction offered by the nitro group to the attainment of a coplanar configuration. Several further examples of inhibition of the hydrogen exchange reaction by ortho substituents have since been discovered and it is now obvious that the ortho effect is as characteristic for this reaction as it is for numerous other reactions of aromatic tertiary amines.[2]

In an effort to test experimentally the validity of this theory of the ortho effect in hydrogen exchange reactions, two independent lines of approach were explored. One obvious method of attack was to vary the size of the ortho substituent in the expectation that as the size of the group becomes small the inhibiting effect should diminish or eventually vanish. The series selected for this purpose was that of the bromo, chloro and fluoro derivatives of dimethylaniline (*cf.* Fig. 1). The second line of attack was based on the argument that if the amino nitrogen were to be linked to the ortho carbon atom in such a way as to form a five-membered ring, as in N-methylindoline (I), which would necessarily be coplanar with the benzene ring, there should be no ortho effect. A similar result was predicted for

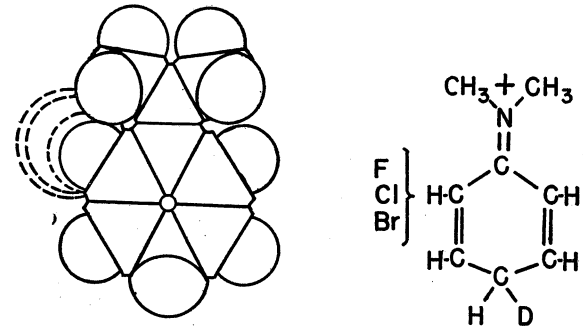
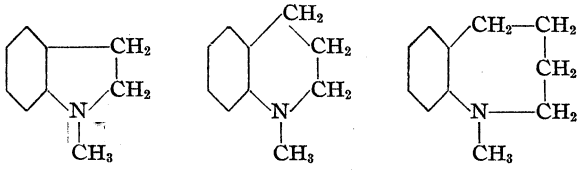


Fig. 1.—On the left, representation based on scale atomic models of the structures indicated on the right. The dotted lines show approximately the relative dimensions of F, Cl and Br.

(1) Brown, Kharasch and Sprowls, *J. Org. Chem.*, in press.

(2) The literature on the subject of ortho effects in the reactions of aromatic tertiary amines, particularly with regard to the reactions with methyl iodide, nitrous acid, diazo compounds, and formaldehyde, is too extensive to be cited here in detail, but the very extensive work of the late Julius von Braun in this field deserves special mention. For a review on the subject of ortho effects in general, see Ludwig Anschütz, *Z. angew. Chem.*, **41**, 691 (1928).

an analogous compound with a six-membered ring, N-methyltetrahydroquinoline (II), though perhaps with less certainty because of the probable slight strain in the coplanar configuration. With a highly puckered seven-membered ring, on the other hand, as in N-methyl-*homo*-tetrahydroquinoline (III), the opportunity for a steric effect of the type under consideration definitely arises and this compound should exhibit the characteristic inhibition of the normal lability of the para and unsubstituted ortho hydrogen atoms.



(I) (II) (III)

The experimental results are entirely in accordance with the predictions. We find a pronounced ortho effect in the failure of *o*-bromodimethylaniline and of *o*-chlorodimethylaniline to undergo hydrogen exchange to any appreciable extent under experimental conditions such that the exchange reactions of the corresponding meta and para isomers are substantially complete. The effect is very much less conspicuous, although not entirely absent, in *o*-fluorodimethylaniline which undergoes hydrogen exchange at an intermediate rate. In the series of cyclic bases, it is observed that N-methylindoline and N-methyltetrahydroquinoline exhibit a very high degree of reactivity in the exchange reaction, the former being more reactive but both exceeding dimethylaniline, whereas N-methyl-*homo*-tetrahydroquinoline exchanges hydrogen at a relatively slow rate. These results provide rather convincing evidence that the key to the situation really lies in the ability of the dialkylamino group to come into the plane of the benzene ring.

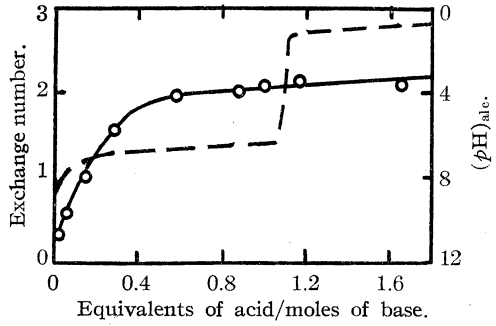


Fig. 2.—The rate of exchange of dimethylaniline in deuteroalcohol with varying amounts of sulfuric acid. The dotted line indicates the estimated $(p\mathrm{H})_{\mathrm{alc.}}$

In the meantime further evidence in support of the mechanism of direct deuteron addition at the site of the exchange (ortho and para carbon atoms) was forthcoming in a study of the effect of acid concentration on the rate of exchange of dimethylaniline in deuteroalcohol solution. As Ingold, Raisin, and Wilson[3] first pointed out, and verified experimentally with reference to the exchange of dimethylaniline in dilute hydrochloric acid, it is a consequence of this mechanism that on increasing the amount of acid the rate of exchange should reach a maximum value which would represent a compromise between the increasing concentration of acid catalyst and the decreasing concentration of free base. Our results on the sulfuric acid catalyzed exchange reaction of dimethylaniline in deuteroalcohol are similar to those obtained by Ingold, Raisin, and Wilson in showing that beyond a certain point the rate of exchange does indeed fail to keep pace with the increasing concentration of acid (*cf.* Fig. 2).

It is characteristic of the ortho effect in the reactions of aromatic tertiary amines that it does not always appear as a completely dominant effect. It is rather an effect of limited magnitude which may be partially or wholly obscured by opposing influences. In the hydrogen exchange reaction the effect is known to be of limited magnitude not only in the case of *o*-fluorodimethylaniline, in which the inhibition of reactivity is only slight, but also in the case of *o*-chlorodimethylaniline which does not exchange hydrogen readily at 110° but does so at 180°. It is therefore of interest in connection with the interpretation of the behavior of more complicated molecules to know the extent to which the ortho effect can be overcome by suitably oriented activating groups. An effect in this direction can be seen in the fact that dimethyl-*p*-xylidine exchanges hydrogen, albeit slowly, while under similar conditions N-dimethyl-*o*-toluidine and 2-dimethylamino-*m*-xylene exhibit no appreciable exchange. In this example the deactivating steric effect of an ortho methyl group is to some

(3) Ingold, Raisin, and Wilson, *J. Chem. Soc.*, 1639 (1936). The fundamental difference between the mechanism proposed by these authors and our mechanism is that they apparently believe the hydrogen exchange to be effected in a single step involving simultaneous proton and deuteron transfers and nothing is indicated with regard to a possible quinonoid structure for the intermediate complex. In our view the formation of a quinoid form of the cation by deuteron transfer is followed by a proton transfer in which the acceptor will not necessarily be the anion derived from the catalyzing acid.

TABLE I

EXCHANGE REACTIONS OF TERTIARY AROMATIC AMINES IN DEUTEROALCOHOL

In all experiments the amount of substance used was 0.0130 mole, the amount of alcohol 0.0850 mole.

Substance	H_2SO_4, cc.	Time, hours	Temp.	Initial % D_2O	Final % D_2O	Exchange number
o-Chlorodimethylaniline	0.02	65	115	2.60	2.60	0
o-Chlorodimethylaniline	.02	140	115	2.60	2.58	0.05
o-Chlorodimethylaniline	.02	72	185	2.60	2.29	.89
o-Chlorodimethylaniline	.02	159	185	2.60	2.20	1.24
m-Chlorodimethylaniline	.02	65	115	2.60	1.90	2.43
p-Chlorodimethylaniline	.02	65	115	2.60	2.06	1.73
o-Bromodimethylaniline	.02	65	115	2.60	2.60	0
o-Bromodimethylaniline	.02	140	115	2.60	2.59	.02
m-Bromodimethylaniline	.02	65	115	2.60	1.88	2.53
p-Bromodimethylaniline	.02	65	115	2.60	2.08	1.7
o-Fluorodimethylaniline	.02	65	115	2.60	2.41	0.52
o-Fluorodimethylaniline	.02	140	115	2.60	2.27	.96
N-Dimethyl-*o*-toluidine	.02	90	115	2.30	2.30	0
N-Dimethyl-*o*-toluidine	.08	70	115	2.25	2.26	0
2-Dimethylamino-*m*-xylene	.02	90	115	2.30	2.30	0
2-Dimethylamino-*m*-xylene	.08	90	115	2.25	2.26	0
N-Dimethyl-*p*-xylidine	.02	70	115	2.30	2.24	0.20
5-Dimethylaminotetralin	.02	74	115	2.29	2.24	.19
α-Dimethylaminonaphthalene	.02	41	115	2.76	2.29	1.36
Dimethylaniline	.01	24	60	2.81	2.75	0.12
N-Methylindoline	.01	24	60	2.80	2.25	1.58
N-Methyltetrahydroquinoline	.01	24	60	2.74	2.42	0.87
N-Methyl-*homo*-tetrahydroquinoline	.01	44	60	2.79	2.78	0
N-Methyl-*homo*-tetrahydroquinoline	.02	70	120	2.77	2.57	0.85

extent alleviated by the normal activating effect of a meta methyl group. A similar case is provided by 5-dimethylaminotetralin, which undergoes hydrogen exchange slowly. These results provide a clue to the behavior of α-dimethylaminonaphthalene, which can be regarded, formally at least, as an ortho substituted amine but which shows a high degree of reactivity in the hydrogen exchange reaction. We suppose that the steric inhibition which might be expected is very nearly compensated by the activating effect of the benzo group. It is to be anticipated that the steric factor in such a molecule could be greatly increased by substituents in the 8-position and experiments are in progress to test this prediction.[4]

It will be obvious, in view of the parallel occurrence of ortho effects in the hydrogen exchange reaction and in coupling, nitrosation, and condensation reactions of aromatic amines, that the elucidation of the nature of the effect for one type of reaction has important implications with regard to the others. There appears to be no obstacle in the way of extending the principles and the experimental approach of the present work to these related reactions, and in fact much of the necessary data is already available in the literature. In subsequent papers an attempt will be made to show how this extension can be carried out.

(4) The α-dialkylaminoanthraquinones present a similar picture in so far as the steric relationships are concerned and it seems possible that this may be the origin of many of the anomalies to be encountered in the chemistry of these substances.

TABLE II

HYDROGEN EXCHANGE OF DIMETHYLANILINE WITH VARYING AMOUNTS OF ACID[a]

H_2SO_4, cc.	Acid/base	Initial % D_2O[b]	Final % D_2O	Exchange number
0	0	2.83	2.81	0
0.005	0.014	2.81	2.68	0.32
.020	.058	2.78	2.56	.57
.050	.14	2.74	2.38	1.01
.100	.29	2.69	2.19	1.56
.200	.58	2.58	2.02	1.97
.300	.88	2.48	1.95	2.01
.342	1.00	2.44	1.91	2.10
.400	1.17	2.39	1.87	2.15
.500	1.46	2.29	1.81	2.09

[a] These experiments were carried out with mixtures containing 0.0130 mole of dimethylaniline, 0.085 mole of alcohol, and the amount of sulfuric acid shown in the table. The reactions were allowed to proceed at 60° for sixty-nine hours. [b] The initial concentrations have been corrected for the dilution of the deuterium by the normal hydrogen of the sulfuric acid.

Experimental

Experimental Procedure.—The procedure for carrying out exchange reactions in deuteroalcohol described by

TABLE III

PHYSICAL CONSTANTS OF THE TERTIARY AMINES AND SOME OF THE INTERMEDIATES

Substance	B. p. °C.	B. p. Mm.	$n^{20}D$	Notes
Dimethylaniline	188	750	1.5582	
o-Chlorodimethylaniline	207.5–208.5	749	1.5524	
m-Chlorodimethylaniline	239–240	747	1.5732	
p-Chlorodimethylaniline	231–232	746	(M. p. 35.5°)	
o-Bromodimethylaniline	107–108	14	1.5750	
m-Bromodimethylaniline	133–134	14	1.5988	
o-Nitrofluorobenzene	188	750		*a*
o-Fluorodimethylaniline	69–70	16	1.5173	
N-Dimethyl-*o*-toluidine	180	750	1.5255	
2-Dimethylamino-*m*-xylene	193–194	748	1.5138	
N-Dimethyl-*p*-xylidine	199	745	1.5223	
5-Aminotetralin	149–152	15	1.6044	
5-Dimethylaminotetralin	134–134.5	16	1.5608	
α-Dimethylaminonaphthalene	129	10	1.6224	
N-Methylindole	123–124	20	1.6060	*b*
N-Methylindoline	102	20	1.5682	
N-Methyltetrahydroquinoline	105–106	8	1.5843	*c*
homo-Tetrahydroquinoline	114–115	10	1.5751	
N-Methyl-*homo*-tetrahydroquinoline	105–106	10	1.5597	*d*

[a] The mixture of the ortho and para derivatives which was obtained on nitrating fluorobenzene, and which contained approximately 13% of the ortho compound, was separated without difficulty by fractional distillation at 50 mm. pressure using a 1-meter column packed with glass helices. [b] This compound was prepared by the method of Koizumi, Kowski, and Titani, *Bull. Jap. Chem. Soc.*, **13**, 645 (1938), and was reduced to N-methylindoline by the method of Wenzing, *Ann.*, **239**, 246 (1887). Other methods for the preparation of the latter which were first tried gave unsatisfactory results. [c] The compound assumes a bright red color when exposed to air and the rate of coloration is enormously accelerated by traces of acid. In the exchange experiments the samples were distilled into reaction tubes under high vacuum without subsequent exposure to air. Under these conditions no color developed in the control experiments and only a slight yellow color in the tubes containing acid. [d] The methylation of *homo*-tetrahydroquinoline was carried out by refluxing equal volumes of the amine, methyl iodide, and methyl alcohol for three hours, resulting in a 65% yield of the tertiary amine as compared with a 20% yield reported by v. Braun and Seemann.[9]

Kharasch, Brown, and McNab,[5] and later modified,[1,6] has been improved as a result of the discovery[7] that significant errors can arise from isotopic fractionation in the distillation of ethyl alcohol at reduced pressure. In order to minimize these errors the distillations are now carried out at atmospheric pressure and care is exercised in collecting the same fraction in each distillation. With these precautions a constant decrease, amounting to 0.8% of the concentration of deuterium, was obtained. Control experiments, in which no catalyst was added, were carried out with each compound and in no case did we find evidence of exchange in the absence of added acid.

Experimental Results.—The experimental results are given in tabular form in Tables I and II. The extent of hydrogen exchange is expressed in terms of the "exchange number," which is used here as a matter of convenience,[8] and which is derived from the data by means of the relation: $n = (a/s)(D_1 - D_2)/D_2$, where a/s is the molar ratio of alcohol to substance, and D_1 and D_2 are the initial and final concentrations of deuterium in the alcohol. Since the unit of deuterium concentration does not enter into the result, it is unnecessary to transform the analytical data from mole % D_2O in the water of combustion, in which form they are obtained and are given in the tables, to mole % C_2H_5OD in the alcohol.

Corrections were applied for the dilution of the deuterium by the normal hydrogen of the sulfuric acid added. In the series of experiments recorded in Table II, this correction becomes quite large with the higher concentrations of acid and there is some uncertainty as to how it should be applied.

Materials.—The tertiary amines required for this work have been described previously and were prepared by the methods given in the literature, the principal exception being the preparation of N-methyl-*homo*-tetrahydroquinoline which was carried out by a less laborious route than the original one of v. Braun and Seemann.[9] Extensive use was made of the acetic anhydride treatment as a method of purifying tertiary amines, and in connection with the possible occurrence of secondary amines as impurities in certain cases it may be mentioned that the amino hydrogen exchanges rapidly in the absence of added catalyst and thus the control experiments served also as a check on the purity of the substances.

The physical constants of the materials used in the exchange experiments, and also of some of the intermediates required in the preparations, are given in Table III.

(5) Kharasch, Brown, and McNab, *J. Org. Chem.*, **2**, 36 (1937).

(6) Brown and Eberly, unpublished work.

(7) Widiger and Brown, THIS JOURNAL, **61**, 2453 (1939).

(8) Since equilibrium data are in most cases not yet available the true degree of completion of the reactions cannot be given. Experience indicates that the limiting value of the "exchange number" in reactions involving C–H hydrogens is less than the actual number of exchanging hydrogen atoms per molecule by 15–20%.

(9) Von Braun and Seemann, *Ber.*, **55**, 3824 (1922).

A careful examination of the problems involved in the synthesis of N-methyl-*homo*-tetrahydroquinoline by the method of v. Braun and Seemann[9] led to the discovery that γ-(*o*-aminophenyl)-butyric acid, one of the later intermediates, could be prepared more conveniently by the Beckmann rearrangement of the *p*-toluenesulfonic ester of α-tetraloneoxime.[10] This method was adopted and the subsequent steps were carried out essentially as described by v. Braun and Bartsch[11] and by v. Braun and Seemann.[9]

α-Tetralone.—The following method was used for the preparation at a reasonable cost of the relatively large quantities of α-tetralone needed for the above-mentioned synthesis. Air is blown gently for a period of one hundred hours through a suspension of finely powdered copper oxide in tetralin maintained at 90°. The suspension is then allowed to settle and the liquid decanted. Upon fractional distillation at reduced pressure 80% of the tetralin is recovered and there is obtained in 20% yield a mixture of α-tetralol and α-tetralone containing 50–75% of the latter. This product is dissolved in an equal volume of acetic acid and treated in the cold with an equal weight of chromic acid dissolved in a small quantity of water. After the addition of chromic acid is complete, the solution is allowed to warm to room temperature and is maintained at room temperature for six hours. The product is then isolated by the usual methods, yield 90% based on tetralin consumed, b. p. 134° (15 mm.).

α-Tetraloneoxime.—The oxime was prepared using a technical grade of neutral hydroxylamine sulfate, recrystallized from 50% alcohol using a little Norite; yield 90%, m. p. 102°.

(10) Schroeter, *Ber.*, **63**, 1323 (1930).

(11) Von Braun and Bartsch, *ibid.*, **45**, 3376 (1912).

Summary

Some further examples of the inhibition of the acid catalyzed hydrogen exchange reactions of dimethylaniline derivatives by ortho substituents are reported.

In support of the theory that the ortho effect is primarily a steric effect having to do with the tendency of an ortho substituent to block the formation of quinonoid structures, it is shown that the inhibition of hydrogen lability caused by an ortho fluorine atom is much less than that caused by an ortho chlorine atom. A more decisive test of the theory is provided by a study of the exchange reactions of the cyclic bases, N-methylindoline, N-methyltetrahydroquinoline, and N-methyl-*homo*-tetrahydroquinoline. The first two of these, having bicyclic structures which are coplanar or nearly so, were observed to exchange hydrogen readily, while the third, in which the heterocyclic ring must be highly puckered, exhibited the inhibition of reactivity which is characteristic of ortho substituted tertiary amines.

CHICAGO, ILLINOIS RECEIVED JUNE 26, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

Inactivation of Tyrosinase in the Oxidation of Catechol

BY B. J. LUDWIG AND J. M. NELSON

When catechol is oxidized by means of an excess of the oxidase, tyrosinase, two atoms of oxygen are consumed per mole of the substrate. If, however, less than a sufficient amount of the enzyme is used, then the enzyme becomes inactivated before the catechol is completely oxidized (curves I and III, Fig. 1).

The inactivation of one unit of catecholase[1] has been found to involve a definite amount of oxygen uptake. In fact the amount of oxygen required for the inactivation may be used as a quantitative measure of the amount of catecholase present in a given preparation of the enzyme, provided the latter has been purified sufficiently. Crude tyrosinase preparations[2] are apt to contain from the plant, serving as the source, catechol or catechol derivatives and phenols which are aerobically oxidized by the enzyme, or tend to form with the latter inactive complexes. For this reason crude tyrosinase preparations often tend to lose activity on standing. These concomitant substances are usually lost when the purification has reached the stage, in the case of tyrosinase from the common mushroom, *Psalliota campestris*, when 1 mg. dry weight is equivalent to 80 or more catecholase units (for definition of units see legend Fig. 1). Sufficiently purified tyrosinase preparations from the last-mentioned source require for complete inactivation an uptake of 100 ± 5 cu. mm. of oxygen per catecholase unit (column 4, Table I).

It has been shown by Parkinson (unpublished) in these laboratories and also by others[3,4] that in

(1) Since tyrosinase catalyzes the oxidation of both catechol and *p*-cresol, the terms catecholase and cresolase have been used for the respective enzymic activities.

(2) M. W. Onslow, "Principles of Plant Biochemistry," University Press, Cambridge, England, 1931, p. 131.

(3) F. Kubowitz, *Biochem. Z.*, **299**, 32 (1938).

(4) D. Keilin and T. Mann, *Proc. Roy. Soc.* (London), **B125**, 187 (1938).

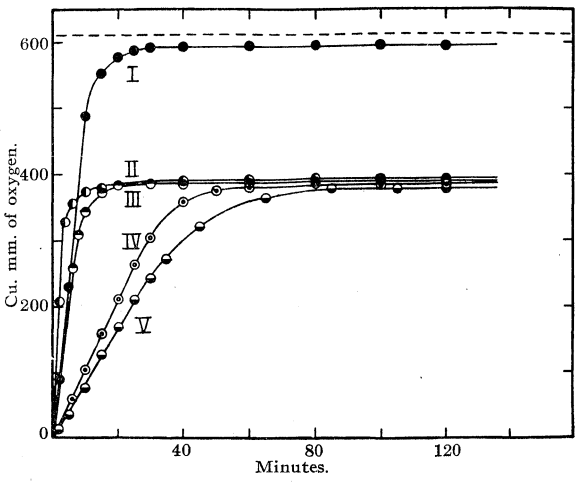


Fig. 1.—Showing oxygen uptake when catechol is oxidized aerobically in the presence of tyrosinase. Barcroft differential respirometer (ref. 5) used. Temp. 25°. Contents of control flasks differed from that in reaction flasks by substituting an equal volume of water in place of the enzyme solution. Curve I shows the complete oxidation (2 atoms of oxygen) of catechol when sufficient enzyme is used. Reaction mixture in reaction flask: 3 cc. 0.2 *M* phosphate buffer (*p*H of final reaction mixture 6.7), 1 cc. gelatin solution (5 mg.), 2 cc. tyrosinase solution (8.0 catecholase units) and sufficient water to make the final reaction mixture 8 cc.; 1 cc. catechol solution (3 mg.) was added from the side arm to the reaction mixture at zero time. Curve III shows inactivation of the tyrosinase when less enzyme (4 units) and more catechol (4 mg.) was used than in the experiment corresponding to curve I. Otherwise reaction mixture for experiment (curve III) same as that represented by curve I. After the expiration of ninety minutes 2 mg. more catechol was added to each of the two above reaction mixtures. In the case of the mixture corresponding to curve I, further oxidation took place, showing the enzyme to be still active, while in the case of the mixture (curve III) no further uptake of oxygen occurred, showing that the enzyme was no longer active. Curves II, IV and V are discussed in a later section of the text. They show that the amount of oxygen corresponding to complete inactivation is influenced neither by the length of time the enzyme is exposed to the reaction mixture nor by the rate at which the catechol is oxidized or by the concentration of the oxygen in the reaction mixture. The reaction mixtures used in these experiments were the same as that used in the experiment for curve III, but the composition of the gases in the reaction vessel differed: II 100% oxygen, III 21% O_2 (air), and IV 2% oxygen and 98% nitrogen. In the experiment corresponding to curve V, the air in the flask was replaced by nitrogen, the final traces of oxygen being removed by alternately evacuating and reflushing the flask with nitrogen. The catechol was then added to the main reaction flask and the latter shaken for forty minutes, after which time the nitrogen was replaced by a 2% oxygen–98% nitrogen mixture, and the oxygen uptake measured. 2% oxygen was used here, instead of air, in order to slow down the rate of the reaction and permit equilibrium conditions to be attained before appreciable oxygen consumption occurred. A comparison of the curves IV and V reveals that although a slightly different rate of oxygen consumption resulted, nevertheless, the total oxygen uptake, before inactivation of the enzyme was complete, was the same in the two experiments. The slower rate evidenced by curve V may be attributed to the initial lack of dissolved oxygen in the reaction mixture. The tyrosinase used in the above mentioned experiments was obtained from the common mushroom, *Psalliota campestris*, and contained about 320 catecholase units per γ of copper. For definition of catecholase units see paper by Adams and Nelson (ref. 6).

the case of reasonably purified preparations of tyrosinase the catecholase activity is proportional to the copper content. It therefore follows that the amount of oxygen required for the inactivation of catecholase is proportional to the copper content (3.3×10^4 cu. mm. of oxygen per γ of copper, column 6, Table I). The first three values in column 6 are low and indicate that an appreciable amount of copper, inactive toward catechol, is present in preparations C101A, B and D. This may be due to foreign copper proteins being present in these relatively impure preparations as has been suggested by Keilin and Mann or to the presence of inactivated enzyme, removable by further purification.

The cresolase activity, determined according to the Graubard and Nelson method as modified by Adams and Nelson, appears to bear no relation to the amount of oxygen consumed in the complete inactivation of the enzyme (column 7, Table I).

In Part B, Table I, data are presented for tyrosinase preparations from sources other than *Psalliota campestris*. These data indicate that the amount of oxygen consumed for the complete inactivation of these tyrosinases is different. In the case of the wild mushroom, *Lactarius piperatus*, an oxygen uptake of 400 ± 15 cu. mm. is required for the inactivation of one unit (catecholase). Since Dalton (unpublished) has shown that the catecholase activity of the tyrosinase from this source is also proportional to the copper content (42 units per γ of copper), it follows that the total oxygen required to inactivate the amount of enzyme equivalent to one γ of copper, in this case, is about 1.7×10^4 cu. mm. This value is approximately one-half of 3.3×10^4 cu. mm., the corresponding value for the enzyme from *Psalliota campestris*.

This inactivation of tyrosinase resulting when the enzyme catalyzes the oxidation of catechol has been ascribed by several workers[7,8] to the *o*-benzoquinone formed in the oxidation of the catechol. The fact that the inactivation persists when the reaction is allowed to take place in the presence of sodium benzenesulfinate is an argument against this view. Bordner and Nelson[9] have shown that sodium benzenesulfinate combines almost quantitatively with *o*-benzoquinone, thereby rendering the latter inactive.

Further evidence that *o*-benzoquinone does not

(5) Dixon, "Manometric Methods," University Press, Cambridge, England, 1934.

(6) M. H. Adams and J. M. Nelson, THIS JOURNAL, **60**, 2474 (1938).

(7) D. Richter, *Biochem. J.*, **28**, 901 (1934).

(8) C. R. Dawson and J. M. Nelson, THIS JOURNAL, **60**, 250 (1938).

(9) C. A. Bordner and J. M. Nelson, *ibid.*, **61**, 1507 (1939).

TABLE I

Prepn.	Units enzyme per mg. dry wt.	Units enzyme per γ copper	Av. O_2 uptake per unit enzyme inactivated, cu. mm.	Total O_2 uptake per mg. dry wt., cu. mm.	Total O_2 uptake per γ copper, cu. mm.	Ratio: catecholase units/cresolase units
			Part A			
C101A	83	175	100	0.83×10^4	1.8×10^4	6.7
C101B	110	136	98	0.98	1.3	6.1
C101D	282	234	103	2.9	2.4	6.4
C101C	363	342	95	3.4	3.2	8.0
C101E	472	344	101	4.7	3.5	11.3
C95	500	322	95	3.2	3.1	3.1
C100	480	320	95	4.7	3.1	5.3
C102	445	365	96	4.3	3.5	8.3
C106	487	310	98	4.8	3.1	11.4
C94	...	...	185	...	...	2.2
C96	...	...	210	...	...	1.7
C97	75	...	162	1.2	...	2.6
			Part B			
Lactarius piperatus	98	42	402	3.9	1.7	0.1
Irish potato	...	...	190	...	...	.6
Sweet potato	...	...	320	...	...	...
Puff ball	...	...	750	...	...	.05
Dolichos lablab	...	...	>1500	...	...	1.2

All the tyrosinase preparations mentioned in Part A were obtained from the common mushroom, *Psalliota campestris* The fresh mushrooms were ground in a meat grinder, and the ground pulp frozen. The frozen material was then placed in an equal volume of water and allowed to stand overnight to thaw out. The material was then filtered, the residue pressed dry in a hydraulic press and the pressed juice and filtrate combined. The latter was treated with an equal volume of cold acetone, the precipitate filtered off, dissolved in water and made 0.6 saturated with ammonium sulfate. The precipitate from the ammonium sulfate treatment was redissolved in water and made *p*H 4.8 by adding 2% trichloroacetic acid. The precipitate thus obtained was centrifuged off, discarded and the supernatant liquid remaining was brought to *p*H 7 by means of dilute ammonium hydroxide. The solution thus obtained was treated with just enough alumina to adsorb about 15% of the enzyme together with some of the accompanying impurities. After filtering off the alumina, the filtrate remaining was made 0.6 saturated with ammonium sulfate, the precipitate formed filtered off and redissolved in a small amount of water and dialyzed against glass-distilled water. The dialyzed solution contained preparation C101A. The greater portion of the solution containing preparation C101A was treated with enough alumina to adsorb the enzyme completely. The enzyme was eluted from the alumina by means of disodium phosphate, filtered and the solution concentrated by making it 0.6 saturated with ammonium sulfate, filtering off the precipitate, redissolving in a small amount of water and dialyzing against glass-distilled water. The solution thus prepared contained preparation C101B. The major portion of the latter solution was adjusted to *p*H 7.4 by 0.1 *M* ammonium hydroxide, treated with a small amount of recently prepared tricalcium phosphate and filtered. The filtrate, which contained most of the enzyme, was made 0.4 saturated with ammonium sulfate, the precipitate obtained dissolved in water and the *p*H adjusted to 6.5 by 0.1 *M* ammonium hydroxide. The enzyme in the latter solution was adsorbed to alumina, eluted with disodium phosphate and dialyzed. The solution thus obtained contained preparation C101C. The tyrosinase in a portion of the solution containing the preparation C101C was adsorbed to alumina, eluted with disodium phosphate and the solution obtained made 0.3 saturated with ammonium sulfate. The precipitate obtained was dissolved in water and dialyzed. This solution contained preparation C101D. The filtrate remaining after the treatment of the solution from which preparation C101D was obtained, with 0.3 saturated ammonium sulfate still contained considerable enzyme which was not precipitated under those conditions. This portion of the tyrosinase was precipitated by making the above mentioned filtrate 0.4 saturated with ammonium sulfate. The precipitate thus obtained was dissolved in water, dialyzed and the resulting solution contained preparation C101E. Preparations C95, C100, C102 and C106 were obtained from different lots of mushrooms (*Psalliota campestris*), and were purified by procedures similar to those described above. Preparations C94, C96 and C97 were also from *Psalliota campestris* but only partly purified.

exert a destructive effect on tyrosinase is shown by the data represented graphically in Fig. 2. In one of these experiments (curve II) the enzyme was allowed to react with only a fraction of the amount of catechol necessary to inactivate it completely. The active enzyme remaining after the oxidation of this initial addition of catechol was shaken in the Warburg apparatus for forty minutes in the presence of the *o*-benzoquinone previously formed, and then an excess of catechol was added to the reaction vessel, whereupon further consumption of oxygen occurred. The total oxygen uptake was found to be the same as in the case of the control (curve I) in which the enzyme was allowed to react on an excess of catechol at the start.

The inactivation of tyrosinase in the presence of an excess of catechol is not influenced by the rate at which the catechol is oxidized, hence the length of time at which the enzyme is exposed to the reaction mixture is without effect on its activity. This fact is brought out by comparing the oxygen uptakes necessary for inactivation when the oxidation took place rapidly in the pres-

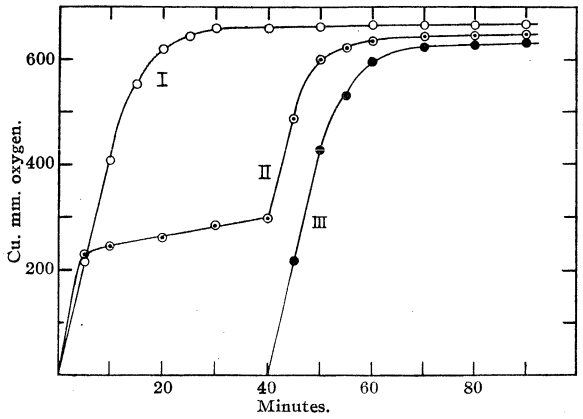


Fig. 2.—Showing that the products of the enzymatic oxidation of catechol are without destructive effect on the enzyme. Warburg respirometer, 25°. Reaction mixture: 2 cc. of tyrosinase solution (8 units), 3 cc. of 0.2 *M* phosphate buffer (final *p*H 4.3), 1 cc. of 0.5% gelatin (5 mg.) solution and 1.5 cc. of water. Final volume was 8 cc. The catechol (7.5 mg.) was added from a side-arm in experiment (curve I) at zero time; in experiment (curve III) the same amount of catechol was added after the rest of the reaction mixture had been shaken in the Warburg flask for forty minutes; in experiment (curve II) the catechol was added in two portions, one portion (2.25 mg.) was introduced at zero time by means of a "dangling tube" (Dixon[9]) and the remainder (5.25 mg.) from the side-arm after the expiration of forty minutes. At completion of the experiments further addition of catechol brought about no more oxygen uptake, showing the tyrosinase to be inactive. Tyrosinase from *Psalliota campestris* was used in the above experiment. A low *p*H was used because *o*-benzoquinone is less fugitive in acid solutions.[10]

ence of 100% oxygen and when the rate was slow in the presence of 2% oxygen and 98% nitrogen (curves II and IV, Fig. 1). Permitting the tyrosinase to remain in contact with the catechol and the other components of the reaction mixture, but in the absence of oxygen, had no inactivating effect on the enzyme. This fact is shown by Curve V, Fig. 1, which represents an experiment in which the enzyme was introduced into the reaction mixture in the absence of oxygen. After the expiration of forty minutes a mixture of 2% oxygen and 98% nitrogen was introduced and the oxygen uptake measured.

The data given in Table II show that using the amount of oxygen consumed in the inactivation of a given amount of enzyme as a measure, the inactivation is independent of the hydrogen-ion concentration between *p*H 5 and 7.5.

The temperature at which the inactivation is permitted to take place does, however, influence the amount of oxygen uptake required to bring about complete inactivation. At 25° the oxygen uptake, as already stated, is 100 ± 5 cu. mm. per unit for tyrosinase from *Psalliota campestris*. At 35° this value drops to about 80 cu. mm. of oxygen.

(10) C. R. Dawson and B. J. Ludwig, THIS JOURNAL, **60**, 1617 (1938).

TABLE II

SHOWING THE INFLUENCE OF *p*H ON THE TOTAL OXYGEN CONSUMPTION PER UNIT OF CATECHOLASE (*Psalliota campestris*) INACTIVATED, WHEN THE LATTER WAS PERMITTED TO ACT ON AN EXCESS OF CATECHOL

Warburg respirometer; temp. 25°; reaction mixture: 1 cc. tyrosinase solution (4 units); 1 cc. gelatin solution (5 mg.); 3 cc. 0.2 *M* phosphate buffer solution (except for the first two in which phosphate–citrate was used); sufficient water to make final volume 8 cc.; 1 cc. catechol solution (4 mg.) added from the side-arm.

*p*H of reacn. mixt.	4.0	4.3	4.8	5.2	5.8
Cu. mm. O_2 per unit of enzyme inactivated	67	86	90	95	95
*p*H of reacn. mixt.	6.2	6.6	7.6	8.1	8.6
Cu. mm. O_2 per unit of enzyme inactivated	95	95	93	82	78

The oxidation of a definite amount of catechol is necessary for the complete inactivation of a given quantity of tyrosinase, irrespective of the concentration of the catechol in the reaction mixture. This was shown by oxidizing various amounts of catechol in the presence of an excess of a suitable reducing agent, such as ascorbic acid. Such a reducing agent converts the quinone as fast as it is formed to catechol, thereby maintaining a constant supply of catechol during the course of the reaction. Under these conditions it was found that although the rate of oxygen uptake was influenced by the amount of catechol present, the total oxygen consumed per unit of catecholase inactivated was independent of the concentration of catechol used, and was the same as when the enzyme was allowed to act in the presence of an excess of catechol (curves II and III, Fig. 3).

Tyrosinase from *Psalliota campestris* is incapable of catalyzing the oxidation of hydroquinone, but the latter like ascorbic acid reduces *o*-benzoquinone. Hence, through the medium of catechol, tyrosinase oxidizes ascorbic acid to dehydroascorbic acid and hydroquinone to *p*-benzoquinone. It is therefore possible to maintain a low concentration of catechol constant in the reaction mixture by means of hydroquinone, just as when ascorbic acid is used as the reductant. However, the presence of hydroquinone allows the reaction to continue for a longer time, and as a result, the total oxygen consumed before the enzyme is inactivated is much greater than that consumed when the enzyme is allowed to act in the presence of an excess of catechol (curves I and II, Fig. 3). This difference in behavior when these substances are used with catechol as the substrate makes it apparent that whereas both

function as reductants of *o*-benzoquinone and tend to keep the supply of catechol constant, hydroquinone, in addition, exerts a protective influence on the tyrosinase.

In order to gain further information concerning the nature of the protective action on the enzyme exhibited by hydroquinone under these conditions, a study was made of the effect of varying the ratio of hydroquinone to catechol on the rate of oxygen uptake and on the total amount of oxygen consumed during the inactivation of the enzyme. Using a constant concentration of catechol in the reaction mixture, it was found that the rate of oxygen uptake was practically independent of the amount of hydroquinone present. On the other hand, the total volume of oxygen consumed per unit of catecholase inactivated was found to increase with increasing amounts of hydroquinone.

Additional evidence has been obtained which suggests that the protective action shown by the hydroquinone might be due to a tendency of this substance to combine with the enzyme. It was found that benzoic acid, when added to the reaction mixture in concentrations equal approximately to that of the catechol used, produced a marked inhibitory effect on the rate of oxygen uptake. Yet the total oxygen uptake consumed per unit of catecholase inactivated was unchanged. This inhibition due to benzoic acid can be seen by comparing curves II and III with curves IV and V, respectively, in Fig. 3. Furthermore, upon adding to the reaction mixture a sufficient quantity of benzoic acid (*p*H adjusted to 7) to inhibit completely the enzymic action, and subsequently subjecting the reaction mixture to dialysis, it was found that the enzyme, dialyzed free of benzoic acid, had regained all of its original activity.

The behavior of the benzoic acid toward the tyrosinase–catechol reaction suggests that tyrosinase exerts its catalytic action by first combining with the substrate to form a complex, this combination being of such a nature that it is reactive toward molecular oxygen. In such a mechanism, benzoic acid acts as an inhibitor simply by competing with the substrate for the space available at the active enzyme center.

Only compounds of certain molecular configuration are capable of combining with the enzyme, the tendency being dependent on the molecular structure. Of those substances which can combine with the enzyme, only a few are capable of becoming activated sufficiently so that they are

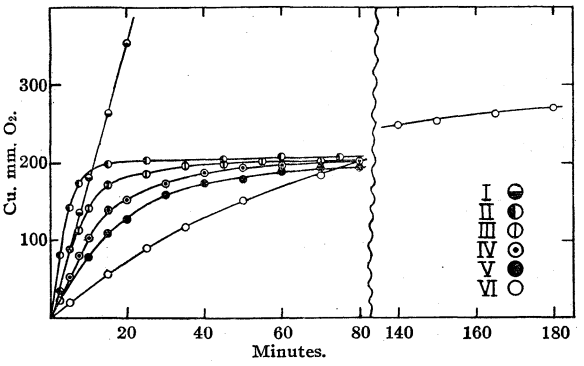


Fig. 3.—Showing the effects of ascorbic acid, hydroquinone, *p*-cresol and benzoic acid on the inactivation of tyrosinase. Tyrosinase prepared from *Psalliota campestris*. Temp. 25°, Barcroft respirometer (Dixon[3]). Curve II: inactivation of enzyme in the presence of an excess of catechol. Reaction mixture was 3 cc. of 0.2 *M* phosphate buffer (final *p*H 7.0), 1 cc. of gelatin (5 mg.), 1 cc. of tyrosinase solution (2 catecholase units), sufficient water to make final volume 8 cc. and 1 cc. of catechol solution (4 mg.) in side-arm. Curve III, showing that ascorbic acid only reduces the *o*-benzoquinone back to catechol without influencing the amount of oxygen uptake required for inactivation. Reaction mixture was same as for expt. II except a 1.5 cc. of solution containing 0.1 mg. of catechol and 5 mg. of ascorbic acid in side-arm. Curve I, showing the difference in effect on the reaction when hydroquinone is used in place of ascorbic acid as in expt. III. Reaction mixture same as for expt. III except 5 mg. of hydroquinone in place of the 5 mg. of ascorbic acid. Curve IV shows the inhibiting influence of benzoic acid on the oxidation of catechol by tyrosinase. Reaction mixture was same as for expt. II except that the reaction flask contained in addition 1 cc. of 0.1 *M* sodium benzoate. Curve V, showing the inhibiting influence of benzoic acid on the oxidation of catechol in the presence of ascorbic acid. Reaction mixture was the same as for expt. III except that reaction flask contained in addition 1 cc. of 0.002 *M* sodium benzoate. Curve VI, showing the protective action against the inactivation of the enzyme by *p*-cresol. Reaction mixture was same as for expt. II except 1 cc. of a solution containing 4 mg. *p*-cresol and 0.1 mg. catechol in side-arm. In all experiments the contents of the side arm were transferred to the main reaction vessel at zero time, when the mixture had attained the temperature of the thermostat. The control flasks in each experiment contained the same reaction mixture except that water replaced the enzyme solution.

oxidized by the oxygen which also takes part in the complex. On this basis the difference in effect manifested by ascorbic acid, *p*-cresol, benzoic acid and hydroquinone on the tyrosinase–catechol reaction becomes clear. Ascorbic acid does not have a suitable configuration to permit it to combine with the enzyme molecule; hence when it is added to the tyrosinase–catechol reaction mixture, it behaves simply as a reductant of the *o*-quinone. On the other hand, according to some observations of Gregg (unpublished) *p*-cresol combines more readily with tyrosinase (*Psalliota campestris*) than does catechol. When the latter is added to a reaction mixture containing the enzyme and an equal amount of the cresol, the course of the reaction is practically the same as if no catechol[11] had been added. Benzoic acid

(11) Except the trace necessary to remove the initial lag period occurring in the enzyme oxidation of the *p*-cresol.

seems to combine with the enzyme to about the same extent as catechol, but is not sufficiently activated by the enzyme to become oxidized. Hydroquinone also combines with tyrosinase and like benzoic acid is not activated sufficiently, when combined with the enzyme, to become oxidized. Unlike benzoic acid, however, it resembles ascorbic acid, as has been mentioned above, in that it acts as a reductant toward *o*-benzoquinone. The protective action of the hydroquinone on the activity of tyrosinase may also be due to its tendency to combine with the enzyme. *p*-Cresol also tends to protect tyrosinase, as is shown by curve VI in Fig. 3, and it, too, as has been pointed out, seems to have a strong tendency to combine with the enzyme. The inactivation of the enzyme takes place in the process of the reaction and is not due to the reactants nor to the reaction products present in the reaction.

One substance which might be suspected of inactivating the enzyme in the tyrosinase–catechol reaction is hydrogen peroxide. The latter is known to inactivate many enzymes. Dawson and Ludwig,[10] however, were unable to detect any formation of peroxide in this reaction, and reached the conclusion that if it is formed it must be used up in performing some intermediary function at a rate faster than its rate of formation. Therefore, if hydrogen peroxide, or some activated form of oxygen, is responsible for the inactivation, the inactivation must occur during the process of the oxidation of the catechol. As a matter of fact, in the light of our present knowledge, the cause of the inactivation of tyrosinase, when it catalyzes the oxidation of catechol, is still unknown.

Summary

It has been found when tyrosinase, from *Psalliota campestris*, is inactivated in the oxidation of catechol, that:

1. The inactivation, at 25°, involves a constant uptake of oxygen: 100 ± 5 cu. mm. per unit of enzyme, or 3.3×10^4 cu. mm. per γ of copper.

2. This amount of oxygen is independent of: (a) the rate of oxidation of the catechol; (b) the concentration of oxygen; (c) the hydrogen-ion concentration between *p*H 5 and 7.5; (d) the ratio of catecholase activity to cresolase activity; (e) but is dependent on temperature.

3. The inactivation is not due to any products, known to be formed, in the oxidation of the catechol, but occurs at the time the catechol is oxidized.

4. Tyrosinase from different sources consumes different amounts of oxygen per unit of catecholase inactivated. The total oxygen consumed in the inactivation of purified preparations from *Lactarius piperatus*, at 25°, is 400 ± 15 cu. mm. per unit or 1.7×10^4 cu. mm. per γ of copper.

5. Hydroquinone, when used in excess with low concentration of catechol, besides serving as a reductant of *o*-benzoquinone, exerts a protective influence against inactivation of the enzyme. Ascorbic acid, also a reductant toward *o*-benzoquinone, exerts no protective influence.

6. Benzoic acid exerts a retarding influence on the activity of the enzyme toward catechol, but has no protective action.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, BANTING INSTITUTE, UNIVERSITY OF TORONTO]

Oxidation of 1,2-Glycols or 1,2,3-Polyalcohols by Means of Lead Tetraacetate in Aqueous Solution

BY ERICH BAER, J. M. GROSHEINTZ AND HERMANN O. L. FISCHER

Criegee[1] found that lead tetraacetate oxidizes 1,2-glycols by breaking the bond between the hydroxyl-carrying carbon atoms, thereby forming aldehydes and ketones. This cleavage reaction takes place quantitatively at room temperature; its velocity depends greatly on the structure of the glycol and the *solvent* in which the reaction takes place. The method has found extensive application both in analytical and preparative procedures. The discoverer contended that non-aqueous solvents only can be used, *e. g.*, benzene, nitrobenzene, chloroform, di- and tetrachlorethane or glacial acetic acid. Considerable emphasis was placed on the drying of such solvents.

The same oxidative cleavage of glycols can be carried out in aqueous solution with periodic acid according to Malaprade.[2] This method is very suitable for the titration of glycols, and frequently has been used whenever it is desirable to work in water.

One of us (E. B.) observed that, contrary to prevailing views, the glycol cleavage with lead tetraacetate also may be carried out in moist organic solvents and even in aqueous solution, if the velocity of oxidation be higher than that of the hydrolysis of the oxidizing agent. Since the lead is easily removed quantitatively by dilute sulfuric acid, we believe that this modification will greatly extend the applicability of Criegee's method of oxidative glycol cleavage.

In preliminary qualitative experiments lead tetraacetate was added to aqueous solutions of glycerol, *d*-mannitol, *d*-glucose and *d*-mannose, either as a concentrated solution in glacial acetic acid or in a finely powdered form. In both cases the aqueous solution generally remained clear. Although slight brown turbidities sometimes occurred due to local excess of the reagent, these disappeared very rapidly. The end of the reaction is indicated by the immediate formation of a permanent brown precipitate of lead oxides. These compounds contained up to six adjacent hydroxyl groups and therefore a mixture of oxidation products, giving mixed precipitates with substituted hydrazines, resulted.

In order to make a quantitative study of the oxidation with lead tetraacetate in aqueous solution we investigated the cleavage of 1,2–5,6-diacetone-*d*-mannitol and of pinacol. We chose these compounds since they possess only a single pair of vicinal hydroxyl groups and further because the oxidation of these substances (in organic solvents) is unambiguous and was already familiar to us.[3] Further, the cleavage products are easily determined quantitatively. A concentrated solution of the equivalent amount of lead tetraacetate in acetic acid was added to an aqueous solution of 1,2–5,6-diacetone-*d*-mannitol. Oxidation took place immediately and the acetone-*d*-glyceraldehyde which was formed was hydrolyzed quickly to *d*-glyceraldehyde in the presence of the dilute acetic acid. The amount of aldehyde present was equal to 99% of the theoretical yield. By oxidation of *d*-glyceraldehyde with bromine, *d*-(−)-glyceric acid was obtained in a yield of 76%. This is a convenient way of preparing *d*-(−)-glyceric acid and its derivatives. The procedure for preparing *d*-(−)-glyceric acid has been included at the end of this paper. Its antipode may be prepared similarly from *l*-glyceraldehyde[3c] recently synthesized by us.

The pinacol was oxidized in the same manner as above described and the yield of acetone was 95% of the theoretical.

The results of our quantitative studies of the oxidation of *α-glycols* with lead tetraacetate in aqueous solutions indicate that these reactions follow the same course and go as thoroughly to completion in water as in non-aqueous solvents—a finding quite unexpected in view of Criegee's insistence on the necessity of drying all solvents.

From glycols containing two hydroxyl groups we turned our attention to compounds with three adjacent hydroxyl groups. Previous experiments[4] had already shown that compounds such as

(1) Rudolf Criegee, *Ann.*, **481**, 275 (1930); *Ber.*, **64**, 260 (1931); *Angew. Chem.*, **50**, 153 (1937); this last article contains a review of the literature concerned.

(2) Malaprade, *Compt. rend.*, **186**, 382 (1929).

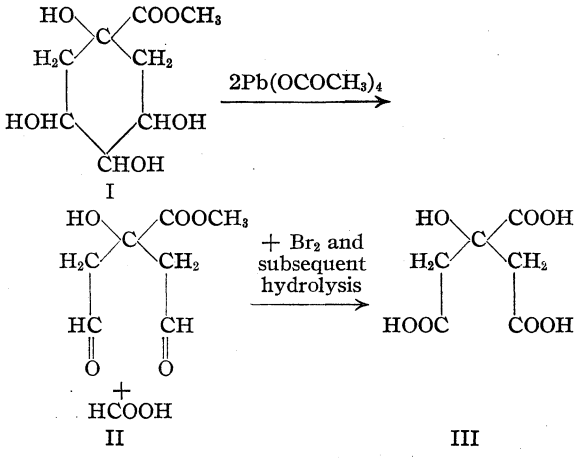
(3) (a) Criegee, *Ber.*, **64**, 264 (1931); (b) H. O. L. Fischer and E. Baer, *Helv. Chim. Acta*, **17**, 622 (1934); (c) E. Baer and H. O. L. Fischer, THIS JOURNAL, **61**, 761 (1939); and (d) *J. Biol. Chem.*, **128**, 463 (1939).

(4) H. O. L. Fischer and Dangschat, *Helv. Chim. Acta*, **17**, 1196 (1934); **17**, 1200 (1934); **18**, 1204 (1935).

quinic acid (1 mole) and shikimic acid (1 mole) could be oxidized with periodic acid (2 moles) in aqueous solution. Dialdehydes were formed and the central carbon atom was split out as formic acid.

In order to test the usefulness of lead tetraacetate for this reaction, we studied the oxidation of the methyl ester of quinic acid and found, in agreement with our expectations, that one mole of quinic acid methyl ester (I) in aqueous solution formed one mole of dialdehyde (II) and one mole of formic acid, using up two moles of lead tetraacetate.[5]

The reaction takes place according to the equation



Titration according to the method of Willstätter and Schudel showed an amount of dialdehyde present in the aqueous solution equal to the theoretical. The dialdehyde was then oxidized by bromine to the stable citric acid (III) which was isolated in a yield of 86% of the theoretical.

Experimental

A. Glycol Cleavage

I. Lead Tetraacetate Oxidation of 1,2–5,6-Diacetone-*d*-mannitol.—A colorless solution of 4.43 g. of lead tetraacetate (0.01 mole) in 25 cc. of warm glacial acetic acid[6] was added rapidly with constant agitation to a solution of 2.63 g. of diacetone-*d*-mannitol (m. p. 121–122°)[3d] (p. 466) (0.01 mole) in 60 cc. of water. The oxidation took place instantaneously and the mixture remained perfectly clear. After a few minutes 20 cc. of 1 *N* sulfuric acid was added, and the precipitate of lead sulfate was separated by centrifuging. During this procedure the cleavage product, acetone-*d*-glyceraldehyde, hydrolyzed quickly to *d*-glyceraldehyde and acetone in the acid solution. Acetone was removed by evaporation *in vacuo* and the concentrate was made up to 50.00 cc. with distilled water (solution I). The product was not isolated at this stage. The precipitation of the 2,4-dinitrophenylhydrazone (m. p. 155–156°) and dimedone compound (m. p. 198°; $[\alpha]_D$ +198°) from the above solution confirmed our expectation that the product of the reaction would be the same (*i. e.*, *d*-glyceraldehyde) in water as in non-aqueous solvents. The yield was determined by the method of Willstätter and Schudel.[7] In three such titrations, 5.00 cc. of solution I required 39.2, 39.4 and 39.6 cc. of 0.1 *N* iodine solution, equivalent to 176, 177 and 178 mg. of aldehyde, respectively. The yield was therefore 98.8% of the theoretical.

Solution I was dextro-rotatory, $[\alpha]^{20}D$ +9.0°. We already have reported[8] the occurrence of solutions of glyceraldehyde with low specific rotation and have described a method for converting this material to a form with the characteristic maximal specific rotation of +14°.

II. Lead Tetraacetate Oxidation of Pinacol.—A colorless solution of 4.43 g. of lead tetraacetate (0.01 mole) in 30 cc. of warm glacial acetic acid was added gradually with gentle agitation to 1.18 g. of pinacol (0.01 mole) dissolved in 50 cc. of distilled water. After a few minutes[9] 5 cc. of 5 *N* sulfuric acid was added, and the precipitated lead sulfate was separated by centrifuging. A perfectly clear solution was obtained, containing only the cleavage product, acetone (0.02 mole). The solution was then made up to 100.0 cc. with distilled water and the acetone determined quantitatively by the method of Messinger.[10] Two 5.0-cc. portions of the solution required 56.8 and 57.3 cc. of 0.1 *N* iodine solution, respectively, which correspond to 55.0 and 55.4 mg. of acetone, respectively; yield, 95% of the theoretical.

B. Cleavage of 1,2,3-Polyalcohols

The oxidation of quinic acid methyl ester was carried out in two different ways with equally good results. (a) The lead tetraacetate dissolved in glacial acetic acid was added slowly to the aqueous solution of the substance to be oxidized, as described in the case of pinacol and diacetone-mannitol. (b) The aqueous solution of the substance to be oxidized was poured into a saturated solution of lead tetraacetate in glacial acetic acid. We shall describe the latter method only, since the inverted order of procedure is an interesting variation of the oxidation with lead tetraacetate in aqueous solution.

Lead Tetraacetate Oxidation of Quinic Acid Methyl Ester.—A solution of 6.18 g. of quinic acid methyl ester (0.03 mole) in 50 cc. of distilled water was poured into a mixture of 25 cc. of glacial acetic acid and 26.58 g. of lead tetraacetate (0.06 mole). The crystals of lead tetraacetate dissolved slowly as the oxidation proceeded. After ten minutes, 125 cc. of 1 *N* sulfuric acid was added, the solution was made up to 500.0 cc. and the precipitate

(5) Cases in which more lead tetraacetate is required will be described in a subsequent paper. (J. G.)

(6) The glacial acetic acid was warmed only for the purpose of dissolving the lead tetraacetate in a minimal quantity of solvent, thus keeping the ratio of water and acid as much as possible in favor of the water.

(7) Willstätter and Schudel, *Ber.*, **51**, 780 (1918).

(8) H. O. L. Fischer and E. Baer, *Helv. Chim. Acta*, **19**, 524 (1936); refs. 3b and 3c.

(9) The velocity of this reaction is much higher in aqueous solution than in organic solvents. Probably this will be the case for other compounds also.

(10) Messinger, *Ber.*, **21**, 3366 (1888).

of lead sulfate was removed by centrifuging. The dialdehyde formed was determined by titration according to Willstätter and Schudel; 25 cc. of the solution used up 61.0 cc. of 0.1 *N* iodine solution: dialdehyde calculated, 208.8 mg.; found, 211.0 mg.

For the oxidation of the dialdehyde the solution was freed from the excess of sulfuric acid by dropwise addition of barium acetate and diluted to 300 cc. with distilled water; 15 g. of bromine was added and the resulting mixture was placed in a tightly sealed bottle and allowed to stand for two days with occasional shaking. The excess bromine was removed by aeration, the hydrobromic acid formed was removed with silver acetate and the excess silver was precipitated with hydrogen sulfide. The mixture was then evaporated to dryness and the remaining citric acid monomethyl ester was saponified by boiling for half an hour with 60 cc. of 2 *N* sodium hydroxide. An amount of 1 *N* sulfuric acid (120 cc.) equivalent to the sodium hydroxide used was added and the solution evaporated to dryness under reduced pressure. The *citric acid* was separated from the sodium sulfate by extraction of the residue with ethyl acetate; 4.9 g. of crude citric acid was obtained (86% yield). Recrystallization from water yielded pure citric acid (m. p. 151°).

Preparation of *d*-(—)-glyceric acid.[11]—To an aqueous solution of *d*-glyceraldehyde prepared as described on page 2608, Col. 1, from 25 g. of diacetone-*d*-mannitol,[3d] 40 g. of bromine was added and the solution was shaken for two hours. After standing at room temperature for an additional fifteen hours, the excess bromine was removed by aeration and the bromide ions by shaking with silver carbonate or acetate. The silver ions were precipitated by hydrogen sulfide. The solution was then evaporated at 40° (10 mm.) to a dry sirup of constant weight; 15.4 g. (76% of the theoretical) of glyceric acid was obtained.

Preparation of *d*-Glyceric Acid Methyl Ester (Dextrorotatory).—Eleven grams of glyceric acid together with 250 cc. of dry methyl alcohol, containing 1.5% of hydrochloric acid (gas), was refluxed for twenty-four hours. After shaking the liquid for twelve hours with finely powdered silver carbonate, the silver salts were removed by centrifuging. The methyl alcohol was evaporated at reduced pressure and the residue was distilled *in vacuo:* yield, 11.5 g. (92% of the theoretical) of glyceric acid methyl ester; b. p. (8 mm.) 114–116°. Calculated for $C_4H_8O_4$ (120): C, 40.00; H, 6.70. Found: C, 39.96; H, 6.70. *Optical rotation* in homogeneous substance: $\alpha^{26}D$ +5.92 (1-dm. tube, d^{26}_4 1.279, $[\alpha]^{26}D$ +4.7).[12]

Preparation of the Calcium Salt of *d*-Glyceric Acid.—Eight grams of *d*-glyceric acid methyl ester was added to a solution of 2.47 g. of calcium hydroxide in 40 cc. of distilled water. After warming on the water-bath for one hour, the solution was neutralized with a few drops of 5 *N* hydrochloric acid and filtered, while still hot. Warm ethanol was then added until the clear and hot solution became turbid and the mixture was allowed to cool in the refrigerator; 8.0 g. of calcium salt was precipitated after six hours (84% yield). Calcd. for $(C_3H_5O_4)_2Ca\cdot 2H_2O$ (286): Ca, 13.99. Found: Ca, 13.95. *Optical rotation* of the calcium salt containing 2 moles of crystal water, in aqueous solution: 1-dm. tube, c = 5.19, $\alpha^{20}D$ +0.67°, $[\alpha]^{20}D$ +12.9°.[13]

Summary

It has been shown that oxidation with lead tetraacetate can be carried out quantitatively in *aqueous* solution and in water-containing solvents. This observation that the reaction does not always require dry organic solvents enlarges the field of its application. Lead tetraacetate yields the same oxidation products in water as in organic solvents, except in rare cases where secondary hydrolytic reactions may occur.

(11) Wohl and Freudenberg, *Ber.*, **56**, 309 (1923).

(12) Frankland and Turnbull, *J. Chem. Soc.*, 459 (1914).

(13) E. Fischer and Jacobs, *Ber.*, **40**, 1069 (1907); Wohl and Schellenberg, *ibid.*, **55**, 1404 (1922).

TORONTO, CANADA RECEIVED JULY 5, 1939

[CONTRIBUTION NO. 150 FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, THE UNIVERSITY OF TEXAS]

The Nitrogen Compounds in Petroleum Distillates. XV. Counter-Current Acid Extraction of Kero Bases. Isolation of 2,4-Dimethyl-8-*n*-propylquinoline

BY W. NELSON AXE[1] AND J. R. BAILEY

Introduction

It has been reported previously[2] that a satisfactory separation of 2,3-dimethyl-8-*n*-propyl- and 2,3,4,8-tetramethylquinoline from associated bases in the 300° boiling range of kero bases was accomplished by supplementing the conventional methods of processing petroleum bases with so-called fractional degassing of their acid sulfite solution under aeration.

In Jantzen's monograph,[3] the author reports the isolation of the following products from coal tar bases (b. p. 238–266°), through employment of counter-current extraction: quinoline, each of the seven monomethylquinolines, 2,8-dimethylquinoline,[4] isoquinoline, 1- and 3-methylisoquinoline, 1,3-dimethylisoquinoline, two $C_{10}H_9N$ bases (probably 6-methyl- and 5- or 7-methylisoquino-

(1) Research Department, Phillips Petroleum Company, Bartlesville, Oklahoma.

(2) W. N. Axe and J. R. Bailey, THIS JOURNAL, **60**, 3028 (1938).

(3) Ernst Jantzen, "Das fraktionierte Destillieren und das fraktionierte Verteilen," Verlag Chemie, Berlin, 1932, pp. 117–137.

(4) Isolated from California petroleum by Lake and Bailey, THIS JOURNAL, **55**, 4143 (1933).

line, respectively), and a C_7H_5NS compound (a thioisoquinoline?). Of these sixteen products, relatively few had been encountered by previous investigators in processing coal tar bases.

Lately, through employment of counter-current extraction,[5] 2,4-dimethyl-8-ethylquinoline was obtained from the kero base fraction of b. p. 292–293°.[6]

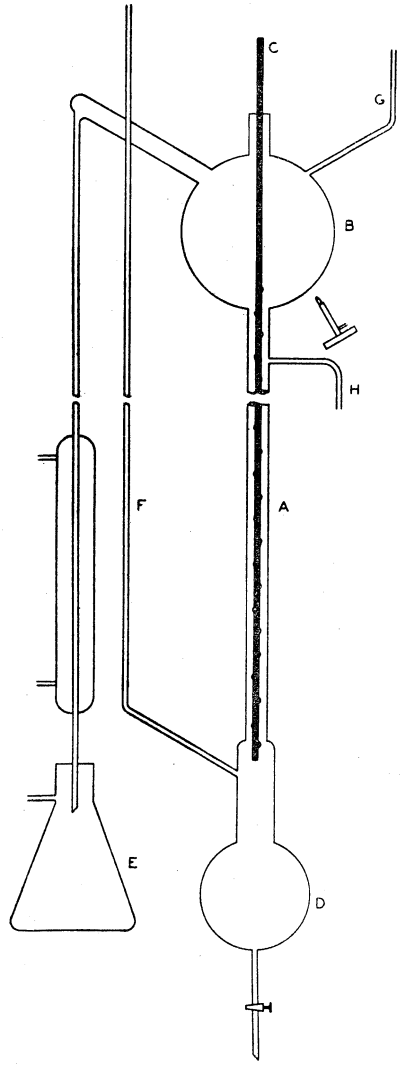


Fig. 1.—All-glass countercurrent extraction equipment. A, extraction column, height 125 cm., internal diameter 1.1 cm.; B, boiler from which solvent is distilled progressively into E; C, stirrer with nodes—above B is a bell-cup type mercury seal; F, inlet tube for bases in petroleum ether solution into B; G, inlet tube for dilute hydrochloric acid into B; H, outlet tube for withdrawal of base fraction in petroleum ether at the end of each extraction; D, reservoir for base-hydrochloride solution which is run off as desired.

(5) The column used was designed by Schutze, Quebedeaux and Lochte, *Ind. Eng. Chem., Anal. Ed.*, **10**, 676 (1938), Fig. 3.

(6) W. N. Axe, THIS JOURNAL, **61**, 1017 (1939).

We find in separation of mixtures of aromatic petroleum bases that fractional degassing of their acid sulfites, because of the simplicity in operation, can be employed to advantage frequently in their partial separation, preliminary to the use of exhaustive counter-current extraction.

This paper deals with the isolation of a $C_{14}H_{17}N$ base[2] by the extraction method and its identification as 2,4-dimethyl-8-*n*-propylquinoline through degradation and synthesis. The formation of 2,4-dimethylquinoline-8-carboxylic acid in chromic acid oxidation was confirmed by the usual comparison with an authentic sample of this preparation.[6] This showed the original base to be an 8-*n*- or isopropyl homolog of 2,4-dimethylquinoline. The *n*-propyl derivative was synthesized from acetyl acetone and *o*-amino-*n*-propylbenzene[2] and was proved to be the $C_{14}H_{17}N$ kero base.

Experimental

The preliminary work carried out for assembling the 292–293° fraction of aromatic base, known to contain the $C_{14}H_{17}N$ quinoline homolog, has been published previously.[2]

Prior to counter-current extractions, the base mixture was processed through acid sulfites to yield 10% of 2,3-dimethyl-8-ethylquinoline.[7]

Figure 1 shows the construction of the unit employed in counter-current extraction. The bases are dissolved in petroleum ether in the volume ratio of 1:2. Enough 2 *N* hydrochloric acid is used for the partial neutralization of the bases and the acid is diluted to a volume equal to that of the petroleum ether solution of bases. The final concentration of the acid in all extractions was close to 1.5 *N*. The bases are fed in at the bottom of the column through F and the acid above the column through G, an approximately equal flow-rate of the two solutions being maintained through stopcock control of the proportioning ratio. The maximum throughput without reducing contact efficiency is around 80 cc. of bases per hour. Thorough interdispersion of the acid and base solutions is accomplished by operating the stirrer at the maximum speed allowable without producing emulsions. At the end of the extraction, the petroleum ether solution containing Base Fraction I is run off through H. From their hydrochlorides collected in D, the bases are recovered and carried through a second partial extraction to yield Base Fraction II. Table 1 summarizes the final results from a repetition of the above procedure so as to obtain a total of seven fractions.

To effect separation of the component bases, the separate fractions were processed as follows: (1) picration was carried out in hot acetone; (2) the acetone-insoluble picrates were recrystallized from glacial acetic acid; (3) the acetone-soluble picrates were recrystallized from alcohol, followed by liberation of the bases from the alcohol-insoluble salts; (4) the bases obtained from the

(7) C. L. Key and J. R. Bailey, *ibid.*, **60**, 763 (1938).

TABLE I

EXTRACTION OF AROMATIC BASES IN THE 292–293° RANGE

Fraction	Vol., cc.	$n^{25}D$	d^{20}_4	Bases isolated	Yield, %
1	76	1.5760	1.0035	2,3-Me_2-8-*n*-PrQ[a]	21
2	40	1.5770	1.0039	2,3-Me_2-8-*n*-PrQ	22
3	70	1.5774	1.0057	2,3-Me_2-8-*n*-PrQ	14
				2,4-Me_2-8-*n*-PrQ	5
4	80	1.5820	1.0166	2,3-Me_2-8-EtQ	11
				2,4-Me_2-8-*n*-PrQ	8
5	50	1.5848	1.0203	2,3-Me_2-8-EtQ	3
6	47	1.5886	1.0246	None	
7	70	1.5920	1.0309	None	

[a] In this paper, the abbreviations Me_2, Et, Pr and Q denote dimethyl, ethyl, propyl and quinoline, respectively. In this and subsequent tables, *yield* applies to the volume of base in each fraction.

picrates in (3) were dissolved in dilute hydrochloric acid and converted to zinc chloride salts, with subsequent recrystallization from a dilute zinc chloride–hydrochloric acid solution. Step 2 in several fractions yielded 2,3-dimethyl-8-ethyl- and 2,3-dimethyl-8-*n*-propylquinoline. 2,4-Dimethyl-8-*n*-propylquinoline was encountered in Step 4 in processing fractions 3 and 4.

Characterization and Proof of Structure of the $C_{14}H_{17}N$ Base as 2,4-Dimethyl-8-*n*-propylquinoline

Zinc Chloride Salt.—This salt crystallizes in lustrous oblique parallelograms melting at 225–226°.

Anal. Calcd. for $(C_{14}H_{17}N\cdot HCl)_2\cdot ZnCl_2$: C, 55.33; H, 5.96; Cl, 23.34. Found: C, 55.14; H, 6.08; Cl, 23.12.

Free Base.—Prepared from the zinc chloride salt, the base is a colorless, viscous liquid with the following constants: b. p. 298° (747 mm.); $n^{25}D$ 1.5748; d^{20}_4 0.9992.

Anal. Calcd. for $C_{14}H_{17}N$: C, 84.42; H, 8.54. Found: C, 84.71; H, 8.56.

Phthalone.—On heating the base and phthalic anhydride at 200° for four hours, an orange yellow phthalone is formed which, after recrystallization from alcohol, melts at 198–199°.

Anal. Calcd. for $C_{22}H_{19}O_2N$: C, 80.21; H, 5.81. Found: C, 80.15; H, 5.90.

2,4-Dimethylquinoline-8-carboxylic Acid.—To a boiling solution of 5 g. of base in 6 *N* sulfuric acid is added slowly 15 g. of potassium dichromate in 12 cc. of concentrated sulfuric acid diluted with 25 cc. of water. The oxidation is complete in one hour and the carboxylic acid melting at 241–242° can be isolated in a yield of 45%.[2] This product, like an authentic sample of 2,4-dimethylquinoline-8-carboxylic acid, crystallizes from alcohol in long, slender needles melting at 241–242°. A mixed melting point of the two preparations showed no depression. This degradation product established a 2,4-dimethyl-8-*n*- or isopropyl structure for the original base.

Anal. Calcd. for $C_{12}H_{11}O_2N$: C, 71.64; H, 5.47. Found: C, 71.38; H, 5.44.

2,4-Dimethylquinoline.—Soda-lime distillation of the above carboxylic acid gives a liquid base, the picrate of which crystallizes from alcohol in long needles, melting at 194°. This salt was recognized as the suspected 2,4-dimethylquinoline picrate by the exceptional property of a rapid color change from bright yellow to brown on exposure to sunlight. Further confirmation of structure was obtained by the usual mixed melting point method.

Anal. of picrate. Calcd. for $C_{17}H_{14}O_7N_4$: C, 52.85; H, 3.64. Found: C, 52.92; H, 3.75.

Synthesis of 2,4-Dimethyl-8-*n*-propylquinoline.—Synthesis of the base from ortho-*n*-propylaniline[2] and acetylacetone[8] was confirmed by the same melting point for the individual and mixed picrates of the synthetic base and the kero base.

As a comparative study of the effectiveness of countercurrent extraction and degassing of acid sulfites in separation of 2,3-dimethyl-8-*n*-propylquinoline and 2,3,4,8-tetramethylquinoline,[9] the data in Tables II and III are submitted.

TABLE II

EXTRACTION OF AROMATIC BASES IN THE 303° RANGE

Fraction	Vol., cc.	$n^{25}D$	d^{20}_4	Bases isolated	Yield, %
1	28	1.5720	0.9955	2,3-Me_2-8-*n*-PrQ	4.5
2	62	1.5748	0.9988	2,3-Me_2-8-*n*-PrQ	11.5
3	60	1.5760	1.0017	2,3-Me_2-8-*n*-PrQ	17.5
4	32	1.5760	1.0080	2,3-Me_2-8-*n*-PrQ	23.0
5	75	1.5774	1.0024	2,3-Me_2-8-*n*-PrQ	14.0
6	66	1.5792	1.0057	2,3-Me_2-8-*n*-PrQ	1.2
7	72	1.5810	1.0088	None	
8	62	1.5828	1.0137	None	
9[a]	35	1.5834	1.0147		
10[a]	67	1.5872	1.0211		
11[a]	63	1.5896	1.0245		
12[a]	35	1.5916	1.0280		
13	62	1.5935	1.0328	None	
14	72	1.5960	1.0398	2,3,4,8-Me_4Q	29.0

[a] No attempt was made to isolate bases from these fractions.

TABLE III

EFFECT OF METHOD OF SEPARATION ON YIELDS OF PURE BASES

Extraction type	Charge B. p., °C.	$n^{25}D$	$C_{14}H_{17}N$, %	$C_{13}H_{15}N$, %
Fractional degassing	300	1.5850	1.8	0.8
Counter-current extraction	303	1.5855	4.7	2.5

In Table IV are results obtained in the separation of four well-known kero quinoline homologs through countercurrent extraction of an aromatic base fraction in the 280–283° range.

TABLE IV

EXTRACTION OF AROMATIC BASES IN THE 280–283° RANGE

Fraction	Vol., cc.	$n^{25}D$	d^{20}_4	Bases isolated	Yield, %
1	55	1.5724	1.0095	2,3-Me_2Q	33
2	35	1.5706	1.0083	2,3-Me_2-8-EtQ	20
3	55	1.5766	1.0069	2,3,8-Me_3Q	26
4	65	1.5840	1.0301	2,3,8-Me_3Q	25

(8) *Cf.* Königs and Mengel, *Ber.*, **37**, 1325, 1333 (1904).

(9) *Cf.* ref. 2 for the discovery of these quinoline homologs through employment of the degassing procedure.

Summary

This paper deals with the isolation through counter-current hydrochloric acid extraction of a new kero base, 2,4-dimethyl-8-*n*-propylquinoline, the structure of which was established by chromic acid oxidation to a $C_{11}H_{10}NCOOH$ acid, previously obtained in the Texas Laboratory by a similar oxidation of the kero base, 2,4,8-trimethylquinoline. This orientation was confirmed by synthesis, in which acetylacetone and *o*-*n*-propylaniline were the intermediates.

AUSTIN, TEXAS RECEIVED MAY 19, 1939

[CONTRIBUTION NO. 161 FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, THE UNIVERSITY OF TEXAS]

The Nitrogen Compounds in Petroleum Distillates. XVI. Use of Multiple Acid Extraction in Isolation of 2,3,4-Trimethyl-8-ethylquinoline

BY RICHARD A. GLENN AND J. R. BAILEY

Introduction

In a systematic investigation in the Texas Laboratory of kero quinoline homologs from crude bases furnished by the Union Oil Company of California, the 310° fraction was processed through cumulative extraction[1] in order to segregate the aromatic components in satisfactory concentration. In further refining, the latter material in the 305–315° range was processed through multiple acid-extraction.[2]

This method of separation yielded a $C_{14}H_{17}N$ base which degradation and synthesis revealed as 2,3,4-trimethyl-8-ethylquinoline. In chromic acid oxidation a $C_{12}H_{12}NCOOH$ acid was obtained which proved the replacement of an *ethyl* by *carboxyl*. The 8-position of the ethyl follows from the fact that the acid was identical with one previously obtained by chromic acid oxidation of 2,3,4,8-tetramethylquinoline.[3] Its structure was confirmed by synthesis from methylacetylacetone and *o*-aminoethylbenzene.[4]

Experimental

In carrying out multiple acid-extraction with 4000 cc. of aromatic bases in the 305–315° range, the procedure charted by Morton[5] was followed. By this method the bases were resolved into ten fractions of varying volume. Next, separate fractions were carried through one fractional distillation. The physical constants, including boiling point, density and refractivity, of each of the 95 distillation cuts were determined for comparative purposes.

In the present work only fractions IX 14, IX 15, X 12 and X 13, in the 314–319° range, were of interest, because lower boiling fractions had been investigated previously. From all of this material on picration in alcohol, crystalline salts, free of smears, separated. However, in further purification, the four fractions were combined and carried through counter current extraction using the equipment described in the preceding paper by Axe and Bailey.[6]

TABLE I

COUNTER CURRENT EXTRACTION DATA

Cut	Volume, cc.	$n^{25}D$	d^{25}_4
1	22	1.5841	1.0174
2	36	1.5878	1.0237
3	21	1.5888	1.0277
4	30	1.5920	1.0386

Isolation of 2,3,4-Trimethyl-8-ethylquinoline.—From Fractions 1, 2 and 3, this base[7] was separated as the picrate which after four recrystallizations from 60% acetic acid was obtained in lemon-colored, long rectangular microscopic plates, melting at 216° without decomposition. This salt is readily soluble in glacial acetic acid but only sparingly soluble in other common solvents.

Anal. Calcd. for $C_{20}H_{20}O_7N_4$: C, 56.07; H, 4.71; N, 13.08. Found: C, 56.00; H, 4.51; N, 13.11.

Free Base.—The base was liberated from the picrate and recrystallized from methyl alcohol in ill-defined microscopic plates. The following constants were determined: m. p. 52.5–53.0°; b. p. 320°; $n^{54}D$ 1.5798. Methyl alcohol has proved a selective solvent in recrystallization of 2,3,4-trimethyl kero quinolines alkylated at position 8.[3]

Anal. Calcd. for $C_{14}H_{17}N$: C, 84.42; H, 8.54; N, 7.03. Found: C, 84.23; H, 8.29; N, 7.19.

2,3,4-Trimethylquinoline-8-carboxylic Acid.—To a boiling solution of 1 g. of the base in 6 *N* sulfuric acid, a mixture of 2.5 g. of potassium dichromate, 3.8 g. of sulfuric acid and 4.2 g. of water is added slowly. The reaction is complete in twelve hours. The solution is cooled, made alkaline with ammonium hydroxide, acidified with acetic acid and extracted with chloroform. The acid crystallizes from alcohol in needles melting at 233.5–234.0°. A mixed

(1) Perrin and Bailey, THIS JOURNAL, **55**, 4136 (1933).

(2) Ernst Jantzen, "Das fraktionierte Destillieren und das fraktionierte Verteilen," Verlag Chemie, Berlin, 1932, pp. 117–137.

(3) Axe and Bailey, THIS JOURNAL, **60**, 3031 (1938).

(4) Combes, *Bull. soc. chim.*, [2] **49**, 91 (1888).

(5) Morton, "Laboratory Technique in Organic Chemistry," McGraw-Hill Book Company, Inc., New York, N. Y., 1938, p. 200.

(6) Axe and Bailey, THIS JOURNAL, **61**, 2609 (1939).

(7) None of the base was found in Fraction 4, but here 24 g. of the crude picrate of 2,3,4,8-tetramethylquinoline was encountered (Axe and Bailey, reference 3).

melting point determination with an authentic sample of 2,3,4-trimethylquinoline-8-carboxylic acid[3] showed no depression.

Anal. Calcd. for $C_{13}H_{13}O_2N$: C, 72.04; H, 6.11; N, 6.51. Found: C, 72.03; H, 5.87; N, 6.72.

Phthalone.—Molar amounts of phthalic anhydride and base are heated together for four hours at 190°. The melt is recrystallized from 70% acetic acid in yellow microscopic plates melting at 253°.

Anal. Calcd. for $C_{22}H_{19}O_2N$: C, 80.24; H, 5.77; N, 4.26. Found: C, 80.01; H, 5.48; N, 4.31.

Nitrate.—Concentrated nitric acid added to an alcohol or ether solution of the base precipitates the nitrate which recrystallizes from alcohol in tetragonal truncated pyramids, melting with decomposition at 159.5–160.0°.

Anal. Calcd. for $C_{14}H_{17}N\cdot HNO_3$: C, 64.10; H, 6.91; N, 10.69. Found: C, 64.33; H, 6.96; N, 10.51.

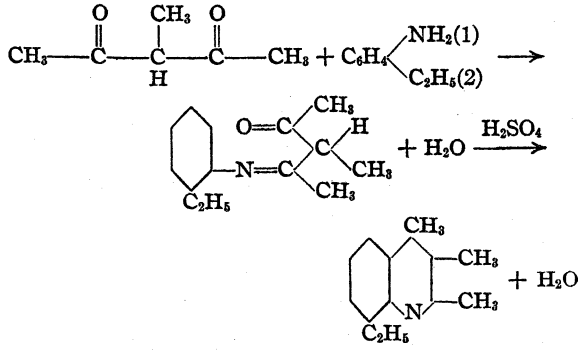
Acid Sulfate.—On addition of concentrated sulfuric acid to an alcohol or acetone solution of the free base, the acid sulfate precipitates and recrystallizes from water in microscopic fan-like needles melting without decomposition at 245–246°.

Anal. Calcd. for $C_{14}H_{17}N\cdot H_2SO_4$: SO_4, 32.32. Found: SO_4, 32.26.

Hydrochloride.—This salt is prepared by passing hydrogen chloride into an ether solution of the base. It crystallizes difficultly from acetone in fan-like microscopic needles, melting without decomposition at 203–204°.

Anal. Calcd. for $C_{14}H_{17}N\cdot HCl$: Cl, 15.05. Found: Cl, 15.25.

Synthesis of 2,3,4-Trimethyl-8-ethylquinoline.—As outlined below, methylacetylacetone[8] is condensed in two steps[9] with *o*-aminoethylbenzene.[10] A mixed melt of the purified synthetic base and the kero base gave no depression.



It is of interest to note that the spread in refractive index and in density obtained by multiple acid extraction compares favorably with that obtained by Axe[6] in counter-current extraction of a lower boiling base fraction. However, it may be emphasized that multiple acid extraction, unlike counter-current extraction, admits of a minimum of supervision and the processing of large quantities of bases in one operation.

Summary

This paper deals with multiple acid extraction in the isolation of a new $C_{14}H_{17}N$ kero base, 2,3,4-trimethyl-8-ethylquinoline. Its structure has been established by chromic acid oxidation to a $C_{12}H_{12}NCOOH$ acid, identical with the acid Axe and Bailey reported from a similar oxidation of 2,3,4,8-tetramethylquinoline. This structure was confirmed through synthesis of the base from methylacetylacetone and *o*-ethylaniline.

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(8) Auwers and Jacobsen, *Ann.*, **426**, 227 (1922).
(9) Von Braun, Gmelin and Petzold, *Ber.*, **57**, 387 (1924).
(10) Axe, THIS JOURNAL, **61**, 1017 (1939).

[CONTRIBUTION NO. 162 FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, THE UNIVERSITY OF TEXAS]

The Nitrogen Compounds in Petroleum Distillates. XVII. The Use of Multiple Acid Extraction in Isolation of 2,3,4-Trimethyl-8-*n*-propylquinoline

BY LESLIE M. SCHENCK AND J. R. BAILEY

Introduction

In multiple extraction of a pyrolysis distillate from transformer oil bases, furnished by the Union Oil Company of California, a new $C_{15}H_{19}N$ base, b. p. 330°, was isolated in the form of the picrate. To determine whether a *pyrolysis* or a *preformed* product was involved, a search was made for this particular base among the *aromatic* kero bases in the 320–330° range. Multiple extraction was also employed here, and the $C_{15}H_{19}N$ base was encountered in greatly increased yield, due probably to its presence in very small amount in high-boiling transformer oil bases.

The $C_{15}H_{19}N$ compound on chromic acid oxidation was converted to a $C_{12}H_{12}NCOOH$ acid which proved identical with the oxidation product of both 2,3,4,8-tetramethylquinoline[1] and 2,3,4-trimethyl-8-ethylquinoline.[2] In this way orientation of the base as a 2,3,4-trimethyl-8-propylquinoline was established. In determining the

(1) Axe and Bailey, THIS JOURNAL, **60**, 3028 (1938).
(2) See preceding paper by Glenn and Bailey, THIS JOURNAL, **61**, 2612 (1939).

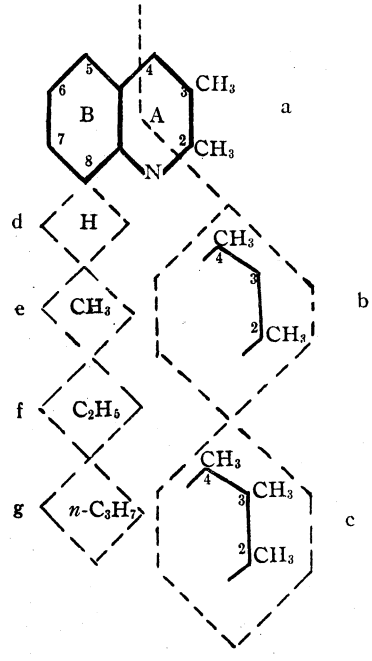
nature of the propyl group it was necessary to supplement degradation by synthesis. Accordingly, in anticipation of an *n*- and not an isopropyl, a Combes synthesis[3] with the intermediates methylacetylacetone and *o*-*n*-propylaniline was carried out. The product obtained proved identical with the kero base.

The subjoined diagram shows an interesting relationship between eleven of the twelve quinoline homologs so far isolated from California petroleum. The base not included is 2,8-dimethylquinoline. A futile search was made for 2,3,4-trimethylquinoline.[4,5] With this exception, the recent discovery of 2,3,4-trimethyl-8-ethylquinoline and 2,3,4-trimethyl-8-*n*-propylquinoline completes the series.

DIAGRAM I

TWELVE QUINOLINE HOMOLOGS OCCURRING IN STRAIGHT-RUN DISTILLATES OF CALIFORNIA PETROLEUM

A and B refer to the Py- and Bz-nuclei, respectively.
Aa, Ab and Ac show variation in methylation in the Py-nucleus.
Bd, Be, Bf and Bg show the substituent, if any, at position 8.
2,3,4-Trimethylquinoline (AcBd) has not been found.
2,8-Dimethylquinoline, a known kero base, is omitted.



Experimental

Our limited supply of pyrolyzed transformer oil bases (600 cc.) was carried through cumulative extraction,[6] followed by exhaustive fractional distillation. Fractions over a boiling range of 240–360° were obtained. Several multiple acid extractions[7] of each fraction yielded on picration small quantities of several known bases previously isolated in this Laboratory. After recombinations in the order of *n*-values of the extraction fractions in the 340° range, cumulative extraction and counter current extraction yielded in the first fraction (Table I) only 100 mg. of 2,3,4-trimethyl-8-*n*-propylquinoline.

TABLE I

BASE FRACTIONS FROM COUNTER CURRENT EXTRACTION

Fraction	$n^{25}D$	Vol., cc.
1	1.6143	4
2	1.6195	5
3	1.6154	8

Since the meager amount of the new base obtained above was insufficient for even a complete analysis, 13.5 liters of kero bases with $n^{20}D$ 1.5698 and b. p. 320–330° were cumulatively extracted and an aromatic fraction, 3.7 liters with $n^{20}D$ 1.5841, was obtained. Below are tabulated the results obtained in processing this material through multiple acid extraction.

TABLE II

FRACTIONAL ACID EXTRACTION

Fraction	B. p., °C.	Volume, cc.	$n^{20}D$
1	317	705	1.5760
2	319	715	1.5794
3	322	713	1.5829
4	323	711	1.5853
5	323	740	1.5890

Picrates were prepared in alcohol from 100 cc. of no. 5. Three 80-g. batches of crystalline salts were obtained. For purification, the picrates were converted to nitrates and acid sulfates with recrystallization at each stage, followed by reconversion to picrates. Since only 2,3,4-trimethyl-8-ethylquinoline[2] was encountered, the search for the 8-propyl homolog was shifted to Fraction 3, Table II. This material was further processed through a second multiple extraction, the tabulated results being given in Table III.

TABLE III

SECOND MULTIPLE EXTRACTION

Fraction	B. p., °C.	Volume	$n^{20}D$
1	325	62	1.5755
2	322	65	1.5749
3	315	60	1.5784
4	316	68	1.5798
5	326	62	1.5807
6	323	66	1.5807
7	317	63	1.5818
8	318	68	1.5805
9	320	61	1.5835
10	320	70	1.5810

2,3,4-Trimethyl-8-*n*-propylquinoline Nitrate.—Fractions 5 and 6 were combined and dissolved in five volumes of 1:10 acetone–ether mixture. On addition of concen-

(3) Combes, *Bull. soc. chim.*, [2] **49**, 91 (1888).
(4) Combes, *Compt. rend.*, **106**, 143 (1888).
(5) Braun, Gmelin and Petzold, *Ber.*, **57**, 387 (1924).
(6) Perrin and Bailey, THIS JOURNAL, **55**, 4136 (1933).
(7) *Cf.* Morton, "Laboratory Technique in Organic Chemistry," McGraw-Hill Book Co., Inc., New York, 1938, p. 200.

trated nitric acid in slight excess, 28 g. of nitrate separated from which the base was liberated and converted to the picrate. The picrate after digestion with benzene was changed through the liberated base to the nitrate, a *selective* salt for this base. The nitrate crystallizes from acetone–ether in long slender needles melting with decomposition at 160.1°.

Anal. Calcd. for $C_{15}H_{19}N \cdot HNO_3$; C, 65.18; H, 7.23. Found: C, 64.99; H, 7.32.

Base.—This odorless base crystallizes from methyl alcohol in fine radiating needles and has the following constants: m. p. 69–70°; b. p. 330°; $n^{70}D$ 1.5618; $n^{44}D$ 1.5731.

Anal. Calcd. for $C_{15}H_{19}N$: C, 84.45; H, 8.98; N, 6.57. Found: C, 84.62; H, 9.12; N, 6.41.

Picrate.—This salt which, with the exception of glacial acetic acid, is difficultly soluble in ordinary solvents, crystallizes from 50% acetic acid in long lemon colored hexagonal needles melting undecomposed at 211–211.5°.

Anal. Calcd. for $C_{21}H_{22}O_7N_4$: C, 57.07; H, 5.01; N, 12.66. Found: C, 56.85; H, 5.08; N, 12.45.

Acid Sulfate.—On the addition of the calculated amount of concentrated sulfuric acid to the base in acetone, this salt precipitates. It crystallizes from *t*-butyl alcohol in small irregular platelets melting without decomposition at 230.5–231°.

Anal. Calcd. for $C_{15}H_{19}N \cdot H_2SO_4$: SO_4, 30.86. Found: SO_4, 30.91.

Hydrochloride.—This hygroscopic salt separates on passing dry hydrogen chloride into an ether solution of the base. No solvent was found for its recrystallization. It forms small lustrous ill-defined crystals melting undecomposed at 221–222°.

Anal. Calcd. for $C_{15}H_{19}N \cdot HCl$: Cl, 14.23. Found: Cl, 14.59.

2,3,4-Trimethylquinoline-8-carboxylic Acid.—The base (0.44 g.) is dissolved in a sufficient amount of 12 *N* sulfuric acid to redissolve the initially precipitated acid sulfate and to the boiling solution 2.25 g. of potassium dichromate in 3 g. of concentrated sulfuric acid and 15 cc. of water is added dropwise over a period of forty minutes. The reaction mixture is made alkaline with ammonium hydroxide and then acidified with acetic acid. The chloroform extracted acid crystallizes from ethyl alcohol in long slender needles melting sharply and undecomposed at 234°; yield 0.090 g. A mixed melt of this product with an authentic sample of 2,3,4-trimethylquinoline-8-carboxylic acid[1] showed no depression.

Anal. Calcd. for $C_{13}H_{13}O_2N$: C, 72.53; H, 6.07; N 6.51. Found: C, 72.23; H, 5.89; N, 6.48.

Synthesis of the Base.—In preparation of the intermediate, *o*-*n*-propylaniline from *n*-propylbenzene,[8] the procedure of Axe and Bailey[1] was followed. Molecular amounts of this base and methylacetylacetone are condensed in two steps,[5] with a yield of about 90%. The usual melting point comparison of the kero and synthetic bases established their identity.

Summary

This paper deals with multiple acid extraction in the isolation of a new $C_{15}H_{19}N$ kero base, 2,3,4-trimethyl-8-*n*-propylquinoline. Its structure has been established by chromic acid oxidation to a $C_{12}H_{12}NCOOH$ acid identical with the acid obtained by Axe and Bailey through a similar oxidation of 2,3,4,8-tetramethylquinoline. This structure was confirmed through synthesis of the base from methylacetylacetone and *o*-*n*-propylaniline.

(8) *Cf.* Cohen, "Practical Organic Chemistry," The Macmillan Co., London, 1928, p. 155.

AUSTIN, TEXAS RECEIVED MAY 19, 1939

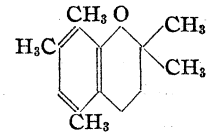
[JOINT CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA AND THE RESEARCH LABORATORIES OF MERCK & CO., INC.]

The Chemistry of Vitamin E. XVIII. Condensation of Phenols and Hydroquinones with Allylic Alcohols, Allylic Halides, and Conjugated Dienes[1]

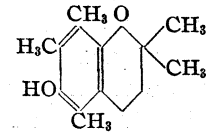
BY LEE IRVIN SMITH, HERBERT E. UNGNADE, J. R. STEVENS AND C. C. CHRISTMAN

In a previous paper[2] it was shown that isoprene could be condensed with 2,3,5-trimethylphenol to give the chroman I, and with trimethylhydroquinone to give the analogous chroman II. The same chroman, II, was obtained by condensing trimethylhydroquinone with γ,γ-dimethylallyl bromide.[3]

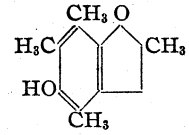
Several years ago Claisen[4] reported that allylic



I



II



III

carbinols as well as appropriate diols which gave dienes when catalytically dehydrated, would con-

(1) Paper XVII, THIS JOURNAL, **61**, 2424 (1939). Presented at the 98th meeting of The American Chemical Society, Boston, Mass., September, 1939.

(2) Paper VI on Vitamin E, *J. Org. Chem.*, **4**, 309 (1939).

(3) Paper V on Vitamin E, *ibid.*, **4**, 305 (1939).

(4) German Patent 394,797 (1924).

dense with phenols to give chromans. This type of condensation has been modified for the preparation of α-tocopherol from trimethylhydroquinone and phytol by Bergel, Copping, Jacob, Todd and Work[5] and by us also.

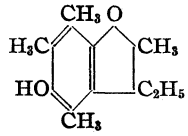
Claisen implied that when allylic carbinols and diols condensed with phenols, the first step in the reaction involved formation of the diene which then condensed with the phenol, and when it was found that phytadiene could be condensed with trimethylhydroquinone to produce α-tocopherol,[2] Claisen's mechanism appeared to offer a common explanation for the formation of tocopherols from hydroquinones and phytyl bromide, phytol or phytadiene. In harmony with this conception was the formation of the chromans I and II when either γ,γ-dimethylallyl bromide or isoprene was used.

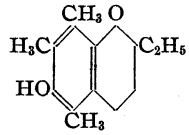
This mechanism, however, offers some difficulties when considered in the light of known facts regarding the addition of phenols to double bonds. In the first place, allyl alcohol, bromide and chloride all condense with 2,3,5-trimethylhydroquinone to give coumaran III and it is obvious that the diene-allene- cannot be an intermediate in this case unless an unusual mode of addition of the hydroquinone is postulated. Second, in some of the reactions between conjugated dienes and phenols, hydroquinones and their derivatives, allylic phenols or their HX addition products are formed and these may be cyclized in a separate operation, giving rise to the same cyclic compound whether the reaction is carried out in one step or in two.[2,4,6] With a substituted diene such as isoprene, therefore, it is again difficult to interpret the reaction as a direct addition of the phenol to the diene without assuming an unusual mode of addition, since the intermediate is known to contain a γ,γ-dimethylallyl group.

In order to reach a decision as to whether or not the diene is an intermediate, we have condensed ethylvinylcarbinol (IV) and pentadiene-1,3 (V) with trimethylhydroquinone under identical conditions. Since the diene to be expected

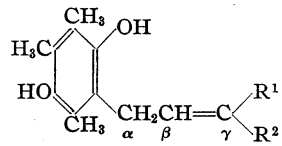
$CH_3CH_2CHOHCH{=}CH_2$ (IV)
$CH_3CH{=}{=}CHCH{=}CH_2$ (V)

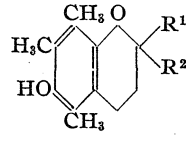
by dehydration of IV is V, these two substances should give identical products when condensed with the hydroquinone, providing that the diene is an intermediate. Actually, however, the two products are different. Although the structures of these products have not been proved definitely, tentatively we regard the products from ethylvinylcarbinol and pentadiene as the coumaran VI and the chroman VII, respectively.


VI

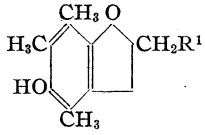

VII

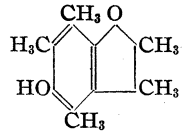
Thus, the diene cannot be an intermediate in the formation of VI, and it is therefore necessary to devise some other mechanism which will account for the known products obtained in these condensations when dienes, allylic alcohols and halides are used. While such a mechanism cannot at present be stated with certainty, the following is at least in harmony with present knowledge.


VIII


IX

(a) In the case of the halides and alcohols, the first step involves nuclear "allylation" without rearrangement. Thus a primary allylic alcohol (or halide), such as allyl alcohol or phytol (or their halides), would give the intermediate allylic phenol VIII. The second step, the cyclization, may be regarded as an addition of the phenolic hydroxyl group to the double bond, in accordance with Markownikoff's rule and hence, when R^1 and R^2 are alkyl groups, the product would be a chroman (IX); when R^1 and R^2 are hydrogen, the


X


XIII

product would be a coumaran (III); while when R^1 is alkyl and R^2 is hydrogen, the product might be either the chroman (IX) or the coumaran (X) although the former is produced in all cases which have so far been investigated.

(b) When the diene is used, the first intermediate is the 1,4-addition product of the acidic catalyst (proton), (whether the addition is really 1,4 or is 1,2 followed by rearrangement). This intermediate then "allylates" the phenol directly,

(5) Bergel, Copping, Jacob, Todd and Work, *J. Chem. Soc.*, 1382 (1938).

(6) Claisen, *Ann.*, **401**, 26 (1913); *ibid.*, **442**, 210 (1935); *Ber.*, **58**, 279 (1925).

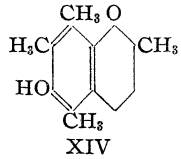
and the cyclization proceeds in a second step as outlined under (a).

Thus pentadiene-1,3 (V), isoprene, 2,3-dimethylbutadiene, phytadiene, and other similarly constituted dienes with terminal CH_2 groups (XI, R^1, R^2, R^3 = H or alkyl) all give the same products as would be obtained by using the halide or

$$R^1CH{=}C(R^2){-}C(R^3){=}CH_2 \quad (XI)$$
$$R^1CH_2C(R^2){=}C(R^3)CH_2X \quad (XII)$$

alcohol XII (R^1, R^2, R^3 = H or alkyl, X = OH or halogen). On the other hand, the secondary and probably also the tertiary allylic alcohols and halides give products different from those obtained from the related dienes and this regardless of whether the alcohols and halides are single substances or mixtures of allylic isomers, so long as one of the allylic isomers is not related to the diene as XII is to XI.

In accordance with this scheme, trimethylhydroquinone and methylvinylcarbinol give the coumaran XIII; crotyl bromide gives the chroman XIV, although the product is very difficult to purify and is probably contaminated with the isomeric coumaran (X, R = CH_3)[7] or with the coumaran XIII, derived from 3-chlorobutene-1, the allylic isomer of crotyl chloride.



XIV

In connection with this work, certain improvements in procedure have been discovered which make it possible to use the cheaper allylic chlorides instead of the bromides, and also an improved procedure for condensing the allylic alcohols with phenols and hydroquinones has been devised. The latter, applied to the condensation of trimethylhydroquinone and phytol, constitutes, we believe, the best procedure so far developed for the preparation of α-tocopherol. The yield is not only better, but the product is more readily purified than that obtained by any method so far known to us. These details are given in the experimental section.

Experimental Part

Condensations with Allylic Alcohols

2,4,6,7-Tetramethyl-5-hydroxycoumaran (II).—Trimethylhydroquinone (1 g.), allyl alcohol (1 cc.), zinc chloride (0.3 g.) and benzene (5 cc.) were sealed into a Carius tube and the mixture was heated for three and one-half hours at 200°. The product was dissolved in petroleum ether and the solution was washed with water. The organic layer was allowed to stand for a day, and then filtered. The filtrate was evaporated and the residue was steam distilled. The distillate deposited a solid (200 mg.) on cooling. After crystallization from petroleum ether, the substance melted at 127–128° and did not depress the melting point (129–130°) of a specimen made by another method.[3]

2,3,4,6,7-Pentamethyl-5-hydroxycoumaran (XIII).—Trimethylhydroquinone (1 g.), methylvinylcarbinol (1 cc.), zinc chloride (0.3 g.) and benzene (5 cc.) were heated in a Carius tube for three hours at 200°. The product was crystallized directly from petroleum ether; yield 70 mg. After repeated crystallization first from dilute ethanol and then from petroleum ether, the white substance melted at 119.5–120.5°.

Anal. Calcd. for $C_{13}H_{18}O_2$: C, 75.73; H, 8.74. Found: C, 75.82; H, 8.68.

The coumaran is very soluble in 95% ethanol, somewhat soluble in aqueous ethanol, and soluble in ether and petroleum ether. It gives a positive phenol test (Folin), reduces alcoholic silver nitrate slowly, shows a positive Furter reaction, and gives a greenish-yellow color with cold concd. sulfuric acid. This color turns to orange-yellow when ferric chloride is added.

2,4,6,7-Tetramethyl-3-ethyl-5-hydroxycoumaran (VI).—Trimethylhydroquinone (2 g.), ethylvinylcarbinol (2 cc.), zinc chloride (0.6 g.) and benzene (5 cc.) were heated in a Carius tube for one hour at 150°, one hour at 150–200°, followed by one hour at 200°. The product was steam distilled and the solid in the distillate was crystallized first from petroleum ether and then from dilute methanol. The white solid melted at 88–89°; a mixture of VI and VII (m. p. 113–114°) melted at 77.5–81°.

Anal. Calcd. for $C_{14}H_{20}O_2$: C, 76.36; H, 9.09. Found: C, 76.54; H, 9.50.

The substance gives a positive phenol test (Folin) and a red color with nitric acid in absolute ethanol (Furter). It reduces alcoholic silver nitrate and gives a bright greenish-yellow color with cold concd. sulfuric acid.

2,5,7,8-Tetramethyl-2-isohexyl-6-hydroxy-chroman (?).—Trimethylhydroquinone (2 g.), geraniol (3 cc.), zinc chloride (0.6 g.) and benzene (5 cc.) were heated in a Carius tube for one hour at 150° and one hour at 200°. The product was diluted with ether and washed with water. The ether solution was filtered and the filtrate evaporated. The unsaturated chroman was extracted from the residue with petroleum ether; after removal of the petroleum ether, the chroman was taken up in methanol and reduced in the presence of a platinum oxide catalyst. The catalyst was filtered off, the solvent was evaporated, and the residue was distilled under high vacuum. The main fraction boiled at 110–115° (thermometer in the liquid) under 10^{-6} mm. Although the product was not obtained analytically pure, it showed the properties of a 6-hydroxychroman, *viz.*, positive Furter reaction, positive Folin test, yellow color with cold concd. sulfuric acid, and it reduced alcoholic silver nitrate.

2,4,6-Trimethyl-7-allyl-5-hydroxycoumaran and 2,4,6-Trimethyl-5-hydroxycoumaran.—*m*-Xylohydroquinone (5

(7) Karrer and Escher, *Helv. Chim. Acta*, **22**, 264 (1939).

g.), allyl alcohol (5 cc.), zinc chloride (1.5 g.) and benzene (10 cc.) were heated in a Carius tube at 150° for one hour and then at 200° for one hour. The product was steam distilled, but only traces of oil appeared in the distillate. The residue was an oil soluble in hot carbon tetrachloride. It brominated rapidly. It was considered to be mostly the trimethylallylcoumaran, although it was not obtained analytically pure.

α-Tocopherol.—Trimethylhydroquinone (200 g.) and fused zinc chloride (100 g.) were dissolved in acetic acid (800 cc.). The solution was refluxed gently (oil-bath temperature 125–130°) under an atmosphere of nitrogen, and with stirring phytol (400 g.) was added slowly (one hour). After refluxing for two hours longer, the mixture was poured over ice (several kilograms) and extracted with ether several times. The ether layer was washed with dilute potassium hydroxide several times, then with water, and dried over sodium sulfate. The ether was removed in an atmosphere of nitrogen, and the residue refluxed for an hour with a solution of potassium hydroxide (40 g.) in methanol (2000 cc.). The solution was poured over ice and worked up as before; then the treatment with alcoholic potassium hydroxide was repeated twice more. The concentrate (470 g.) finally was degassed and then distilled in a molecular still. A small amount (5–10%) of low boiling material came over first, followed by the tocopherol at 145–150°. The distillate was dissolved in petroleum ether (5 volumes) and stirred, in the presence of nitrogen, with an equal weight of aluminum oxide. The suspension was filtered and the filtrate distilled as before. The distillate had a pale yellow color and its absorption spectrum was identical with that of natural α-tocopherol.

Condensation with Dienes

2-Ethyl-5,7,8-trimethyl-6-hydroxychroman (VII).—Trimethylhydroquinone (2.74 g.), pentadiene-1,3 (1.23 g.), zinc chloride (0.3 g.) and sulfuric acid (1 drop) were refluxed in acetic acid (30 cc.) for an hour. The product was poured into water and the solid removed and crystallized several times from petroleum ether. It melted at 115–116°; mixed with VI, m. p. 77.5–81°.

Anal. Calcd. for $C_{14}H_{20}O_2$: C, 76.36; H, 9.1. Found: C, 76.06; H 9.11.

The substance gives a yellow color with cold concd. sulfuric acid, a positive Folin test, a positive Furter reaction, and reduces alcoholic silver nitrate.

Other examples of condensations between dienes and phenols or hydroquinones already have been reported.[2]

Condensations with Allylic Halides, Particularly Chlorides

Allyl chloride reacts with trimethylhydroquinone under the same condition as does the bromide, and the product in both cases is the known 2,4,6,7-tetramethyl-5-hydroxycoumaran. When crotyl chloride is used, the product is a mixture which consists predominantly of 2,3,4,6,7-pentamethyl-5-hydroxycoumaran (XIII), the same substance as is obtained when methylvinylcarbinol is used in the condensation. The crotyl chloride used in this experiment was obtained from the isomeric mixture of crotyl and methylvinylcarbinyl chloride by fractionation; the formation of XIII can be explained by an isomerization of the halide, which is known to occur at elevated temperatures and in the presence of acidic catalysts, particularly hydrochloric acid.

$$CH_3CH{=}CHCH_2Cl \rightleftharpoons CH_3CHClCH{=}CH_2$$

Crotyl chloride also will react with trimethylhydroquinone at atmospheric pressure, using benzene as a solvent, zinc chloride as the catalyst, and an inert atmosphere. The reaction with the chloride occurs as readily as it does with the bromide.

2,4,6,7-Tetramethyl-5-hydroxycoumaran (III).—Trimethylhydroquinone (1 g.), and allyl chloride (5 cc.) were heated in a tube at 150° for three hours. The product, isolated and purified as described above, weighed 600 mg. and had a melting point and mixed melting point of 130.6–131°.

2,3,4,6,7-Pentamethyl-5-hydroxycoumaran (XIII).—Trimethylhydroquinone (1 g.), and pure crotyl chloride (4 cc.) were heated in a tube at 150° for four hours. The product (400 mg.) was dissolved out with ether and crystallized from petroleum ether. After several crystallizations, the product melted at 117–117.5° and showed no depression in melting point when mixed with a specimen of XIII prepared from methylvinylcarbinol. It gave an acetate, melting point 70.5–71°. Using the procedure of Karrer, and substituting pure crotyl chloride for crotyl bromide, the product was the same. A repetition of Karrer's experiment,[3] using the isomeric mixture of crotyl bromide and methylvinylcarbinyl bromide, again gave predominantly this same substance, although the product was a mixture.

2,4,6-Trimethyl-7-allyl-5-hydroxycoumaran. — *m*-Xylohydroquinone (5 g.) and allyl bromide (10 cc.) were heated in a tube at 150° for three hours. The product was dissolved out with ether and steam distilled. Only traces of it came over into the distillate. The residue, when distilled under 10 mm. pressure from a sausage flask, gave a distillate consisting of a pale yellow, viscous oil, the properties of which corresponded with those of the product obtained from the hydroquinone and allyl alcohol (see above).

Summary

1. Allylic alcohols can be condensed directly with phenols and hydroquinones, thus avoiding the necessity of converting the alcohols into halides.

2. Although dienes also can be condensed with phenols and hydroquinones, the dienes are not always intermediates in the condensations when allylic alcohols and halides are used, for the products are not always the same.

3. A mechanism is proposed for these condensations, which, though not proved, correlates the facts well.

4. Allylic chlorides condense with phenols and hydroquinones as well as the bromides do.

5. An improved procedure is given for the preparation of α-tocopherol from trimethylhydroquinone and phytol.

MINNEAPOLIS, MINNESOTA, AND
RAHWAY, NEW JERSEY RECEIVED JULY 12, 1939

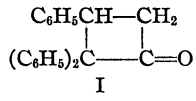
(8) Karrer, *Helv. Chim. Acta*, **21**, 946 (1938).

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

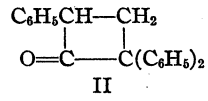
The Reaction between Diphenylketene and Phenylacetylene[1]

BY LEE IRVIN SMITH AND HARVEY H. HOEHN[2]

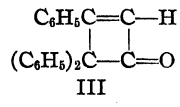
In a previous paper[3] it has been shown that the addition product obtained from diphenylketene and cyclopentadiene is a cyclobutanone derivative. Staudinger and Suter[4] added diphenylketene to styrene, and likewise regarded the product as a cyclobutanone derivative, I or II. At first these authors favored structure II with the more hindered carbonyl group, because the substance failed to form a phenylhydrazone or a benzal derivative but later,[5] when it was discovered that the product, on alkaline cleavage, gave α,α,β-triphenylbutyric acid, formula II was abandoned in favor of I. It has been shown recently[6] that formula I is really correct, although the cleavage product is actually β,γ,γ-triphenylbutyric acid, which Staudinger and Rheiner mistook for the α,α,β-acid.



I



II



III

The facile formation of cyclobutanone derivatives is often observed in reactions between ketenes and unsaturated compounds, and in connection with earlier work[3] Agre[7] had sought to obtain further evidence that styrene and diphenylketene reacted to form a cyclobutanone derivative. His plan of attack involved addition of diphenylketene to phenylacetylene; assuming that styrene and phenylacetylene added to the ketene in the same way, then reduction of the adduct III from the acetylenic hydrocarbon should give the adduct II of the ethylenic hydrocarbon.

Contrary to the statement of Staudinger,[8] phenylacetylene and diphenylketene can be made to react with the production in excellent yield of a crystalline compound melting at 143–144°. Beyond showing that this product had the composition required by formula III and that its chemical properties were quite unusual for a compound of this structure, Agre did no further work upon it.

In the present communication, it is shown that this adduct is not a cyclobutanone derivative at all, but is 3,4-diphenyl-α-naphthol, IV, an isomer of III. Analysis and molecular weight determinations showed the composition to be $C_{22}H_{16}O$. The substance was readily soluble in (methyl) alcoholic potassium hydroxide; it gave a positive phenol reaction (Folin) and in the Grignard machine showed one active hydrogen atom and no addition of the reagent. It formed an acetate (IX) and a methyl ether (X), and it coupled with diazotized sulfanilic acid to give the azo compound XIII.

The adduct (IV) formed a monobromo derivative (V) which was still a phenol for it could be converted into an acetate (XI) or a methyl ether (XII). This bromophenol (V) was readily soluble in aqueous alkali, hence was more strongly acidic than the parent compound IV.

The adduct IV was extremely sensitive to oxidizing agents, even turning brown in air in a few days. It decolorized permanganate instantly, and depending upon the conditions and upon the oxidizing agent used, a variety of products was obtained. Using permanganate or chromic acid under mild conditions, the oxidation led to a product, insoluble in carbonate solution, whose structure has not yet been determined. Using potassium dichromate under vigorous conditions, the products were *o*-benzoylbenzoic and benzoic acids. The formation of these oxidation products eliminated the possibility that the adduct IV was 1,4-diphenyl-β-naphthol, since the latter compound would have produced *o*-dibenzoylbenzene on oxidation.

Oxidation of the bromo derivative V by chromic acid in acetic acid or oxidation of the phenol IV by lead tetraacetate produced a bright red solid (VI) having the properties of a 1,2-naphthoquinone. Reduction of VI by zinc and acetic acid or by sodium hydrosulfite gave colorless solutions, which in the air rapidly turned red and de-

(1) Presented at the 98th meeting of the American Chemical Society, Boston, Mass., September, 1939.

(2) Abstracted from a thesis by Harvey H. Hoehn, submitted to the Graduate Faculty of the University of Minnesota, in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

(3) Smith, Agre, Leekley and Prichard, THIS JOURNAL, **61**, 7 (1939).

(4) Staudinger and Suter, *Ber.*, **53**, 1092 (1920).

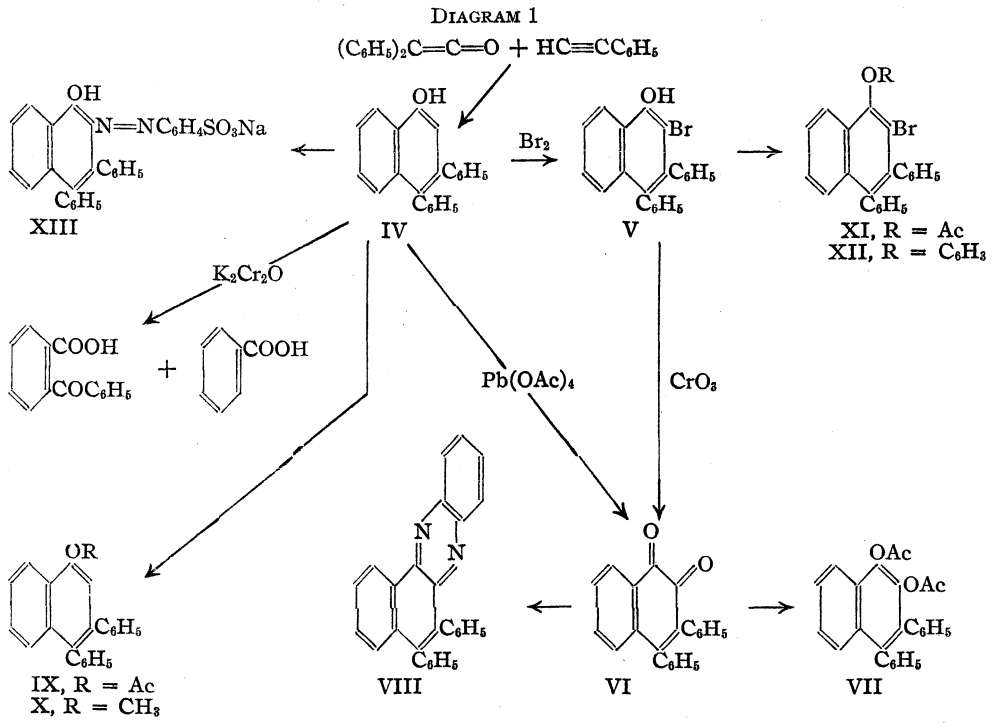
(5) Staudinger and Rheiner, *Helv. Chim. Acta*, **7**, 8 (1924).

(6) Bergmann and Bergmann, *J. Chem. Soc.*, 727 (1938).

(7) C. L. Agre, Ph.D. Thesis, University of Minnesota, 1937, p. 77.

(8) Staudinger, *Ann.*, **356**, 94 (1907).

DIAGRAM 1

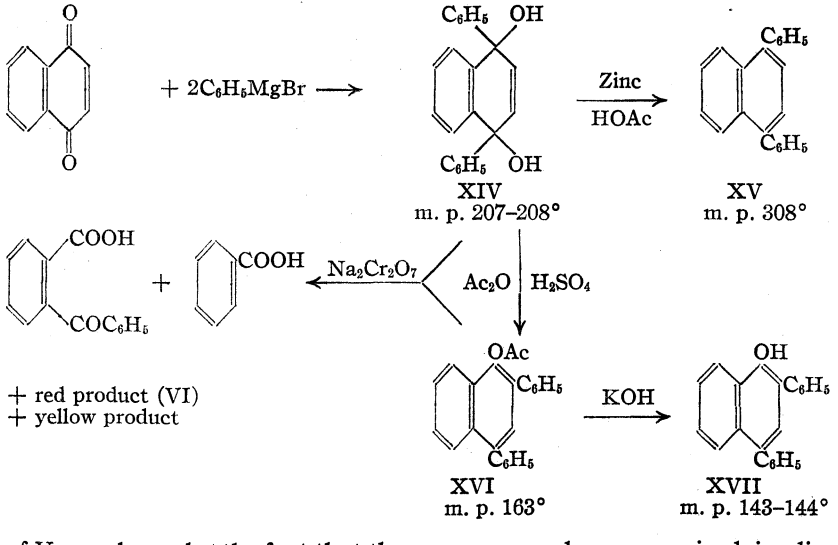


posited VI when the reducing agent was removed. Reductive acetylation of VI gave a colorless diacetate, VII. Finally, the *o*-quinone structure of VI was definitely settled by conversion of VI to a phenazine, VIII. That the azo group of XIII occupies the same position as the bromine atom of V was shown by the fact that the azo compound on reductive cleavage followed by oxidation of the intermediate amine (not isolated) also gave the red quinone VI.

These transformations, which are shown in diagram 1, are all explained adequately by structure IV, 3,4-diphenyl-α-naphthol, for the product of the reaction between diphenylketene and phenylacetylene.

Although the reactions shown in diagram 1 definitely prove that the adduct IV is a diphenyl naphthol with the two phenyl groups located in positions 3 and 4, these results do not definitely locate the hydroxyl group, for the reactions shown would be just as consistent with the β- as with the α-naphthol structure. In order to locate the hydroxyl group, an independent synthesis of IV was undertaken. Some years ago Franssen[9] studied the addition of phenylmagnesium bromide to 1,4-napthoquinone; his results, using the structures which he assigned, are summarized in diagram 2.

DIAGRAM 2

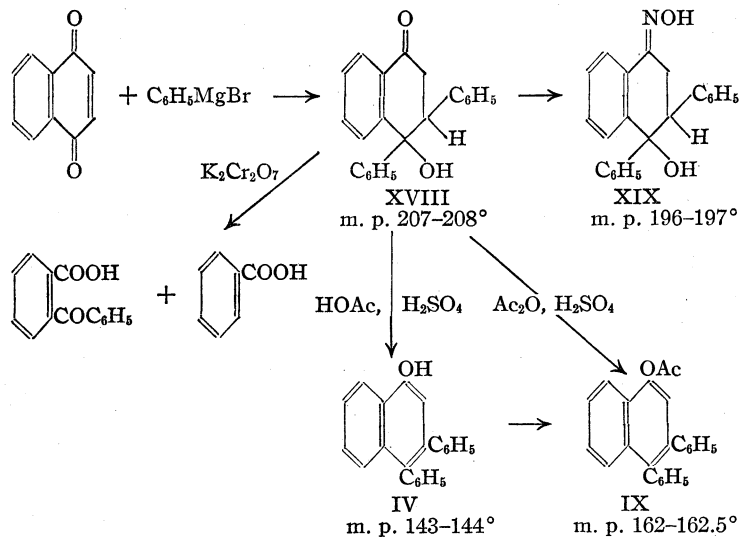


Franssen's work was of interest in connection with the present work, since the melting points of two of his products, XVI and XVII, coincided with

(9) Franssen, *Bull. soc. chim.*, [4] **37**, 902 (1925).

two obtained in this work, those of IX and IV, respectively. That is, Franssen reported a phenol and its acetate which had the same melting points as the phenol IV and its acetate obtained by an entirely different series of reactions. It followed almost certainly that Franssen's compounds and ours were identical, but this could not be the case if the structures assigned by Franssen were correct. Franssen's evidence for structure XIV rested primarily upon the conversion of XIV into 1,4-diphenylnaphthalene, XV. But this compound since has been synthesized by Weiss, Abeles and Knapp[10] and by Allen and Gilman,[11] who report that it melts at 135–137° and 134–136°, respectively, and not at 308° as does Franssen's compound XV. Another serious objection to Franssen's formulations is that the production of *o*-benzoylbenzoic and benzoic acids by oxidation of XIV and XVI, and the conversion of XIV into XVI, must both involve rearrangements. Crawford[12] showed that phenylmagnesium bromide added to 2,3-dimethyl-1,4-naphthoquinone to give a variety of products, the relative amounts of which depended largely upon the relative amounts of the quinone and Grignard reagent. She showed that when two moles of phenylmagnesium bromide was added to the quinone, the product formed in largest amount was the one resulting from a 1,4-addition to the conjugated system followed by a 1,2-addition to the other carbonyl group. Franssen's products could be reconciled with ours if this same type of reaction were assumed in the case of 1,4-naphthoquinone. To test this point, Franssen's work was repeated. The products which we obtained and their relationships are shown in diagram 3.

DIAGRAM 3



When 1,4-naphthoquinone was added to a large excess (5 moles) of phenylmagnesium bromide the addition product XVIII, identical with Franssen's XIV, resulted. That this substance possessed a carbonyl group was shown by the formation of an oxime (XIX). When XVIII was subjected to the action of acetic and sulfuric acids, or to the action of acetic anhydride, it was transformed into the naphthol IV and the acetate IX, respectively. These transformations can be understood readily on the basis of structure XVIII for the primary product, for the tertiary hydroxyl group in position 4 would be expected to be eliminated readily under the conditions used, giving the naphthol IV directly, or its acetate IX. Structure XVIII also serves to explain the observed oxidation products; Franssen's XIV should give, not the observed oxidation products, but *o*-dibenzoylbenzene, none of which was obtained by Franssen nor by us. It follows, therefore, that Franssen's formulation of the reaction, and the structure of his products, are incorrect. His XIV must be replaced by XVIII; and his XVI and XVII must be replaced by IX and IV, respectively. What Franssen's hydrocarbon XV can be, it is not possible as yet to say. We have observed similar high melting products when certain of our products are oxidized, but we have not, as yet, been able to establish the structure of any of these. Certainly, however, Franssen's XV is not 1,4-diphenylnaphthalene.

When the results of these two syntheses, and the degradation of the products, are considered and assembled, the proof appears quite definite that diphenylketene reacts with phenylacetylene to produce 3,4-diphenyl-α-naphthol, IV. The reaction between this as well as other ketenes and acetylenic compounds appears to be quite general, and the hydrogen atom in the acetylene is not apparently necessary, for diphenylketene and diphenylacetylene also give a crystalline addition product. Consideration of the limits of

(10) Weiss, Abeles and Knapp, *Monatsh.*, **61**, 162 (1932).
(11) Allen and Gilman, THIS JOURNAL, **58**, 937 (1936).
(12) Crawford, *ibid.*, **57**, 2000 (1935).

this reaction and also of the mechanism will, however, be reserved for later communications.

Experimental Part[13]

Addition of Diphenylketene to Phenylacetylene: 3,4-Diphenyl-α-naphthol (IV).—Diphenylketene (1.94 g., 0.01 mole) and phenylacetylene (1.02 g., 0.01 mole) were mixed and allowed to stand at room temperature. After about ten hours, the mixture became very viscous and shortly thereafter a yellow solid separated. After standing for three days, the solid was washed with a little petroleum ether (b. p. 28–38°) and then was recrystallized from petroleum ether (b. p. 90–100°). The white needles weighed 2.4 g. and melted at 139–141°. After crystallization twice more, the product melted at 143–144°.

Anal. Calcd. for $C_{22}H_{16}O$: C, 89.19; H, 5.71; mol. wt., 296. Found: C, 89.23; H, 5.80; mol. wt., 296. Calcd. for structure IV: active H, 1.0; carbonyl, 0. Found: active H, 0.97; carbonyl, 0.

The magnesium compound resulting from this determination, on acidification, gave IV, m. p. 143–144°.

The naphthol IV also was produced when a solvent was used, but the reaction was much slower and the yield much less. This undoubtedly was the cause of Staudinger's report that no reaction occurred, for he operated with 0.1 molar solutions. Diphenylketene (17.4 g.), phenylacetylene (9.3 g.) and petroleum ether (18 g., b. p. 57–70°) were allowed to stand for one week in an atmosphere of carbon dioxide. The solid was removed and crystallized from a mixture of petroleum ether and benzene. It weighed 13 g. (50%) and melted at 143–144°.

Apparently the naphthol IV exists in two forms, one melting at 143–144°, and the other at 154°. In the early experiment it was observed frequently that the substance, after melting at 143–144°, would crystallize as the temperature was raised slowly, and then remelt at 154°. In the later stages of the work, however, this phenomenon, which was observed independently by C. L. Agre and one of us (H. H. H.) could not be duplicated.

3,4-Diphenyl-α-acetoxynaphthalene (IX).—The naphthol (5 g.) was dissolved in acetic anhydride (30 cc.) containing a drop of sulfuric acid and the solution was heated to the boiling point. The product, isolated by pouring the reaction mixture over ice, formed white cubes when recrystallized from ethanol. The yield was 5.5 g., and the melting point was 162–162.5°.

Anal. Calcd. for $C_{24}H_{18}O_2$: C, 85.17; H, 5.37. Found: C, 84.86; H, 5.22.

3,4-Diphenyl-α-methoxynaphthalene (X).—The naphthol (500 mg.) and dimethyl sulfate (1.5 cc.) were dissolved in methanol (5 cc.). The solution was heated and stirred, and to it was slowly added a solution of potassium hydroxide (1 g.) in methanol (10 cc.). After refluxing for thirty minutes, water (75 cc.) was added. The precipitate was washed with Claisen's alkali (10 cc.) and then with water. The substance (400 mg.) was then recrystallized, first from alcohol–acetone and then from alcohol. It formed white cubes melting at 203–203.5°.

Anal. Calcd. for $C_{23}H_{18}O$: C, 88.99; H, 5.85. Found: C, 88.74; H, 5.85.

(13) Microanalyses by J. W. Opie, C. O. Guss and H. H. Hoehn.

3,4-Diphenyl-1-methoxy-2-nitronaphthalene.—Although the naphthol IV could not be nitrated (see below), the methyl ether X (200 mg.) in acetic acid (2 cc.) was nitrated readily by addition of nitric acid (0.08 cc.). The mixture was heated to the boiling point and then cooled. The nitro compound (70 mg.) which separated was removed and crystallized from ethanol. It formed yellow needles which melted at 202°.

Anal. Calcd. for $C_{23}H_{17}O_3N$: C, 77.72; H, 4.83. Found: C, 77.99; H, 4.78.

Oxidation of the Naphthol IV. (a) By Lead Tetraacetate.—This is the best preparative method for **3,4-diphenyl-1,2-naphthoquinone, VI.** The naphthol IV (296 mg.) and lead tetraacetate (800 mg.) were refluxed in acetic acid (10 cc.) for five hours. The solution was poured onto ice (100 g.) and most of the acetic acid was neutralized by adding saturated aqueous sodium carbonate. The mixture, containing an orange red precipitate, was extracted with chloroform. The chloroform was removed and the red residue was taken up in hot ethanol and filtered while hot. On cooling, the filtrate deposited orange red needles (130 mg.) which softened at 245° and melted at 247–248°. The melting point was not depressed by addition of a specimen of VI made from the bromonaphthol V; this latter specimen was carefully purified (m. p. 249–250° and was analyzed (see below).

(b) **Oxidation by Nitric Acid.**—The naphthol IV could not be nitrated; all attempts to do so led only to oxidation, the chief product being the red quinone VI although the yield was poor. The naphthol (1 g.) was dropped into a well-stirred mixture of nitric acid (1 cc.), sulfuric acid (2 cc.) and chloroform (10 cc.). After stirring the mixture for thirty minutes at room temperature, water was added, the chloroform layer was removed and the aqueous layer extracted with chloroform. The combined chloroform solutions were washed with bicarbonate and then with water. Removal of the chloroform left a red residue, which when worked up as described above gave 70 mg. of the quinone VI, m. p. 246–247°. The only other products were uncrystallizable oils.

(c) **Oxidation by Dichromate.**—The naphthol IV (1 g.) and potassium dichromate (3 g.) were refluxed in acetic acid (30 cc.) for eight hours. The green solution was poured onto ice (100 g.) and some of the excess acetic acid was neutralized with saturated carbonate. The mixture was extracted with benzene; the benzene was then extracted with sodium hydroxide (10%) and the alkaline extract was acidified and steam distilled. From the distillate benzoic acid (100 mg.), m. p. and mixed m. p. 121°, was isolated. From the residue in the distillation flask *o*-benzoylbenzoic acid (440 mg.) was isolated. This substance was identified as the hydrate after crystallization from water; m. p. and mixed m. p. 95°. From the residual benzene solution there was isolated a small amount (80 mg.) of a yellow solid melting at 280–286° which was not investigated further.

Reduction of the Quinone VI.—The quinone (140 mg.) in acetic acid (10 cc.) and water (1 cc.) was heated with zinc (20 mesh) for an hour. The red color of the quinone disappeared within ten minutes. The mixture was diluted with water, decanted from the zinc, and extracted with ether. The ether solution rapidly turned red, and re-

moval of the ether left red crystals of VI. Practically all of the starting material was recovered. Essentially the same results were obtained when VI was reduced by sodium hydrosulfite.

Reductive Acetylation: 1,2-Diacetoxy-3,4-diphenylnaphthalene (VII).—The quinone (50 mg.) and fused sodium acetate (50 mg.) were dissolved in acetic anhydride (1 cc.), a little zinc dust was added, and the mixture was heated to boiling. The red color faded at once. The zinc was filtered off and the filtrate was diluted with water. The solid (64 mg.) was removed and crystallized from dilute ethanol. It formed white needles which melted at 166–167°.

Anal. Calcd. for $C_{26}H_{20}O_4$: C, 78.76; H, 5.09. Found: C, 78.48; H, 5.15.

Phenazine (VIII).—The quinone VI (95 mg.) and *o*-phenylenediamine (60 mg.) were heated in alcohol (20 cc.) for thirty minutes on the steam-bath. After about five minutes, yellow crystals of the phenazine began to separate. The solid (110 mg.) was removed from the cooled mixture and recrystallized from alcohol–benzene. It formed yellow needles which melted at 274–275°.

Anal. Calcd. for $C_{28}H_{18}N_2$: C, 87.93; H, 4.75. Found: C, 87.92; H, 4.71.

Coupling Reaction of IV. The Azo Compound XIII.—Sulfanilic acid dihydrate (1.6 g.) was dissolved in sodium carbonate solution (15 cc., 2.5%) and sodium nitrite (0.56 g.) was added. The solution was poured into a mixture of ice (8 g.) and hydrochloric acid (1.5 cc.). To this suspension of the diazonium compound was added a solution of the naphthol IV (2.2 g.) and sodium acetate (0.6 g.) in acetic acid (30 cc.). The mixture was allowed to stand at room temperature for four hours, with occasional shaking. The red solid (2.8 g.) was filtered off and dried. It was not analyzed.

Reductive Cleavage of the Azo Compound: The Quinone VI.—The red compound XIII (1 g.), sodium hydrosulfite (0.4 g.) and sodium hydroxide (0.2 g.) were dissolved in water (20 cc.) and the solution was boiled. More hydrosulfite (0.5 g.) and alkali (0.5 g.) were added. The red color disappeared, and a white solid (the amino naphthol) separated when the solution was cooled. This solid was filtered off as rapidly as possible; the filtrate turned black within a few minutes. The white solid was boiled with aqueous ferric chloride and the mixture was extracted with chloroform. Evaporation of the chloroform left a red residue which, recrystallized from ethanol–ether, melted at 246–247° and showed no depression in melting point when mixed with a specimen of VI made by oxidation of IV or V.

Attempts to purify the intermediate **2-amino-3,4-diphenyl-α-naphthol** by crystallization failed, for solutions of it oxidized in the air very rapidly and turned black.

2-Bromo-3,4-diphenyl-α-naphthol (V).—The naphthol IV (2 g.) in ether (10 cc.) was stirred and brominated by the slow addition of bromine (0.35 cc.) in ether (10 cc.). Stirring was continued for thirty minutes after all of the bromine was added. Water was added, the ether layer was separated, washed with bisulfite and the solvent was evaporated. The residue, when crystallized twice from methanol, formed white needles (2.05 g.) melting at 157–158°.

Anal. Calcd. for $C_{22}H_{15}OBr$: C, 70.39; H, 4.03. Found: C, 70.6; H, 3.82.

2-Bromo-3,4-diphenyl-α-acetoxynaphthalene (XI).—The bromonaphthol V (100 mg.) was acetylated by heating it in acetic anhydride (2 cc.) containing a drop of sulfuric acid. The product (120 mg.), isolated in the usual way and crystallized from ethanol, formed white needles melting at 199–200°.

Anal. Calcd. for $C_{24}H_{17}O_2Br$: C, 69.06; H, 4.11. Found: C, 69.03; H, 4.28.

2-Bromo-3,4-diphenyl-1-methoxynaphthalene (XII).—The bromonaphthol V (750 mg.) was dissolved in sodium methoxide solution (prepared from 60 mg. of sodium and 20 cc. of methanol), and dimethyl sulfate (3 cc.) was added slowly. After stirring the mixture for an hour, sodium hydroxide (4 cc., 40%) was added and the mixture was poured into water and extracted with ether. The ether was evaporated and the residue (500 mg.) was crystallized twice from alcohol. The product separated in fine white needles melting at 209–210°.

Anal. Calcd. for $C_{23}H_{17}OBr$: C, 70.95; H, 4.41. Found: C, 70.52; H, 4.45.

Oxidation of the Bromonaphthol: 3,4-Diphenyl-1,2-naphthoquinone (VI).—A solution of the bromonaphthol V (0.5 g.) in acetic acid (10 cc.) was heated on the steam-bath, and to it was added chromic acid (150 mg.). After heating for two hours, the mixture was poured into water. The product was removed and crystallized twice from ethanol. It weighed 150 mg. The m. p. was 249–250°; when mixed with a specimen of VI prepared from the naphthol IV, the substance melted at 247–248°.

Anal. Calcd. for $C_{22}H_{14}O_2$: C, 85.13; H, 4.54. Found: C, 85.24; H, 4.84.

4-Hydroxy-3,4-diphenyl-α-tetralone (XVIII).—1,4-Naphthoquinone (20 g.) suspended in ether (500 cc.) was added slowly (two hours) to a solution of phenylmagnesium bromide prepared in the usual way from magnesium (16 g.), bromobenzene (99 g.) and ether (500 cc.). The color became first wine red and then orange. After adding all of the quinone, the mixture was stirred and refluxed for five hours. The reaction mixture, which contained a brown, sticky precipitate, was poured into ice and hydrochloric acid (150 cc.). The ether layer was separated, and the tetralone suspended in it was filtered off. The aqueous layer was thoroughly extracted with ether, the ether solutions were combined and the solvent was distilled off. The tetralone, separated during removal of the ether, was removed from time to time. The solids were combined and digested with chloroform. Most of the sparingly soluble red impurity was removed by filtering the hot solution. The filtrate was decolorized with charcoal, and the chloroform solution was concentrated and alcohol was added. The cooled solution deposited white plates of the tetralone XVIII (8.1 g.) melting at 207°. This is the same substance reported by Franssen as having structure XIV.

Anal. Calcd. for $C_{22}H_{18}O_2$: C, 84.04; H, 5.78. Found: C, 83.93; H, 5.87.

Oxime XIX.—The tetralone XVIII (400 mg.), hydroxylamine hydrochloride (1 g.), sodium hydroxide (2 cc., 20%), water (6 cc.) and ethanol (20 cc.) were refluxed

for fifteen minutes, giving a clear solution. Most of the alcohol was distilled off and the residual solution, on cooling, deposited white plates of the oxime XIX (500 mg.) melting at 195–196°. Recrystallization from alcohol gave a product melting at 196–197°.

Anal. Calcd. for $C_{22}H_{19}O_2N$: C, 80.20; H, 5.82. Found: C, 80.09; H, 6.21.

Oxidation.—The tetralone XVIII (1 g.) and potassium dichromate (3 g.) were refluxed in acetic acid (30 cc.) for six hours. The green solution was poured into water (100 cc.) and most of the acetic acid was neutralized with sodium carbonate. Some sticky, orange material rose to the top of the solution; this was removed with a spatula. The aqueous solution was extracted with benzene, and the benzene solution then extracted with sodium hydroxide solution (10%). The alkaline extraction was acidified and steam distilled. From the distillate, benzoic acid (200 mg.), m. p. and mixed m. p. 121°, was isolated. The residue in the distilling flask was extracted with ether; from the ether extract, *o*-benzoylbenzoic acid (hydrate) (520 mg.), m. p. and mixed m. p. 88–90°, was isolated. From the sticky orange solid originally found in the oxidation, a very small amount of the red quinone VI, m. p. and mixed m. p. 245°, was isolated by repeated crystallization from alcohol.

Naphthol IV.—The tetralone XVIII (500 mg.), acetic acid (15 cc.) and sulfuric acid (5 drops) were boiled for thirty minutes and then poured into water. The pinkish solid was removed, dissolved in alcohol and the solution decolorized with charcoal. The alcohol was boiled off and replaced by petroleum ether (b. p. 90–100°). On cooling white needles of 3,4-diphenyl-α-naphthol IV (430 mg.) were deposited. These had a melting point and mixed melting point of 142–143° and showed the phenomenon of solidification after melting with remelting at 153–154° (see above under properties of IV). This is the same substance reported by Franssen as having structure XVII.

Acetate IX.—The tetralone XVIII (1 g.), acetic anhydride (7.5 cc.) and sulfuric acid (1 drop) were boiled for fifteen minutes. The cooled solution was poured onto ice and the pinkish solid (m. p. 160–162°) was removed. The solid was dissolved in chloroform and the solution was decolorized with charcoal. Most of the chloroform was removed, alcohol was added and the solution was cooled. White cubes of the acetate IX (950 mg.), m. p. and mixed m. p. 162–162.5°, were obtained. This is the same substance reported by Franssen as having structure XVI.

Summary

1. Diphenylketene and phenylacetylene react by addition to form, in good yield, 3,4-diphenyl-α-naphthol, IV.

2. The structure of the naphthol was proved by degradation and by an independent synthesis from 1,4-naphthoquinone and phenylmagnesium bromide.

3. The work of Franssen on the addition of phenylmagnesium bromide to 1,4-naphthoquinone has been repeated and his structures for the products have been shown to be incorrect. These have been supplanted by the correct structures.

4. The reaction between diphenylketene and acetylenes appears to be quite general, although no solvent, or quite concentrated solutions, must be used in order to bring about a reaction. As yet the mechanism of this reaction is not known, but observations to be reported later indicate that an acetylenic hydrogen atom is not involved because diphenylacetylene also reacts with the ketene.

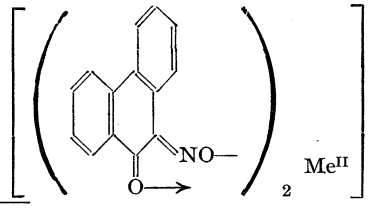
MINNEAPOLIS, MINNESOTA RECEIVED JULY 12, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF WASHINGTON]

Ortho-quinone Monoxime Inner Complexes

BY HELMUT M. HAENDLER WITH GEORGE MCP. SMITH

Recently, Ciusa,[1] in work on phenanthrenequinone, observed that the monoxime behaved as do α-isonitroso ketones in reacting even in extremely dilute solutions with salts of cobalt, nickel, and iron. The divalent cobalt and nickel inner complexes obtained were of regular composition, having the structure



In general, cobalt, nickel, and copper form inner complexes more readily than do other metals. To determine, however, the extent to which other inner complexes of this group would form, various metals were tested with phenanthrenequinone monoxime and other oximes possessing the chelating group C, C–NOH, O.[2]

Inner complexes of cadmium, copper, lead, manganese, and uranyl with phenanthrenequinone monoxime were prepared, and complexes of copper, lead, manganese, nickel, and uranyl with chrysenequinone monoxime also were prepared. In all cases except that of the uranyl compounds

(1) Ciusa, *Gazz. chim. ital.*, **66**, 591 (1936).

(2) Haendler and Geyer, THIS JOURNAL, **60**, 2813 (1938).

TABLE I

INNER COMPLEXES OF PHENANTHRENEQUINONE MONOXIME (PqxH) AND CHRYSENEQUINONE MONOXIME (CxH)

Inorg. salt	Solvent for inorg. salt	Color	M. & P. No.	Formula	% yield	Metal analyses, % Calcd.	Found
$Cd(OAc)_2$	Alcohol	Brownish orange	5-D-12	$[Cd \rightleftarrows (Pqx)_2]$[a]	80	Cd, 20.2	20.1
$Cu(OAc)_2$	Water	Chocolate-brown	7-E-11	$[Cu \rightleftarrows (Pqx)_2]$	80	Cu, 12.5	12.5
$Pb(OAc)_2$	Water	Light brown	7-C-12	$[Pb \rightleftarrows (Pqx)_2]$	85	Pb, 31.8	31.5
$Mn(OAc)_2$	Water	Yellowish brown	15-J-8	$[Mn \rightleftarrows (Pqx)_2]$	80	Mn, 11.0	11.3
$UO_2(OAc)_2$	Alcohol	Bright yellow	9-L-8	$[UO_2 \rightleftarrows (Pqx)_2 \cdot 2C_2H_5OH]$	95	*b*	
$UO_2(OAc)_2$[c]	Alcohol	Brick red	5-J-11	$[UO_2 \rightleftarrows (Pqx)_2]$	90	U, 33.3	33.0
$Cu(OAc)_2$	Water	Red-brown	8-J-5	$[Cu \rightleftarrows (Cx)_2]$	80	Cu, 10.4	10.4
$Pb(OAc)_2$	Alcohol	Red-brown	8-J-7	$[Pb \rightleftarrows (Cx)_2]$	70	Pb, 27.6	27.7
$Mn(OAc)_2$	Alcohol	Olive green	15-L-7	$[Mn \rightleftarrows (Cx)_2]$	95	Mn, 9.2	9.4
$NiCl_2$	Alcohol	Green-brown	16-A-12	$[Ni \rightleftarrows (Cx)_2]$	75	Ni, 9.7	9.8
$UO_2(OAc)_2$	Alcohol	Yellow-orange	9-L-10	$[UO_2 \rightleftarrows (Cx)_2 \cdot 2C_2H_5OH]$	80	*d*	
$UO_2(OAc)_2$[e]	Alcohol	Orange-brown	5-H-12	$[UO_2 \rightleftarrows (Cx)_2]$	75	U, 29.2	28.8

[a] Forms unstable greenish black addition compound with pyridine. [b] Ratio of $[UO_2 \rightleftarrows (Pqx)_2] : C_2H_5OH$ determined. Calcd. 1:2. Found 1:1.95, 1:2.10. [c] Made by heating the alcohol addition compound to 100°. [d] Ratio of $[UO_2 \rightleftarrows (Cx)_2] : C_2H_5OH$ determined. Calcd. 1:2. Found 1:1.96. [e] Made by heating the alcohol addition compound to 100°.

the simple inner complex formed. In the case of the uranyl complex, a compound containing two moles of ethyl alcohol, probably coördinated directly to the uranyl, first precipitated and then decomposed on heating to the normal inner complex.

In addition to the complexes described, tests[3] on these two oximes indicate that chromium, mercury (I), palladium, rhodium, and zinc also form complexes.

Retenequinone monoxime exhibits the same reactive tendencies as the two oximes used; the colors shown, however, are somewhat duller than those of the phenanthrenequinone monoxime complexes but not as dark as those of the chrysenequinone monoxime compounds. 2-Nitrophenanthrenequinone monoxime gives colors duller than the phenanthrenequinone monoxime complexes but also somewhat duller than those from the 4-nitro isomer. Whether these indications will be supported by observations on other types of complexes remains to be seen.

It originally was intended to measure the absorption spectra of these complexes, but due to their insolubility this plan was, of necessity, abandoned. We hope, however, to carry out this phase of the problem with certain complexes which seem to show greater promise from the standpoint of solubility.

The description of color is so vague that it was felt a more tangible reference would be useful. All the complexes prepared have been classified according to the color charts of Maerz and Paul,[4] by assigning them what we have termed the M. and P. No., being the actual color plate reference of the compound.

(3) Haendler, *J. Chem. Education*, **16**, 66 (1939).

(4) Maerz and Paul, "Dictionary of Color," McGraw-Hill Book Co., Inc., New York, N. Y.

Experimental

Phenanthrenequinone Monoxime.—Phenanthrene, purified by the method of Bachmann,[5] was oxidized to the quinone as described by Jakubowitsch and Worobjowa,[6] purified by the method of Moore and Huntress,[7] and converted to the monoxime by Goldschmidt's procedure[8]; m. p. 158–159°.

Chrysenequinone Monoxime.—Purified chrysene[9] was oxidized and converted to the oxime according to Graebe and Hönigsberger[10]; m. p. 162–163°.

Inner Complexes.—The complexes of phenanthrenequinone monoxime ($C_{14}H_9NO_2$ = PqxH) and chrysenequinone monoxime ($C_{18}H_{11}NO_2$ = CxH) were prepared by treating a hot alcohol solution of a slight excess of the oxime with either an alcohol or water solution of the metallic salt and adjusting the *p*H of the mixture with ammonium hydroxide or acetic acid until coagulation of the precipitate occurred. The compounds, after filtration, were purified by extraction of the excess organic compound with alcohol. The complexes are extremely stable, insoluble in practically all organic solvents commonly available, soluble with decomposition in warm glacial acetic acid, and are only slightly attacked by mineral acids in most cases. For the sake of simplicity the preparational data are presented in tabular form.

Summary

1. Several new inner complexes of phenanthrenequinone monoxime and chrysenequinone monoxime have been prepared.

(5) Bachmann, THIS JOURNAL, **57**, 557 (1935).

(6) Jakubowitsch and Worobjowa, *J. prakt. Chem.*, **143**, 281 (1935).

(7) Moore and Huntress, THIS JOURNAL, **49**, 1328 (1927).

(8) Goldschmidt, *Ber.*, **16**, 2178 (1883).

(9) Liebermann, *Ann.*, **158**, 306 (1871).

(10) Graebe and Hönigsberger, *Ann.*, **311**, 262 (1900).

2. Tests have shown the existence of other inner complexes of these and also other quinone oximes.

3. An increase in the complexity of the substituent groups on the organic compounds tested appears to cause a darkening in the color of the metal complexes.

SEATTLE, WASH. RECEIVED JULY 12, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

The Entropy of Hydrogen Cyanide. Heat Capacity, Heat of Vaporization and Vapor Pressure. Hydrogen Bond Polymerization of the Gas in Chains of Indefinite Length

BY W. F. GIAUQUE AND R. A. RUEHRWEIN

This paper reports the results of low temperature calorimetric measurements on solid and liquid hydrogen cyanide. The data have been used to calculate the entropy of hydrogen cyanide gas and the experimental result has been compared with the value calculated from available band spectrum data.

It has been shown by Sinosaki and Hara[1] and by Felsing and Drake[2] that hydrogen cyanide gas is partially polymerized, and it is therefore necessary to apply a correction in obtaining the entropy of HCN from the entropy of the actual gas.

The measurements were made in a calorimeter with the laboratory designation Gold Calorimeter III which has been described previously.[3] The standard thermocouple which had been compared with a helium gas thermometer[3] was compared with oxygen and hydrogen vapor pressures during the course of this work. Agreement was found to within 0.05° at all temperatures measured. The resistance thermometer was calibrated directly in terms of the vapor pressure of hydrogen for temperatures below 20°K.

Preparation and Purity of Hydrogen Cyanide.—Hydrogen cyanide was prepared by a method described by Perry and Porter.[4] 18 Normal sulfuric acid was dropped on sodium cyanide until enough gas had been generated to make 300 cc. of liquid hydrogen cyanide. The gas from the generator was passed through 2 tubes of anhydrous calcium chloride and 3 tubes of phosphorus pentoxide. All of the tubes were 30 cm. long and 3 cm. in diameter. A considerable amount of a dark brown product was left in the reaction vessel.

The collected liquid was distilled three times, a portion being discarded at the beginning and end of each distillation. A purified portion of 135 cc. remained. This was distilled in a vacuum-jacketed column, for a reason to be discussed later. The whole system could be subjected to a high vacuum and between each distillation the hydrogen cyanide was solidified by means of liquid air and pumped with a mercury diffusion pump.

The material was a clear colorless liquid and it remained so even after a portion had been allowed to stand at room temperature for about one year.

From the slight rise in heat capacity below the melting point, due to premelting, the liquid-soluble solid-insoluble impurity was estimated to be of the order of one mole in one hundred thousand moles of hydrogen cyanide.

An interesting phenomenon was observed when the solidified hydrogen cyanide was warmed from or cooled to liquid air temperatures in a glass bulb. Intense flashes of bluish-white light were emitted in the temperature range 100 to 200°K. both on warming or cooling. The static discharge probably was due to strains set up in the solid by an unequal rate of temperature change. The discharge was accompanied by a cracking sound characteristic of crystals breaking under strain. The temperature range of the effect was obtained roughly by sealing a well into the glass bulb so that a thermocouple could be introduced.

The above effect is an interesting demonstration of the necessity of providing glass bulbs with a protective sheath to prevent contact of such materials with liquid air in case of breakage. It appears that solid hydrogen cyanide cooling in contact with liquid air would be practically certain to explode although we did not try it. Electrostatic effects in some degree are to be expected when such materials are fractured.

The Melting Point and Vapor Pressure of Hydrogen Cyanide.—A summary of the melting point investigation is given in Table I.

The values of the vapor pressure are given in Table II. The measurements were made by means of a Société Génévoise cathetometer with a precision of 0.002 cm., used as a comparison instrument with a standard meter. The standard acceleration of gravity was taken as 980.665 cm. sec.$^{-2}$ and the acceleration at this location as 979.973 cm. sec.$^{-2}$. The meniscus height corrections were taken from the work of Cawood and Patterson[5] and the corrections to international

(1) Sinosaki and Hara, *Tech. Repts. Tohôku Univ.*, **8**, 297 (1929).
(2) Felsing and Drake, THIS JOURNAL, **58**, 1714 (1936).
(3) Giauque and Egan, *J. Chem. Phys.*, **5**, 45 (1937).
(4) Perry and Porter, THIS JOURNAL, **48**, 299 (1926).
(5) Cawood and Patterson, *Trans. Faraday Soc.*, **29**, 514 (1933).

TABLE I

MELTING POINT OF HYDROGEN CYANIDE

0°C. = 273.10°K.

Time	% melted	T, °K. resistance thermometer	T, °K. Thermocouple
1-26-38			
10:46 P.M.	Heated into melting point		
1-27-38			
1:20 P.M.	10	259.863	259.85
2:10 P.M.	10	259.854	259.85
3:48 P.M.	Supplied heat		
6:20 P.M.	40	259.850	259.86
7:02 P.M.	40	259.855	259.86
8:00 P.M.	Supplied heat		
10:00 P.M.	70	259.861	259.86
11:00 P.M..	70	259.857	259.86
11:35 P.M.	70	259.858	259.86
	Accepted value		259.86

cm. of Hg were made by means of data given in the "I.C.T."[6]

Several vapor pressure observations were made on the solid but it became evident that the results were slightly high due to the presence of a small amount of solid in the line just above the calorimeter. For this reason these observations are omitted. In solidifying the substance for calorimetric measurements this was avoided by the sudden introduction of an atmosphere of helium with the material at the freezing point and practically all solid. Cooling was then accomplished before diffusion could take place. The possibility that helium might be entrapped in the solid with subsequent diffusion during the vapor pressure measurements caused us to forego this method of keeping the tube open in that case.

TABLE II

VAPOR PRESSURE OF HYDROGEN CYANIDE

0°C. = 273.10°K.

T, °K. Resistance thermometer	P inter. cm. Hg	$P_{obsd.}-P_{calcd.}$	$T_{obsd.}-T_{calcd.}$	Remarks
259.854	14.040	Triple point		10% melted
259.855	14.040	Triple point		40% melted
259.858	14.048*	Triple point		70% melted
259.856	14.040	0.000	0.000	Value accepted
265.083	18.170	− .006	.007	Liquid
268.017	20.915	.004	− .004	Liquid
272.004	25.178	.012	− .010	Liquid
276.221	30.411	− .008	.006	Liquid
280.090	36.003	.003	− .002	Liquid
285.020	44.284	− .012	.007	Liquid
289.929	54.043	.005	− .002	Liquid
295.015	65.873	− .016	.006	Liquid
298.801	76.016	.015	− .005	Liquid

(6) "International Critical Tables," McGraw-Hill Book Co., Inc., New York, 1926, Vol. I.

The data in Table II have been represented by and compared with the equation

Liquid hydrogen cyanide, 259.86 to 298.8°K.

$$\log_{10}P \text{ (inter. cm. Hg)} = -\frac{1600.8}{T} - 0.0017835\,T + 7.77114 \qquad (1)$$

The temperatures are given to 0.001° only because of relative accuracy. The triple point value marked with an asterisk was given no weight because a slight superheating of the surface may have occurred when the solid was nearly all melted and that which remained was at the bottom of the container due to its greater density.

From Equation 1 the boiling point of hydrogen cyanide was determined to be 298.80°K.

The melting and boiling point temperatures obtained by various observers are given in Table III.

TABLE III

MELTING AND BOILING POINT TEMPERATURES OF HYDROGEN CYANIDE

M. p., T, °K.	B. p., T, °K.	Observer
259	299	Gautier[7] (1869)
262	298	Nef[8] (1895)
259.70	...	Tammann[9] (1899)
259.76	...	Lespieau[10] (1905)
259.70	298.7	Bredig and Teichmann[11] (1925)
258.24	298.75	Perry and Porter[4] (1926)
260.08	298.8	Sinosaki and Hara[12] (1927)
259.86	298.80	This research

The Heat Capacity of Hydrogen Cyanide.—The heat capacity data are given in Table IV, and are shown graphically in Fig. 1. The amount was determined by condensing the substance in an evacuated bulb which was weighed. This was especially convenient since hydrogen cyanide boils a little above room temperature. The molecular weight was taken as 27.026 and 3.3721 moles were used for the measurements; 4.1832 international joules was taken as one calorie. The heat capacity observations were corrected for vaporization into the small volume of calorimeter and line at all temperatures where the effect was appreciable. This correction which involves no appreciable inaccuracy utilized the data of Sinosaki and Hara[1] on the density of liquid hydrogen cyanide and the density of the

(7) Gautier, *Ann. chim. phys.*, [4] **17**, 121 (1869).
(8) Nef, *Ann.*, **287**, 325 (1895).
(9) Tammann, *Ann. Physik*, **68**, 576 (1899).
(10) Lespieau, *Compt. rend.*, **140**, 855 (1905).
(11) Bredig and Teichmann, *Z. Elektrochem.*, **31**, 449 (1925).
(12) Sinosaki and Hara, *Tech. Reports, Tohôku Univ.*, **6**, No. 3, 19 (1927).

TABLE IV

THE HEAT CAPACITY OF HYDROGEN CYANIDE

0°C. = 273.10°K. (molecular weight = 27.026) 3.3721 moles in calorimeter.

Series	T, °K.	ΔT	C_p, cal./deg./mole	Series	T, °K.	ΔT	C_p, cal./deg./mole
I	14.77	1.029	0.372	II	166.30	1.812	10.70
I	16.85	2.333	0.523	III	166.40	3.370	10.72
I	19.04	1.669	0.746	II	168.23	1.784	10.81
I	21.64	3.410	1.013	III	169.55	2.665	11.93*
I	25.82	5.047	1.423	II	170.20	1.920	12.19*
I	29.79	2.818	1.864	III	171.27	0.674	11.68*
I	32.85	3.104	2.232	II	172.31	2.022	11.23*
I	36.10	3.260	2.607	III	172.73	2.074	10.93
I	39.43	3.321	3.005	II	174.42	2.041	10.95
I	43.43	4.532	3.477	III	175.81	3.789	10.96
I	47.67	3.883	3.940	I	177.04	6.334	11.01
I	51.72	4.060	4.412	II	177.58	3.720	11.04
I	56.15	4.649	4.877	II	181.51	3.611	11.19
I	60.53	4.161	5.275	I	183.61	6.065	11.25
I	65.00	4.775	5.628	I	190.30	5.788	11.52
I	69.81	4.885	6.042	I	196.32	5.569	11.76
I	74.68	4.868	6.428	I	202.10	5.350	12.02
I	79.79	5.377	6.795	I	207.76	5.272	12.22
I	84.93	4.958	7.158	I	213.43	5.542	12.49
I	89.95	5.029	7.456	I	224.74	5.254	13.08
I	94.97	5.150	7.718	I	230.94	5.440	13.42
I	102.06	4.725	8.126	I	236.66	5.228	13.77
I	106.94	4.485	8.349	I	242.51	5.525	14.09
I	111.60	4.809	8.599	I	248.43	5.304	14.47
I	116.85	5.482	8.833	I	254.14	5.110	14.79
I	122.48	5.215	9.034		259.86	Melting point	
II	124.67	8.848	9.121	IV	266.57	4.112	16.92
I	127.73	4.976	9.244	V	271.33	6.049	16.85
II	133.19	8.234	9.453	IV	271.76	4.870	16.82
I	133.34	4.736	9.468	IV	277.15	4.790	16.84
I	138.42	5.219	9.631	V	277.97	5.898	16.95
II	141.10	7.705	9.780	IV	282.77	5.083	16.86
I	143.62	4.986	9.882	V	284.63	5.784	16.92
I	148.75	5.012	10.04	IV	288.48	4.978	16.93
II	149.34	8.852	10.12	V	291.12	5.648	17.01
I	154.04	5.242	10.27	IV	294.02	4.509	16.94
II	157.89	8.319	10.42	V	297.12	5.090	16.96
I	159.29	5.053	10.44	IV	298.34	2.976	16.88
II	163.70	3.346	10.63		298.80	Boiling point	
I	164.43	4.869	10.62				

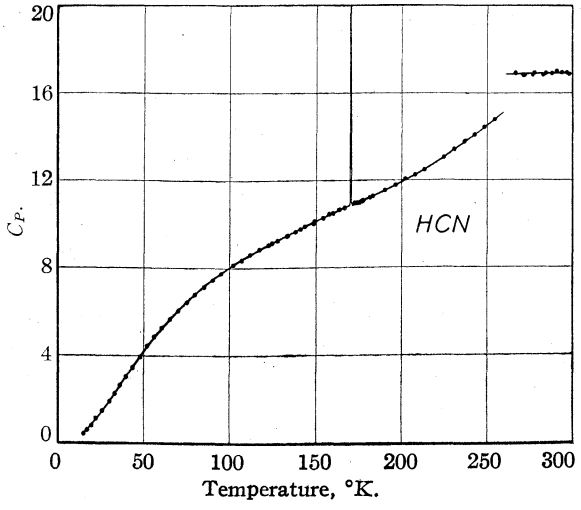


Fig. 1.—Heat capacity in calories per degree per mole of hydrogen cyanide.

solid was estimated with sufficient accuracy from rough observations during the preparation of the material. A smooth curve through the data should give the heat capacity to within 0.2% above 35°K. At 20°K. the inaccuracy may be about ±1% and at 15°K. about ±5%. Values taken from a smooth curve are given in Table V.

TABLE V

THE HEAT CAPACITY OF HYDROGEN CYANIDE

Values taken from smooth curve through the data. Molecular weight, 27.026.

T, °K.	C_p cal. deg.$^{-1}$ mole^{-1}	T, °K.	C_p, cal. deg.$^{-1}$ mole^{-1}
15	0.382	160	10.48
20	0.835	170	11.20
25	1.336	170.37	31 maximum
30	1.886	180	11.12
35	2.470	190	11.50
40	3.069	200	11.90
45	3.646	210	12.32
50	4.214	220	12.82
60	5.230	230	13.37
70	6.058	240	13.95
80	6.817	250	14.55
90	7.456	259.86	Melting point
100	8.008	260	16.82
110	8.520	270	16.86
120	8.938	280	16.90
130	9.333	290	16.94
140	9.730	298.80	Boiling point
150	10.11	300	16.97

A narrow region of high heat capacity occurred near 170°K. as is shown in Fig. 1. The points marked with asterisks in Table IV are not plotted in Fig. 1 because the temperature interval used was too large to allow them to be considered as values of differential heat capacity in this region of rapid variation. When the effect was first noted, during some preliminary observations, it was thought that it might be due to impurity, so the hydrogen cyanide was removed and fractionated in a vacuum-jacketed column. This produced no change in the effect.

Attainment of thermal equilibrium was a little less rapid in the region 140 to 170°K. and in order to determine whether the region of high heat capacity was due to some false equilibrium in the solid, the material was allowed to stand at approximately 165°K. for three days. No change in the effect was found.

In order to determine the entropy connected with the above effect, the total energy absorbed over a temperature of several degrees was measured. While the heat absorption was not sharp,

it was possible, without much arbitrariness, to subtract what may be considered the normal $\int C_p dT$ over the interval and thus assign a value to the heat effect accompanying the phenomenon. These values are given in Table VI. The first three values given correspond to the measurements made before the material was removed for fractionation in the column. The differences between the several values are somewhat greater than might be expected but we do not feel that any significance is to be attached to the variations.

The effect was also studied by means of cooling rate observations in this region. The temperature of the heavy metal cylinder which surrounded the calorimeter was set a little below that of the calorimeter, which thus cooled very slowly. The rate of cooling in the region of normal heat capacity was 0.0103° per minute while at the maximum of the heat capacity curve the rate decreased to 0.0044° per minute. The cooling rates give the best available information as to the character of the curve. The maximum heat capacity of 31 cal. deg.$^{-1}$ mole^{-1} occurred at 170.37°K. The cooling curve data, which are shown in Fig. 2, were also used to calculate a value for the total heat effect. This value is included in Table VI. The agreement of the results obtained by heating and cooling shows that no appreciable irreversibility is involved.

TABLE VI

MOLAL ENERGY ABSORPTION OF HYDROGEN CYANIDE NEAR 170°K.

Amounts given are in calories per mole above the heat corresponding to the "normal" heat capacity. Maximum heat capacity at 170.37°K.

No. of energy increments	Temp. interval	Heat input cal. mole^{-1}	$\int C_p dT$	ΔH cal. mole^{-1}
	Before fractionation			
1	167.166–173.499	99.34	94.80	4.5
	A few % melted, stood 10 hrs. resolidified			
2	169.231–173.320	64.93	61.15	3.8
3	168.198–173.759	87.48	83.15	4.3
	Material removed from calorimeter and fractionated			
0	From graphical integration of cooling rate			3.2
2	168.224–171.969	59.36	55.26	4.1
10	167.690–171.749	63.43	59.89	3.5
1	168.574–172.490	61.30	58.22	3.1
			Mean value	3.8

The entropy change corresponding to the 3.8 cal. mole^{-1} is only 0.022 cal. deg.$^{-1}$ mole^{-1}. The physical process which results in such a small change in entropy must be one involving the actions of large groups of hydrogen cyanide molecular units.

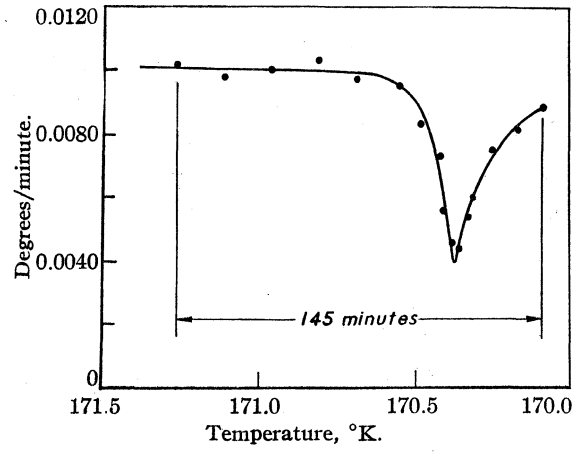


Fig. 2.—Cooling rate curve for hydrogen cyanide near 170°K.

As has been pointed out by Smyth and McNeight,[13] the low dielectric constant of the solid precludes any possibility of appreciable molecular rotation in the crystalline state and the hydrogen bond polymerization to be discussed later in this paper should be effective in preventing rotation.

The Heat of Fusion of Hydrogen Cyanide.—The determinations were made in the usual manner, each measurement was started somewhat below the melting point and ended somewhat above. Corrections for the $\int C_p dT$ were made. The results are given in Table VII.

TABLE VII

MOLAL HEAT OF FUSION OF HYDROGEN CYANIDE

Melting point 259.86°K. 0°C. = 273.10°K. Molecular weight, 27.026.

Temp. interval	Heat added per mole	$\int C_p dT$	ΔH, cal. mole^{-1}
257.400–263.844	2142.5	132.8	2010
257.388–263.975	2144.7	135.8	2009
257.030–264.166	2155.3	147.0	2008
		Average value	2009

The Heat of Vaporization of Hydrogen Cyanide.—The heat of vaporization was measured at constant pressure, the gas being absorbed in a bulb containing 150 cc. of 4 *M* sodium hydroxide and arranged with a mercury trap at the bottom. Only the lower half of the calorimeter heater was used to supply energy and hydrogen cyanide was evaporated only from the upper part of the calorimeter. The data are given in Table VIII, which also lists a value obtained from the vapor pressure observations represented by Equation 1. In using the equation

$$\Delta H \text{ vaporization} = \frac{dP}{dT} T \Delta V$$

(13) Smyth and McNeight, THIS JOURNAL, **58**, 1723 (1936).

we have made use of the liquid and gas density data of Sinosaki and Hara[1] which are discussed later in this paper. $(PV/RT) = 0.9239$ at 1 atmosphere and 298.80°K., which leads to a gas volume of 22,655 cc. per mole of HCN at the boiling point. The molal volume of the liquid is 40 cc. at this temperature.

TABLE VIII

HEAT OF VAPORIZATION OF HYDROGEN CYANIDE

Boiling point 298.80°K. 0°C. = 273.10°K. Molecular weight, 27.026.

Moles evap.	Time, min.	ΔH cal., deg.$^{-1}$ mole^{-1}
0.21455	45	6007
.22473	45	6031
.22549	45	6033
.22656	45	6035
	Average value	6027
Calcd. from vapor pressure Equation 1		6083

The value of the heat of vaporization obtained from the vapor pressure data is given no weight in comparison with the calorimetric value.

The Entropy of Hydrogen Cyanide from Calorimetric Data.—A summary of the entropy calculation for the equilibrium mixture of hydrogen cyanide and its associated forms at the boiling point is given in Table IX.

TABLE IX

THE ENTROPY OF HYDROGEN CYANIDE

0–15°K., Debye extrapolation, $h\nu/k = 160$	0.126
15–259.86°K., Graphical	16.770
Heat absorption above normal C_p near 170.37 = 3.8/170.37	0.022
Fusion, 2009/259.86	7.731
259.86–298.80°K., Graphical	2.360
Entropy of liquid at 298.80°K.	27.01
Vaporization, 6027/298.80	20.17
	47.18
Gas imperfection correction	0.03
Entropy of 27.026 g. of gas at 298.80°K.	47.21

The correction for gas imperfection was made by assuming Berthelot's equation of state and the critical constants for hydrogen chloride

$$T_c = 324.5°\text{K.},^{14}\ P_c = 83\ \text{atm.}^{14}$$
$$\Delta S = S_{\text{ideal}} - S_{\text{actual}} = 27\ RT_c^3P/32\ T^3P_c$$
$$= 0.03\ \text{cal. deg.}^{-1}\ \text{mole}^{-1}$$

Although Berthelot's equation does not hold for an associated gas, the above estimate should be fairly accurate since the gas consists largely of the monomer.

(14) Pickering, *J. Phys. Chem.*, **28**, 97 (1924).

The Polymerization of Hydrogen Cyanide Gas.—In order to calculate the entropy of monomeric hydrogen cyanide gas from the above results, it is necessary to consider the association of the substance. Sinosaki and Hara[1] have made a very extensive investigation of the gas density of hydrogen cyanide as a function of temperature and pressure and more recently Felsing and Drake[2] have reported single observations at each of three temperatures which show that association exists.

The results in this paper are based on the work of Sinosaki and Hara and we have not used their observations at pressures below 0.3 atmosphere because the accuracy limitations of gas density measurements make them unsuitable for the accurate determination of the extent of association. In making corrections for gas imperfection the equation $PV = RT(1 + \lambda P)$ was used and λ was taken as -0.0056 at the boiling point of hydrogen cyanide, this being the value for hydrogen chloride considered to be a Berthelot gas. Similarly values of λ were obtained at other temperatures. The value of λ for associated forms is undoubtedly larger but it may be shown readily that it is unimportant to consider the difference. The critical data of hydrogen cyanide were not used to calculate λ because it may be shown that a considerable amount of the polymer is present at the critical point. The effect of variation of λ will be discussed later.

The first calculations were based on the assumption that

$$2\text{HCN} = (\text{HCN})_2$$

represented the polymerization with

$$K = \frac{\alpha/2(1 - \alpha/2)}{(1 - \alpha)^2P}$$

where α represents the fraction of the material in the dimeric form and

$$1 - \alpha/2 = \frac{(PV)_{\text{observed}}}{RT(1 + \lambda P)}$$

$(PV)_{\text{observed}}$ was taken as the volume of one mole on a monomeric basis. The values of K calculated showed a very considerable decrease with decreasing pressure at the several temperatures and even impossibly large values of λ could not appreciably alter the trend. Calculations based on the presence of some hydrogen isocyanide assumed to be out of equilibrium with hydrogen cyanide and the formation of dimers in the various possible combinations did not satisfy the data.

The assumption of specific formation of a trimer

gave impossible results and indicated that the average polymer was intermediate between a dimer and trimer and thus the presence of both.

It is evident that if the equilibrium constants calculated on the assumption of dimer formation are plotted, the true constant for the formation of $(HCN)_2$ will be obtained by extrapolating the values to zero pressure. Values so obtained are shown in Table X, together with the false values corresponding to one atmosphere to show the trend.

TABLE X

EQUILIBRIUM CONSTANTS FOR THE REACTION 2HCN = $(HCN)_2$

T, °K.	$K(p=0) \times 10^2$ True	$K(p=1) \times 10^2$ False
273.1	9.5	...
303.0	5.6	8.6
333.1	3.4	4.2
373.1	2.0	2.3
462.3	1.0	1.0

The logarithms of the values of the constants given in the second column of Table X fall nearly on a straight line when plotted against the reciprocal of the absolute temperature and may be represented by the equation

$$\log_{10}K_D = (717/T) - 3.616 \qquad (2)$$

where K_D is the equilibrium constant for dimer formation.

K_T for the reaction

$$3HCN = (HCN)_3$$

was then calculated at the several temperatures.

$$K_T = \frac{\beta/3(1-\alpha/2-2\beta/3)^2}{(1-\alpha-\beta)^3P^2} \qquad (3)$$

where α and β are the fractions associated to dimer and trimer, respectively, and

$$(1 - \alpha/2 - 2\beta/3) = \frac{(PV)_{\text{observed}}}{RT(1 + \lambda P)} \qquad (4)$$

Values of K_T obtained by means of the above equations decreased somewhat with decreasing pressure. Again extrapolating to zero pressure, the values 0.055, 0.0087, 0.0030 and 0.0013 atm.$^{-2}$ are found for K_T at the temperatures 273.1, 303.0, 333.1 and 373.1°K., respectively. These results can be represented by the equation

$$\log_{10}K_T = (1905/T) - 8.320 \qquad (5)$$

If hydrogen cyanide forms both a dimer and trimer, one might reasonably ask whether higher polymers are not present also and there are good reasons for believing this to be the case. The trend in K_T with pressure is in the right direction to indicate higher polymers but this places too great a strain on the gas density to be considered as more than a suggestion. However, Kumler[15] has explained the phenomenally high dielectric constants of such liquids as hydrogen cyanide and hydrogen fluoride by assuming chains due to hydrogen bond formation and it is difficult to see any other explanation for the high electric moment.

There is no evident limit to the length of the hydrogen cyanide chains possible by such a mechanism except that the longer groupings are less stable thermodynamically. Equations 2 and 5 may be used as a basis for estimating the fractions of higher polymers.

Bauer, Beach and Simons[16] recently have presented electron diffraction evidence which indicates that hydrogen fluoride gas consists principally of zig-zag chains due to hydrogen bonds.

There are two simple tests which may be applied to Equations 2 and 5 to judge their reasonableness. First: the entropy change in the formation of the dimer should roughly approximate the Trouton value for the reduction by one of the number of moles of gas by a condensation process and the change for trimer formation should be about twice that for the above quantity. Second: the heat of formation for the trimer from the monomer should be of the order of twice the value for the dimer. The following values are found

$$\Delta S^\circ_D = -16.5 \text{ cal. deg.}^{-1} \text{ mole}^{-1}$$
$$\Delta S^\circ_T = -38 \text{ cal. deg.}^{-1} \text{ mole}^{-1}$$
$$\Delta H^\circ_D = -3{,}280 \text{ cal. mole}^{-1}$$
$$\Delta H^\circ_T = -8{,}720 \text{ cal. mole}^{-1}$$

Taking the increments between the dimer and trimer values as more representative of further additions, a general equation may be written as

$$\Delta F^\circ = -RT \ln K_n = \Delta H^\circ - T\Delta S^\circ \qquad (6)$$
$$= 7600 - 5440n - T(26.5 - 21.5n) \qquad (7)$$

where n is the number of molecules combined in the polymer.

From Equation 7 and equations similar to Equation 3, the fractions associated in the various polymers have been calculated and are given in Table XI.

Since deuterium bonds would be expected to be stronger than those of hydrogen gas density measurements on deuterium cyanide should show a larger, more easily studied, polymerization.

(15) Kumler, THIS JOURNAL, **57**, 600 (1935).
(16) Bauer, Beach and Simons, *ibid.*, **61**, 19 (1939).

TABLE XI

FRACTIONS OF HYDROGEN CYANIDE GAS IN THE STRAIGHT CHAIN SERIES OF POLYMERS

T = boiling point = 298.80°K., P = 1 atmosphere.

Polymer	Fraction
Dimer	0.0988
Trimer	.0268
Tetramer	.0064
Pentamer	.0015
Hexamer	.0003
Heptamer	.00004

The question also arises as to whether hydrogen bond polymerization does not occur to a small extent in gaseous water and we believe that it can be answered in the affirmative in the following way. From the gas density data as summarized by Keenan and Keyes,[17] $\lambda = -0.016$ atm.$^{-1}$ for saturated vapor at the boiling point. If the specific effects due to hydrogen bonds could be eliminated, the λ for hydrogen sulfide should be larger than that for water at the same temperature. Berthelot's equation of state represents the gas density of hydrogen sulfide quite accurately at ordinary temperatures and it seems safe to assume that it does so at the boiling point of water. λ is found to be -0.004 and from this we conclude that hydrogen bond association exists to the extent of about 3% in gaseous water at one atmosphere and 373.1°K. A larger effect would be anticipated in the case of deuterium oxide gas.

The Entropy of Monomeric Hydrogen Cyanide.—The entropy of the equilibrium mixture in hydrogen cyanide gas is given by the expression

$$S^\circ_{\text{mixture}} = (1 - \alpha - \beta - \ldots)\, S^\circ_{\text{HCN}} + \alpha/2\, S^\circ_{\text{D}} + \beta/3\, S^\circ_{\text{T}} + \ldots - R(1 - \alpha/2 - 2\beta/3 - \ldots) [N_{\text{M}} \ln N_{\text{M}} + N_{\text{D}} \ln N_{\text{D}} + N_{\text{T}} \ln N_{\text{T}} + \ldots] \quad (8)$$

$$= S^\circ_{\text{HCN}} + \alpha/2\, \Delta S^\circ_{\text{D}} + 2\beta/3\, \Delta S^\circ_{\text{T}} + \ldots + R\,(1 - \alpha/2 - 2\beta/3 - \ldots)\, \Sigma\, N \ln N \quad (9)$$

$$S^\circ_{\text{HCN}} = S^\circ_{\text{mixture}} - \alpha/2\, \Delta S^\circ_{\text{D}} - \beta/3\, \Delta S^\circ_{\text{T}} - \ldots + R \left[(1 - \alpha - \beta - \ldots) \ln \frac{(1 - \alpha - \beta - \ldots)}{(1 - \alpha/2 - 2/3\beta - \ldots)} + \alpha/2 \ln \frac{\alpha/2}{(1 - \alpha/2 - 2/3\beta - \ldots)} + \beta/3 \ln \frac{\beta/3}{(1 - \alpha/2 - 2/3\beta - \ldots)} + \ldots \right] \quad (10)$$

The total entropy correction to be added to the value for the entropy of the equilibrium mixture on account of polymerization is 0.73 cal. deg.$^{-1}$ mole^{-1}, of which only 0.05 cal. deg.$^{-1}$ mole^{-1} is due to all polymers higher than the trimer.

(17) "Thermodynamic Properties of Steam," Keenan and Keyes, John Wiley and Sons, Inc., New York, 1936.

To test the importance of the particular choice of λ, the calculations were repeated with $\lambda = -0.025$ atm.$^{-1}$. With the larger λ the 0.03 cal. deg.$^{-1}$ mole^{-1} correction for ordinary gas imperfection, given in Table IX, is increased to 0.12 cal. deg.$^{-1}$ mole^{-1}. It is sufficient to include only polymers up to and including the trimer in making the comparison. The following result was obtained

$\lambda = -0.025$: correction = 0.12 + 0.57 = 0.69 cal. deg.$^{-1}$ mole^{-1}

$\lambda = -0.0056$: correction = 0.03 + 0.68 = 0.71 cal. deg.$^{-1}$ mole^{-1}

The difference of 0.02 cal. deg.$^{-1}$ mole^{-1} for such a large variation of λ makes it evident that the final result does not depend appreciably on the particular value selected as the best estimate.

Comparison of the Entropy Values from Calorimetric and Spectroscopic Data.—The necessary molecular data for calculating the entropy were taken from the band spectrum observations of Bartunek and Barker,[18] who give a summary of previous observers. The moment of inertia, I, is 18.72×10^{-40} g. cm.^{2} and the observed vibrational quanta for excitation to the first level of each type are 2089.0, 712.1 and 3312.9 cm.$^{-1}$ respectively. The 712.1 cm.$^{-1}$ corresponds to the bending motion and has a weight of 2.

$$S_{\text{Translation}} = 3/2\, R \ln M + 5/2\, R \ln T - R \ln P - 2.300$$

$$S_{\text{Rotation}} = R \ln IT + 177.676$$

The vibrational entropy was calculated by means of the Einstein formula. The nuclear spins of H, C and N are $1/2$, 0 and 1, respectively; thus the spin contribution is $R \ln (2 \times 1/2 + 1)(2 \times 1 + 1) = R \ln 6 = 3.560$ cal. deg.$^{-1}$ mole^{-1}. A comparison of the entropy values at the boiling point 298.80°K. and at 298.10°K. is given in Table XII. The value 48.23 cal. deg.$^{-1}$ mole^{-1} for 298.10°K. is identical with the result of a similar calculation made by Gordon,[19] who also considered

TABLE XII

COMPARISON OF CALORIMETRIC AND SPECTROSCOPIC VALUES FOR THE ENTROPY OF HYDROGEN CYANIDE

Temperature, °K.	298.80	298.10
Equilibrium gas, actual	47.18±0.1	...
Equilibrium gas, ideal	47.21	...
Correction for polymerization	0.73	...
HCN ideal, experimental	47.94	47.92
HCN spectroscopic less nuclear spin contribution	48.25	48.23
Correction for nuclear spin	3.56	3.56
Absolute entropy, cal. deg.$^{-1}$ mole^{-1}	51.81	51.79

(18) Bartunek and Barker, *Phys. Rev.*, **48**, 516 (1935)

(19) Gordon, *J. Chem. Phys.*, **5**, 30 (1937).

the effect of polymerization. However, Gordon was unaware of the experiments of Sinosaki and Hara[1] and thus was led to assume that only a dimer was formed.

The experimental value is 0.31 cal. deg.$^{-1}$ mole^{-1} lower than the one obtained from molecular data. We believe that not more than 0.1 cal. deg.$^{-1}$ mole^{-1} of this can be attributed to calorimetric error. The weakest point in the calculation appears to be the strain placed on the gas density observations in obtaining the temperature coefficients of the association constants. The density measurements of Sinosaki and Hara[1] have been made with great care but the amounts of polymeric forms decrease so rapidly with increasing temperature that high accuracy is not to be expected when the data are used to calculate association constants. Here, as in so many other cases of equilibrium measurements, the onset of error is gradual and the straight line obtained with a log K *vs.* $1/T$ plot must not be taken too seriously.

The net correction for the presence of polymers is only 0.73 cal. deg.$^{-1}$ mole^{-1}; the entropy terms in Equation 10 which are based on the temperature coefficient of gas density amount to 1.28 cal. deg.$^{-1}$ mole^{-1}. Thus we conclude that the entropy obtained from the third law of thermodynamics is in agreement with the value obtained from molecular data.

The entropy value 48.23 cal. deg.$^{-1}$ mole^{-1}, which does not include the nuclear spin effect, is the one which should be used in ordinary thermodynamic calculations for monomeric hydrogen cyanide. The entropy of liquid hydrogen cyanide at 298.1 is 26.97 cal. deg.$^{-1}$ mole^{-1}.

We thank Dr. T. M. Powell for assistance with the measurements.

Summary

The heat capacity of solid and liquid hydrogen cyanide has been measured from 14 to 300°K.

The melting and boiling points were found to be 259.86 and 298.80°K., respectively (0°C. = 273.10°K.).

The heat of fusion is 2009 cal. mole^{-1}.

An energy absorption of 3.8 cal. mole^{-1} occurred over a small temperature range with a maximum at 170.37°K.

The heat of vaporization at the boiling point was determined calorimetrically to be 6027 cal. mole^{-1}.

The vapor pressure of liquid hydrogen cyanide has been measured and the data have been represented by the equation liquid, 259.86 to 298.9°K.

$$\log_{10}P \text{ (inter. cm. Hg)} = -(1600.8/T) - 0.0017835\,T + 7.77114$$

The triple point pressure is 14.040 inter. cm. Hg.

The available gas density data on hydrogen cyanide have been used to show that multiple polymerization exists. The data are taken to indicate indefinite straight chain hydrogen bond polymerization in the gas, as suggested by Kumler for the liquid, in explanation of its abnormally high dielectric constant. The fraction of the gas in the various polymeric forms up to the heptamer has been calculated.

It has been estimated that hydrogen bond polymerization occurs in saturated water vapor to the extent of 3% at the boiling point.

The data and the third law of thermodynamics have been used to calculate the entropy of monomeric hydrogen cyanide gas at 298.10°K. and 1 atm. The experimental value 47.92 cal. deg.$^{-1}$ mole^{-1}, which contains a small possible error on account of uncertainty in the temperature coefficients of the polymerization reactions, is in agreement with the value 48.23 cal. deg.$^{-1}$ mole^{-1}, calculated from the band spectrum data.

The entropy of liquid hydrogen cyanide at 298.1°K. is 26.97 ± 0.05 cal. deg.$^{-1}$ mole^{-1}.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

The Influence of Ionic Strength on the Quenching of Fluorescence in Aqueous Solutions

BY R. W. STOUGHTON AND G. K. ROLLEFSON

The quenching of fluorescence in solution has usually been discussed as a deactivation of the photoactivated molecule by a collision with the quenching ion in which some energy is transferred to the quencher. Such a process is analogous to the type assumed in the discussion of gaseous systems. A more specific picture to adopt for the mechanism of quenching would be to say that the activated molecule and the quencher react to form an intermediate, such as is assumed in the discussion of rates of reaction, and that when this intermediate decomposes into the original molecules, neither is in a state which can radiate. At first it may seem that there is no essential difference between the two views but there is a definite difference to be expected for the effect of ionic strength on the efficiency of a quencher. In this paper we shall show that the quenching process behaves exactly as a second order reaction.

According to the interionic attraction theory, the limiting law for the effect of ionic strength on the activity coefficient of an ion in water at 25° is

$$\log \gamma = -0.5\, z^2\mu^{1/2} \qquad (1)$$

in which γ is the activity coefficient, z the charge on the ion and μ the ionic strength. This shows that the activity of an ion at a given concentration will decrease as the ionic strength is increased. If the quenching action of ions in solution on fluorescence is considered as simply a collision of the second kind and it is assumed that the number of effective collisions is determined by the activities of the colliding molecules, it follows that raising the ionic strength will decrease the quenching efficiency of a given ion. On the other hand, if the quenching process is analogous to the rate of a bimolecular reaction involving ions in solution, the effect which will be observed will depend on the nature of the molecules involved. Thus it has been found that the logarithm of the rate constant for an ionic reaction is given by

$$\log k = \log k_0 + 0.5\ \Delta z^2\mu^{1/2}$$

or

$$(2/\Delta z^2) \log k/k_0 = \mu^{1/2} \qquad (2)$$

in which k is the rate constant at ionic strength μ, k_0 is the constant at $\mu = 0$, and Δz^2 is the difference between the square of the charge of the intermediate complex formed from the reactants and the sum of the squares of the charges of the reactant molecules. On the basis of this equation raising the ionic strength may increase, decrease, or have no effect on the quenching action depending on the sign of Δz^2. The three possibilities may be illustrated by writing the equations

$$M^{-*} + X^- \rightleftarrows MX^{--} \longrightarrow M^- + X^- \quad \Delta z^2 = 2 \quad (3)$$

$$M^* + X^- \rightleftarrows MX^- \longrightarrow M + X^- \quad \Delta z^2 = 0 \quad (4)$$

$$M^{+*} + X^- \rightleftarrows MX \longrightarrow M^+ + X^- \quad \Delta z^2 = -2 \quad (5)$$

The first step is written as reversible in accordance with the assumption usually made in deriving equation (2). It must be stressed, however, that the validity of that equation as a limiting law rests on an experimental basis and is independent of any assumptions which may be made in justifying it on theoretical grounds. Furthermore, the application of the equation to the quenching of fluorescence is independent of the nature of the products in (3), (4) and (5) except that the molecules of the fluorescent substance must be regenerated.

In the following paragraphs we present data on twelve systems in all of which the quenching changes in the way predicted for a bimolecular ionic reaction. The limiting law is not strictly valid at the concentrations used but the deviations observed are within the same range as found for electrolytes such as the alkali halides and halogen acids.

Materials.—The KNO_3, $NaClO_4$, KCl, KBr, KI, KCNS, $AgNO_3$, quinine sulfate and acridone used in these experiments were C. P. grade. The fluorescein was reprecipitated by dissolving it in an alkaline solution and acidifying. The anthracenesulfonic acid was prepared by a method outlined in the literature.[1] The acridone sulfonic acid was prepared by heating acridone and fuming sulfuric acid in the presence of glacial acetic acid to 100°, diluting, removing the excess sulfuric acid with barium hydroxide and evaporating to dryness.

Apparatus.—The apparatus is shown in Fig. 1. Light from the Heraeus type mercury arc S passed through the lens L and the filter F and excited the fluorescent solution in the cell C, which was placed in the water thermostat B. F was a no. 586 Corning filter and transmitted only the group of mercury lines around 3660 Å. The fluorescent light from C passed through the filter F′, which absorbed

(1) *Chem. Zentr.*, **83**, II, 1413 (1912).

all ultraviolet light, and onto the photocell P_1. In order to compensate for fluctuations in the arc, light from the same source was allowed to pass through the same type of filter F and illuminate a second photocell P_2. The currents of the two photocells were balanced with a potentiometer. With this arrangement the potentiometer readings were proportional to the intensity of light falling on P_1 when adjustment was made so that no current flowed through the galvanometer G. The linearity of the potentiometer readings as the light intensity was varied was verified by placing calibrated screens between F' and P_1.

Method.—All the solutions used in these experiments were kept in a thermostat at 25°, and mixing was done immediately before the measurements were taken to prevent the possibility of photoöxidation on standing. The thermostat in which the cell was placed was also kept at 25°.

The potentiometer reading obtained when the cell C was filled with a dye solution at a definite hydrogen ion concentration and at a definite ionic strength was recorded as I_0. Similar readings were taken at various concentrations of the quenching salt and recorded under the heading I. From these data values of the quenching constant k were calculated using the equation

$$I/I_0 = 1/(1 + kC_q)$$

where C_q is the concentration of the quenching ion.

In order to test the validity of the present explanation for the quenching of fluorescence, the charge on the fluorescent substance in solution had to be known. It was possible to fix the molecular species present by using the proper hydrogen ion concentration. Two different sets of data were recorded in the case of fluorescein: one in 0.001 M perchloric acid ensuring the presence of only the un-ionized molecules and one in 0.001 M potassium hydroxide to ensure having only the divalent negative ion in solution. All the measurements with quinine sulfate were taken in 0.01 M nitric acid, so that the substance would be in the form of the divalent positive ion. No acid or base was added in the case of acridone, anthracenesulfonic acid or acridonesulfonic acid since acridone exists only as the neutral molecule and the other two are strong acids.

The values of k at a given ionic strength were determined for various concentrations of the quenching salts in the cases of fluorescein with potassium iodide in both acid and basic solutions and quinine sulfate with potassium chloride and bromide and silver nitrate. It was found that k depended only slightly on the concentration of the quencher. The variations that were observed showed a slight increase with increasing concentration with the negative ions but with Ag^+ there was a decrease. In order to separate the effect of ionic strength from any variations of this type, values of k were determined in which the concentration of the quenching salt was kept constant and the ionic strength varied by adding sodium perchlorate in the case of fluorescein and potassium nitrate in all other cases. Small corrections were made for the quenching of quinine sulfate by potassium nitrate. No measurable quenching was observed by either potassium nitrate or sodium perchlorate with the other dyes. The results are given in the tables.

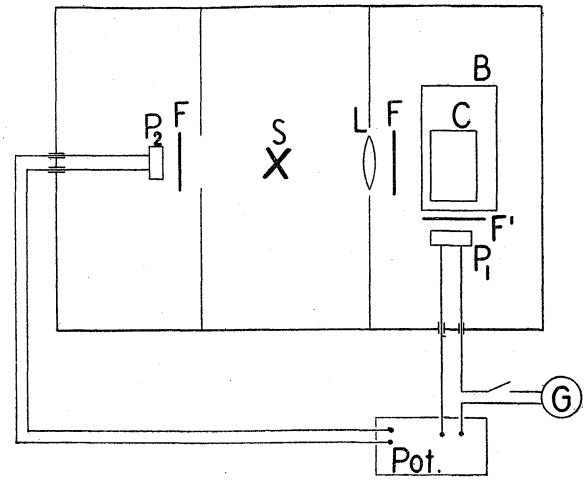

Fig. 1.—Diagram of apparatus.

TABLE I

QUENCHING OF QUININE SULFATE (c = 0.0004 M) AT 25°

μ	I/I_0	k
By 0.025 M Silver Nitrate		
0.0367	0.882	5.3
.0617	.858	6.6
.1117	.840	7.6
.2117	.786	10.9
.4117	.720	15.5
By 0.005 M KBr		
0.0217	0.370	340
.0317	.393	308
.0417	.417	280
.0617	.438	256
.1117	.513	190
.2117	.531	176
.4117	.569	152
By 0.005 M KCl		
0.0217	0.438	256
.0617	.510	192
.1117	.562	156
.2117	.612	126
.4117	.666	100

TABLE II

QUENCHING OF FLUORESCEIN ($c = 1 \times 10^{-4}$ M) BY KI AT 25°

μ	I/I_0	k	C_{KI}
	In 0.001 M KOH		
0.031	0.745	11.4	0.03
.051	.732	12.2	.03
.101	.705	14.0	.03
.201	.550	16.4	.05
.301	.544	16.8	.05
	In 0.001 M $HClO_4$		
0.031	0.635	19.2	0.03
	.615	20.9	.03
.041	.558	19.8	.04
.051	.638	18.8	.03
	.621	20.3	.03
	.490	20.8	.05
	.500	20.0	.05
.091	.483	21.4	.05
	.508	19.4	.05
.101	.500	20.0	.05
	.333	20.0	.1
.201	.513	19.0	.05
	.330	20.5	.1
	.336	19.8	.1

TABLE III

QUENCHING OF ACRIDONE (SATD. SOLN.) AT 25°

μ	I/I_0	k
	By 0.01 M KI	
0.01	0.522	92
.05	.521	92
.11	.516	94
.21	.517	93.5
	By 0.025 M $AgNO_3$	
0.025	0.765	12.2
.125	.763	12.4
.425	.745	13.6

TABLE IV

QUENCHING OF ANTHRACENESULFONIC ACID ($c = 1 \times 10^{-4}$ M) AT 25°

μ	I/I_0	k
	By 0.05 M KI	
0.05	0.640	11.3
.10	.598	13.5
.25	.560	15.8
.45	.550	16.3
.55	.526	18.0
.85	.523	18.2
	By 0.025 M $AgNO_3$	
0.025	0.440	51.0
.050	.474	44.4
.125	.550	32.8
.425	.576	29.5
.525	.567	30.5
.905	.533	35.0

Fluorescein in Table II represents the first dye studied. Results in this case were not as reproducible as they were in the later work due to slight improvements in the method and apparatus made after the studies on fluorescein. Also in Table II the values of k are given for more than one value of the concentration of the quencher.

TABLE V

QUENCHING OF ACRIDONE SULFONIC ACID ($c = 5 \times 10^{-5}$ M) AT 25°

μ	I/I_0	k
	By 0.05 M $AgNO_3$	
0.05	0.697	8.7
.15	.717	7.9
.25	.725	7.6
.45	.722	7.7
.65	.709	8.2
.85	.692	8.9
	By 0.01 M KI	
0.0105	0.620	62.0
.03	.591	69.0
.05	.580	72.5
.11	.568	76.0
.21	.552	81.0
.31	.551	82.0
.41	.538	86.0
.51	.535	86.5
.81	.536	86.5
	By 0.01 M KCNS	
0.01	0.698	43.3
.05	.663	51.0
.11	.648	54.5
.21	.634	57.5
.31	.629	59.0
.41	.624	60.0
.51	.626	60.0
.81	.620	61.0

Discussion

From the data in Tables I to V, values of $(2/\Delta z^2) \log k$ were determined and plotted against $\mu^{1/2}$. The values of Δz^2 were obtained by subtracting the sum of the squares of the charges of the reacting ions from the square of the charge of the intermediate complex formed. The quenching ions in these reactions were the negative ions of the potassium halides and potassium thiocyanate used, and the silver ion in the case of silver nitrate. The charges on the dye ions were discussed before. Thus the Δz^2 values for the reactions of the quenching of fluorescence of quinine sulfate by potassium iodide and silver nitrate would be as follows

$$Q^{++*} + I^- \rightleftharpoons QI^+ \longrightarrow Q^{++} + I^- + \text{energy} \qquad \Delta z^2 = -4$$

$$Q^{++*} + Ag^+ \rightleftharpoons QAg^{+++} \longrightarrow Q^{++} + Ag^+ + \text{energy} \qquad \Delta z^2 = +4$$

Q^{++*} and Q^{++} representing the activated and unactivated quinine ions, respectively.

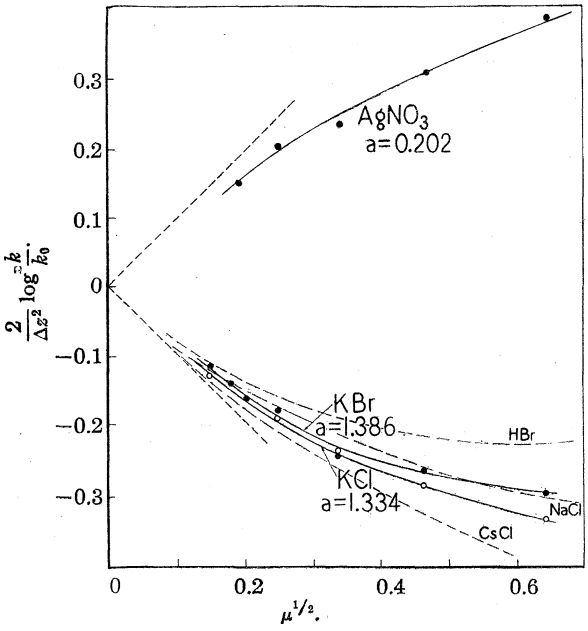

Fig. 2.—Quenching of fluorescence of quinine sulfate by $AgNO_3$, KBr and KCl.

In order properly to compare the $(2/\Delta z^2)\log k$ *vs.* $\mu^{1/2}$ curves obtained with known activity coefficient curves, it was necessary to determine the value of $\log k_0$. This determination was accomplished by drawing in the limiting curve of slope ± 1 in the position which seemed most appropriate and extending it to the ordinate. The value of the ordinate at this intersection was taken as $(2/\Delta z^2)\log k_0$, and the entire curve was shifted by this amount toward the origin by moving it parallel to the $(2/\Delta z^2)\log k$ axis. This method was equivalent to plotting $(2/\Delta z^2)\log k/k_0$ *vs.* $\mu^{1/2}$ and it brought all the curves into the same region for comparison. The results are shown in Figs. 2, 3, 4, 5 and 6.

The values of a here represent $(2/\Delta z^2)\log k_0$. The dotted lines of slope $+1$ and -1 represent the limiting slope predicted by the Debye–Hückel theory. The activity coefficient curves for hydrobromic acid, sodium chloride, and cesium chloride are shown dotted in Fig. 2 for comparison.

The possibility of explaining the quenching of fluorescence as due to the tying up of part of the dye ions by complex formation with the quenching ions before activation of the dye was considered. Absorption measurements were made on solutions of quinine sulfate, fluorescein and acridone sulfonic acid in the presence and absence of the quenching ions used in each case. These measurements were taken with such concentrations of the dyes that about 50% of the incident light was absorbed. A negligible decrease in absorption in the presence of the quenching salts was noted in all cases except those involving Ag^+, where a small increase (less than 1%) was observed. Since it is very improbable that the complexes in all cases would have the same absorption coefficients as the dye molecules

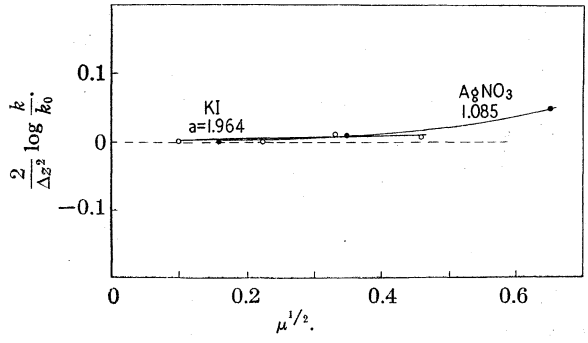

Fig. 4.—Quenching of fluorescence of acridone by silver nitrate and potassium iodide.

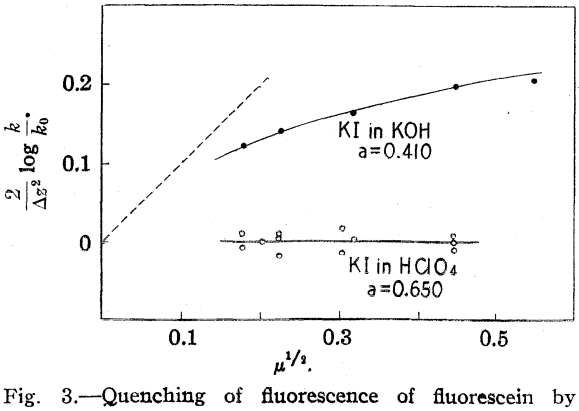

Fig. 3.—Quenching of fluorescence of fluorescein by potassium iodide in acid and basic solutions.

themselves, these results may be interpreted as eliminating the possibility of explaining the quenching by complex formation before activation of the dye.

It may be well to emphasize here the importance of fixing the molecular species in solution of those dyes which are weak electrolytes. For our purpose the charge on the ions had to be known, and it was pointed out by Desha, Sherrill and Harrison[2] and later by Eisenbrand[3] that the form of the molecules due to the value of *p*H has an enormous effect on the intensity of fluorescent

(2) Desha, Sherrill and Harrison, THIS JOURNAL, **48**, 1493 (1926).
(3) Eisenbrand, *Z. physik. Chem.*, **A144**, 441 (1929).

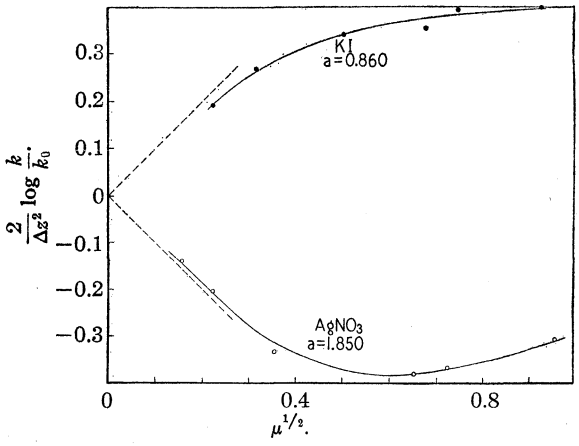

Fig. 5.—Quenching of fluorescence of anthracene sulfonic acid by silver nitrate and potassium iodide.

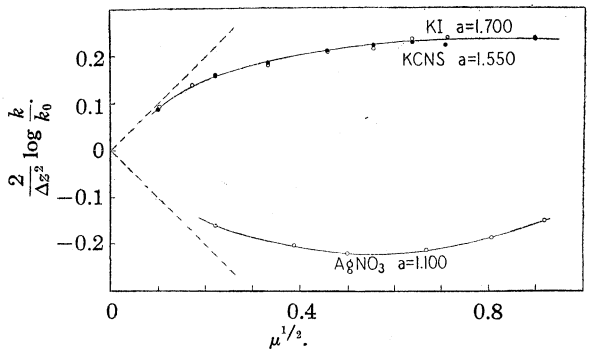

Fig. 6.—Quenching of fluorescence of acridone sulfonic acid by $AgNO_3$, KI and KCNS.

light in the region of hydrogen ion where dissociation takes place. This ensuring of a single definite molecular species in solution has been overlooked by many investigators of fluorescence quenching.

From the data presented it can be seen that the variations of values of $(2/\Delta z^2) \log k/k_0$ with varying ionic strength are of the same type and magnitude as those known to occur in ordinary bimolecular reactions. In every case the curves are of the required form and in every case the increase or decrease of the values of the quenching constants at low values of μ is in accordance with the sign of Δz^2. In view of these results and the considerations of the previous paragraphs, it follows that the quenching is due to an ordinary bimolecular reaction between the activated dye molecules and the quenching ions.

It must be pointed out here that in the present paper no attempt is made to attribute the decrease in fluorescence intensity with increasing dye concentration to the ionic strength effect on the quencher. Only the quenching due to known non-fluorescing quenching ions was explained in this way.

From the results of the present work the study of the quenching of fluorescence seems to offer a very convenient means for studying a simple bimolecular reaction. The first step of such a process may be determined directly without having to consider the products formed as is usually the case. A perhaps even more useful possibility is to reverse the process used here, that is, assume the reaction to be of the ordinary bimolecular type and then determine the molecular species involved by a study of the variations of log k with varying ionic strength. Such an application should be of considerable importance in determining the form of the ions present in non-aqueous solutions.

Summary

The quenching constants at various values of ionic strength were determined for the quenching of fluorescence of quinine sulfate by potassium chloride and bromide and silver nitrate; of fluorescein by potassium iodide in acid and basic solutions; of acridone by potassium iodide and silver nitrate; of anthracene sulfonic acid by potassium iodide and silver nitrate and of acridone sulfonic acid by potassium iodide, potassium thiocyanate and silver nitrate.

The values of $(2/\Delta z^2) \log k$ were plotted against $\mu^{1/2}$ and in every case the curves obtained were of the same type as those expected for an ordinary bimolecular reaction.

Absorption measurements were made with the dye solutions in the presence and absence of the quenching ions. Only a negligible change of absorption was observed, thus eliminating the possibility of explaining the quenching as due to complex formation of the dye with the quencher before excitation of the former.

The quenching in all cases appeared to be due to an ordinary bimolecular reaction between the quenching ion and the activated dye molecule.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, OREGON STATE COLLEGE]

Studies on Hydrazine: The Heat of Formation of Hydrazine and of Hydrazine Hydrate*

BY ALBERT M. HUGHES, R. J. CORRUCCINI AND E. C. GILBERT

In order to extend previous results from this Laboratory on the thermochemistry of hydrazine and its compounds in aqueous solution,[1] attention has been turned to heats of combustion. For this a new calorimeter has been constructed, in which, however, the adiabatic principle of the earlier work has been retained.[1a]

Apparatus and Method

In the construction of the calorimeter the general principles and restrictions laid down by White[2] were followed closely. Certain details, however, are pertinent. Automatic temperature control by means of a 17-junction thermel, high sensitivity galvanometer and Weston Photronic cell, and electrolytic heating is the same as in the earlier apparatus.[1a] For the combustion a Parr double valve Illium bomb of 360 cc. capacity was used. The 3-mm. pegs with which it was originally provided were replaced by pegs 12 mm. high which allowed more effective circulation of water around it. The bomb was held in an oval calorimeter of approximately 2000 cc. capacity. This in turn was contained in a submarine jacket with a 12-mm. air gap between the two. The water was stirred by means of a chain driven stirrer and synchronous motor. The heat of stirring was of the order of 0.0001° per minute. The stirrer shaft contained a bakelite insert to minimize heat transfer. The ignition leads were led through copper tubing immersed in the outer bath for the same reason.

A temperature difference of 0.0002° between the calorimeter and the outer bath could be detected by the thermel galvanometer. During the runs the divergence never amounted to more than 0.0006°, and that only for brief intervals during the combustion. The automatic heating was augmented during the rapid temperature rise by the manual addition of hot water. There was a lag of approximately four seconds in the temperature equalization between the calorimeter and the outer bath.

The temperature was measured by means of a Leeds and Northrup platinum resistance thermometer, a "Mueller-type" thermometer bridge, and a Leeds and Northrup galvanometer (2285-b). Resistance could be read under the optimum conditions accurately to 0.00001 ohm. The bridge was newly calibrated in terms of the international ohm.[3] The bomb was provided with special crucible supports constructed by the Parr Instrument Co., having screw binding posts. Heavy platinum wires led from these to a point near the charge to be burned. The charge was ignited by heating an exactly measured (2–3 cm.) piece of iron wire (no. 36) electrically using a 14-volt transformer. The energy introduced by the heating and combustion of this wire was determined by a series of blank runs, the mean result being 0.00019 ohm (0.0019°) for 3 cm.

The same mass of water was used in the calorimeter each time within 0.1 g. The mass of the charge was determined to 0.00001 g. The crucible for holding the charge was of very thin platinum, a factor which seemed to minimize carbon formation.

The bomb was washed out several times with oxygen at 4–5 atm. to remove residual air. Nitric acid formed in the combustions was determined by titration of the bomb washings with standard base, using brom cresol green as indicator. For the heat of formation of nitric acid at 25° and constant volume the value of 13,960 cal. mole^{-1} was used.[4] This correction was of considerable importance in the compounds burned for this investigation.

The same pressure of commercial oxygen, 30 atm. absolute, was used in every run, and 1 g. of water was added to the bomb.

The results are referred to the standard temperature of 25°, by using in each instance an initial temperature of 25 ± 0.1°, and calculations involving the heat capacity of the products of the reaction. This procedure was adopted because of uncertainty regarding the heat capacity of the reactants.

Calibration of the Calorimeter

The energy equivalent of the calorimeter was determined by the combustion of benzoic acid (Standard Sample 39e) supplied by the Bureau of Standards. The isothermal heat of combustion of this sample at 25° is given as 26,419 int. joules per gram true mass when burned under standard conditions.[5] The ratio of mass of acid and water to volume of the bomb being not quite "standard" a small correction ensues[5] (p. 491), which gives a value of 26,418 int. joules developed by the combustion of one gram of benzoic acid under the bomb conditions of this calorimeter. For convenience in making heat capacity calculations and in interpreting results, the results of this paper are largely expressed in conventional calories derived from the international joule by dividing by the factor 4.1833.[6]

Independent determinations were made by two operators (A. M. H. and R. J. C.) and the results are shown in Table I.

Heat of Combustion of Hydrazine Hydrate

Purification.—Purification of this compound is difficult on account of its instability and ease of oxidation, factors which also complicate the problem of securing uncon-

* Published with the approval of the Monographs Publication Committee, Oregon State College, as Research Paper No. 23, School of Science, Department of Chemistry.

(1) (a) Cobb and Gilbert, THIS JOURNAL, **57**, 35 (1935); (b) *ibid.*, **57**, 39 (1935); (c) Bushnell and Gilbert, *ibid.*, **57**, 2611 (1935); (d) Bushnell, Gilbert and Hughes, *ibid.*, **59**, 2142 (1937).

(2) White, "The Modern Calorimeter," The Chemical Catalog Co., New York, 1928.

(3) Mueller, National Bureau of Standards, Sci. Paper 288.

(4) (a) Becker and Roth, *Z. Elektrochem.*, **40**, 835 (1934); (b) Huffman, THIS JOURNAL, **60**, 1171 (1938).

(5) Jessup and Green, *Bur. Standards J. Research*, **13**, 496 (1934).

(6) Rossini, *Chem. Rev.*, **18**, 233 (1936).

TABLE I

CALIBRATION OF CALORIMETER WITH BENZOIC ACID AT 25°

Sample	True mass benz. acid, g.	Corr.[b] temp. rise Ohms	Corr.[b] temp. rise Degrees	Energy from b. a. int. joules	Energy from HNO_3 joules	Heat capacity calor. and products, int. joules deg.$^{-1}$	Heat capacity products, deg.$^{-1}$	Energy equiv. of calor., joules deg.$^{-1}$	Dev. from mean
1[a]	1.00134	0.24853	2.4764	26454.7	2.5	10683.6	16.9	10666.7	−0.6
2	1.00543	.24929	2.4840	26538.7	3.7	10685.3	16.9	10668.4	+1.1
3	0.99810	.24772	2.4683	26368.8	2.2	10683.7	16.9	10666.8	−0.5
4	1.02603	.25461	2.5370	27106.7	2.5	10685.5	17.0	10668.5	+1.2
5	0.98751	.24510	2.4422	26089.0	2.5	10683.5	16.9	10666.6	−0.7
10	.98488	.24450	2.4362	26019.5	6.3	10682.8	16.9	10665.9	−1.4
13[c]	.62341	.15475	1.5420	16468.7	6.3	10684.5	16.1	10668.4	+1.1
14[c]	.62438	.15499	1.5443	16494.3	3.8	10683.0	16.1	10666.9	−0.4
15[c]	1.08859	.27017	2.6920	28759.4	5.5	10685.0	17.2	10667.8	+ .5
						Mean energy equivalent, int. joules deg.$^{-1}$		10667.3	± .8
						calories deg.$^{-1}$		2550.0	± .2

[a] Expts. 1–5 were performed by A. H., the remainder by R. C. [b] Corrected for heat of stirring, evaporation, etc., and for "ignition" energy. [c] (Fused.)

taminated samples in the glass ampoules, a necessary step in the process. The freezing point curve for the system hydrazine–water has been established recently by Semishin.[7] From this it appears that upon freezing, any solution of hydrazine and water containing between 30 and 60% hydrazine should yield crystals of the hydrate (m. p. −46.8°). This was attempted with the apparatus used for anhydrous hydrazine and described below, but the product obtained after two recrystallizations contained hydrazine in nearly 5% excess over the amount needed to make the hydrate. Combustions were run on this material and are reported with the other results. Since the heat of solution of anhydrous hydrazine in the hydrate is not known, no worthwhile conclusions may be drawn from these values except as they indicate the reproducibility of the combustion process, with a given sample. A number of samples of Kahlbaum hydrazine hydrate "pro analysi" (99.8–100.5%) were available and the procedure finally adapted was the same as that used in the earlier work,[1d] which was to take the distilled Kahlbaum preparation, determine the hydrazine content by the iodic acid method[8] (which in our experience is the most accurate available) and add the proper amount of water to give the exact composition of the hydrate (64.03% N_2H_4) (all weights reduced to vacuum). This material was then used for filling the ampoules for combustion. The air in the ampoules was replaced by hydrogen, and hydrate introduced by evacuation in a hydrogen-filled desiccator. They were filled completely, sealed off and used for combustion runs within a few hours. The results are shown in Table II.

The precision of the analysis rather than of the combustion is presumably the limiting factor. Combustions conducted on samples of hydrate from widely different batches over a year apart and by different individuals gave quantitative agreement, however.[9] The only impurity to be obvious would be ammonia, but tests for this substance were negative. Since the heat of combustion of ammonia is higher than that of hydrazine, its presence would give high results.

(7) Semishin, *J. Gem. Chem.* (*U. S. S. R.*), **8**, 654 (1938).

(8) Bray and Cuy, THIS JOURNAL, **46**, 858 (1924).

(9) Albert L. Hughes, Master's Thesis, Oregon State College, 1938.

TABLE II

THE ISOTHERMAL HEAT OF COMBUSTION OF HYDRAZINE HYDRATE AT 25°

Sample	True mass, g.	Total heat[b] evolved at 25°, cal.	Heat from HNO_3, cal.	$-\Delta U_B/m$, cal. g.$^{-1}$	Deviation from mean
1[a]	1.70351	5,186.1	18.6	3,033.4	
2[a]	1.88990	5,756.6	21.0	3,034.8	
3[a]	1.73356	5,275.0	20.1	3,031.3	
4	1.89781	5,588.8	19.5	2,934.7	−0.5
5	1.49717	4,408.9	13.6	2,935.9	+ .7
6	1.57381	4,635.6	15.4	2,935.6	+ .4
7	1.95292	5,751.9	19.8	2,935.7	+ .5
8	1.75321	5,161.8	17.3	2,934.3	− .9
			Mean $-\Delta U_B/m$	= 2,935.2	±0.6 cal. g.$^{-1}$

$-\Delta U_B$ = 146,936 ± 30 cal. mole^{-1}

[a] The samples checked by analysis to contain 0.0539% by wt. N_2H_4 and 0.9461% $N_2H_4 \cdot H_2O$, hence were not used in further calculations. [b] Corrected for heat of stirring, evaporation, etc., and for the ignition energy.

Purity of the Reaction.—A question also of considerable importance is that of the purity of the reaction and the absence of side reactions. The following products that might conceivably occur were tested for in the bomb washings: nitrites,[10] ammonia[10] (p. 468), hydrazoic acid, and excess hydrazine hydrate. None was found, except in a few bad runs there was some unburned hydrate, apparently from splashing. Flattening the sides of the ampoules and filling them fuller seemed to obviate this difficulty.

Calculation of Results.—Due to the fact that hydrazine hydrate contains only nitrogen, hydrogen and oxygen, it was necessary to depart from the classical equations of Washburn[11] for the heat capacity of the products. The pure reaction for the combustion is

$$N_2H_4 \cdot H_2O(liq) + O_2(g) \longrightarrow N_2(g) + 3H_2O(liq)$$

from which it may be seen that the only pressure change will be due to oxygen used in the forma-

(10) Mahin, "Quantitative Analysis," 4th ed., McGraw-Hill Book Co., Inc., N. Y., 1932, p. 473.

(11) Washburn, *Bur. Standards J. Research*, **10**, 525 (1933).

tion of the small amount of nitric acid and ferric oxide. Also the appearance of nitrogen, mole for mole, for the oxygen consumed otherwise further simplifies the problem, since their thermodynamic properties may be considered equal. Due however to the large amount of water formed, a significant correction is introduced. From the figures of Washburn[11] (p. 556) and making due allowance for the water present as vapor at 25°, the mass of liquid water after the combustion will be

$$(m_w + 54.06m_h/50.06 - 0.0068)$$

where m_w = mass of water initially placed in the bomb and m_h = mass of hydrate burned.

Any correction for the heat of dilution of nitric acid is disregarded since Becker and Roth[4a] have shown that this may be done safely. Allowance was made, however, for the fact that the specific heat of the resultant nitric acid solution is significantly less than that of pure water. The final expression developed for the heat capacity of the products for an average charge of hydrate is

$$S_F = 5.01(n_{O_2} - \phi_{HNO_3} - \phi_{Fe}) + 0.965\ (m_w + 54.06\ m_h/50.06 - 0.0068) + 0.7\ V + 0.158\ m_{Fe} + 0.0024\ \text{cal.}_{15}\ \text{deg.}^{-1}$$

using the notation of Washburn. All other calculations followed the usual procedure and need not be described.

Heat of Combustion of Anhydrous Hydrazine

Purification.—Kahlbaum hydrazine hydrate was dehydrated with sodium hydroxide in an all-glass apparatus with a fractionating column by the method of Raschig[12] and the product which analyzed variously 99–100% pure was subjected to fractional crystallization in the apparatus shown in Fig. 1, in an atmosphere of dry hydrogen. In this apparatus the hydrazine could be crystallized repeatedly and melted with no exposure to moisture, oxygen or ground-glass surfaces. Since the f. p. is in the neighborhood of 2.0°, the manipulation and temperature control is much simpler than for the hydrate, which perhaps accounts for the lack of success with the latter. The material froze in the arm A to give beautiful, long, loose crystals of the anhydrous hydrazine. When about two-thirds was frozen the apparatus was turned so the residual liquid could be forced out through the platinum filter plate F and side tube B by hydrogen pressure. The solid was then melted and the process repeated. The material thus obtained analyzed to be 99.90% anhydrous hydrazine. Two samples were prepared by freezing and one was prepared by dehydration of the hydrate by barium oxide followed by fractional distillation. The procedure for filling the ampoules was the same as for the hydrate. The results of the combustion are shown in Table III. In calculating the heat capacity of the products the same

(12) Raschig, *Ber.*, **43**, 1927 (1910).

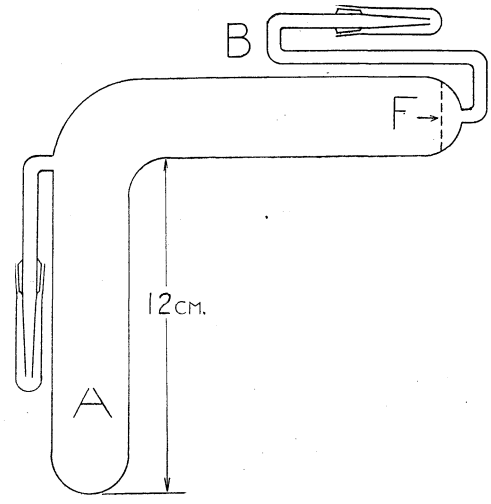


Fig. 1.—Device for fractional crystallization of hydrazine in an inert atmosphere.

equation was used as for the hydrate, due allowance being made for the different amount of water produced.

TABLE III

THE ISOTHERMAL HEAT OF COMBUSTION OF HYDRAZINE AT 25°

Sample	True mass, g.	Total heat[a] evolved at 25°, cal.	Heat from HNO_3 cal.	$-\Delta U_B/m$, cal. g.$^{-1}$	Deviation from mean
2(b)	1.28528	5,979.8	25.4	4,633.2	+0.3
2(c)	1.13373	5,274.6	24.9	4,630.7	−2.2
3(b)	1.49549	6,955.7	26.5	4,633.4	+0.5
3(d)	1.09253	5,087.4	24.1	4,634.2	+1.3
(X)				4,630.7	

Mean $-\Delta U_B/m$ for 99.90% N_2H_4 = 4,632.9 ±1.1 cal. g.$^{-1}$

Calcd. mean $-\Delta U_B/m$ for 100% N_2H_4 = 4,637.6 cal. g.$^{-1}$

Calcd. $-\Delta U_B$ = 148,635 ± 30 cal. mol^{-1}

[a] Corrected for heat of stirring, evaporation, etc., and for ignition energy.

(X) This value was obtained by A. L. H. (Thesis, ref. 9) with a different calorimeter, on hydrazine prepared by fractional distillation of the hydrate from barium oxide, but not analyzed.

Discussion of Results

The heat quantity obtained, $-\Delta U_B$, is the heat of the reaction under bomb conditions and to be useful should be converted to $-\Delta U_R$, the heat evolved by the reaction in the reference state of 1 atm. and 25°. Following the system of Washburn as closely as the difference in types of reaction permitted, this correction proved to amount to 0.003% and was disregarded, $-\Delta U_B$ and $-\Delta U_R$ being taken as equal. From the stoichiometric reaction also it may be seen that $-\Delta U_R = -\Delta H_R$ the heat of the isothermal reaction at constant pressure.

On this basis the results permit some interesting calculations.

(1) $-\Delta H^{\circ}_{298.1}$, the heat of formation of the compounds may be obtained from $-\Delta H_R$ with the use of $-68{,}318.1$ cal.[13] as the heat of formation of liquid water at 25°. For the hydrate is thus obtained

(a) $N_2(g) + 2H_2(g) + H_2O(liq) \longrightarrow N_2H_4 \cdot H_2O(liq)$ $\Delta H^{\circ}_{298.1} = 10{,}300$ cal.

and for anhydrous hydrazine, from the combustion data

(b) $N_2(g) + 2H_2(g) \longrightarrow N_2H_4(liq)$ $\Delta H^{\circ}_{298.1} = 12{,}000$ cal.

Incorporating with (a) the following quantity previously found in this Laboratory by direct measurement[1d]

$N_2H_4(liq) + H_2O(liq) \longrightarrow N_2H_4 \cdot H_2O(liq)$ $\Delta H^{\circ}_{298.1} = -1800$ cal.

a slightly different figure is obtained for (b), *i. e.*

$$\Delta H^{\circ}_{298.1} = 12{,}100 \text{ cal.}$$

(2) In converse manner, the difference between the molal heat of combustion of the hydrate and anhydrous hydrazine should give the heat of hydration. Thus is found

$N_2H_4(liq) + H_2O(liq) \longrightarrow N_2H_4 \cdot H_2O(liq)$ $\Delta H_{298.1} = -1700$ cal. (± 45)

in comparison with the value -1800 cal. found by dilution measurements.[1d] Both of these quantities are obtained by differences and errors are magnified.

(3) From (1) and (2) may be obtained, by using a mean value $\Delta H^{\circ}_{298.1} = 12{,}050$ cal. for hydrazine, and the following quantity[1d]

$N_2H_4(liq) + Aq. \longrightarrow N_2H_4 \cdot Aq$ $\Delta H_{298.1} = -3890$ cal.

a value for the heat of formation in dilute solution;

$N_2(g) + 2H_2(g) + Aq \longrightarrow N_2H_4 \cdot Aq$ $\Delta H_{298.1} = 8160$ cal.

(13) Rossini, *Bur. Standards J. Research*, **22**, 407 (1939).

From earlier thermochemical work, by indirect calculation, Bichowsky and Rossini[14] give three estimates for this quantity, *viz.*, +3500, +4500, and +5800 with apparent preference for the middle value. From the lack of agreement among themselves it would seem that little dependence may be placed on these earlier values.

(4) From $\Delta H^{\circ}_{298.1}$ for anhydrous hydrazine and its heat of vaporization ($\Delta H_v = +10{,}200$ cal. at 25°) reported recently by Hieber and Woerner,[15] $-\Delta H^{\circ}_{298.1}$ for the formation of hydrazine gas may be found. Our figures yield a value for this quantity $\Delta H^{\circ}_{298.1}$ (gas) = 22,250 cal., which compares interestingly with a value calculated from theoretical reasoning by Pauling,[16] of 22,100 cal. (0.96 e. v. mole^{-1}).

Grateful acknowledgment is due the National Research Council and the General Research Council of this College for financial assistance which made this work possible.

Summary

1. An adiabatic calorimeter for precise determinations of heats of combustion has been described briefly, along with its calibration.

2. Heats of combustion for hydrazine and hydrazine hydrate have been determined.

3. The standard heat of formation of hydrazine, liquid and gas; hydrazine hydrate, liquid and aqueous; and the heat of hydration of anhydrous hydrazine have been calculated.

CORVALLIS, OREGON RECEIVED JULY 10, 1939

(14) Bichowsky and Rossini, "The Thermochemistry of Chemical Substances," Reinhold Publishing Corp., N. Y., 1936, p. 217.

(15) Hieber and Woerner, *Z. Elektrochem.*, **40**, 252 (1934).

(16) Pauling, THIS JOURNAL, **54**, 3570 (1932).

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

The Electron Diffraction Investigation of the Molecular Structures of Ethyl Chloride, Ethyl Bromide, Isopropyl Chloride, Isopropyl Bromide, Methyl Chloroform and Isocrotyl Chloride[1]

BY J. Y. BEACH AND D. P. STEVENSON[2]

In a previous paper[3] we determined by the electron diffraction method the bond angles and bond distances in *t*-butyl chloride and *t*-butyl bromide. The bond distances in methyl chloride[4] and methyl bromide[5] also have been studied previously. In this paper we shall report an electron diffraction investigation of the molecular structures of ethyl chloride, ethyl bromide, isopropyl chloride and isopropyl bromide. This completes the investigation of the compounds derived from methyl chloride or methyl bromide by replacing zero, one, two or three hydrogen atoms by methyl groups. It is found in all cases that the distortion of the bond angles from the tetrahedral value is less than about 3°. However, we observe a trend in the bond angles which is probably real in going from the simpler molecules to the more complicated molecules. The interatomic distances are found to agree with those predicted by the table of covalent radii.

Methyl chloroform was studied for a comparison with *t*-butyl chloride. Methyl chloroform can be considered to be derived from *t*-butyl chloride by replacing the methyl groups by chlorine atoms and the chlorine atom by a methyl group.

In an electron diffraction investigation of phosgene and the chloroethylenes[6] it was found that the interatomic distance for a carbon–chlorine bond adjacent to a double bond is less than the carbon–chlorine bond distance in saturated compounds. The present study of isocrotyl chloride constitutes an extension of that investigation.

The electron diffraction apparatus used in this investigation is similar to the one described by Brockway.[7] The electron wave length, λ, was 0.0590 Å. The photographs were interpreted by the visual method[8] and by the modified radial distribution method. The theoretical scattering formula used in the visual method is $I = \Sigma_i \Sigma_j Z_i Z_j \sin sr_{ij}/sr_{ij}$. Z_i is the atomic number of the ith atom, r_{ij} is the distance between the ith and j^{th} atoms and $s = (4\pi \sin \theta/2)/\lambda$ where θ is the angle of scattering. Both sums are taken over all the atoms in the scattering molecule. The radial distribution method[9] has recently been improved[10] to give more detailed and reliable results. The coefficients in the radial distribution function were obtained from the visually estimated intensities by multiplying them by $s^2e^{-as^2}$ where $se^{-as^2} = 0.1$ for the largest ring. We have used this modification of the radial distribution method throughout this paper.

Ethyl Chloride.—Kahlbaum ethyl chloride was used without further purification. The photographs showed eight measurable maxima. The

TABLE I

ETHYL CHLORIDE

Values in parentheses not included in the average.

Max.	Min.	I	s_0	s^a	s^a/s_0
1		9	3.22	3.29	(1.021)
	2		4.16	3.75	(0.901)
2		20	5.15	5.07	.984
	3		6.40	6.33	.989
3		18	7.50	7.62	1.016
	4		8.31	8.70	(0.955)
4		5	9.47	9.20	(1.029)
	5		10.62	10.56	0.994
5		12	11.91	12.05	1.012
	6		13.24	13.29	1.004
6		8	14.47	14.42	0.997
	7		15.63	15.67	1.003
7		1	16.56	16.79	1.013
	8		17.71	17.50	0.988
8		3	18.90	18.85	.997
				Average	1.000

C–Cl = 1.76 Å.
long C–Cl = 2.74 Å.

[a] Calculated for a model having a ratio of carbon–chlorine to carbon–carbon distance of 1.76/1.54 and a C–C–Cl angle of 112°.

(1) Most of these results were presented to the American Chemical Society at Baltimore, April, 1939.

(2) Now National Research Fellow in Chemistry at the California Institute of Technology.

(3) J. Y. Beach and D. P. Stevenson, THIS JOURNAL, **60**, 475 (1938).

(4) L. E. Sutton and L. O. Brockway, *ibid.*, **57**, 473 (1935).

(5) H. A. Lévy and L. O. Brockway, *ibid.*, **59**, 1662 (1937).

(6) L. O. Brockway, J. Y. Beach and L. Pauling, *ibid.*, **57**, 2693 (1935).

(7) L. O. Brockway, *Rev. Modern Phys.*, **8**, 231 (1936).

(8) L. Pauling and L. O. Brockway, *J. Chem. Phys.*, **2**, 867 (1934).

(9) L. Pauling and L. O. Brockway, THIS JOURNAL, **57**, 2684 (1935).

(10) Ch. Degard, *Bull. Soc. Sci. Liège*, February, 1938; V. F. H. Schomaker, paper presented to the American Chemical Society at Baltimore, April, 1939. The modification of the radial distribution method used in this paper is not identical with the modification proposed by Schomaker.

observed values of $s(s_0)$ for the maxima and minima and the visually estimated intensities of the maxima are given in Table I. The fourth maximum is close to the third and is difficult to measure. The eight-term radial distribution function is shown in Fig. 1, curve A. The two principal peaks at 1.76 and 2.74 Å. represent the two carbon–chlorine distances in the molecule.

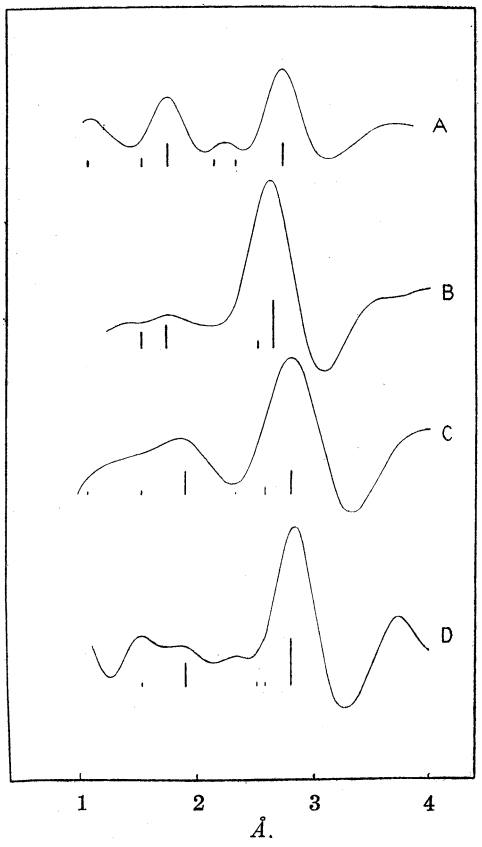


Fig. 1.—Modified radial distribution function for: A, ethyl chloride; B, isopropyl chloride; C, ethyl bromide; D, isopropyl bromide. The vertical lines indicate the final values for the interatomic distances and their importance.

The smaller peaks represent, less reliably, the less important distances in the molecule. In calculating the theoretical intensity curves the ratio of the carbon–chlorine distance to the carbon–carbon distance was taken to be 1.76/1.54. This was the only ratio tried as it gave a final value for the carbon–carbon distance of 1.54 Å., the value we assume to be correct. Other ratios lead to different carbon–carbon distances. No attempt was made to determine the motion of the methyl groups as their orientation has a negligible effect on the theoretical scattering curve.

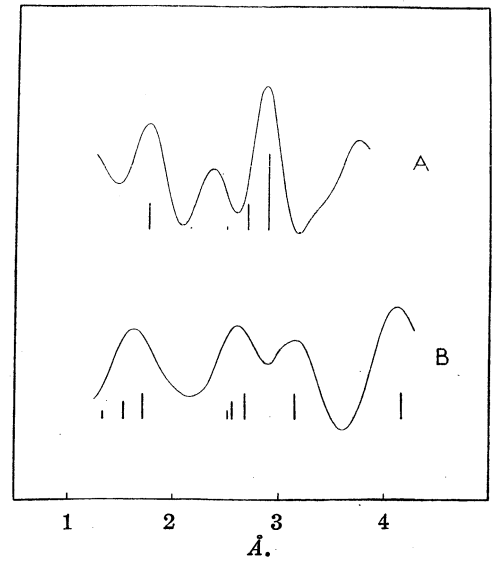


Fig. 2.—Modified radial distribution function for: A, methyl chloroform and B, isocrotyl chloride. The vertical lines indicate the final values for the interatomic distances and their importance.

For the purpose of calculating curves we assumed them to be oriented so that the hydrogen atoms avoided as much as possible the atoms on the other end of the molecule. Theoretical intensity curves were calculated for values of the C–C–Cl angle of 109° 28′ (tetrahedral), 112° and 114° 30′. These curves are shown in Fig. 3. The 112° curve agrees best with the photographs.

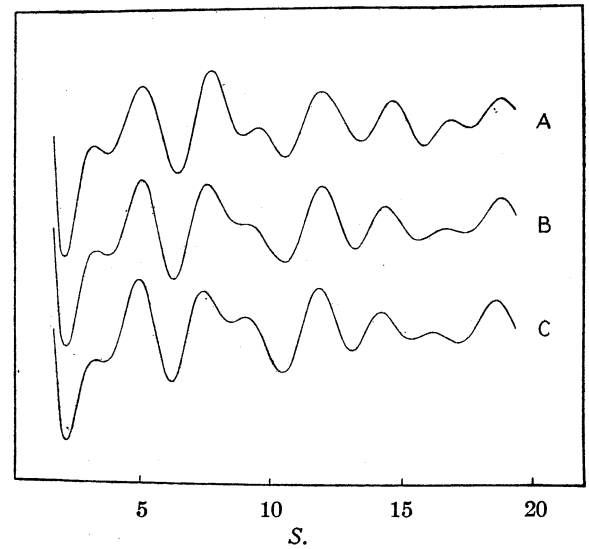


Fig. 3.—Theoretical intensity curves for ethyl chloride. The C–C–Cl angle is: curve A, 109° 28′; curve B, 112°; curve C, 114° 30′. The ratio of carbon–chlorine distance to carbon–carbon distance is 1.76/1.54.

The seventh maximum on the 109° 28′ curve is higher than on the photographs. The 114° 30′ curve is unsatisfactory because the fourth maximum, or shelf, is too high. Quantitative comparison of the photographs with the 112° curve is made in Table I.

The final results are: carbon–chlorine bond distance, 1.76 ± 0.02 Å.; long carbon–chlorine distance, 2.74 ± 0.02 Å.; C–C–Cl angle, 111° 30′ ± 2°. The carbon–carbon and carbon–hydrogen distances were assumed to be 1.54 and 1.09 Å., respectively.

Ethyl Bromide.—Eastman Kodak Co. ethyl bromide was purified by fractional distillation. The electron diffraction photographs showed six measurable maxima. The values of s_0 for the maxima and minima and the visually estimated intensities of the maxima are tabulated in Table II. The six-term radial distribution function is shown in Fig. 1, curve C. The two peaks at 1.87 and 2.81 Å. represent the two carbon–bromine distances in the molecule. In calculating the theoretical intensity curves the methyl group was assumed to possess a static configuration in which the hydrogen atoms avoid as much as possible the atoms on the other end of the molecule. The carbon–hydrogen distance was assumed to be 1.09 Å. and all bond angles except the C–C–Br angle were assumed to be tetrahedral. Curves were calculated for models in which the ratio of the carbon–bromine distance to the carbon–carbon distance was 1.91/1.54, the C–C–Br angle ranging from 107° 30′ to 113° 30′. These curves are shown in Fig. 4. When the C–C–Br angle is greater than the tetrahedral angle the fourth maximum on the calculated curves is much too low. A curve intermediate between curves A and B resembles the photographs most closely. Quantitative comparison of the photographs with both curves A and B is made in Table II. Theoretical intensity curves were also calculated for models in which the ratio of the carbon–bromine distance to the carbon–carbon distance were given values of 1.87/1.54 and 1.95/1.54. Decreasing the carbon–bromine distance has the same effect on the calculated curves as increasing the C–C–Br angle and therefore is impossible. Increasing the carbon–bromine distance is unsatisfactory because the fourth and fifth maxima merge into one.

TABLE II

ETHYL BROMIDE

Values in parentheses not included in the averages.

Max.	Min.	I	s_0	s^a	s^a/s_0	s^b	s^b/s_0
1		10	3.09	3.06	(0.990)	3.13	(1.013)
	2		3.91	3.75	(.958)	3.91	(0.999)
2		16	5.01	4.77	.951	4.87	.971
	3		5.98	5.96	.996	6.04	1.010
3		13	7.16	7.22	1.008	7.28	1.017
	4		8.13	8.52	1.047	8.70	1.070
4		5	9.31			10.10	(1.085)
	5		10.20			10.81	(1.060)
5		2	11.36	11.15	0.982	11.30	0.995
	6		12.36	12.46	1.008	12.53	1.014
6		4	13.84	13.73	0.992	13.84	1.000
				Average	0.998		1.010
				C–Br = 1.91 Å.		C–Br = 1.93 Å.	
				long C–Br = 2.81 Å.		long C–Br = 2.81 Å.	

[a] Calculated for a model having a ratio of carbon–bromine to carbon–carbon distance of 1.91/1.54 and a C–C–Br angle of 109° 28′. [b] Calculated for a model having a ratio of carbon–bromine to carbon–carbon distance of 1.91/1.54 and a C–C–Br angle of 107° 30′.

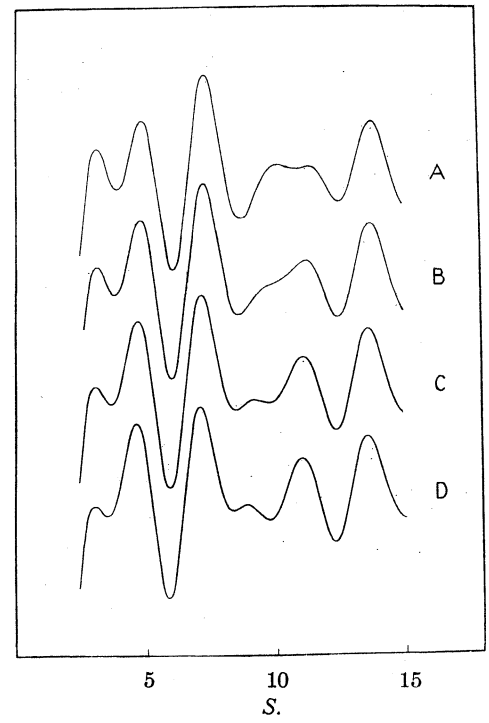


Fig. 4.—Theoretical intensity curves for ethyl bromide. The C–C–Br angle is: curve A, 107° 30′; curve B, 109° 28′; curve C, 111° 30′; curve D, 113° 30′. The ratio of the carbon–bromine distance to the carbon–carbon distance is 1.91/1.54.

Taking the results of the quantitative comparisons together with the radial distribution function we arrive at the final results: carbon–bromine bond distance, 1.91 ± 0.02 Å.; long carbon–bromine distance, 2.81 ± 0.02 Å.; C–C–Br angle, 109 ± 2°.

Isopropyl Chloride.—Eastman Kodak Co. isopropyl chloride was purified by fractionation in a

thirty-inch (76-cm.) column. The photographs show six measurable maxima. The fifth is better defined than the fourth. The values of s_0 for the maxima and minima and the intensities of the maxima are listed in Table III. The radial distribution function is shown in Fig. 1, curve B. The principal peak at 2.64 Å. is an unresolved combination of the long carbon–carbon distance and the two equal long carbon–chlorine distances. If the carbon–carbon distance is 2.52 Å., the value which would obtain if the carbon–carbon bond distance were 1.54 Å. and the C–C–C angle were 109° 28′, then the long carbon–chlorine distance would be 2.66 Å. To make this calculation it is assumed that the observed position of the radial distribution peak is a weighted mean of the two contributing distances, the weighting factors being the importance of the interatomic distance in the scattering function. If all the bond angles in the molecule are tetrahedral and the carbon–chlorine and carbon–carbon distances are 1.76 and 1.54 Å., respectively, then the long carbon–chlorine distance would be 2.70 Å. The value 2.66 Å. obtained from the radial distribution function indicates that the C–C–Cl angle is somewhat less than the tetrahedral value or that the bond distances just assumed are too great. We shall assume that the carbon–carbon distance has the value 1.54 Å., and show that the carbon–chlorine distance is not appreciably less than 1.76 Å., but that the C–C–Cl angle is slightly less than the tetrahedral value.

TABLE III

ISOPROPYL CHLORIDE

Values in parentheses not included in the average.

Max.	Min.	I	s_0	s^a	s^a/s_0	s^b	s^b/s_0
1		10	3.22	2.95	(0.916)	3.02	(0.938)
	2		4.14	3.90	(.943)	3.96	(.957)
2		9	5.43	5.15	(.949)	5.23	(.963)
	3		6.44	6.37	.989	6.44	1.000
3		7	7.70	7.55	.980	7.65	0.993
	4		8.62	8.68	1.008	8.87	1.030
4		4	9.96	9.41	0.945	9.66	0.970
	5		10.91	10.78	.988	10.92	1.001
5		3	12.35	12.21	.989	12.34	0.999
	6		13.35	13.47	1.009	13.57	1.016
6		1	14.83	14.41	0.972	14.68	0.990
				Average	0.985		1.000
				C–Cl = 1.73		C–Cl = 1.76	
				long C–Cl = 2.66		long C–Cl = 2.66	

[a] Calculated for a model having a C–C–C angle of 109° 28′, a C–C–Cl angle of 109° 28′ and a ratio of carbon–chlorine to carbon–carbon distance of 1.76/1.54. [b] Calculated for a model having a C–C–C angle of 111° 30′, a C–C–Cl angle of 107° 30′ and a ratio of carbon–chlorine to carbon–carbon distance of 1.76/1.54.

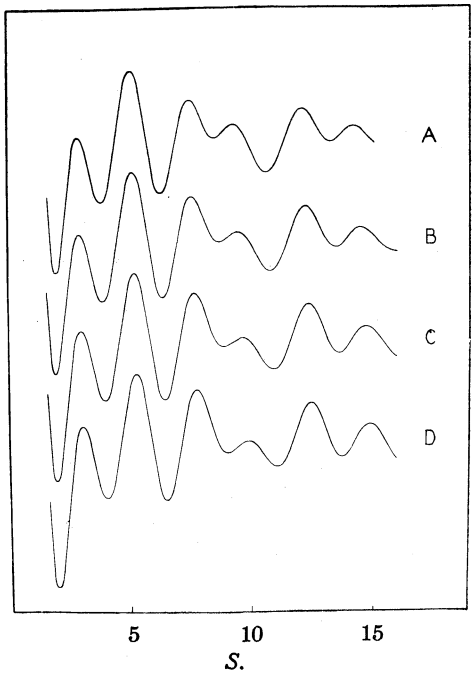


Fig. 5.—Theoretical intensity curves for isopropyl chloride. The C–C–C angle and the C–C–Cl angle, respectively, are: curve A, 107° 30′ and 111° 30′; curve B, 109° 28′ and 109° 28′; curve C, 111° 30′ and 107° 30′; curve D, 113° 30′ and 106°. The ratio of the carbon–chlorine distance to the carbon–carbon distance is 1.76/1.54 for all four curves.

A theoretical intensity curve was first calculated for the model having all tetrahedral angles and a ratio of carbon–chlorine distance to carbon–carbon distance of 1.76/1.54. This curve is in satisfactory qualitative agreement with the photographs and is shown in Fig. 5, curve B. Quantitative comparison of the photographs with this curve is made in Table III. This comparison leads to a carbon–carbon distance of 1.52 Å., 0.02 Å. less than the value we assume to be correct. Quantitative comparison with curves for models having a larger C–C–Cl angle lead to still smaller values for the carbon–carbon distance so these models are discarded. Curve C, Fig. 5, calculated for a model having a C–C–Cl angle of 107° 30′, is in satisfactory qualitative agreement with the photographs. Quantitative comparison is made in Table III. Curve D, Fig. 5, calculated for a model in which the C–C–Cl angle is 106°, is unsatisfactory because the fourth maximum is too low. Models having a ratio of carbon–chlorine distance to carbon–carbon distance much different from 1.76/1.54 are not in satisfactory qualitative agreement with the photographs or lead to values for the carbon–carbon distance different from 1.54.

The results in Table III and the radial distribution function lead to the final results: carbon–chlorine distance, 1.75 ± 0.02 Å.; long carbon–chlorine distance, 2.66 ± 0.03 Å.; C–C–Cl angle 109 ± 3°; C–C–C angle 110 ± 3°.

Isopropyl Bromide.—Eastman Kodak Co. isopropyl bromide was purified by fractional distillation. The photographs possess eight measurable maxima, the seventh being the most difficult to measure. The values of s_0 for the maxima and minima and the intensities of the maxima are given in Table IV. The radial distribution function is shown in Fig. 1, curve D. The large peak at 2.84 Å. represents the long carbon–bromine distance. This peak is not shifted appreciably by the long carbon–carbon distance because the long carbon–bromine distance is of much greater importance in the scattering function. The value calculated for this distance from a tetrahedral bond angle and 1.91 and 1.54 Å. for the carbon–bromine and carbon–carbon bond distances, respectively, is 2.82 Å. The two small peaks at 1.53 and 1.86 Å. represent less reliably the carbon–carbon and carbon–bromine bond distances.

TABLE IV

ISOPROPYL BROMIDE

Values in parentheses not included in the average.

Max.	Min.	I	s_0	s^a	s^a/s_0	s^b	s^b/s_0
1		18	3.00	2.85	(0.950)	2.86	(0.953)
	2		3.94	3.78	(.960)	3.85	(.977)
2		20	5.10	4.88	(.957)	4.95	(.971)
	3		6.03	6.02	.999	6.06	1.005
3		17	7.21	7.16	.993	7.25	1.005
	4		8.24	8.31	1.009	8.42	1.022
4		11	9.64	9.41	0.977	9.55	0.991
	5		10.50	10.47	.997	10.67	1.016
5		4	11.56	11.47	.992	11.68	1.010
	6		12.57	12.54	.996	12.68	1.007
6		7	13.79	13.72	.995	13.83	1.003
7		1	15.77	16.50	(1.047)	16.60	(1.052)
8		1	18.04	18.11	1.004	18.21	1.010
				Average	0.996		1.008
				C–Br = 1.90 Å.		C–Br = 1.93 Å.	
				long C–Br = 2.81 Å.		long C–Br = 2.81 Å.	

[a] Calculated for a model in which the C–C–C angle and the C–C–Br angle are both equal to 109° 28′ and the ratio of the carbon–bromine distance to the carbon–carbon distance is 1.91/1.54. [b] Calculated for a model in which the C–C–C angle and the C–C–Br angle are equal to 111° 30′ and 107° 30′, respectively, and the ratio of the carbon–bromine distance to the carbon–carbon distance is 1.91/1.54.

Theoretical intensity curves were calculated for models in which the C–C–C angle ranged from 107° 30′ to 113° 30′, the C–C–Br angle ranged from 106° to 111° 30′ and the ratio of the carbon–bromine distance to the carbon–carbon distance varied from 1.87/1.54 to 1.95/1.54. Curve A, Fig. 6, is calculated for a model having tetrahedral angles and a ratio of carbon–bromine distance to carbon–carbon distance of 1.91/1.54. This curve is in good qualitative agreement with the photographs and quantitative comparison is made in Table IV. When the C–C–Br angle is decreased below 107° 30′, the seventh maximum becomes too prominent (see curve C, Fig. 6). When this angle is made larger than 111° 30′ the seventh maximum is too low. When the photographs are compared quantitatively with curves for models in which the ratio of the carbon–bromine distance to the carbon–carbon distance is different from 1.91/1.54, a carbon–carbon distance is obtained which differs from the value 1.54. These models are therefore eliminated.

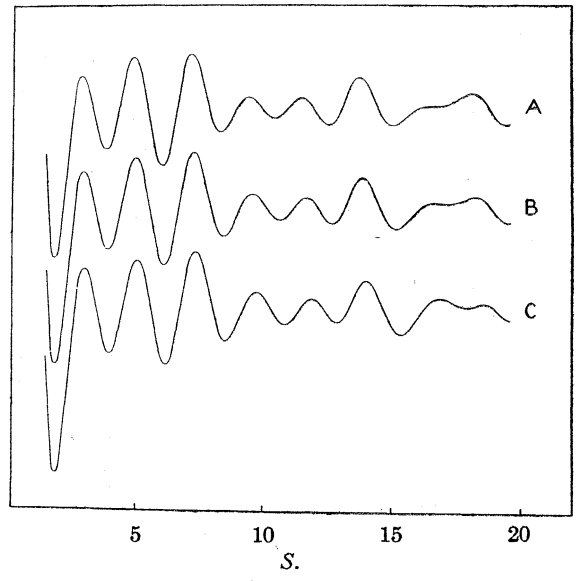


Fig. 6.—Theoretical intensity curves for isopropyl bromide. The C–C–C angle and the C–C–Br angle, respectively, are: curve A, 109° 28′ and 109° 28′; curve B, 111° 30′ and 107° 30′; curve C, 113° 30′ and 106°. The ratio of the carbon–bromine distance to the carbon–carbon distance is 1.91/1.54 for all three curves.

The quantitative comparisons in Table IV and the radial distribution function lead to the final results: carbon–bromine bond distance, 1.91 ± 0.03 Å.; long carbon–bromine distance 2.81 ± 0.03 Å., C–C–C angle, 109° 28′ ± 3°; C–C–Br angle 109° 28′ ± 3°.

Methyl Chloroform.—Eastman Kodak Co. methyl chloroform was purified by fractional distillation. The photographs show eight measurable maxima. The values of s_0 for the maxima and minima and the intensities of the maxima

TABLE V

METHYL CHLOROFORM

Values in parentheses not included in the average.

Max.	Min.	I	s_0	s^a	s^a/s_0
1		16	2.95	2.75	(0.937)
	2		4.05	3.75	(.926)
2		20	5.15	4.91	(.953)
	3		6.27	6.12	.976
3		16	7.34	7.31	1.010
	4		8.38	8.36	0.998
4		12	9.33	9.31	.998
	5		10.57	10.41	.985
5		14	11.50	11.61	1.010
	6		12.83	12.77	0.996
6		7	13.78	13.87	1.006
	7		14.78	14.74	0.997
7		5	15.73	15.76	1.002
	8		16.88	16.95	1.004
8		3	17.91	18.19	1.016
			Average		1.000

C–Cl = 1.76 Å.
Cl–Cl = 2.88 Å.

[a] Calculated for a model having tetrahedral bond angles and a ratio of carbon–chlorine distance to carbon–carbon distance of 1.76/1.54.

are given in Table V. The radial distribution function, shown in Fig. 2, curve A, possesses two large peaks at 1.75 and 2.87 Å. The first peak represents the carbon–chlorine bond distance. The second is due principally to the chlorine–chlorine distance. It is shifted slightly by the long carbon–chlorine distance. If this distance is taken to be 2.70 Å. calculated from a tetrahedral bond angle, a carbon–chlorine distance of 1.76 Å. and a carbon–carbon distance of 1.54, the chlorine–chlorine distance must be about 2.92 Å. This value indicates that the Cl–C–Cl angle is slightly greater than the tetrahedral value. Theoretical intensity curves were calculated for models having a Cl–C–Cl angle of from 109° 28′ to 114° 30′. The ratio of carbon–chlorine distance to carbon–carbon distance was taken to be 1.76/1.54. No attempt was made to determine the movement of the methyl group. The calculated curves are shown in Fig. 7. The 109° 28′ curve is in satisfactory qualitative agreement with the photographs. Quantitative comparison is made in Table V. Curve B is unsatisfactory because the sixth maximum is too low. Curve C is unsatisfactory because it leads to a carbon–carbon distance less than 1.54 Å. The final results for methylchloroform are: carbon–chlorine distance, 1.76 ± 0.02 Å.; chlorine–chlorine distance, 2.89 ± 0.03 Å.; Cl–C–Cl angle, 110 ± 2°.

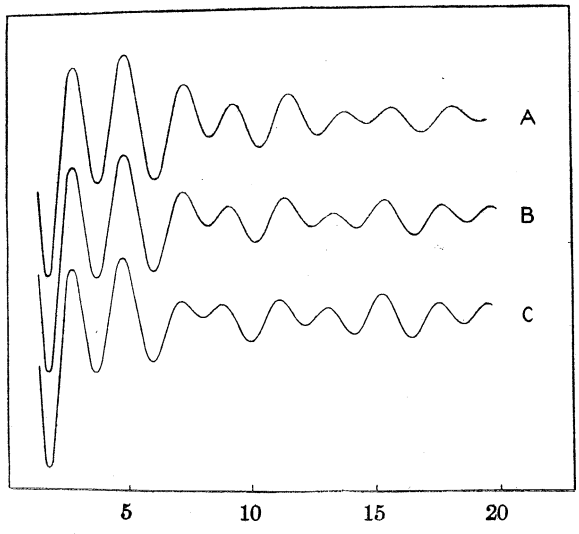


Fig. 7.—Theoretical intensity curves for methyl chloroform. The C–C–Cl angle is: curve A, 109° 28′; curve B, 112°; curve C, 114° 30′. The ratio of the carbon–chlorine distance to the carbon–carbon distance is 1.76/1.54.

Isocrotyl Chloride.—The isocrotyl chloride, $(CH_3)_2CCHCl$, used in this investigation was an Eastman Kodak Co. product which was carefully fractionated in a thirty-inch (76-cm.) distilling column. The photographs show seven maxima, the third being close to the second and difficult to read. An eighth maximum is visible but no reliable measurements could be made on it. The radial distribution function is shown in Fig. 2, curve B. The peak at 1.63 Å. is composed of the carbon–carbon single bond distance and the carbon–chlorine bond distance. If the carbon–carbon single bond distance is assumed to be 1.54 Å. and the observed position of the peak is a weighted mean, then the carbon–chlorine distance is 1.70 Å. The peak at 2.61 Å. consists of the next longer carbon–chlorine distance and the distance between methyl carbon atoms. If the carbon–carbon distance is 2.52 Å. (calculated from a tetrahedral bond angle and a bond distance of 1.54 Å.) the carbon–chlorine distance is 2.64 Å. The peaks at 3.15 and 4.12 Å. represent the two longest carbon–chlorine distances.

In calculating theoretical intensity curves only models were considered which were planar (except for hydrogen atoms) and which had a carbon–carbon single bond distance of 1.54 Å. The methyl groups were assumed to be stationary. Curves were calculated for ten models. The C–C–C angle was varied from 109° 28′ to 112°, the C–C–Cl angle was varied from 125° 16′ to 122° and the ratio of the carbon–chlorine dis-

tance to the carbon–carbon double bond distance was varied from 1.76/1.34 to 1.72/1.34. Some of the calculated curves are shown in Fig. 6. The difficultly measurable third maximum appears, at most, as a shelf, so while it can be included in the radial distribution function it cannot be used in the quantitative comparisons between curves and photographs. Curves A and B are both for models in which the C–C–C angle and the C–C–Cl angle are tetrahedral and the C–C–Cl angle is 125° 16′. The ratio of the carbon–chlorine distance to the carbon–carbon double bond distance is 1.76/1.54 for curve A and 1.72/1.54 for curve B. Both curves are unsatisfactory because the fifth maximum is not sufficiently prominent. Curve C differs from curve B in that the C–C–Cl angle has been decreased to 122°. This curve is in satisfactory qualitative agreement with the photographs. Quantitative comparison is made in Table VI. If the C–C–C angle is increased much above the tetrahedral value, the fifth maximum again becomes too small.

The final results, obtained from Table VI and from the radial distribution function, are: carbon–chlorine bond distance, 1.72 ± 0.02 Å.; C–C–Cl angle, 123 ± 2°; C–C–C angle 111 ± 3°.

TABLE VI

ISOCROTYL CHLORIDE

Values in parentheses not included in the average.

Max.	Min.	I	s_0	s^a	s^a/s_0
1		7	3.23	3.10	(0.960)
	2		4.11	3.86	(.939)
2		12	4.92	5.05	1.026
3		5	6.35	...	...
	4		7.28	6.97	0.957
4		7	8.12	8.06	.993
	5		9.08	9.25	1.019
5		3	10.08	10.47	1.039
	6		11.53	11.40	0.989
6		4	12.55	12.50	.996
	7		13.53	13.62	1.007
7		1	14.45	15.20	1.052
				Average	1.008

C–Cl 1.73 Å.

[a] Calculated for a model having a C–C–C angle of 109° 28′, a C–C–Cl angle of 122° and a ratio of carbon–chlorine distance to carbon–carbon double bond distance of 1.72/1.34.

Discussion

In studying the structure of molecules as complicated as the molecules discussed in this paper it is not possible to determine all of the structure parameters from the electron diffraction data alone. In the case of these molecules we have not attempted to rule out, on the basis of the electron diffraction data, all of the structures bearing no geometrical relation to the conventional chemical structural formula. The number of conceivable (not chemically conceivable) arrangements of, say, ten atoms is tremendous and we have made no attempt to ascertain which non-chemical arrangements, if any, are compatible with the data. In all cases we have assumed that the structure of the molecule was essentially determined by the chemical structural formula, and then proceeded to determine the bond distances and bond angles. We have not attempted to determine the carbon–hydrogen bond distance for in all cases the hydrogen atoms contribute so little to the total electron scattering of the molecule that their positions can be assumed without fear of affecting the other results even though the assumptions are not accurate. We assumed throughout that the carbon–hydrogen bond distance is 1.09 Å., the value found for methane.[11] No attempt was made to determine the orientation of the methyl groups about the carbon–carbon bonds, and in calculating the theoretical intensity curves it was assumed that the hydrogen atoms avoid other atoms and each other as much as possible. Also, we have assumed the value 1.54 Å. for the carbon–carbon single bond distance. This distance is known with certainty from the X-ray study of

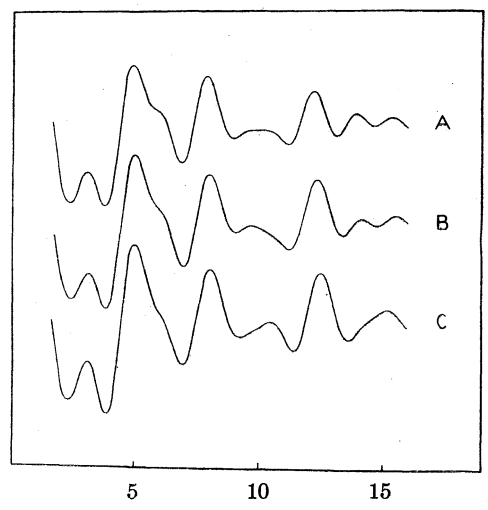


Fig. 8.—Theoretical intensity curves for isocrotyl chloride. The C–C–C angle is 109° 28′ in all three curves. The C–C–Cl angle is 125° 16′ in curves A and B, and 122° in curve C. The ratio of the carbon–chlorine distance to the carbon–carbon double-bond distance is 1.76/1.34 in curve A, and 1.72/1.34 in curves B and C.

(11) Ginsburg and Barker, *J. Chem. Phys.*, **3**, 668 (1935).

diamond[12] and the electron diffraction studies of a large number of saturated hydrocarbons.[13]

The C–C–Cl bond angles in ethyl chloride, isopropyl chloride and *t*-butyl chloride[3] are 111° 30′ ± 2°, 109 ± 3° and 107 ± 2°, respectively. These three values are equal to the tetrahedral angle within the experimental error. However, we believe the trend in angles to be real.

The fact that the C–C–Cl angle in *t*-butyl chloride is less than the tetrahedral value shows that the exchange repulsions and electrostatic repulsions between the methyl groups together with the electrostatic attraction of the chlorine atom for the hydrogen atoms is greater than the steric repulsion between the chlorine atom and the methyl groups. The C–C–Cl angle in methyl chloroform is 109 ± 2°. This molecule is similar to *t*-butyl chloride, the groups attached to the central carbon atom merely being interchanged. Here again the bond angle between unlike groups is less than the tetrahedral value. In both compounds the electrostatic repulsion of like groups and attraction of unlike groups determines the direction of the distortion of the bond angles from the tetrahedral values. The steric repulsions between attached groups in these two molecules must be roughly equal.

The C–C–Br angles in ethyl bromide, isopropyl bromide and *t*-butyl bromide are 109 ± 2°, 109° 28′ ± 3° and 107° 30′ ± 2°. The trend, observed in the case of the chlorides, while present is not pronounced.

The carbon chlorine single bond distance given by the table of covalent radii[13,14] is 1.76 Å. The carbon–chlorine distance observed in methyl chloride[4] is 1.77 ± 0.02 Å. The carbon–chlorine distances observed in ethyl chloride, isopropyl chloride and *t*-butyl chloride[3] are 1.76 ± 0.02 Å., 1.75 ± 0.03 Å. and 1.78 ± 0.03 Å., respectively. In methylchloroform the carbon–chlorine distance is 1.76 ± 0.03 Å. The carbon–chlorine distance in methyl chloride in which zero, one, two or three hydrogen atoms are replaced by methyl groups is found to be in agreement with the value given by the table of covalent radii.

The carbon–bromine distances in methyl bromide,[5] ethyl bromide, isopropyl bromide and *t*-butyl bromide are 1.91 ± 0.06 Å., 1.91 ± 0.02 Å., 1.91 ± 0.03 Å. and 1.92 ± 0.03 Å. The value given by the table of covalent radii for this distance is 1.91 Å. Here, as in the case of the chlorides, complete agreement is found.

In isocrotyl chloride, $(CH_3)_2CCHCl$, we have assumed the carbon–carbon single bond distance to be 1.54 Å., the value given by the table of covalent radii,[13,14] and found to obtain in isobutene.[13] The carbon–carbon double bond distance was assumed to be 1.34 Å., the value given by the table of covalent radii and found in ethylene[13] and allene.[13] The carbon–hydrogen bond distance was assumed to be 1.09 Å., the methane[11] value. The carbon–chlorine distance was found to be 1.72 ± 0.02 Å. The difference of 0.04 Å. between this value and the value found for the compounds discussed above is very probably real and is in fact not surprising. The effect of an adjacent double bond on a carbon–chlorine bond distance already has been observed. It was found in the case of the chloroethylenes[6] that the carbon–chlorine bond distance is less than the normal value; the shortening is greatest in the case of vinyl chloride and decreases as the number of chlorine atoms is increased. The shortening in isocrotyl chloride, 0.04 Å., is not so great as in vinyl chloride, 0.08 Å. As both compounds have one atom adjacent to the double bond this is at first surprising. The shortening in isocrotyl chloride is about the same as the shortening in trichloroethylene. The presence of two methyl groups decreases the shortening approximately as much as two chlorine atoms. This shows that there is some conjugation of the carbon–carbon single bonds with the double bond, decreasing the shortening in isocrotyl chloride to about the same extent that the additional chlorine atoms decrease the shortening in trichloroethylene. This conjugation will have some effect on the carbon–carbon single bond distance which we assumed to be 1.54 Å. The shortening of a single bond adjacent to a triple bond has been observed in methylacetylene[15,16] to be 0.08 Å. The shortening of a carbon–carbon single bond adjacent to a benzene ring is negligible. The carbon–carbon single bond distance in hexamethylbenzene is 1.53 Å.[17] We would, therefore, estimate the carbon–carbon single bond distance in isocrotyl chloride to be between 1.51 and 1.53 Å.

(12) "Strukturbericht."

(13) L. Pauling and L. O. Brockway, THIS JOURNAL, **59**, 1223 (1937).

(14) L. Pauling and M. L. Huggins, *Z. Krist.*, **87A**, 205 (1934).

(15) L. Pauling, H. D. Springall and K. J. Palmer, THIS JOURNAL, **61**, 927 (1939).

(16) G. Herzberg, F. Patat and H. Verleger, *J. Phys. Chem.*, **41**, 123 (1937).

(17) L. O. Brockway, paper presented to the American Chemical Society at Baltimore, Md., April, 1939.

This will not affect materially the carbon–chlorine distance of 1.72 Å. we obtained assuming 1.54 Å.

Of the compounds discussed in this paper only ethyl chloride and ethyl bromide have been studied previously by the electron diffraction method.[18] The results were: 1.81 ± 0.1 Å. for the carbon–chlorine distance in ethyl chloride and 2.07 ± 0.07 Å. for the carbon–bromine distance in ethyl bromide. Both of these values are somewhat higher than the values reported by us. We believe our values to be more reliable because of the advances which have been made in electron diffraction technique since the other work was done.

Summary

Electron diffraction has been used to determine the molecular structures of ethyl chloride, ethyl bromide, isopropyl chloride, isopropyl bromide, methyl chloroform and isocrotyl chloride. The results are given in Table VII.

TABLE VII

Compound	C–Cl distance, Å.	C–C–Cl angle
Ethyl chloride	1.76 ± 0.02	111° 30′ ± 2°
Isopropyl chloride	1.75 ± 0.03	109 ± 3°
	C–Br	C–C–Br
Ethyl bromide	1.91 ± 0.02	109 ± 2°
Isopropyl bromide	1.91 ± 0.03	109° 28′ ± 3°
	C–Cl	C–C–Cl
Methylchloroform	1.76 ± 0.02	109 ± 2°
Isocrotyl chloride	1.72 ± 0.02	123 ± 2°

PRINCETON, NEW JERSEY RECEIVED JULY 28, 1939

(18) L. Bru, *Anal. soc. espan. fis. quim.*, **31**, 115 (1933).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE UNIVERSITY OF NORTH CAROLINA]

The Constitution of Natural Tannins. VI.[1] Coloring Matters Derived from 2,5-Dihydroxyacetophenone

BY ALFRED RUSSELL AND SAMUEL FRIEND CLARK[2]

The material already reported includes a description of polyhydroxychalcones derived from various 2-hydroxy ketones (notably resacetophenone, phloracetophenone, and gallacetophenone) and hydroxyaldehydes (notably protocatechualdehyde, vanillin, *m*-hydroxybenzaldehyde, and *p*-hydroxybenzaldehyde). By reduction of these 2′-hydroxychalcones with zinc dust and dilute alcoholic acids are obtained light colored amorphous products; when these amorphous products are water-soluble (those derived from protocatechualdehyde only), they are qualitatively indistinguishable from natural phlobatannins. On various grounds it is probable that the amorphous products are flavopinacols hydroxylated on the patterns of the parent chalcones; for the sake of simplicity they are formulated as of the *bis* type, although their structure may be more complicated.

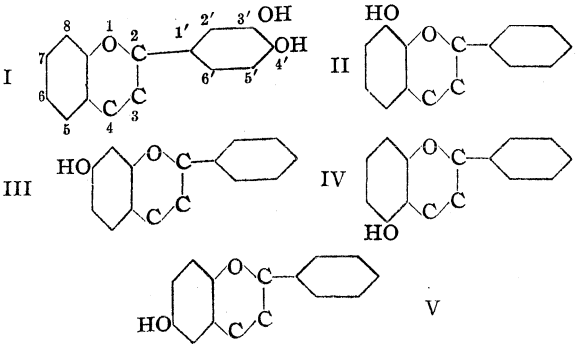
To continue the series so far described, polyhydroxychalcones derived from the various hydroxyaldehydes with three other hydroxy ketones should be examined; these ketones are the dihydroxyacetophenones, 2,3-, 2,6- and 2,5-. The reason for selecting 2,3-dihydroxyacetophenone is the frequent occurrence of catechol as a fission product of natural materials, it not being at all certain that this always comes from a benzopyran compound hydroxylated in the 3′,4′-positions (I)—an hydroxyl group may in some cases be located in the 8-position (II) (the second one ortho to the first appearing after fission). 2,6-Dihydroxyacetophenone must be included because of the frequent occurrence of resorcinol, not necessarily resulting from a compound hydroxylated in the 7-position (III) but possibly from a compound hydroxylated in the 5-position (IV). 2,5-Dihydroxyacetophenone is selected because of the occasional occurrence of quinol as a decomposition product of natural materials, suggesting a benzopyran compound hydroxylated in the 6-position (V). In particular, the monomethyl ether of quinacetophenone has been isolated as a decomposition product of a yellow coloring matter from a European variety of stemless primrose.[3] Moreover, Nierenstein[4] has reported finding quinol amongst the decomposition products of quebracho tannin.

(1) The present paper forms a continuation of a series of five articles published in the Journal of the Chemical Society; Russell and co-workers, *J. Chem. Soc.*, 218, 1066, 1506, 1940 (1934); 421 (1937); cf. also Russell, *Chem. Rev.*, **17**, 155 (1935).

(2) From a dissertation submitted to the Faculty of the University of North Carolina in partial fulfilment of the requirements for the degree of Doctor of Philosophy, June, 1939.

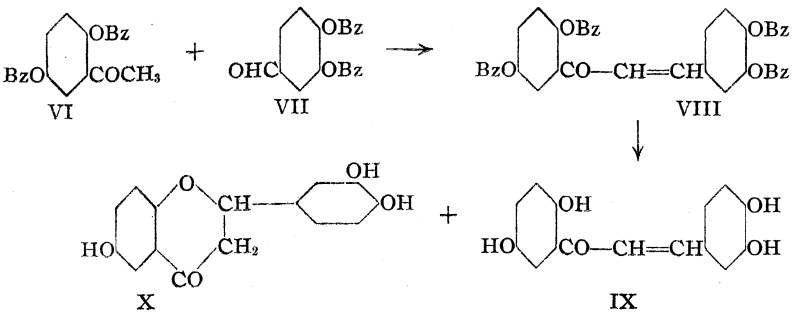
(3) Goris and Canal, *Compt. rend.*, **200**, 1990 (1935).

(4) Nierenstein, *Collegium*, 65 (1905).



I II III IV V

There are now described syntheses of polyhydroxychalcones,[5] flavanones, and anthocyanidins derived from 2,5-dihydroxyacetophenone (quinacetophenone) and various hydroxyaldehydes. The anthocyanidins are of the luteolinidin type,

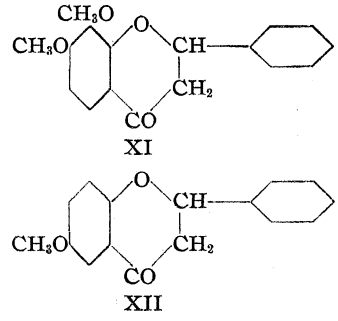


VI VII VIII IX X

containing no hydroxyl group in the 3-position. There is also included a qualitative comparison of the amorphous reduction product of 3,4,2′,5′-tetrahydroxychalcone—*bis*-(6,3′,4′-trihydroxy)-flavopinacol—with natural hemlock and mimosa tannins in aqueous solution.

The synthesis of a typical stable polyhydroxychalcone may be outlined first. Quinacetophenone dibenzoate (VI) was condensed with protocatechualdehyde dibenzoate (VII) in solution of dry ethyl acetate using anhydrous hydrogen chloride to give 3,4,2′,5′-tetrabenzoyloxychalcone (VIII). This, by debenzoylation with alcoholic potassium hydroxide, gave 3,4,2′,5′-tetrahydroxychalcone (IX) and 6,3′,4′-trihydroxyflavanone (X). The chalcone is stable in the sense of remaining unchanged by ordinary laboratory treatment of the dry solid. However, an easy equilibrium exists between the flavanone and chalcone in dilute alcoholic solution, the formation of the flavanone being favored at higher temperatures. This made the task of isolating a pure sample of the chalcone extremely difficult.

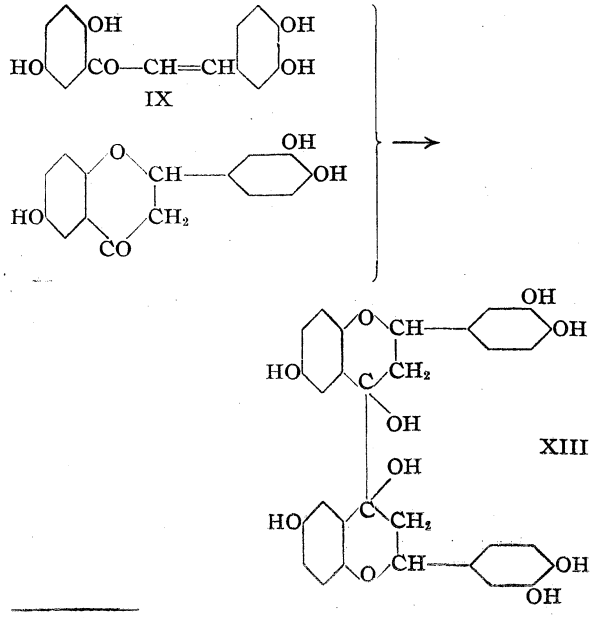
The ready formation of flavanone has been noted by v. Kostanecki,[6] who has isolated flavanone to the exclusion of chalcone in two cases (XI and XII). Further, it is in concordance with



XI XII

the suggestion of Wheeler[7] that this process of making polyhydroxychalcones might, in some instances, give rise to some quantity of flavanone.

Reduction of pure 6,3′,4′-trihydroxyflavanone (X), or of a mixture of flavanone and 3,4,2′,5′-tetrahydroxychalcone (IX) consisting mostly of the latter, with zinc dust and alcoholic hydrochloric acid, gave an amorphous light red material—*bis*-(6,3′,4′-trihydroxy)-flavopinacol (XIII).



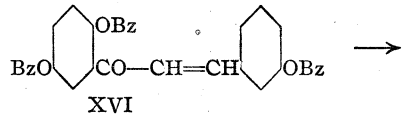
IX XIII

(5) The numbering system used for the hydroxychalcones is that of *Chemical Abstracts*, following the original system of v. Kostanecki. The benzene ring nearer the carbonyl group bears the prime numbers. It is to be noted that this is contrary to the English system of the *British Chemical Abstracts* and the *Journal of the Chemical Society*.

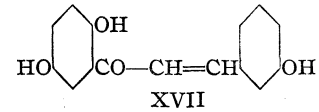
(6) Woker, v. Kostanecki and Tambor, *Ber.*, **36**, 4235 (1903); v. Kostanecki and Lampe, *ibid.*, **37**, 773 (1904).

(7) Nadkarni and Wheeler, *J. Chem. Soc.*, 1320 (1938).

Similarly to the above-described synthesis of a polybenzoyloxychalcone, the preparation of seven other polybenzoyloxychalcones was accomplished. These were 4,2′,5′-tribenzoyloxychalcone (XIV) from *p*-hydroxybenzaldehyde, 3,2′,5′-tribenzoyloxychalcone (XVI) from *m*-hydroxybenzaldehyde, 4,2′,5′-tribenzoyl-oxy-3-methoxychalcone (XIX), vanillin, 2,2′,5′-tribenzoyloxychalcone (XXI) from salicylaldehyde, 2,4,2′,5′ - tetrabenzoyloxychalcone (XXV) from resorcylaldehyde, 2,4,2′,5′-tetrabenzoyloxy-6-methylchalcone (XXVIII) from orcylaldehyde, and 2,4,6,2′,5′-pentabenzoyloxychalcone (XXXI) from phloroglucinaldehyde. With the exception of the last one, which is an oil, the polybenzoyloxychalcones are pale yellow, difficultly crystalline and without sharp melting points.



XVI



XVII

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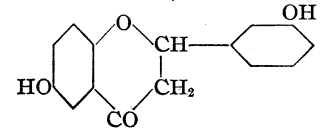
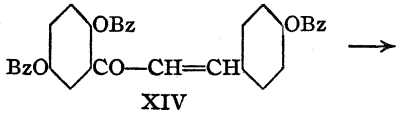


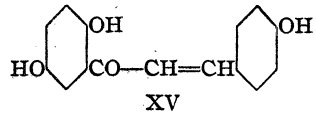
XVIII

Considerable difficulty was experienced in effecting debenzoylation of the polybenzoyloxychalcones without causing fission of the products to initial materials. Even under the mild conditions of saponification finally adopted, the product required was always accompanied by some quantity of quinacetophenone (the hydroxyaldehydes are more soluble and do not appear). This is evidenced by the fact that, although the yield of polybenzoyloxychalcone was upward of 70% of the theoretical, the actual yield of polyhydroxychalcone and other products by hydrolysis in many cases was below 40% of the theoretical. It is clear that the polyhydroxychalcones hydroxylated on the 2′,5′-pattern are particularly sensitive to alkaline fission. Thus, the results were so varied as to necessitate separate description.

The synthesis of 4,2′,5′-trihydroxychalcone (XV) proceeded comparatively smoothly with some accompanying quinacetophenone, but no flavanone.



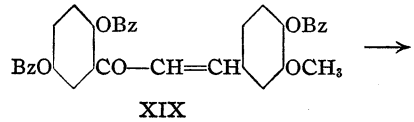
XIV



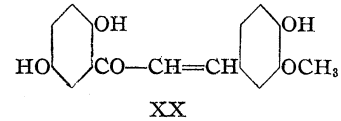
XV

The synthesis of 3,2′,5′-trihydroxychalcone (XVII) furnished some difficulty, because the chalcone was accompanied by quinacetophenone and almost an equal quantity of 6,3′-dihydroxyflavanone (XVIII). The equilibrium between chalcone and flavanone was more evenly balanced in this instance than in that first described (IX and X); consequently, the separation of the two substances by fractional crystallization from dilute alcohol was comparatively easy.

4,2′,5′-Trihydroxy-3-methoxychalcone (XX) was prepared with some accompanying decomposition. In this case the benzoyloxychalcone more stubbornly resisted the action of alkali and was recovered in part. No flavanone could be found, although it appears probable that repetition of the synthesis here or in the case of 4,2′,5′-trihydroxychalcone might yield some quantity of flavanone.



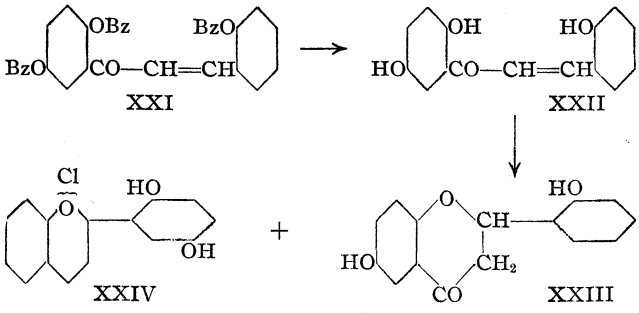
XIX



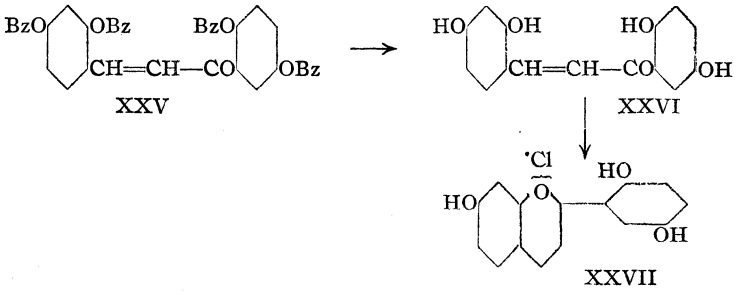
XX

In those cases where the liberated hydroxychalcone had an hydroxyl group in the 2-position, acidification of the alkaline solution after debenzoylation caused cyclization to the anthocyanidin. Thus, 2,2′,5′-trihydroxychalcone (XXII) gave 2′,5′-dihydroxy-2-phenylbenzopyrylium chloride (XXIV) on boiling with 10% hydrochloric acid. The accompanying production of 6,2′-dihydroxyflavanone (XXIII) in considerable quantity was noted. It is believed to be a rare occurrence for a flavanone to be formed in competition with an anthocyanidin.

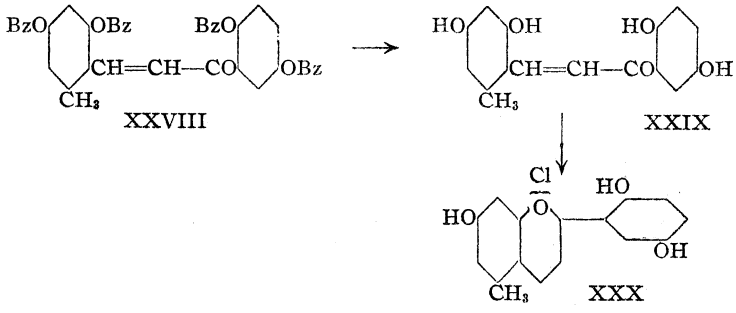
The benzoyloxychalcone (XXV) from resorcylaldehyde was converted to the anthocyanidin—7,2′,5′-trihydroxy-2-phenylbenzopyrylium chlo-



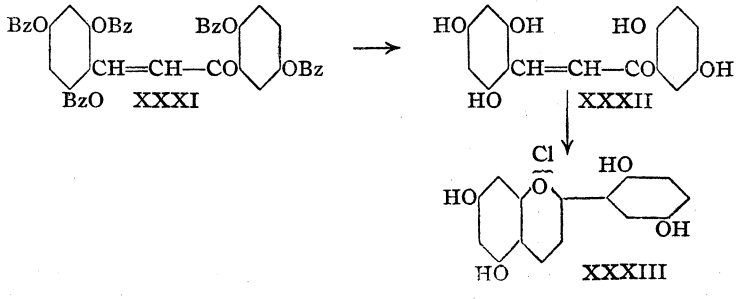
ride (XXVII)—through the intermediate hydroxychalcone (XXVI).



Similarly, the benzoyloxychalcone (XXVIII) from orcylaldehyde was converted to 7,2′,5′-trihydroxy-5-methyl-2-phenylbenzopyrylium chloride (XXX).



Finally, the synthesis of 5,7,2′,5′-tetrahydroxy-2-phenylbenzopyrylium chloride (XXXIII) was accomplished from the benzoyloxychalcone (XXXI). Some difficulty was experienced in isolating this substance due to the usual decomposition and its appreciable water solubility.



The polyhydroxychalcones are various shades of orange, the color deepening as the number of hydroxyl groups increases, and are definitely crystalline with sharp melting points. The anthocyanidins are red in color and are associated with water of crystallization, as R. Robinson[8] previously has noted in other instances. The flavanones are white crystalline substances with a faint yellowish tinge. The flavopinacol is a light red amorphous powder that is difficult to dry and retains traces of solvents with great obstinacy—its analysis was not attempted.

In view of the relationship between chalcone and flavanone exhibited in the present work, it may be that such a relationship exists in other series. For example, Kurth[9] has reported the synthesis of yellow 3,4,2′,3′,4′ - pentahydroxychalcone, m. p. 249°, by the action of cold alkali on gallacetophenone and protocatechualdehyde, followed by acidification and crystallization from dilute alcohol. This substance was previously reported by Russell[2] as a deep orange material, m. p. 233°. Since the color of polyhydroxychalcones deepens (yellow-deep orange) as the number of hydroxyl groups increases, it is possible that Kurth's product is the corresponding flavanone. Moreover, the fact that it gave a pentabenzoate is not relevant evidence that it is a pentahydroxychalcone, as many instances are on record[10] where acylation of hydroxyflavanones produced the fully acylated chalcones corresponding.

The table below gives a qualitative comparison, by means of various reagents, of *bis*-(6,3′,4′-trihydroxy)-flavopinacol with natural hemlock and mimosa tannins, using approximately 1% aqueous solutions. It will be seen that the resemblance is very close.

Experimental

Quinacetophenone.—This ketone was prepared more than twenty times. A typi-

(8) *Cf.* Irvine and Robinson, *J. Chem. Soc.*, 2091 (1927).

(9) Kurth, THIS JOURNAL, **61**, 861 (1939).

(10) *Cf.* Asahina, Shinoda and Inubuse, *J. Pharm. Soc. Japan*, **48**, 207 (1928); *C. A.*, **22**, 2946 (1928), for discussion.

TABLE I

Reagent	*bis*-(6,3′,4′-Trihydroxyflavopinacol)	Hemlock tannin	Mimosa tannin
Alcoholic $FeCl_3$	Dark green color	Dark green color	Dark blue-violet color
Aqueous $FeCl_3$	Dark green color; dark ppt.	Dark green color; dark ppt.	Dark blue-violet color; dark ppt.
Gelatin	Dirty white ppt.	Dirty white ppt.	Dirty white ppt.
Lead acetate	Light colored ppt. soluble in acetic acid	Light colored ppt. soluble in acetic acid	Light colored ppt. soluble in acetic acid
Boiling dil. HCl (phlobaphene reaction)	Solution reddens slowly and red-brown ppt. separates	Solution reddens slowly and red ppt. separates	Solution reddens slowly and red ppt. separates
Bromine water	Immediate heavy yellow ppt.	Immediate heavy yellow ppt.	Immediate heavy orange ppt.
Calcium hydroxide	Faint green ppt. with blue-violet fluorescence	Pink color; faint pink ppt.	Violet color; faint violet ppt.
Sodium sulfite	Yellow color	Pink color	Pink color
HCHO + HCl	Ppt. on warming	Ppt. on warming	Ppt. on warming
Nitrous acid	Immediate brown ppt.	Immediate brown ppt.	Immediate brown ppt.
Copper sulfate	No change in color; addition of NH_3 gives dark ppt.	Faint green color; addn. of NH_3 gives heavy dark ppt.	Faint green color; addn. of NH_3 gives heavy dark ppt.
Aqueous NH_3	Solution darkens slowly	Solution darkens slowly	Solution darkens slowly
Potassium dichromate	Brown precipitate	Brown precipitate	Brown precipitate
Potassium ferricyanide	Yellow-orange color, turning orange-brown on NH_3 addition	Orange-red on NH_3 addition	Orange-red on NH_3 addition
Hide powder	Absorbed quantitatively	Absorbed quantitatively	Absorbed quantitatively

cal run is cited. Quinol (100 g.) was dissolved in boiling glacial acetic acid (200 cc.). Freshly fused zinc chloride (400 g.) was added, and the mixture refluxed for an hour. The temperature rose to 150–165°, and the solution became dark red. At the end of the reflux period the solution was poured into ice water. The precipitated crude quinacetophenone was recrystallized from dilute alcohol with several charcoal treatments. Quinacetophenone crystallized in greenish-yellow plates, m. p. 200–201°. The yield averaged 20–25%, being rather low due to the necessity of heavy charcoaling to free the ketone from colored material.

Preparation of Aldehydes.—Protocatechualdehyde was prepared by the method of Pauly[11] from piperonal. Resorcylaldehyde, orcylaldehyde, and phloroglucinaldehyde were prepared by the Adams modification[12] of the Gattermann reaction, using the corresponding phenol, zinc cyanide, and dry hydrogen chloride in ice-cold ether solution. Vanillin, salicylaldehyde, *p*-hydroxybenzaldehyde, and *m*-hydroxybenzaldehyde were the best Eastman Kodak Co. grade.

Preparation of Benzoates.—The same method was employed for all benzoates. The ketone or aldehyde (0.3 mole) was dissolved in pyridine (150 cc.) and benzoyl chloride in 10–15% excess of that required to benzoylate all hydroxy groups was added with shaking over a period of ten minutes. The mixture was warmed on the steam-bath for twenty to thirty minutes and then set aside overnight at room temperature. The mixture was poured into cold water (1500 cc.) and stirred until the benzoate solidified. It was usually tan to light brown in color. The crude material was washed thoroughly with water and finally with dilute hydrochloric acid. It was then recrystallized from alcohol (charcoal) and dried in the air. The yields were in the range 65–90%, depending on the purity of the initial material. The benzoates were all colorless, although quinacetophenone dibenzoate was difficult to obtain free from yellow coloration.

TABLE II

Benzoate	M. p., °C.	% yield
Quinacetophenone	113	88
p-Hydroxybenzaldehyde	89	81
m-Hydroxybenzaldehyde	37–38	65
o-Hydroxybenzaldehyde	B. p. 208 (15 mm.)	60
Vanillin	97	73
Protocatechualdehyde	75	78
Resorcylaldehyde	98	85
Orcylaldehyde	134–135	82
Phloroglucinaldehyde	130	46

***m*-Benzoyloxybenzaldehyde.**—This benzoate apparently has not been reported before. It melted at a rather low temperature, which necessitated dissolving it in alcohol at room temperature and immersing the solution in a freezing mixture of salt and ice to induce crystallization. It crystallized in colorless prismatic needles, m. p. 37–38°.

Anal. Calcd. for $C_{14}H_{10}O_3$: C, 74.3; H, 4.5. Found: C, 74.2; H, 4.5.

Resorcylaldehyde Dibenzoate.—This benzoate has not been reported previously. It crystallized from alcohol in clusters of colorless prismatic needles, m. p. 98°. *Anal.* Calcd. for $C_{21}H_{14}O_5$: C, 72.8; H, 4.1. Found: C, 72.5; H, 4.1.

Orcylaldehyde Dibenzoate.—This benzoate has not been reported previously. It crystallized from alcohol as a mass of white felted needles, m. p. 134–135°. *Anal.* Calcd. for $C_{22}H_{16}O_5$: C, 73.3; H, 4.5. Found: C, 73.1; H, 4.5.

General Method for Benzoyloxychalcones.—Quinacetophenone dibenzoate (0.07 mole) and the aldehyde benzoate (0.07 mole) were dissolved in anhydrous ethyl acetate (350–400 cc.) (dried over calcium chloride, distilled, and stored over sodium sulfate). Dry hydrogen chloride was passed in for two to five days at ice temperatures. The

(11) Pauly, *Ber.*, **40**, 3098 (1907).

(12) Adams and Levine, THIS JOURNAL, **45**, 2373 (1923).

solution turned in color from a pale yellow to a clear dark red. When the solution had been thoroughly saturated for at least a day, it was evaporated on the steam-bath to a thick red sirup. On triturating with cold alcohol, the material usually hardened after ten minutes. It was boiled with alcohol (100 cc.) to remove initial materials, cooled to room temperature, and the alcohol decanted. The material was considered sufficiently pure for conversion to the free hydroxychalcone. For analysis a sample of the benzoyloxychalcone was recrystallized from alcohol, in which it was difficultly soluble.

It had been found previously[1] that benzoyloxychalcones retained alcohol rather tenaciously, which tended to disturb the analytical results. The benzoyloxychalcones were dried in a vacuum desiccator over sodium hydroxide for several days at room temperature. The analytical results were in rather good agreement with the calculated values, considering the nature of the substances.

General Method for Hydroxychalcones.—The preparation of the free hydroxychalcones from the benzoyloxychalcones constituted an unexpected and stubborn problem. The debenzoylation of benzoyloxychalcones derived from resacetophenone and phloracetophenone proceeded smoothly under the conditions previously described.[1] Repetition of this work in the case of 4,2′,4′-trihydroxychalcone and 4,2′,4′-trihydroxy-3-methoxychalcone gave the expected results without difficulty. The method of debenzoylation involved solution of the benzoyloxychalcone in acetone, replacement of acetone by alcohol, slow addition under nitrogen of an aqueous solution of twice the theoretical quantity of potassium hydroxide, distillation of the alcohol over a period of three to four hours, cooling, and finally acidification of the solution to precipitate the hydroxychalcone.

When this method was applied to representative benzoyloxychalcones in the quinacetophenone series, hydrolytic fission of the molecule occurred at the double bond, and quinacetophenone appeared on acidification. The aldehydes were soluble and did not appear. Numerous modifications of the procedure were tried with the view to decreasing the extent of fission at the double bond. It was thought that the excess of potassium hydroxide together with the extended heating period were responsible for the decomposition. (The heating period was quite long due to the large amount of alcohol required to dissolve the benzoyloxychalcones, which seem more insoluble than those of other series.) Accordingly, the following scheme finally was worked out.

The benzoyloxychalcone from the above preparation was introduced into a 3-necked, 1-liter flask, so placed in a steam-bath that most of the surface could be heated directly by the live steam. The small necks of the flask were fitted with a dropping funnel and a tube bent downward for distillation. The large neck bore a mercury-seal stirrer and a gas inlet tube. Alcohol (500–600 cc.) was added and brought to boiling with mechanical stirring under an atmosphere of nitrogen. No attempt was made to dissolve the benzoyloxychalcone completely. An aqueous solution of potassium hydroxide (1 g. excess over requisite theoretical quantity in 200 cc. of water) was added over a period of forty to sixty minutes to the boiling solution. The color turned from a pale yellow to a dark red, and all suspended matter disappeared. Distillation of the alcohol was continued for an hour longer until the original volume was collected.

The solution was then chilled in an ice-bath and acidified with dilute sulfuric acid (20 cc. of concd. acid in 50 cc. of water). The precipitated chalcone and benzoic acid were filtered off and washed with cold water. Separation of the benzoic acid was effected either with cold sodium bicarbonate solution or with hot benzene in a Soxhlet. The specific method employed is described in each case below. The resulting hydroxychalcone contained quinacetophenone and in certain instances flavanone. These were separated by fractional crystallization from dilute alcoholic solutions, the quinacetophenone being more soluble than the hydroxychalcone and the flavanone less soluble. Due to the apparently unavoidable decomposition and to the tedious separation required, the yields (calculated on the basis of quinacetophenone dibenzoate) were much lower than those previously reported.[2]

4,2′,5′-Tribenzoyloxychalcone.—Quinacetophenone dibenzoate (0.07 mole) and *p*-benzoyloxybenzaldehyde (0.07 mole) were converted to the benzoyloxychalcone, a pale yellow semi-crystalline solid, m. p. 134–136°. The yield was 31 g. (78%). *Anal.* Calcd. for $C_{36}H_{24}O_7$: C, 76.0; H, 4.3. Found: C, 75.3; H, 4.5.

4,2′,5′-Trihydroxychalcone.—The benzoyloxychalcone (31 g.) was debenzoylated as described above. The hydroxychalcone was separated from benzoic acid by extraction of the latter with cold dilute sodium bicarbonate solution (12 g. sodium carbonate in 200 cc. of water saturated with carbon dioxide). The chalcone was filtered, washed with cold water, and recrystallized from 35% alcohol (600 cc.). The yield was 10 g. (56%). The crystals were orange-yellow prismatic needles, m. p. 222–224°. *Anal.* Calcd. for $C_{15}H_{12}O_4$: C, 70.3; H, 4.7. Found: C, 70.3; H, 4.8. No trace of flavanone could be found.

3,2′,5′ - Tribenzoyloxychalcone.—Quinacetophenone dibenzoate (0.07 mole) and *m*-benzoyloxybenzaldehyde (0.07 mole) were converted to the benzoyloxychalcone, a light yellow semi-crystalline solid, m. p. 174–175°. The yield was 27 g. (67%). *Anal.* Calcd. for $C_{36}H_{24}O_7$: C, 76.0; H, 4.3. Found: C, 75.6; H, 4.4.

3,2′,5′-Trihydroxychalcone.—The benzoyloxychalcone (27 g.) was debenzoylated as described above. The hydroxychalcone was separated from benzoic acid by extraction of the latter with cold dilute sodium bicarbonate solution (12 g. sodium carbonate in 250 cc. of water saturated with carbon dioxide). The chalcone was filtered and washed with cold water. The product proved to be a mixture, containing quinacetophenone, chalcone, and flavanone. The chalcone was finally separated by fractional crystallization from 20% alcohol as orange needles, m. p. 204–206°. The yield was 3.5 g. (20%). *Anal.* Calcd. for $C_{15}H_{12}O_4$: C, 70.3; H, 4.7. Found: C, 70.2; H, 4.8.

6,3′-Dihydroxyflavanone.—The flavanone was separated from the corresponding chalcone by fractional crystallization. It was finally crystallized in colorless needles, having faint yellow coloration, m. p. 234–236°, from 70% alcohol (charcoal). The yield was 2.0 g. (12%). *Anal.* Calcd. for $C_{15}H_{12}O_4$: C, 70.3; H, 4.7. Found: C, 70.4; H, 4.9.

4,2',5' - Tribenzoyloxy - 3 - methoxychalcone.—Quinacetophenone dibenzoate (0.07 mole) and vanillin benzoate (0.07 mole) were converted to the benzoyloxychalcone, a pale yellow semi-crystalline solid, m. p. 145–147°. The yield was 37 g. (88%).

Anal. Calcd. for $C_{38}H_{26}O_8$: C, 74.2; H, 4.4. Found: C, 74.1; H, 4.5.

4,2',5'-Trihydroxy-3-methoxychalcone.—The benzoyloxychalcone was debenzoylated as described above. The hydroxychalcone was separated from benzoic acid by extraction of the latter with cold dilute sodium bicarbonate solution (12 g. sodium carbonate in 250 cc. of water saturated with carbon dioxide). The chalcone was dissolved in dilute alcohol and filtered. The residue was unconverted benzoyloxychalcone (10 g.). The hydroxychalcone crystallized in dark orange needles, m. p. 172–173°. The yield was 5 g. (46%). *Anal.* Calcd. for $C_{16}H_{14}O_5$: C, 67.1; H, 4.9. Found: C, 67.1; H, 5.0. No trace of flavanone could be found.

3,4,2',5' - Tetrabenzoyloxychalcone.—Quinacetophenone dibenzoate (0.14 mole) and protocatechualdehyde dibenzoate (0.14 mole) were converted to the benzoyloxychalcone, a pale yellow semi-crystalline solid, m. p. 182–184°. The yield was 75 g. (78%). *Anal.* Calcd. for $C_{43}H_{28}O_9$: C, 75.0; H, 4.1. Found: C, 74.7; H, 4.2.

3,4,2',5'-Tetrahydroxychalcone.—The benzoyloxychalcone was debenzoylated as described above. The chalcone was separated from benzoic acid by extraction of the latter with hot benzene in a Soxhlet. (The 3,4-dihydroxy grouping increases the water solubility of the chalcone to the point where the sodium bicarbonate solution would dissolve an appreciable amount. Since the benzene solubility is at the same time decreased, this method of separation was used successfully.) The crude material was recrystallized from dilute alcohol (1 liter). The recrystallized product obtained weighed 25 g. (66%). However, it was found to be a mixture of chalcone and flavanone. Attempted fractional crystallization from dilute alcohol seemed to establish the equilibrium between chalcone and flavanone in favor of the latter. Consequently, only a small amount of pure chalcone (less than a gram) was obtained. It crystallized in dark orange micro-crystals, m. p. 225–227°. *Anal.* Calcd. for $C_{15}H_{12}O_5$: C, 66.1; H, 4.5. Found: C, 65.8; H, 4.6.

6,3',4'-Trihydroxyflavanone.—The flavanone was separated from the chalcone by fractional crystallization and finally by the action of charcoal. It crystallized in a mass of white felted needles with a slight yellowish tinge, m. p. 218–220° (dec.). *Anal.* Calcd. for $C_{15}H_{12}O_5$: C, 66.1; H, 4.5. Found: C, 66.1; H, 4.5.

2,2',5'-Tribenzoyloxychalcone.—Quinacetophenone dibenzoate (0.07 mole) and salicylaldehyde benzoate (0.07 mole) were converted to the benzoyloxychalcone, a bright yellow semi-crystalline solid, m. p. 137–139°. The yield was 32.5 g. (82%). *Anal.* Calcd. for $C_{36}H_{24}O_7$: C, 76.0; H, 4.3. Found: C, 75.6; H, 4.3.

2',5'-Dihydroxy-2-phenylbenzopyrylium Chloride.—The benzoyloxychalcone (27.5 g.) was debenzoylated as described above. The free hydroxychalcone was precipitated with hydrochloric acid and separated from benzoic acid by extraction of the latter with cold dilute sodium bicarbonate solution (11 g. of sodium carbonate in 150 cc. water saturated with carbon dioxide). The resulting material was recrystallized from 10% alcoholic hydrochloric acid, separation from a considerable quantity of quinacetophenone being effected. The recrystallized product (3.5 g.) proved to consist of chalcone, flavanone, and a very small quantity of anthocyanidin. The anthocyanidin was separated from the chalcone and flavanone by extraction of the latter two substances with ether in which the salt was not soluble. The anthocyanidin (less than 1 g.) formed a reddish micro-crystalline powder, m. p. 175° (dec.). *Anal.* Calcd. for $C_{15}H_{11}O_3Cl \cdot {}^1/_2H_2O$: Cl, 12.5. Found: Cl, 12.6. It gave a red solution in acid and a blue solution in sodium carbonate.

6,2'-Dihydroxyflavanone.—This substance, separated from the colored material as described above, was recrystallized from dilute alcohol. It apparently is formed in preference to the anthocyanidin. It crystallized in very pale yellow prismatic needles, m. p. 178–180° (dec.). *Anal.* Calcd. for $C_{15}H_{12}O_4 \cdot H_2O$: C, 65.8; H, 5.1. Found: C, 66.2; H, 5.1. No attempt was made to isolate the chalcone of which only a trace was present.

2,4,2',5'-Tetrabenzoyloxychalcone.—Quinacetophenone dibenzoate (0.07 mole) and resorcylaldehyde dibenzoate (0.07 mole) were converted to the benzoyloxychalcone, a yellow crystalline solid, m. p. 137–139°. The yield was 39 g. (81%). *Anal.* Calcd. for $C_{43}H_{28}O_9$: C, 75.0; H, 4.1. Found: C, 74.7; H, 4.2.

7,2',5'-Trihydroxy-2-phenylbenzopyrylium Chloride.—The benzoyloxychalcone (34 g.) was debenzoylated as described above. The hydroxychalcone was precipitated by the addition of hydrochloric acid and was separated from benzoic acid by extraction of the latter with cold dilute sodium bicarbonate solution (12 g. sodium carbonate in 200 cc. of water saturated with carbon dioxide). The product was crystallized from dilute alcoholic 10% hydrochloric acid. The yield of anthocyanidin was 7 g. (39%). A portion was recrystallized for analysis. It separated as a dark red microcrystalline powder, m. p. 190° (dec.). Its solution in acid was red and in sodium carbonate blue. *Anal.* Calcd. for $C_{15}H_{11}O_4Cl \cdot 5^1/_2H_2O$: Cl, 9.1. Found: Cl, 9.1.

2,4,2',5' - Tetrabenzoyloxy - 6 - methylchalcone.—Quinacetophenone dibenzoate (0.07 mole) and orcylaldehyde dibenzoate were converted to the benzoyloxychalcone, a pale yellow semi-crystalline solid, m. p. 125–127°. The yield was 42 g. (86%).

Anal. Calcd. for $C_{44}H_{30}O_9$: C, 75.2; H, 4.3. Found: C, 74.7; H, 4.5.

7,2',5' - Trihydroxy - 5 - methyl - 2 - phenylbenzopyrylium Chloride.—The benzoyloxychalcone (37 g.) was debenzoylated as described above. The hydroxychalcone was precipitated with hydrochloric acid and separated from the benzoic acid by extraction of the latter with hot benzene in a Soxhlet. The brown residue was crystallized from dilute alcoholic 10% hydrochloric acid as dark, red, iridescent plates, m. p. 285–287° (dec.). Its solution in acid was red and in sodium carbonate blue. *Anal.* Calcd. for $C_{16}H_{13}O_4Cl \cdot H_2O$: Cl, 11.0. Found: Cl, 11.1.

2,4,6,2',5' - Pentabenzoyloxychalcone.—Quinacetophenone dibenzoate (7 g.) and phloroglucinaldehyde tribenzoate (9 g.) were converted to the benzoyloxychalcone, a

yellow oil, which was not analyzed but transformed into the anthocyanidin.

5,7,2′,5′-Tetrahydroxy-2-phenylbenzopyrylium Chloride.—The benzoylchalcone was debenzoylated as described above. The hydroxychalcone was precipitated with hydrochloric acid and was separated from benzoic acid by extraction of the latter with cold dilute sodium bicarbonate solution. The residue was crystallized from 10% hydrochloric acid in which it was very soluble. The dark red crystal mass was extracted with ether, leaving less than a gram of anthocyanidin. It was a brownish-red crystalline powder, m. p. above 300°. *Anal.* Calcd. for $C_{15}H_{11}O_6Cl.2H_2O$: Cl, 10.4. Found: Cl, 10.3. It gave a red solution in acid and blue in sodium carbonate.

bis-**(6,3,′4′-Trihydroxy)-flavopinacol.**—This flavopinacol, possessing the possible phlobatannin structure, was prepared by reduction of pure 6,3′,4′-trihydroxyflavanone (1 g.) and also by reduction of a mixture (1 g.) of flavanone and 3,4,2′,5′-tetrahydroxychalcone, consisting mostly of the latter. The flavanone (or mixture of chalcone and flavanone) was dissolved in alcohol (40 cc.) and zinc dust (5 g.) and concd. hydrochloric acid (12 cc.) were added. The solution was boiled for five minutes, during which time the color changed from dark orange (in the case of the mixture) to a pale yellow. The solution was filtered from unreacted zinc and nearly neutralized with sodium bicarbonate, a tan precipitate separating. The solution was saturated with sodium chloride and extracted without filtering with two portions (75 cc. each) of ethyl acetate. The ethyl acetate was dried over sodium sulfate overnight and evaporated on the steam-bath. Most of the remaining solvent was removed in a vacuum desiccator over sodium hydroxide. The final product was a light red friable solid, retaining traces of solvent with great tenacity. It was readily soluble in acetone, alcohol, and ethyl acetate and partially soluble in water. The water-soluble portion was qualitatively indistinguishable from natural phlobatannins such as mimosa and hemlock tannins, as indicated in the table above. No analysis was attempted.

Summary

1. The production of a new flavopinacol from quinacetophenone and protocatechualdehyde is reported. This substance is qualitatively indistinguishable from such natural phlobatannins as hemlock and mimosa tannins.

2. New benzoyloxychalcones, hydroxychalcones, flavanones, and anthocyanidins derived from quinacetophenone are reported.

3. The peculiar sensitivity of 2′,5′-hydroxychalcones to alkali is noted.

CHAPEL HILL, N. C. RECEIVED JULY 1, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE CITY COLLEGE, THE COLLEGE OF THE CITY OF NEW YORK]

Alkanolamines. VII. Condensation Products of Monoethanolamine and the Isomeric Dichloronitrobenzenes

BY CHESTER B. KREMER AND AARON BENDICH

The activation of a halogeno or nitro group on the benzene nucleus by the presence of other substituted groups is well known. The reactions among such molecules and the amino alcohols were originally investigated in these laboratories. This present paper records our findings with the isomeric dichloronitrobenzenes.

Quite recently, Waldkötter[1] has extended our findings dealing with the condensing ability of monoethanolamine. In general, however, he has dealt with benzene molecules which are quite heavily substituted in the nucleus and contain, usually, at least two nitro groups on the ring. Under such conditions, it is frequently an active nitro group that is split out on condensing with the amino alcohol rather than a halogeno group. Work carried out in our laboratories checks exactly with these results. Our investigations, however, have not been limited to reactions with the ethanolamines and we expect to publish these data in our next article.

The preparation of all six dichloronitrobenzenes is not an easy task. The 2,5- and 3,4-isomers are readily available, but the others are usually prepared through a number of intermediate syntheses. The fundamental researches dealing with the preparation of most of the isomers were carried out by Beilstein and Kurbatow[2] and improved and extended by Holleman and Reiding[3] and Holleman and De Mooy.[4] In preparing the 3,5- and the 2,6-dichloronitrobenzenes we followed their procedures with slight modifications. 2,4-Dichloronitrobenzene usually is prepared by the nitration of *m*-dichlorobenzene. We synthesized this material from a by-product formed in the synthesis of 2,6-dichloronitrobenzene. An outline of the complete synthesis of these three dichloronitrobenzenes is given in Chart I.

Theoretically, it should be possible to obtain

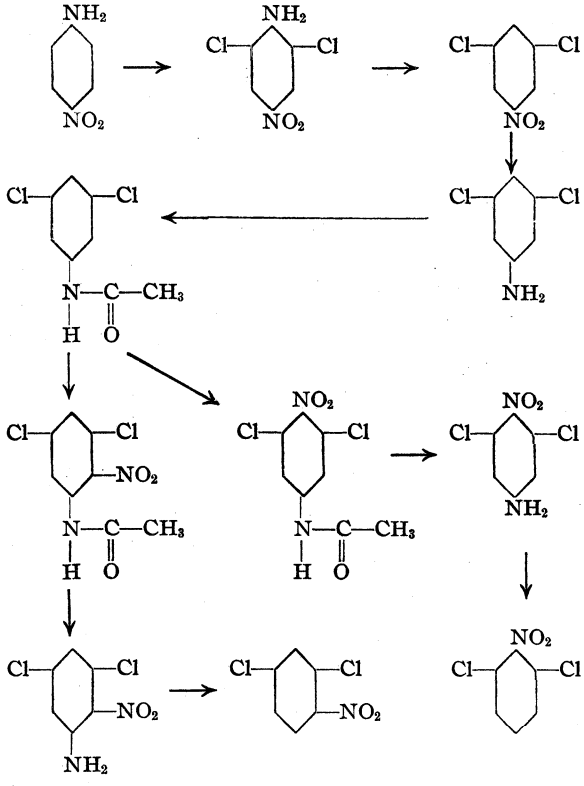
(1) Waldkötter, *Rec. trav. chim.*, **57**, 1294 (1938).

(2) Beilstein and Kurbatow, *Ann.*, **196**, 228 (1879).

(3) Holleman and Reiding, *Rec. trav. chim.*, **23**, 357–379 (1904).

(4) Holleman and De Mooy, *ibid.*, **35**, 1–66 (1916).

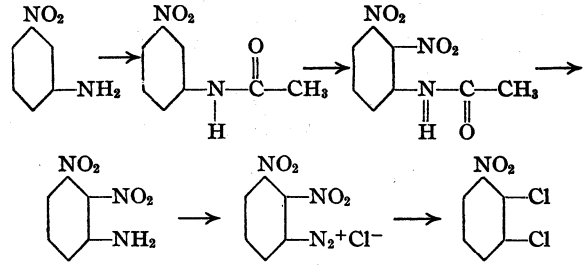
CHART I



2,4- and 2,6-dichloronitrobenzenes by nitration in a suitable medium, followed by diazotization, of 2,4-dichloroaniline. Our preliminary results with this nitration were uniformly unsuccessful; but recently we have been able to obtain some very small yields of the desired products. We hope to be able to develop further this line of work.

2,3-Dichloronitrobenzene can be prepared by chlorinating *o*-chloronitrobenzene in the presence of antimony chloride. Holleman and Reiding[3] used this method but it is not conducive to the preparation of large amounts of material. With this in mind, Holleman and De Mooy[4] devised a synthesis of the compound by taking advantage of the fact that when 2,3-dinitroaniline is involved in a Sandmeyer reaction to replace the amine group with halogen, not only is the amine group replaced but also the ortho nitro group. In their synthesis of 2,3-dinitroaniline, they nitrated *m*-nitroacetanilide according to the procedure of Wender.[5] It is claimed that a mixture of three isomers, with the desired product constituting about 50% of the whole, is obtained. We tried this nitration several times and found that it gave most unsatisfactory results. We therefore devised a different method of nitration. By treating *m*-nitroacetanilide with fuming nitric acid (sp. gr. 1.50) at room temperature we were able to obtain a product which after one recrystallization from ethanol gave a melting point of 185–186°. With this method, 30 g. of the *m*-nitroacetanilide yielded 25 g. of the desired product and there could be recovered 6 g. of low-melting isomers. The steps involved in the synthesis of 2,3-dichloronitrobenzene are given in Chart II.

CHART II



The condensations between the amino alcohol and the dichloronitrobenzenes were carried out in the usual reflux apparatus, using propyl or butyl alcohol as solvent and magnesium oxide as an acid binding agent.

All of the nitro condensation products were highly colored solids varying from yellow to red with the exception of 2-(6-chloro-2-nitroanilino)-ethanol which was a red liquid. The reduced products were white solids with the exception of 2-(6-chloro-4-aminoanilino)-ethanol, which apparently is a liquid.

Experimental

Preparation of the Dichloronitrobenzenes.—The 2,5- and 3,4-dichloronitrobenzenes were obtained from the Eastman Kodak Co.

3,5-Dichloronitrobenzene.—One hundred and thirty-eight grams of *p*-nitroaniline is mixed with 2 liters of concentrated hydrochloric acid and 60 g. of potassium chlorate added slowly, care being taken to keep the temperature around 70°. When the reaction is complete, the whole is poured into 2 liters of water, the crude 2,6-dichloro-4-nitroaniline removed by filtration and washed free of acid. Varying amounts of 4-nitro-2-chloroaniline are usually found mixed with the desired dichlorinated product. The two can be separated by treatment with hot alcohol.

The 2,6-dichloro-4-nitroaniline is air dried and 105 g. is then added to a mixture of 375 cc. of ethanol and 100 g. of concentrated sulfuric acid in a flask equipped with reflux condenser and automatic stirrer. Thirty-six grams of sodium nitrite is added and the mixture heated on the water-bath for about one hour. This is followed by steam

(5) Wender, *Jahresber.*, **42**, 775 (1889).

distillation. Seventy grams of the 3,5-dichloronitrobenzene distil over, is filtered and recrystallized from ethanol; m. p. 65°.

2,6-Dichloronitrobenzene.—Ninety-six grams of 3,5-dichloronitrobenzene is added to 350 cc. of hydrochloric acid (sp. gr. 1.19) in 150 cc. of water and 180 g. of finely divided tin is added gradually until the reduction is complete. Two hundred grams of sodium hydroxide is then added and the whole steam distilled. About 70 g. of 3,5-dichloroaniline melting at 51° is obtained. The product is recrystallized from dilute ethanol.

The dichloroaniline is dissolved in 50 cc. of glacial acetic acid and 100 cc. of 45% acetic anhydride in glacial acetic acid is added. The acetanilide separates out instantly and forms a compact mass. After standing for four hours, it is diluted with water, filtered and air dried. The yield is quantitative and the product melts at 186°.

Fifty grams of the acetanilide is treated with 250 g. of fuming nitric acid (sp. gr. 1.51) until nitration is complete. The mixture is poured into water, whereupon a mixture of two isomers, 3,5-dichloro-4-nitroacetanilide and 3,5-dichloro-2-nitroacetanilide, precipitates out. These are separated by treatment with hot benzene, the former compound being quite insoluble in the hot solvent. The product is washed several times with hot benzene and finally recrystallized from dilute ethanol; m. p. 222°.

Ten grams of the 3,5-dichloro-4-nitroacetanilide is dissolved in 40 g. of concentrated sulfuric acid and warmed for a half hour around 110°. This solution is then poured into 150 cc. of ethanol; 3 g. of sodium nitrite is added and the mixture refluxed on the water-bath until evolution of nitrogen ceases. This is followed by steam distillation. There is obtained 6.5 g. of the 2,6-dichloronitrobenzene. This is recrystallized from ethanol and then vacuum distilled; b. p. 100–101°, 4–5 mm. pressure. Whereas the literature reports this compound as yellow, our product was pure white and melted at 70.5°.

2,4 - Dichloronitrobenzene.—3,5 - Dichloro - 2 - nitroacetanilide is prepared as described above. After separation from the 3,5-dichloro-4-nitroacetanilide, which is also produced at the same time, by means of hot benzene, the desired isomer is quite pure and melts at 138°. This compound is treated identically as described above for the other isomer and results in the same yield. A light yellow solid is obtained which melts at 34° and can be purified further by vacuum distillation; b. p. 105–107° at a pressure of 3–4 mm. and 132–133° at a pressure of 13–14 mm.

2,3-Dichloronitrobenzene.—One hundred and thirty-eight grams of *m*-nitroaniline was acetylated according to Kaufmann[6] by mixing a concentrated solution of the aniline in benzene with 105 g. of acetic anhydride and refluxing for one hour. The mixture is cooled, the acetanilide filtered and air dried. It melts at 154–155°.

The acetanilide was nitrated as follows: 30 g. was treated with 60 cc. of fuming nitric acid (sp. gr. 1.50) at 20° for one hour. The resulting mixture was poured onto crushed ice and the resulting yellow product filtered and washed free of acid. Recrystallization from a relatively large volume of ethanol yielded 25 g. of a near white solid melting at 186–187°. Evaporation of the mother liquor yielded 6–8 g. of isomers melting at 100°.

The dinitroacetanilide was treated with four times its volume of concentrated sulfuric acid and heated at 110° for half an hour. The mixture was poured onto crushed ice, the resulting orange solid filtered off and the 2,3-dinitroaniline recrystallized from a small volume of ethanol; m. p. 127°.

One hundred and eleven grams of the 2,3-dinitroaniline was treated with 128 cc. of concentrated hydrochloric acid and the mixture poured into an ice-cold concentrated solution containing 38 g. of sodium nitrite. To this solution was added dropwise a solution of cuprous chloride in hydrochloric acid prepared according to van der Linden.[7] The mixture was stirred at room temperature for ten minutes and then refluxed over a free flame for half an hour. It was then cooled with ice and filtered. The filtered solid was steam distilled and the material coming over in the steam distillate recrystallized from ethanol. The 2,3-dichloronitrobenzene is white and melts at 61°. It can be purified further by vacuum distillation.

Condensation Reactions

These were run in a solvent, usually normal butyl alcohol, and in some cases magnesium oxide was employed as an acid binder.

Reactions Using Magnesium Oxide.—One-tenth of a mole of the dichloronitrobenzene was dissolved in 50 cc. of warm butanol and 0.1 mole of magnesium oxide was suspended in the solution. A reflux apparatus with mechanical stirrer and dropping funnel was employed. The suspension was heated until the alcohol refluxed gently and then slightly more than 0.1 mole of monoethanolamine was added dropwise and the mixture refluxed for several hours. The whole was filtered clear of any excess magnesium oxide and then steam distilled. On cooling the residue in the distillation flask, the condensed product separated out as a solid (with one exception) and was filtered off. It was then recrystallized from the appropriate solvent. The products obtained with the various dichloronitrobenzenes along with other data are given in Table I.

A somewhat modified procedure was followed in several cases with excellent results. Instead of butanol, propanol was employed as solvent in these runs. After refluxing the reaction mixture as described above and filtering off the magnesium oxide, the alcohol solution was cooled in ice, whereupon a goodly portion of the condensed product separated out. This was filtered off and the over-all yield materially increased by throwing the filtrate into water, whereupon further precipitation of the desired product occurred. This method obviates the use of steam distillation but requires a longer reaction period due to the lower boiling point of the propanol.

Reactions without Magnesium Oxide.—These were run practically the same as described above with the exception that the molar ratio of the monoethanolamine was two or three times that of the dichloronitrobenzene. When propanol was used as the solvent, the steam distillation was omitted as described above.

Reaction between 3,4-Dinitrochlorobenzene and Monoethanolamine.—This reaction was run to assist in proving the structure of the condensation product obtained

(6) Kaufmann, *Ber.*, **42**, 3480 (1909).

(7) Van der Linden, *Rec. trav. chim.*, **30**, 315 (1911).

TABLE I

SUBSTITUTED ANILINO ETHANOLS

Compound, ethanol	Yield, %	Cryst. from	M. p., °C. Corr.	Nitrogen, % Calcd.	Found
2-(6-Chloro-2-nitroanilino)-	60		155–157/2 mm. (b. p.)	12.93	12.87
2-(5-Chloro-2-nitroanilino)-	88	Dil. EtOH	116	12.93	13.07
2-(4-Chloro-2-nitroanilino)-	70	*n*-BuOH	107.5	12.93	13.04
2-(3-Chloro-2-nitroanilino)-	13	Dil. EtOH	78.5	12.93	13.15
2-(6-Chloro-4-nitroanilino)-	64	Toluene	120	12.93	13.05
2-(6-Chloro-2-aminoanilino)-			135–137/2 mm. (b. p.)	15.01	15.06
2-(5-Chloro-2-aminoanilino)-	90	Toluene	104.5	15.01	15.00
2-(4-Chloro-2-aminoanilino)-	90	Benzene	122.5	15.01	15.17
2-(3-Chloro-2-aminoanilino)-	85	Toluene	74	15.01	14.88
2-(6-Chloro-4-aminoanilino)-			Oil, dec. at 185° (1 mm.)		

with 2,4-dichloronitrobenzene. The procedure was the same as just described. The product obtained is identical with that formed in condensing 2,4-dichloronitrobenzene with the amino alcohol.

Reductions

All reductions of the nitro compounds were carried out using sodium hydrosulfite in a weakly alkaline medium. Yields were practically quantitative in most cases. The properties of these reduced products are included in Table I.

Discussion

In certain of the dichloronitrobenzenes, two chloro groups are capable of replacement. This is the case with the 2,4- and the 2,6-isomers. In all of the other isomers only one chloro group is capable of replacement as the other is in the meta position to the activating nitro group and, as proved by work in these laboratories with amino alcohols, and in analogous work with ammonia, sodium methoxide and potassium sulfide as recorded in the literature,[4,8] such a chloro group is inactive. In the case of 3,5-dichloronitrobenzene both of the chloro groups are in the meta position and no condensation whatsoever occurs here.

That only one of the two chlorine atoms is removed in condensing either 2,4- or 2,6-dichloronitrobenzene with monoethanolamine is shown by both quantitative and qualitative analyses. In the case of the 2,6-isomer it makes no difference which chlorine is removed; the resulting compound would be the same. It then only becomes a question of determining which of the two chlorine atoms in the 2,4-isomer reacts. It is definitely established that the one ortho to the nitro group is mobile. This is proved by condensing 3,4-dinitrochlorobenzene in the same manner as described for the dichloronitrobenzenes. The product obtained is identical with that obtained in condensing 2,4-dichloronitrobenzene.

It is interesting to compare the ability of the dichloronitrobenzenes to condense with monoethanolamine, with those condensations involving ammonia, substituted amines and sodium methoxide. Much of this latter work has been carried out by Holleman and his co-workers.[3,4] They find the most reactive isomer to be the 2,4. The remaining order is 3,4, 2,5, 2,3 and 2,6. Our results check fairly well with those presented in the literature. There can be no doubt that 2,6-dichloronitrobenzene is the least reactive, the yields seldom exceeding 15% even after long periods of refluxing. We find, however, that 2,5-dichloronitrobenzene appears to react more readily with monoethanolamine than the 3,4-compound, which is at variance with the findings of Holleman; but in general our order of reactivity follows closely his order of "speed of reaction."

Summary

1. A study of the preparation of the isomeric dichloronitrobenzenes has been made.

2. The reaction between the dichloronitrobenzenes and monoethanolamine in a neutral solvent has been studied.

3. A report is made upon the preparation and properties of several new chloronitroanilino and chloroaminoanilino ethanols.

RECEIVED JUNE 27, 1939

(8) Kremer, THIS JOURNAL, **59**, 1681 (1937); Blanksma, *Rec. trav. chim.*, **28**, 105–112 (1909); Körner, *Gazz. chim. ital.*, **4**, 305–446 (1876); Beilstein and Kurbatow, *Ber.*, **11**, 2056–2057 (1879).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

Synthesis of Iodinated Benzoylbenzoic Acids and Anthraquinones[1]

BY ROBERT W. HIGGINS AND C. M. SUTER

Although many halogenated anthraquinones have been prepared, the known iodine derivatives are limited in number. The 1- and 2-iodoanthraquinones have been obtained from the amines[2] and 1,5-diiodoanthraquinone has been prepared from the diamine.[3] The action of iodine and sodium nitrite in fuming sulfuric acid upon anthracene yields a mixture of mono- and diiodoanthraquinones of unknown structure[4] whose physical properties were not recorded. It has been reported[5] that the action of iodine on anthraquinone in 70% oleum at 180° yields a complex mixture of products of which a tri-, a tetra- and a penta-iodoanthraquinone were isolated. The tetra compound was characterized by its high melting point (500°). The only attempt so far made to prepare an iodinated anthraquinone by a nuclear synthesis was that of Eckert and Klinger.[5] They found that the benzoyltetraiodobenzoic acid obtained from tetraiodophthalic anhydride and benzene when heated with concentrated sulfuric acid at 190–200° lost iodine but nevertheless there resulted a 20% yield of a tetraiodoanthraquinone, m. p. 476° (dec.), which they believed was not the 1,2,3,4-compound. Attempts to bring about ring closure by the use of aluminum chloride resulted in evolution of iodine and hydrogen chloride with formation of a diiodoanthraquinone (m. p. 290–292°) of unknown structure.

Lawrance[6] found that tetraiodophthalic anhydride condensed readily with toluene but ring closure was not attempted. The conversion of benzoyltetrabromobenzoic acid to the anthraquinone[7] has been brought about by heating with 13% oleum and a variety of substituted anthraquinones has been prepared from the benzoylbenzoic acids resulting from the action of tetrachlorophthalic anhydride upon benzene derivatives.[8]

Since Pratt and Perkins[9] have shown that the di- and triiodophthalic anhydrides obtained by partial iodination of phthalic anhydride in oleum can be separated it was decided to investigate the condensation of these with representative aromatic compounds under various conditions. The condensation of the 3,4-, 4,5- and 3,6-di-, and the 3,4,6-triiodophthalic anhydrides with benzene occurs readily in the presence of two molecular equivalents of aluminum chloride. The products from the 3,4- and 4,5-diiodo anhydrides are purified readily by crystallizing their potassium salts from hot water. On the other hand, the potassium salts of the acids obtained from the 3,4,6-triiodo- and tetraiodophthalic anhydrides do not separate from water readily. No effort has so far been made to determine which of the two possible acids results from the 3,4-diiodo anhydride and benzene but the ease of ring closure indicates that it is 2-benzoyl-3,4-diiodobenzoic acid. The 3,4,6-triiodo anhydride yields a mixture in practically equal amounts of the two possible isomeric acids.

Ring closure of the three benzoyldiiodobenzoic acids was effected readily with 100% sulfuric acid. With a lower concentration iodine elimination occurred. The 2,3-diiodoanthraquinone corresponds in melting point to the diiodoanthraquinone obtained by Eckert and Klinger[5] through the action of aluminum chloride upon benzoyltetraiodobenzoic acid. The identity of these acids is reasonable as the iodine atoms in the 1,4-positions are eliminated easily. Attempts to condense phthalic anhydride with *m*-diiodobenzene under a variety of conditions were unsuccessful. It was thought that from the benzoylbenzoic acid so obtained it might be possible to prepare the unknown 1,3-diiodoanthraquinone.

Conversion of the two isomeric benzoyltriiodobenzoic acids into 1,2,4-triiodoanthraquinone occurred under narrowly defined conditions in yields of about 25%. In view of these results various attempts were made to induce a similar reaction with benzoyltetraiodobenzoic acid under conditions where iodine was not eliminated but without success, confirming previous reports.[5]

The results of some preliminary experiments designed to prepare iodinated hydroxyanthraqui-

(1) Presented before the Organic Division of the American Chemical Society at the Milwaukee meeting September, 1938.

(2) Laube, *Ber.*, **40**, 3566 (1907); **37**, 60 (1904).

(3) Scholl, Hass, Meyer and Seer, *ibid.*, **62B**, 107 (1929).

(4) Varma and Subramanyam, *C. A.*, **25**, 2994 (1931).

(5) Eckert and Klinger, *J. prakt. Chem.*, [2] **121**, 281 (1929).

(6) Lawrance, THIS JOURNAL, **43**, 2577 (1921).

(7) Hofmann, *Monatsh.*, **36**, 805 (1915).

(8) For examples see Ruggli and Brunner, *Helv. Chim. Acta*, **8**, 155 (1925); Waldmann, *J. prakt. Chem.*, **147**, 331 (1937); Underwood and Walsh, THIS JOURNAL, **57**, 940 (1935).

(9) Pratt and Perkins, *ibid.*, **40**, 219 (1918).

nones may be mentioned. Although phthalic anhydride condenses with veratrole and with 4-chloroveratrole without undue difficulty, so far it has not been possible to bring about reaction of either of these ethers with 4,5-diiodophthalic anhydride or the tetraiodo compound. On the other hand, anisole and the methyl ethers of *o*- and *m*-cresol react readily with both anhydrides. Further work on this aspect of the investigation is in progress.

Considerable difficulty was encountered in the analysis of iodinated anthraquinones for iodine. The usual procedure with the Parr bomb gave only partial decomposition of the compounds. The Stepanow method using sodium and alcohol gave erratic results which were high until it was found that digestion of the silver iodide precipitate for several hours with dilute nitric acid gave consistent results on both known compounds and the iodinated anthraquinones. The intermediate benzoylbenzoic acids were titrated in aqueous alcohol solution with standard alkali using thymol blue as the indicator.

Experimental

Iodophthalic Acids.—Iodination of phthalic anhydride was conducted according to the procedures of Pratt and Perkins.[9] The low temperature iodination gave the more satisfactory results. In the original directions where separation of the 4,5-diiodophthalic acid is effected by precipitation with a definite volume of "acetic acid," the volume given refers to 6 *N* acid; the use of 100% acetic acid gave a mixture of iodinated acids. In the precipitation of the 3,4,6-triiodo acid 18 cc. of 6 *N* acetic acid gave better results than the 10 cc. specified in the original. The volumes of concentrated hydrochloric acid found necessary in the later stages of the separation checked those specified by Pratt and Perkins. The precipitates obtained by this separation procedure required considerable purification before the products gave satisfactory melting points and the yields of iodophthalic anhydrides isolated were distinctly lower than the amounts of nearly pure acids obtained in the original preparation would suggest. From 780 g. of phthalic anhydride, 1270 g. of iodine, and 2500 g. of 50% oleum after heating for six days at 70–80° were obtained 100 g. of 4,5-diiodophthalic anhydride, m. p. 215–216°, 147 g. of the 3,4,6-triiodo anhydride, m. p. 220–223° (further crystallization raised this to 226–227°); 325 g. of the 3,4-diiodo anhydride, m. p. 194–196° and 395 g. of 3,6-diiodo anhydride, m. p. 228–231°. In addition, smaller amounts of the compounds having somewhat lower melting points were isolated.

2-Benzoyl-4,5-diiodobenzoic Acid.—A mixture of 5 g. of diiodophthalic anhydride, 3.65 g. (10% excess over two molecular equivalents) of aluminum chloride and 40 ml. of benzene was refluxed for twenty-four hours, poured into cold water and the benzene steam distilled out. The water-insoluble residue was filtered and then treated with hot potassium carbonate solution which left only a trace of undissolved material. The solution upon cooling deposited the potassium benzoylbenzoate which was redissolved in hot water and the solution acidified. Crystallizing the precipitate from dilute alcohol gave 4.8 g. of product melting[10] at 244–245°. This corresponds to an 80% yield.

Anal. Calcd. for $C_{14}H_8O_3I_2$: neut. equiv., 478. Found: neut. equiv., 481, 481.

2-Benzoyl-3,4-(?)-diiodobenzoic Acid.—By a procedure exactly analogous to that used in the preceding section, there was obtained a 65% yield of the benzoylbenzoic acid from the 3,4-anhydride. The m. p. was 223–224°. Only one product was isolated. When the time of heating was shortened to nine hours the yield was about the same.

Anal. Calcd. for $C_{14}H_8O_3I_2$: neut. equiv., 478. Found: neut. equiv., 476, 478, 481.

2-Benzoyl-3,6-diiodobenzoic Acid.—The potassium salt of the benzoylbenzoic acid from the 3,6-anhydride did not crystallize readily from aqueous solution. Acidification of the solution and crystallization of the precipitate from dilute alcohol gave a 60% yield of acid of m. p. 218–220°.

Anal. Calcd. for $C_{14}H_8O_3I_2$: neut. equiv., 478. Found: neut. equiv., 482, 482, 476.

2-Benzoyl-3,4,6- and 3,5,6-triiodobenzoic Acids.—From 32.6 g. (0.061 mole) of 3,4,6-triiodophthalic anhydride, 18.1 g. (0.136 mole) of aluminum chloride and 200 ml. of benzene after twenty-one hours of refluxing was obtained 37 g. of product soluble in potassium carbonate solution. Heating the product in concentrated hydrochloric acid did not produce a yellow color, indicating that no appreciable amount of anhydride was unreacted. Refluxing the product with 400 ml. of 95% alcohol for forty-five minutes left an insoluble residue amounting to 20 g. which melted at 252–262°. This residue was extracted with hot dioxane, leaving a small amount (2.4 g.) of inorganic material. Concentrating and cooling the dioxane solution gave 13.5 g. of acid melting at 257–258° and a second crop of 2.8 g. melting at 254–257°.

Cooling the alcohol solution gave 10.7 g. of the low melting isomer, m. p. 224–227°, and then further smaller fractions which were practically pure. A total of 16.3 g. of the high melting and 14.4 g. of the low-melting isomer were obtained. The purest samples of these melted at 257–258° and 225–227°, respectively.

Anal. Calcd. for $C_{14}H_7O_3I_3$ (m. p. 257–258°): neut. equiv., 604. Found: neut. equiv., 607, 602.

Anal. Calcd. for $C_{14}H_7O_3I_3$ (m. p. 225–227°): neut. equiv., 604. Found: neut. equiv., 600, 613.

2,3-Diiodoanthraquinone.—To 40 g. of 100% sulfuric acid at 140° was added gradually over thirty minutes with stirring 2 g. of 2-benzoyl-4,5-diiodobenzoic acid. The mixture was then cooled to 70–80° and diluted slowly by adding small pieces of ice. The mixture was filtered and the precipitate warmed with aqueous potassium carbonate to remove any unreacted acid. The insoluble portion was crystallized from benzene and acetic acid and then melted at 291–292°. The yield was 1.6 g. or 80% of the theoretical amount.

(10) All melting points are corrected.

Anal. Calcd. for $C_{14}H_6O_2I_2$: I, 55.21. Found: I, 55.0, 55.3.

1,2-Diiodoanthraquinone.—This was prepared in a manner similar to that used with the 2,3-isomer. It crystallized in orange-red plates from a benzene–toluene mixture and melted at 236–237°.

Anal. Calcd. for $C_{14}H_6O_2I_2$: I, 55.21. Found: I, 55.6, 55.6.

1,4-Diiodoanthraquinone.—From heating 2 g. of 2-benzoyl-3,6-diiodobenzoic acid with 75 g. of 100% sulfuric acid at 100° for two hours, was obtained 1.1 g. (60%) of the anthraquinone. After crystallizing from alcohol it melted at 218–219°.

Anal. Calcd. for $C_{14}H_6O_2I_2$: I, 55.21. Found: I, 55.4, 55.3, 55.7.

1,2,4-Triiodoanthraquinone.—A. Two grams of the high-melting benzoyltriiodobenzoic acid was added to 60 g. of 100% sulfuric acid kept at 105° over a thirty-minute period with stirring and the mixture heated and stirred for thirty minutes longer. It was then cooled and poured on ice and the resulting colloidal suspension coagulated by heating on the steam-bath. The precipitate was then treated with dilute sodium hydroxide. The red residue upon crystallization from acetic acid yielded 0.5 g. of product melting at 202–204°. This is about 25% of the theoretical amount. Alterations in these conditions did not improve the yield.

B. From treatment of the low-melting benzoyltriiodobenzoic acid as in A was obtained 0.4 g. of the anthraquinone. After two crystallizations from acetic acid the m. p. was 202–203.5°.

Anal. Calcd. for $C_{14}H_6O_2I_2$: I, 64.84. Found: I, 64.9, 65.0.

Summary

1. The condensation of di- and triiodophthalic anhydrides with benzene and aluminum chloride gives good yields of the benzoylbenzoic acids.

2. Ring closure of benzoyldiiodobenzoic acids is readily effected by treatment with 100% sulfuric acid. The triiodo compounds give smaller yields of the triiodoanthraquinones.

3. Veratrole and 4-chloroveratrole do not condense readily with iodinated phthalic anhydrides. Work upon the synthesis of iodinated hydroxyanthraquinones is being continued.

EVANSTON, ILLINOIS RECEIVED JULY 7, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF EX-LAX, INC.]

3,3′-Dimethyl-4,4′-dihydroxybenzophenone

BY MAX H. HUBACHER

During the progress of some work being carried out recently, it became necessary to prepare a quantity of 3,3′-dimethyl-4,4′-dihydroxybenzophenone. This was done by a caustic potash fusion of *o*-cresolphthalein.[1]

Since the properties of the compound prepared from *o*-cresolphthalein did not agree with those recorded by Doebner and Schroeder,[2] an investigation of this discrepancy was made in order to determine the true properties of this material. These chemists obtained a compound which they designated as dioxydimethylbenzophenone, melting at 138°, by caustic potash fusion of *o*-cresolbenzein. For an analysis they report, calculated for $C_{15}H_{14}O_3$: C, 78.51; found, 78.19. Evidently, an error was made in calculation as the value for carbon is 74.36.

A caustic potash fusion of *o*-cresolbenzein produced no trace of a compound melting at 138°. Instead, a product melting at 247° was obtained which was identical with that from *o*-cresolphthalein. That the compound of melting point 247° was the expected 3,3′-dimethyl-4,4′-dihydroxybenzophenone was confirmed by analysis and the preparation of the diacetyl derivative and the mono and dimethyl ethers. On prolonged fusion with caustic potash, the benzophenone was converted into *o*-cresol and 3-methyl-4-hydroxybenzoic acid.

Experimental[3]

3,3′-Dimethyl-4,4′-dihydroxybenzophenone (I).—Seventy grams of potassium hydroxide was heated in a nickel crucible to 260–265° (oil-bath temperature) and 10 g. of *o*-cresolphthalein of m. p. 224–225° was stirred in. After ten minutes, the melt was poured into 1.5 liters of water and acidified with hydrochloric acid. The 6.60 g. of crude was crystallized from 75 cc. of glacial acetic acid; 4.85 g. (69.3%) of (I), melting at 246–247° was obtained. A second crystallization or a sublimation *in vacuo*[4] at 180° gave a pure product, melting point 247.0–247.8°. It formed colorless needles from 20% ethanol and rectangular plates from acetic acid. It dissolved in both sodium hydroxide or concd. sulfuric acid with yellow color.

(1) A. v. Baeyer, *Ann.*, **202**, 126 (1880); W. R. Orndorff and W. R. Barrett, THIS JOURNAL, **46**, 2488 (1924).

(2) O. Doebner and G. Schroeder, *Ann.*, **257**, 74 (1890).

(3) All melting points are corrected.

(4) All the sublimations were done in a vacuum produced by a CenCO-HyvAC pump guaranteed to produce a vacuum of 0.3 micron.

Anal. Calcd. for $C_{15}H_{14}O_3$: C, 74.36; H, 5.82; mol. wt., 242. Found: C, 74.42; H, 5.95; mol. wt. (Rast, in camphor), 237, 241.

The aqueous mother liquor from the crude (I) yielded 1.09 g. of benzoic acid.

3,3′-Dimethyl-4,4′-diacetoxybenzophenone was prepared by refluxing 2.42 g. of (I), 3.1 g. of acetic anhydride, 10 cc. of acetic acid and one drop of concd. sulfuric acid; 3.11 g. (95%) was obtained. The pure compound formed thin plates from ethanol and melted at 106.8–107.2°.

Anal. Calcd. for $C_{19}H_{18}O_5$: C, 69.91; H, 5.56. Found: C, 70.21; H, 5.53.

3,3′-Dimethyl-4,4′-dimethoxybenzophenone (II).—To 2.42 g. of (I) in 60 cc. of normal sodium methylate was added 5.0 g. of dimethyl sulfate and the mixture refluxed for one hour. After the evaporation of the methanol and taking up in water, the alkali insoluble portion weighed 0.85 g. After sublimation *in vacuo* at 100°[4] and crystallization from 50% ethanol, the dimethyl ether (II) melted at 113.7–114.2° (silky needles).

Anal. Calcd. for $C_{17}H_{18}O_3$: C, 75.52; H, 6.71. Found: C, 75.71; H, 6.83.

3,3′-Dimethyl-4,4′-dimethoxybenzophenoneoxime.—1.35 g. of (II) and 0.70 g. of hydroxylamine hydrochloride in 4 cc. of pyridine were heated for three hours to 90°. The oxime (1.41 g.) melted at 160.9–161.2° after crystallizations from ethanol.

Anal. Calcd. for $C_{17}H_{19}O_3N$: N, 4.91. Found: N, 5.14.

3,3′-Dimethyl-4-methoxy-4′-hydroxybenzophenone.—The alkali soluble portion from the methylation of (I) above weighed 1.61 g. After sublimation *in vacuo* at 180°,[4] followed by several crystallizations from ethanol, the pure monomethyl ether melted at 203.7–204.2°.

Anal. Calcd. for $C_{16}H_{16}O_3$: C, 74.96; H, 6.29; OCH_3, 12.11. Found: C, 74.77, 75.57; H, 5.91, 6.55; OCH_3, 11.97.

Fusion of *o*-Cresolbenzein with Potassium Hydroxide.—Five grams of *o*-cresolbenzein[2] and 30 g. of potassium hydroxide were heated for ten minutes at 260–265° (oil-bath temperature). The crude, after one crystallization from glacial acetic acid, weighed 2.31 g. (61%) and melted at 246.0–247.3°. Neither a mixture of this material with (I) nor a mixture of the diacetyl derivatives showed a depression of the melting points.

Fusion of (I) with Potassium Hydroxide.—Ten grams of (I) prepared from *o*-cresolphthalein and 50 g. of potassium hydroxide were heated for one hundred and ten minutes at 280°. The fusion was poured into water and saturated with carbon dioxide. The ether extract was distilled, the fraction boiling at 186–190°, weighing 3.77 g. The 2,4-dinitrophenyl ether prepared from this fraction melted at 88.4–88.8° and showed no depression when mixed with a known sample of 2,4-dinitrophenyl *o*-cresyl ether of m. p. 88.7–90.0°.

The aqueous solution was acidified and the precipitate purified by sublimation at 160° *in vacuo* (5.41 g.), a crystallization from water, followed by a second sublimation. The 3-methyl-4-hydroxybenzoic acid melted at 173.9–175.0°.[5] Neutralization equiv. calcd. 152, found 151.3. The methyl ether melted at 195.9–196.2°[6] and the ethyl ester at 95.0–96.6°.[7]

Summary

3,3′-Dimethyl-4,4′-dihydroxybenzophenone was made by caustic potash fusion of *o*-cresolphthalein and of *o*-cresolbenzein. Its diacetyl derivative and the mono and dimethyl ethers were prepared. The structure was shown by its conversion into *o*-cresol and 3-methyl-4-hydroxybenzoic acid.

The 3,3′-dimethyl-4,4′-dihydroxybenzophenone reported by Doebner and Schroeder as melting at 138° is incorrect.

BROOKLYN, N. Y. RECEIVED JUNE 3, 1939

(5) F. Tiemann and C. Schotten, *Ber.*, **11**, 777 (1878), gave a m. p. of 172–175° for 3-methyl-4-hydroxybenzoic acid.

(6) C. Schall, *ibid.*, **12**, 825 (1879), reported a m. p. of 192–193° for the 3-methyl-4-methoxybenzoic acid.

(7) K. Auwers, *ibid.*, **39**, 3174 (1906), gave a m. p. of 98–99° for the ethyl ester of 3-methyl-4-hydroxybenzoic acid.

[CONTRIBUTION FROM THE STERLING CHEMISTRY LABORATORY, YALE UNIVERSITY]

The Use of Triiodophenyl Ethers for the Identification of Alkyl Halides

BY ROBERT D. DREW AND JULIAN M. STURTEVANT

In a recent paper proposing the use of sodium saccharin as a reagent for the preparation of derivatives of alkyl halides, Merritt, Levey and Cutter[1] have pointed out that the types of derivatives for these compounds previously investigated are relatively difficult to prepare. Another convenient type of derivative is suggested by the work of Brenans[2] and Daniels and Lyons,[3] who found certain ethers of 2,4,6-triiodophenol to be nicely crystalline substances. In the present work a convenient standardized method of preparation has been devised using the sodium salt of triiodophenol and the alkyl halide dissolved in absolute alcohol, and several new ethers have been prepared. As found by Merritt, Levey and Cutter[1] in the case of sodium saccharin, most alkyl chlorides react very slowly with sodium triiodophenolate.

Experimental

Five grams of 2,4,6-triiodophenol and an equivalent amount of the alkyl halide are added to 22 cc. of a solution of sodium ethylate (12.3 g. of sodium dissolved in 1 liter of absolute ethyl alcohol), and the solution is refluxed for thirty minutes, or until a precipitate of sodium halide has formed. After filtering, the solution is cooled and diluted with water, the precipitate filtered and recrystallized from alcohol or dilute alcohol. About 1 g. of product is obtained after three or four successive recrystallizations. Some of the lower melting ethers separate from the cooled reaction mixture as liquids. In these cases the mixture is allowed to settle, the supernatant liquid decanted, and the product recrystallized from alcohol. One such recrystallization is usually sufficient to produce a solid product. A slightly longer period of reflux is found to give better results in these cases.

TABLE I

2,4,6-TRIIODOPHENYL ETHERS

Halide used	M. p., °C. (corr.)	Empirical formula	% iodine Calcd.	% iodine Found	
Methyl iodide[a]	98.5	$C_7H_5I_3O$	...	...	...
Ethyl bromide[a]	83.5	$C_8H_7I_3O$	76.16	76.49	76.12
n-Propyl bromide[a]	82.0	$C_9H_9I_3O$	74.11	73.94	73.77
Isopropyl bromide	43.0	$C_9H_9I_3O$	74.11	73.82	73.89
n-Butyl bromide	66.0	$C_{10}H_{11}I_3O$	72.13	71.83	71.55
Isobutyl bromide	48.0	$C_{10}H_{11}I_3O$	72.13	71.91	71.63
n-Amyl bromide	47.0	$C_{11}H_{13}I_3O$	70.25	70.03	69.70
n-Hexyl bromide	44.5	$C_{12}H_{15}I_3O$	68.49	68.37	68.34
Benzyl chloride[a]	122.5	$C_{13}H_9I_3O$	67.76	67.51	67.73
β-Phenylethyl bromide	88.0	$C_{14}H_{11}I_3O$	66.12	66.16	65.59
γ-Phenyl-*n*-propyl bromide	63.5	$C_{15}H_{13}I_3O$	64.54	64.57	64.46
p-Nitrobenzyl bromide	207.5	$C_{13}H_8I_3NO_3$	62.73	63.10	62.65
Ethylene bromohydrin	137.5	$C_8H_7I_3O_2$	73.81	73.82	73.94
Ethyl bromoacetate[b]	124.0	$C_{10}H_9I_3O_3$	68.25	67.94	67.92
Ethyl α-bromopropionate	80.5	$C_{11}H_{11}I_3O_3$	66.58	66.65	66.30

[a] Ethers previously prepared by Brenans.[2] Brenans also prepared the allyl ether, melting at 113–114°, from allyl iodide. [b] Previously prepared by Daniels and Lyons,[3] who found the melting point to be 128.5°.

In Table I are listed the corrected melting points and the analyses (by the Parr bomb method) of the various ethers prepared by this method. It was found in all cases where the melting points are close together that a mixed melting point shows a large depression.

Summary

The use of 2,4,6-triiodophenol as a reagent for the identification of alkyl halides has been found to be satisfactory. Several new alkyl triiodophenyl ethers have been prepared, and their melting points determined.

NEW HAVEN, CONN. RECEIVED JULY 1, 1939

(1) Merritt, Levey and Cutter, THIS JOURNAL, **61**, 15 (1939).
(2) Brenans, *Bull. soc. chim.*, **25**, 819 (1901).
(3) Daniels and Lyons, THIS JOURNAL, **58**, 2646 (1936).

[CONTRIBUTION FROM THE WALKER LABORATORY OF THE RENSSELAER POLYTECHNIC INSTITUTE]

The Reaction of Tetrahydrofuran and 2,5-Dimethyltetrahydrofuran with Acyl Halides[1]

BY JOHN B. CLOKE AND FREDERICK J. PILGRIM

The need for certain δ-halogenobutyl and similar esters led us to study the action of acyl halides on tetrahydrofuran. In the case of acetyl chloride, the reaction gave not only δ-chlorobutyl acetate (I), as was anticipated, but also at least two other products whose properties correspond to the acetate of ditetramethylene glycol chlorohydrin, *i. e.*, δ-(δ-chlorobutoxy)-butyl acetate (II) and to the related compound (III)

$$CH_3COCl + \underbrace{CH_2CH_2CH_2CH_2O} \longrightarrow$$

$$\underset{(I)}{CH_3CO_2(CH_2)_4Cl} + \underset{(II)}{CH_3CO_2(CH_2)_4O(CH_2)_4Cl} + \underset{(III)}{CH_3CO_2(CH_2)_4O(CH_2)_4O(CH_2)_4Cl}$$

Since the yield of δ-chlorobutyl acetate by the foregoing process was but 42% in one run and somewhat better than 50% in another, zinc chloride was added to the reaction mixture in view of its well-known action in the fission of ethers. In one run we employed an amount of anhydrous zinc chloride corresponding to that used by Underwood[2] for the preparation of esters from ordinary ethers, but this led to the formation of much sludge and only 10% of the desired ester. However, it was found eventually that by decreasing the amount of zinc chloride to a few milligrams, a 76% yield of (I) and some of the higher boiling products (II and III) could be obtained. Similar results were obtained in the preparation of analogous δ-chloro esters from both tetrahydrofuran and 2,5-dimethyltetrahydrofuran. However, acetyl bromide gave bromoacetates which could not be separated easily from the accompanying dibromide. Likewise, in our work thus far on the action of acetyl fluoride on tetrahydrofuran we have not yet separated in a state of purity the several products formed.

The δ-chlorobutyl acetate can be methyl alcoholized to give tetramethylene chlorohydrin. It also will give tetramethylene chlorobromide, although the optimum conditions for this reaction have not yet been ascertained.

(1) The data reported herein have been taken from a thesis presented to the Rensselaer Polytechnic Institute in 1939 by Frederick John Pilgrim in partial fulfilment of the requirements for the degree of Bachelor of Science in Chemistry.

(2) Underwood and Wakeman, THIS JOURNAL, **52**, 387 (1930); Underwood, Bari and Toone, *ibid.*, **52**, 4087 (1930).

Experimental Part

Furan.—The major part of the required furan was prepared in batches by the decarboxylation of 500 g. of furoic acid in the presence of 500 cc. of refined quinoline and 3 g. of cupric oxide[3] contained in a 2-liter flask, which was heated in an oil-bath to 225°. The furan and carbon dioxide mixture was passed through a soda-lime tower, which was immersed in water at 75°, when the furan was liquefied by the use of a spiral condenser cooled by circulating ice water. The crude furan, obtained in yields of about 150 cc. per hour, was dried and distilled, giving approximately 85% yields.

Tetrahydrofuran.—The furan was hydrogenated in 200-g. lots in the presence of 20 g. of Raney nickel[4] at initial pressures ranging from 800–1500 pounds per sq. in. (55–100 atm.) in an American Instrument Co. high pressure hydrogenator. Yields of about 97% of tetrahydrofuran were obtained.

δ-Chlorobutyl Acetate (1) Reaction of Acetyl Chloride with Tetrahydrofuran without a Catalyst.—In the first run on the preparation of δ-chlorobutyl acetate, 185 g. (2.57 moles) of tetrahydrofuran[5] was boiled with 435 g. (5.55 moles) of redistilled acetyl chloride for twelve hours in an all-glass apparatus. The acetyl chloride and most of the unchanged tetrahydrofuran (A) were then distilled in the water-bath, leaving 242 g. of crude residue (B). The recovered acetyl chloride–tetrahydrofuran mixture (A) was then boiled again for twelve hours, whereby 60 g. of crude product (C) and another distillate (D) were obtained. The repetition of the process on the distillate (D) gave a further 14 g. yield of crude product (E), where the process was discontinued.

Two distillations of the combined residues (B), (C), and (E) gave 164 g. of δ-chlorobutyl acetate of b. p. 90–92° at 21 mm., 91 g. of product (F) of b. p. 157–165° at 20 mm. and a third product (G) of boiling point 165 to 200° at 23 mm. with intermediate fractions. The redistillation of (F) gave 74 g. of product of b. p. 165–167° at 24 mm., whereas (G) gave a product of b. p. 175–178° at 10 mm. (°C., uncorr.).

The foregoing process gave a 42.5% yield of δ-chlorobutyl acetate.[6] Various preparations boiled as follows: 78–79° at 15 mm., 90–91° at 20 mm., and 92–93° at 22 mm. Our material possessed a density d^{20}_4 of 1.0805 and a refractive index $n^{20}D$ of 1.43439, which correspond to a molecular refractivity, M_D of 36.29 as compared with the calculated value of 36.43.

Anal. Calcd. for $C_6H_{11}O_2Cl$: Cl, 23.56. Found: Cl, 23.47, 23.47.

(3) Gilman and Louisinian, *Rec. trav. chim.*, **52**, 156 (1933); Wagner and Simons, *J. Chem. Ed.*, **13**, 265 (1936); Starr and Hixon, THIS JOURNAL, **56**, 1595 (1934); Shepard, Winslow and Johnson, *ibid.*, **52**, 2083 (1930).

(4) Cloke and Ayers, *ibid.*, **56**, 2144 (1934); Heisig, *ibid.*, **61**, 525 (1939).

(5) We are indebted to H. Tennent and C. Wear for this material.

(6) Bennett and Heathcoat, *J. Chem. Soc.*, 268 (1929).

The redistilled product (F) of b. p. 165–167° at 24 mm. possessed a density, d^{20}_4, of 1.0471 and a refractive index, $n^{20}D$, of 1.44474, which correspond to a molecular refractivity, M_D, of 56.85. The molecular refractivity calculated for the compound $CH_3COOCH_2CH_2CH_2CH_2OCH_2CH_2CH_2CH_2Cl$ is 56.54.

Anal. Calcd. for $C_{10}H_{19}O_3Cl$: Cl, 15.94. Found: Cl, 16.05, 16.09, 16.27.

The redistilled product (G) of b. p. 175–178° at 10 mm., of which only a few grams were obtained, possessed a chlorine content corresponding to the formula $CH_3COO(CH_2)_4O(CH_2)_4O(CH_2)_4Cl$.

Anal. Calcd. for $C_{14}H_{27}O_4Cl$: Cl, 12.01. Found: Cl, 12.61, 12.58, 12.54.

δ-Chlorobutyl Acetate. (2) Reaction of Acetyl Chloride with Tetrahydrofuran in the Presence of Zinc Chloride.—In view of the long period of heating required to bring about the interaction of acetyl chloride and tetrahydrofuran, anhydrous zinc chloride was added with the expectation that it would increase the yield. In the first run, 261 g. (3.32 moles) of acetyl chloride was added gradually to 111 g. (1.54 moles) of tetrahydrofuran and 53.2 g. (0.39 mole) of anhydrous zinc chloride in an all-glass apparatus, which was protected from the entrance of atmospheric moisture. Much heat was evolved at first and the reaction mixture turned dark. At the end of twelve hours of refluxing a considerable amount of sludge was found to have been formed in the flask. The mixture was extracted with ether, the ethereal solution was washed with water, dried over calcium chloride and distilled, giving only a 10% yield of δ-chlorobutyl acetate and a small amount of fraction boiling from 96–160° at 25 mm.

Subsequent runs, summarized in Table I, led to the use of a 10–20 mg. portion of zinc chloride, a period of refluxing of about an hour and the direct distillation of the mixture without the hydrolysis procedure mentioned above. Run 10, made in this way, gave 72 g., a 76% yield, of δ-chlorobutyl acetate and 9 g. of the higher boiling products, which account for most of the tetrahydrofuran.

TABLE I

Run	CH_3COCl	Tetrahydrofuran	$ZnCl_2$	Yield, G.	%	Time reflux, hr.	Remarks
1	261 g.	111 g.	53.2 g.	20	10	12	Heavy sludge
2	135	66	10	30	20	1.5	Heavy sludge
3	212	90	2	36	14	2	Light sludge
4	94	48	7.3	30	27	No	Heavy sludge
5	94	48	0.5	40	38	1	Light sludge
6	94	48	0.3	54	52	1	Light sludge
7	94	48	0.1	54	52	2.5	Light sludge
8	94	48	10 mg.	71	70	0.5	No sludge, no discoloring
9	65	50	10 mg.	72	71	0.5	No discoloring
10	65	50	10 mg.	79	76	1.5	Direct distn.

(3) Reaction of Acetyl Chloride with Tetrahydrofuran in the Presence of Anhydrous Aluminum Chloride.—A weight of 48 g. (0.67 mole) of tetrahydrofuran and 94 g. (1.12 moles) of acetyl chloride was allowed to react in the presence of 1 g. of anhydrous aluminum chloride. The reaction, which was very violent, gave much sludge and a poor yield of δ-chlorobutyl acetate. No attempts were made to find the optimum amount of catalyst.

δ-Chlorobutyl Propionate.—When 93 g. (1.01 moles) of propionyl chloride, 70 g. (0.98 mole) of tetrahydrofuran and 15 mg. of zinc chloride were allowed to react for one hour, hydrolyzed and distilled, δ-chlorobutyl propionate was obtained in a 73% yield together with some higher boiling products. The propionate had a b. p. of 93.5–94.5° at 15 mm. and 101.5–102.5° at 20 mm.; d^{20}_4 1.0537; $n^{20}D$ 1.43640; M_D (calcd.) 40.99; M_D (found), 40.84.

Anal. Calcd. for $C_7H_{13}O_2Cl$: Cl, 21.56. Found: Cl, 21.38, 21.63.

δ-Chlorobutyl *n*-Butyrate.—A one and one-half hour period of heating 50 g. (0.69 mole) of tetrahydrofuran, 90 g. (0.85 mole) of *n*-butyryl chloride and 10 mg. of zinc chloride gave a 62% yield of the chlorobutyl butyrate and a small amount of higher fractions. It is probable that a longer period of refluxing would improve the yield. The ester had a b. p. of 105.5–106.5° at 15 mm., and 112.5–113.5° at 20 mm.; d^{20}_4 1.0302; $n^{20}D$ 1.43791; M_D (calcd.), 45.61; M_D (found), 45.54.

Anal. Calcd. for $C_8H_{15}O_4Cl$: Cl, 19.87. Found: Cl, 20.21, 20.08.

δ-Chlorobutyl Benzoate.—A mixture of 110 g. (0.52 mole) of benzoyl chloride, 50 g. (0.69 mole) of tetrahydrofuran and 10 mg. of zinc chloride, when refluxed for an hour, gave a 54.5% yield of δ-chlorobutyl benzoate and considerable higher boiling material. In this case the tetrahydrofuran was used in excess in order to see what effect this would have on the yield of chlorobutyl benzoate, which in this single run was less than in the case of the aliphatic esters. The product was an oily liquid of b. p. 140–142.5° at 4 mm.; d^{20}_4 1.1429; $n^{20}D$ 1.52028; M_D (calcd.), 55.92; M_D(found), 56.54.

Anal. Calcd. for $C_{11}H_{13}O_2Cl$: Cl, 16.69. Found: Cl, 16.61, 16.58.

δ-Bromobutyl Acetate.[7]—The reaction of 50 g. (0.69 mole) of tetrahydrofuran and 90 g. (0.73 mole) of acetyl bromide in the presence of 5 mg. of zinc chloride took place with the evolution of much heat. At the end of one hour of refluxing, 109 g. of a fraction of b. p. 87–93° at 15 mm. was obtained. The redistillation of this gave a product of b. p. 89.5–92° at 15 mm., which, however, gave consistently high values for bromine. The same discrepancy was also noted after five further distillations. The values for the density (d^{20}_4 1.4921) and refractive index ($n^{20}D$ 1.46799), likewise, gave a molecular refractivity (M_D 37.91) which did not correspond with that computed for the ester (M_D 39.33) from the atomic refractivities of Auwers and Eisenlohr, assuming molecular weights. The impurity responsible for these discrepancies is doubtless tetramethylene dibromide.

Anal. Calcd. for $C_6H_{11}O_2Br$: Br, 41.00. Found: Br 46.63.

δ-Bromobutyl Benzoate.[8]—A mixture of 100 g. (0.54 mole) of benzoyl bromide and 35 g. (0.49 mole) of tetrahydrofuran was allowed to react in the presence of 10 mg. of zinc chloride. After the vigor of the reaction had subsided, the mixture was refluxed for one-half hour and then distilled at 9 mm., giving 94 g. of δ-bromobutyl benzoate

(7) Grishkevich-Trokhimovskii, *J. Russ. Phys.-Chem. Soc.*, **48**, 901 (1916); *C. A.*, **11**, 785 (1917).

(8) V. Braun, *Ber.*, **46**, 1782 (1913).

(76%) of b. p. 155–157°; d^{20}_4 1.3539, and $n^{20}D$ of 1.53694, together with some high boiling fractions; M_D (calcd.), 58.92; M_D (found), 59.26.

Anal. Calcd. for $C_{11}H_{18}O_2Br$: Br, 31.11. Found: Br, 31.16, 31.25, 31.09.

2,5 - Dimethyltetrahydrofuran.—Redistilled Eastman Kodak Co. 2,5-dimethylfuran of b. p. 91–94° (10 parts) was reduced in the presence of Raney nickel (1 part) in a high pressure hydrogenator as in the case of the furan itself. However, high temperatures must be avoided during the hydrogenation. The reduced product boiled from 89–91° (uncorr.), which is somewhat less than the boiling points reported for the compound prepared by other methods.

α-Methyl-δ-chloroamyl Acetate.—A mixture of 106 g. (1.06 mole) of 2,5-dimethyltetrahydrofuran and 204 g. (2.83 mole) of acetyl chloride was allowed to react in the presence of 10 mg. of zinc chloride. The mixture was then refluxed for one-half hour, carefully hydrolyzed and then worked up in the usual way, giving 145 g. of the chloro ester, a yield of 77%. The product had a b. p. of 85.5–87° at 15 mm. or 94–95° at 20 mm.; d^{20}_4 1.0132; $n^{20}D$ 1.43288; M_D (calcd.), 45.74; M_D (found), 45.67.

Anal. Calcd. for $C_8H_{15}O_2Cl$: Cl, 19.87. Found: Cl, 20.16, 20.30.

α-Methyl-δ-bromoamyl Acetate.—The reaction of 50 g. (0.5 mole) of 2,5-dimethyltetrahydrofuran, 70 g. (0.57 (mole of acetyl bromide and 5 mg. of zinc chloride took place with considerable violence. From the mixture 75 g. of product of b. p. 105–107° at 20 mm. was obtained. Although several redistillations were made, no ester could be obtained whose analysis corresponded to pure α-methyl-δ-bromoamyl acetate, as in the case of the δ-bromobutyl acetate, probably on account of the presence of dibromide.

Anal. Calcd. for $C_8H_{15}O_2Br$: Br, 35.85. Found: Br, 38.44, 38.37, 38.60.

Tetramethylene Chlorohydrin.—A mixture of 60 g. of δ-chlorobutyl acetate, 120 cc. of methanol and 0.7 cc. of concd. hydrochloric acid was warmed at 40° for three and a half days. At the end of this period most of the methyl acetate and methanol was removed by distillation under diminished pressure, being careful not to overheat the residue, since the tetramethylene chlorohydrin gives hydrogen chloride and tetrahydrofuran when heated.[9] A further quantity of 60 cc. of methanol was then added to the residue, and this mixture was again heated at 50° for six hours and then at 30° for seventeen, when the mixture was distilled, giving 36.5 g. of the δ-chlorobutanol of b. p. 64–65° at 3 mm., an 80% yield.

Summary

Acetyl chloride will react with tetrahydrofuran to give δ-chlorobutyl acetate with certain other products. The yield of δ-chloro ester is improved by the addition of a trace of zinc chloride. Other acyl halides react similarly both with the tetrahydrofuran and 2,5-dimethyltetrahydrofuran.

The work is being continued and extended.

(9) Kirner and Richter, THIS JOURNAL, **51**, 2505 (1929).

TROY, N. Y. RECEIVED JULY 26, 1939

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY OF PRINCETON UNIVERSITY]

Studies in the Ketone Sugar Series. IX. The Validity of Hudson's Rules of Isorotation in the *l*-Sorbose Series. β-Ethylsorboside and its Tetraacetate

BY EUGENE PACSU

By the discovery[1] of the true α-pentaacetylfructose <2,6> and by the subsequent[2] interconversion of this substance and the β-pentaacetate, there has become known for the first time in the ketose group an α,β-pair, the mutual relationship of the members of which has been definitely proved. According to Hudson's rules of isorotation, the different a_x constants that may be calculated from this true α,β-pair and the β-derivatives of *d*-fructose should be of general applicability for all the ketoses and their derivatives. These a_x constants, with the exception of a_{OH} for chloroform solution, have been found to be throughout larger than the corresponding A_x constants in the aldose series. Difference between the values of a_x and A_x is, of course, to be expected, since the constants represent, in the latter series, the molecular rotations of carbon atom 1, H–C–X, whereas in the ketose series they express the rotational values of carbon atom 2, ROH_2C–C–X, where R designates a hydrogen atom in the free ketoses and their glycosides, and an acetyl group in the acetylated products. According to the rules of isorotation, the difference in structure or configuration of the basal chain, b_x, of the ketoses should not alter to any large extent the values of the a_x constants. If large deviations be found, it would not necessarily follow that the principle of optical superposition as applied by Hudson is of no general validity, because it is possible that the deviating "constants" have been calculated from the molecular rotations of com-

(1) Pacsu and Cramer, THIS JOURNAL, **57**, 1944 (1935).
(2) Cramer and Pacsu, *ibid.*, **59**, 711 (1937).

TABLE I

l-SORBOSE AND ITS DERIVATIVES WITH THEIR MELTING POINTS, MOLECULAR WEIGHTS, SPECIFIC AND MOLECULAR ROTATIONS, AND CALCULATED ROTATIONS

Substance[a]	M. p., °C.	Mol. wt.	$[\alpha]_D$	Mol. rot.	$[\alpha]_D$ calcd. from $a_x + b_{\alpha,\beta}$	$[\alpha]_D$ calcd. from $a_x + b_\alpha$ and $a_x + b_\beta$
α-Sorbose tetraacetate	100.8	348	−19.4	− 6,750	− 36.8	−17.2
α-Sorbose pentaacetate	97.0	390	−56.4	−22,000	− 71.6	−54.1
α-Acetochlorosorbose	67.0	367	−83.4	−30,600	−108.5	−89.9
α-Methylsorboside tetraacetate	89.5	362	−52.6	−19,100	− 71.7	[−52.6]
α-Ethylsorboside tetraacetate	75.0	376	−54.6	−20,500	− 76.4	−58.2
β-Sorbose pentaacetate	113.8	390	74.4	29,000	96.8	79.4
β-Methylsorboside tetraacetate	75.0	362	79.8	28,900	98.7	[79.8]
β-Ethylsorboside tetraacetate	86.0	376	82.7	31,000	102.5	84.3
α-Methylsorboside	122.0	194	−88.7	−17,200	−134.0	[−88.7]
α-Ethylsorboside	116.0	208	−73.9	−15,400	−120.0	−77.4
β-Methylsorboside	106.2	194	39.0	7,600	84.5	[39.0]
β-Ethylsorboside	...	208	31.0	6,500	73.5	31.2
α-Sorbose	161.0	180	−43.1	− 7,850	− 92.5	−43.3

[a] The rotations of the acetates refer to chloroform solutions and those of the other substances to aqueous solutions.

pounds which are not true α,β-stereoisomeric pairs. The history of the application of Hudson's rules in sugar chemistry shows that such errors frequently have been made in the past. Only a few years ago it was discovered[3] that neither "α"-pentaacetylfructose nor "α"-chloroacetylfructose possesses any ring structure in its molecule. Yet, the rotations of these compounds had been used together with those of the true β-compounds for calculations at a time when the correctness of the assigned structural formulas of these "α"-compounds had not been questioned. Also in the aldose series it recently has been shown[4] that the α-ethyl- and α-benzylthioglucosides are furanosides and not the diastereoisomers of the pyranoid β-compounds as earlier workers had believed.

In view of all these recent cases, where the apparent invalidity of Hudson's rules has been traced back to erroneous assumptions regarding the chemical structures of the "α,β-pairs," it appears to be necessary to ascertain the stereochemical relationship of the constituents of a reference pair, before using their rotational data for computations. This seems to be of special importance in instances where the results of the calculations indicate a failure of the principle of optical superposition. Such a failure of Hudson's rules has been recorded by Schlubach and Graefe[5] in their paper dealing with the preparation of new *l*-sorbose derivatives and with the numerical relationship of rotations in the *l*-sorbose series.

From the known α-tetraacetate of *l*-sorbose the authors have prepared the α-pentaacetate and the α-acetochloro compound. From the latter, by the replacement of the chlorine atom with an acetoxyl or methoxyl group, the β-pentaacetate and the β-methylsorboside tetraacetate have been obtained. Deacetylation of the glycoside has yielded the β-methylsorboside. Since the publication of Schlubach's work, Whistler and Hixon[6] have prepared the α-ethylsorboside and its tetraacetate, and in the Experimental Part of this paper the corresponding β-isomers are described. In the preparation of the latter compounds it has been found that the reaction between α-acetochlorosorbose and ethyl alcohol, just as in the fructose series, does not give rise exclusively to the true β-ethylsorboside tetraacetate. This sorboside is only the product of a side reaction, the main reaction being the formation of a new ethylsorboside tetraacetate possessing ortho ester structure. On account of its sirupy nature, the latter compound has not been investigated closely. Table I contains the data of all the *l*-sorbose derivatives which have been used for calculations in the present publication.

In carrying out their computations, Schlubach and Graefe have assumed that the two methylsorbosides and their acetates constitute true α,β-stereoisomeric pairs. From the molecular rotations of these pairs they have obtained $b_{\text{sorb.}} = -4800$[7] and $b_{\text{sorb. ac.}} = 4900$. Using these values, Schlubach and Graefe have calculated from the molecular rotations of the α-derivatives the different a_x constants; these values were found to be 4400 to 9250 units smaller than those

(3) Pacsu and Rich, THIS JOURNAL, **54**, 1697 (1932); **55**, 3018 (1933).
(4) Green and Pacsu, *ibid.*, **59**, 1205 (1937).
(5) Schlubach and Graefe, *Ann.*, **532**, 211 (1937).
(6) Whistler and Hixon, THIS JOURNAL, **60**, 563 (1938).
(7) The authors give +4800, which is obviously a clerical error.

of the corresponding constants determined by Pacsu and Cramer[1] from the rotations of the whole group of the fructose derivatives (Table II).

TABLE II

COMPARISON OF THE a_x VALUES OF SCHLUBACH AND GRAEFE[5] AND THE CORRESPONDING a_x VALUES DETERMINED FOR THE KETOSES BY PACSU AND CRAMER[1]

	a_x values (S. and G.) (for acetylated sorbose derivatives in chloroform)	a_x values (P. and C.) (for acetylated fructose derivatives in chloroform)	Difference
a_{OH}	12,300	17,750	−5,450
a_{OMe}	24,000	30,850	−6,850
a_{OEt}	25,400[a]	33,650	−8,250
a_{OAc}	26,900	32,850	−5,950
a_{Cl}	35,500	44,750	−9,250
	For deacetylated sorbose derivatives in water	For deacetylated ketose derivatives in water	
a_{OMe}	12,400	21,200	−8,800
a_{OEt}	15,700[a]	20,100	−4,400
a_{OH}	3,050[a]	11,800[a,b]	−8,750

[a] Addition of the present author. [b] Calculated from the rotation of the basal chain in the two methylfructosides <2,6>, $b_{fruct.} = -12,200$, and the initial rotation of β-fructose (−24,000).

Furthermore, it has been pointed out by Schlubach and Graefe that if the calculations be based on the molecular rotations of the two sorbose pentaacetates instead of the acetylated methylsorbosides, the value of $b_{sorb.\ ac.}$ becomes only 3500 instead of 4900, and all the a_x values will be 1400 units smaller. This fact could be regarded as an indication that there might be a difference in the structure of the α- and β-derivatives, since the substitution of an acetoxyl group for a methoxyl group should not influence the rotation of the basal chain to such a large extent. The other fact that the a_x values in the sorbose series deviate so greatly (4400–9250 or more) from the a_x values for the fructose derivatives could be construed as confirmatory evidence that once again incorrect "α,β-pairs" have been used for calculations. However, application of the periodic acid oxidation method of Jackson and Hudson[8] gave results which indicate that both the α- and β-sorbosides possess pyranoid ring structures. Such a structure already has been established by Whistler and Hixon[9] for the α-alkylsorbosides. Therefore, the results of the above calculations would appear to indicate a complete failure of Hudson's rules in the ketose series (column 6, Table I). However, it will be shown in the following calculations that *the isorotation rules hold closely in the sorbose series provided that the a_x constants for the fructose derivatives are applied separately to the α- and β-sorbose derivatives.*

From the molecular rotation of α-methylsorboside tetraacetate (−19,100) and the a_{OMe} constant for the fructose series, the value of the basal chain is calculated to be $b_{\alpha\text{-sorb. ac.}}$[10] = 11,750, from the equation: $-19,100 = -30,850 + b_{\alpha\text{-sorb. ac.}}$ Combination of $b_{\alpha\text{-sorb. ac.}}$ with the different a_x constants for the fructose derivatives gives the calculated specific rotations of *all the α-sorbose derivatives.* The values obtained agree satisfactorily with those found by experiment (column 7, Table I). From the molecular rotation of β-methylsorboside tetraacetate a new value for the basal chain, $b_{\beta\text{-sorb. ac.}} = -1950$, is obtained from the equation: $28,900 = 30,850 + b_{\beta\text{-sorb. ac.}}$ Combination of this new value with the a_x constants for the fructose series gives the specific rotations of *all the β-sorbose derivatives.* Again, the agreement between calculated and observed values is quite satisfactory (column 7, Table I). Similar results are obtained if calculations be carried out by the use of the molecular rotations of the two methylsorbosides. From the [M] value of α-methylsorboside (−17,200) and $a_{OMe} = 21,200$, which is the constant for the fructose derivatives, the value of the basal chain is calculated to be $b_{\alpha\text{-sorb.}} = 4000$ from the equation: $-17,200 = -21,200 + b_{\alpha\text{-sorb.}}$ From the molecular rotation of the β-methylsorboside (7600) a new value for the basal chain is calculated to be $b_{\beta\text{-sorb.}} = -13,600$, from the equation: $7600 = 21,200 + b_{\beta\text{-sorb.}}$. Combination of the respective basal chain values with the a_x constants for the fructose series gives the rotations of the α- and β-sorbose derivatives, the agreement between calculated and found values being satisfactory (column 7, Table I).

The principle that underlies these calculations is Hudson's glycoside-sugar corollary[11] from his rules of optical isorotation. He showed that the difference between the molecular rotation of a given glycoside and that of its parent sugar, $A_{OMe} - A_{OH}$, has the same numerical value (10,000) and the proper sign throughout the sugar group. He found it "a very noteworthy fact that the normal value of the difference holds for

(8) Jackson and Hudson, THIS JOURNAL, **58**, 378 (1936); *Science*, **85**, 51 (1937); THIS JOURNAL, **59**, 994 (1937).

(9) Whistler and Hixon, *ibid.*, **59**, 2047 (1937).

(10) The symbols b_α, b_β and $b_{\alpha,\beta}$ indicate that their values were obtained from the α-form, or β-form, or the α,β-pair of the sugar derivatives.

(11) Hudson, THIS JOURNAL, **47**, 268 (1925).

mannose and rhamnose," although "these sugars . . . exhibit a considerable and similar deviation from the principle of optical superposition when the rotations of their respective α and β forms are compared." He also suggested that "the known α forms of mannose ($[\alpha]_D$ + 30) and methyl mannoside (+79), rhamnose (−7.7) and methyl rhamnoside (−62.5) . . . possess ring structures common to the respective members of each pair" and "that the β forms of these sugars, the rotations of which have been shown to differ from those of the respective α forms by a much smaller amount than is required by the principle, possess rings that are different from those of the α forms." At present, it is recognized that "rings that are different" cannot in these cases be rings that differ in the *number* of their members (pyranoid and furanoid rings), since the α- and β-derivatives of these sugars and also those of *l*-sorbose and *d*-fructose possess six-membered rings throughout. It seems probable that the difference may be ascribed to a new type of isomerism that is not apparent in the customary α,β-stereoisomeric formulas, an isomerism which very well can be accounted for by the existence of any or all of the two possible *trans* and six *cis* ring conformations[12] constituted on the Sachse principle. The numerical value of this new factor (F) can be obtained easily from either equation

$$[M]_\alpha = + A_x + (B_{\alpha,\beta} + F) \text{ and}$$
$$[M]_\beta = - A_x + (B_{\alpha,\beta} - F)$$

where A_x represents the "normal" values valid for *all* the aldoses. Until the exact physical significance of F is fully understood and it becomes definitely known for which particular sugars this additional optical factor must be considered, it is only a matter of convenience to assume that F = 0 in the arabinose–glucose series, where the majority of the most common aldoses belong. Consequently, the A_x values obtained from the α,β-stereoisomeric pairs of these sugars and derivatives will represent the "normal" values valid for *all* the aldoses. From α-methylmannopyranoside ($[M]_\alpha$ = 15,250) and β-methylmannopyranoside ($[M]_\beta$ = −13,200), the value of the basal chain is calculated to be $B_{\alpha,\beta\text{-man.}}$ = 1025. These two substances do not obey Hudson's rules, since the half of the difference of their rotations gives A'_{OMe} = 14,225, instead of the "normal" value of A_{OMe} = 18,700, obtained from the members of the arabinose–glucose series. From either modified equation: $[M]_\alpha = A_{OMe} + (B_{\alpha,\beta\text{-man.}} + F)$ and $[M]_\beta = -A_{OMe} + (B_{\alpha,\beta\text{-man.}} - F)$ the value of F is calculated to be −4475. This represents the numerical value of the contribution of the new optical factor (ring conformation) to the total rotation of the molecule. According to the above arbitrary assumption, this factor does not occur, or it cancels out, in the glucose type of sugars. By the aid of F the rotation of α-mannose is calculated to be $[M]_\alpha = A_{OH} + (B_{\alpha,\beta\text{-man.}} + F)$, that is: 8450 + 1025 − 4475 = 5000, where A_{OH} = 8450 represents the "normal" value obtained from the members of the glucose type of aldoses for *all* the aldehyde sugars. Similarly, the molecular rotation of β-mannose is calculated from the equation: $[M]_\beta = -A_{OH} + (B_{\alpha,\beta\text{-man.}} - F)$ to be −2950. Then the specific rotation of α-mannose becomes 5000/180 = 28° and that of β-mannose, −2950/180 = −16.4°, which values agree excellently with the observed respective values of +29.9 and −16.3°.

In the ketose group the values of $a_{OMe} - a_{OH}$ for α-*l*-sorbose and β-*d*-fructose and their corresponding methyl glycosides are constant (9500) and practically identical with those for the aldoses (10,000).[13] However, the a_x values from the sorbose derivatives are entirely at variance with the a_x constants calculated from the fructose derivatives (Table II). Here again, just as in the aldose group, at present, it is only a matter of convenience to decide which values should be chosen as the "normal" values valid for *all* the ketoses, that is, which one of the two ketoses possesses *strictly* comparable b parts in its α- and β-forms. It is suggested that until no contradictory evidence is discovered, the a_x values derived from the fructose derivatives should be used as the "normal" values for all the ketoses. Then in the calculation of the rotations of those ketoses and their derivatives which do not obey Hudson's rules, *e. g.*, *l*-sorbose, a factor F must be added to the value of $b_{\alpha,\beta}$ for all the α-forms and subtracted from $b_{\alpha,\beta}$ for all the β-isomers. From α-methylsorbopyranoside ($[M]_\alpha$ = −17,200) and β-methylsorbopyranoside ($[M]_\beta$ = 7600) the constant $b_{\alpha,\beta}$ = −4800 is obtained. From either equation: $[M]_\alpha = -a_{OMe} + (b_{\alpha,\beta\text{-sorb.}} + F)$ and $[M]_\beta = a_{OMe} + (b_{\alpha,\beta\text{-sorb.}} - F)$, where a_{OMe} = 21,200 represents the "normal" value obtained

(12) Haworth, "The Constitution of Sugars," Edward Arnold and Co., London, 1929, p. 91.

(13) Since all the A_x constants for the aldoses are different from the a_x constants for the ketoses, the agreement is probably fortuitous.

from the two methylfructopyranosides, the value of F is calculated to be 8800. Addition of $F = 8800$ to $b_{\alpha,\beta\text{-sorb.}} = -4800$ gives $b_{\alpha\text{-sorb,}} = 4000$ for all the α-sorbose derivatives and subtraction of $F = 8800$ from $b_{\alpha,\beta\text{-sorb.}} = -4800$ gives $b_{\beta\text{-sorb.}} = -13{,}600$ for all the corresponding β-isomers. Similarly, from the acetylated α- and β-methylsorbopyranosides $F = 6850$ is obtained, which when added to, or subtracted from, $b_{\alpha,\beta\text{-sorb. ac.}} = 4900$, gives $b_{\alpha\text{-sorb. ac.}} = 11{,}750$ for all the acetylated α-sorbose derivatives and $b_{\beta\text{-sorb. ac.}} = -1950$ for all the corresponding β-forms. The very satisfactory agreement between the values calculated on this basis and the actually observed values of all the *l*-sorbose derivatives (column 7, Table I) leads to the conclusion that Hudson's rules of isorotation hold closely in the *l*-sorbose series and that measurements of the factor F for various sugars may furnish evidence concerning ring conformations.

Addendum.—The possibilities of the construction of two *trans*- and six *cis*-models of sugars on the Sachse principle have been discussed and explored by Haworth.[12] However, our attempts to build up these different forms by using the latest atom models[14] based on the true atomic dimensions resulted in the surprising discovery that only one *trans*- and one *cis*-conformation of a hexopyranose could be constructed. The skeleton models of these two conformations are shown in the sketches Figs. 1 and 2.

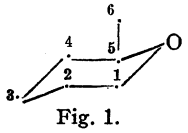


Fig. 1.

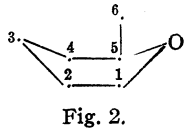


Fig. 2.

In any other conformation more or less obstruction occurs between certain atoms or atomic groups such as the terminal —CH_2OH group, the hydrogen atom and the hydroxyl group of one or more ring carbon atoms, thus making the construction of the molecule impossible. Since theoretical considerations[15] indicate that the *cis*-forms would seem to be unstable due to large repulsion both in the ring and among the subsidiary groups, there remains only one *trans*-form (Fig. 1) from which all the hexopyranoses and their derivatives must be derived. Under such circumstances the physical significance of F appears to be the disturbing effect of the different orientation of the hydroxyl groups in the α and β-isomers of certain sugars. The occurrence of such disturbances at present cannot be predicted beyond some empirical rules, neither can the effect be measured by any chemical or physical methods. In many instances the optical effect of the orientation appears to be negligible (glucose–arabinose series) but for various sugars (mannose, sorbose, etc.) it must be eliminated from the calculations by the introduction of factor F, a characteristic constant for each of these sugars. If this conclusion regarding the nature of F be correct, then the numerical value of this factor must remain the same not only for one particular sugar and its glycosidic derivatives but for any other similarly constructed sugar and its corresponding derivatives. The structure of rhamnose is very similar to that of mannose, consequently the orientation of the hydroxyl groups should not differ to any great extent in the two sugars. Indeed, the numerical value of the factor for *d*-mannose ($F = -4475$) is practically equal and opposite to that for rhamnose ($F = 4650$, obtained from α- and β-methyl-*l*-rhamnopyranoside) which belongs to the *l*-series. By the use of this factor the initial rotations of α- and β-*l*-rhamnose are calculated to be $-5.3°$ and $41.0°$, respectively. Jacobi[16] observed $-5°$ and Hudson[17] measured $-7.7°$ for the α-form, and Fischer[18] gave $31.5°$ for the β-form of a sample which probably was not quite pure.

Experimental Part

Preparation of β-Ethylsorboside Tetraacetate.—Twelve grams of α-sorbose tetraacetate was dissolved in 150 cc. of absolute ether and the solution saturated with dry hydrogen chloride at $-70°$ in a pressure bottle. After having been warmed up to 0° for twelve hours, the solution was cooled and the bottle opened. The solution was evaporated four times with ether to a sirup, rotating $-67°$ in chloroform. Attempts at crystallization of the acetochloro compound from the sirupy product failed. In order to convert it into the glycoside, the crude acetochlorosorbose was shaken with absolute ethyl alcohol and silver carbonate for several hours, then the reaction mixture was filtered and the filtrate treated with hydrogen sulfide to remove traces of silver salts. After filtration with activated carbon, the solution was evaporated to a sirup, which was stirred vigorously for ten minutes in 100 cc. of boiling water containing one drop of 0.1 N hydrochloric acid. The latter operation was necessary in order to decompose the large quantity of ortho ester formed from the

(14) Fisher–Hirschberger Atom Models, Fisher Scientific Co., Pittsburgh, Pa.

(15) Gorin, Kauzmann and Walter, *J. Chem. Phys.*, **7**, 327 (1939).

(16) Jacobi, *Ann.*, **272**, 170 (1892).

(17) Hudson, THIS JOURNAL, **48**, 1424 (1926).

(18) Fischer, *Ber.*, **29**, 324 (1896).

acetochloro compound, which ortho ester prevented the crystallization of the true glycoside. The resulting solution containing sorbose tetraacetate, which is the decomposition product of the ortho ester, and oily drops of the partially soluble β-ethylsorboside tetraacetate, was cooled and extracted with 200 cc. of benzene in several portions. The latter solution was then extracted repeatedly with water until the aqueous extract no longer reduced Fehling's solution. The benzene solution was dried over anhydrous sodium sulfate, then evaporated to a sirup, whose 15-cc. ether solution, on addition of 30 cc. of petroleum ether, deposited 2.5 g. of crystalline β-ethylsorboside tetraacetate. After repeated recrystallization from the same solvents, the substance melted at 86° and showed $[\alpha]^{20}D$ 82.7, $[\alpha]^{20}C$ 66.0 and $[\alpha]^{20}Hg_I$ 98.0 in chloroform solution (0.200 g. of substance, 10 cc. of solution, 2-dm. semimicro tube; rotations 3.31, 2.64 and 3.92° to the right, respectively). In an acetyl estimation, 0.3762 g. of the substance required 40.3 cc. of decinormal alkali; calcd. for four acetyls, 40.0 cc.

The same compound was obtained from the acetochlorosorbose, which was prepared according to Schlubach and Graefe from the reaction of sorbose tetraacetate and liquid hydrogen chloride in an autoclave at 0°. Also in this case a large quantity of ortho ester accompanied the formation of the glycoside. The crystalline β-methylsorboside tetraacetate of Schlubach and Graefe was obtained readily by either method after the ortho ester, the main product of the reaction, had been decomposed by very dilute acid.

β-Ethylsorboside.—A solution of 0.05 g. of metallic sodium in 5 cc. of absolute methyl alcohol was added to 4 g. of β-ethylsorboside tetraacetate dissolved in 5 cc. of the same solvent.[19] After two days the solution was evaporated to leave a colorless sirup, which was extracted with cold absolute ethyl alcohol. The substance, a colorless product, has not yet been obtained in crystalline form. Its specific rotation was 31.0° in water solution (0.4324 g. in 25 cc. rotated 1.07° to the right; 2-dm. tube). Reacetylation gave back the crystalline β-ethylsorboside tetraacetate.

Oxidation of α-Methylsorboside and β-Ethylsorboside by Periodic Acid.—Jackson and Hudson[8] showed that the cleavage type of oxidation by periodic acid of the glycosides provides a new method for the determination of ring structure. Differentiation between the pyranosides and furanosides of the pentoses and hexoses is based on the fact that, on treatment by periodic acid, the pyranosides give rise to one mole of formic acid whereas the furanosides yield no formic acid under similar experimental conditions. Application of this method to the α- and β-sorbosides resulted in the formation of nearly one equivalent of formic acid which was obtained by distillation under diminished pressure of the reaction mixture. This result is regarded as a definite proof of the pyranoid ring structure present in both alkyl sorbosides.

(19) Zemplén and Pacsu, *Ber.*, **62**, 1613 (1929).

Twenty cc. of a 0.1 molar solution of crystalline periodic acid was added to 10 cc. of a 0.1 molar aqueous solution of the glycoside. After sixteen hours of standing at room temperature, the solution was mixed with 20 cc. of decinormal sodium hydroxide solution, then transferred into a 250-cc. distilling flask and evaporated to dryness under diminished pressure at a bath temperature of 45 to 50°. The receiver flask containing 10 cc. of the same standard alkali solution was cooled by running water during the distillation. The residue was then dissolved in 10 cc. of distilled water and the solution was evaporated *in vacuo*, the distillate being collected in the same receiver. Titration of the content of the receiver by decinormal acid solution showed that 9 cc. and 8.6 cc. of 0.1 molar formic acid was obtained from α-methylsorboside and β-ethylsorboside, respectively, instead of the theoretical yield of 10 cc.

Acknowledgment is made to Dr. C. S. Hudson for the *l*-sorbose used in this investigation. The author also wishes to thank Dr. J. W. Green for his helpful assistance in the experimental work.

Summary

It has been shown that Hudson's rules of isorotation hold closely in the *l*-sorbose series provided that the a_x constants for the ketoses are applied separately to the α- and β-derivatives.

The rotations of the α- and β-isomers can be calculated by introduction of factor F in the equations: $[M]_\alpha = -a_x + (b_{\alpha,\beta} + F)$ and $[M]_\beta = a_x + (b_{\alpha,\beta} - F)$. The numerical value of F has been determined to be 6850 for the acetylated and 8800 for the deacetylated products. Similarly, by introduction of a factor (F) in the equations, the rotation of α- and β-mannose can be calculated from the "normal" A_{OH} value for the aldoses. It is suggested that F represents the numerical value of the contribution of a new optical factor (ring conformations) to the total rotation of the molecule.

It has been found that the reaction between α-acetochlorosorbose and methyl or ethyl alcohol gives rise to the ortho esters, as the main products and only to a small quantity of the true β-alkylsorboside tetraacetates. Crystalline β-ethylsorboside tetraacetate has been obtained and the pyranoid ring structure of α-methyl- and β-ethylsorboside has been proved by the periodic acid oxidation method of Jackson and Hudson.

PRINCETON, NEW JERSEY RECEIVED FEBRUARY 24, 1939

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY OF PRINCETON UNIVERSITY]

Studies in the Ketone Sugar Series. X. The Synthesis of a New Disaccharide, 1-β-Glucosidofructose, and the Structure of Turanose and Melezitose[1]

BY EUGENE PACSU, E. JUSTIN WILSON, JR., AND LADISLAS GRAF

In 1926 Zemplén and Braun[2] prepared hendecamethylmelezitose which on controlled hydrolysis gave 2,3,4,6-tetramethylglucose and heptamethylturanose. On further hydrolysis the latter substance gave rise to the same tetramethylglucose and a sirupy trimethylfructose with $[\alpha]_D$ 30° in water and 25° in alcohol solution. Using the method of elimination for structure determination, Zemplén and Braun concluded that their product was the 1,3,4-trimethylfructose. On this basis and on the assumption that melezitose was a derivative of sucrose which at that time was believed to possess a 2,6-ring in its fructose constituent, Zemplén and Braun also concluded that melezitose contained a glucosidic group at the fifth carbon atom of the fructose portion of the molecule and that turanose was a 5-glucosidofructose. After Haworth and Hirst[3] had shown that the fructose constituent of sucrose did not belong to the pyranoid type but contained a 2,5-ring, Zemplén[4] pointed out that in such case turanose was a 6-glucosidofructose and melezitose was the corresponding 6-glucosido derivative of sucrose. Zemplén's results and conclusions were later confirmed by Miss Leitch[5] with the exception that she reported the rotation 55.5° in alcohol solution for the sirupy trimethylfructose. In 1931 Pacsu[6] found that on treatment with triphenylmethyl chloride and subsequent acetylation turanose gave rise to a triphenylmethyl derivative and its pentaacetate. He considered this fact as evidence of the presence of three primary hydroxyl groups in turanose. This discovery together with the results of the methylation experiments of Zemplén and of Leitch led him to the conclusion that the formulas of turanose and melezitose originally suggested by Zemplén and Braun were the more probable. In a series of investigations Pacsu[7] subsequently prepared and studied the properties of the acetohalogeno derivatives, the methylglycosides and the acetates of turanose. For reasons discussed in Part VII[7e] several of these derivatives were described as ortho esters. Especially the existence of five octaacetates made it necessary that other than normal structures should be assigned to some of them in order to avoid conflict with the accepted structure of turanose. During the later phase of these investigations, however, it became increasingly difficult, if not impossible, to reconcile the new experimental facts with either the 5- or the 6-glucosidofructose formula of turanose. Striking difference between the properties of the true, crystalline 1,3,4-trimethylfructose[8] (m. p. 75°; $[\alpha]^{18}D$ −52° in water solution) and those of the similarly named sirupy product of Zemplén and of Leitch also indicated that error must have been made in the structure determination of this important key substance and, consequently, the structures assigned to both turanose and melezitose were incorrect. If positions 5 and 6 in the fructose portion of turanose are thus eliminated from the possibilities where the disaccharide linkage might occur, there remain only carbon atoms 1, 3 and 4 for such union. If the glucosidic group were combined with carbon atom 4, the osazone of turanose[9] would be identical with maltosazone. This, however, is not the case.[10] Hence the glucosidic group must be attached on either carbon atom 1 or carbon atom 3. The fact that turanose gives an osazone does not *a priori* eliminate carbon atom 1 as a possible place for the disaccharide linkage. It is entirely conceivable that the ketone group and the adjacent secondary alcoholic group of a 1-glucosidofructose might react with phenylhydrazine to give a 2,3-osazone. Similarly constructed osazones have been reported[11] in the literature.

(1) This work was begun in the first semester of the academic year 1937-38 in the II. Chemical Institute of the Royal Hungarian University at Budapest, where the senior author spent his sabbatical leave. The experiments carried out in that Institute with Dr. Ladislas Graf, University Assistant, were later repeated and concluded in this Laboratory with Mr. E. Justin Wilson, Jr., Research Assistant on Special Funds from the Rockefeller Foundation.

(2) Zemplén and Braun, *Ber.*, **59**, 2230 (1926).

(3) Haworth and Hirst, *J. Chem. Soc.*, 1858 (1926).

(4) Zemplén, *Ber.*, **59**, 2539 (1926).

(5) Leitch, *J. Chem. Soc.*, 588 (1927).

(6) Pacsu, THIS JOURNAL, **53**, 3099 (1931).

(7) (a) Part I, Pacsu, *ibid.*, **54**, 3649 (1932); (b) Part II, Pacsu, *ibid.*, **55**, 2451 (1933); (c) Part III, Pacsu and Rich, *ibid.*, **55**, 3018 (1933); (d) Part VI, Cramer and Pacsu, *ibid.*, **59**, 711 (1937); (e) Part VII, Pacsu and Cramer, *ibid.*, **59**, 1059 (1937).

(8) (a) Hibbert and Tipson, *ibid.*, **52**, 2582 (1930); (b) Challinor, Haworth and Hirst, *J. Chem. Soc.*, 676 (1934).

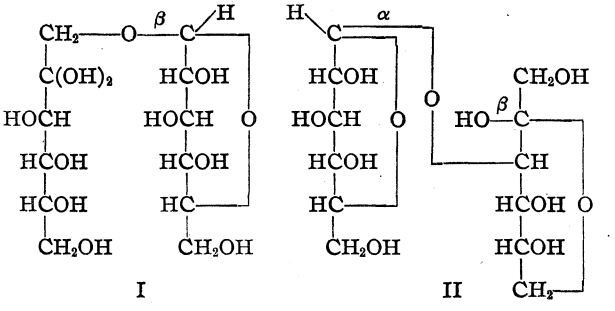
(9) Fischer, *Ber.*, **17**, 583 (1884).

(10) Isbell and Pigman, *Bur. Standards J. Research*, **20**, 787 (1938).

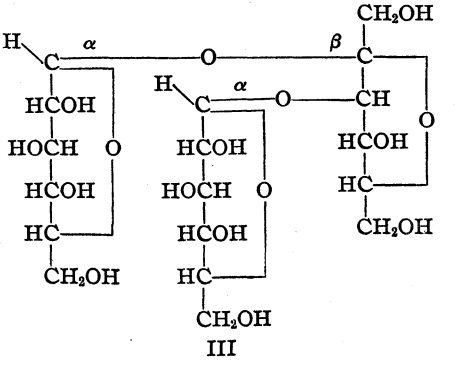
(11) (a) De Bruyn and van Ekenstein, *Rec. trav. chim. de Pays-Bas*, **16**, 270, 277 (1897); (b) Nef, *Ann.*, **357**, 296 (1907).

For the investigation of this problem with all its implications regarding the structure of turanose and melezitose, 1-β-glucosidofructose was prepared in the following way. The starting material, 2,3-4,5-diacetone-β-fructopyranose[12] was condensed with tetraacetyl-1-bromoglucose by means of the Königs–Knorr reaction as modified by Reynolds and Evans.[13] The product of the reaction was 1-tetraacetyl-β-glucosido-2,3-4,5-diacetone-β-fructopyranose with m. p. 162–163° and $[\alpha]^{20}D$ −32.9° in chloroform solution. Deacetylation of this compound resulted in the formation of 1-β-glucosido - 2,3 - 4,5-diacetone - β - fructopyranose with m. p. 174–175° and $[\alpha]^{20}D$ −45.6° in water solution. On removal of the two acetone residues by controlled acid hydrolysis, this substance gave rise to the desired disaccharide, 1-β-glucosidofructose with m. p. 132–135° and $[\alpha]^{20}D$ −59.2° in water solution. The new sugar crystallized from its aqueous solution with two molecules of water, of which one was probably chemically bound. It reduced Fehling's solution but unlike turanose it was not fermented by yeast and no mutarotation could be observed in its aqueous solution. The latter fact lent support to the view that the substance represented a derivative of the open-chain fructose hydrate (I). Although the new disaccharide was obviously different from turanose there remained the possibility that the difference was caused by an α,β-isomerism similar to that in the cellobiose–maltose pair. The α-glucosidic linkage in turanose has been proved[14] by Bridel and Aagaard and the presence of a β-glucosidic linkage in the new disaccharide follows from the fact that the sugar was prepared from acetylbromoglucose. It was, therefore, of great interest to investigate whether or not the 1-β-glucosidofructose will give an osazone as readily as turanose. It was found that under normal experimental conditions no osazone was formed from the new sugar. However, in the presence of an excess of acetic acid or if the heating with phenylhydrazine was extended to thirty minutes, a slight precipitation occurred and the isolated substance was identified as glucosazone.[15]

From the results of these experiments it became evident that turanose and 1-β-glucosidofructose were two entirely different sugars. Consequently the α-glucosidic group in turanose must be attached on carbon atom 3 of the fructose constituent as the only possible position left for the disaccharide linkage. Since Isbell and Pigman[10] have shown that crystalline turanose exhibits a pyranose–furanose mutarotation, the structure of this sugar has now become definitely established as 3-α-glucosido-β-fructopyranose represented by formula II.



As to the structure of melezitose, the identity of the potential disaccharide fructose< >glycopyranose presents an interesting problem. Unlike turanose this disaccharide cannot be isolated in a free state and it may be sucrose with a 2,5-ring in the fructose part or a ring isomer of sucrose with a fructopyranose constituent. This problem is now under investigation in this Laboratory and the results so far obtained indicate that in all probability the structure of melezitose corresponds to formula III.



With the recognition of the true structure of turanose as 3-α-glucosidofructose, it became necessary to revise the chemical formulas assigned to all the

(12) (a) Fischer, *Ber.*, **28**, 1165 (1895); (b) Ohle and Koller, *ibid.*, **57**, 1571 (1924).

(13) Reynolds and Evans, THIS JOURNAL, **60**, 2559 (1938).

(14) (a) Bridel and Aagaard, *Bull. soc. chim. biol.*, **9**, 884 (1927); (b) Aagaard, *Tidskr. Kemi Bergwaesen*, **8**, 5, 16, 35 (1928).

(15) By condensation of 12 g. of their supposed [Brigl and Schinle, *Ber.*, **66**, 325 (1933); Part II, Note 9, Pacsu, THIS JOURNAL, **55**, 2451 (1933)] 2,3,4,5-tetraacetylfructopyranose with 6 g. of acetylbromoglucose Helferich and Bredereck [*Ann.*, **465**, 166 (1928)] obtained 0.2 g. of a crystalline octaacetate (m. p. 129° and $[\alpha]^{20}D$ 14.1° in chloroform solution) of 1-β-glucosidofructose. On deacetylation of this acetate the authors obtained a small quantity of an amorphous product which was found to give glucosazone in a very small yield when treated with phenylhydrazine "in the customary manner."

TABLE I

DESIGNATION OF THE INCORRECT AND THE TRUE STRUCTURAL FORMULAS OF TURANOSE DERIVATIVES AND THE M. P. AND SPECIFIC ROTATION OF THE SUBSTANCES

Present incorrect designation	M. p., °C.	$[\alpha]^{20}D$ in chloroform solution	Designation of the correct structural formula
"First octaacetylturanose"[a] (Hexaacetyl-β-turanose<2,6>-2,3-*l*-semiorthoacetic anhydride)	216–217	20.5°	Octaacetyl-3-α-glucosido-β-fructopyranose
"Fourth octaacetylturanose"[a] (Hexaacetyl-β-turanose<2,6>-2,3-*d*-semiorthoacetic anhydride)	194–195	103.2°	Octaacetyl-3-α-glucosido-α-fructopyranose
"Fifth octaacetylturanose"[b] (β-Octaacetylturanose)	Sirup	67.4°	Octaacetyl-3-α-glucosido-β-fructofuranose
"Second octaacetylturanose"[a] (α-Octaacetylturanose)	158	107.0°	Octaacetyl-3-α-glucosido-α-fructofuranose
"Third octaacetylturanose"[a,c] (Octaacetyl-*keto*-turanose)	96	126.2°	Octaacetyl-3-α-glucosido-*keto*-fructose
"Stable chloroacetylturanose"[a] (Hexaacetyl-β-turanose<2,6>-2,3-*l*-orthoacetyl chloride)	165	− 0.4°	Heptaacetyl-2-chloro-3-α-glucosido-β-fructopyranose
"Stable bromo-acetylturanose"[a] (Hexaacetyl-β-turanose<2,6>-2,3-*l*-orthoacetyl bromide)	133–134	−30.5°	Heptaacetyl-2-bromo-3-α-glucosido-β-fructopyranose
"Stable iodo-acetylturanose"[a] (Hexaacetyl-β-turanose<2,6>-2,3-*l*-orthoacetyl iodide)	105–106	−54.2°	Heptaacetyl-2-iodo-3-α-glucosido-β-fructopyranose
Heptaacetylturanose[d] (ortho ester structure with *l*-configuration)	140–141	37.0°	Heptaacetyl-3-α-glucosido-β-fructopyranose
"Normal" β-methylturanoside heptaacetate[d]	188–189	27.5°	Heptaacetyl-3-α-glucosido-β-methylfructopyranoside
"Normal" β-methylturanoside[d,e]	173–174	3.6°[f]	3-α-Glucosido-β-methylfructopyranoside
Heptaacetyl-β-methylturanoside with ortho ester structure[d]	162–164	80.0°	Hexaacetyl-1,2-[methoxyl-ethylidene]-3-α-glucosido-β(?)-fructopyranose
"γ"-(3)-Monoacetyl-β-methylturanoside[d]	137	114.6°[f]	1,2-[Methoxyl-ethylidene]-3-α-glucosido-β(?)-fructopyranose

[a] Note (7a). [b] Note (7d). [c] Note (7c). [d] Note (7b). [e] This substance was originally described as a sirup. Later it was obtained in long needles from alcohol solution and showed the indicated constants. [f] In water solution.

derivatives which were previously prepared from this sugar. In this revisionary work it was found that all the experimental facts accumulated during the past investigations could be interpreted excellently on the basis of the new formula. In Table I a list is given of the more important turanose derivatives with their incorrect designations as they now appear in the literature. The last column contains the names of the correct chemical formulas which are based on experimental facts and on the true structure of turanose. Since it is impractical to designate turanose derivatives possessing the furanoid or pyranoid fructose constituent by retaining the word "turanose," the scientific name of 3-α-glucosidofructose has been used throughout because this permits the precise designation of any structural difference.

The acetohalogeno derivatives, the methylglycosides and the acetates of 1-β-glucosidofructose are now being investigated in this Laboratory.

Experimental Part

2,3–4,5-Diacetone-β-fructopyranose.—This substance was prepared by a slightly modified procedure of Ohle and Koller.[12b] Forty cc. of concentrated sulfuric acid was added drop by drop with mechanical stirring to one liter of acetone in an ice–salt mixture. The solution was then shaken on the machine at room temperature with 50 g. of fructose. After three hours of shaking the solution became clear and it was made alkaline with concentrated ammonia solution; the ammonium sulfate was filtered off and the clear filtrate was evaporated *in vacuo* yielding a solid residue or a sirup. This was dissolved in hot water containing about 25% ethyl alcohol and the hot solution was filtered with activated carbon. The resulting clear, orange-colored solution was treated with water until a slight cloudiness developed; then it was warmed up again and allowed to cool and crystallize. Large prismatic crystals of pure β-diacetonefructose were obtained. On concentration *in vacuo* the mother liquor yielded additional crystals. After one recrystallization from dilute alcohol, the substance had m. p. 96–97° and $[\alpha]^{20}D$ −33.0° in water solution. These values are in good agreement with those recorded[12a,b] in the literature; total yield, 47 g.

1-Tetraacetyl-β-glucosido-2,3–4,5-diacetone-β-fructopyranose.—The condensation of β-diacetonefructose with acetylbromoglucose was carried out according to the procedure of Reynolds and Evans[13] for the preparation of gentiobiose. Twenty-six g. of β-diacetonefructose, 25 g. of silver oxide prepared according to Helferich and Klein,[16] 100 g. of Drierite and 100 g. of absolute chloroform were placed in a 500-cc. three-necked flask equipped with a mercury-sealed stirrer, calcium chloride tube and a separatory funnel. The mixture was stirred for one hour to ensure the absence of moisture, then 5 g. of iodine was added after the manner of Helferich and co-workers.[17] A solution of 42 g. of acetylbromoglucose in 150 cc. of absolute chloroform was then added in one hour to the reaction mixture under vigorous stirring at room temperature. After twenty-four hours of continuous stirring the apparatus was fitted with a condenser and the stirring was continued at 55–60° for one hour. The reaction mixture was filtered through a layer of activated carbon, the filtrate was concentrated *in vacuo* and the crystalline residue was dissolved in 200 cc. of hot ethyl alcohol. Upon cooling the disaccharide derivative separated in colorless needles which were recrystallized from alcohol; yield, 30

(16) Helferich and Klein, *Ann.*, **450**, 219 (1926).
(17) Helferich, Bohn and Winkler, *Ber.*, **63**, 990 (1930).

to 35 g.; m. p. 162–163°; $[\alpha]^{20}D$ −32.9° in chloroform solution (*c*, 2.374). The substance was insoluble in cold water, slightly soluble in hot water and petroleum ether, soluble in cold ether. In an acetyl estimation 0.4666 g. of the substance was dissolved in 22 cc. of pure acetone. This solution required 31.75 cc. of decinormal alkali, whereas the value calculated for tetraacetyl-1-glucosido-β-diacetonefructose is 31.63 cc.

Anal. Calcd. for $C_{26}H_{38}O_{16}$: C, 52.85; H, 6.48. Found: C, 53.14; H, 6.47.

1 - β - Glucosido - 2,3 - 4,5 - diacetone - β - fructopyranose.—The deacetylation of the tetraacetate was carried out by a small quantity of sodium methoxide according to the method of Zemplén and Pacsu.[18] Sixty grams of the acetate in 300 cc. of methyl alcohol was heated on the water-bath for thirty minutes with 15 cc. of a 0.2 *N* methyl alcoholic sodium methoxide solution. After treatment with activated carbon the solution was concentrated *in vacuo* and the solid residue was crystallized from hot absolute alcohol. From the mother liquor, after treatment with activated carbon, additional crystals were obtained; yield, 42 g.; m. p. 174–175°; $[\alpha]^{20}D$ −45.6° in water solution (*c*, 0.986).

Anal. Calcd. for $C_{18}H_{30}O_{11}$: C, 51.15; H, 7.16. Found: C, 51.27; H, 7.22.

1-β-Glucosidofructose.—The conditions for the removal of the two acetone residues without simultaneously hydrolyzing the disaccharide linkage were established by quantitative estimation of the increase during hydrolysis of the reducing power of the acid solution. A 0.5179-g. sample of the diacetone derivative was dissolved in 50 cc. of 5% acetic acid, then the solution was transferred to a flask for heating in the water-bath. For reduction determination by the Bertrand method, 4-cc. samples were withdrawn at certain intervals of time and diluted to 20 cc. The permanganate solution used was standardized against a solution containing 0.3010 g. of pure glucose in 100 cc. of water. Twenty cc. of this solution required 18.22 cc. of the potassium permanganate solution, so that 1 cc. of the latter was equivalent to 6.2 mg. of copper. The results are summarized in Table II.

TABLE II

HYDROLYSIS AT 100° OF THE ACETONE GROUPS IN 0.5179 G. OF 1-β-GLUCOSIDO-β-DIACETONEFRUCTOSE DISSOLVED IN 50 CC. OF 5% ACETIC ACID. OPTICAL ROTATIONS AND COPPER REDUCING POWER

Hours	Observed rotation	$[\alpha]^{20}D$	Cc. of permanganate soln. for 4-cc. samples	Mg. of Cu	Mg. of sugar (calcd. as glucose)
0.16	−0.45°	−43.4°	..	..	..
0.42	− .38	..	..	..	..
1.50	− .38	..	2.35	14.6	7.0
3.5	− .48	..	4.0	24.8	12.0
5.5	− .50	−59.8 (calcd. as free sugar)	4.40	27.3	13.5
17.7	− .38	....	4.45	27.6	13.8
23.0	− .30	....	4.85	30.1	15.0
41.5	− .24	....	5.00	31.0	15.4

It is seen from the table that in the presence of 5% acetic acid about six hours of heating is sufficient to remove the acetone residues. At that time a 4-cc. sample of the solution, as used for the reduction determination, should contain 33.4 mg. of the new sugar. From the figure (13.5 mg.) obtained it follows that the reducing power of the disaccharide is only 40% of that of glucose. For the conversion of 40 g. of the diacetone derivative into the free sugar, eight 5-g. samples were dissolved each in 500 cc. of 5% acetic acid and the solutions were heated on the water-bath at 100° for six hours. After this time the batches were united and the solution was concentrated *in vacuo* at 45° to a crystalline mass. This was treated repeatedly with water, each time the solvent being evaporated *in vacuo* to ensure the removal of the acetic acid. Finally the hot aqueous solution of the residue was allowed to stand at 0° and crystallize. Colorless, fine needles of pure 1-β-glucosidofructose dihydrate were obtained. On concentration *in vacuo* the mother liquor yielded additional crystals: total yield, 30.5 g. After one recrystallization from water the substance had m. p. 132–135° and $[\alpha]^{20}D$ −59.2° in water solution (*c*, 1.3328; first reading, eight minutes after addition of solvent). The rotation remained constant during an observation period of one day. The new sugar is difficultly soluble in cold water, hot methyl alcohol and hot dioxane, and practically insoluble in ethyl alcohol. It is regarded as an open-chain derivative of fructose hydrate (I).

Experiments carried out in fermentation saccharimeters showed that while yeast was capable of fermenting turanose very readily in distilled water to give carbon dioxide, it was without any effect on the new disaccharide.

On account of the difficult solubility of the sugar in suitable solvents the usual methods of molecular weight determination could not be employed. Finally by the aid of Menzies' differential thermometer[19] the molecular weight of the sugar in methyl alcohol was determined in a special ebullioscopic apparatus[20] as being 381 instead of the calculated value of 378. For analysis the substance was dried at room temperature over concd. sulfuric acid in a vacuum desiccator to constant weight.

Anal. Calcd. for $C_{12}H_{22}O_{11}\cdot 2H_2O$: C, 38.07; H, 6.93. Found: C, 37.76; H, 6.73.

Osazone Test on 1-β-Glucosidofructose.—When 0.5 g. of the sugar in 5 cc. of hot water was heated on the water-bath with a filtered solution of 0.5 g. of phenylhydrazine (3 moles) and 0.3 g. of glacial acetic acid (3 moles) in 5 cc. of water, the solution remained almost colorless for ten minutes. On continued heating the solution became yellow and after thirty minutes a very small precipitation of osazone took place. After filtration the solution was heated with 1 cc. of glacial acetic acid for thirty minutes, during which time a somewhat larger quantity of osazone separated. In another experiment 0.2 g. of the sugar was heated in 10 cc. of water with 0.4 g. of phenylhydrazine (6 moles) and the same amount of glacial acetic acid (10 moles). In twelve minutes a brown colored osazone separated which was filtered off. After additional heating for twenty minutes, the solution again deposited a brown colored substance. The combined solids were purified with moist ethyl acetate; yield, 70 mg. of light yellow crystals; m. p. 204–206°; $[\alpha]^{20}D$ −65.5°, in a mixture of

(18) Zemplén and Pacsu, *Ber.*, **62**, 1613 (1929).

(19) Menzies, THIS JOURNAL, **43**, 2309 (1921).

(20) Menzies and Wright, Jr., *ibid.*, **43**, 2314 (1921).

six parts of absolute alcohol and four parts of pyridine (c, 0.58). After one day the rotation became constant at $-34.5°$. On the basis of these data the substance was identified as pure glucosazone.

Summary

The present structures of turanose and melezitose are based on the supposed 1,3,4-trimethylfructose, a sirupy product obtained by Zemplén and by Leitch from the fully methylated melezitose. The existence of the true, crystalline 1,3,4-trimethylfructose and the number and properties of the octaacetates and other derivatives of turanose indicate that neither carbon atom 5 nor carbon atom 6 of the fructose part of turanose can carry the glucosidic linkage. Carbon atom 4 is also eliminated because turanosazone is not identical with maltosazone. If carbon atom 1 were the position of the linkage, 1-β-glucosidofructose would be the β-glycosidic isomer of turanose. This new disaccharide has been synthesized by condensation of acetylbromoglucose with β-diacetonefructose and subsequent hydrolysis of the acetyl and isopropylidene groups. The synthetic sugar is entirely different from turanose and unlike the latter it does not give an osazone except for a small quantity of glucosazone. Turanose, therefore, must be 3-α-glucosidofructose and melezitose the corresponding sucrose derivative. Based on the true formula of turanose the correct structures of the more important turanose derivatives are given.

PRINCETON, NEW JERSEY RECEIVED AUGUST 1, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Infrared Absorption Studies of Some Glycols and Ethoxyalcohols

BY F. T. WALL AND W. F. CLAUSSEN

It has been recognized for some time that hydroxy compounds such as the alcohols and acids can undergo association through the formation of hydrogen bonds.[1,2] This association can lead to the formation of well-defined dimers in certain cases, or to the formation of polymers of indefinite size. Thus the monocarboxylic acids form definite dimers,[3] whereas water and the alcohols can associate to form aggregates of varying sizes.[4]

It has been observed further that certain hydroxy compounds such as water not only can associate with themselves,[5] but also can bond to other molecules such as the ethers.[6] Ethyl ether has no active hydrogens, and so cannot form hydrogen bonds by itself, but its oxygen readily can take part in the formation of a hydrogen bond by serving as an acceptor for an active hydrogen atom from another molecule.

In addition to molecules bonding to others of the same kind or to suitable molecules of a different kind, it also has been found that internal bonding, giving rise to ring formation, can occur in certain cases. This type of bonding known as "intramolecular" bonding (to be distinguished from "intermolecular" bonding) occurs, for example, in o-nitrophenol,[7] and salicyl aldehyde,[8] in which cases a stable six-membered ring containing a hydrogen bond is formed.

Evidence for the above-described effects has been provided in numerous ways, but one of the most convenient methods is through the study of infrared absorption. Infrared studies show that, whereas a certain absorption frequency to be associated with an OH group is generally present in hydroxy compounds, that frequency is shifted by an appreciable amount when hydrogen bonding occurs.[1,8] The shifted or hydrogen bond frequency occurs at wave lengths higher than is found for the fundamental OH, and the magnitude of the shift is usually sufficiently large so as to leave no doubt that a change in the nature of the hydroxyl group has taken place.

The effects discussed above were first observed for the simple hydroxy compounds, by themselves or in combination with simple ethers. It was accordingly felt desirable to investigate by means of infrared absorption studies the association of the glycols and ethoxyalcohols. It is clear from their structures that these molecules offer the possibility of not only associating with one another,

(1) Errera, *Helv. Chim. Acta*, **20**, 1373 (1937).
(2) Buswell, Rodebush and Roy, THIS JOURNAL, **60**, 2239 (1938).
(3) Pauling and Brockway, *Proc. Natl. Acad. Sci.*, **20**, 336 (1934).
(4) Zachariasen, *J. Chem. Phys.*, **3**, 158 (1935).
(5) Morgan and Warren, *J. Chem. Phys.*, **6**, 666 (1938).
(6) Unpublished work of Mr. I. T. Krohn of this Laboratory.
(7) Buswell, Dietz and Rodebush, *J. Chem. Phys.*, **5**, 501 (1937).
(8) Hilbert, Wulf, Hendricks and Liddell, *Nature*, **135**, 147 (1935).

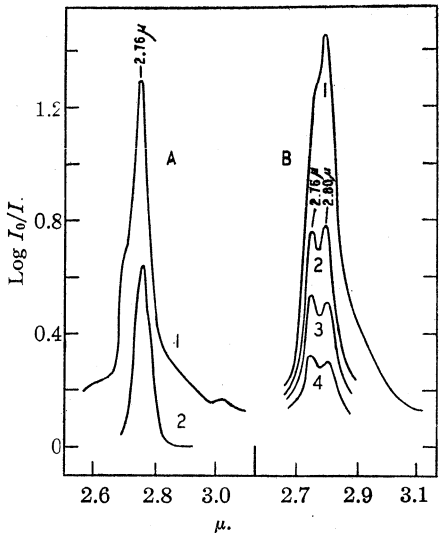


Fig. 1.—A, Ethylene glycol (1) saturated solution, (2) 1/4 saturated solution; B, propylene glycol (1) saturated solution, (2) 1/2 saturated solution, (3) 1/4 saturated solution, (4) 1/8 saturated solution. Cell length, 10.18 cm.

but that they might also undergo intramolecular bonding when the chain length is suitable. It was the purpose of these studies to find out which effect or to what extent both effects take place when these compounds are introduced into an inert solvent like carbon tetrachloride.

Substances Used.—The glycols studied were ethylene, propylene, butylene, pentamethylene, hexamethylene, decamethylene and octadecamethylene glycols. Of these, ethylene and propylene glycols have been investigated previously,[9] but under different conditions, so that it was felt desirable to repeat them here. Most of these compounds were obtained from the preparation stock rooms of our organic chemistry division. However, the pentamethylene glycol was specially prepared by the hydrolysis of pentamethylene dibromide in an alkaline water–alcohol solution. Octadecamethylene glycol was prepared under the direction of Professor C. S. Marvel by the reduction of the corresponding ester of the dibasic acid with sodium and alcohol. All of these compounds were carefully distilled or recrystallized, the physical constants being recorded in Table I.

TABLE I

		°C., Mm.
Ethylene glycol	B. p.	88/10
Propylene glycol	B. p.	105/10
Butylene glycol	B. p.	124/ 8
Pentamethylene glycol	B. p.	104/ 4
Hexamethylene glycol	M. p.	42
Decamethylene glycol	M. p.	70
Octadecamethylene glycol	M. p.	91

(9) Barnes, Bonner and Condon, *J. Chem. Phys.*, **4**, 772 (1936).

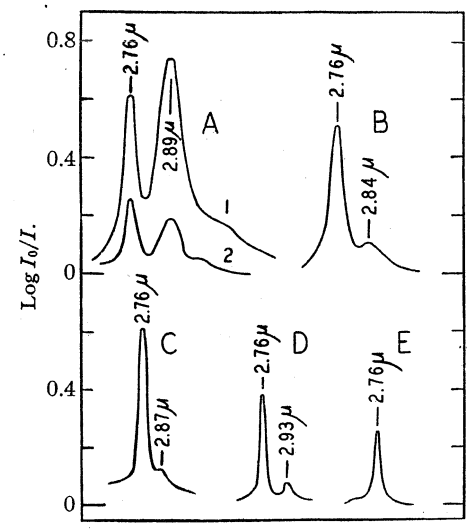


Fig. 2.—A, Butylene glycol (1) satd. solution, (2) 1/4 saturated solution; B, pentamethylene glycol, satd. soln.; C, hexamethylene glycol, satd. soln.; D, decamethylene glycol, satd. soln.; E, octadecamethylene glycol, satd. soln. Cell length, 10.18 cm.

With the exception of 2-ethoxyethanol-1 ("cellosolve"), which is commercially available, all of the ethoxyalcohols used in these studies were prepared in this Laboratory. 3-Ethoxypropanol-1 was synthesized from propylene chlorohydrin and sodium ethylate. 4-Ethoxybutanol-1 was prepared from the monosodium derivative of tetramethylene glycol and ethyl bromide. 5-Ethoxypentanol-1 was made by hydrolyzing the product from the reaction of equimolar quantities of pentamethylene dibromide and sodium ethylate. These ethoxy alcohols were carefully fractionally distilled, and the resulting boiling points are recorded in Table II.

TABLE II

Compound	B. p., °C.
Ethyl cellosolve	132
3-Ethoxypropanol-1	158–159
4-Ethoxybutanol-1	181
5-Ethoxypentanol-1	75–80 (4 mm.)

Experimental

The technique employed for the absorption studies has been described previously.[2] The spectroscope used was of the prism type, the rock salt prism being on a Littrow–Wadsworth mounting. The source of radiation was a Nernst glower, and the intensity of the beam was measured

by means of a thermocouple–galvanometer arrangement. In some cases a Moll amplifier[10] was used to increase the deflections.

The glycols were not very soluble in carbon tetrachloride, so approximately saturated solutions which were about 0.002 molar were used for the most part. In some cases more dilute solutions were investigated in order to study the effect of concentration. The solutions were placed in absorption cells of length 10.18 cm.

The ethoxyalcohols were more soluble than the glycols so they were studied for a concentration range from 0.004 to 0.256 molar. In the case of the ethoxyalcohols, the length of the cell times the concentration of the solute was kept constant for the different runs, so that the radiation passed the same amount of material in each case.

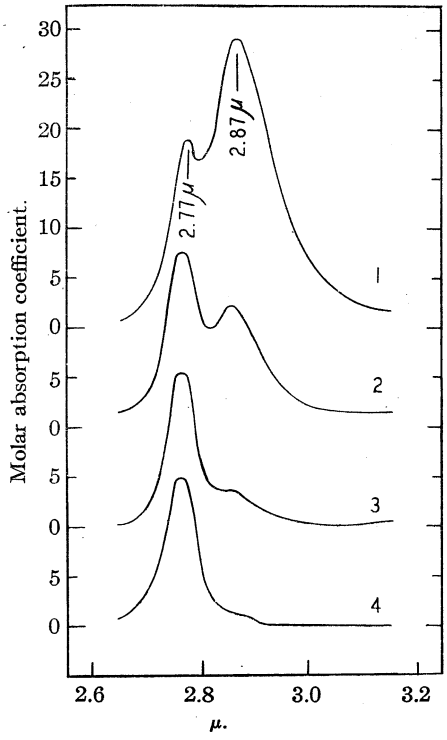


Fig. 3.—2-Ethoxyethanol-1 (1) 0.256 *M* in 0.162-cm. cell, (2) 0.064 *M* in 0.640-cm. cell, (3) 0.016 *M* in 2.53-cm. cell, (4) 0.004 *M* in 10.18-cm. cell.

The results of the experimental investigation are shown in Figs. 1 to 6. For the glycols the values of log I_0/I are plotted against wave length where I_0/I is the ratio of the intensities of light transmitted by pure solvent to that transmitted by the same length of solution. For the ethoxyalcohols, there are plotted the molar extinction coefficients defined as

$$K = \frac{1}{cd} \log \frac{I_0}{I}$$

where c is the concentration in moles per liter and d is the length of the cell in centimeters. The published curves show the absorption only in the 2.8 μ region. It should be added that all the molecules show absorption in the neighborhood of 3.35 μ and beyond, which is due to carbon–hydrogen absorption. Since we are concerned here only with hydrogen bonding possibilities, the carbon–hydrogen absorption is not included in the curves.

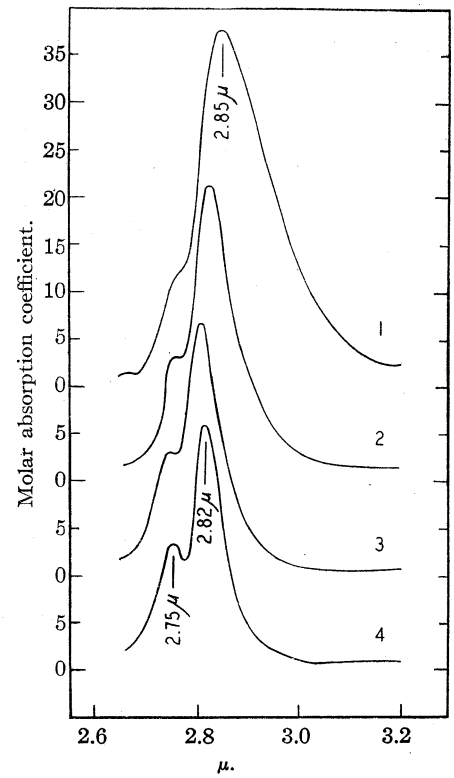


Fig. 4.—3-Ethoxypropanol-1 (1) 0.256 *M* in 0.162-cm. cell, (2) 0.064 *M* in 0.640-cm. cell, (3) 0.016 *M* in 2.53-cm. cell, (4) 0.004 *M* in 10.18-cm. cell.

Discussion of Results

The results for the glycols are somewhat difficult to interpret because their limited solubility in carbon tetrachloride prevented their study over a wide concentration range. Ethylene glycol gives no evidence for a bonded peak, but does show the fundamental OH at 2.76 μ. The failure to bond might well be due to the low concentration.

A saturated solution of propylene glycol shows a peak at 2.80 μ with a shoulder on the short wave length side. Upon dilution, using the same length cell, however, this shoulder can be resolved into an absorption maximum at 2.76 μ. Upon further dilution the 2.80 μ peak becomes relatively less im-

(10) Moll and Burger, *Phil. Mag.*, **50**, 724 (1925).

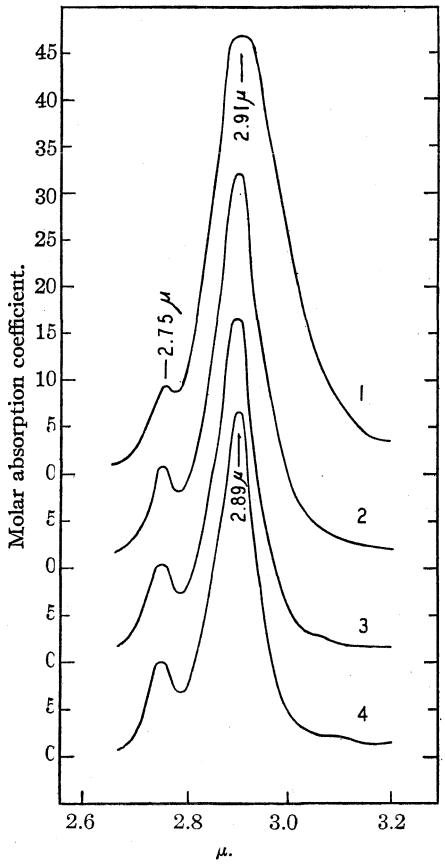


Fig. 5.—4-Ethoxybutanol-1 (1) 0.256 *M* in 0.162-cm. cell, (2) 0.064 *M* in 0.640-cm. cell, (3) 0.016 *M* in 2.53-cm. cell, (4) 0.004 *M* in 10.18-cm. cell.

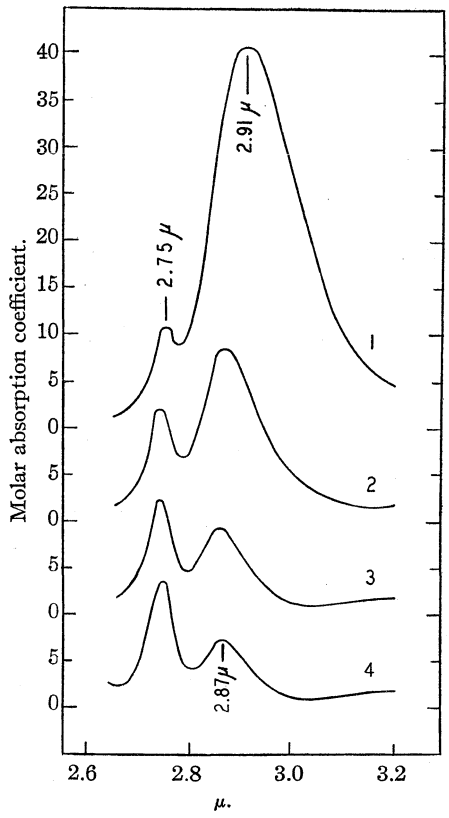


Fig. 6.—5-Ethoxypentanol-1 (1) 0.256 *M* in 0.162-cm. cell, (2) 0.064 *M* in 0.640-cm. cell, (3) 0.016 *M* in 2.53-cm. cell, (4) 0.004 *M* in 10.18-cm. cell.

portant suggesting that it is due partly to association. In the light of the results obtained for the ethoxyalcohols, the association peak for propylene glycol very likely is due to intramolecular bonding. It is possible that two non-linear hydrogen bonds are formed when the ends of propylene glycol are joined together. Such non-linear bonds would show a much smaller shift in frequency from the fundamental OH than would a regular hydrogen bond, which is in agreement with the observation.

Butylene glycol shows two well-defined peaks at 2.89 μ and 2.76 μ. Upon dilution the 2.89 μ absorption maximum goes down considerably suggesting that it is largely due to association. However, some ring formation is to be expected. The 2.76 μ absorption is due of course to the fundamental OH vibration.

The penta-, hexa-, and decamethylene glycols all show two maxima, a strong fundamental OH and a weaker bonded peak. In the case of these molecules ring formation is not probable. Octadecamethylene glycol gave evidence only for the fundamental OH frequency.

The ethoxyalcohols provide a much more interesting set of data because of their greater solubility. Each of these compounds shows two peaks, one due to the fundamental OH and the other due to the hydrogen bonded OH. Since the absorption results for these molecules were obtained by keeping $c \times d$ constant, the relative heights of the peaks have a quantitative significance capable of immediate interpretation. For each compound, the bonded or higher wave length peak decreased in height as the concentration was lowered. However, the decrease was not the same in each instance. By plotting the height of the bonded peak against concentration (Fig. 7), an idea as to what is taking place can be obtained. By extrapolating those curves to zero concentration, one can determine the molar hydrogen bond absorption at infinite dilution.

At infinite dilution, any hydrogen bonding must be of the intramolecular (ring form) type. This

follows from equilibrium considerations. The extrapolation in Fig. 7 shows that there is no bonding whatsoever for the ethoxyethanol at infinite dilution. This means that any bonding which the molecule undergoes in actual solutions must be of the intermolecular type. On the other hand, the substituted propanol and butanol show considerable bonding even at infinite dilution. This is to be attributed to ring formation. Moreover, ethoxypentanol shows only small hydrogen bonding at zero concentration. This can be associated with the fact that the pentanol would form a ring too long for stability.

It appears from these results that the most stable rings involving hydrogen bonds contain 6 or 7 atoms, including the hydrogen. These numbers are greater by one than those usually given for rings involving only the ordinary electron pair type of bond. No explanation seems immediately forthcoming as to why a five-membered hydrogen bond ring should be unstable, yet there seems to be no doubt as to the absence of ring formation in 2-ethoxyethanol-1.

Conclusion

The infrared absorption spectra of carbon tetrachloride solutions of various glycols and ethoxyalcohols have been studied in the neighborhood of 2.8 μ. The results show that the ethoxyalcohols can associate through the formation of intermolecular hydrogen bonds. Also the substituted propanol and butanol can form stable rings, whereas ethoxyethanol shows no evidence of ring formation. The glycols likewise demonstrate hydrogen bonding, but the evidence for their precise behavior is not conclusive because of their limited solubility.

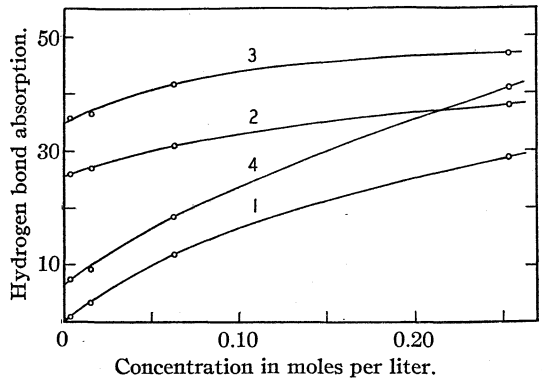


Fig. 7.—Heights of hydrogen bond peaks (1) 2-ethoxyethanol-1, (2) 3-ethoxypropanol-1, (3) 4-ethoxybutanol-1, (4) 5-ethoxypentanol-1.

The authors are indebted to Professors W. H. Rodebush and A. M. Buswell for many helpful suggestions and for their kind interest in the work.

URBANA, ILLINOIS RECEIVED JULY 5, 1939

[CONTRIBUTION FROM THE SCHOOL OF PHYSICS, THE PENNSYLVANIA STATE COLLEGE]

On the Degassing of Hydrogen-Charged Palladium

BY F. D. BENNETT[1]

For a long time experimenters have recognized that palladium sorbs very great quantities of hydrogen gas. Metals such as iron and nickel are known to sorb hydrogen and other gases in varying quantities, portions of which are held tenaciously even when the metals are heated to the melting point in vacuum. While there is considerable indirect evidence suggesting that palladium releases its sorbed gas quickly at comparatively low temperatures, apparently no direct measurements have been made of the degassing of palladium in vacuum.

In a recent investigation of the palladium–hydrogen equilibrium by Gillespie and Galstaun,[2] a series of pressure–composition isotherms over the range 80–313° is presented and several palladium hydrides postulated to explain the existence of certain discontinuities in the isotherms.

In the preparation of the palladium black with which these experiments were carried out, Gillespie and Galstaun reduced palladosammine chloride in hydrogen. The black was degassed of hydrogen at 500° in a stream of carbon dioxide and then cooled. It was further degassed in an evacuated Pyrex bulb by heating with a hand torch until the glass began to soften. The black was then transferred to the reaction bulb and hydrogen admitted in order to clean up adsorbed oxygen.

(1) Graduate Assistant in Physics at The Pennsylvania State College.

(2) Gillespie and Galstaun, THIS JOURNAL, 58, 2565 (1936).

Further degassing was carried out at the experimental temperatures[3] (200–313°).

Question has been raised[4] as to whether the procedure used by Gillespie and Galstaun was sufficient to remove all significant amounts of hydrogen from the palladium sample before the measurements were taken. The possibility of a small amount remaining in the palladium even under very strenuous degassing was suggested. Such a residual amount might cause serious error in the concentration values used by Gillespie and Galstaun and correction of the error would necessitate assumption of different hydrides from those mentioned.

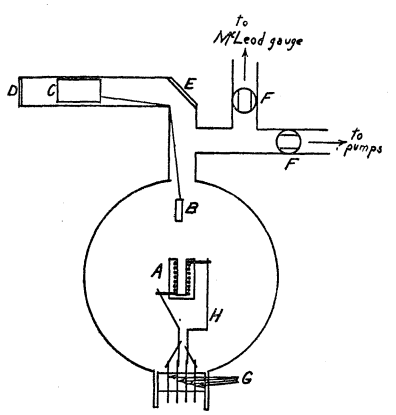


Fig. 1.

The work of Gutbier[5] and Kemmerer[6] on the determination of the atomic weight of palladium is open to similar objection, *viz.*, that neither of these investigators made certain that the palladium samples used were free of hydrogen. Kemmerer's technique differs from that of Gutbier in that Kemmerer allowed the hydrogen-treated sample to cool from 955° to room temperature in an atmosphere of nitrogen while the highest temperature at which degassing might have taken place in Gutbier's treatment was about 500°.

The purpose of this investigation is to make some quantitative determination of the degassing of hydrogen-charged palladium at various temperatures up to the melting point of palladium and to determine whether a considerable amount of hydrogen is retained at low temperatures (200–600°).

The experimental work is divided into two sections, the first of which deals with the degassing of palladium over the temperature range 650–1553°; the second covers the degassing experiments at temperatures 180–440°.

Experimental. I

Apparatus.—Figure 1 shows a schematic representation of the degassing apparatus which consists essentially of a small high-temperature furnace in a closed system with auxiliary mechanism for evacuation of system, introduction of the palladium sample and measurement of pressure changes. A refers to the crucible, B to the metallic palladium sample suspended by a thin tungsten wire from a soft-iron cylindrical shell C. The shell may be moved by magnets outside the system and the palladium lowered into the furnace at will. D is a plane piece of Pyrex sealed onto the tube; E is an aluminized mirror sealed in and inclined so that the interior of the crucible may be seen by viewing through D. F and F are mercury seal stopcocks. G indicates four 60 mil tungsten leads sealed into the bulb. H shows the 40 mil nickel wires used to support the crucible and conduct current to the tungsten furnace winding. All interior connections are spot-welded. 110 v. d. c. through a suitable system of control rheostats was used to heat the furnace. A current of 9.5 amp. was sufficient to attain the highest temperatures used—about 1600°.

The furnace itself consists of a 20 mil tungsten winding embedded in zirconium oxide shaped in crucible form. Crucible dimensions do not exceed 2 cm. each way. Zirconium chloride added to the oxide paste served as a binder until the whole had been fired by a hand torch.

Samples and Charging.—In these experiments metallic palladium rod was used instead of palladium black. The electrolytic charging method was found to be the only efficient method of charging the solid samples.

Dilute sulfuric acid (5% by weight) was used as the electrolyte in the charging cell. The sample of palladium was made the cathode of the cell and held by a platinum electrode sealed through glass under an inverted 50-cc. buret filled with the electrolyte. The hydrogen given off at the cathode either entered the palladium sample or came off in gaseous form and was collected in the buret. By passing a known charge through the cell and observing the amount of gas collected, the amount of hydrogen sorbed by the palladium could be deduced. In reducing the amount of gas collected to N. T. P. correction was made for the vapor pressure of the solution which was assumed sufficiently dilute to be considered the same as pure water. No correction was made for the amounts of hydrogen in solution in the electrolyte; these were so small as to be negligible (0.00016 g. of hydrogen dissolves in 100 g. of water at 20° and 1 atm. hydrogen pressure).

The palladium sample was charged past equilibrium by this electrolytic method, but on standing lost gas until approximate equilibrium was reached. After several chargings a nearly constant H/Pd ratio was obtained and at this ratio the sample was considered completely charged.

(3) This use of hydrogen to clean up adsorbed oxygen was not mentioned specifically in Gillespie and Galstaun's paper, but Dr. Gillespie in written communication with Dr. W. R. Ham (of The Pennsylvania State College) stated that the clean-up technique was used and has been described by him in a previous paper: Gillespie and Hall, THIS JOURNAL, **48**, 1207 (1926).

(4) Dr. W. R. Ham raised this question in the unpublished correspondence with Dr. Gillespie.

(5) Gutbier, *J. prakt. Chem.*, N. F., **79**, 235 (1909).

(6) Kemmerer, THIS JOURNAL, **30**, 1701 (1908).

Degassing.—For degassing, the charged sample was cut in half and one part left under the buret while the other was sealed into the degassing chamber. In this way a check was had on the amount of gas given up by the sample in the sealed chamber during the time prior to actual degassing.

The general technique of degassing was as follows. The furnace was heated to the highest temperature to be used in the degassing process and the system thoroughly degassed. Then the furnace was cooled to approximately 650°, system closed off and palladium introduced to furnace. Large amounts of hydrogen were liberated, but pressure change was not measured until furnace and gas had been cooled down to room temperature. The system was then evacuated thoroughly, closed off and furnace and sample again degassed at 650° to determine the amount of hydrogen sorbed when furnace and sample were cooled in the atmosphere of liberated hydrogen. This correction proved to be slightly more than 1%.

After evacuation at 650° the system was again closed off and temperature raised to 1550° in order to melt the palladium. Pressure change over the range was recorded.

Experimental. II

Apparatus.—Figure 2 shows a schematic diagram of the degassing apparatus used for the low temperature measurements. A refers to a heavy nickel tube about 14″ (35.5 cm.) long with inside diameter $^3/_8$″ (1 cm.) and outside diameter $^{13}/_{16}$″ (2.1 cm.) situated in the nichrome wound electric furnace D. B refers to water coolers brazed onto the ends of the nickel tube to cool the de Khotinsky joints E where the nickel tube is sealed to the glass tubing which makes up the remainder of the system. C is the chromel-alumel thermocouple used to measure furnace temperatures. Its leads pass out through de Khotinsky plugs F. I represents the charged sample of palladium which is attached by a stiff nichrome wire to a small piece of soft iron which may be moved by means of magnets from the outside. G and H indicate mercury seal stopcocks and K denotes the mercury manometer on which pressure changes may be read. For this series of experiments stopcock G was closed and manometer alone was used.

Samples and Charging.—A thin palladium tube about 3 mm. in diameter and 3 cm. long was used. The tube was charged by the electrolytic method exactly as described in the first section except that no particular effort was made to reach the final equilibrium charge each time. After several electrolyses the sample would spontaneously degas to a certain extent and when this occurred the tube was considered sufficiently charged.

Degassing.—The charged sample was attached to the nichrome wire and sealed into the system. The furnace was heated to the experimental temperature desired and system allowed to degas for several hours at this temperature. Then stopcock H was closed and the palladium sample introduced to the furnace. At this point time and manometer readings were recorded. Usually the degassing of the sample started within one minute from the time of introduction into the furnace and continued for a considerable period of time, especially at the lower temperatures. When the manometer reading remained constant for several minutes the degassing was taken to be complete; the sample was withdrawn and the furnace shut off so that the system could come to room temperature. When the system was cool, manometer, temperature and barometric pressure readings were taken. These together with the volume of the system allowed calculation of the amount of gas liberated by the palladium.

It was thought for a time that the low-temperature degassing might not be complete or that the furnace and palladium might re-sorb considerable quantities of hydrogen and to detect these the system was evacuated cold, closed off and heated several hundred degrees higher than the experimental temperature, whereupon the sample was readmitted and degassed further. It was found that the hydrogen given off during this process was about 3% of the total at the lowest temperature and negligible at the three higher ones.

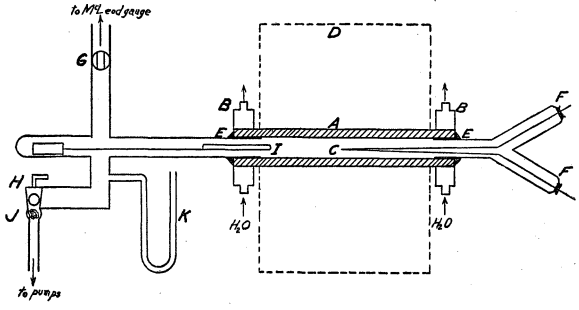


Fig. 2.

Experimental Data and Results

TABLE I

CHARGING DATA

Wt. of sample, 0.690 g.; H_1, cc. of hydrogen collected in buret during electrolysis (reduced to N. T. P.); H_2, cc. of hydrogen given up on standing (reduced to N. T. P.).

No.	Current, mils	Time, min.	H_1, cc.	Initial H/Pd	H_2, cc.	Final H/Pd
I	0.150	89.5	51.5	0.577	0	0.577
II	.150	60.8	50.8	.753	2.6	.718
III	.150	55.5	51.8	.800	5.3	.727
IV	.150	54.7	51.8	.800	6.9	.705
V	0	0	0	.705	0.5	.698

TABLE II

DEGASSING DATA

Wt. of sample, 0.336 g.; vol. of system, 1300 cc.; H indicates cc. hydrogen at N. T. P.

Temp., °C.	Pressure change μ	H, cc.	H/Pd
650	15,600	24.6	0.700
650	156	0.25	.007
650	43	0.07	.002
1553	17	neg.	..
			Total 0.709

TABLE III

Degassing temp., °C.	Degassing time	H/Pd Apparent	H/Pd Correction	H/Pd Charge	% Variation
181	14 hrs.	0.619	0.017	0.618	3
225	50 min.	.676	...	.665	2
297	3 min.	.665	...	.671	1
438	1 min.	.646	...	.672	4

Discussion

Table I gives the charging data and calculations. From Table I we see that the first electrolysis was sufficient to bring the ratio of hydrogen to palladium atoms to 0.577. This charge was evidently well below equilibrium because no hydrogen was lost on standing. Further electrolysis succeeded in raising the charge as high as 0.800, but on standing hydrogen was lost spontaneously until the ratio fell to about 0.700. This loss of hydrogen was easy to follow visually, for on breaking the current bubbles of hydrogen continued to come from the sample until the equilibrium charge was reached.

Row V shows the amount of hydrogen lost over a two-day period after the fourth electrolysis, and 0.698 represents the stable charge ratio of the sample at room temperature. Observations on the control sample show no further loss of hydrogen during the remainder of the time prior to actual degassing.

This final, stable charge is in good agreement with results of von Samson-Himmelstern[7] who found, on electrolytically charging palladium at 20°, stable charge values from 0.70 to 0.80. Of his seven determinations, four lie between 0.70 and 0.72.

The 30° isotherm of Gillespie and Hall[8] shows that at an external hydrogen pressure of 500 mm. about 72.5 cc. of hydrogen is sorbed by each gram of palladium. This amount is equivalent to an atomic ratio of about 0.69. From the curvature of the isotherm it seems likely that a moderate increase in external pressure would have brought the equilibrium charge up to 0.70.

Table II shows the degassing data and calculated results. At 650° an initial large change in pressure is recorded. The succeeding pressure changes represent the amount of gas taken up by the furnace and sample upon cooling in the liberated hydrogen.

The apparent concentration of hydrogen in palladium as shown by the 650° degassing is 0.709. This value is in close agreement with that of the known initial charge, 0.698. The variation here is about 1.6%, which is within the experimental error.

The degassing at 1553°, the melting point of palladium, gave rise to a very small pressure change and indicated that a negligible amount of hydrogen was given off.

Table III shows the results of degassing a charged sample at four temperatures lower than 650°. Of these four trials the first at 181° was the only one in which any appreciable amount of hydrogen came off during the second degassing. The 0.619 apparent H/Pd came off over a period of fourteen hours at 181° and the 0.017 correction came off in less than a minute at about 300°. Thus the total charge indicated for this trial was about 0.636 H/Pd.

The variations between the H/Pd ratio as shown by degassing and the H/Pd ratio calculated from electrolytic charging data are from 1 to 4%. These variations are erratic and are due to experimental error.

Within the uncertainty of the experiment these data show that massive hydrogen-charged palladium degasses completely and rapidly in vacuum at temperatures as low as 300°. Below this temperature degassing occurs, but takes place over much greater lengths of time and at temperatures below 200° is probably not complete.

While these data apply strictly to massive palladium, similar results obtain without doubt for palladium black. Massive palladium is notoriously more difficult to use in equilibrium experiments because of the slowness with which it takes up or gives off hydrogen. One would expect the degassing of palladium black to be somewhat more rapid than that of massive palladium, but otherwise essentially the same.

Summary

A stable charge of hydrogen in palladium is obtained by the electrolytic method such that the ratio H/Pd is equal to 0.698. This value agrees well with the existing experimental data on the subject.

It is shown within the limits of experimental error that all of the important amounts of hydrogen in a charged sample of massive palladium are driven off by degassing in vacuum at temperatures as low as 300°. Below this temperature degassing occurs but at much slower rates and with less probability of completion.

Further degassing up to the melting point shows negligible liberation of hydrogen.

No correction for unremoved hydrogen in the atomic weight of palladium as determined by Gutbier[5] and Kemmerer[6] is indicated. The assumption of Gillespie and Galstaun[2] that their samples of palladium black were sufficiently well degassed by treatment at 650° and over the range 200–300° is correct.

(7) Von Samson-Himmelstern, *Z. anorg. Chem.*, **186**, 337 (1930).

(8) L. J. Gillespie and F. P. Hall, THIS JOURNAL, **48**, 1212 (1926).

STATE COLLEGE, PENNA. RECEIVED APRIL 3, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF DUKE UNIVERSITY]

Saturated Standard Cells with Small Temperature Coefficients. IV. The Addition of Various Sulfates to the Electrolyte of the Weston Cell

BY W. C. VOSBURGH, PAUL F. DERR, GERALD R. COOPER AND BARBARA PETTENGILL

Modification of the saturated Weston cell by the addition of bismuth to the amalgam and the double salt of sodium and cadmium sulfates to the electrolyte in excess gives a saturated cell of smaller temperature coefficient than that of the normal Weston cell.[1] Some cells made by the addition of other sulfates and double sulfates to the electrolyte of the Weston cell have now been studied.

The details of the preparation and measurement of the cells were essentially as described previously.[1a] The amalgam was a 10% cadmium amalgam, except as otherwise noted. The added salt was sometimes added merely in the form of the specially purified simple salt, with the expectation that any double salt formation necessary for stable equilibrium would take place within the cell. Care was taken to provide an excess of hydrated cadmium sulfate, except as mentioned below. In some of the cells the proper double salt was added, along with cadmium sulfate. Enough sulfuric or acetic acid was added to the electrolytes to make them either 0.01 molar with respect to sulfuric acid or about 0.07 molar with respect to acetic acid.

The cells in Table I all contained hydrated cadmium sulfate as one solid phase, and contained a second solid salt which was either the salt in the first column, or a hydrate of this, or a double salt formed from this salt and cadmium sulfate. The cells were kept at 25° until the electromotive forces were constant and then measured at other temperatures. The temperatures were probably correct within 0.05°. For comparison, data for sodium sulfate from a previous paper[1a] and for the Weston cell (no added salt), and for the amalgam cell,[1] Cd(Bi,Hg)/Cd^{++}/Cd(Hg) have been added. The last was included because it was found that the cells of lowest temperature coefficient could be made by the use of a cadmium–bismuth amalgam instead of cadmium amalgam. The electromotive force of such a cell can be calculated by combination of the data for a Weston-type cell (made with cadmium amalgam) with that for the amalgam cell as if the two were connected in series. The temperature coefficient of the combination cell is the algebraic sum of the coefficients of the amalgam cell and the Weston-type cell.

(1) (a) Paper II, Vosburgh, Guagenty and Clayton, THIS JOURNAL, **59**, 1256 (1937); (b) Paper III, Vosburgh and Parks, *ibid.*, **61**, 652 (1939).

TABLE I

MODIFIED WESTON CELLS CONTAINING AS SOLID PHASES HYDRATED CADMIUM SULFATE AND AN ADDITIONAL SULFATE OR DOUBLE SULFATE

Sulfate added	No. of cells	E_{25}, v.	$E_t - E_{25}$, v. × 10^5 15°	20°	30°	35°
(Amalgam cell)[a]	...	0.00170	−55	−32	36	78
(Weston cell)	...	1.01805	40	23	−26	− 56
(Na_2SO_4 cell)[b]	...	1.01668	45	24	−28	− 64
Li_2SO_4	3	1.01411	52	28	−31	− 66
K_2SO_4	5	1.01769	41	23	−24	− 56
$(NH_4)_2SO_4$	2	1.01598	118	64	−71	+343
$CaSO_4$	2	1.01801	46	25	−27	− 57
$Al_2(SO_4)_3$	1	1.01612	42	21	−27	− 57
$Ce_2(SO_4)_3$	2	1.01779[c]	45	25	−27	− 59
$Zr(SO_4)_2$	2	1.01737[d]	43	24	−28	− 58

[a] Ref. 1. [b] Ref. 1a. [c] The two cells differed by 0.1 mv. [d] The two cells differed by 0.2 to 0.25 mv.

From the data in Table I it can be seen that the cell containing lithium sulfate when combined with the amalgam cell should give a cell of lower temperature coefficient than the sodium sulfate cell.

A number of cells were made in which the electrolyte was saturated with cadmium and lithium sulfates[2] and the amalgam was cadmium–bismuth. These cells were made in four different groups and at different times. All were more or less disturbed by temperature changes, and sometimes they assumed new electromotive forces that seemed constant after changes in temperature. This could not be ascribed to impurities, because one pair of these cells which behaved abnormally was made at the same time and so far as possible with the same materials as three of the potassium sulfate cells of Table I, and the latter behaved normally.

The lithium sulfate cells shown in Table II have two objections as standards in comparison with the sodium sulfate cells,[1a] they are more variable and they have an electromotive force somewhat different from saturated and unsaturated Weston cells. The temperature coefficient has the low value predicted. The disagreement

(2) Parks, Patterson and Vosburgh, THIS JOURNAL, **59**, 2141 (1937).

of Cells 817–822 in temperature coefficient may be the result of temperature hysteresis, which was somewhat pronounced in these cells.

TABLE II

MODIFIED WESTON CELLS CONTAINING LITHIUM SULFATE AND CADMIUM–BISMUTH AMALGAM

Cells	E_{25}, v.	$E_t - E_{25}$, v. × 10^5 15°	20°	30°	35°
(Calcd.)	1.01581	−3	−4	5	12
817–22	1.01593	+4	+5	0	..
831–34	1.01591	−6	−5	4	13
837, 839–40[a]	1.01587	...	−4	7	13
841–42	1.01597	...	+1	6	5

[a] These cells had an electromotive force of 1.01581 v. at 25° which was constant for several weeks when first prepared.

A few cells were made in which the electrolytes were saturated with a double salt of cadmium sulfate and potassium or ammonium sulfate together with an excess of potassium or ammonium sulfate. These cells had cadmium amalgams. In one group of these cells the electrolyte was saturated with both the double salt[3] $K_2SO_4 \cdot CdSO_4 \cdot 1^1/_2H_2O$ and potassium sulfate, and in another the electrolyte was saturated with the double salt[4] $(NH_4)_2SO_4 \cdot CdSO_4 \cdot 6H_2O$ and ammonium sulfate. Both cells had electromotive forces larger than that of the Weston cell, and much larger temperature coefficients. The results are shown in Table III.

TABLE III

CELLS CONTAINING A DOUBLE SALT OF CADMIUM SULFATE BUT NO CADMIUM SULFATE SOLID PHASE

No. of cells	Solid phases	E_{25}, v.	$Et - E_{25}$, v. × 10^5 20°	30°
2	$K_2SO_4 \cdot CdSO_4 \cdot 1 \cdot 5H_2O$; K_2SO_4	1.04780	79	− 75
3	$(NH_4)_2SO_4 \cdot CdSO_4 \cdot 6H_2O$; $(NH_4)_2SO_4$	1.05975	378	−401

In the previous paper on the sodium sulfate cells[1a] the most important data were for cells between one and two months old. The same cells, nos. 749–758, have now been observed for a much longer time, and some others of the same kind have been made. A new group, Cells 761–764, was made by Dr. Roger G. Bates. They were like Cells 754–758, the electrolyte having been made by the saturation of 0.1 *M* acetic acid solution with cadmium sulfate and the double salt. The amalgam for all these cells was cadmium–bismuth. Three of the newer group of cells when newly prepared agreed within 0.01 mv. with Cells 749–758. The fourth was 0.02 to 0.04 mv. lower.

Cells 749–758 eight months after they were prepared agreed almost exactly with the values reported previously. At that time, Cells 750, 752 and 754 were withdrawn from the group for a test at room temperature. From Cells 761–764, Cell 764 was taken for test at room temperature and Cell 763 was accidentally broken. The remaining nine cells of the two groups were observed from time to time at constant temperature, and their record is given in Table IV. While these cells have shown no change in two years larger than the error of measurement, a group of unsaturated Weston cells could be expected to decrease in electromotive force by something of the order of magnitude of 0.1 mv.[5] during that time.

TABLE IV

ELECTROMOTIVE FORCES OF MODIFIED WESTON CELLS CONTAINING SODIUM SULFATE AT VARIOUS AGES

Cells	E_{25} − 101,800, volts × 10^5 3 mo.	8	13	17–23	24–29
749, 751, 753	41	41	41	41	40
755–758	39	38	38	38	38
761–762	37	37	..	37	36

Four of the sodium sulfate modified cells were measured occasionally for a period of more than eight months at room temperature. The cells were mounted in wooden boxes to ensure uniformity of temperature.[6] The temperature as measured inside one of the boxes varied from 20 to 28.7°, while the average electromotive force of the four varied from 1.01835 to 1.01845 when no correction for temperature was applied. A correction for temperature would reduce the variation considerably.

It may be concluded that the sodium sulfate cell is more nearly constant in electromotive force at constant temperature than the unsaturated Weston cell, for periods of over two years at least. Its variation under ordinary room-temperature conditions is not large enough to cause serious error for many purposes if it should be used as a standard.

Summary

Modified Weston cells were prepared in which the electrolytes were saturated with two sulfate salt phases, one phase being either hydrated cad-

(3) Benrath and Thönnessen, *Z. anorg. allgem. Chem.*, **203**, 408 (1932).

(4) Malhotra and Suri, *J. Phys. Chem.*, **34**, 2106 (1930).

(5) (a) Vosburgh, *J. Optical Soc. Am.*, **11**, 59 (1925); (b) Smith, *Rev. Sci. Instruments*, **5**, 425 (1934).

(6) For the mounting of these cells and for some of the electromotive force measurements the authors are indebted to Mr. Harry Pfann.

mium sulfate or a double salt of cadmium sulfate. These cells were measured at different temperatures.

The temperature coefficient of the cell containing lithium sulfate was such that if made with cadmium–bismuth amalgam it would have a temperature coefficient less than that of the sodium sulfate cell previously reported.

A number of the lithium sulfate cells with ternary amalgams were not as constant or reproducible as the sodium sulfate cell.

Further observations on the constancy and reproducibility of the sodium sulfate cell are reported.

DURHAM, N. C. RECEIVED AUGUST 4, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF ST. JOHN'S UNIVERSITY]

The System Li_2SO_4–$Al_2(SO_4)_3$–H_2O at 0°

BY HAROLD A. HORAN AND JOHN A. SKARULIS

Systematic studies of the ternary system Li_2SO_4–$Al_2(SO_4)_3$–H_2O have been carried out at 30°[1] and at 0°[2] and in both cases it was concluded that the only solid phases in equilibrium were $Li_2SO_4 \cdot H_2O$ and $Al_2(SO_4)_3 \cdot 18H_2O$. In the study at 0°, the solubility of pure lithium sulfate was found to be 25.43%, while for aluminum sulfate the value found was 27.02%. The former value differs considerably from that found by Friend,[3] namely, 26.51%, which was determined using carefully prepared and purified lithium sulfate and employing an analytical method which was direct and not subject to appreciable error. The aluminum sulfate value given above is considerably higher than the values found by Poggiale[4] and by Kremann and Hüttinger[5] and definitely lower than a recently found value[6] of 27.97%. The large differences in the values for both salts undoubtedly are due to differences in the purity of materials used, methods of obtaining equilibrium and the analytical methods employed.

Rather recently the existence and properties of a lithium alum have been reported.[7] The alum is supposedly formed at temperatures in the neighborhood of 0° although no definite temperature is mentioned.

In view of these claims as well as the disagreements in solubilities mentioned above, it was thought advisable to reinvestigate the ternary system at 0°, taking special care as to the materials used, methods of obtaining equilibrium and methods of analysis.

(1) Schreinemakers and de Waal, *Chem. Weekblad*, **3**, 539 (1906).
(2) Sanders and Dobbins, *J. Phys. Chem.*, **35**, 3086 (1931).
(3) Friend, *J. Chem. Soc.*, **128**, 2330 (1929).
(4) Poggiale, *Ann. chim. phys.*, [3] **8**, 463 (1843).
(5) Kremann and Hüttinger, *Jahrb. K. K. geol. Reichsanst.*, **58**, 645 (1908).
(6) Dobbins and Addelston, *J. Phys. Chem.*, **39**, 637 (1935).
(7) Spencer, *Nature*, **138**, 169 (1936).

Purification of Materials

Lithium Sulfate.—Reagent grade (Merck) lithium carbonate was recrystallized from hot water according to the method of Kraus and Burgess.[8] After drying, this salt was used to neutralize 6 *N* sulfuric acid. This solution was heated to boiling and slowly evaporated. The lithium sulfate which crystallized out was separated from the solution, drained and washed with 95% alcohol and then dried at 130°. It was then heated in platinum to expel traces of sulfuric acid.

Aluminum Sulfate.—The problem of obtaining hydrated aluminum sulfate of known composition for use in making up complexes offered some difficulties. Hill and Kaplan[9] attempted to prepare the octadecahydrate by allowing the recrystallized salt to come to constant composition in desiccators over some partially dehydrated aluminum sulfate, which consisted of a mixture with the next lower hydrate, the supposed $16H_2O$. This procedure was not wholly successful in that the salt thus produced usually contained more than the required amount of water (as revealed by aluminum determinations on the material). This also has been the experience of Smith.[10] It is questionable whether occluded water is removed by this method of drying. It is believed that the slow crystallization of aluminum sulfate is favorable to the occlusion of considerable amounts of water.

The material used in this investigation was prepared in the following manner. Reagent grade (Merck) aluminum sulfate was dissolved in water at 60° to make a solution of sp. gr. 1.33. The filtered solution was cooled slowly to room temperature. The crystals were filtered off and sucked as dry as possible. After washing with 95% alcohol, the crystals were again sucked as dry as possible. In order to free the crystals of occluded water, they were effloresced in vacuum desiccators over sulfuric acid. The desiccators were evacuated repeatedly to remove the alcohol. The salt, in a finely divided condition, was placed in small amounts (5–10 g.) on petri dishes in desiccators over a saturated solution of sodium bromide dihydrate. Analysis of the salt for aluminum by the quinolate method[11]

(8) Kraus and Burgess, THIS JOURNAL, **49**, 1227 (1927).
(9) Hill and Kaplan, *ibid.*, **60**, 551 (1938).
(10) Private communication from Mr. Norman Smith at New York University.
(11) Kolthoff and Sandell, THIS JOURNAL, **50**, 1900 (1928).

TABLE I

ISOTHERM AT 0° FOR Li_2SO_4–$Al_2(SO_4)_3$–H_2O

Line no.	Solution Wt. % $Al_2(SO_4)_3$	Solution Wt. % Li_2SO_4	Original complex Wt. % $Al_2(SO_4)_3$	Original complex Wt. % Li_2SO_4	Wet residue Wt. % $Al_2(SO_4)_3$	Wet residue Wt. % Li_2SO_4	Solid phase
1	0.0	26.50	...	...	...	...	$Li_2SO_4 \cdot 1H_2O$
2	1.90	25.08	...	...	...	...	$Li_2SO_4 \cdot 1H_2O$
3	7.27	21.21	5.75	34.39	...	...	$Li_2SO_4 \cdot 1H_2O$
4	10.48	18.91	...	...	5.18	52.85	$Li_2SO_4 \cdot 1H_2O$
5	15.17	15.55	13.11	25.03	...	...	$Li_2SO_4 \cdot 1H_2O$
6	16.83	14.45	16.22	16.99	...	...	$Li_2SO_4 \cdot 1H_2O$ + $Al_2(SO_4)_3 \cdot nH_2O$[a]
7	16.82	14.46	25.74	11.81	...	...	$Li_2SO_4 \cdot 1H_2O$ + $Al_2(SO_4)_3 \cdot nH_2O$[a]
8	17.76	13.07	20.42	12.19	...	...	$Al_2(SO_4)_3 \cdot nH_2O$[a]
9	18.17	12.92	...	...	35.04	6.58	$Al_2(SO_4)_3 \cdot nH_2O$[a]
10	21.56	7.86	...	...	33.82	4.95	$Al_2(SO_4)_3 \cdot nH_2O$[a]
11	23.78	4.64	26.01	4.35	...	...	$Al_2(SO_4)_3 \cdot nH_2O$[a]
12	25.74	2.30	...	...	...	...	$Al_2(SO_4)_3 \cdot nH_2O$[a]
13	27.50	0.0	...	...	...	...	$Al_2(SO_4)_3 \cdot nH_2O$[a]

[a] n is not definitely decided in this study. It may be between 15 and 18 H_2O.

revealed progressive hydration. After a month's time, during which the salt was stirred thoroughly each day, aluminum determinations revealed little if any further change in composition. At this time the aluminum value was 8.34%, considerably higher than that required at $Al_2(SO_4)_3 \cdot 18H_2O$, *i. e.*, 8.09%. In the belief that the vapor pressure within the desiccators was insufficient fully to hydrate the salt, it was transferred to desiccators over a saturated solution of sodium chloride.[12] Little change was observed in three weeks time. Aluminum determinations at this time were 8.30%. The salt was definitely homogeneous and there was no evidence of further change. This aluminum value corresponds closely to that required by $Al_2(SO_4)_3 \cdot 17H_2O$, namely, 8.32%. The salt was kept in the desiccators until needed for making up complexes. In making these the salt was weighed, by difference, from a glass-stoppered container into the solubility tubes. The percentage anhydrous aluminum sulfate in the complexes was calculated from the aluminum (quinolate) value obtained on a representative sample taken while the former were being made up.

Experimental

In several cases complexes containing accurately known amounts of anhydrous lithium sulfate, hydrated aluminum sulfate and water were prepared. In other cases the compositions of the original complexes were not known accurately. The mixtures, contained in 60-ml. glass-stoppered tubes, were rotated for two weeks in a well insulated bath maintained at 0 ± 0.05°. Samples were removed at the end of ten days and again at the end of two weeks and aluminum determinations on both showed that equilibrium had been reached. These samples were removed with a previously cooled pipet fitted with a filter. In the cases where the compositions of the original complexes were not known accurately, samples of the residues were collected on a filter kept near the temperature of the bath, and the excess mother liquid quickly removed. These wet residues were transferred as quickly as possible to weighing bottles.

(12) Kolthoff and Sandell, "Textbook of Quantitative Inorganic Analysis," The Macmillan Co., New York, N. Y., 1936, p. 123.

For analysis, aluminum was determined as the quinolate.[11] The combined filtrate and washings from this precipitation were evaporated to approximately 25 ml. At this point a mixture of concentrated hydrochloric acid and nitric acid (10 ml. to 5 ml.) was introduced along with sufficient sulfuric acid to convert the lithium to sulfate. The solution was then evaporated to fumes of sulfur trioxide. The residue was washed into a large platinum crucible. After the introduction of a drop or so of sulfuric acid, the solution was evaporated to incipient dryness in a radiator. The excess of sulfuric acid was expelled and the residue gently ignited. The lithium was then weighed as the sulfate. Several blank determinations on solutions containing no lithium revealed a constant blank of 1.5 mg. In the analyses this amount was deducted from the weight of the residues. The amounts of lithium sulfate weighed in most cases were greater than 0.15 g. The entire procedure was tested successfully many times on solutions containing known amounts of lithium sulfate and aluminum sulfate, the ratio of the two being varied considerably.

The data are given in Table I and the results are represented graphically in Fig. 1.

Discussion of Results

The solubility of pure aluminum sulfate at 0° has been found to be 27.50%.[13] This is considerably different from previously accepted values.[2,4,5,6] It is close to the values obtained for the same salt 25° by Hill and Kaplan[9] and Smith,[10] *viz.*, 27.39 and 27.89%, respectively. In the light of this it is questioned whether the solid phase in equilibrium at 25° is the same as that at 0°.

The solubility found for pure lithium sulfate at 0° agrees well with that of Friend[3] and is definitely higher than that of Sanders and Dobbins.[2]

(13) The solubility of unrecrystallized Merck reagent grade aluminum sulfate, which according to the label had as main impurities alkali sulfates 0.15%, free acid 0.12%, was determined in the same manner and found to be 27.70%.

No lithium alum has been found at 0°. Its formation at lower temperatures is still a possibility. In this study only two solid phases were found to exist. One is definitely lithium sulfate monohydrate. On the aluminum sulfate side, in addition to being too few in number, the extrapolations are too scattered due to slight variations in the composition of the aluminum sulfate used in making up the complexes as well as accidental errors in the analyses to be significant in the designation of the formula of the hydrate in equilibrium with the saturated solutions. Similar scattering in the extrapolations was found by Hill and Kaplan[9] when working with aluminum sulfate.

In previous ternary investigations involving aluminum sulfate as one of the phases, the octadecahydrate has been assumed to be the solid phases over a considerable range of temperatures although in the few cases where the tie lines were extrapolated, large deviations from the theoretical values were evident.

Additional work is being carried out in this Laboratory in an attempt to decide the hydration of aluminum sulfate at 0° as well as at other temperatures. The results of this work will be reported later.

The isothermally invariant point for this system has been found to be 16.83% aluminum sulfate and 14.45% lithium sulfate. This is considerably different than the previously reported value[2] at this temperature.

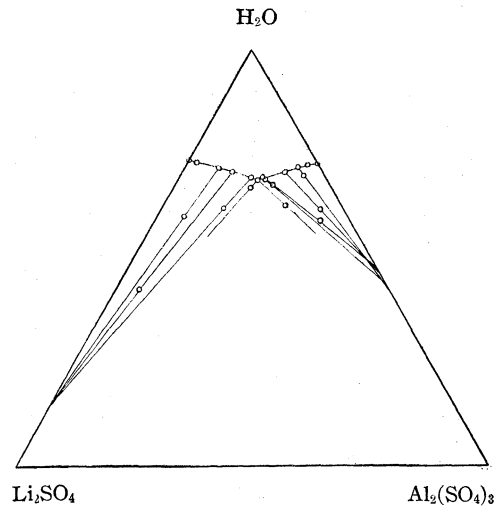


Fig. 1.—0° Isotherm: Li_2SO_4–$Al_2(SO_4)_3$–H_2O.

Summary

Solubility measurements are given for the system Li_2SO_4–$Al_2(SO_4)_3$–H_2O at 0°. There is no evidence of double salt formation or solid solution.

A new value for the solubility of aluminum sulfate at 0° is given.

The degree of hydration of aluminum sulfate in contact with a saturated solution at 0° has not been determined with certainty. The previous assumptions of the existence of the octadecahydrate at this temperature have been questioned.

BROOKLYN, N. Y. RECEIVED JUNE 1, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING OF THE STATE COLLEGE OF WASHINGTON]

Binary Liquid Systems. I. Vapor–Liquid Equilibria in the System Carbon Tetrachloride–Ethyl Acetate

BY PHILIP W. SCHUTZ

In a survey of the behavior and properties of homogeneous binary liquid systems it became of interest to investigate the system carbon tetrachloride–ethyl acetate. A careful search of the literature showed that the only vapor–liquid equilibria data available, covering the complete range of composition for this system, were those due to Tyrer.[1] These data have been quoted in the "International Critical Tables" and other similar compilations. Unfortunately, a careful scrutiny of these data shows that they are most probably in error. When the vapor and liquid compositions given are plotted against the boiling temperature (at 745 mm. in this case) as the concentration of carbon tetrachloride increases from zero mole per cent., both curves show the normal behavior for a system which exhibits a minimum boiling mixture. The behavior continues normal until the composition of the azeotropic mixture is reached (about 51 mole per cent.) at which point the vapor and liquid curves *cross* instead of becoming *tangent*. The vapor curve then continues to lie below the liquid curve through the rest of the concentration range. This behavior leads to the theoretically impossible situation of a system ex-

(1) Tyrer, *J. Chem. Soc.*, **101**, 81 (1912).

hibiting a minimum boiling point and at the same time giving at all concentrations, except that of the azeotropic mixture, a vapor which is richer in one component, carbon tetrachloride in this case, than the liquid in equilibrium with it. Because of these facts, it was deemed advisable to repeat the equilibrium measurements on this system.

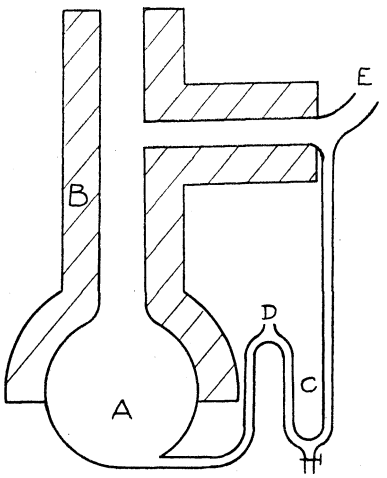


Fig. 1.—Cross section of apparatus: A, boiling flask; B, asbestos lagging; C, condensate receiver and return to boiling flask; D, pressure equalizing vent, kept loosely covered during operation; E, condenser attached here. Thermometer and internal electrical heater not shown.

Experimental

Carbon Tetrachloride.—Merck technical carbon tetrachloride was treated with a mixture of 50% potassium hydroxide solution and ethyl alcohol and subsequently with concentrated sulfuric acid as suggested by Fieser.[2] After removing the dissolved acid by washing with water, the material was dried for several hours over calcium chloride and finally for twenty-four hours over phosphorus pentoxide. The dried material was distilled through a twenty-inch (51-cm.) packed column under heavy reflux, and a fraction boiling at 73.50° under 687.0 mm. collected for use. The boiling range was not detectable on a thermometer graduated in 0.1°. The refractive index of this product ($n^{20}D$) was 1.46023.

Ethyl Acetate.—Merck technical ethyl acetate was washed with saturated sodium carbonate and then with saturated calcium chloride. After drying for twenty hours over calcium chloride, it was distilled in the column mentioned above. A fraction boiling between 73.9 and 74.2° at 685 mm. was then dried over phosphorus pentoxide for several weeks and refractionated. Material taken as product from this fractionation boiled at 74.10 ± 0.05° under 685.0 mm. and had a refractive index ($n^{20}D$) of 1.37239.

Apparatus and Method.—The apparatus used consisted of a 250-cc. round-bottomed distilling flask on which the usual side-arm was replaced by a piece of 12 mm. i. d. glass tubing. It was so arranged that the condensed vapor was returned continuously to the distilling flask. The detail of this arrangement is shown in Fig. 1. The entire vapor space, up to the point at which the condensate return line was attached, was enclosed in three-quarters of an inch (2 cm.) of asbestos paper in order to minimize fractionation in this section. That this was accomplished is indicated by the fact that the results obtained were not affected by a two-fold change in the rate of distillation. Had there been an appreciable amount of fractionation, this would not have been true. The condensate trap had a volume of about 2 cc. In order to avoid the possibility of error due to condensate from the beginning of a run being trapped in the short length of tubing (volume about 0.25 cc.), leading to the ungreased stopcock, a small volume of condensate was drawn off slowly about the middle of the run and discarded. In no case did this amount to more than 0.5 cc. In making a run the flask was charged with 100–125 cc. of mixture and heating begun with the internal electrical heater. After distillation had attained its maximum rate, it was continued for forty-five minutes, when the heating was stopped and the condensate sample withdrawn into a small tightly stoppered vial. The boiling liquid sample was removed by tilting the whole apparatus and filling the condensate trap. This was done three or four times, and the material drawn off was discarded in order to rinse the trap. The next filling was then withdrawn as a sample. Both samples were put into a thermostat at 20.00 ± 0.02° and analyzed by means of a Pulfrich refractometer whose temperature was controlled by a stream of water from the same thermostat. All of the concentrations are judged to be accurate to at least ±0.1 mole per cent. Temperatures were measured with a mercury-glass thermometer which was checked against a Bureau of Standards calibrated thermometer. The recorded temperatures are accurate to ±0.03°. No effort was made to control the pressure, all runs being made at the normal barometric pressure here. During the period of these runs, it did not vary by more than 1 mm. from 685 mm. (corrected to 0°).

Discussion of Results

TABLE I

VAPOR–LIQUID EQUILIBRIA AT 685 MM.

T, °C.	Mole % CCl_4 in vapor	Mole % CCl_4 in liquid	$n^{20}D$ of liquid
73.40	100	100	1.46023
72.57	87.1	89.4	1.45044
72.12	76.5	79.2	1.44122
71.81	67.5	69.3	1.43238
71.62	61.0	61.3	1.42527
71.57	58.7	58.8	1.42277
71.57	57.7	57.2	1.42157
71.63	52.8	51.3	1.41627
71.74	45.9	42.9	1.40893
71.95	38.9	35.2	1.40223
72.20	32.4	28.0	1.39607
72.76	20.2	15.9	1.38569
73.30	10.0	7.3	1.37836
74.01	0.8	0.5	1.37280
74.10	0.0	0.0	1.37239

(2) Fieser, "Experiments in Organic Chemistry," D. C. Heath and Company, 1935, p. 308.

The data are presented in Table I. Because of the difficulty of reproducing on a small scale a plot of temperature *vs.* composition when the liquid and vapor are so nearly alike, this plot has been omitted. On a large-scale plot all of the points fall on smooth curves with no deviations as large as those given above. It is evident from these data that this system behaves in the normal manner for systems exhibiting a minimum boiling mixture. The azeotropic mixture contains 58.2 mole per cent. carbon tetrachloride and boils at 71.56° under 685 mm. pressure.

In Table II are given the various data available on the azeotropic constants for this system at different pressures. The values attributed to Tyrer were obtained after a careful consideration of his data and do not agree with those given in the International Critical Tables.[3]

Inspection of Table II shows that the rate of change of composition of the azeotrope with pressure is decreasing as the pressure decreases. This behavior is just the reverse of that found in numerous other systems which have been investigated over a range of pressures.[4] Because of this apparent difference in behavior, this system is being investigated over a wide pressure range in order to verify this difference with a single set of data.

(3) "International Critical Tables," McGraw-Hill Book Co., Inc., New York, N. Y., 1928, Vol. III, p. 312.

(4) (a) Wade and Merriman, *J. Chem. Soc.*, **99**, 997 (1911). (b) Merriman, *ibid.*, **103**, 628, 1790 (1913); (c) Vrevsky, *Z. physik. Chem.*, **81**, 1 (1912); **83**, 551 (1913).

TABLE II

AZEOTROPIC DATA AT DIFFERENT PRESSURES

P, mm.	B. p., °C.	Mole % CCl_4	Observer
760	74.75	43	Young,[5] Lecat[6]
745	74.04	51.0 ± 0.5	Tyrer[1]
685.0	71.56	58.2	This paper
318.8	49.99	67.4	Zawidzki[7]

The refractive index–composition curve falls just slightly below the straight line joining the indices of the two pure components. The maximum deviation comes at 50 mole per cent., and the curve appears to be symmetrical about this point.

Summary

The system carbon tetrachloride–ethyl acetate has been investigated at 685 mm. and found to behave as expected for a system having a minimum boiling mixture, contrary to indications from other data.

(5) Young, "Distillation Principles and Processes," Macmillan and Company, London, 1922, p. 52.

(6) Lecat, "L'azeotropisme," Lamertin, Brussels, 1918, p. 136.

(7) Zawidzki, *Z. physik. Chem.*, **35**, 129 (1900).

PULLMAN, WASH. RECEIVED JULY 15, 1939

[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY, THE UNIVERSITY OF CHICAGO]

The Peroxide Effect in the Addition of Reagents to Unsaturated Substances. XXII. The Addition of Hydrogen Bromide to Trimethylethylene, Styrene, Crotonic Acid, and Ethyl Crotonate

BY CHEVES WALLING,[1] M. S. KHARASCH AND F. R. MAYO

Recently we described an abnormal addition of hydrogen bromide to 2-bromo-2-butene under peroxidic conditions in dilute pentane solution, and commented upon the efficacy of this method of obtaining the abnormal addition of this reagent.[2] Further interesting results, with the aid of this technique, now have been obtained with several more olefins.

Addition of Hydrogen Bromide to Trimethylethylene.—In 1904 Ipatieff and Dechanov[3] observed that, while treatment of trimethylethylene with hydrogen iodide or aqueous hydrobromic acid yielded exclusively the tertiary halide, addition of hydrogen bromide in 60% acetic acid gave 10–25% of *s*-isoamyl bromide (2-methyl-3-bromobutane). A similar result was reported by Michael and Zeidler.[4] Recently, however, Smith[5] has indicated that *t*-amyl bromide is the sole product of the addition of hydrogen bromide to this olefin and that peroxides are without effect upon the course of the reaction, but unfortunately he does not describe the experimental conditions employed. The latter conclusion is contradicted by the results of this investigation, as shown in Table I. In the absence of a solvent and air and in the presence of an inhibitor, a

(1) Du Pont Fellow 1938–1939.

(2) Walling, Kharasch and Mayo, THIS JOURNAL, **61**, 1711 (1939).

(3) Ipatieff and Dechanov, *Chem. Zentr.*, **75**, II, 961 (1904).

(4) Michael and Zeidler, *Ann.*, **385**, 271 (1911).

(5) Smith, *Chemistry and Industry*, **57**, 561 (1938).

product containing 95% of the normal addition product, *t*-amyl bromide (I), results. Addition in pentane solution containing lauroyl peroxide yields as much as 64% of the abnormal addition product, 2-methyl-3-bromobutane (II). When the peroxide is replaced by diphenylamine, the product is chiefly normal, indicating that reversal is not due to the solvent itself.

$$(CH_3)_2C{=}CHCH_3 \xrightarrow{HBr} (CH_3)_2CBrCH_2{-}CH_3 \quad (I)$$

$$(CH_3)_2C{=}CHCH_3 \xrightarrow[HBr]{Peroxides} (CH_3)_2CH{-}CHBr{-}CH \quad (II)$$

Experiments in the presence of peroxides in ethyl bromide[6] and nitrobenzene gave 60 and 100% of normal product, respectively. A similar if less pronounced difficulty in detecting abnormal addition in nitrobenzene solution has been observed in the addition of hydrogen bromide to isobutylene.[7]

TABLE I

THE ADDITION OF HYDROGEN BROMIDE TO TRIMETHYLETHYLENE

Expt.	Substance added	Moles[a]	Yield, %	% *t*-Amyl bromide By index of refraction	% *t*-Amyl bromide By hydrolysis
VII	Diphenylamine[b]	0.02	73	100	95
IX	Hydroquinone[b]	0.03	83	94	93
III	....	...	68	70	71
XII	....	...	73	70	75
IV	Lauroyl peroxide	0.01	73	82	80
XVI	Lauroyl peroxide	0.01	81	76	74
VIII	Diphenylamine	0.02	66	79	77
	Pentane	6.0			
I	Lauroyl peroxide	0.05	70	52	40
	Pentane	10.00			
II	Lauroyl peroxide	0.05	66	40	36
	Pentane	10.00			
V	Pentane[c]	10.00	72	46	41
XI	Lauroyl peroxide	0.05	55	(109)	100
	Nitrobenzene	10.00			
XIV	Lauroyl peroxide	0.05	65	64	60
	Ethyl bromide	10.00			

[a] In moles per mole of ethylene derivative. [b] Vacuum technique employed.[2] [c] Reaction mixture illuminated with 500-watt incandescent lamp during addition.

A possible explanation of the failure of Smith to obtain evidence of abnormal addition to trimethylethylene lies in the ease with which the abnormal product undergoes isomerization. Thus, treatment of methylisopropylcarbinol or isopropylethylene with hydrogen bromide yields, respectively, 79[4] (p. 284) and 48%[8] of the tertiary halide. In order to avoid this complication in the work reported here, any prolonged contact of the addition products with hydrogen bromide was avoided, and all distillations were carried out at reduced pressure.

Addition of Hydrogen Bromide to Styrene.—Although it is generally considered that the product obtained by adding hydrogen bromide to styrene is α-phenylethyl bromide, it has been observed that thiophenol,[9,10] thioglycolic acid,[11] and bisulfite[12] all add abnormally to this olefin to yield β-phenylethyl derivatives. Also, a method has been described in the patent literature[13] for treating styrene with hydrogen bromide at 95° in ethylbenzene solution in the presence of benzoyl peroxide. Under these conditions, it is claimed that the product contains 92% β-phenylethyl bromide.

TABLE II

THE ADDITION OF HYDROGEN BROMIDE TO STYRENE

Expt.	Substance added	Moles[a]	Yield, %	Product α-Phenylethyl bromide, %
V	Diphenylamine[b]	0.02	65	100
VII	Diphenylamine[b]	0.02	70	100
II	....	...	70	95
VIII	....	...	85	100
VI	Diphenylamine	0.02	65	95
	Pentane	6.00		
IX	Lauroyl peroxide	0.01	80	93
III	Ascaridole	0.05	70	45
	Pentane	10.00		
I	Ascaridole	0.05	60	42
	Pentane	7.0		
IV	Lauroyl peroxide	0.02	70	29
	Pentane	10.00		
X	Lauroyl peroxide[c]	0.02	75	20
	Pentane	6.0		

[a,b] Have the same significance as in Table I. [c] Hydrogen bromide passed in during several hours.

Accordingly, it was of especial interest to investigate this problem. It has now been found that in absence of solvent styrene adds hydrogen bromide almost instantaneously to form α-phenylethyl bromide (III), and that even the presence of added peroxide does not lead to the formation of over 7% of the abnormal product (Table II).

(6) The result recorded in Table I was obtained with ethyl bromide purified by washing thoroughly with sulfuric acid, followed by fractionation. Two experiments with ordinary commercial ethyl bromide (which apparently contained alcohol or ether, as it darkened sulfuric acid) gave only the normal product, a result which seems reasonable in view of the ability of alcohol to inhibit reactions involving bromine atoms.

(7) Kharasch and Potts, THIS JOURNAL, **58**, 57 (1936).

(8) Michael and Leupold, *Ann.*, **379**, 296 (1911).

(9) Posner, *Ber.*, **38**, 646 (1905).

(10) Ashworth and Burkhardt, *J. Chem. Soc.*, 1791 (1928).

(11) Holmberg, *J. prakt. Chem.*, **141**, 93 (1934); Kharasch, Read and Mayo, *Chemistry and Industry*, **57**, 752 (1938).

(12) Kharasch, May and Mayo, *J. Org. Chem.*, **3**, 175 (1938).

(13) Société des usines chimiques Rhône-Poulenc, British Patent 438,820 (1935); *C. A.*, **30**, 2993 (1936).

However, when the normal reaction is retarded by working in dilute pentane solution and peroxides are added, products may be isolated which contain as much as 80% of β-phenylethyl bromide (IV). There seems to be no reason to doubt that greater dilution and the slower addition of the halogen acid would result in an even greater percentage of this product.

$$C_6H_5CH{=}CH_2 \xrightarrow{HBr} C_6H_5CHBrCH_3 \quad (III)$$

$$C_6H_5CH{=}CH_2 \xrightarrow[HBr]{Peroxides} C_6H_5CH_2CH_2Br \quad (IV)$$

Addition of Hydrogen Bromide to Crotonic Acid and Ethyl Crotonate.—Preliminary investigation in this Laboratory has found only one product (the usual β-bromo derivative) in the addition of hydrogen bromide to acrylic, crotonic and bromocrotonic acids[14] in both the presence and absence of oxygen and peroxides. Furthermore, no reversal of addition has been obtained with bromomaleic,[15] bromofumaric,[15] and tetrolic acid,[16] although in the latter case there is evidence that the products obtained in the presence of peroxides are stereoisomeric with those obtained in the absence of these materials.

We can now report that even in the presence of a peroxide, illumination, and dilution with a solvent such as pentane, the only products of the addition of hydrogen bromide to crotonic acid and ethyl crotonate are the β-bromo derivatives.

Discussion

It is well established and is further shown in this paper that the normal addition of hydrogen bromide to olefins in which the double bond is not at the end of a hydrocarbon chain or is conjugated with a benzenoid nucleus proceeds with great rapidity. The present work shows that when these addition reactions are carried out in dilute pentane solution the normal reaction is retarded, and considerable abnormal addition of hydrogen bromide is observed. The previous paper in this series reached a similar conclusion in the case of 2-bromo-2-butene.

However, even though these conditions markedly retard the addition of hydrogen bromide to crotonic acid and its ethyl ester, no reversal of the direction of addition could be observed under even the most favorable conditions; neither do peroxides markedly accelerate the addition of hydrogen bromide to these substances in dilute pentane solution as they do in the case of other olefins.[17] This fact may indicate that the chain mechanism postulated for abnormal addition[18] is inoperative in the case of ethylenic bonds conjugated with a carboxyl or similar group. However, the alternative explanation cannot be excluded, that the mechanisms of both normal and abnormal addition lead, in the case of these compounds, to the formation of the same product. Indeed this explanation is to some extent supported by the reaction of tetrolic acids cited previously.

Experimental

Trimethylethylene and Hydrogen Bromide.—**Trimethylethylene** was prepared from Eastman *t*-amyl alcohol. Four hundred grams was placed in a distilling flask equipped with an efficient condenser and a "cold finger" in the neck of the flask to minimize the distillation of alcohol. Thirty cubic centimeters of concentrated sulfuric acid was added, and the flask heated on a steam-bath. Distillation of the product (together with a little alcohol and water) began almost at once, and the reaction was practically complete in two hours. The distillate was washed with sodium carbonate solution, dried over calcium chloride, and distilled through a 1.5-meter packed column. Two fractionations yielded 114 g. (36%) of trimethylethylene, b. p. 37.6–38.0° (744 mm.).

Addition of hydrogen bromide was carried out as indicated in Table I. Seven grams (0.1 mole) of trimethylethylene was used in all experiments. The pentane employed was a 30–35° fraction free from unsaturated material obtained from the Skelly Oil Company, Tulsa, Oklahoma. Hydrogen bromide was passed in (at room temperature except in vacuum experiments) and seemed to react as rapidly as it was added. After the removal of solvent the products were distilled at 100 mm. through a Podbielniak column. The yield recorded in the table is the amount of distillate collected at 47–52°. In the experiment in nitrobenzene the addition products were quickly distilled from the reaction mixture at reduced pressure and then fractionated.

Preliminary experiments on a redistilled sample of Kahlbaum *t*-amyl bromide, $n^{20}D$ 1.4420, indicated that it was hydrolyzed to the extent of 95% in fifteen minutes at 100° in 80% aqueous acetone, and that under the conditions of the experiment this amount presumably represented an equilibrium, as longer heating produced no fur-

(14) Kharasch and McNab, unpublished work.

(15) Kharasch, Mansfield and Mayo, unpublished work.

(16) Grigorieff, Ph.D. Dissertation, University of Chicago, 1939.

(17) As an example, 0.1 mole of crotonic acid in 1.2 moles of pentane kept saturated with hydrogen bromide at about 20° reacted only to the extent of 40% in six hours, despite strong illumination and the presence of 0.0025 mole of lauroyl peroxide. In absence of solvent, crotonic acid, if warmed to start the reaction, will absorb the theoretical amount of hydrogen bromide in a few minutes. Propylene, by way of contrast, is subject to abnormal addition, and, while it undergoes the normal reaction in absence of solvent at a rate roughly comparable with crotonic acid, it reacts completely with hydrogen bromide in a few minutes in dilute pentane solution in the presence of only traces of peroxides (Mayo and Savoyias, kinetic investigation now in progress in this Laboratory).

(18) Kharasch, Engelmann and Mayo, *J. Org. Chem.*, **2**, 288 (1937).

ther hydrolysis. Similarly, when the products of experiments I, II, and V were combined and carefully fractionated into four portions, the third and fourth fractions (which presumably contained the greatest proportion of 2-methyl-3-bromobutane) were hydrolyzed by this procedure to the extent of 17.9 and 5.7%, respectively. As it seemed likely that even the highest boiling fraction contained some *t*-amyl bromide, it was assumed for purposes of calculation that 2-methyl-3-bromobutane was not measurably hydrolyzed under these conditions. Accordingly, 0.3 g. of the addition products was weighed out into Pyrex tubes of about 10 cc. capacity, and 5 cc. of 80% aqueous acetone added. The tubes were then sealed and placed in boiling water for fifteen minutes. After cooling and opening, the liberated acid was titrated with standard base.

As an additional check, the indices of refraction of all products were determined, and the percentage of normal and abnormal product calculated. Although results by both methods are included in Table I, we consider those obtained by hydrolysis to be the more accurate. The index of refraction of 2-methyl-3-bromobutane was found to be $n^{20}D$ 1.4453 by extrapolation.

Styrene and Hydrogen Bromide.—Styrene used in this investigation was obtained from the Bakelite Corporation, Bloomfield, New Jersey. As it contained hydroquinone to prevent polymerization, it was distilled *in vacuo* shortly before use. Experiments were performed as indicated in Table II. In all experiments, 10.4 g. of styrene was used; 9 g. of hydrogen bromide was passed in (at room temperature in all except vacuum experiments) and in no case did addition appear to require more than a few minutes. The products were worked up by distillation through a Podbielniak column at a pressure of 9 mm. of mercury. The yield recorded in Table II is based upon the weight of the fraction collected. In cases of addition in pentane, the solvent was removed before distillation by evaporation at atmospheric pressure.

For analysis, 0.2 g. of the product was weighed out into a Pyrex tube of about 10 cc. capacity, and 5 cc. of 80% aqueous acetone added. After sealing and heating for two hours in boiling water, the liberated acid was titrated with standard base. Experiments with samples of known composition indicated that, under these conditions, hydrolysis proceeded to the extent of 95% with α-phenylethyl bromide as compared with less than 2% with β-phenylethyl bromide.

As a further check, the addition product of experiment I (Table II) were treated with alcoholic potassium hydrosulfide,[19] and the potassium salts of the resulting mercaptans allowed to react with 2,4-dinitrochlorobenzene according to the procedure of Bost, Turner, and Norton.[20] From the reaction mixture, β-phenylethyl 2,4-dinitrophenyl sulfide was obtained in yellow pearly plates (m. p. after crystallization from alcohol 87–88°). Similar treatment of the product from experiment II yielded α-phenylethyl 2,4-dinitrophenyl sulfide (orange crystals, m. p. after crystallization from alcohol 108–109°).

Addition to Crotonic Acid and Ethyl Crotonate.—Two sets of conditions were chosen as favoring the abnormal reaction. (a) One-tenth mole of crotonic acid or ethyl crotonate, 0.0025 mole of lauroyl peroxide, and 1.0 to 1.2 moles of pentane were placed in a Pyrex bomb tube and cooled to −80°. One-eighth mole of hydrogen bromide was passed in, the tube sealed, and allowed to warm to room temperature. After standing overnight, the tubes were opened, the solvent evaporated off, and the products distilled under reduced pressure. (b) Hydrogen bromide (0.14–0.16 mole) was condensed in a Pyrex tube cooled to −80°. By carefully raising the tube from the cooling-bath, a very slow stream of hydrogen bromide could be obtained. This was bubbled very slowly through another Pyrex vessel containing 0.1 mole of the unsaturated material and 0.0025 mole of lauroyl peroxide in 1.2 moles of pentane. During the addition the vessel was illuminated by a 500-watt incandescent lamp at a distance of 15 cm. and cooled to about 20° by a stream of water. After three to six hours the product was worked up as described under (a). Under these conditions, crotonic acid added hydrogen bromide to the extent of 40% in six hours, while in the case of ethyl crotonate the reaction was virtually complete in three hours.

Fifteen-hundredths gram of the crotonic acid addition product was weighed into a flask, and 2.00 ml. of 1.942 *N* potassium hydroxide solution added. After standing for one hour at room temperature the mixture was diluted with water and titrated with standard acid. Under these conditions hydrogen bromide was liberated from known α- and β-bromobutyric acids to the extent of 3 and 98%, respectively. By this method all samples obtained by the addition of hydrogen bromide to crotonic acid contained over 95% of the β-bromo acid. A different method of analysis was used for the ester addition products on account of the partial hydrolysis of the esters. Three-tenths gram of the addition product was weighed out and 2.0 cc. of 1.8 *N* alcoholic potassium hydroxide added. After one minute the mixture was diluted with water and acidified with nitric acid. After addition of an excess of standard silver nitrate solution, the mixture was back titrated with ammonium thiocyanate solution. Under these conditions the α- and β-bromo esters liberated 1.3 and 99.3%, respectively, of the theoretical bromide ion. By this method, all samples obtained by addition of hydrogen bromide to ethyl crotonate contained 97% or more of ethyl β-bromobutyrate.

Summary

1. Trimethylethylene adds hydrogen bromide in the absence of oxygen and peroxides to give *t*-amyl bromide. Under conditions of peroxide catalysis the product contains as much as 64% of the abnormal product, 2-methyl-3-bromobutane.

2. Styrene adds hydrogen bromide in the absence of oxygen and peroxides to give α-phenylethyl bromide. Under conditions of peroxide catalysis and in the presence of solvent the product contains as much as 80% β-phenylethyl bromide.

3. In presence or absence of peroxides, crotonic acid and ethyl crotonate yield only β-bromobutyric acid and ethyl β-bromobutyrate, respectively.

CHICAGO, ILLINOIS RECEIVED AUGUST 3, 1939

(19) Sontag, *Ann. Chim.*, (11) **1**, 428 (1934).

(20) Bost, Turner, and Norton, THIS JOURNAL, **54**, 1985 (1932).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OKLAHOMA AGRICULTURAL AND MECHANICAL COLLEGE]

The Composition of the Seeds of Sapindus Drummondii[1,2]

BY O. C. DERMER AND L. T. CREWS

The tree *Sapindus drummondii* H. and A., commonly known as Western Soapberry or Wild Chinaberry, is widely distributed in the southwestern part of the United States. Its clusters of yellow translucent fruits or "berries" ripen in the fall and remain on the tree during the winter. Each drupe-like fruit contains a round, black, hard-shelled seed which averages 0.4 g. in weight as compared to 1 g. for the whole fruit. The reputedly toxic pericarp is rich in a saponin which has been employed as a soap substitute, while the polished seeds have been used as primitive ornaments.

The only published chemical data on this fruit[3] show that whole fruits from Oklahoma contain 8%, and their seed kernels 43%, of a non-drying oil.

Experimental

The fruits used in this work were gathered in December and January from trees in the Cimarron River valley near Coyle, Oklahoma. After several months the slightly sticky outer pulp was removed by hand and preserved for an intended investigation of the saponin present. Nearly all the seeds were ground whole, for kernels could be separated from shells only by tedious hand sorting.

Since it is well known that different methods of extraction of an oil remove different kinds and proportions of other substances, some of the meal (1–2 kg.) was percolated with ether, some with petroleum ether, and some was warmed and pressed hydraulically to remove the oil. The oils thus obtained, after the removal of any solvent and filtration, gave substantially the same constants. The seed kernels were found to contain 42.7% of ether-soluble materials,[4] whereas the whole seeds contained 23–24%.

The oil was greenish-brown to yellow-brown in color and had the characteristic but not unpleasant odor and taste of the seed kernels. It did not become rancid readily. The usual physical properties and chemical constants were determined by standard methods[5] unless otherwise specified. The results, in Table I, show the limits of variation of characteristics of the oils extracted by different methods.

TABLE I

CHEMICAL AND PHYSICAL CHARACTERISTICS OF THE OIL

Specific gravity, 25°/25°	0.903–0.917
Refractive index, $n^{25}D$	1.4704–1.4722
Acid value	0.3–0.9
Saponification value	213–219
Iodine no. (Hanus)	81.5–83.5
Thiocyanogen no.	63.9–67.2
Unsaponifiable matter, %	1.2
Reichert–Meissl no.	0.0
Polenske no.	0.0
Acetyl value	14.5
Unsaturated acids, %	74–77,[a] 82[b]
Saturated acids, %	17–20,[a] 13[b]

[a] Calculated from iodine number and thiocyanogen number. [b] Observed by separation and weighing, and corrected for impurities.

The air-dry exhausted meal was analyzed with the following results: protein 21.3%; crude fiber 18.0;[6] ash 3.70%; moisture 8.40%. It contained starch (iodine test) but no reducing sugars.

Fatty Acids.—Saturated acids were best separated from unsaturated acids by low-temperature crystallization of the free acids from acetone.[7] The unsaturated fraction gave a negative hexabromide test for linolenic acid. The presence of oleic acid was confirmed by its conversion to elaidic acid, but bromination of the unsaturated fraction in petroleum ether at −10° gave no precipitate of linoleic acid tetrabromide, probably owing to the solvent action of the large amount of oleic acid dibromide present. From the iodine number and the thiocyanogen number of the original oil it can be estimated that there were present about 60–65% of oleic acid and 15% of linoleic acid.

Fractional crystallization of portions of the mixed saturated acids (iodine numbers 5.0–28) led to the isolation of palmitic acid, m. p. 61.5–62.5°, and stearic acid, m. p. 68.5–69.5°, identified by melting points and mixture melting points. No others could be found, although average molecular weights obtained by either direct titration or saponification of the saturated fraction from different runs indicated the presence of an acid higher than stearic acid in the series.

When a portion of the saturated acids derived from the oil extracted with petroleum ether was distilled at 1 mm., a few crystals of alkali-insoluble material were isolated from the highest-boiling fraction and about an equal amount from the residue in the still. After recrystallization from alcohol, these waxy crystals melted at 63–64° and about 130° (indefinite), respectively. They were proved to be alkanes by their insolubility in even hot concentrated sulfuric acid. The known occurrence of

(1) This is an abstract of a thesis submitted by Mr. Crews in partial fulfilment of the requirements for the degree of Master of Science at the Oklahoma Agricultural and Mechanical College in 1939.

(2) The authors wish to express their thanks to members of the Department of Botany for help in identifying the plant, and to Dr. J. E. Webster for apparatus and suggestions.

(3) Report of the Chief of the Bureau of Chemistry and Soils, U. S. Department of Agriculture, 1938, p. 7.

(4) Determined by Dr. J. E. Webster.

(5) Jamieson, "Vegetable Fats and Oils," Chemical Catalog Co., Inc. New York, 1932.

(6) Association of Official Agricultural Chemists, "Methods of Analysis," Washington, D. C., fourth edition, 1935, p. 30.

(7) Brown and Stoner, THIS JOURNAL, **59**, 3 (1937); *cf.* Hartsuch *ibid.*, **61**, 1142 (1939).

saturated hydrocarbons in seed coats and the ability of seeds of *Sapindus drummondii* to take a high polish suggest that these alkanes came from the unremoved seed coats rather than from the kernels. Such complications in fat chemistry have been remarked before.[8]

The seed oils of the following relatives of *Sapindus drummondii* have been studied: *Schlichera trijuga*,[5] *Naphelium lappaceum*,[5] *Nephelium mutabile*,[5] *Sapindus trifoliatus*,[5] *Ungnadia speciosa*,[5] *Sapindus mukurossi*,[9] and *Sapindus marginatus*.[10] The iodine number of the seed oil of *Sapindus drummondii* is higher than that of any of the others except *S. marginatus;* this is in agreement with the observation that, among related plants, growth in a cooler climate connotes greater unsaturation of the oil. The principal difference between the oil of *S. drummondii* and that of any of its relatives, however, appears to be its lack of *n*-eicosanic (arachidic?) acid.

(8) Schuette, Cowley and Chang, THIS JOURNAL, **56**, 2085 (1934).
(9) Kafuku and Hata, *J. Chem. Soc. Japan*, **55**, 369 (1934).
(10) G. S. Jamieson, unpublished work.

Summary

1. The physical and chemical characteristics of the seed oil of *Sapindus drummondii* have been determined.

2. The fatty acids present consist chiefly of oleic acid, accompanied by smaller amounts of linoleic, palmitic and stearic acids.

STILLWATER, OKLA. RECEIVED JULY 20, 1939

[CONTRIBUTION FROM THE DIVISION OF INDUSTRIAL AND CELLULOSE CHEMISTRY, MCGILL UNIVERSITY]

Studies on Lignin and Related Compounds. XLVI. The Action of Ozone on Isolated Lignins[1]

BY RODGER M. DORLAND, W. LINCOLN HAWKINS AND HAROLD HIBBERT

The action of ozone on lignin preparations has been studied by a number of workers but the identifiable fragments split off by this treatment have been too small to be of any real value in the elucidation of the structure of lignin. Thus Phillips and Goss[2] isolated anisic acid in small yield by the action of ozone on methylated alkali lignin obtained from corn cobs. Bell, Hawkins, Wright and Hibbert[3] have noted the formation of acetone in the ozonization of birch formic acid lignin. In general it may be said that, when a lignin is subjected to the action of ozone, there results, after treating the resulting product with water, a water-insoluble lignin and an aqueous solution. This latter solution contains mainly a water-soluble, lignin-like material and oxalic acid. The more prolonged the treatment with ozone, the smaller is the resulting water-insoluble and the greater the water-soluble fraction. This action is accompanied by a decrease in the methoxyl content of the ozonized lignin.

In connection with studies being carried out in these Laboratories on the mechanism of the solubilization of lignins by means of aqueous bisulfite solution, it was observed that formic[4a] and acetic acid[4b] lignins are insoluble in aqueous bisulfites but that after a carefully controlled ozonization in formic acid solution they become completely soluble.

The increase in the solubility in sulfite "cooking liquor" and the decrease in the methoxyl content of the lignin with increasing degree of ozonization were studied by carrying out a series of ozonizations on identical samples of birch formic acid lignin using increasing amounts of ozone. The resulting ozonized samples were then analyzed for methoxyl and the quantitative solubility in sulfite "cooking liquor" was determined (Table I).

TABLE I

THE ACTION OF OZONE ON BIRCH FORMIC ACID LIGNIN

G. of O_3 reacting per 2 g. of lignin	Water-insoluble fraction % yield	Water-insoluble fraction % OCH_3	Original minus final OCH_3	% solubility in sulfite liquor of ozonized lignin
0.167	95	15.9	2.7	36
.290	88	13.9	4.7	61
.368	68	11.7	6.9	88
.404	72	12.5	6.1	78
.396	73	12.6	6.0	73
.405	65	11.5	7.1	82
.463	60	11.8	6.8	80
.544	53	10.9	7.7	93

These results expressed graphically (Fig. 1) show that both the loss in methoxyl and the increased solubility in sulfite liquor vary directly with the amount of ozone employed. From these data it was possible to calculate the approximate amount

(1) From a thesis submitted to the Faculty of Graduate Studies and Research, McGill University, by Rodger M. Dorland in partial fulfilment of the requirements for the Degree of Doctor of Philosophy, May, 1939. Paper XLV, THIS JOURNAL, **61**, 2204 (1939).
(2) Phillips and Goss, THIS JOURNAL, **55**, 3466 (1933).
(3) Bell, Hawkins, Wright and Hibbert, *ibid.*, **59**, 598 (1937).
(4) (a) Lieff, Wright and Hibbert, *ibid.*, **61**, 1477 (1939); (b) A. Bell, Ph.D. Thesis, McGill University, 1937.

of ozone necessary to give a completely bisulfite soluble lignin. Accordingly, birch formic acid[4a] and birch acetic acid[4b] lignins were treated with ozone to the required degree and the sulfonic acids prepared by the customary "sulfite cook."

The lignin sulfonic acid prepared by cooking yellow birch wood meal with acid sodium sulfite yields, on alkaline cleavage, 2.7% vanillin and 2.8% syringaldehyde based on the weight of lignin.[5] Acetosyringone, but not acetovanillone, also has been isolated from the same waste sulfite liquor although the yield was much smaller, being of the order of 0.8%.[6] Accompanying this was a small quantity of pyrogallol 1,3-dimethyl ether amounting to 0.2%.[7] In view of these results it was of interest to determine the action of alkali on the sulfonated, ozonized birch lignins. The sulfonated, ozonized, birch formic acid lignin yields, on alkaline cleavage, only guaiacyl derivatives, namely, vanillin and acetovanillone, and in approximately equal amounts (1%). The same results have been observed in the case of the corresponding ozonized acetic acid lignin, the yields being of the order of 2.7% also based on the weight of lignin. Presumably this is the first time that acetovanillone has been obtained from a hard wood waste sulfite liquor since Leger and Hibbert[6] found only acetosyringone.

There are two possible explanations as to why no syringyl analogs were found in the present investigation. In the first place the formic and acetic acid lignins which were used had been subjected previously to a solvent fractionation and in both cases the vanillin and acetovanillone were obtained from fractions of the crude lignin having the lowest methoxyl content. It is also to be noted that the formic and acetic acid lignins, previous to sulfonation, were subjected to the action of ozone and there is thus the possibility that, if syringyl groups did exist, they might have been split off as part of the water-soluble fraction. This latter possibility is at present under investigation.

Experimental

The Loss in Methoxyl and the Increase in Solubility in Sulfite Liquor of Birch Formic Acid Lignin with Respect to the Degree of Ozonization.—A 2.0-g. sample of formic acid lignin[4a] (18.6% OCH_3) was dissolved in 50 cc. of formic acid (95%) and at 0° ozone was passed into this solution for varying lengths of time. The amount of ozone delivered by the machine was determined at intervals by passing the gas through a neutral potassium iodide solution for a definite period of time and titrating with standardized thiosulfate the iodine liberated on acidification. The gas passing out of the lignin solution was also treated in a similar manner in order to determine the amount of ozone not absorbed by the solution. When the ozonization was complete the formic acid was removed by distillation under reduced pressure, 300 cc. of water added to the residue and the solution refluxed for thirty minutes. On cooling, the water-insoluble lignin was filtered off, washed with water, dried at 60° (20 mm.) and then weighed.

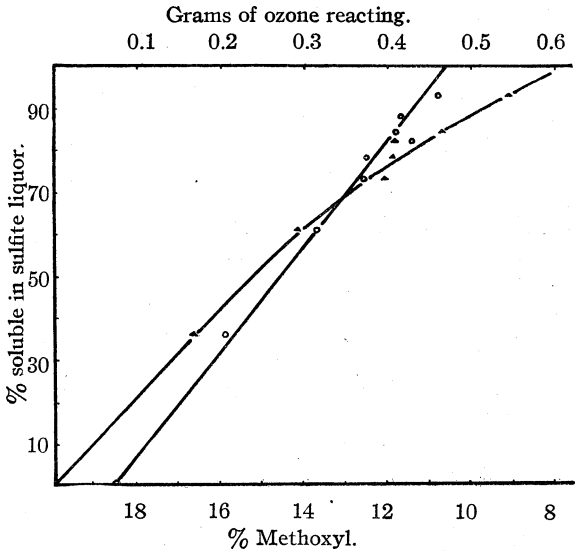


Fig. 1.—The action of ozone on birch formic acid lignin: ▲, increase in solubility of birch formic acid lignin in sulfite liquor with increasing ozonization; O, increase in solubility of birch formic acid lignin in sulfite liquor with loss in methoxyl.

The ozonized lignin was analyzed for methoxyl and the solubility in sulfite liquor determined in the following manner. Exactly 0.100 g. of the lignin was sealed in a small glass bomb with 6 cc. of sodium bisulfite "cooking liquor" (6.0% total and 1.15% combined sulfur dioxide) and the bomb placed in a toluene vapor bath (110°) for twelve hours. On completion of the cook the bomb was cooled to 0°, opened, and the contents washed into a small, tared, centrifuge cup. The insoluble lignin was centrifuged off, washed with water, and dried overnight at 60° (20 mm.). The per cent. soluble in the sulfite liquor was then calculated by difference. These results have been summarized in Table I.

The Isolation of Vanillin and Acetovanillone from Ozonized Birch Formic Acid Lignin.—Ten grams of birch formic acid lignin (15.5% OCH_3)[4a] was dissolved in 400 cc. of formic acid (95%) and at 0° this solution was treated with 2.56 g. of ozone over a period of eight hours, during which time 2.34 g. of ozone was absorbed by the solution. The solvent was then removed under reduced pressure and the residue refluxed for one hour with one liter of water. Upon cooling, the water-insoluble fraction was filtered off, washed with water and dried. This product

(5) Hawkins, Wright and Hibbert, THIS JOURNAL, **59**, 2447 (1937).
(6) Leger and Hibbert, *ibid.*, **60**, 565 (1938).
(7) Leger and Hibbert, *Can. J. Research*, **16B**, 151 (1938).

was ground to a fine powder and again refluxed with one liter of water for forty-five minutes. The lignin was then filtered, washed and dried: yield 6.9 g.; 8.3% OCH_3; 95% soluble in bisulfite "cooking liquor" after heating at 110° for twelve hours.

Sodium bisulfite liquor (200 cc. containing 6.0% total and 1.15% combined SO_2) and 6.8 g. of the ozonized lignin were heated in a stainless steel bomb to 110° over a period of one and one-half hours. The bath was held at 110° for four hours and then raised to 130° for an additional eight hours. Upon cooling, the contents of the bomb were filtered and the volume of the filtrate made up to 500 cc. with water. The insoluble material after drying weighed 0.8 g.

A portion of the filtrate (100 cc.) was freed from inorganic material by dialysis against running distilled water for seven days. On evaporating the solution to dryness a relatively pure sample of the sulfonated lignin product was obtained; analysis, 3.3% OCH_3, 6.6% sulfur.

The alkaline cleavage of the sulfonated product was carried out by adding 70 g. of sodium hydroxide to 290 cc. of the crude liquor and heating this at 135° for twelve hours under an atmosphere of oxygen-free nitrogen. The solution was cooled, just acidified with 50% sulfuric acid and extracted continuously with benzene for forty-eight hours. The benzene extract was shaken out ten times with 15-cc. portions of 5% sodium bisulfite; this latter solution was acidified and the sulfur dioxide removed under reduced pressure. The solution was then filtered and the volume made up to 200 cc. The total aldehydes present were determined by adding 10 cc. of an aqueous solution of 2,4-dinitrophenylhydrazine hydrochloride to a 20-cc. aliquot of the solution. After standing for six hours the precipitate was filtered on to a tared sintered glass funnel, washed and dried at 105°; weight, 0.1005 g. or 1.3%, calculated as vanillin based on the lignin in the liquor.

The remaining 180 cc. of solution was extracted continuously with ether. The residue after the removal of the ether was sublimed at 61° (2 mm.) yielding 0.040 g. of a crystalline product. Recrystallization from petroleum ether (80–90°) gave white, feathery crystals, m. p. 81–82°. A mixed m. p. with an authentic sample of vanillin showed no depression. The yield of the vanillin based on the lignin was 1.1%.

The benzene extract of the acidified alkaline cleavage product, left after the extraction with bisulfite, was evaporated to dryness under reduced pressure. The residue was sublimed at 150° (2 mm.). Resublimation of this product at 90° (2 mm.) yielded 0.055 g. of crystalline material. Recrystallization from petroleum ether (80–90°) gave white crystals, m. p. 111–112°. A mixed melting point with an authentic sample of acetovanillone showed no depression. The yield of acetovanillone based on the lignin was 1.2%.

The Isolation of Vanillin and Acetovanillone from Ozonized Birch Acetic Acid Lignin.—Twelve grams of birch acetic acid lignin (18.8% OCH_3)[4b] was dissolved in 300 cc. of formic acid and at 0° the solution then treated with 2.16 g. of ozone over a period of five and one-half hours, during which time 1.84 g. of ozone was absorbed by the solution. The solvent was removed under reduced pressure and the residue refluxed with one liter of water for forty-five minutes. Upon cooling, the water-insoluble fraction was filtered off, washed with water and dried. This product was ground to a fine powder and again refluxed with one liter of water for forty-five minutes. The ozonized lignin was then filtered, washed and dried; yield 5.4 g.; 13.3% OCH_3; 95% soluble in sulfite liquor at 110° for twelve hours.

Five grams of the ozonized lignin and 200 cc. of the above sodium bisulfite "cooking liquor" were heated in a stainless steel bomb to 110° over a period of one and one-half hours and the bath then maintained at that temperature for twelve hours. The bomb was cooled, the contents filtered and the volume of the filtrate made up to 250 cc. with water. The insoluble material after drying weighed 0.02 g.

A portion of the filtrate (50 cc.) was purified by dialysis against running distilled water for seven days. The sulfonated product was obtained by evaporating the solution to dryness; 6.4% OCH_3; 6.15% sulfur.

The alkaline cleavage of this sulfonated product was carried out by adding 33.6 g. of sodium hydroxide to 140 cc. of the crude, filtered liquor and heating the mixture at 135° for twelve hours under an atmosphere of oxygen-free nitrogen. The cooled reaction product was just acidified with 50% sulfuric acid and extracted continuously with benzene for forty-eight hours. This benzene extract was then shaken out with bisulfite solution, as previously described, the bisulfite solution acidified, the sulfur dioxide removed, solution filtered and made up to a volume of 250 cc. The total aldehydes present were determined as the 2,4-dinitrophenylhydrazones on a 20-cc. aliquot of this solution; yield 0.0208 g. or 4% calculated as vanillin based on the lignin in the liquor.

The subsequent ether extract of the remaining acidified bisulfite solution was worked up in the same manner as described previously. The residue on sublimation and recrystallization yielded 0.075 g. of white crystals, m. p. 82–83°. The mixed m. p. with an authentic sample of vanillin showed no depression. The yield of vanillin based on the lignin was 2.7%.

The benzene extract of the acidified alkaline cleavage solution, after extraction with the bisulfite, was worked up in a similar manner and yielded 0.075 g. of crystalline material, m. p. 112–113°. The mixed m. p. with an authentic sample of acetovanillone showed no depression. The yield of acetovanillone based on the lignin was 2.7%.

Acknowledgments.—The authors wish to thank the Canadian National Research Council for the grant of a Bursary to one of them (R. M. D.).

Summary

Isolated lignins, obtained by extraction with formic and acetic acids, and which are normally insoluble in aqueous bisulfite solution, have been shown to yield soluble sulfonic acids after a prior treatment of the lignin with ozone.

Sulfonic acids obtained in this manner from birch formic and acetic acid lignins have been shown to yield vanillin and acetovanillone on alkaline cleavage. Presumably this is the first

time that acetovanillone has been obtained from a lignin sulfonic acid prepared from a hard wood.

An increase in solubility in aqueous bisulfite solution and a decrease in methoxyl content of formic acid lignin with increasing ozonization have been shown to take place.

MONTREAL, CANADA RECEIVED AUGUST 4, 1939

[CONTRIBUTION FROM THE U. S. DEPT. OF AGRICULTURE, FRUIT AND VEGETABLE BY-PRODUCTS LABORATORY,[1] AND THE DEPARTMENT OF CHEMISTRY OF THE STATE COLLEGE OF WASHINGTON]

Enzymic Preparation of *d*-Galacturonic Acid[2]

BY H. H. MOTTERN AND H. L. COLE

d-Galacturonic acid has been available only in limited quantities. Three methods have been used for its preparation: synthesis from galactose,[3] acid hydrolysis of pectic substances,[4] and enzymic hydrolysis of pectic substances.[4b,5] Although materials such as pectin with a galacturonic acid content of approximately 70%, are readily available, because of the lack of definite knowledge concerning the nature of the starting materials, complicated procedures, and low yields, *d*-galacturonic acid has remained a rare chemical.

Because of recent interest in the possible biological significance[6] of *d*-galacturonic acid, it is desirable to have a method whereby *d*-galacturonic acid can be prepared free from contamination with heavy metals and in quantity at nominal cost. A method which is the subject of this report has now been developed which for the first time makes it possible to prepare readily large or small quantities of the pure acid. A commercial pectinase preparation converts commercially available polygalacturonic acid[7] into galacturonic acid in good yields. This method is not subject to interference by side reactions such as decarboxylation to the acid and the formation of furan derivatives, which interfere with crystallization.[8] Disadvantages of Ehrlich's methods[4b,5] were that they employed the use of a little known "pectolsaure," and an enzyme from a special mold described as "*Penicillium Ehrlicii*."

(1) Food Research Division Contribution No. 418.

(2) Abstracted from a portion of a thesis submitted to the Graduate School of the State College of Washington by H. H. Mottern in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

(3) Sell and Link, THIS JOURNAL, **60**, 1813 (1938).

(4) (a) Morell, Bauer and Link, *J. Biol. Chem.*, **105**, 15 (1934); (b) Ehrlich and Guttmann, *Biochem. Z.*, **259**, 100 (1933).

(5) Ehrlich, Guttmann and Haensel, *ibid.*, **281**, 93 (1935).

(6) Manville, Bradway and McMinnis, *Am. J. Digestive Diseases Nutrition*, **3**, 570 (1936); Sullivan and Manville, *Am. J. Pub. Health*, **27**, 1108 (1937).

(7) Obtained from California Fruit Growers Exchange, Products Division, Ontario, California.

(8) Link and Niemann, THIS JOURNAL, **52**, 2474 (1930).

Experimental Part

Preparation of Polygalacturonic Acid.—One hundred grams of powdered apple or citrus pectin[9] was suspended in 250 cc. of 50% ethanol in a mixing bowl of 2 liters capacity which was provided with an egg-beater type stirrer. Since adequate stirring could not be accomplished with a common motor-driven laboratory stirrer it was necessary to use the egg-beater type. When the pectin had been thoroughly wetted by the ethanol and was uniformly dispersed, 10 g. of calcium chloride[10] dissolved in 250 cc. of water was added. The mixture was stirred until the pectin had taken up the aqueous solution and then 250 cc. of 3 *N* sodium hydroxide solution measured ready for use was added promptly. Stirring was continued until the mixture formed a smooth pasty mass. It was permitted to stand for fifteen minutes, after which any clear supernatant liquor was decanted. The mixture was neutralized with hydrochloric acid and sufficient excess added to give a concentration of about 1.5%, and boiled for ten minutes while being vigorously stirred. The polygalacturonic acid was filtered with suction and washed with water containing 10 cc. of concentrated hydrochloric acid per liter. The hydrochloric acid was removed by washing with 50% ethanol. The product was dried by washing several times with ethanol and then with ethyl ether. Yields of 75–80 g. were obtained. Polygalacturonic acid in the moist state may be used directly for the preparation of galacturonic acid.

Enzymic Hydrolysis of Polygalacturonic Acid to Galacturonic Acid.—Seventy-five grams of dry polygalacturonic acid (or the equivalent of the moist preparation obtained as described above) was suspended in 750 cc. of water, which had been warmed to 40°, in a mixing bowl which was provided with an egg-beater type stirrer and while stirring 75 cc. of 3 *N* sodium hydroxide solution was added. The mixture formed a smooth viscous mass. After dispersion the *p*H was adjusted to between 3.7 and 4.0 by the addition of measured amounts of 3 *N* sodium hydroxide or 3 *N* sulfuric acid solutions. To the mixture was then added 3.75 g. of "Pectinol 100D."[11] The mixture was

(9) Ordinary commercial fast-setting powdered pectin was satisfactory without purification.

(10) The calcium salt was used to control the degree of swelling of the pectic acid particles so that a grainy precipitate was obtained which could be satisfactorily filtered and washed.

(11) This preparation is "Pectinase 46 AP" standardized by the addition of diatomaceous earth. It was obtained from Röhm and Haas Co., Bristol, Penna.

next placed in a bottle and sufficient toluene was added to prevent mold growth. The bottle, stoppered with cork, was kept at a temperature of 35–40° for ten days.

At the end of the hydrolysis period[12] (usually less than ten days) the calculated amount of dilute sulfuric acid was added to set free the galacturonic acid from its sodium salt. The hydrolyzate was clarified by filtration using infusorial earth as a filter aid and was concentrated to a thick sirup under vacuum. The sirup was purified by the addition of five volumes of 95% ethanol and three volumes of ethyl ether, which precipitated sodium sulfate, ethanol insoluble fractions of the enzyme preparation, and any unhydrolyzed polygalacturonic acid. After standing for twelve hours the ethanol–ether solution of galacturonic acid was decanted from the residue and evaporated to a thick sirup under vacuum. Crystallization,[13] which required approximately twenty-four hours for completion, was hastened by adding small amounts of 95% ethanol and seeding with a few crystals of galacturonic acid. The acid was triturated with cold 90% ethanol, filtered, and washed with ethanol. It was purified further by dissolving in 50% ethanol, treating with charcoal, filtering, and recrystallizing after the addition of sufficient ethanol to make the ethanol concentration 75%. The yield from 75 g. of polygalacturonic acid was 20 g. of the purified product. The m. p. was 113–115° (uncorr.).[14]

(12) Indicated by treating a test portion with fresh enzyme for twenty-four hours and showing no increased reduction of Fehling's solution over previous samples.

(13) Direct crystallization of α-*d*-galacturonic acid from the purified hydrolyzate depends upon the use of starting materials which will not yield substances such as sugars interfering with crystallization.

Acknowledgment.—The writers are indebted to the California Fruit Growers Exchange, Research Department, Ontario, California for citrus pectin, to General Foods Corporation, New York City, for apple pectin, and to Röhm and Haas Co., Bristol, Penna., for pectinase preparations. Acknowledgment is also made to Dr. I. A. Manville, University of Oregon School of Medicine, for helpful suggestions and criticisms.

Summary

A method has been developed for the quantity preparation of *d*-galacturonic acid by the action of a pectinase enzyme on polygalacturonic acid.

(14) Link and Nedden, *J. Biol. Chem.*, **94**, 307 (1931).

PULLMAN, WASHINGTON RECEIVED APRIL 15, 1939

[CONTRIBUTION FROM THE BAILEY CHEMICAL LABORATORY OF THE UNIVERSITY OF KANSAS]

Iodo Derivatives of Phenyl Ether. II. Studies in Orientation

BY R. Q. BREWSTER AND H. S. CHOGUILL

Substances containing two or more benzene rings offer numerous problems in orientation. A given substituent may enter one of the nuclei at a certain position while another substituent may take an entirely different location. The experiments here reported were undertaken in order to obtain more information on these orientation effects in the phenyl ether series. Such knowledge was desirable in the continuation of a study of the iodinated derivatives of phenyl ether[1] which has been conducted in this Laboratory. Much work upon this subject has been done by several other investigators[2] using particularly those phenyl ether derivatives containing substituents of halogens, acetamino, nitro and to some extent methoxy groups. The present work is concerned primarily with the derivatives of 2-methoxy- and 4-methoxyphenyl ether. Since the methoxy radical is one of the more strongly directing groups, it would be expected that 4-methoxyphenyl ether would undergo substitution at position 3 and so it does upon nitration, 3-nitro-4-methoxyphenyl ether being the sole product.[2c] We find that halogenation however introduces the halogen atom at position 4′. If that position should be occupied, the halogen attaches itself to the carbon atom at 3 unless the substituent at 4′ is a group such as hydroxy or amino which exceeds the methoxy group in orienting power. Likewise the methoxy group is the controlling factor in the nitration of 2-methoxyphenyl ether as the product obtained is 5-nitro-2-methoxyphenyl ether, yet halogens substitute at position 4′ and take position 5 only if 4′ is occupied. In the halogenation of 4-nitrophenyl ether or 2-nitrophenyl ether, McCombie, Macmillan and Scarborough[2b] showed that a halogen enters at 4′, *i. e.*, para to the ether oxygen and always in the non-nitrated nucleus. The strong preference of a halogen for a position para to the ether oxygen is shown in the iodination of 4-methoxy-2′-nitrophenyl ether where the iodine takes position 4′ (Compound XIII) in spite of the presence of a nitro group in the same ring. However, in the iodination of 2-methoxy-4-nitro-

(1) Brewster and Strain, THIS JOURNAL, **56**, 117 (1934).

(2) (a) Scarborough and colleagues, *J. Chem. Soc.*, 2361 (1929); (b) *ibid.*, 529 (1931); (c) Lea and Robinson, *ibid.*, 411 (1926); (d) Oesterlin, *Monatsh.*, **57**, 31 (1931); (e) Raiford, Thiessen and Wernert, THIS JOURNAL, **52**, 1205 (1930).

TABLE I

No.	Ref.	Phenyl ether	Source	Procedure	M. p., °C.	Analyses, %	Calcd.	Found
I	5	4-Methoxy-4′-iodo		C	115	I,	38.95	38.62
II	6	Benzoyl der. of 4-hydroxy			97	C,	78.61	78.30
						H,	4.83	4.75
III		Benzoyl der. of 4-hydroxy-4′-iodo	II	C	122	I,	30.53	30.40
IV	7	4-Hydroxy-4′-iodo	III		116	I,	40.70	40.82
V	8	4-Methoxy-3-amino		F	70	N,	6.51	6.42
		Acetyl der. of V			148	N,	5.45	5.39
VI	9	4-Methoxy-3-iodo	V	H	76	I,	38.95	38.70
VII	10	4-Methoxy-3-bromo	V	H	55	Br,	28.67	28.79
VIII	11	4-Methoxy-3-bromo-4′-iodo	I, VII	D, C	88	Br,	19.75	19.85
						I,	31.36	31.50
IX	12	4-Methoxy-3,4′-diiodo	I, VI, XI	C, H	101	I,	56.20	55.80
X	13	4-Methoxy-3-nitro-4′-iodo	I	E	92	I,	34.23	33.95
XI	14	4-Methoxy-3-amino-4′-iodo	X	G	85	I,	37.24	36.95
XII	15	4-Methoxy-2′-nitro		A	77	N,	5.71	5.87
XIII		4-Methoxy-2′-nitro-4′-iodo	XII	C	70	I,	34.23	34.28
XIV	16	4-Methoxy-2′-amino-4′-iodo	XIII	G	102	I,	37.24	37.15
XV	17	4-Methoxy-2′-,-3-dinitro	XII	E	132	N,	9.66	9.45
XVI	17	4-Methoxy-2′,4′-dinitro		A	110	N,	9.66	9.55
XVII	18	2 Methoxy-4′-iodo		H	B. p. 228 (28 mm.)	I,	38.95	38.80
XVIII	18	2-Methoxy-5-nitro-4′-iodo	XVII, XX	E, C	115	I,	34.24	33.90
XIX	19	2-Methoxy-5-iodo-4′-nitro		C	109	I,	34.24	33.97
XX	20	2-Methoxy-5-nitro		E	72	N,	5.71	5.64

phenyl ether the iodine atom is directed to position 5 even though position 4 is unoccupied, *i. e.*, the methoxy group exceeds the 4-nitrophenoxy radical in power of orientation.

Experimental

The laboratory procedures used in these experiments are of standard types and are referred to in the table by letters as follows: A, preparation of phenyl ethers by the Ullmann reaction[3]; B, the modified Ullmann reaction using nitrofluorobenzene[4] in place of nitrochlorobenzene; C, iodination by heating on the steam-bath with iodine monochloride in acetic acid solution for one or two hours; D, bromination in acetic acid solution; E, nitration with nitric acid (d. 1.42) in acetic acid solution; F, reduction of nitro compounds free from halogen substituents with hydrogen and the Adams platinum catalyst; G, reduction of nitro compounds containing halogen with iron powder in

(3) *Org. Syntheses*, **14**, 66 (1934).

(4) Rarick, Brewster and Dains, THIS JOURNAL, **55**, 1289 (1933).

(5) Potassium phenate and 4-bromoanisole according to the procedure of Oesterlin[2d] gave a 70% yield of 4-methoxyphenyl ether while bromobenzene and hydroquinone monomethyl ether gave only a 20% yield. Iodination of 4-methoxyphenyl ether gave I which was also obtained from 4-methoxy-4′-aminophenyl ether by the Sandmeyer reaction. The samples made by both methods were identical by a mixed melting point test.

(6) 4-Methoxyphenyl ether (100 g.) was heated with anhydrous aluminum chloride (65 g.) for one hour in an oil-bath at 130°. Fifteen grams of additional aluminum chloride was then added and the temperature raised to 140–150° for another hour after which the mass was cooled and poured into water; yield of 4-hydroxyphenyl ether, 75 g., m. p. 84°. It forms the benzoyl derivative readily upon shaking with benzoyl chloride and alkali.

(7) Thirty grams of III was hydrolyzed to IV by boiling with 100 cc. of ethyl alcohol and 50 cc. of 20% sodium hydroxide solution for one hour; yield 20 g.

(8) Nitration of 4-methoxyphenol ether in acetic acid solution[2c] gave a 70% yield of 4-methoxy-3-nitrophenyl ether which gave practically a quantitative yield of V upon reduction.

(9) For diazotization 22.5 g. (0.1 mole) of V was dissolved in 300 cc. of water and 50 cc. of concentrated sulfuric acid and cooled in ice. Crystals of the sulfate separated but redissolved readily upon diazotization with 7.5 g. of sodium nitrite which was added all at once. After ten minutes 5 g. of urea was added, the solution filtered and poured into 25 g. of potassium iodide in 100 cc. of water.

(10) Distils at 182–187°, ten mm.

(11) Compound VIII was obtained both by the bromination of I and the iodination of VII. The two samples were purified from ethyl alcohol and from ligroin and showed no lowering of the melting point on mixing.

(12) Produced by iodination of either I or VI and through the diazo reaction from XI.

(13) No. X was also obtained by iodination of 4-methoxy-3-nitrophenyl ether. Both specimens were shown to be identical by a mixed melting point.

(14) The Sandmeyer reaction with XI gave IX.

(15) Obtained in 70% yield from *o*-nitrochlorobenzene and hydroquinone monomethyl ether.

(16) Deamination of XIV gave I showing that the iodination of XII occurred at 4′.

(17) Compound XV, produced by the nitration of XII, most probably has the composition here assigned as it was not identical with XVI made from 2,4-dinitrochlorobenzene and hydroquinone monomethyl ether.

(18) For conversion to a solid derivative, XVII was nitrated in acetic acid solution giving XVIII. The location of the iodine atom at position 4′ in XVII was established by its synthesis from 2-methoxy-4′-aminophenyl ether through the Sandmeyer reaction. This sample also gave XVIII upon nitration. The fact that the nitro group in XVIII was at position 5 was shown by the preparation of an identical sample by iodination of XX.

(19) In the iodination of 2-methoxy-4′-nitrophenyl ether the iodine enters at 5, producing compound XIX, identical by mixed melting point with a sample prepared from 4-nitrofluorobenzene and the potassium salt of 2-methoxy-5-iodophenol (4-iodoguaiacol).

(20) Lea and Robinson[2c] obtained compound XX by the nitration of 2-methoxyphenyl ether but considered that the nitro group most probably took position 6. We proved that its location was at 5 by synthesis of 2-methoxy-5-nitrophenyl ether, identical with XX by a mixed melting point, from potassium phenate and 2-methoxy-5-nitrobromobenzene.

acetic acid solution; and H, replacement of an amino group by halogen through the Sandmeyer reaction. Other explanatory comments are given in the footnotes.

Summary

The study of the orienting effect of the methoxy group in phenyl ether derivatives has been extended. In determining this orientation a group of new compounds has been prepared and the structure of each proved.

LAWRENCE, KANSAS RECEIVED AUGUST 4, 1939

[CONTRIBUTION FROM THE ORGANIC LABORATORIES OF THE UNIVERSITY OF FLORIDA]

Derivatives of Piperazine. XVIII. Synthesis of Substituted Piperazines and the Hydrolysis of Amines

BY J. P. BAIN[1] AND C. B. POLLARD

It has been shown that N-phenylpiperazine[2] may be prepared readily by heating a mixture of aniline and diethanolamine hydrochlorides. We have found that this method cannot be extended conveniently to the preparation of C-substituted piperazines from arylamines and diisopropanolamine. We have shown that piperazines may be prepared from amino alcohols[3] using the catalytic alkylation methods of Paden and Adkins[4] and Hill and Adkins.[5] This paper reports an extension of the synthesis of piperazines by this method and the formation of alcohols by hydrolysis of amines under catalytic alkylation conditions. This interesting side reaction does not appear to have been reported by other investigators.

Experimental

N-Cyclohexylamines were prepared by passing ethylene oxide into a methanol solution of cyclohexylamine. After removal of the solvent at atmospheric pressure the amino alcohols were distilled at 10 mm. pressure. N-Cyclohexylethanolamine distilled at 118° and N-cyclohexyldiethanolamine at 175°. The neutral equivalents of these compounds were determined using methyl red as the indicator: N-cyclohexylethanolamine, neut. equiv. calcd. 143.2, found 143.0; $n^{25}D$ 1.4842; N-cyclohexyldiethanolamine, neut. equiv. calcd. 187.3, found 187.2; $n^{25}D$ 1.4927.

N-Phenyldiisopropanolamine was prepared by heating one mole of aniline with two moles of propylene oxide in 300 cc. of dioxane to 170° in a bomb for several hours. The product was a viscous straw-colored liquid boiling at 184–185° at 10 mm.; N calcd. 6.69, found 6.60.

N-*p*-Tolyldiisopropanolamine was prepared similarly. After removal of solvent the product solidified and was recrystallized several times from hexane and from diisopropyl ether as slightly pink needles, m. p. 112°; N calcd. 6.27, found 6.20.

1,4-Dicyclohexylpiperazine was prepared by two methods. (a) Six hundred ml. of dioxane containing 1 mole each of cyclohexylamine and N-cyclohexyldiethanolamine was heated to 250–270° and shaken for three to four hours in hydrogen at a pressure of 34 atmospheres with 25 g. of copper–chromium oxide catalyst. After filtration from the catalyst and removal of the dioxane, the reaction mixture was distilled at 10 mm. pressure. The first fraction of 20 g., boiling at 60–61°, was identified as cyclohexanol by conversion to the phenylurethan, m. p. 82.5°. The second fraction, 19 g., boiling at 109–110°, was not identified. The third fraction, distilling between 170° at 10 mm. and 200° at 5 mm. partly solidified on cooling. Recrystallized first from pentane and then from aqueous methanol it yielded the piperazine in 20% yield, m. p. 118°. For analysis it was converted to the sparingly soluble dihydrobromide: Br calcd. 38.77, found (gravimetric) 38.76, neut. equiv. calcd. 206, found (by titration with phenolphthalein in the presence of benzene to remove the free amine as formed). (b) Cyclohexylethanolamine treated under the same conditions gave the piperazine in the same yield as well as the two low boiling fractions.

1-Cyclohexyl-2,6-dimethyl-4-phenylpiperazine, b. p. 205–210° at 2 mm., was prepared in 20% yield from cyclohexylamine and N-phenyldiisopropanolamine. The dihydrobromide was used for analysis: N calcd. 6.45, found 6.41; Br calcd. 36.81, found 36.83.

1-Cyclohexyl-2,6-dimethyl-4-*p*-tolylpiperazine, prepared from cyclohexylamine and N-*p*-tolyldiisopropanolamine, boiling at 175–230° at 5 mm., 15% yield, was converted to the hydrobromide and recrystallized from water; for the monohydrobromide, Br calcd. 21.72, found 21.67.

Cyclohexanol from Cyclohexylamine.—Sixty grams of cyclohexylamine, 300 ml. of dioxane, 20 ml. of water and 20 g. of copper–chromium oxide catalyst were placed in a bomb under 500 lb./sq. in. (34 atm.) hydrogen pressure and heated at 260–270° for four hours with shaking. After removal of low boiling material the product was fractionated at 10 mm. The fraction boiling at 55–65° was acidified and the neutral material extracted with ether. The neutral material distilled at 60–61° at 10 mm. and was identified as cyclohexanol by conversion to the phenylurethan, m. p. 82.5°. The yield of the pure alcohol was 20%.

(1) This paper is abstracted from a portion of a dissertation submitted by J. P. Bain to the Graduate Council of the University of Florida in partial fulfilment of the requirements for the degree of Doctor of Philosophy, May, 1939.

(2) Pollard and MacDowell, THIS JOURNAL, **56**, 2199 (1934).

(3) Bain and Pollard, *ibid.*, **61**, 532 (1939).

(4) Paden and Adkins, *ibid.*, **58**, 2487 (1936).

(5) Hill and Adkins, *ibid.*, **60**, 1033 (1938).

Diethylcyclohexylamine was prepared from cyclohexylamine and diethyl sulfate. Primary and secondary amines were removed with benzenesulfonyl chloride. The product boiled at 68.5–69 at 10 mm.; neut. equiv. calcd. 155.3, found 156.1.

Cyclohexanol was prepared from diethylcyclohexylamine in 33% yield under the conditions used for the hydrolysis of cyclohexylamine. Seventy-eight grams of diethylcyclohexylamine was treated with 300 ml. of 50% aqueous dioxane and 23 g. of copper–chromium oxide catalyst at 270–280° without hydrogen pressure. The product boiling at 50–68° at 10 mm. was acidified and extracted with ether. Only about 1 g. of neutral material was obtained. The amine hydrochlorides were treated with alkali and the free amines fractionated at 10 mm. The fraction boiling at 53.5–56° weighed 12 g. and gave a neutral equivalent of 133.0 (calculated for mono- and diethylcyclohexylamines, 127.2 and 155.3, respectively). This product on treatment with sodium nitrite and hydrochloric acid yielded 5 g. of a pale yellow oil, b. p. 127–128° at 12.5 mm. The literature[6] gives 130° at 12 mm. as the boiling point of N-nitrosoethylcyclohexylamine.

Summary

1. A number of new piperazine derivatives have been prepared from amino alcohols by catalytic alkylation.

2. The formation of alcohols from amines under catalytic alkylation conditions has been reported. This side reaction may account in part for the poor yields obtained in certain alkylations.

3. The generality and applicability of this reaction is being studied.

(6) Heilbron, "Dictionary of Organic Compounds," Vol. II, 1936, p. 27.

GAINESVILLE, FLORIDA RECEIVED JULY 13, 1939

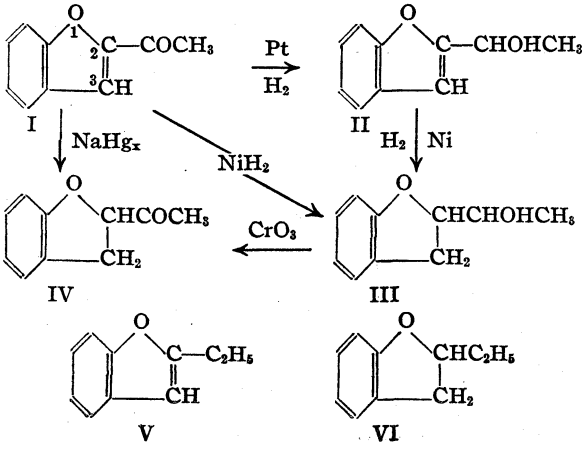
[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Derivatives of Coumaran. VI. Reduction of 2-Acetobenzofuran and its Derivatives

BY R. L. SHRINER AND JOHN ANDERSON

In an investigation concerned with the preparation of 2-substituted coumarans, the catalytic hydrogenation of 2-acetobenzofuran and some of its derivatives was studied.

It has been found possible to obtain the two alcohol reduction products of 2-acetobenzofuran (I) by catalytic hydrogenation provided the appropriate catalyst is employed. Hydrogenation with a platinum catalyst results in the formation of 2-(1-hydroxyethyl)-benzofuran (II) while a Raney nickel catalyst leads to the formation of 2-(1-hydroxyethyl)-coumaran (III). The coumaran (III) also can be obtained from the benzofuran (II) by hydrogenation in the presence of Raney nickel.



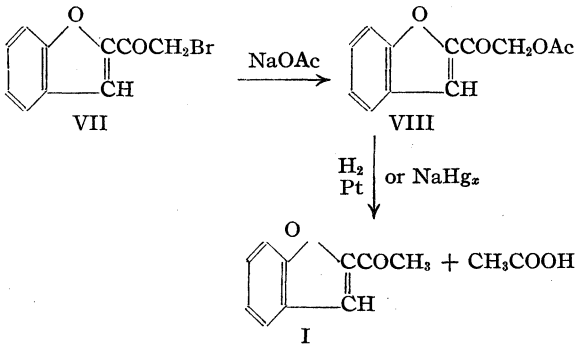
Hydrogenation in the presence of colloidal platinum resulted in a mixture of II, III, 2-ethylbenzofuran (V) and 2-ethylcoumaran (VI). No 2-acetocoumaran (IV) was found among the products of catalytic reduction. A sample of this ketone was made by oxidation of the alcohol (III) and by a sodium amalgam reduction of 2-acetobenzofuran. It was characterized by its semicarbazone.

The catalytic reduction of 2-acetobenzofuran thus follows a course different from that of the closely related benzalacetone, which is smoothly reduced to benzylacetone[1] first and then undergoes further reduction to 4-phenyl-2-butanol. The results constitute further evidence that catalytic hydrogenation of α,β-unsaturated ketones occurs by 1,2-addition[1] and not by 1,4-addition[2] as is the case in reduction by chemical means.[3] In this particular case the double bond in the 2,3-position probably is stabilized to some extent by resonance in the benzofuran nucleus.

ω-Acetoxy-2-acetobenzofuran (VIII) was prepared by bromination of 2-acetobenzofuran, followed by treatment of the resulting ω-bromo-2-acetobenzofuran (VII) with sodium acetate.

An unusual reaction took place when ω-acetoxy-2-acetobenzofuran (VIII) was subjected to

(1) Kern, Shriner and Adams, THIS JOURNAL, 47, 1147 (1925).
(2) Straus and Grindel, *Ann.*, 439, 276 (1924).
(3) Conant and Cutter, *J. Phys. Chem.*, 28, 1105 (1924).



catalytic hydrogenation. It was found that the major portion of the reacting material underwent cleavage to acetic acid and 2-acetobenzofuran (I). In the reductions when only one mole of hydrogen was absorbed, 2-acetobenzofuran was obtained as the cleavage product while mixtures of reduction products of 2-acetobenzofuran were obtained when more than one mole of hydrogen was absorbed. Sodium amalgam reduction of ω-acetoxy-2-acetobenzofuran in acetic acid solution resulted in a similar cleavage producing a mixture of the reduction products of 2-acetobenzofuran.

It seemed possible that this cleavage reaction might be general for phenacyl esters but catalytic reduction of phenacyl acetate in the presence of platinum oxide gave a good yield of 1-phenyl-2-acetoxyethanol and only a very small amount of methylphenylcarbinol and acetic acid.

Experimental

2-Acetobenzofuran.—This substance was prepared from salicylaldehyde and chloroacetone according to the method of Stoermer, Chydenius and Schinn.[4] A 60% yield of colorless crystals melting at 74–75° was obtained.

ω-Bromo-2-acetobenzofuran.—The method for the preparation of this compound was indicated by Calov and Stoermer[5] but these authors gave neither detailed directions for the preparation nor analysis of the product. A solution of 25.0 g. of bromine in 200 cc. of carbon disulfide was added dropwise, with stirring, into a solution of 25.0 g. of 2-acetobenzofuran in 200 cc. of the same solvent. The bromine was added during a period of two hours and at the end of this time the carbon disulfide was removed by evaporation to leave a yellow solid residue. The pure product, which exists in the form of white needles with a melting point of 90–91°, was obtained in a yield of 34 g. by recrystallizing the residue twice from ethanol. The yield was 91% of the theoretical.

Anal. Calcd. for $C_{10}H_7BrO_2$: C, 50.24; H, 2.95; Br, 33.42. Found: C, 50.52; H, 3.16; Br, 33.25.

ω-Acetoxy-2-acetobenzofuran.—A solution of 50 g. of sodium acetate trihydrate, 25.0 g. of ω-bromo-2-acetobenzofuran and 5 cc. of 6 *N* hydrochloric acid in 500 cc. of 50% ethanol was refluxed for one and a half hours. The mixture was poured into 500 cc. of ice water and the crude product was removed by filtration. The product was purified by recrystallization from ethyl acetate to give 17 g. (74%) of yellow needles which had a melting point of 86–87°.

Anal. Calcd. for $C_{12}H_{10}O_4$: C, 66.05; H, 4.62. Found: C, 66.29; H, 4.72.

2-(1-Hydroxyethyl)-benzofuran.—A mixture of 16.0 g. of acetobenzofuran in 100 cc. of absolute ethanol and 0.1 g. of platinum oxide was shaken in an atmosphere of hydrogen at a pressure of 2 to 3 atmospheres for six hours. At the end of this time one mole of hydrogen had been absorbed and the absorption had ceased. The catalyst was removed by filtration and the ethanol was removed by distillation from an oil-bath at 150°. The residue solidified to give the product, which had a melting point of 41°, in a quantitative yield. Recrystallization of the product by dissolving it in a small amount of ether at room temperature and cooling in a dry ice–acetone bath did not raise the melting point. The product boiled at 147° under a pressure of 19 mm. but purification by distillation did not raise the melting point.

Anal. Calcd. for $C_{10}H_{10}O_2$: C, 74.05; H, 6.22. Found: C, 74.25; H, 6.33.

The phenylurethan of the product was prepared by heating equimolecular quantities of the alcohol and phenyl isocyanate on a steam-bath for five hours. The mixture was taken up in carbon tetrachloride and filtered. Evaporation of the carbon tetrachloride at room temperature caused precipitation of the phenylurethan in crystalline form. It was recrystallized from a mixture of one part of benzene and two parts of low-boiling petroleum ether to give white needles with a melting point of 102–103°.

Anal. Calcd. for $C_{17}H_{15}NO_3$: N, 4.98. Found: N, 5.11.

Previous investigators[6] described 2-(1-hydroxyethyl)-benzofuran and its phenylurethan but the alcohol was reported to have a melting point of 37° and the phenylurethan to have a melting point of 126°.

2-(1-Hydroxyethyl)-coumaran from 2-(1-Hydroxyethyl)-benzofuran.—To a solution of 8 g. of 2-(1-hydroxyethyl)-benzofuran in 100 cc. of absolute ethanol there was added 2 g. of Raney nickel. The mixture was shaken in an atmosphere of hydrogen at a pressure of two to three atmospheres. One mole of hydrogen was absorbed in fourteen hours and the absorption ceased. The ethanol was removed by distillation and the residue subjected to vacuum distillation. The entire residue distilled at 145° under a pressure of 20 mm. to yield 6.5 g. (81%) of the product as a colorless, viscous liquid with the following constants: d^{25}_{25} 1.1138; $n^{25}D$ 1.5470; M_D found 46.7, M_D calcd. 45.9.

Anal. Calcd. for $C_{10}H_{12}O_2$: C, 73.14; H, 7.37. Found: C, 72.94; H, 7.38.

This compound was reported by former investigators[6] to have a density of 1.506 at 18°.

The phenylurethan of the above compound was prepared by heating equimolecular quantities of the compound

(4) Stoermer, Chydenius and Schinn, *Ber.*, **57**, 75 (1924).
(5) Calov and Stoermer, *Ann.*, **312**, 322 (1900).
(6) Stoermer and Shaffer, *Ber.*, **36**, 2869, 2871 (1903).

and phenyl isocyanate on a steam-bath for eight hours. The reaction mixture was taken up in glacial acetic acid and poured into ice water to cause separation of the crude phenylurethan. It was recrystallized from a mixture of one part of benzene and two parts of low-boiling petroleum ether to give white needles which melted at 115–116°.

Anal. Calcd. for $C_{17}H_{17}NO_3$: N, 4.95. Found: N, 5.16.

The phenylurethan of 2-(1-hydroxyethyl)-coumaran was formerly reported[6] to have a melting point of 73° but it seems probable that this was a mixture of the phenylurethans of 2-(1-hydroxyethyl)-coumaran and 2-(1-hydroxyethyl)-benzofuran.

2-(1-Hydroxyethyl)-coumaran from 2-Acetobenzofuran.—To a solution of 25 g. of acetobenzofuran in 120 cc. of absolute ethanol there was added 8 g. of Raney nickel and the mixture was shaken in an atmosphere of hydrogen at a pressure of two to three atmospheres. Two moles of hydrogen was absorbed in thirty-six hours and the absorption ceased. The solution was filtered, the ethanol removed by distillation, and the residue fractionally distilled to yield 22.5 g. of 2-(1-hydroxyethyl)-coumaran which was identical in all its properties with that prepared by hydrogenation of 2-(1-hydroxyethyl)-benzofuran. The yield by this method of preparation was 90% of the theoretical.

Hydrogenation of 2-Acetobenzofuran in the Presence of Colloidal Platinum.—To a solution of 24 g. of 2-acetobenzofuran in 100 cc. of absolute ethanol there was added 1.0 g. of Norite, 0.1 g. of chloroplatinic acid and 0.05 g. of platinum oxide. The mixture was shaken in an atmosphere of hydrogen at a pressure of two to three atmospheres and one mole of hydrogen was absorbed in nine minutes. The catalyst was removed by filtration and the ethanol by distillation. The only pure compound which could be isolated from the residue was unchanged acetobenzofuran.

A second reduction was carried out in which two moles of hydrogen were absorbed. The product was isolated as above and consisted of two definite fractions. The lower-boiling fraction weighed 5.5 g., distilled at 99–100° under a pressure of 19 mm. and had the following constants: d^{20}_{20} 1.0196; $n^{20}D$ 1.5475.

Anal. Calcd. for $C_{10}H_{10}O$: C, 82.16; H, 6.89. Calcd. for $C_{10}H_{20}O$: C, 81.04; H, 8.16. Found: C, 81.92; H, 7.56.

This product was evidently a mixture of 2-ethylbenzofuran and 2-ethylcoumaran. The higher-boiling fraction weighed 7.5 g. and distilled at 144–145° under a pressure of 19 mm. It was a mixture of 2-(1-hydroxyethyl)-coumaran and 2-(1-hydroxyethyl)-benzofuran.

Chromic Anhydride Oxidation of 2-(1-Hydroxyethyl)-coumaran.—To a solution of 14.5 g. of 2-(1-hydroxyethyl)-coumaran in 40 cc. of glacial acetic acid there was added, with stirring, 58.0 g. of a 10% solution of chromic anhydride in glacial acetic acid. The oxidizing solution was added in portions over a period of forty-four hours and the mixture was stirred for twelve hours longer at room temperature and seven hours at 80°. The reaction mixture was poured into 700 cc. of water and the resulting solution was treated with sodium bicarbonate until all of the acetic acid was neutralized. The neutral solution was extracted with 400 cc. of ether in four portions, the ether extract was dried over calcium chloride and the ether removed by evaporation. The methyl ketone portion of the concentrate was then isolated by shaking in saturated sodium bisulfite solution and removing the bisulfite addition compound by filtration. The bisulfite addition product weighed 7 g., which is 29% of the theoretical yield. The bisulfite addition compound was decomposed by shaking it in 2% sulfuric acid, the free ketone was extracted with ether and the ether solution dried over calcium chloride. After the calcium chloride was removed by filtration and the ether by evaporation, the crude ketone was treated with semicarbazide hydrochloride and sodium acetate in ethanol solution in the usual manner and the semicarbazone which formed was recrystallized five times from 50% ethanol to give white needles with a melting point of 168–169°.

Anal. Calcd. for $C_{11}H_{13}N_3O_2$: N, 19.17. Found: N, 19.20.

Since 2-acetocoumaran semicarbazone has been reported[4] to have a melting point of 192°, it was thought advisable to determine the melting point of a mixture of the product described above and 2-acetobenzofuran semicarbazone which would be the impurity most likely to be present in the compound previously described because the investigators had obtained their 2-acetocoumaran from sodium amalgam reduction of 2-acetobenzofuran. It was found that the addition of small quantities of 2-acetobenzofuran semicarbazone (m. p. 217°) to the semicarbazone obtained above raised the melting point to the neighborhood of 190°.

A sodium amalgam reduction of 2-acetobenzofuran, using a much larger excess of sodium amalgam than that given in the directions of Stoermer, Chydenius and Schinn,[4] resulted in the formation of a ketone the semicarbazone of which melted at 168–169° and which proved to be identical with the semicarbazone obtained above.

Hydrogenation of ω-Acetoxy-2-acetobenzofuran. (a) **With Platinum Oxide.**—A solution of 7.5 g. of ω-acetoxy-2-acetobenzofuran in 60 cc. of absolute ethanol and 1.5 g. of platinum oxide was shaken with hydrogen at 3 atmospheres pressure. One mole equivalent of hydrogen was absorbed in ten minutes and the reaction was stopped at this point. The catalyst was removed by filtration, the solvent distilled and the residue fractionated.

The forerun was treated on a watch glass with piperazine hexahydrate and the piperazonium salt which formed was recrystallized from *n*-butanol. It melted at 208–209° and comparison with an authentic sample of piperazinium diacetate[7] showed that they were identical and proved the presence of acetic acid in the reduction mixture. The main fraction boiled at 147–148° at 20 mm. and solidified on standing. Recrystallization from alcohol yielded 4.2 g. of colorless crystals melting at 74–75° and which were identical with 2-acetobenzofuran.

A second reduction was carried out using only 0.2 g. of catalyst. At the end of forty-eight hours 1.8 mole equivalents had been absorbed.

Fractionation of the products yielded 6.0 g. of a liquid which boiled at 146–148° at 18 mm. and 2.4 g. which boiled at 180–200° at 18 mm. The lower boiling fraction was redistilled and a middle fraction taken for analysis.

(7) Pollard, Adelson and Bain, THIS JOURNAL, 56, 1759 (1934).

Anal. Calcd. for $C_{10}H_8O_2$: C, 74.99; H, 5.03. Calcd. for $C_{10}H_{10}O_2$: C, 74.05; H, 6.22. Calcd. for $C_{10}H_{12}O_2$: C, 73.14; H, 7.37. Found: C, 74.97; H, 6.64.

The analyses indicate that this material is probably a mixture of acetobenzofuran and its reduction products. Had the acetoxy group not been cleaved, the carbon and hydrogen analyses would both have yielded much lower values.

A third reduction was carried out in which a solution of 10.0 g. of acetoxyacetobenzofuran in 150 cc. of cyclohexane was shaken with hydrogen at 2 to 3 atmospheres pressure in the presence of 5.0 g. of Raney nickel. No hydrogen was absorbed in three hours and 0.1 g. of platinum oxide was added to the reaction mixture. One mole of hydrogen was then absorbed in twenty-four hours and absorption ceased at this point. The catalyst was removed by filtration and the solvent by distillation to leave a residue which solidified. Recrystallization of the residue yielded 4.3 g. of 2-acetobenzofuran.

(b) **With Raney Nickel in Ethanol.**—Hydrogenation with Raney nickel in ethanol at 2 to 3 atmospheres pressure took place slowly. Acetic acid was identified as one product but the remainder consisted of a mixture which could not be separated readily.

Sodium Amalgam Reduction of ω-Acetoxy-2-acetobenzofuran.—To a solution of 10.0 g. of ω-acetoxy-2-acetobenzofuran in 300 cc. of 60% acetic acid there was added in small portions, over a period of twenty-four hours, 600 g. of 3% sodium amalgam. The solution which had been stirred and kept at room temperature throughout the time of addition was then diluted with an equal volume of water, neutralized with the calculated quantity of 5% sodium hydroxide solution and extracted with ether. The ether extract was dried over calcium chloride and the ether was removed by distillation to leave a liquid residue. Fractional distillation of the residue gave a product which weighed 6.2 g. and boiled at 115–130° at 6 mm. Refractionation of this product gave 4.5 g. of material boiling at 115–120° and 1.2 g. boiling at 120–130°. The lower boiling material was again fractionated and the middle portion taken for analysis.

Anal. Calcd. for $C_{10}H_8O_2$: C, 74.99; H, 5.03. Calcd. for $C_{10}H_{10}O_2$: C, 74.05; H, 6.22. Found: C, 74.16; H, 6.09.

All portions of the product were treated with semicarbazide hydrochloride and sodium acetate in ethanol solution to yield a semicarbazone which melted at 200–201°. This semicarbazone gave the following analytical data.

Anal. Calcd. for $C_{13}H_{15}N_3O_4$: N, 15.16; C, 56.30; H, 5.42. Calcd. for $C_{11}H_{11}N_3O_2$: N, 19.35; C, 60.81; H, 5.11. Calcd. for $C_{11}H_{13}N_3O_2$: N, 19.17; C, 60.26; H, 5.98. Found: N, 19.38; C, 60.52; H, 5.66.

This semicarbazone is evidently a mixture of the semicarbazones of 2-acetobenzofuran and 2-acetocoumaran. The analyses show that under these conditions the acetoxy group is cleaved in a manner similar to the cleavage in the catalytic hydrogenations and that the ketone portion of the product is a mixture of 2-acetobenzofuran and 2-acetocoumaran.

Hydrogenation of Phenacyl Acetate.—A solution of 25.0 g. of phenacyl acetate in 200 cc. of absolute ethanol was shaken with hydrogen at two to three atmospheres pressure in the presence of 0.2 g. of platinum oxide. One mole of hydrogen was absorbed in three and one-half hours and the reduction was stopped at this point. The catalyst was removed by filtration and the ethanol by distillation. The residue was distilled and 1 cc. of distillate collected. This was treated with piperazine hydrate and the salt which resulted recrystallized from *n*-butanol. It melted at 208–209°, corresponding to piperazinium diacetate. The remainder was fractionally distilled to yield 1.8 g. of material boiling at 90–140° under a pressure of 25 mm. and 19.5 g. of material boiling at 163–168° under a pressure of 25 mm. The main fraction was redistilled and it boiled almost entirely at 136–137° under a pressure of 6 mm. and a middle fraction showed the following constants: d^{20}_{20} 1.1438; $n^{20}D$ 1.5260; M_D calcd. for 1-phenyl-2-acetoxyethanol, 48.0; M_D found, 48.4.

Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 66.80; H, 6.65.

The lower boiling fraction was redistilled and the fraction which boiled at 190–205° was treated with α-naphthyl isocyanate at room temperature for ten hours to give a reaction mixture which was extracted with 250 cc. of petroleum ether. The petroleum ether extract was evaporated at room temperature to give a crude α-naphthyl urethan which was recrystallized from petroleum ether to give white needles with a melting point of 94–96°. Since this substance was not obtained in sufficient quantities to allow further purification by recrystallization, it was subjected to analysis.

Anal. Calcd. for $C_{19}H_{17}NO_2$: N, 4.81. Found: N, 4.96.

Evidently this lower boiling fraction contained a small amount of phenylmethylcarbinol which formed the above urethan.

Summary

Catalytic reduction of 2-acetobenzofuran with platinum and hydrogen produced 2-(1-hydroxyethyl)-benzofuran. With hydrogen and nickel 2-(1-hydroxyethyl)-coumaran was formed. 2-Acetocoumaran was obtained by a sodium amalgam reduction of 2-acetobenzofuran and by oxidation of 2-(1-hydroxyethyl)-coumaran.

ω-Acetoxy-2-acetobenzofuran was cleaved by reducing agents to 2-acetobenzofuran and acetic acid.

URBANA, ILLINOIS RECEIVED JULY 21, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Vinyl Chloride Polysulfone[1]

BY C. S. MARVEL AND L. H. DUNLAP

Vinyl chloride is unique among the olefins which have been found to combine with sulfur dioxide to give polysulfones since it yields a polymer having two olefin units to one sulfur dioxide unit.[2] In the work previously reported no evidence for the exact structure of the polymer was obtained. Hence a further study of this problem has been made.

When vinyl chloride polysulfone is hydrolyzed with 20% sodium hydroxide and volatile products are removed rapidly from the reaction flask in a current of steam, an aldehyde is produced.[2] This aldehyde has now been identified definitely as acetaldehyde. During the hydrolysis not only is the aldehyde formed but at the same time all of the chlorine is removed from the organic molecule as sodium chloride and practically all of the sulfur remains in organic combination. These facts make it possible to assign a definite structure (I) to vinyl chloride polysulfone.

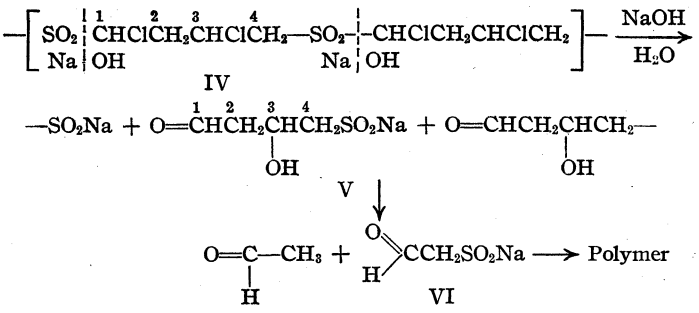
$$-[SO_2CHClCH_2CHClCH_2]_n-$$
I

$$-[SO_2CHClCH_2CH_2CHCl]_n-$$
II

$$-[SO_2CH_2CHClCHClCH_2]_n-$$
III

The three most probable structures for the polymer are those represented by formulas I, II and III in which there are four carbon atoms between the sulfone groups. It is conceivable that vinyl chloride could dimerize to a butylene derivative which then would form a polysulfone. But all of the polysulfones which are derived from olefins are degraded by liquid ammonia and by dilute alkalies to yield cyclic disulfones.[3] Vinyl chloride polysulfone does not show this behavior.

Only structure I can account for the hydrolysis of the polymer to yield acetaldehyde and a sulfur-containing organic residue, according to the following scheme.



The α-halogen sulfone linkage should break readily to yield the aldehyde on carbon 1 (IV and V). The hydrolysis of the chlorine atom on carbon 3 then gives a β-hydroxy aldehyde, which by a retrograde aldol reaction would give acetaldehyde and an aldehydo sulfinic acid (VI) which would be expected to polymerize in the alkaline reaction medium.

A polymer of structure II would be expected to yield succindialdehyde which would polymerize in the alkaline medium and no acetaldehyde could form. A polymer of structure III might hydrolyze to a glycol but the primary sulfone linkage would not break readily under the conditions used in our experiments.

Further experiments on the pyrolysis of vinyl chloride polysulfone in dioxane solution have shown that the reaction is very complex and both hydrogen chloride and sulfur dioxide are lost. No definite polymeric residue seems to be formed. Liquid ammonia removes the chlorine from the polymer forming ammonium chloride and considerable sulfur dioxide is also removed from the polymer. The reaction is not clean cut and definite polymeric products could not be isolated from the reaction mixture.

Experimental

Alkaline Hydrolysis of Vinyl Chloride Polysulfone.—In a 1-liter distilling flask were placed 4.8 g. of powdered vinyl chloride polysulfone and 100 cc. of 20% aqueous sodium hydroxide. A current of steam was passed through this mixture, the distillate was cooled in a long condenser and collected below the surface of a solution containing 1 g. of 2,4-dinitrophenylhydrazine, 10 cc. of concentrated sulfuric acid and 75 cc. of ethanol. After about one hour of steam distillation the distillate was worked up to yield the aldehyde 2,4-dinitrophenylhydrazone. The yield was 0.35 g. (6.2% of the theoretical amount). In another run

(1) This is the tenth communication on polysulfones. For the ninth see, THIS JOURNAL, **60**, 1603 (1938).

(2) Marvel and Glavis, *ibid.*, **60**, 2622 (1938).

(3) Staudinger and Ritzenthaler, *Ber.*, **68**, 455 (1935); Hunt and Marvel, THIS JOURNAL, **57**, 1691 (1935); Glavis, Ryden and Marvel, *ibid.*, **59**, 707 (1937).

2.8 g. of polymer gave 0.2 g. (6.1%) of the 2,4-dinitrophenylhydrazone derivative. The derivative was carefully recrystallized from alcohol and then melted at 160°. Acetaldehyde 2,4-dinitrophenylhydrazone melts at 164.5°[4] and a mixture of an authentic specimen with the derivative isolated from the above hydrolysis melted at 162°.

Anal. Calcd. for $C_8H_8N_4O_4$: C, 42.8; H, 3.57. Found: C, 43.05; H, 3.68.

An authentic specimen of propionaldehyde 2,4-dinitrophenylhydrazone, m. p. 151° (lit. 155°[5]), was mixed with the derivative obtained in the above hydrolysis and the mixture melted at 140–144°.

The alkaline residue remaining in the distilling flask after the steam distillation was filtered to remove aldehyde resin and other insoluble material and analyzed for chloride, sulfite and sulfate. No sulfites were found. Precipitation of the sulfate with barium chloride showed that 3.72–4.22% out of the 16.9% of the sulfur originally present in the polymer had been converted to sulfate. Of the 37.6% of chlorine originally present in the polysulfone, 35.5% was present in this filtrate as chloride ion.

Action of Liquid Ammonia on Vinyl Chloride Polysulfone.—Many experiments were tried adding liquid ammonia to the polymer and vice versa. The liquid ammonia was then allowed to evaporate and the residue treated with water and filtered. Extensive analyses of the water solution and the insoluble part showed that the chlorine was entirely removed from the polymer as ammonium chloride. Considerable sulfur was removed as ammonium sulfite. The remaining polymeric products were not uniform in character and varied over a considerable range in their sulfur content.

Pyrolysis in Dioxane.—When small quantities of vinyl chloride polysulfone were suspended in dioxane and the mixture heated to boiling under a reflux condenser, gas was evolved. This gas consisted of a mixture of hydrogen chloride and sulfur dioxide. No vinyl chloride could be detected among the volatile products. In fact no organic material except dioxane was carried over through the reflux condenser. Analysis of the residual polymeric materials showed that they varied widely in sulfur content.

(4) Strain, THIS JOURNAL, **57**, 758 (1935).
(5) Allen, *ibid.*, **52**, 2955 (1930).

Summary

1. Alkaline hydrolysis of vinyl chloride polysulfone produces acetaldehyde which is evidence that the polymeric unit in this material is —$CHClCH_2CHClCH_2SO_2$—.

2. The polymer does not give a clean-cut reaction with liquid ammonia and pyrolysis causes loss of both hydrogen chloride and sulfur dioxide.

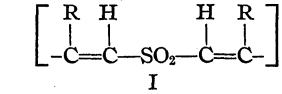
URBANA, ILLINOIS RECEIVED JULY 24, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

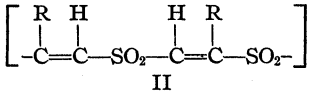
Acetylene Polysulfones. XI.[1] The Compound $C_{10}H_{16}SO_2$ from 1-Pentynepolysulfone and Some Experiments on Other Acetylenepolysulfones

BY C. S. MARVEL AND W. W. WILLIAMS

When acetylenes of the type RC≡CH combine with sulfur dioxide, the polysulfone formed has one remaining double union for each acetylene unit.[2] The arrangement of these units in the polymer may be either that shown in formula I or



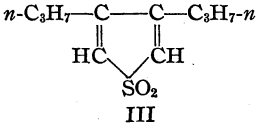
I



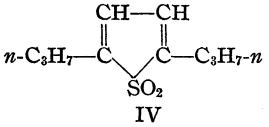
II

that in formula II or the polymer may consist of a random mixture of these units. The present work was undertaken in order to add to our knowledge concerning these compounds.

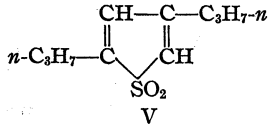
It was found[2] that heating a solution of 1-pentynepolysulfone $(C_5H_8SO_2)_n$ gave a crystalline solid of the composition $C_{10}H_{16}SO_2$ which tentatively was considered to be a di-*n*-propylthiophene sulfone (III, IV or V). This product must



III



IV



V

be formed by the loss of sulfur dioxide from two units of polymer and hence knowledge of its structure would make it possible to assign a definite formula for the polymer.

A more detailed study of the pyrolysis of 1-pentynepolysulfone in dioxane has been made. The reaction proceeds to some equilibrium stage. Isolation of the unchanged polymer and repetition of the pyrolysis in fresh dioxane gives more of the decomposition product. By using this stepwise

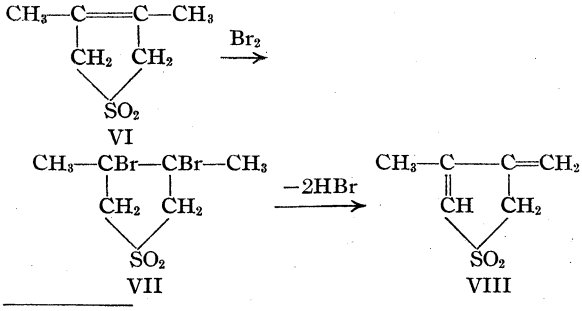
(1) For the tenth communication on polysulfones, see THIS JOURNAL, **61**, 2709 (1939).
(2) Ryden and Marvel, *ibid.*, **58**, 2047 (1936).

procedure it has been possible to increase the yield of the crystalline sulfone to 22% on the basis of the polysulfone which is used up in the process. It has not been possible to obtain other crystalline products from 1-pentynepolysulfone. Neither has it been possible to pyrolyze other acetylene-polysulfones to give a product similar to the $C_{10}H_{16}SO_2$ compound.

Evidence that this crystalline degradation product has an α,β-unsaturated sulfone linkage has been obtained by a study of its addition reactions. Sodiomalonic ester adds readily to give a product of the expected composition.[3] Reduction of the cyclic sulfone with zinc and acetic acid yields a dihydro compound. This reaction must proceed by a 1,4-addition of hydrogen with a resulting shift of the double union to the 3,4-position in the ring (III, IV or V) as otherwise this reduction would be expected to give a tetrahydro compound.

Catalytic reduction of the cyclic sulfone using hydrogen at three atmospheres and a platinum oxide–platinum black catalyst[4] gave another dihydro compound. The catalyst was poisoned rather quickly during this reaction. Since this dihydro compound is isomeric with the one formed by a 1,4-addition of hydrogen, it must be the 1,2-addition product. However, if it is the result of 1,2-addition of hydrogen to one of the structures III, IV or V, the resulting molecule would still be an α,β-unsaturated compound and would be expected to reduce with zinc and acetic acid. This could not be accomplished.

One or the other of these reduction products may be derived from a rearranged form of the cyclic sulfone. Backer and Strating[5] have shown that the cyclic sulfone (VIII) obtained by the addition of sulfur dioxide to 2,3-dimethylbutadiene



followed by bromination and removal of two molecules of hydrogen bromide has only one double bond in the ring.

The sulfone (III, IV or V) obtained by the pyrolysis of 1-pentynepolysulfone might have a similar structure but the fact that Backer and Strating's compound (VIII) adds bromine, whereas our compound does not, seems to cast doubt on this possibility.

The polysulfones derived from acetylenes have an α,β-unsaturated sulfone linkage[6] (I or II) and therefore would be expected to show the characteristics of simpler molecules containing this system.[3] Attempts to add sodiomalonic ester, the Grignard reagent and hydrogen from zinc and acetic acid all resulted in degradation of the polymers without the formation of products which could be characterized.

X-Ray diffraction patterns of the polysulfones from 1-pentyne, 1-hexyne, 1-heptyne, 1-nonyne and 1-pentadecyne have been furnished us by Dr. S. T. Gross. Fibered samples obtained by extruding the hot sample through a conical orifice were used. The patterns were prepared at 5 cm. using radiation from a copper target Phillips metallix diffraction X-ray tube. A nickel filter furnishing approximately monochromatic K-radiation was used. An analysis of the patterns will be reported later by Dr. Gross. It is of interest to note that the patterns are much better defined than any which have been obtained with olefin polysulfones. It is possible that the many asymmet-

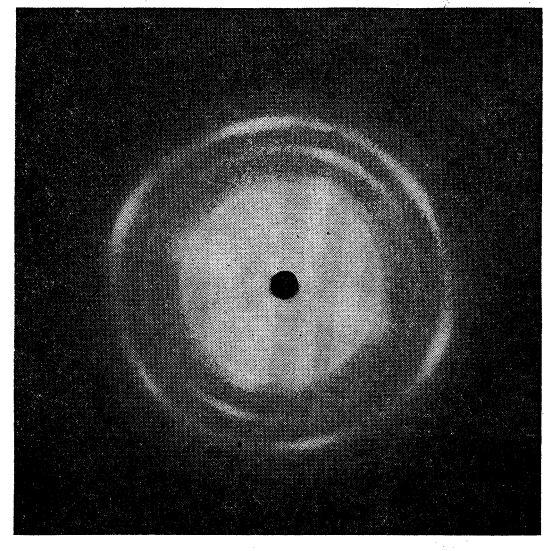


Fig. 1.—Pentyne polysulfone.

(3) Kohler and Potter, THIS JOURNAL, **57**, 1316 (1935), have shown this reaction is characteristic of α,β-unsaturated sulfones.

(4) Adams, Vorhees and Shriner, "Org. Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1932, p. 452.

(5) Backer and Strating, *Rec. trav. chim.*, **53**, 525 (1934); **54**, 170 (1935).

(6) This fact was called to our attention by Dr. H. R. Turner.

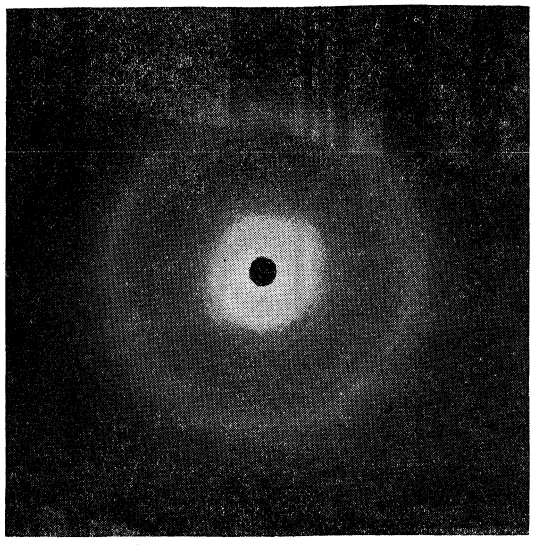


Fig. 2.—Hexyne polysulfone.

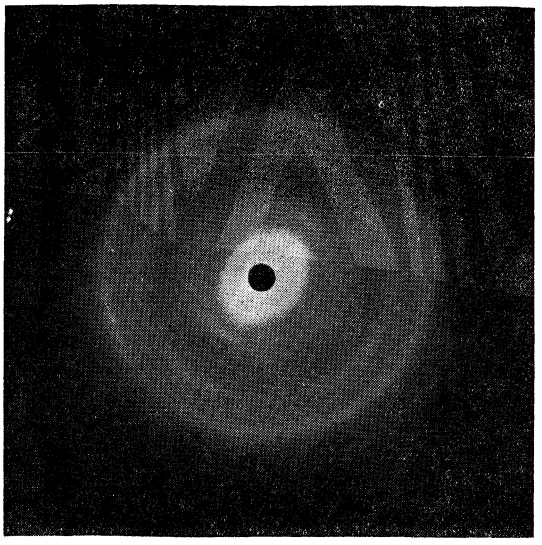


Fig. 4.—Nonyne polysulfone.

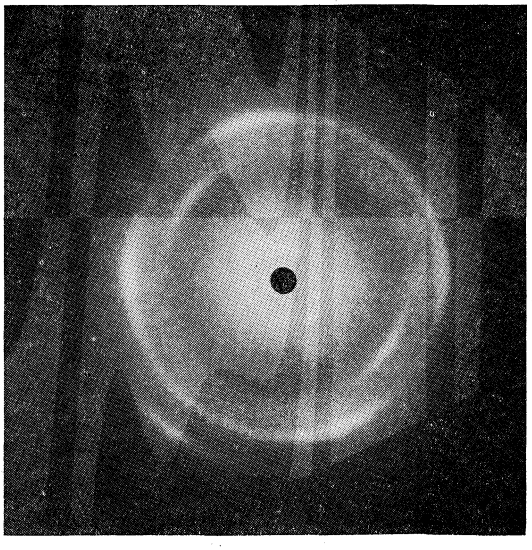


Fig. 3.—Heptyne polysulfone.

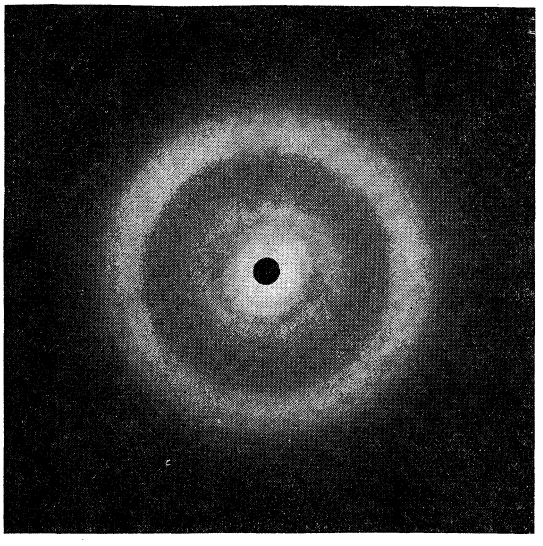


Fig. 5.—Pentadecyne polysulfone.

ric centers in the latter are responsible for their less sharp patterns.

Attempts to prepare a polysulfone from acetylene itself proved futile.

Experimental

Heat Degradation of 1-Pentynepolysulfone.—In general the polymer was decomposed by boiling its dioxane solution as previously described.[2] The yields have been improved and the details of a typical experiment follow.

A solution of 10 g. of 1-pentynepolysulfone in 500 cc. of dioxane was heated under reflux condenser for about fifty hours. The evolution of sulfur dioxide had nearly stopped at this time. The dioxane was removed by boiling under reduced pressure and ether was added to the brownish residue. The ether solution was filtered and the residue again extracted with ether. The ether extracts were combined, washed with 5% sodium hydroxide solution and then with water. The alkaline extract turned orange-red during the extraction. The ether layer was dried over anhydrous sodium sulfate, filtered and most of the ether removed by distillation on a steam cone. The last of the ether was removed in a desiccator under reduced pressure. The brownish residue containing some crystals was allowed to stand for about a day in the refrigerator to permit as much crystallization as would occur. This residue, which resembled apple butter, was spread on a clay plate and allowed to stand about a day. The residual material was scraped off and crystallized from dilute alcohol. Norite was used to remove the color. The material thus obtained amounted to 0.3 to 0.4 g. (3.5–5.3%) of product melting at 88°.

In one run 10 g. of polysulfone in 400 cc. of purified

dioxane was heated under a reflux condenser in a current of nitrogen for about one hundred twenty-five hours. The evolved sulfur dioxide was led into standard alkali and titration showed that 8.5% of the total sulfur dioxide in the polymer came off in this time. Evaporation of the dioxane and extraction of the residue with ether left 6.6 g. of polymer which sulfur analysis showed to be essentially unchanged. The yield of crystalline monosulfone in this run was 0.3 g. (3.48% on total polymer or 11.5% on polymer destroyed).

In another set of experiments 30-g. samples of the polymer in 500 cc. of dioxane were heated for about twenty-four hours, then the unchanged polymer was isolated, put in fresh dioxane and heated again for twenty-four hours. This was repeated until practically no unchanged polymer was left. Only one such experiment is recorded for illustration.

	Heating				
	First	Second	Third	Fourth	Fifth
G. polymer	30	24	18.3	14.0	10.7
Cc. dioxane	500	300	250	200	200
Hours refluxing	24	25	26	25	35
G. polymer lost	6	5.7	4.3	3.3	2.7
G. crystalline $C_{10}H_{16}SO_2$	0.88	0.8	0.71	0.43	0.28
% yield based on polymer used	19.4	18.5	21.8	17.1	13.7

Careful fractional distillation of the dioxane from one of the decomposition experiments showed a low boiling fraction which contained a small amount of 1-pentyne. This was identified as the mercury derivative by means of Johnson and McEwen's reagent.[7] Known 1-pentyne gave a derivative melting at 117–118°, the alkyne from the pyrolysis gave a derivative melting at 116–119°; the mixture of the two melted at 116–119°.

An acidic substance was always present in the dioxane after the heating period but no definite acidic product could be separated.

Reactions of $C_{10}H_{16}SO_2$.—As noted previously[2] the sulfone would not add bromine but did decolorize alkaline potassium permanganate solution.

The addition of sodiomalonic ester was accomplished by treating 0.7 g. of ethyl malonate in about 5 cc. of benzene with sodium until the salt was formed. The excess sodium was removed and 60 cc. of benzene added. To the suspension thus obtained was added 0.44 g. of the sulfone. The reaction mixture was heated for three hours on a steam-bath, cooled, washed with water until the washings were neutral, and the benzene removed. The excess malonic ester was removed by distillation under reduced pressure. When the residue was cooled and dried on a clay plate, 0.56 g. of white crystals remained. Crystallization from alcohol gave a product melting at 104.5–105°.

Anal. Calcd. for $C_{17}H_{28}O_6S$: S, 8.9. Found: S, 8.6.

Attempts to add a second mole of malonic ester to this product were ineffective and the starting material was recovered.

Reduction with zinc and acetic acid was carried out by dissolving 0.41 g. of the sulfone in 50 cc. of glacial acetic acid and boiling the mixture for seven hours with 10 g. of zinc. The hot mixture was then filtered from undissolved zinc, the zinc washed with hot acetic acid, and then the combined acetic acid solutions diluted with water. The solution turned cloudy but no crystals separated. The solvent was then removed through a Widmer column and the residue was dissolved in ether. After removal of the ether the residue was finally induced to crystallize from low-boiling petroleum ether. The product thus obtained melted at 49–50° on a hot-stage microscope. Analysis showed it to be a dihydro derivative of the sulfone.

Anal. Calcd. for $C_{10}H_{18}SO_2$: C, 59.35; H, 8.97. Calcd. for $C_{10}H_{20}SO_2$: C, 58.76; H, 9.87. Found: C, 59.43; H, 9.06.

Catalytic reduction of 2.86 g. of the sulfone in 50 cc. of absolute alcohol with hydrogen in the presence of 0.1 g. of platinum oxide–platinum black[4] in a low pressure reduction apparatus[8] for twenty hours gave a solution with a faint odor of hydrogen sulfide. The platinum catalyst was removed by filtration. The solution was cooled in a dry ice–acetone bath and the solid collected in a filter. The solid thus obtained was twice recrystallized from ether by cooling the solution in a dry ice–acetone bath. This product melted at 56.5–57° on a hot-stage microscope.

Anal. Calcd. for $C_{10}H_{18}SO_2$: C, 59.35; H, 8.97. Found: C, 59.55, 59.43; H, 8.88, 8.90.

A mixture of this compound with the dihydro derivative which melted at 49–50° melted below 44°. This dihydro compound could not be further reduced with zinc and acetic acid.

Attempts to Add Reagents to the Acetylene Polysulfones.—When 5 g. of 1-pentynepolysulfone in 225 cc. of glacial acetic acid was boiled under a reflux condenser with 15 g. of powdered zinc for thirteen hours, some hydrogen sulfide was liberated. After isolating the polymer it was found to have the melting point (200–208°) characteristic of the original 1-pentynepolysulfone.[2] Attempts to reduce 1-nonynepolysulfone with zinc and acetic acid were also unsuccessful. Similarly attempts to reduce dioxane solutions of 1-nonynepolysulfone, propynepolysulfone and 1-pentynepolysulfone with hydrogen in the presence of platinum oxide–platinum black[4,8] were unsuccessful.

The carefully dried polysulfones from 1-pentyne, 1-hexyne, 1-heptyne, 1-nonyne and phenylacetylene dissolved in an ether solution of ethylmagnesium bromide with the evolution of gas and the formation of amber to red colored solutions. Attempts to follow the gas liberation quantitatively gave unreproducible results. Recovery of the polymers from the solution showed that considerable degradation had taken place in this reaction. No evidence for a simple addition was obtained.

Sodiomalonic ester in dry benzene did not add to 1-pentynepolysulfone in the cold and when the mixture was warmed the polymer was degraded.

Attempts to Obtain Acetylene Polysulfone.—Various attempts to bring about the combination of acetylene and sulfur dioxide at atmospheric pressure and under the pressure of a solution of acetylene in acetone and sulfur dioxide were made. Ascaridole was used as a catalyst. Ethyl alcohol was also added to some of the mixtures. In the experiments at atmospheric pressure acetylene was bubbled through the cold reaction mixture. No evidence of polymer formation was ever obtained.

(7) Johnson and McEwen, THIS JOURNAL, 48, 469 (1926).

(8) Adams and Vorhees, ref. 4, p. 53.

Summary

1. The pyrolysis of 1-pentynepolysulfone to yield a crystalline sulfone, $C_{10}H_{16}SO_2$, has been studied further and evidence that the new sulfone has a cyclic unsaturated sulfone structure has been described. No similar products have been obtained from other acetylenepolysulfones by pyrolysis.

2. Attempts to add reagents to the α,β-unsaturated sulfone systems present in the acetylene polysulfones resulted in degradation of the polymers.

3. Some X-ray diffraction patterns of typical acetylenic polysulfones have been recorded.

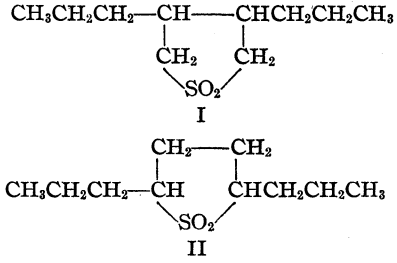
URBANA, ILLINOIS RECEIVED JULY 24, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Polysulfones. XII.[1] The Synthesis of 3,4- and 2,5-Di-*n*-propyltetrahydrothiophene-1,1-dioxides

BY C. S. MARVEL AND W. W. WILLIAMS

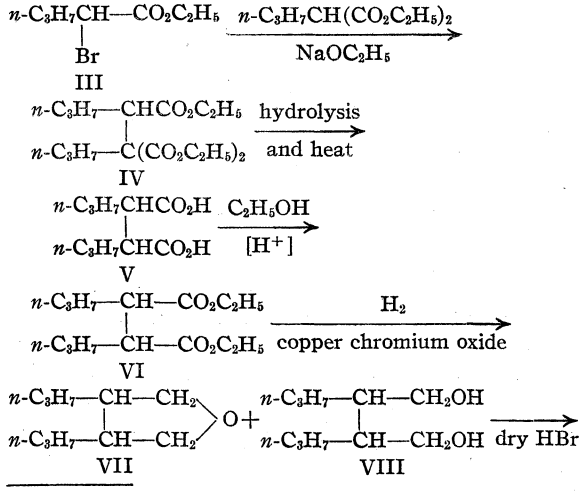
The pyrolysis of 1-pentynepolysulfone in dioxane has yielded a cyclic unsaturated sulfone which is probably a di-*n*-propylthiophene oxide.[2] The positions of the alkyl groups are uncertain as they may be 3,4, 2,5 or 2,4. In order to have available related compounds of known structure, we have now synthesized the 3,4- and the 2,5-di-*n*-propyltetrahydrothiophene-1,1-dioxides (I and II).



I

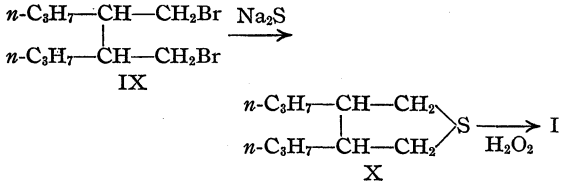
II

The synthesis of the 3,4-di-*n*-propyl derivative (I) has been accomplished by the following reactions.



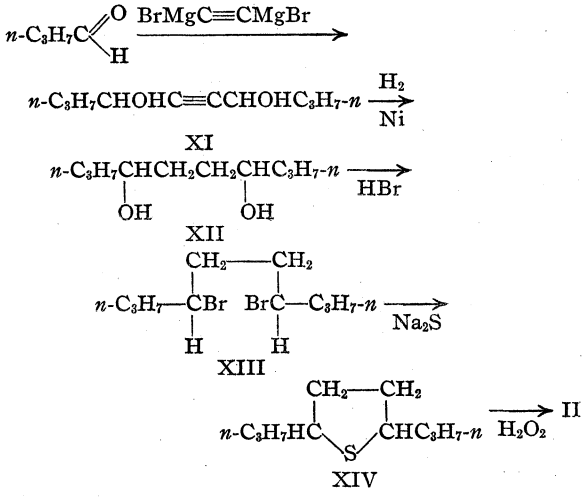
(1) For the eleventh communication on polysulfones, see THIS JOURNAL, **61**, 2710 (1939).

(2) Ryden and Marvel, *ibid.*, **58**, 2047 (1936); see also ref. 1.



The di-*n*-propylsuccinic acid has been prepared previously by Bone and Sprankling[3] from cyanoacetic ester but the procedure described in the experimental part of this communication worked more smoothly for us.

The synthesis of the 2,5-di-*n*-propyl derivative has been accomplished by the following reactions.



4,7-Decanediol has been prepared previously by Bogert and Slocum[4] but the details of their process were not available to us at the time the above synthesis was performed.

2,5-Di-*n*-propyltetrahydrothiophene-1,1-diox-

(3) Bone and Sprankling, *J. Chem. Soc.*, **77**, 654 (1900).

(4) Bogert and Slocum, *Am. Perfumer*, **18**, 621 (1924); *C. A.*, **18**, 1271 (1924).

ide (II) is a liquid. By use of its refractive index and density it is possible to assign a refractive constant of 8.7 to the sulfone group.

Experimental

4,4,5-Tricarboethoxyoctane (IV).—A regular malonic ester synthesis using 469 g. of ethyl *n*-propylmalonate, 500 cc. of dry xylene, 53.4 g. of sodium and 490 g. of ethyl α-bromovalerate and heating for fifteen hours gave 454.4 g. (59%) of a product boiling at 182–183° (1 mm.); d^{20}_{20} 1.0170; $n^{20}D$ 1.4393.

Anal. Calcd. for $C_{17}H_{30}O_6$: C, 61.78; H, 9.16. Found: C, 61.91; H, 8.95.

α,α′-Di-*n*-propylsuccinic Acid (V).—A solution of 405 g. of the above ester in 1250 g. of aqueous 40% potassium hydroxide was refluxed overnight. About 300 cc. of water was distilled from the flask and heating was continued for two days, after which time the solution became nearly homogeneous. A few drops of unsaponified material was removed by ether extraction and then the solution was cooled to 0° and hydrochloric acid was added until the solution was distinctly acid to congo paper. When the solution warmed up to room temperature carbon dioxide was evolved rapidly. The organic acid was extracted with ether and the ether evaporated. There remained a nearly quantitative yield of the mixture of diastereoisomers of the desired acid. Recrystallization of a sample from benzene gave the *cis*-form[3] melting at 115–117°. The *trans*-form never was isolated in an entirely pure form.

Ethyl α,α′-Di-*n*-propylsuccinate (VI).—The mixed isomers of the acid were esterified with ethyl alcohol in the presence of sulfuric acid. The ester was obtained in about 87% yield based on the acid not recovered; b. p. 86–87° (less than 1 mm.); d^{20}_{20} 0.9568; $n^{20}D$ 1.4302.

Anal. Calcd. for $C_{14}H_{26}O_4$: C, 66.58; H, 10.38. Found: C, 65.53; H, 10.22.

Catalytic Reduction of Ethyl α,α′-Di-*n*-propylsuccinate.—The ester was reduced by the general method for ester reduction described by Adkins.[5]

A solution of 70.7 g. of ester in 125 cc. of dioxane was refluxed with a few grams of Raney nickel catalyst for two hours to remove catalyst poisons. The nickel catalyst was removed by filtration and 7.1 g. of copper–chromium oxide catalyst was added. The reaction mixture was placed in a steel bomb under a hydrogen pressure of over 4400 lb. per square inch (300 atm.) at a temperature of 260°. The pressure drop noted in about twenty hours indicated the reduction was complete. The catalyst was removed by filtration and the reaction mixture was fractionally distilled through a Widmer column. The first fraction boiling at 55–63° (1–2 mm.) weighed 23.2 g. (54.2%) and was identified as 3,4-di-*n*-propyltetrahydrofuran (VII). Redistillation gave a product, b. p. 40–42° (less than 1 mm.); d^{20}_{20} 0.8683; $n^{20}D$ 1.4369.

Anal. Calcd. for $C_{10}H_{20}O$: C, 76.84; H, 12.91. Found: C, 76.82; H, 12.92.

After removal of the furan a second fraction boiling at 63–83° (1 mm.) amounting to 26 g. was obtained and a residue weighing 2 g. remained. Redistillation of the residue gave a liquid boiling at 103° (less than 1 mm.); d^{20}_{20} 0.9378; $n^{20}D$ 1.4563. Analysis showed this fraction to be the expected 2,3-di-*n*-propyl-1,4-butanediol (VIII).

Anal. Calcd. for $C_{10}H_{22}O_2$: C, 68.89; H, 12.74. Found: C, 68.76; H, 12.71.

1,4-Dibromo-2,3-di-*n*-propylbutane (IX).—No very satisfactory procedure for obtaining the dibromide was worked out in detail. The furan (44.1 g.) and the glycol (6 g.) obtained as above were heated to 125° for about ten hours with dry hydrogen bromide in glacial acetic acid and the samples of impure bromide were obtained. These crude products were mixed and again heated to 125° for fifteen hours with hydrogen bromide in glacial acetic acid but analysis of the best fractions indicated there was incomplete reaction. Finally the crude material from this treatment was heated to 128–154° for about fifty hours with dry hydrogen bromide slowly bubbling through the mixture. This product was washed with sodium carbonate solution, then water and dried. Redistillation gave 34.2 g. of product boiling at 81–94° (about 1 mm.). The best fraction boiling at 94° (about 1 mm.) had the following properties: d^{20}_{20} 1.3834; $n^{20}D$ 1.4971.

Anal. Calcd. for $C_{10}H_{20}Br_2$: C, 40.00; H, 6.72. Found: C, 40.68; H, 6.88.

3,4-Di-*n*-propyltetrahydrothiophene (X).—In a 200-cc. three-necked flask equipped with a dropping funnel, stirrer, and reflux condenser was placed 125 cc. of an alcoholic solution of sodium sulfide.[6] The alcohol was heated to boiling and the stirrer started. Then 14.7 g. of 1,4-dibromo-2,3-di-*n*-propylbutane in 15 cc. of absolute alcohol was added from the dropping funnel over a period of one hour. Boiling was continued about ten hours and then the cooled reaction mixture was poured into 265 cc. of 25% sodium chloride solution. The organic sulfide was extracted with petroleum ether (b. p. 35–38°), the extract was dried and then distilled. A second run using 15.5 g. of the bromide and other equivalent reagents was made and mixed with the above. From the two runs 13.4 g. (77.5%) of 3,4-di-*n*-propyltetrahydrothiophene was obtained, b. p. 65–66° (1 mm.); d^{20}_{20} 0.9129; $n^{20}D$ 1.4830.

Anal. Calcd. for $C_{10}H_{20}S$: C, 69.68; H, 11.70. Found: C, 69.76; H, 11.73.

3,4-Di-*n*-propyltetrahydrothiophene-1,1-dioxide (I).—To a solution of 11.5 g. of the above tetrahydrothiophene derivative in 25 cc. of glacial acetic acid was added cautiously 35 cc. of 100 volume hydrogen peroxide. The heat developed caused the reaction mixture to boil. The mixture was then heated on a steam-bath for about two hours. Cooling the reaction mixture in the icebox caused some crystals to separate. These were collected on a filter, washed with water and dried at 1 mm. pressure. The yield was 8.75 g. The filtrate and washings were extracted several times with ether and the ether extract dried and concentrated. There remained 3.53 g. of oil which was apparently also cyclic sulfone as no odor of the sulfide remained.

The above solid was examined on a hot-stage microscope and found to consist of irregular scales mixed with

(5) Adkins, "Reactions of Hydrogen with Organic Compounds over Copper–Chromium Oxide and Nickel Catalysts," The University of Wisconsin Press, Madison, Wis., 1937.

(6) Bost and Conn, *Org. Syntheses*, **15**, 72 (1935), John Wiley and Sons, Inc., New York, N. Y., 1935, p. 72.

oily droplets. At 58° it was completely liquid. The solid was purified by dissolving in a little ether and cooling in a dry ice–acetone bath. The glistening white, scale material thus formed melted at 57–59.5° on the hot-stage microscope.

Anal. Calcd. for $C_{10}H_{20}SO_2$: C, 58.77; H, 9.87. Found: C, 58.87; H, 9.80.

5-Decyne-4,7-diol (XI).—To a solution of 1.54 moles of acetylenedimagnesium bromide in ether prepared in the usual manner[7] was added 216.2 g. of *n*-butyraldehyde over a period of one and one-half hours. The mixture was stirred for nearly a day and then poured onto cracked ice, acidified with hydrochloric acid. The ether layer was worked up in the usual manner and 213 g. (41.8%) of a viscous golden oil of b. p. 113–114° (1 mm.) was obtained; d^{20}_4 0.9462; $n^{20}D$ 1.4678.

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66. Found: C, 70.58; H, 10.90.

4,7-Decanediol (XII).—The above acetylenic glycol was divided into two parts for reduction with hydrogen over Raney nickel.[8] In one run 102 g. of glycol, 35 cc. of alcohol and about 5 g. of Raney nickel were placed in the bomb at 25° and 2400 lb. (160 atm.) pressure. The bomb was warmed up to 85° during the reduction. At the end of the reaction the pressure had dropped to 800 lb. (53 atm.). In the other run 111 g. of glycol, 30 cc. of alcohol and about 5 g. of Raney nickel were placed in the bomb at 25° and 4430 lb. (298 atm.) pressure. This run was not heated but the reaction mixture warmed to 75° from the heat of reaction. At the end of the reduction the pressure had dropped to 750 lb. (30 atm.). The two reduction mixtures were united, filtered to remove catalyst and distilled. The portions boiling at 110–112° (1 mm.) solidified in the receiver. The yield was 164 g. (71%). The glycol was recrystallized from petroleum ether (b. p. 65–110°) and then melted at 79–80° on a hot-stage microscope.

Anal. Calcd. for $C_{10}H_{22}O_2$: C, 68.89; H, 12.74. Found: C, 68.94; H, 12.75.

(7) Du Pont, *Ann. chim.*, [8] **30**, 485 (1913); Blomquist and Marvel, THIS JOURNAL, **55**, 1655 (1933).

(8) Covert and Adkins, *ibid.*, **54**, 4116 (1932).

4,7-Dibromodecane (XIII).—Dry hydrogen bromide was passed through the glycol for four hours at 45–60° and then for eighteen hours at 105–115°. The bromide was then distilled. From 112.6 g. of glycol there was obtained 165 g. (85.3%) of bromide, b. p. 106–109° (1 mm.); d^{20}_4 1.3354; $n^{20}D$ 1.4920.

Anal. Calcd. for $C_{10}H_{20}Br_2$: C, 40.00; H, 6.72; Br, 53.28. Found: C, 40.44; H, 6.77; Br, 52.90.

2,5-Di-*n*-propyltetrahydrothiophene (XIV).—Using the same procedure described for the previous cyclic sulfide, 120 g. of 4,7-dibromodecane gave 52.8 g. (77%) of the desired 2,5-di-*n*-propyltetrahydrothiophene, b. p. 74–75° (1 mm.); d^{20}_4 0.8958; $n^{20}D$ 1.4795.

Anal. Calcd. for $C_{10}H_{20}S$: C, 69.68; H, 11.70. Found: C, 69.61; H, 11.65.

2,5-Di-*n*-propyltetrahydrothiophene-1,1-dioxide (II).—The sulfide was oxidized in the same manner described for its isomer. The yield from 33 g. of sulfide was 38 g. of sulfone, b. p. 123–125° (1 mm.); d^{20}_4 1.0408; $n^{20}D$ 1.4719.

Anal. Calcd. for $C_{10}H_{20}SO_2$: C, 58.77; H, 9.87. Found: C, 58.90; H, 9.95.

Using the Eisenlohr values[9] 2.42 for each carbon atom and 1.1 for each hydrogen atom the refractive constant for the $—SO_2—$ group in the above sulfone is calculated as 8.7.

Summary

1. 3,4-Di-*n*-propyltetrahydrothiophene-1,1-dioxide and 2,5-di-*n*-propyltetrahydrothiophene-1,1-dioxide have been synthesized and many intermediates in these syntheses have been characterized.

2. Since 2,5-di-*n*-propyltetrahydrothiophene-1,1-dioxide is a liquid it has been possible to calculate a refractive constant of 8.7 for the sulfone group in this compound.

(9) Cohen, "Organic Chemistry," Edward Arnold, London, 1921, Vol. II, pp. 17–40.

URBANA, ILLINOIS RECEIVED JULY 24, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Saponins and Sapogenins. XIII. The Precipitability of Steroid Sapogenins by Digitonin

BY C. R. NOLLER

Marker and Rohrmann[1] have reported that chlorogenin is precipitated by digitonin, a finding contrary to our previously published experience.[2] They added to a boiling solution of 100 mg. of chlorogenin in 10 cc. of 95% alcohol, a hot solution of 600 mg. of digitonin in 20 cc. of 90% alcohol. We have repeated their experiment and have found that about half of the chlorogenin is indeed precipitated. However, assuming the addition complex to be a 1:1 molecular compound and digitonin to have the formula $C_{56}H_{92}O_{29}$, a 110% excess of digitonin was used and the concentrations were such that the solubility of digitonin at room temperature was exceeded greatly. Thus if 600 mg. of digitonin is dissolved in a hot solution of 10 cc. of 95% alcohol and 20 cc. of 90% alcohol and the solution cooled and inoculated with a trace of digitonin, 455 mg. will crystallize out on standing at room temperature. It is conceivable that this heavy precipitation would bring down a considerable quantity of chlorogenin along with it. In the usual procedure for the preparation of digitonides, one adds a solution of the compound being tested to an equal volume of a 1% solution of digitonin (1 g. in 100 cc. of 90% alcohol) so that there is no danger of digitonin crystallizing since the solubility of digitonin at room temperature is approximately 0.5 g. per 100 cc. of 90% alcohol. Under these conditions chlorogenin does not precipitate.

In view of the extensive use of the test it seemed desirable to attempt to establish a more definite criterion of compound formation with digitonin. The relative solubility of the compound and its components is the only property that can be used conveniently in this series and it would seem that to show compound formation it is necessary to show that the solubility of the digitonide is less than that of either of its components. If a solution of cholesterol or of β-cholestanol in 90% alcohol, saturated at room temperature, is mixed with an equal volume of a saturated solution of digitonin in the same solvent, a precipitate forms almost immediately. Under the same conditions tigogenin yields a precipitate after about twenty minutes, gitogenin after fifteen hours, while sarsasapogenin, chlorogenin, *epi*-coprosterol and *epi*-dihydrocholesterol give no precipitate after standing for five days. If, however, the solutions of the last four compounds are concentrated to half volume to bring the concentration of the compound and of digitonin to that of saturated solutions, all except *epi*-coprosterol give some precipitate after standing for five hours. It is seen therefore that neither condition gives a satisfactory test since before concentration sarsasapogenin, which is known to give a less soluble digitonide than its epimer,[3] did not precipitate whereas after concentration *epi*-dihydrocholesterol, which has the α-configuration, also was precipitated.

One obvious inaccuracy in the use of saturated solutions of the compounds for qualitative tests is that the solubility, and hence the concentration, is different for each compound. A semi-quantitative approach to the problem was made as follows. Five cubic centimeters of a saturated solution of the compound was evaporated to dryness and the residue weighed. This residue was then dissolved by warming with 5 cc. of a saturated solution of digitonin, tightly stoppered and allowed to stand overnight. The precipitate that had formed was filtered the next morning by suction through tared funnels, dried at 80° and weighed. If no precipitate had formed, which was the case with *epi*-dihydrocholesterol, sarsasapogenin and chlorogenin the solutions were inoculated with traces of precipitates that had been formed previously in more concentrated solutions, and allowed to stand for another twenty-four hours and the precipitates filtered. The filtrates were returned to the flasks and allowed to stand an additional three days to be certain that no more precipitate formed. In the case of those compounds that precipitated on mixing 5 cc. of a saturated solution with 5 cc. of digitonin solution, these precipitates after standing overnight were filtered and weighed. Assuming a molecular ratio of 1:1 and a molecular weight for digitonin

(1) Marker and Rohrmann, THIS JOURNAL, **61**, 946 (1939).
(2) Noller and McMillan, *ibid.*, **59**, 1092 (1937).
(3) Askew, Farmer and Kon, *J. Chem. Soc.*, 1399 (1936).

TABLE I

SOLUBILITY PRODUCTS OF STEROID DIGITONIDES

Compound[a]	Soly.[b] in 90% ethyl alcohol, g. per 5 cc.	Digitonide[b] pptd., g.	Compd. pptd., g.	Digitonin pptd., g.	Concn. of compd. in soln., g. per l.	Concn. of digitonin in soln., g. per l.	Soly. prod., mole per l.	Concn. product on mixing equal volumes of satd. solns., mole per l.
Cholesterol	0.0412	0.0285	0.0068	0.0217	3.44		Small	
β-Cholestanol	.0174	.0302	.0072	.0230	1.02		Small	
Tigogenin	.0051	.0165	.0042	.0123	0.09	0.90	1.6×10^{-7}	2.1×10^{-6}
Gitogenin	.0181	.0220	.0057	.0163	2.48	1.00	4.7×10^{-6}	7.2×10^{-6}
epi-Dihydrocholesterol	.0120	.0119	.0029	.0090	1.82	2.46	9.4×10^{-6}	5.3×10^{-6}
Sarsasapogenin	.0170	.0158	.0040	.0118	2.60	1.90	9.7×10^{-6}	7.1×10^{-6}
Chlorogenin	.0404	.0135	.0035	.0100	7.38	2.26	3.1×10^{-5}	1.6×10^{-5}
epi-Coprosterol	.0524	None					Large	
Digitonin	.0213							

[a] For the pure samples of β-cholestanol, m. p. 143–145°, *epi*-dihydrocholesterol, m. p. 185–186°, and *epi*-coprosterol, m. p. 111°, all of which had been purified by means of digitonin, we are indebted to Dr. R. Schoenheimer, for sarsasapogenin, m. p. 192–194°, to Dr. L. F. Fieser, and for gitogenin, m. p. 270–274°, to Dr. W. A. Jacobs. The tigogenin, m. p. 202–207°, and chlorogenin, m. p. 273–276°, were isolated from *Chlorogalum pomeridianum*. [b] For the first three compounds the temperature of the solubility determinations was 23 ± 0.5° and the volume of the mixed solutions 10 cc. For the last five compounds the solubility determinations were made at 25 ± 0.5° and the volume of the mixed solutions was 5 cc.

of 1228, the weight of compound and of digitonin precipitated could be calculated and these values subtracted from the weights originally present gave the amounts of compound and of digitonin remaining in solution. From these data approximate solubility products for the digitonides could be calculated. The results are given in the table.

The solubility products are approximate only since they have been calculated from a single pair of concentrations in each case and no attempt was made to make the determinations more than roughly quantitative. The precipitates were not washed because of their known high solubility; hence they include the material dissolved in the adherent mother liquors. This may be partly compensated by the difficulty of quantitative transfer of the precipitates to the funnels. Where a second filtration was necessary, as in the case of chlorogenin, the weight of precipitate may be too high because of evaporation of the solvent during the first suction filtration, although such evaporation was held to a minimum. It is believed from several duplicate determinations that the error may be of the order of 5 to 10%. That the values are fairly accurate is indicated by the last column of the table which gives the products of the concentrations on mixing equal volumes of saturated solutions of the compounds and of digitonin. In the case of tigogenin and gitogenin these products exceed the solubility product and it is known that these compounds give precipitates under these conditions, whereas the concentration products are less than the solubility products in the case of *epi*-dihydrocholesterol, sarsasapogenin and chlorogenin.

The table shows clearly that tigogenin forms a stable digitonide as previously reported[4] although its precipitation can hardly be called "almost quantitative." Gitogenin, which has been reported as being not precipitated by digitonin,[4] forms a less soluble digitonide than sarsasapogenin whose epimer gives a more soluble digitonide.[3] Hence until the epimers of gitogenin have been prepared and their properties studied, gitogenin should be considered as being precipitable by digitonin. Chlorogenin digitonide on the other hand is considerably more soluble than sarsasapogenin digitonide, and hence tentatively should be considered as belonging to the group not precipitated by digitonin. The necessity of comparing pairs of epimers is shown clearly by the case of *epi*-dihydrocholesterol, which gives a digitonide having a solubility product the same as that of sarsasapogenin, yet they must be considered as belonging to two different stereochemical groups.

Precipitability by digitonin long has been considered to be specific for steroids having an hydroxyl group at C-3 with the same stereochemical configuration as that present in cholesterol.[5] In recent years it has been shown that not only are some compounds which lack this hydroxyl group precipitated by digitonin,[6] but that others con-

(4) Tschesche and Hagedorn, *Ber.*, **68**, 2247 (1935).

(5) Fieser, "Chemistry of Natural Products Related to Phenanthrene," Reinhold Pub. Corp., New York, N. Y., 1937, p. 118.

(6) Butenandt and Mamoli, *Ber.*, **68**, 1847 (1935); Wintersteiner, THIS JOURNAL, **59**, 765 (1937).

taining a C-3 hydroxyl group of the proper configuration are not precipitated by digitonin.[4,7] It thus may even be questionable whether precipitation by digitonin has the same significance for the steroid sapogenins as for the sterols.

Summary

1. The solubility of the digitonides of steroid sapogenins varies considerably and is much greater than that of the digitonides of cholesterol and β-cholestanol. Thus the solubility product of the digitonide of sarsasapogenin, which is known to be the less soluble of two epimeric forms, is practically the same as that of the digitonide of *epi*-dihydrocholesterol, which ordinarily is considered as not precipitable by digitonin.

2. Gitogenin digitonide has a smaller solubility product than sarsasapogenin digitonide and hence gitogenin provisionally must be considered as being the epimer that is precipitated by digitonin.

3. The digitonide of chlorogenin has a much larger solubility product than that of sarsasapogenin and until its epimer is prepared and shown to give a more soluble digitonide, chlorogenin must be considered as the isomer not precipitable by digitonin.

4. It has been shown that the solubility products of steroid digitonides vary so widely that qualitative tests for precipitation are without meaning unless the behavior of both isomers can be compared.

(7) Dimroth, *Ber.*, **69**, 1123 (1936); Reichstein and Gätzi, *Helv. Chim. Acta*, **21**, 1185 (1938).

CONVERSE MEMORIAL LABORATORY
HARVARD UNIVERSITY
CAMBRIDGE, MASSACHUSETTS RECEIVED MAY 8, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. LXXI. Urane Derivatives

BY RUSSELL E. MARKER AND EWALD ROHRMANN

In papers XXIX[1] and XXXVII[2] of this series the isolation from mares' pregnancy urine of uranetriol and uranediol was described. These substances were shown to possess hydroxyl groups at C-11 and both compounds were converted to the same parent hydrocarbon, urane (I), which is believed to differ from pregnane in the configuration at C-9.

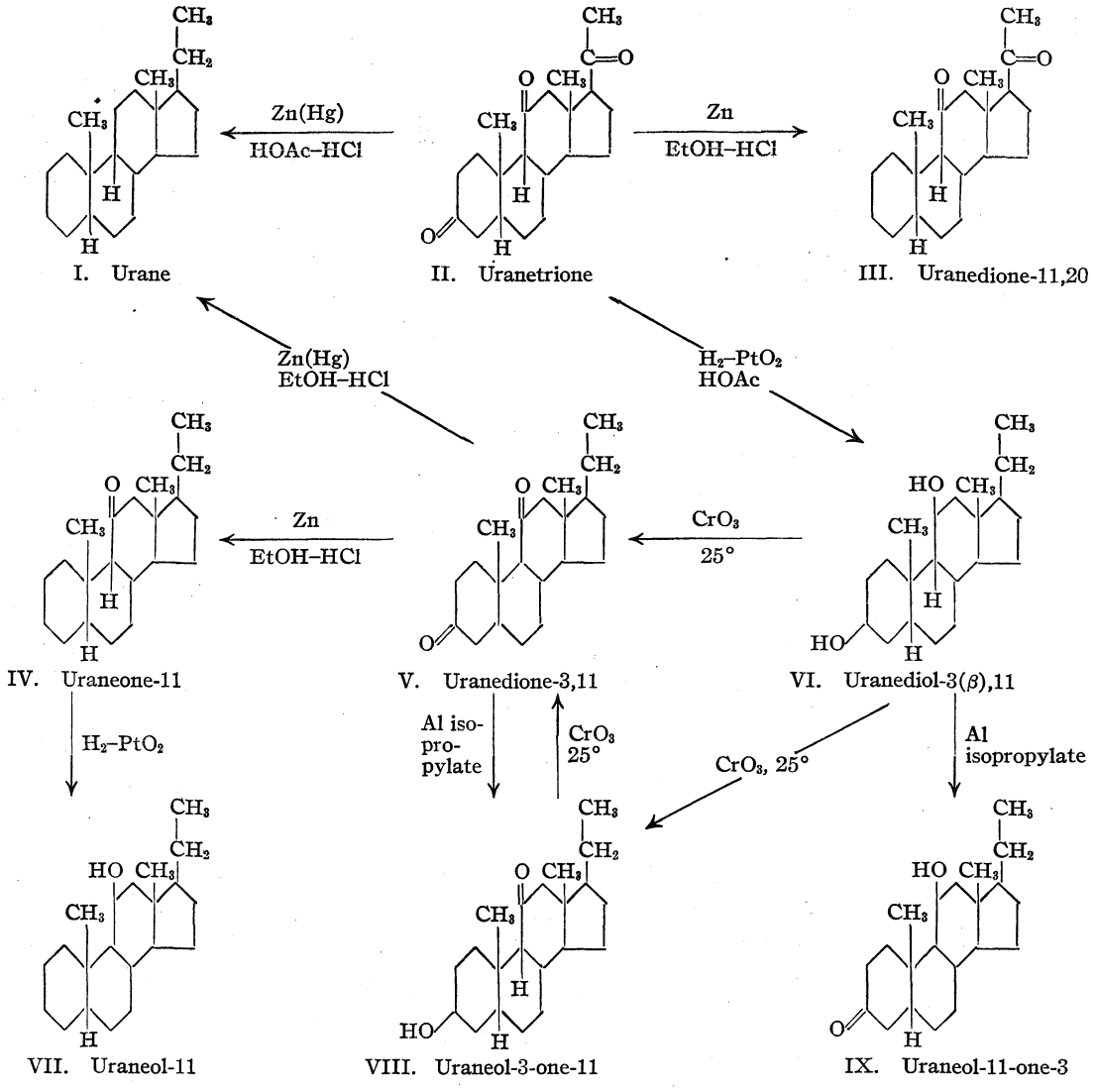
In spite of the close relationship[1,2,3] existing between uranetriol and uranediol, they nevertheless show some unusual and striking differences. We have pointed out previously the fact that on the basis of precipitability with digitonin uranetriol is a 3-α while uranediol is a 3-β compound. There is also a pronounced difference in the reaction of bromouranetrione and bromouranedione with pyridine, the former yielding urenetrione directly while the latter gives largely pyridinium salt which yields urenedione upon destructive distillation. The fact that on the debromination of bromouranedione only one product was obtained suggests that the bromine occupied the C-4 position. Although it appears that the double bond in urenetrione and urenedione may be in the 4,5-position, no definite proof of this point has as yet been obtained.

In the catalytic hydrogenation of uranedione-3,11 (V) the carbonyl group at C-3 is much more easily reduced than that at C-11 and consequently the preparation of uraneol-3(β)-one-11 (VIII) is possible. There was no noticeable *epi* fraction obtained in this reduction. The same product was formed by the reduction of uranedione with aluminum isopropylate. Oxidation of the product with an excess of chromic anhydride gave uranedione.

Uranediol on partial oxidation with chromic anhydride yielded some uraneol-3(β)-one-11 (VIII) in addition to uranedione. No uraneol-11-one-3 was isolated from the oxidation. In the oxidation of uranediol with aluminum isopropylate, however, the oxidation proceeds readily at C-3 and the only ketonic product obtained was uraneol-11-one-3 (IX). This product formed a monoacetate and a monosemicarbazone.

By the Clemmensen reduction of uranedione-3,11 with unamalgamated zinc in ethanol solution, an almost quantitative yield of uraneone-11 (IV) was obtained. This product formed no semicarbazone, but on catalytic hydrogenation yielded uraneol-11 (VII) which formed a monoace-

(1) Marker, Kamm, Oakwood, Wittle and Lawson, THIS JOURNAL, **60**, 1061 (1938).
(2) Marker, Rohrmann and Wittle, *ibid.*, **60**, 1561 (1938).
(3) Marker, Wittle and Oakwood, *ibid.*, **60**, 1567 (1938).



tate. When the Clemmensen reduction was carried out with amalgamated zinc, the main product of the reaction was the hydrocarbon, urane (I).

The Clemmensen reduction of uranetrione (II) with unamalgamated zinc in ethanol solution yielded a diketone which is undoubtedly uranedione-11,20 (III).

This investigation was supported by a grant from the Committee for Research in Problems of Sex, National Research Council. We wish to thank Parke, Davis and Company for the mares pregnancy urine extracts from which the uranediol and uranetriol were isolated.

Experimental Part

Bromouranedione-3,11.—To a solution of 2 g. of uranedione in 40 cc. of acetic acid acidified with 3 drops of 48% hydrobromic acid was added 6.3 cc. of 1.05 *M* bromine in acetic acid. White crystals separated toward the end of the reaction. The reaction mixture was diluted carefully with water and the crystalline solid collected, washed and crystallized from ether to give compact white crystals, m. p. 202–203° dec.

Anal. Calcd. for $C_{21}H_{31}O_2Br$: C, 63.8; H, 7.9. Found: C, 63.4; H, 7.8.

Reaction of Bromouranedione-3,11 with Pyridine.—A mixture of 1.7 g. of bromouranedione-3,11 and 45 cc. of dry pyridine was refluxed for three and one-half hours. Small white plates separated shortly after refluxing was started. These were collected, washed with pyridine and ethanol and dried. The product did not melt below 300°; yield 1.5 g.

Anal. Calcd. for $C_{26}H_{36}O_2$: C, 65.8; H, 7.65. Found: C, 66.1; H, 7.7.

Decomposition of Pyridinium Salt of Bromouranedione-3,11.—The pyridinium salt (1.4 g.) was placed in a glass retort and heated at 5–10 mm. pressure until no more material distilled over. The reaction product was sub-

limed in high vacuum at 90–110°. The sublimate was taken up in ether and the pyridine salts removed by washing with dilute hydrochloric acid and water. The ether was evaporated and the product crystallized from aqueous acetone as white needles, m. p. 168–170°.

Anal. Calcd. for $C_{21}H_{30}O_2$: C, 80.2; H, 9.6. Found: C, 80.5; H, 9.6.

Uraneol-3(β)-one-11 from Uranedione-3,11. (a) **By Aluminum Isopropylate Reduction.**—A mixture of 700 mg. of uranedione, 1.5 g. of aluminum isopropylate (aged, powder) and 50 cc. of isopropyl alcohol was refluxed for fifteen hours. The solvent was distilled off over a period of one hour. The residue was shaken with dilute hydrochloric acid and extracted with ether. The ether was evaporated and the residue dissolved in 20 cc. of hot 95% ethanol and precipitated with a solution of 1 g. of digitonin and 60 cc. of 85% ethanol. A white precipitate separated at once. After standing for two hours this was collected, washed with ethanol, dried and decomposed with pyridine. The product was crystallized from acetone as compact white crystals, m. p. 205–207°. The product gave a 25° depression with uranediol-3(β),11.

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.2; H, 10.8. Found: C, 79.5; H, 11.0.

When refluxed for twenty minutes with acetic anhydride, the product gave an **acetate** which crystallized from aqueous acetone as white needles, m. p. 170.5–172°.

Anal. Calcd. for $C_{23}H_{36}O_3$: C, 76.6; H, 10.1. Found: C, 76.8; H, 10.3.

The *epi* fraction could not be separated readily from unchanged uranedione.

(b) **By Catalytic Hydrogenation.**—A mixture of 400 mg. of uranedione, 300 mg. of Adams catalyst and 120 cc. of absolute ethanol was shaken with hydrogen at 25° and 3 atmospheres pressure for two hours. The mixture was filtered and the filtrate evaporated to a volume of 75 cc. To this hot solution a solution of 1 g. of digitonin in 50 cc. of 95% ethanol was added and the mixture allowed to stand for twelve hours. The digitonide was filtered, washed, dried and decomposed with pyridine. The ether soluble material was crystallized from methanol as white crystals, m. p. 205–208°. This gave no depression with the product obtained by the aluminum isopropylate reduction of uranedione.

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.2; H, 10.8. Found: C, 79.2; H, 10.9.

Oxidation of the diol with chromic anhydride in acetic acid at 25° for one hour yielded a product which crystallized from aqueous acetone as white plates, m. p. 174–177°. This gave no depression with a sample of uranedione, m. p. 175–177°.

The *epi* fraction from the hydrogenation was negligible and was not investigated further.

Uraneol-3-one-11 by Oxidation of Uranediol.—About 5 g. of impure uranediol-3(β),11 obtained from mares pregnancy urine was oxidized in acetic acid at room temperature with 1.5 g. of chromic anhydride. The oxidation mixture which would not crystallize readily was adsorbed in a tower of alumina from benzene–ligroin solution and eluted with benzene. The product was crystallized from ethyl acetate and acetone to give compact white crystals, m. p. 207–209°. This gave no depression with previously prepared samples.

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.2; H, 10.8. Found: C, 79.4, 79.2; H, 10.9, 10.7.

The product was recovered unchanged upon treatment with semicarbazide acetate under the usual conditions.

On refluxing with acetic anhydride the product gave an **acetate** which crystallized from aqueous acetone as white crystals, m. p. 170°. This gave no depression with the acetate of uraneol-3(β)-one-11.

Anal. Calcd. for $C_{23}H_{36}O_3$: C, 76.6; H, 10.1. Found: C, 76.6; H, 10.1.

Uraneol-11-one-3.—A mixture of 1 g. of uranediol, 2 g. of aluminum isopropylate, 15 cc. of cyclohexanone and 50 cc. of dry toluene was refluxed for ten hours. The mixture was cooled, diluted with ether, washed with water and the solvent distilled with steam. The residual oil was treated with 2 g. of Girard's reagent to give approximately 250 mg. of crude ketones. The product was crystallized from ether–pentane as fine white needles, m. p. 169.5–171°.

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.2; H, 10.8. Found: C, 79.1; H, 10.9.

When refluxed for thirty minutes with an excess of acetic anhydride the product gave an **acetate** which crystallized from aqueous acetone as small white plates, m. p. 195–197°.

Anal. Calcd. for $C_{23}H_{36}O_3$: C, 76.6; H, 10.1. Found: C, 76.8; H, 10.1.

When treated with semicarbazide acetate in boiling 80% ethanol for one hour the product yielded a **semicarbazone** which crystallized from dilute ethanol as small white crystals, m. p. 251–253° dec.

Anal. Calcd. for $C_{22}H_{37}O_2N_3$: C, 70.3; H, 9.9. Found: C, 70.5; H, 10.0.

Uraneone-11.—To a boiling mixture of 600 mg. of uranedione-3,11, 60 cc. of 95% ethanol and 10 g. of 20-mesh zinc was added 8 cc. of concentrated hydrochloric acid over a period of three hours. The solution was decanted into water and the mixture extracted with ether. Evaporation of the ether gave a product which crystallized from acetone as white needles, m. p. 135–136.5°, yield 500 mg.

Anal. Calcd. for $C_{21}H_{34}O$: C, 83.4; H, 11.3. Found: C, 83.5; H, 11.5.

The product was recovered unchanged after treatment with semicarbazide acetate for one hour.

Hydrogenation of Uraneone-11.—A mixture of 275 mg. of uraneone-11, 120 cc. of acetic acid and 500 mg. of Adams catalyst was shaken with hydrogen at 3 atmospheres pressure, at 25° for seven hours. The mixture was filtered and the reduction product sublimed in high vacuum at 80–100°. The sublimate was crystallized repeatedly from methanol to give white crystals which melted poorly at 110°.

Anal. Calcd. for $C_{21}H_{36}O$: C, 82.8; H, 11.9. Found: C, 82.5; H, 12.0.

With boiling acetic anhydride the product yielded an **acetate** which crystallized from aqueous acetone as fine white needles, m. p. 140–142°.

Anal. Calcd. for $C_{23}H_{38}O$: C, 79.7; H, 11.1. Found: C, 80.0; H, 11.1.

Uranedione-11,20.—Uranetrione (600 mg.) was reduced by the Clemmensen method as described for uranedione-3,11. After sublimation in high vacuum, the product was crystallized from ether–pentane as white needles, m. p. 199–201°.

Anal. Calcd. for $C_{21}H_{32}O_2$: C, 79.7; H, 10.2. Found: C, 80.0; H, 10.2.

Summary

The following reactions of urane derivatives have been observed:

1. Uranedione on partial oxidation with chromic anhydride yielded uraneol-3(β)-one-11. Uranediol on oxidation with aluminum isopropylate gave uraneol-11-one-3.

2. Mild catalytic hydrogenation of uranedione-3,11 gave uraneol-3(β)-one-11. Similar results were obtained on mild reduction with aluminum isopropylate.

3. Mild Clemmensen reduction of uranedione-3,11 gave uranone-11. Vigorous reduction gave urane. Mild Clemmensen reduction of uranetrione gave uranedione-11,20.

4. Urenedione has been prepared from bromouranedione.

STATE COLLEGE, PENNA. RECEIVED JULY 5, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

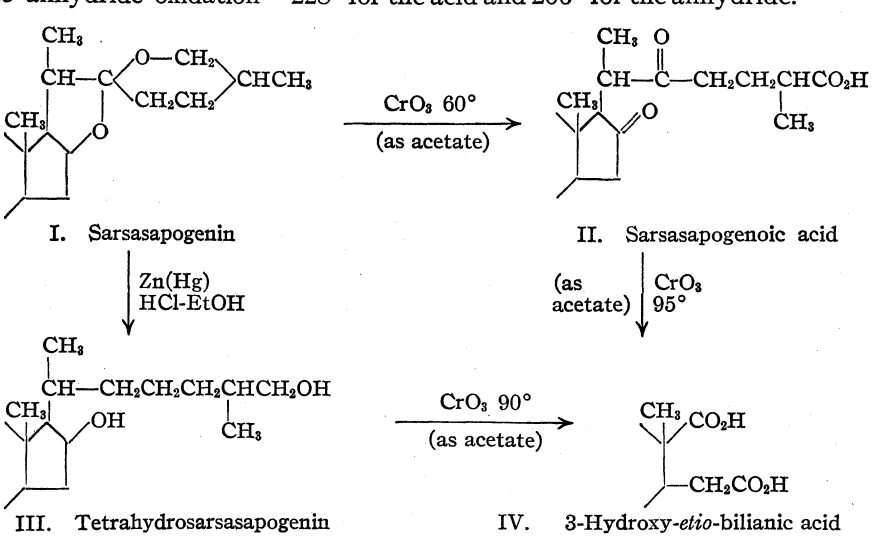
Sterols. LXXII. Oxidation Products of Sarsasapogenin. C_{19} Dibasic Acid

BY RUSSELL E. MARKER AND EWALD ROHRMANN

The fact that sarsasapogenin contains a substituent at C-16 and has by indirect methods been degraded to *etio*-bilianic acid[1] suggests that 3-hydroxy-*etio*-bilianic acid might be expected among the acidic products obtained by the direct oxidation of sarsasapogenin acetate with chromic anhydride.

In extending our investigation of the acidic products from the chromic anhydride oxidation of sarsasapogenin acetate (conducted at 85°), we have isolated from the hydrolyzed acidic fraction in addition to the C_{22} keto acid previously reported[2] a dibasic hydroxy acid of the composition $C_{19}H_{30}O_5$. The acid gives a dimethyl ester with diazomethane. The resulting dimethyl ester was characterized further by the formation of an acetate. Treatment of the acid with acetic anhydride either by refluxing or by the pyridine method resulted in the formation of an acetate anhydride of the composition $C_{21}H_{30}O_5$ which upon alkaline hydrolysis yielded the original acid.

Mild oxidation of the acid followed by Clemmensen reduction yielded a desoxy acid of the composition $C_{19}H_{30}O_4$, m. p. 232°. With acetic anhydride the desoxy acid yielded an anhydride, m. p. 207°. Although no direct comparison was made, the desoxy acid is very probably identical with *etio*-bilianic acid first reported by Wieland[3] and co-workers, who reported a melting point of 228° for the acid and 206° for the anhydride.



I. Sarsasapogenin

II. Sarsasapogenoic acid

III. Tetrahydrosarsasapogenin

IV. 3-Hydroxy-*etio*-bilianic acid

The same hydroxy dibasic acid was obtained in almost 12% yield by the oxidation of sarsasapogenoic acid acetate at 90–95° with chromic anhydride. A similar oxidation of the product ob-

(1) Farmer and Kon, *J. Chem. Soc.*, 414 (1937).

(2) Marker and Rohrmann, THIS JOURNAL, **61**, 1285 (1939).

(3) Wieland, Schlichting and Jacobi, *Z. physiol. Chem.*, **161**, 80 (1926).

tained by the acetylation of tetrahydrosarsasapogenin in pyridine in the cold gave only a poor yield of the dibasic acid. This is in accordance with our recently suggested structure for the tetrahydro compound[4] (III). Such a substance would not be expected to yield readily an easily oxidizable intermediate β-diketone or β-keto acid such as would be formed from our suggested formulation of sarsasapogenoic acid[5] (II).

The fact that sarsasapogenoic acid is oxidized easily to the dibasic acid suggests that it is an intermediate in the oxidation of sarsasapogenin to the bilianic acid.

The recent work of Litvan and Robinson[6] on the conversion of estric acid the dibasic acid from estrone analogous to *etio*-bilianic acid, to estrone suggests a very interesting possible method of converting 3-hydroxy-*etio*-bilianic acid to testosterone.

We wish to thank Parke, Davis and Company for their generous help and assistance in the various phases of this work.

Experimental Part

C_{19} Dibasic Acid. (a) **From Sarsasapogenin Acetate.**—The hydrolyzed acidic fraction obtained from the oxidation of sarsasapogenin acetate with twice its weight of chromic anhydride at 85° was taken up in ether and allowed to stand for several days. The C_{22} keto acid which separated was collected and the filtrate evaporated to a sirup. Upon dilution of the sirup with chloroform, white crystals separated. These were collected, washed with chloroform and crystallized from acetone–chloroform to give a product, m. p. 220–222°.

Anal. Calcd. for $C_{19}H_{30}O_5$: C, 67.4; H, 8.9; neut. equiv., 169. Found: C, 67.2; H, 9.0; neut. equiv., 175.

(b) **From Sarsasapogenoic Acid Acetate.**—The acidic fraction obtained by the chromic anhydride oxidation of sarsasapogenoic acid acetate (3.3 g.) at 90–95° after being freed from most of the C_{22} keto acid was crystallized from chloroform to give 300 mg. of compact white crystals, m. p. 219–222°. This gave no depression with the above sample.

Anal. Calcd. for $C_{19}H_{30}O_5$: C, 67.4; H, 8.9. Found: C, 67.4; H, 9.1.

(c) **From Tetrahydrosarsasapogenin.**—Tetrahydrosarsasapogenin (3 g.) was acetylated with acetic anhydride in pyridine for twenty hours at room temperature. The sirupy product was dissolved in 100 cc. of acetic acid and to this solution heated at 90–95° was added 8 g. of chromic anhydride in 60 cc. of 80% acetic acid over a period of one hour. The mixture was heated for an additional two hours at 95° and the products separated into neutral and acidic fractions in the usual manner. Only a very small amount of neutral material was obtained and this was not investigated further.

The alkaline extract was heated and hydrolyzed by heating for twenty minutes on the steam-bath. The acids obtained would not crystallize. The acid fraction was acetylated with hot acetic anhydride and sublimed in high vacuum, the fraction distilling at 160–180° being collected, hydrolyzed with ethanolic potassium hydroxide and the acid crystallized from chloroform to give 40 mg. of white crystals, m. p. 219–222°. This gave no depression with samples obtained previously.

Anal. Calcd. for $C_{19}H_{30}O_5$: C, 67.4; H, 8.9. Found: C, 67.0; H, 8.9.

Acetate Anhydride of C_{19} Dibasic Acid.—A mixture of 200 mg. of the dibasic acid and 4 cc. of acetic anhydride was refluxed for thirty minutes. The excess acetic anhydride was destroyed with water and the white solid collected and crystallized from aqueous acetone to give small flat white needles, m. p. 203–204°.

Anal. Calcd. for $C_{21}H_{30}O_5$: C, 69.6; H, 8.3. Found: C, 69.6; H, 8.4.

The same product was obtained by allowing the acid (50 mg.) to stand at room temperature for twenty hours with 10 cc. of pyridine and 0.3 cc. of acetic anhydride.

Hydrolysis of the acetate anhydride with ethanolic potassium hydroxide yielded the original dibasic acid.

Dimethyl Ester of Dibasic Acid.—A solution of 200 mg. of the acid in 15 cc. of ether and 2 cc. of methanol was treated with an excess of diazomethane in ether. The solvent was evaporated and the residual sirup crystallized from ether–pentane to give white needles, m. p. 121–122°.

Anal. Calcd. for $C_{21}H_{34}O_5$: C, 68.8; H, 9.3. Found: C, 68.9; H, 9.3.

A mixture of 50 mg. of the dimethyl ester and 3 cc. of acetic anhydride was refluxed for twenty minutes. The excess acetic anhydride was destroyed with water and the oily product crystallized from ether–pentane to give compact white crystals of a **dimethyl ester acetate,** m. p. 103–104°.

Anal. Calcd. for $C_{23}H_{36}O_6$: C, 67.6; H, 8.9. Found: C, 67.6; H, 8.8.

Desoxy Dibasic Acid.—To a solution of 500 mg. of the C_{19} dibasic acid in 20 cc. of acetic acid was added a solution of 300 mg. of chromic anhydride in 8 cc. of 80% acetic acid. After standing at room temperature for one hour the mixture was diluted with water and the precipitated solid taken up in ether. Evaporation of the ether gave a non-crystalline residue. This product was dissolved in 40 cc. of acetic acid and to this solution was added 6 g. of amalgamated zinc (20-mesh) and 20 cc. of concentrated hydrochloric acid. The resulting mixture was refluxed for six hours, diluted with water and extracted with ether. The residue remaining upon evaporation of the ether was refluxed with an excess of ethanolic potassium hydroxide for thirty minutes. Acidification with hydrochloric acid yielded a product which was crystallized from ether–pentane as small white crystals, m. p. 230–232°.

Anal. Calcd. for $C_{19}H_{30}O_4$: C, 70.8; H, 9.4. Found: C, 70.7; H, 9.6.

(4) Marker and Rohrmann, THIS JOURNAL, **61**, 846 (1939).
(5) Marker and Rohrmann, *ibid.*, **61**, 2072 (1939).
(6) Litvan and Robinson, *J. Chem. Soc.*, 1997 (1938).

This gave no depression with a sample, m. p. 228–231°, prepared by oxidizing desoxysarsasapogenin with chromic anhydride at 90–95°.

The desoxy acid (75 mg.), m. p. 230–232°, was refluxed for thirty minutes with acetic anhydride and the reaction product was sublimed in high vacuum at 120–140°. The sublimate was crystallized from ether–pentane to give white needles of the **desoxy anhydride**, m. p. 205.5–207°.

Anal. Calcd. for $C_{19}H_{28}O_3$: C, 75.0; H, 9.3. Found: C, 75.0; H, 9.4.

Treatment of the desoxy anhydride with hot ethanolic potassium hydroxide gave the desoxy acid, m. p. 230–232°.

Summary

The acetates of sarsasapogenin, tetrahydrosarsasapogenin, and sarsasapogenoic acid upon oxidation with chromic anhydride yield a C_{19} dibasic acid, probably 3-hydroxy-*etio*-bilianic acid.

STATE COLLEGE, PENNA. RECEIVED JUNE 17, 1939

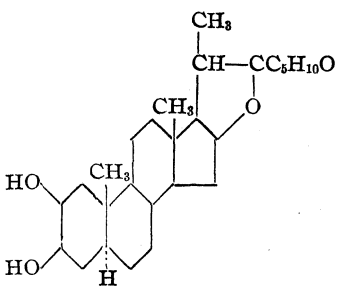
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. LXXIII. Reactions of Digitogenin and Gitogenin

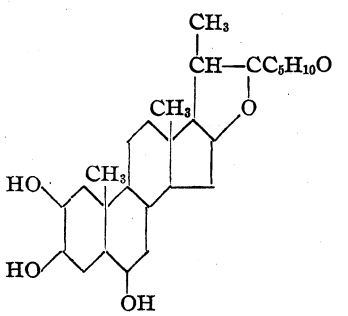
BY RUSSELL E. MARKER AND EWALD ROHRMANN

Although digitogenin (II) and gitogenin (I) were the first steroidal sapogenins to be studied,[1] the chemistry of the substances appears to be still in a somewhat confused state, particularly in regard to the nature of various oxidative degradation products. Unfortunately in all of the oxidation studies which have been reported on these substances no attempt was made to protect the reactive hydroxyl groups and therefore conclusions derived from such studies concerning the nature of the two less reactive oxygens must be regarded as of doubtful value.

The fact that tigogenin has been oxidized to gitogenic acid,[2,3] identical with that obtained by the chromic anhydride oxidation of gitogenin, shows conclusively that gitogenin is of the *allo*-configuration at C-5 and also offers strong support to the work of Tschesche and Hagedorn,[4] concerning the position of the nuclear hydroxyl groups. The evidence concerning the configuration of digitogenin at C-5 is not certain in spite of the fact that it has been degraded to gitogenic acid by the Wolff–Kishner reduction of digitogenic acid, inasmuch as inversion at C-5 may have occurred under the influence of alkali.



I. Gitogenin



II. Digitogenin

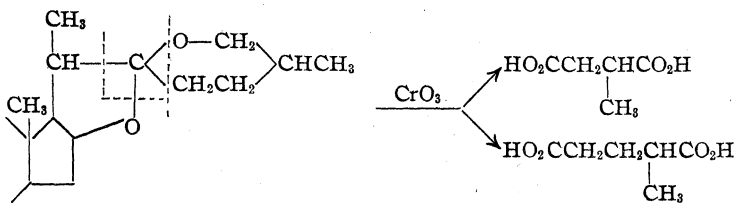
The fact that both α-methylglutaric acid and methylsuccinic acids have been reported from the chromic anhydride oxidation of digitogenic acid[2,4] is in accordance with our recently proposed structure of the sapogenin side chain III.[5] It is no longer necessary to regard the formation of α-methylglutaric acid as arising from the oxidation of the nucleus of the sapogenin as was necessitated by structure IV of Tschesche and Hagedorn.[4,6]

Contrary to Tschesche and Hagedorn,[7] we have found that both digitogenin and gitogenin yield insoluble digitonides, a characteristic which evidently is shown by all of the known steroidal sapogenins.

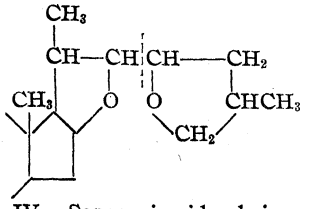
Digitogenin and gitogenin both readily yield dihydro compounds[5] upon catalytic hydrogenation in acidic medium. These dihydro compounds have not been investigated further. The acetates of digitogenin and gitogenin yield with

(1) Fieser, "Chemistry of Natural Products Related to Phenanthrene," Reinhold Publishing Corp., New York, N. Y., 1936.

(2) Tschesche and Hagedorn, *Ber.*, **68**, 1090 (1935).
(3) Jacobs and Simpson, *J. Biol. Chem.*, **110**, 429 (1935).
(4) Tschesche and Hagedorn, *Ber.*, **69**, 797 (1936).
(5) Marker and Rohrmann, THIS JOURNAL, **61**, 846 (1939).
(6) Tschesche and Hagedorn, *Ber.*, **68**, 1412 (1935).
(7) Tschesche and Hagedorn, *ibid.*, **68**, 2247 (1935).



III. Sapogenin side chain



IV. Sapogenin side chain (Tschesche and Hagedorn[7])

bromine characteristic monobromo derivatives. Gitogenin and digitogenin also react with selenium dioxide.

That these two sapogenins are related more closely to tigogenin[8] than to sarsasapogenin is shown further by the fact that they appear to be relatively inert to treatment with alcoholic hydrochloric acid. Attempts to reduce the substances by the Clemmensen method[3] were unsuccessful.

The acetates of the C_{22} lactones of digitogenin and gitogenin were prepared by oxidizing digitogenin triacetate and gitogenin diacetate with chromic anhydride at 90–95°, the yields being comparable to those obtained by similar oxidations of sarsasapogenin and tigogenin acetates. Hydrolysis of the acetate lactones gave the corresponding hydroxy lactones.

We wish to thank Parke, Davis and Company for their generous support and assistance in the various phases of this work. We also wish to thank Mr. Paul H. Williams and Drs. Elmer J. Lawson and H. C. Benedict for their assistance in obtaining the bulbs of *Chlorogalum pomeridianum*.

Experimental Part

Isolation of Gitogenin from Chlorogalum Pomeridianum.—The filtrate remaining after removal of the chlorogenin and tigogenin from *Chlorogalum pomeridianum* was evaporated to dryness and the crystalline residue acetylated by boiling for thirty minutes with a large excess of acetic anhydride. The acetic anhydride was evaporated *in vacuo* and the residue crystallized from acetone to give white needles, m. p. 241–243°. This gave no depression with a sample of gitogenin diacetate prepared from gitogenin isolated from *Digitalis purpurea*.

Anal. Calcd. for $C_{31}H_{48}O_6$: C, 72.1; H, 9.4. Found: C, 72.4; H, 9.5.

Hydrolysis of the acetate with ethanolic potassium hydroxide yielded a product which crystallized from 95% ethanol as fine white needles, m. p. 266–268°. This gave a 25° depression when mixed with chlorogenin. This gave no depression with a sample of gitogenin isolated from *Digitalis purpurea*.

Anal. Calcd. for $C_{27}H_{44}O_4$: C, 74.9; H, 10.2. Found: C, 74.6; H, 10.2.

When heated with an acetic acid solution of selenium dioxide the substance readily yielded a red precipitate.

Gitogenin was recovered unchanged after treatment with amalgamated zinc and hydrochloric acid in alcohol solution for six hours.

Digitogenin from Recovered Digitonin.—To a hot solution of 50 g. of recovered digitonin in 400 cc. of absolute methanol was added a mixture of 100 cc. of concentrated hydrochloric acid, 100 cc. of water and 100 cc. of methanol. The resulting mixture was refluxed for eight hours. The material showed a considerable tendency to froth during the first two hours of refluxing. The mixture was then diluted with water and the white precipitate collected, washed with water and dried. The dried material was treated with Norite in 95% ethanol. Concentration of the alcoholic solution yielded white crystals which were recrystallized from dry benzene to give fine white needles, m. p. 278°.

Anal. Calcd. for $C_{27}H_{44}O_5$: C, 72.3; H, 9.9. Found: C, 72.6; H, 9.8.

The product reacted readily with a hot solution of selenium dioxide in acetic acid. Digitogenin was recovered essentially unchanged after treatment with amalgamated zinc and hydrochloric acid in ethanol solution for five hours.

Dihydrogitogenin.—A mixture of 2 g. of gitogenin diacetate, 1 g. of Adams catalyst and 100 cc. of glacial acetic acid was shaken with hydrogen (3 atmospheres) at 70° for twelve hours. The mixture was filtered and the acetic acid evaporated *in vacuo*. The residual sirup was hydrolyzed for twenty minutes in alcoholic potassium hydroxide. The resulting solution was diluted with water and the mixture extracted with ether and the product crystallized from ethyl acetate to give fine white needles, m. p. 195–197°. The substance gave a precipitate with digitonin. The substance showed no tendency to react with selenium dioxide.

Anal. Calcd. for $C_{27}H_{46}O_4$: C, 74.6; H, 10.7. Found: C, 74.1; H, 10.7.

Tri-*p*-nitrobenzoate of Dihydrogitogenin.—A solution of 100 mg. of dihydrogitogenin and 400 mg. of *p*-nitrobenzoyl chloride in 10 cc. of pyridine was heated on the steam-bath for six hours. After dilution with water the neutral material was crystallized from ether–acetone as pale yellow crystals, m. p. 189–191°.

Anal. Calcd. for $C_{48}H_{55}O_{18}N_3$: C, 65.35; H, 6.3. Found: C, 65.0; H, 6.3.

Dihydrodigitogenin.—This was prepared as described for dihydrogitogenin. The product was crystallized from acetone as white needles, m. p. 184–186°.

Anal. Calcd. for $C_{27}H_{46}O_5$: C, 71.9; H, 10.3; mol. wt.,

(8) Marker and Rohrmann, THIS JOURNAL, **61**, 1516 (1939).

450. Found: C, 71.6, 71.9, H, 10.5, 10.3, mol. wt. (Rast), 434.

Bromogitogenin Diacetate.—To a solution of 300 mg. of gitogenin diacetate in 30 cc. of acetic acid acidified with 2 drops of 48% hydrobromic acid was added 0.6 cc. of 1.05 *M* bromine in acetic acid. The solution was diluted with water and the precipitate collected, washed with water and dried. The product was crystallized from acetone–methanol as white needles, m. p. 219–220° dec.

Anal. Calcd. for $C_{31}H_{47}O_6Br$: C, 62.5; H, 8.0. Found: C, 62.3; H, 8.0.

When reduced with sodium and absolute ethanol the bromo compound yielded gitogenin, m. p. 265–267°.

The bromo compound showed no evidence of reaction when heated with an acetic acid solution of selenium dioxide.

Bromodigitogenin Triacetate.—This was prepared as described for bromogitogenin diacetate. The product was crystallized from aqueous methanol as white crystals, m. p. 142° dec.

Anal. Calcd. for $C_{33}H_{49}O_8Br$: C, 60.6; H, 7.6. Found: C, 60.8; H, 7.6.

Its behavior toward selenium dioxide and sodium and ethanol was analogous to that of the gitogenin compound.

Digitogenin Lactone Triacetate.—To a solution of 3 g. of digitogenin triacetate in 100 cc. of glacial acetic acid heated at 95° was added a solution of 5 g. of chromic anhydride in 60 cc. of 80% acetic acid over a period of one hour. The resulting mixture was heated for an additional ninety minutes. The mixture was evaporated *in vacuo* to a volume of about 50 cc. The residual solution, after dilution with water, was extracted with ether and the ethereal extract washed with 3% sodium hydroxide solution to remove acidic products. The ether was evaporated and the residue crystallized from acetone as compact white crystals, m. p. 281–283°.

Anal. Calcd. for $C_{28}H_{40}O_8$: C, 66.6; H, 8.0. Found: C, 66.7; H, 8.1.

Hydrolysis of the lactone acetate with an excess of ethanolic potassium hydroxide gave the **trihydroxy lactone** which crystallized from acetone as small white crystals, m. p. 279–282°.

Anal. Calcd. for $C_{22}H_{34}O_5$: C, 69.8; H, 9.0; neut. equiv., 378. Found: C, 69.4; H, 9.0; neut. equiv., 379.5.

Gitogenin Lactone Diacetate.—This was prepared from gitogenin diacetate as described for digitogenin lactone triacetate. The material was crystallized from acetone–pentane as compact white crystals, m. p. 248–251°.

Anal. Calcd. for $C_{26}H_{38}O_6$: C, 69.9; H, 8.7. Found: C, 69.7; H, 8.6.

Hydrolysis of the resulting diacetate with ethanolic potassium hydroxide yielded the **gitogenin lactone** which crystallized from ether–acetone as white needles, m. p. 276–278°.

Anal. Calcd. for $C_{22}H_{34}O_4$: C, 72.9; H, 9.5. Found: C, 72.6; H, 9.4.

Treatment of the dihydroxy lactone with benzoyl chloride in pyridine at room temperature for two days gave a **dibenzoate lactone** which, after treatment with Norite, crystallized from aqueous acetone as white needles, m. p. 275–278°.

Anal. Calcd. for $C_{36}H_{42}O_6$: C, 75.75; H, 7.4. Found: C, 76.0; H, 7.5.

Digitonides of Digitogenin and Gitogenin.—To a hot solution of 250 mg. of digitogenin in 35 cc. of 95% ethanol was added a boiling solution of 1.1 g. of digitonin in 35 cc. of 80% ethanol. A precipitate started to separate after thirty minutes and after standing overnight at room temperature the precipitate was collected, washed with 95% ethanol and dried: yield of digitonide, 800 mg. This was dissolved in 10 cc. of pyridine and the resulting solution heated on the steam-bath for twenty-five minutes. The solution was then poured into a mixture of 200 cc. of ether and 15 cc. of methanol. The white precipitate was collected and washed with ether. The filtrate after shaking with dilute hydrochloric acid was evaporated and the residue crystallized from acetone–benzene to give 180 mg. of fine white needles, m. p. 276–279°. This gave no depression with a sample of digitogenin.

Similar results were obtained with gitogenin.

Summary

Gitogenin and digitogenin resemble sarsasapogenin and tigogenin in their behavior toward catalytic hydrogenation, bromination and oxidation with selenium dioxide. They are relatively inactive toward isomerization with hydrochloric acid and Clemmensen reduction.

The C_{22} lactones of digitogenin and gitogenin have been prepared.

STATE COLLEGE, PENNA. RECEIVED JUNE 17, 1939

[CONTRIBUTION FROM THE DIVISION OF DAIRY RESEARCH LABORATORIES, BUREAU OF DAIRY INDUSTRY, U. S. DEPARTMENT OF AGRICULTURE]

The Acetylation of Lactic Esters by Ketene

BY H. V. CLABORN AND LEE T. SMITH

The acetylation of lactic esters was accomplished first by Wislicenus[1] who acetylated ethyl lactate by means of acetyl chloride. He did not, however, report the yield obtained. More recently Burns and his co-workers[2] have used acetic anhydride for the acetylation of methyl, ethyl, butyl, and benzyl lactates. They reported yields of 81, 91, 92, and 70%, respectively. The authors have duplicated these results and in the case of methyl lactate have increased the yield to 92% of the theoretical. The improvement was due to: (1) the fact that the sulfuric acid used to catalyze the reaction was neutralized with calcium carbonate before the fractional distillation and (2) the use of a 24-inch (61-cm.) Widmer fractionating column, which proved very efficient in removing the acetic acid. This method also has been used with good results for acetylating other lactic esters.

Ketene has been used for the acetylation of alcohols,[3] primary amines,[3] amino acids,[4] ethyl mercaptan,[5] carbohydrates,[6] and phenols.[7] Hurd and Williams[5] have found that α-hydroxy acids such as benzilic and mandelic react with two moles of ketene to form acetylbenzilic acetic anhydride and acetylmandelic acetic anhydride, respectively. In order to obtain the corresponding acetoxy acids, it is necessary to decompose these anhydrides. However, the use of ketene for the acetylation of the esters of α-hydroxy acids has not been recorded.

The authors have found that when a trace, one drop per mole, of sulfuric acid[8] is present to catalyze the reaction, ketene reacts very smoothly with the lactic esters, and the yield of the corresponding α-acetoxypropionate obtained is practically the theoretical.

$$\underset{\text{OH}}{\overset{|}{\text{CH}_3\text{CHCOOR}}} + \text{CH}_2{=}\text{CO} \longrightarrow \underset{\text{CH}_3\text{COO}}{\overset{|}{\text{CH}_3\text{CHCOOR}}}$$

Since the lactic esters and the acetylated esters are both liquids, no solvent is necessary. This also makes possible the use of higher temperatures and, consequently, faster rates of reaction. The ketene may be introduced directly into the ester containing the sulfuric acid catalyst. Since the ketene reacts so readily with these esters, it is necessary to use only a slight excess to complete the reaction. This method is simplified further by the fact that the ketene produced by the pyrolysis of acetone may be used without purification. The reaction product requires only an ordinary type distillation for purification and not a fractional distillation as is required to remove the acetic acid when acetic anhydride is used.

In addition to the preparation of methyl, ethyl, butyl, and benzyl α-acetoxypropionates the physical properties of which already have been recorded,[2] *n*-propyl, isopropyl, isobutyl, *n*-amyl, and isoamyl α-acetoxypropionates were prepared both with ketene and with acetic anhydride. Glycol monolactate reacts with two moles of ketene and glycol monolactate diacetate is formed.

$$\underset{\text{OH}}{\overset{|}{\text{CH}_3\text{CHCOOCH}_2\text{CH}_2}}\underset{\text{OH}}{\overset{|}{}} + 2\text{CH}_2{=}\text{CO} \longrightarrow \underset{\text{CH}_3\text{COO}}{\overset{|}{\text{CH}_3\text{CHCOOCH}_2\text{CH}_2}}\underset{\text{CH}_3\text{COO}}{\overset{|}{}}$$

Some of the physical properties of these new compounds are recorded.

Experimental

The ketene used was prepared by the pyrolysis of acetone by the method of Hurd and Williams[5] modified by Williams.[9] The ketene was used directly as it was produced without purification. A typical example is given.

Methyl α-Acetoxypropionate.—Six moles (624 g.) of methyl lactate containing two drops of sulfuric acid was treated with ketene at the rate of 0.28 mole per hour for twenty-two hours (6.16 moles). The exothermic reaction caused the reaction flask to become quite warm after a few minutes, and it was immersed in an ice water-bath until the reaction was complete. No color change took place in the reaction flask until the end of the experiment. Then a yellow color developed which changed to a dark brown on standing overnight. This color change is an indication that the reaction is complete, for apparently it

(1) J. Wislicenus, *Ann.*, **125**, 58 (1863).

(2) Robert Burns, D. T. Jones and P. D. Ritchie, *J. Chem. Soc.*, 400 (1935).

(3) N. T. M. Wilsmore, *ibid.*, **91**, 1939 (1907).

(4) Max Bergmann and F. Stern, *Ber.*, **63B**, 437 (1930).

(5) C. D. Hurd and J. W. Williams, THIS JOURNAL, **58**, 962 (1936).

(6) C. D. Hurd, S. M. Cantor and A. S. Roe, *ibid.*, **61**, 426 (1939).

(7) F. O. Rice, J. Greenberg, C. E. Waters and R. E. Volrath, *ibid.*, **56**, 1760 (1934).

(8) Since this work was completed the work by Hurd[6] has appeared in which sulfuric acid is used to catalyze the reaction of ketene with carbohydrates.

(9) Unpublished work by Dr. J. W. Williams of the University of Maryland.

TABLE I

THE PERCENTAGE YIELD, B. P., SP. GR., AND REF. INDEX OF LACTIC ESTERS

α-Acetoxypropionate esters	B. p. °C.	Mm.	B. p. 763–5 mm.	Yield, % with Ketene	Yield, % with Acetic anhydride	d^{25}_{25}	$n^{25}D$	Empirical formula	Acetyl, % Calcd.	Acetyl, % Found
Methyl	68–73	14		96.4	92					
Ethyl	73–76	11		98.0	91					
n-Butyl	94–97	8		98.0	92					
Isobutyl	90–92	9	205	94.0	87	0.9952	1.4140	$C_9H_{16}O_4$	22.86	22.86
n-Propyl	77–79	7	196	97.0	87	1.0163	1.4123	$C_8H_{14}O_4$	24.70	24.48
Isopropyl	74–78	9	183	96.5	86	0.9920	1.4069	$C_8H_{14}O_4$	24.70	24.53
n-Amyl	101–103	8	227	97.0	87	0.9822	1.4199	$C_{10}H_{18}O_4$	21.27	21.13
Isoamyl	107–110	12	222	96.0	90	0.9838	1.4190	$C_{10}H_{18}O_4$	21.27	21.14
Benzyl	145–148	7	...	96.0	70					
β-Acetoxyethyl*	141–145	10	265	86.0	..	1.1489	1.4297	$C_9H_{14}O_6$	39.45	39.23

* Glycol monolactate diacetate.

is the result of polymerization of the excess ketene. If the reaction mixture is not allowed to stand for a few hours before distillation, this yellow color may later develop in the final distilled product. The reaction product distilled at 68–73° at 14 mm.; yield, 844 g. or 96.4%.

Methyl, isobutyl, *n*-propyl, isopropyl, *n*-amyl and isoamyl lactate were acetylated with acetic anhydride by the method of Burns.[2] Calcium carbonate was added to neutralize only the sulfuric acid used for catalyst, and the reaction product was fractionated in vacuum with a 24-inch (61-cm.) Widmer fractionating column.

Benzyl lactate was prepared from benzyl chloride and sodium lactate.[10]

Acknowledgment.—The authors are grateful to Dr. J. W. Williams for his helpful suggestions and kind permission to copy the ketene lamp designed by him and now in use in his laboratory at the University of Maryland.

(10) M. Gomberg and C. C. Buchler, THIS JOURNAL, **42**, 2064 (1920).

Summary

The methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, isobutyl, *n*-amyl, isoamyl and benzyl lactates and glycol monolactate were acetylated with ketene in the presence of a trace of sulfuric acid as catalyst. The yields were greater than those obtained when acetic anhydride was used, being practically quantitative. Six new compounds were prepared: namely, *n*-propyl, isopropyl, isobutyl, *n*-amyl, and isoamyl α-acetoxypropionates and glycol monolactate diacetate. Some of the physical properties of these compounds are given.

WASHINGTON, D. C. RECEIVED JUNE 8, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF UNIVERSAL OIL PRODUCTS COMPANY]

Synthesis of *t*-Butyl- and *t*-Amylcyclopentane and of their Intermediate Products[1]

BY HERMAN PINES AND V. N. IPATIEFF

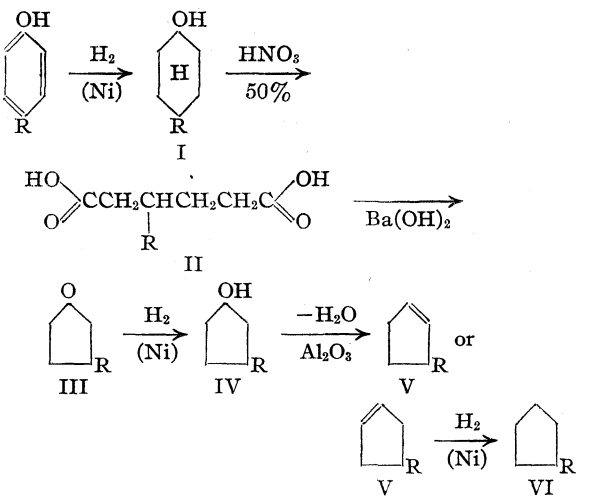
The preparation of *t*-alkylcyclopentanes has not been reported hitherto in the literature. Although the reaction of cyclopentanone with alkylmagnesium halide has been used successfully by others and also in our laboratory[2] for the preparation of several of the alkylcyclopentanes, the use of *t*-butylmagnesium halide did not yield the expected *t*-butylcyclopentanol, which would be an intermediate in the preparation of *t*-butylcyclopentane. Similarly, *t*-butylmagnesium bromide on reacting with cyclopentyl bromide gave only small yields of *t*-butylcyclopentane.

The method described in this paper for the preparation of *t*-alkylcyclopentane consists in cyclicizing alkyladipic acid to alkylcyclopentanone, a method which had been employed for the preparation of methylcyclopentanone. The starting products for the preparation of *t*-butyl- and *t*-amylcyclopentane were, respectively, *p*-*t*-butyl- and *p*-*t*-amylphenol, compounds which are now commercially available. The phenols were converted by catalytic hydrogenation to the corresponding *t*-alkylcyclohexanol; the latter on oxidation with nitric acid solution yielded β-*t*-butyl- and β-*t*-amyladipic acid. The β-*t*-alkyladipic

(1) Presented before the Division of Organic Chemistry at the American Chemical Society Meeting, Baltimore, Md., April 3–6, 1939.

(2) Chavanne and Becker, *Bull. soc. chim. Belg.*, **36**, 591 (1927); Pines and Ipatieff, THIS JOURNAL, **61**, 1076 (1939).

acids were converted into the 3-*t*-alkylcyclopentanones which were characterized by their solid semicarbazones and 2,4-dinitrophenylhydrazones. The yield of the 3-*t*-alkylcyclopentanone obtained based on the 4-*t*-butyl- and 4-*t*-amylcyclohexanol used was of the order of 60–75%. The alkyl cyclopentanone was hydrogenated catalytically to 3-*t*-butyl- and 3-*t*-amylcylopentanol, characterized by the α-naphthylurethans they yield with α-naphthyl isocyanate. The carbinols were dehydrated by the use of aluminum oxide to the olefins and the latter hydrogenated to *t*-butyl- and *t*-amylcyclopentane. The position of the double bond in the *t*-alkylcyclopentane is being investigated. The yields obtained on hydrogenation and dehydrogenation are almost quantitative. The methods of preparation may be illustrated as follows



(R = *t*-Butyl or *t*-Amyl)

Experimental

1. 4-*t*-Alkylcyclohexanol.—The compounds were prepared by hydrogenation in an Ipatieff type electrically heated rotating autoclave of 10 parts of the *p*-*t*-butyl- and *p*-*t*-amylphenols in the presence of 1 part of nickel catalyst with 100 atmospheres of hydrogen at 125°. The hydrogenated product did not contain any unreacted alkylphenol, since it gave a negative test with ferric chloride.

4-*t*-Butylcyclohexanol, m. p. 82° (crystallized from *n*-heptane).

4-*t*-Amylcyclohexanol, m. p. 24–25°, b. p. 154–155° at 40 mm., d^{20}_4 (vac.) 0.9034. *Anal.* Calcd. for $C_{11}H_{22}O$: C, 77.56; H, 13.03. Found: C, 77.50; H, 12.95.

α-Naphthylurethan crystallized twice from heptane, m. p. 113°. *Anal.* Calcd. for $C_{22}H_{29}O_2N$: C, 77.95; H, 8.91. Found: C, 77.79; H, 8.48.

II. β-*t*-Alkyladipic Acids.—These were prepared by the procedure described by Niederl and Smith.[3] Several portions consisting of 1 mole of *t*-alkylcyclohexanol and 560 cc. of 50% nitric acid were heated in the presence of 0.5 g. of ammonium vanadate.

β-*t*-Butyladipic acid (yield 87%) crystallized twice from hot water, m. p. 117° (uncorr.). *Anal.* Calcd. for $C_{10}H_{18}O_4$: C, 59.36; H, 9.44. Found: C, 59.12; H, 9.25.

β-*t*-Amyladipic acid (yield 95%) crystallized twice from hot water, m. p. 77–78°. *Anal.* Calcd. for $C_{11}H_{20}O_4$: C, 61.06; H, 9.31. Found: C, 61.09; H, 9.35.

III. 3-*t*-Alkylcyclopentanone.—One hundred and eighty grams of β-alkyladipic acid was heated in a short-necked distilling flask with 18 g. of barium hydroxide at 280°. Water and alkylcyclopentanone generated during heating were collected in a receiver; at the end of one and one-half to two hours of heating the content of the flask was composed of a solid mass and no more liquid distilled over. The alkylcyclopentanone was separated from the water layer, washed with sodium bicarbonate solution and then dried over anhydrous sodium sulfate.

3-*t*-Butylcyclopentanone (yield 64–70%), boiling point 200–201° at 759 mm., $d^{20}_{vac.}$ 0.9031; n^{20}_D 1.4505. *Anal.* Calcd. for $C_9H_{16}O$: C, 77.07; H, 11.50. Found: C, 76.83; H, 11.43.

Semicarbazone crystallized from 50% ethanol; m. p. 194–194.5° (uncorr.) decomposes. *Anal.* Calcd. for $C_{10}H_{19}N_3O$: N, 21.32. Found: N, 21.26.

2,4-Dinitrophenylhydrazone.—Crystallized from 95% ethanol, m. p. 139° (uncorr.). *Anal.* Calcd. for $C_{15}H_{20}O_4N_4$: N, 17.50. Found: N, 17.53.

3-*t*-Amylcyclopentanone, yield 75–80%, b. p. 120° at 27 mm., $d^{20}_{vac.}$ 0.9159; $n^{20}D$ 1.4601. *Anal.* Calcd. for $C_{10}H_{18}O$: C, 77.85; H, 11.77. Found: C, 78.06; H, 11.72.

Semicarbazone.—Crystallized from 50% ethanol, m. p. 189° (uncorr.). *Anal.* Calcd. for $C_{11}H_{21}N_3O$: N, 19.88. Found: N, 19.66.

2,4-Dinitrophenylhydrazone.—Crystallized from 95% ethanol, m. p. 174.5° (uncorr.). *Anal.* Calcd. for $C_{16}H_{22}O_4N_4$: N, 16.75. Found: N, 16.72.

IV. 3-*t*-Alkylcyclopentanol.—The alcohol was prepared by hydrogenating 10 parts of *t*-alkylcyclopentanone in the presence of 1 part of nickel catalyst at 80° and 100 atmospheres initial hydrogen pressure. When the pressure during hydrogenation decreased to 60 atmospheres, the bomb was recharged to 100 atmospheres. The hydrogenation was considered completed when there was no decrease in hydrogen pressure for a period of two hours.

3-*t*-Butylcyclopentanol.—B. p. 196–198° at 744 mm., $d^{20}_{vac.}$ 0.9006; $n^{20}D$ 1.4574. *Anal.* Calcd. for $C_9H_{18}O$: C, 75.98; H, 12.77. Found: C, 76.11; H, 12.74.

α-Naphthylurethan.—Crystallized from heptane, m. p. 95°. *Anal.* Calcd. for $C_{20}H_{25}O_2N$: C, 77.12; H, 8.09; N, 4.50. Found: C, 76.94; H, 7.60; N, 5.00.

3-*t*-Amylcyclopentanol.—B. p. 217° at 738 mm., $d^{20}_{vac.}$ 0.9114, $n^{20}D$ 1.4656. *Anal.* Calcd. for $C_{10}H_{20}O$: C, 76.84; H, 12.91. Found: C, 77.07; H, 12.76.

α-Naphthylurethan crystallized from heptane, m. p. 82°. *Anal.* Calcd. for $C_{21}H_{27}O_2N$: C, 77.48; H, 8.37; N, 4.30. Found: C, 77.18; H, 8.15; N, 4.57.

V. *t*-Alkylcyclopentenes.—The olefins were prepared by dehydrating *t*-alkylcyclopentanols by passing the carbinols over 40 g. of activated alumina with a rate of 40

(3) Niederl and Smith, THIS JOURNAL, **59**, 717 (1937).

cc. per hour and at a temperature of 345°. The dehydration was quantitative. The olefins were separated from the water, dried over sodium sulfate and distilled over metallic sodium. The position of the double bond in the dehydrated *t*-alkylcyclopentanol is being studied.

***t*-Butylcyclopentene.**—Boiling point by Cottrell[4] method, 139.6° at 760 mm., dT/dP (770 to 730 mm.) = 0.048°/mm., $d^{20}_{vac.}$ 0.8021; $d^{40}_{vac.}$ 0.7861; $n^{20}D$ 1.4421; $n^{20}H_\beta$ 1.4486; $n^{20}H_\alpha$ 1.4397; Δ^{20} (dispersion) 88.8; δ^{20} (specific dispersion) 110.7. *Anal.* Calcd. for C_9H_{16}: C, 87.08; H, 12.92. Found: C, 87.35; H, 12.90.

***t*-Amylcyclopentene.**—B. p. 163–165° at 743 mm., $d^{20}_{vac.}$ 0.8256; $n^{20}D$ 1.4554; $n^{20}H_\beta$ 1.4618; $n^{20}H_\alpha$ 1.4527; Δ^{20} 90.8; δ^{20} 110.0. *Anal.* Calcd. for $C_{10}H_{18}$: C, 86.86; H, 13.14. Found: C, 86.72; H, 13.27.

VI. *t*-Alkylcyclopentane.—This hydrocarbon was prepared by hydrogenating at 60° *t*-alkylcyclopentene in the presence of 10% by weight of nickel catalyst and 100 atmospheres of hydrogen. The hydrogenation proceeded to completion, for the final product was stable toward a nitrating mixture composed of 2 volumes of concentrated sulfuric acid and 1 volume of concentrated nitric acid.

***t*-Butylcyclopentane,** m. p. −96 ± 0.2°, boiling point by Cottrell method 145.2° at 760 mm., dT/dP (770–730 mm.) = 0.052°/mm., $d^{20}_{vac.}$ 0.7911; $d^{40}_{vac.}$ 0.7753; $n^{20}D$ 1.4341; $n^{20}H_\beta$ 1.4396; $n^{20}H_\alpha$ 1.4320; Δ^{20} 76.4; δ^{20} 96.6. *Anal.* Calcd. for C_9H_{18}: C, 85.63; H, 14.37. Found: C, 85.75; H, 14.49.

***t*-Amylcyclopentane.**—Boiling point by Cottrell method 173.9° at 760 mm., dT/dP (770–730 mm.) = 0.054°/mm., $d^{20}_{vac.}$ 0.8071; $d^{40}_{vac.}$ 0.7923; $n^{20}D$ 1.4457; $n^{20}H_\beta$ 1.4511; $n^{20}H_\alpha$ 1.4433; Δ^{20} 78.0; δ^{20} 96.6. *Anal.* Calcd. for $C_{10}H_{20}$: C, 85.63; H, 14.37. Found: C, 85.63; H, 14.25.

Acknowledgment.—The authors wish to express their thanks to Mr. M. Savoyias for the assistance he rendered, to Mr. R. W. Moehl for the analyses and to Mr. R. C. Wackler for the refractometric measurements.

Summary

Synthesis of *t*-butyl- and *t*-amylcyclopentane from *p*-*t*-butyl- and *p*-*t*-amylphenols is described.

The following compounds and their derivatives were synthesized for the first time: 4-*t*-amylcyclohexanol, β-*t*-butyl- and β-*t*-amyladipic acid, 3-*t*-butyl- and 3-*t*-amylcyclopentanone, 3-*t*-butyl- and 3-*t*-amylcyclopentanol, *t*-butyl- and *t*-amylcyclopentene, *t*-butyl- and *t*-amylcyclopentane.

RIVERSIDE, ILLINOIS RECEIVED JULY 19, 1939

(4) Cottrell, THIS JOURNAL, **41**, 721 (1929); Bruun and Hicks-Bruun, *Bur. Standards J. Research*, **6**, 871 (1931).

[CONTRIBUTION NO. 174 FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, THE UNIVERSITY OF TEXAS]

Utilization of Alkoxy Ketones in the Synthesis of Quinolines by the Pfitzinger Reaction

BY LOY B. CROSS[1,2] WITH HENRY R. HENZE

Although the utilization of simple aldehydes and ketones in the synthesis of quinoline acids has received considerable attention, but little effort has been made to use bifunctional carbonyl compounds in this manner. Indeed, Henze[3] has reported the initial investigation in which keto ethers were employed in the Pfitzinger reaction, namely, the preparation of four 3-aryloxy-4-quinaldinecarboxylic acids from the appropriate aryloxyacetones.

Our study of the utilization of keto ethers in the Pfitzinger reaction has been extended to include alkoxy ketones and the condensation of ethoxyacetone and ethoxymethyl ethyl ketone with isatin to produce the corresponding 2-alkyl-3-ethoxycinchoninic acids. However, no evidence has been obtained of the formation of any of the isomeric 2-ethoxyalkylcinchoninic acids.[4] The substituted cinchoninic acids are readily decarboxylated by heating at the temperature of their melting points to form 2-alkyl-3-ethoxyquinolines. Also, these 3-alkoxycinchoninic acids are cleaved at the ether linkage by heating with concentrated hydrochloric acid under pressure. The cinchoninic acids and the 2-alkyl-3-ethoxyquinolines are both extremely resistant to reduction by means of hydriodic acid and red phosphorus and no hydrogenation of the pyridine nucleus was observed. However, 2-ethyl-3-hydroxyquinoline was converted, by means of the reducing action of tin and hydrochloric acid, into 2-ethyl-1,2,3,4-tetrahydroquinoline. An attempt was made to form the phthalone of 3-ethoxyquinaldinic acid by heating with phthalic anhydride. Although the temperature employed was approxi-

(1) From the Ph.D. dissertation of Loy B. Cross, June, 1938.

(2) Present address: Emory University, Atlanta, Ga.

(3) Calaway with Henze, THIS JOURNAL, **61**, 1355 (1939).

(4) Methyl ethyl ketone reacts with isatin in alkaline solution to form both 2,3-dimethylcinchoninic acid [Pfitzinger, *J. prakt. Chem.*, **56**, 283 (1897)] and 2-ethylcinchoninic acid [von Braun, Gmelin and Schultheiss, *Ber.*, **56**, 1344 (1923)].

mately fifty degrees below that of the melting point of the quinoline acid, the product of the reaction proved to be the phthalone of 3-hydroxyquinaldine. The latter was obtained also by phthalonation of 3-hydroxyquinaldine.

Experimental

Preparation of Alkoxy Ketones.—**Ethoxyacetone** was prepared in 65% yield by interaction of 0.9 mole of ethoxyacetonitrile (76.5 g.) and the Grignard reagent produced from one gram atom of magnesium and 1.1 moles of methyl iodide; b. p. 34–36° (corr.) (28 mm.); $n^{20}D$ 1.4000; d^{20}_4 0.9117; *MR* calcd., 26.94; *MR* found, 27.16.

Ethoxymethyl ethyl ketone was prepared in the same manner in 51% yield; b. p. 53–54° (corr.) (24–25 mm.); $n^{20}D$ 1.4065; d^{20}_4 0.9064; *MR* calcd., 31.56; *MR* found, 31.52.

Preparation of 3-Ethoxycinchoninic Acids.—Forty-six grams of isatin (0.313 mole) was dissolved in 200 g. of 33% potassium hydroxide solution, 32 g. of ethoxyacetone (0.314 mole) was added and the mixture was heated under a reflux condenser for twenty-four hours on a steam-bath. The mixture was diluted with water to about 750 cc., decolorized with Norite, cooled with ice, and acidified with a slight excess of acetic acid. The solid which separated was filtered, washed and dried; weight 32 g. (44% yield). After recrystallization from hot water, **3-ethoxy-4-quinaldinecarboxylic acid** melts at 243° (corr.) with decomposition.

Anal. Calcd. for $C_{13}H_{13}NO_3$: C, 67.50; H, 5.67; N, 6.05; neut. equiv., 231.2. Found: C, 67.35; H, 5.67; N, 6.24; neut. equiv., 227.9.

From 60.0 g. of isatin (0.408 mole), dissolved in 300 g. of 33% potassium hydroxide solution, and 52 g. of ethoxymethyl ethyl ketone under the same conditions was obtained 93 g. (92% yield) of crude **2-ethyl-3-ethoxycinchoninic acid** melting at 168–177°. After recrystallization from hot water, colorless needles were obtained melting at 199–201° (corr.) with decomposition.

Anal. Calcd. for $C_{14}H_{15}NO_3$: C, 68.5; H, 6.17; N, 5.71; neut. equiv., 245.3. Found: C, 68.22; H, 6.32; N, 5.69; neut. equiv., 244.8.

In preparing **2-ethyl-3-ethoxy-6-methylcinchoninic acid,** 15 g. of 33% potassium hydroxide solution was used to dissolve 3.28 g. of 5-methylisatin (0.0223 mole) and, after adding 2.6 g. of ethoxymethyl ethyl ketone, the mixture was heated for ten hours under reflux on a steam-bath. The yield of crude product was 3.25 g. (56% of the theoretical). Purification was achieved by solution in 0.3 *N* sodium hydroxide, decolorization with Norite and reprecipitation with 0.3 *N* hydrochloric acid. Thus was obtained 2.25 g. (39% yield) of acid melting at 222° (corr.) with decomposition.

Anal. Calcd. for $C_{15}H_{17}NO_3$: C, 69.47; H, 6.55; N, 5.40; neut. equiv., 259.3. Found: C, 69.26; H, 6.55; N, 5.41; neut. equiv., 258.7.

Decarboxylation of 3-Ethoxy-2-alkylcinchoninic Acids.—Thirty grams of 3-ethoxy-4-quinaldinecarboxylic acid (0.13 mole) was heated in a 125-cc. Claisen distilling flask at 250°. The solid melted and then carbon dioxide was evolved. After heating for thirty minutes, the residual liquid was distilled at 140–141° (corr.) (2–3 mm.); the colorless material, weighing 14.5 g. (59% yield), solidified in the receiver. This product, **3-ethoxyquinaldine,**[5] melts at 68–69° (corr.).

Anal. Calcd. for $C_{12}H_{13}NO$: C, 76.97; H, 7.00; N, 7.49. Found: C, 76.62; H, 6.94; N, 7.21.

In a similar manner, **2-ethyl-3-ethoxyquinoline** was obtained by heating 7 g. of 2-ethyl-3-ethoxycinchoninic acid (0.0286 mole) at 210° which gave a colorless liquid, distilling at 138–140° (corr.) (3–4 mm.) and solidifying in the receiver. The yield of solid melting at 58.5° (corr.) was 2.7 g., corresponding to 47% of the theoretical.

Anal. Calcd. for $C_{13}H_{15}NO$: C, 77.61; H, 7.51; N, 6.97. Found: C, 77.74; H, 7.60; N, 6.98.

Cleavage of 3-Ethoxy-4-quinaldinecarboxylic Acid with Concd. Hydrochloric Acid.—Two grams of 3-ethoxy-4-quinaldinecarboxylic acid was heated with concd. hydrochloric acid in a sealed tube for two hours at 150°. The cooled reaction mixture was neutralized with sodium hydroxide, producing a chrome-yellow precipitate which was purified by solution in alkali and reprecipitation with acid, producing 1.25 g. of material melting at 242–244° (corr.) with decomposition. The product was shown to be **3-hydroxy-4-quinaldinecarboxylic acid.**[6]

Anal. Calcd. for $C_{11}H_9NO_3$: C, 65.03; H, 4.52; N, 6.89. Found: C, 65.75; H, 4.67; N, 6.82.

Cleavage of 2-Alkyl-3-ethoxyquinolines with Concd. Hydrochloric Acid.—Eleven and one-half grams of 3-ethoxyquinaldine and 50 cc. of concd. hydrochloric acid were heated together in a sealed tube for three hours at 180°. The reaction mixture was diluted with a little water and the acid was neutralized with sodium hydroxide. The white solid which separated was filtered, dissolved in dilute alkali and reprecipitated with acid; after drying at 110° the product weighed 8 g. (81.5% yield). When heated, **3-hydroxyquinaldine** darkens at about 250° and melts at 260° (corr.).[7]

Anal. Calcd. for $C_{10}H_9NO$: C, 75.49; H, 5.66; N, 8.80. Found: C, 75.50; H, 5.73; N, 8.68.

In a similar manner, 1 g. of 2-ethyl-3-ethoxyquinoline was heated with 10 cc. of concd. hydrochloric acid in a sealed tube for five hours at 200°. Upon dilution of the reaction mixture with a little water a white crystalline solid separated. The latter was dissolved in alkali and reprecipitated by addition of acetic acid. The yield of **2-ethyl-3-hydroxyquinoline,** of melting point 206–208° (corr.) with decomposition, thus obtained was 0.8 g. (93% of the theoretical).

Anal. Calcd. for $C_{11}H_{11}NO$: C, 76.26; H, 6.41; N, 8.09. Found: C, 75.57; H, 6.57; N, 8.22.

(5) Koenigs and Stockhausen, *Ber.*, **35**, 2556 (1902), report its preparation by the interaction of ethyl iodide and an alcoholic potassium hydroxide solution of 3-hydroxyquinaldine and its m. p. 69–70° (corr.).

(6) The synthesis of this compound, from isatic acid and halogenated acetone, has been reported recently [French patent 784,365, July 22, 1935, through *C. A.*, **30**, 111 (1936)] but no data concerning physical properties were recorded.

(7) Koenigs and Stockhausen, ref. 5, report that 3-hydroxyquinaldine, prepared by condensation of *o*-aminobenzaldehyde and chloroacetone in dilute aqueous sodium hydroxide solution, darkens at 240° (corr.) and melts at 260° (corr.).

Action of Hydriodic Acid and Red Phosphorus on 3-Ethoxyquinolines.—Two grams of 3-ethoxyquinaldine, 1.7 g. of red phosphorus and 20 cc. of hydriodic acid (sp. gr. 1.7) were heated together under reflux for seven days at 150°. The phosphorus was removed from the hot mixture by filtration through asbestos and the filtrate subjected to steam distillation to remove most of the hydrogen iodide. The residual solution was made basic with sodium hydroxide, cooled, extracted with ether, and the ether extract dried over sodium sulfate. The aqueous layer was acidified with acetic acid, causing a white solid to separate. The precipitate was filtered, washed with water and dried yielding material melting at 251–256°. The melting point of a mixture with an authentic sample of 3-hydroxyquinaldine was 253–257°.

Anal. Calcd. for $C_{10}H_9NO$: N, 8.80. Found: N, 8.68.

The ether extract was concentrated on a steam-bath, diluted with alcohol and treated with an alcoholic solution of picric acid. The solution was warmed, diluted with water to faint turbidity and cooled in ice. The bright yellow, crystalline precipitate was recrystallized from dilute alcohol; m. p. 192–194° (corr.).[8]

Anal. Calcd. for $C_{16}H_{12}N_4O_7$: N, 15.05. Found: N, 14.92.

In a similar manner, 6.6 g. of 2-ethyl-3-ethoxyquinoline, 5 g. of red phosphorus and 50 cc. of hydriodic acid (sp. gr. 1.7) were heated together under reflux, but for only twenty-four hours at 140–150°. After removal of the unreacted phosphorus, there separated 3 g. of a cream colored solid which contained iodine and melted at 193–198° (corr.). The melting point of a mixture with an authentic sample of the **hydroiodide of 2-ethyl-3-ethoxyquinoline** was 190–197° (corr.).

The filtrate from the hydroiodide yielded 1 g. of a white solid melting at 206–208° (corr.). Mixed with known 2-ethyl-3-hydroxyquinoline the melting point was 206–208° (corr.).

Attempted Reduction of 2-Ethyl-3-ethoxycinchoninic Acid with Hydriodic Acid and Red Phosphorus.—A mixture of 8.1 g. of 2-ethyl-3-ethoxycinchoninic acid, 5 g. of red phosphorus and 50 cc. of hydriodic acid (sp. gr. 1.7) was heated under reflux at 125° for twenty-four hours. The hot reaction mixture was filtered from phosphorus and cooled, when 2 g. of a chrome-yellow solid separated. After solution in alkali and reprecipitation with acid the product melted at 208–209° (corr.) with decomposition. Additional material was obtained from the filtrate, giving a total yield of 4.5 g., corresponding to 63.5% of the theoretical, of **2-ethyl-3-hydroxycinchoninic acid.**

Anal. Calcd. for $C_{12}H_{11}NO_3$: C, 66.33; H, 5.11; N, 6.45; neut. equiv., 217.2. Found: C, 66.26; H, 5.28; N, 6.67; neut. equiv., 207.6.

In a second attempt at reduction the mixture was refluxed at 140–150° for forty-eight hours with additions of hydriodic acid from time to time until a total volume of 50 cc. of acid had been added. A small amount of the **hydroiodide of 2-ethyl-3-ethoxyquinoline,** m. p. 190–197°, was obtained, but the chief product of the reaction was the bright yellow, crystalline 2-ethyl-3-hydroxycinchoninic acid.

Anal. Calcd. for $C_{13}H_{15}NO \cdot HI$: I, 38.57. Found: I, 39.09.

Phthalonation of Quinaldine Derivatives.—An intimate mixture of 1 g. of 3-hydroxyquinaldine and 1 g. of phthalic anhydride was heated for three hours at 200°. The cooled reaction mixture was dissolved in concd. sulfuric acid and the solution poured over ice. The brown solid which formed was purified by crystallization from glacial acetic acid. The **phthalone of 3-hydroxyquinaldine** is a dark orange colored solid melting at 264–266° (corr.) with decomposition.

Likewise, an intimate mixture of 23 g. of 3-ethoxy-4-quinaldinecarboxylic acid (0.1 mole) and 15 g. of phthalic anhydride (0.1 mole) was heated for five hours at 200°. After recrystallization from glacial acetic acid, the reaction product melted at 264.5–265.5° (corr.) with decomposition. A mixture of this material with the phthalone of 3-hydroxyquinaldine melted at 264–265° (corr.) with decomposition. The yield of phthalone from the carboxylic acid was 10 g., or 34%.

Anal. Calcd. for $C_{18}H_{11}NO_3$: C, 74.73; H, 3.83; N, 4.84; mol. wt., 289.3. Found: C, 74.88; H, 4.30; N, 5.00; mol. wt. (Rast), 298.6.

Reduction of 2-Ethyl-3-hydroxyquinoline.—The reduction of this compound was accomplished in the same manner as that utilized by Reher[9] for the reduction of 2-ethylquinoline. After 23 g. of 2-ethyl-3-ethoxyquinoline (0.15 mole) had been heated with 125 cc. of concd. hydrochloric acid in a sealed tube for five hours at 175°, the solution was diluted with 150 cc. of concd. acid and treated with 77 g. of granulated tin (0.65 gram atom); the mixture was warmed intermittently on a steam-bath until all of the tin had dissolved. Then the solution was saturated with hydrogen sulfide, made basic with sodium hydroxide and subjected to steam distillation. A colorless oil in the distillate was extracted with ether, dried over sodium sulfate and the extract distilled *in vacuo*. The product, **2-ethyl-1,2,3,4-tetrahydroquinoline,**[10] a colorless liquid boiling at 125–127° (corr.) (7 mm.), weighed 5 g. (21% yield); $n^{20}D$ 1.5652; d^{20}_4 1.0178; *MR* calcd., 51.89; *MR* found, 51.54.

Anal. Calcd. for $C_{11}H_{15}N$: C, 81.94; H, 9.38; N, 8.69. Found: C, 81.22; H, 9.33; N, 8.70.

A picrate was formed by the interaction of 2.5 g. of the reduction product and 3.5 g. of picric acid dissolved in 150 cc. of 75% alcohol. Five grams of bright yellow picrate was obtained (83% yield). After recrystallization from 95% alcohol, there was recovered 3.5 g. of the purified **picrate of 2-ethyl-1,2,3,4-tetrahydroquinoline** melting at 143–145° (corr.).

Anal. Calcd. for $C_{17}H_{18}N_4O_7$: N, 14.35. Found: N, 14.34.

Summary

1. Pfitzinger's method has been extended to include the utilization of alkoxy ketones in the initial synthesis of three examples of a new type of substituted cinchoninic acid. The structure of

(8) Pictet and Bunzl, *Ber.*, **22**, 1847 (1889), record that the picrate of quinaldine melts at 191° (corr.).

(9) Reher, *Ber.*, **19**, 2998 (1886).

(10) Reher, ref. 9, reported b. p. 259–263°.

one of these acids has been elucidated through a study of its degradation products.

2. 3-Ethoxycinchoninic acids and 3-ethoxyquinolines resist reduction by means of concd. hydriodic acid and red phosphorus, but the ether linkage is cleaved by this treatment.

3. Both 3-ethoxy-4-quinolinecarboxylic acid and 3-hydroxyquinaldine on phthalonation yield the same phthalone.

AUSTIN, TEXAS RECEIVED AUGUST 14, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, NO. 200]

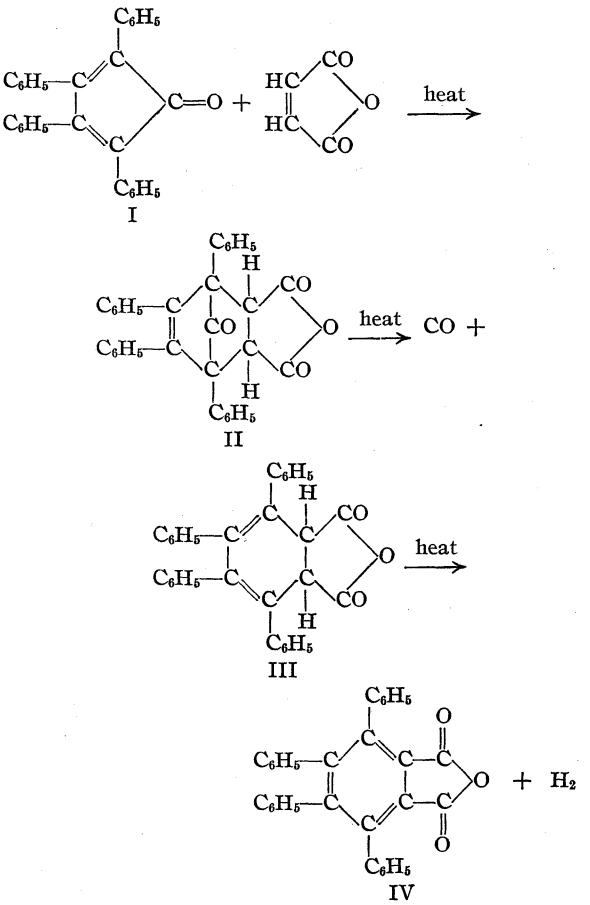
The Reaction of a Thiophene Derivative with Maleic Anhydride

BY DANIEL B. CLAPP[1]

It has been shown by Dilthey and his collaborators[2] that diene syntheses may be carried out readily between various highly arylated cyclopentadienones and maleic anhydride or other ethylenic or acetylenic derivatives. A typical example is the reaction of 2,3,4,5-tetraphenylcyclopentadienone (tetracyclone) (I) with maleic anhydride.[2a] The initial product of this reaction is 3,6-endocarbonyl-3,4,5,6-tetraphenyl-1,2-dihydrophthalic anhydride (II) which on heating successively loses carbon monoxide and hydrogen yielding tetraphenylphthalic anhydride (IV).

In the hope that the same product might be obtained in starting with the sulfur analog of tetracyclone, an attempt was made to bring about a reaction between tetraphenylthiophene (thionessal) and maleic anhydride. By analogy, if an adduct were formed, it might be expected to lose hydrogen sulfide. However, several attempts to carry out this reaction gave completely negative results.

Since it is well known that furan and many of its derivatives will take part readily in diene syntheses, undoubtedly attempts have been made to carry out such syntheses with corresponding thiophene derivatives. However, in a recent review of the Diels–Alder reaction[3] it is stated that no case of a thiophene derivative undergoing this reaction has been recorded. It is evident that the 1,4-conjugate system in thiophene compounds is less active than that present in furan derivatives, the former class being more aromatic in character and resembling benzene derivatives, none of which have been shown to undergo a Diels–Alder reaction. It may be noted that



Schomaker and Pauling[4] recently have shown that electron diffraction results, resonance energies, and other considerations indicate a greater degree of resonance stabilization for thiophene than for furan.

It is possible that the introduction of certain substituents into the thiophene nucleus might so activate the 1,4-system that a diene synthesis could occur. In the case of hydrindene, fixation

(1) Present address: Thompson Chemical Laboratory, Williams College, Williamstown, Mass.

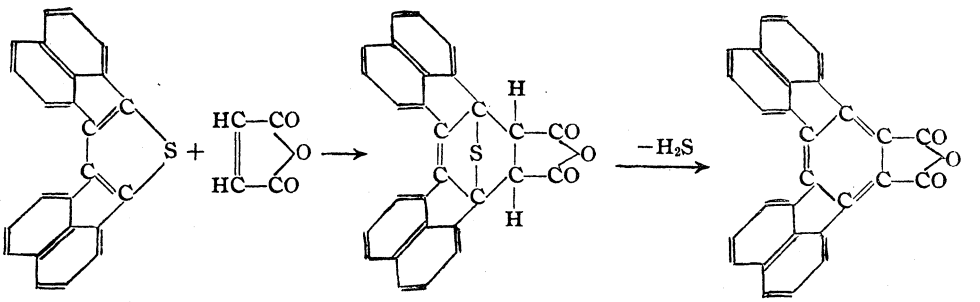
(2) (a) *Ber.*, **66**, 1627 (1933); (b) *ibid.*, **67**, 495, 1959, 2004 (1934); (c) *ibid.*, **68**, 1159 (1935); (d) *ibid.*, **71**, 974 (1938).

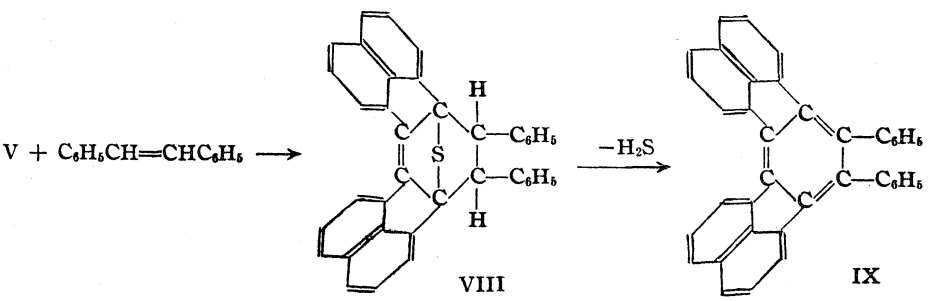
(3) Delaby, *Bull. soc. chim.*, [5] **4**, 765 (1937).

(4) Schomaker and Pauling, THIS JOURNAL, **61**, 1769 (1939).

of the double bonds in the benzene ring, so as to leave a single bond common to the two rings, has been suggested.[5-7] Hence, it might be supposed that the presence of fused five-membered rings in the 2,3- and 4,5-positions of thiophene would increase the activity of the conjugate system, on account of the strain in such a molecule.

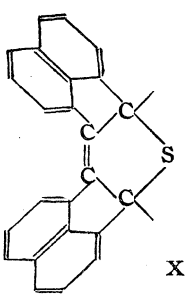
Since the resonance energy in hydrindene has been shown to be practically the same as in benzene,[8] the idea of the fixation of double bonds, at least in hydrindene, is untenable. It has been pointed out[9] that great differences in chemical reactivity may arise from quite small differences in electron distribution. However, the fixation hypothesis is certainly useful for the prediction of reactions and "reaction-structures," even though such structures do not represent completely the molecule in the physical sense.





For the application of this hypothesis to thiophene derivatives, a molecule of the desired type is found in 2,3,4,5-di-(1,8-naphthylene)-thiophene (V). The structure of this substance is indicated by its formation by the sulfur fusion of acenaphthene,[10,11] somewhat analogous to the formation of thionessal by the sulfur fusion of stilbene, and its oxidation to naphthalic anhydride.[10]

In benzene, the internal angle is 120°, which requires a reduction of 5.25° below the corresponding angle in open-chain structures; this necessitates increases in each of the two external angles.[5] Since the internal angles involved in thiophene, if the values calculated by Schomaker and Pauling[4] are assumed, are about 112°, in this case the external angles are increased still more. If it is assumed that these angles are increased proportionally, there will be a greater difference between the β-angle and the α-angle than in the case of benzene. In hydrindene, that structure in which the two greater angles, the β-angles, are included in the 5-ring, will be under the greater strain, since the normal internal angle of this 5-ring (108°) is more nearly equal to the α-angle. In dinaphthylenethiophene, an even greater distortion of the β-angles is required, particularly if the involved internal angles of the 5-ring are assumed to be those in acenaphthene; these latter, according to Banerjee and Sinha,[12] are 97°.



It has been found that dinaphthylenethiophene reacts smoothly with maleic anhydride. If a mixture of these two substances is heated at about 225°, evolution of hydrogen sulfide occurs, and the reaction product, which is obtained in good yield, is undoubtedly 3,4,5,6-di-(1,8-naphthylene)-phthalic anhydride (VII). Confirmation

(5) Mills and Nixon, *J. Chem. Soc.*, 2510 (1930).
(6) Sidgwick and Springall, *ibid.*, 1532 (1936).
(7) Fieser and Lothrop, THIS JOURNAL, **58**, 2050 (1936).
(8) *Ann. Reports*, **34**, 219 (1937).
(9) Sutton and Pauling, *Trans. Faraday Soc.*, **31**, 939 (1935).
(10) Dziewonski, *Ber.*, **36**, 966 (1903).
(11) Rehlander, *ibid.*, **36**, 1586 (1903).
(12) Banerjee and Sinha, *Indian J. Phys.*, **11**, 21 (1937).

of its structure is desirable, and this problem is being attempted. It may be noted that the substance resembles in its appearance and properties certain of the highly arylated phthalic anhydrides prepared by Dilthey.[2] In spite of numerous essays, isolation of the intermediate addition product (VI) has not been accomplished, but this is not surprising in view of the temperature necessary to initiate the reaction.

By the reaction of V with stilbene, 1,2-diphenyl-3,4,5,6-di-(1,8-naphthylene)-benzene (IX) is obtained. A similar reaction appears to take place with cinnamic acid, hydrogen sulfide being evolved steadily, but as yet no pure substance has been isolated from the reaction product.

The reactivity and unsaturated character of dinaphthylenethiophene is indicated by preliminary experiments on the formation of dissociable addition products with chlorine and bromine, details of which will be reported later. These experiments together with the intense red color of dinaphthylenethiophene are, in some degree, suggestive of a diradical structure (X) for the substance.

The work is being extended, and the reactions of other thiophene derivatives with various ethylenic and acetylenic compounds are being studied.

Experimental

2,3,4,5-Di-(1,8-naphthylene)-thiophene.—This substance was obtained by fusion of acenaphthene and sulfur according to the directions of Dziewonski[10] and Rehlander.[11] It was purified by vacuum sublimation at 2.5 mm. and a bath temperature of 260°, followed by recrystallization from xylene; red needles, m. p. 285.5–286° (corr.).

3,4,5,6-Di-(1,8-naphthylene)-phthalic Anhydride.—An intimate mixture of dinaphthylenethiophene (0.12 g.) and maleic anhydride (0.4 g.) was introduced into a test-tube fitted with a long air-condenser. The mixture was heated in a bath, maintained at 225°, for fifteen minutes. The reaction mixture was cooled, broken up, and heated with water; the undissolved solid was then filtered off, dried, finely ground, and boiled with 10 cc. of potassium hydroxide solution (5%). The phthalic anhydride, which was largely unattacked by this treatment, was filtered off, dried, and twice recrystallized from phenyl ether; yield 0.08 g. (60%); yellow needles, decomposing without melting about 385°; almost insoluble in common solvents and aqueous alkali; slightly soluble in alcoholic alkali.

Anal. Calcd. for $C_{28}H_{12}O_3$: C, 84.83; H, 3.06. Found: C, 84.45, 84.72; H, 3.00, 2.97.

1,2-Diphenyl-3,4,5,6-di-(1,8-naphthylene)-benzene.—Dinaphthylenethiophene (0.5 g.) and maleic anhydride (0.5 g.) were heated at a bath temperature of 310–320° for nine hours, at the end of which time evolution of hydrogen sulfide was complete. The reaction mixture was dissolved in benzene, and a crude product was precipitated by the addition of methyl alcohol. On sublimation at 3 mm. and a bath temperature of 255–260°, 0.25 g. of yellow material was obtained, which was recrystallized three times from benzene–methyl alcohol; yield 0.11 g. (14%); greenish yellow crystals, with pronounced yellow-green fluorescence in ultraviolet light; m. p. 290–291° (corr.).

Anal. Calcd. for $C_{38}H_{22}$: C, 95.36; H, 4.64; mol. wt., 478.5. Found: C, 95.21; H, 4.72; mol. wt. (Rast), 473.

Summary

3,4,5,6-Di-(1,8-naphthylene)-phthalic anhydride and 1,2-diphenyl-3,4,5,6-(1,8-naphthylene)-benzene have been obtained from 2,3,4,5-di-(1,8-naphthylene)-thiophene by reaction with maleic anhydride and stilbene, respectively.

RECEIVED AUGUST 1, 1939

[CONTRIBUTION FROM THE OTHO S. A. SPRAGUE MEMORIAL INSTITUTE AND THE DEPARTMENTS OF PATHOLOGY AND MEDICINE, THE UNIVERSITY OF CHICAGO]

Substituted Dialuric and Hydurilic Acids[1]

BY C. M. MARBERG AND D. W. STANGER

In the study of the ideational background underlying certain psychoses in which there is a barrier to communication, there is need for a drug which will permit the physician to establish contact with the patient. Intravenously, sodium-5,5-isoamylethylbarbituric acid has this property[2] to a limited extent. It has the disadvantage that the interview is terminated after a few minutes by the hypnotic effect of the drug. As part of a program to investigate some barbituric acid derivatives from this point of view, we decided to prepare and study the bibarbituric acids, 5,5′-diethylhydurilic and 5,5′-diisoamylhydurilic acid. As by-products in one method of preparation of these compounds, we also obtained the 5-hydroxy barbituric acids, ethyldialuric and isoamyldialuric acids.

Upon intraperitoneal injection of aqueous solutions of the sodium salts of these barbituric acid derivatives into rats, the following results were obtained. Sodium diethylhydurilate, in a dose of 500 mg. per kg. caused no depression. Sodium diisoamylhydurilate, up to 200 mg. per kg., caused no depression, but caused death by circulatory failure in a dose of 500 mg. per kg. Sodium ethyldialurate and sodium isoamyldialurate caused no depression in doses as high as 2 g. per kg. The results of further pharmacological tests will be published in detail elsewhere.

It was first planned to prepare the 5,5′-disubstituted bibarbituric acids from a tetraethyl ester prepared by the reaction of a monobromo-monoalkyl-substituted malonic diethyl ester and the sodium salt of a monoalkyl-substituted malonic diethyl ester. This should permit the ultimate synthesis of unsymmetrical as well as symmetrical dialkyl bibarbituric acids. Two difficulties were encountered. First, the yield of the bimalonic tetraethyl ester was poor, 21 to 24% in the case of the symmetrical diethyltetracarbethoxyethane. This is in agreement with the work of Bischoff,[3] who obtained only a 17% yield of the same ester. Second, attempts to prepare diethylbibarbituric acid, 5,5′-diethylhydurilic acid, from the symmetrical diethyltetracarbethoxyethane by condensation with urea in the usual manner with sodium ethylate were unsuccessful; unchanged ester was recovered. Conrad and Bischoff[4] failed to condense symmetrical tetracarbethoxyethane with urea in the presence of phosphorus oxychloride or phosphorus pentachloride.

The oxidation of the 5-monosubstituted barbituric acids to form 5,5′-disubstituted hydurilic acids, reported by Aspelund,[5] appeared to offer the best method. The preparation of the 5-ethyldialuric and 5,5′-diethylhydurilic acids was repeated and two new compounds, 5-isoamyldialuric and 5,5′-diisoamylhydurilic acids were prepared. For characterization, a benzoyl derivative of the 5-isoamyldialuric acid was prepared and the acid was also hydrolyzed to the isoamyltartronic acid.

Experimental Part

5-Ethylbarbituric Acid.—This acid was prepared according to the method of Fischer and Dilthey as described by v. Merkatz.[6] Our product melted at 196–196.5°.[7]

5-Ethyldialuric Acid.—This acid was prepared according to the method of Aspelund[5] and melted at 224.5–225°.

5,5′-Diethylhydurilic Acid.—This acid was prepared according to the directions of Aspelund[5] and melted with decomposition at 328°. Aspelund reports that it melts above 310° with previous darkening and evolution of gas.

5-Isoamylbarbituric Acid.—This acid was prepared by the Fischer–Dilthey synthesis following Volwiler's[8] directions, and melted at 246–246.5°.

5-Isoamyldialuric Acid.—The preparation of this acid was carried out according to the method of Aspelund[5] with slight modifications. A mixture of 2.1 g. of monoisoamylbarbituric acid and 25 cc. of 3% hydrogen peroxide was refluxed for an hour. The crystals obtained on cooling weighed 1.57 g. when dry and melted at 179.5–180°. Concentration of the mother liquor to 5 cc. increased the yield by 0.46 g., m. p. 176.5°.

Twelve and seven-tenths grams of isoamylbarbituric acid was ground to a fine paste with a small amount of water and transferred to a 1-liter Erlenmeyer flask with 100 cc. of water. After adding 1.5 cc. of concentrated sulfuric acid, the barbituric acid was oxidized by the slow addition of 0.2 *N* potassium permanganate solution from a dropping funnel. The flask was well shaken during the addition

(1) Presented before the Division of Medicinal Chemistry at the meeting of the American Chemical Society, Boston, Massachusetts, September 12, 1939.

(2) Bleckwenn, *Arch. Neurol. Psychiatry*, **24**, 365–372 (1930).

(3) Bischoff, *Ber.*, **21**, 2085 (1888).

(4) Conrad and Bischoff, *Ann.*, **214**, 70 (1882).

(5) Aspelund, *J. prakt. Chem.*, **136**, 329–344 (1933).

(6) Von Merkatz, *Ber.*, **52**, 869 (1919).

(7) Stem corrections have been applied to all melting points recorded in this paper.

(8) Volwiler, THIS JOURNAL, **47**, 2239 (1925).

and heated from time to time to decolorize the permanganate. When 400 cc. had been used and the suspension in the flask was at the boiling point, the further addition was continued until the brown color no longer could be discharged by boiling. This required an additional 200 cc. together with 1 cc. of concentrated sulfuric acid. When the suspension was cool, the brown solid was collected on a Büchner funnel, well washed with water and dried; yield 8.4 g. The filtrate and washings were combined and concentrated to 50 cc. On cooling, crystals of crude isoamyldialuric acid were obtained; yield 4.4 g. The acid was purified by boiling an aqueous solution with norite, filtration and crystallization: yield 3.4 g., m. p. 179.5°. The melting point of a mixture of the isoamyldialuric acid obtained by this procedure with that obtained by the peroxide oxidation showed no depression.

Anal. Calcd. for $C_9H_{14}O_4N_2 \cdot 2H_2O$: H_2O, 14.40. Fonud: H_2O, 14.12. Calcd. for $C_9H_{14}O_4N_2$: C, 50.46; H, 6.59; N, 13.08. Found: C, 50.56; H, 6.36; N, 12.86.

Hydrolysis of 5-Isoamyldialuric Acid.—One-half gram of the acid was added to a solution of 2 g. of sodium hydroxide in 4 cc. of water. Foaming and vigorous evolution of ammonia resulted, and the flask was placed in a steam oven overnight. The residue was dissolved in water, the solution made acid to congo red paper with hydrochloric acid and extracted with ether. The ether extract was concentrated to a small volume, a few cc. of benzene added, and the solution boiled to remove the ether. On cooling, 0.22 g. of isoamyltartronic acid was obtained, which melted with evolution of gas at 134.5°. The melting point of a mixture of this acid and isoamyltartronic acid prepared by the hydrolysis of bromo-isoamylmalonic diethyl ester, method of Braun and Nelles,[9] showed no depression.

5-Benzoyl-5-isoamyldialuric Acid.—One-half gram of 5-isoamyldialuric acid was added to 5 cc. of benzoyl chloride and the mixture was heated slowly to 200–210° in an oil-bath. Solution was almost immediate, followed by gradual evolution of hydrogen chloride. On cooling, crystals were obtained by scratching the walls of the flask with a stirring-rod. The reaction mixture was transferred to a centrifuge tube with ligroin and the crystals were washed several times with this solvent. The slightly brown crystals were dissolved in alcohol, boiled with norite, filtered, and the filtrate diluted with water. After standing for several days the crystals which formed were collected; yield 0.5 g. and m. p. 210.5–216°.

Anal. Calcd. for $C_{16}H_{18}O_6N_2$: N, 8.80. Found: N, 8.88.

5,5′-Diisoamylhydurilic Acid.—This acid which was present in the insoluble residue from the preparation of 5-isoamyldialuric acid by the permanganate method was dissolved in acetone and filtered from the manganese oxide. The acetone was diluted with water and the crystals which formed on standing were collected and air-dried; yield 5.3 g. The acid darkened and melted with decomposition at 290°.

Anal. Calcd. for $C_{18}H_{26}O_6N_4 \cdot 2H_2O$: H_2O, 8.37. Found: H_2O, 8.34. Calcd. for $C_{18}H_{26}O_6N_4$: C, 54.81; H, 6.65; N, 14.21. Found: C, 54.82; H, 6.52; N, 14.06.

We wish to thank Dr. Carl Pfeiffer for the pharmacological testing of our compounds, and Dr. H. A. Shonle, of Eli Lilly and Company, for the gift of certain chemicals which were used in the course of this work.

Summary

A new bibarbituric acid derivative, 5,5′-diisoamylhydurilic acid, and a new 5-hydroxybarbituric acid, isoamyldialuric acid, have been prepared. Solutions of the sodium salts of these compounds and of the corresponding ethyl compounds have no appreciable effect when injected into rats.

CHICAGO, ILLINOIS RECEIVED JUNE 9, 1939

(9) Braun and Nelles, *Ber.*, **66B**, 1466 (1933).

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF THE GENERAL ELECTRIC CO.]

Vapor Pressures and Accommodation Coefficients of Four Non-Volatile Compounds. The Vapor Pressure of Tri-*m*-cresyl Phosphate over Polyvinyl Chloride Plastics

BY FRANK H. VERHOEK AND A. L. MARSHALL

The vapor pressures and accommodation coefficients of the non-volatile organic compounds useful as plasticizers are data of fundamental importance in interpreting the losses of plasticizers which occur from plastics under certain conditions. Such data are given below for pure samples of di-*n*-butyl phthalate, tri-*m*-cresyl phosphate, tri-*p*-cresyl phosphate, and dibenzyl sebacate. The experimental methods employed were: measurements of the rate of effusion of saturated vapor through various tubes and through a small hole in a thin plate; measurements of the rate of evaporation from a free surface; measurements of the vapor pressure by a static method similar to that of Hickman, Hecker and Embree.[1] The vapor pressures of tri-*m*-cresyl phosphate over polyvinyl chloride plastics in which it served as plasticizer were determined by the static method.

(1) Hickman, Hecker and Embree, *Ind. Eng. Chem., Anal. Ed.*, **9**, 264 (1937).

Experimental Details

Method I. (Figs. 1 and 1a.)—The saturated vapor effused through the Fernico tube T (length 2.00 cm., diameter 0.498 cm.). The apparatus was immersed up to the vacuum side-arm in a constant-temperature bath.

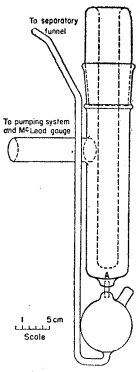


Fig. 1.

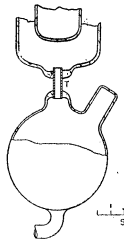


Fig. 1a.

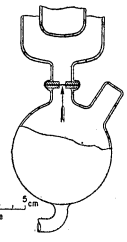


Fig. 2.

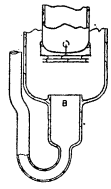


Fig. 3.

After the bath had been heated to a temperature in the region where measurements were to be made, the apparatus was evacuated, liquid air was placed in the condensing tube and the liquid (whose flow was controlled by the stopcock of a separatory funnel) was run slowly into the 300-cc. reservoir bulb. When the bulb was one-third full, giving an evaporating surface about 30 sq. cm. in area, the separatory funnel was sealed off below the stopcock. After further evacuation to remove any residual air that may have remained in the liquid, the vacuum was broken behind the liquid air trap and the liquid air sucked out of the condensing tube. When the latter had come to room temperature it was removed, washed with ether and replaced. The apparatus was then quickly exhausted; when the pressure had fallen below 10 microns, the condensing tube was refilled with liquid air, the time of this filling being taken as zero time for the experiment. When effusion had proceeded long enough for a suitable quantity of vapor—usually about 30 mg.—to condense on the liquid air tube, the experiment was stopped by breaking the vacuum. The condensate was then washed into a weighed platinum dish with 15–20 cc. of ether, which subsequently was evaporated so that the weight of condensate could be determined. Three or more experiments were made at each temperature and the average taken in calculating the vapor pressure; individual experiments agreed with each other to within 2 or 3%. The temperatures of the individual experiments conformed to no sequence; the last experiment on each substance was always carried out at the temperature of the first; these measures were taken to detect any change in the nature of the material under investigation. No evidence of any such change was observed with the four compounds in question. In certain cases, the reproducibility of the method was tested by making duplicate runs on separate charges of material; these results, which are in satisfactory agreement, are given under Method I, in Columns A and B of the tables below. The refractive index of the distillate was the same as that of the liquid being studied and in the case of tri-*m*-cresyl phosphate the distillate gave the correct percentage of phosphorus by analysis.

Method I'.—In the hope of measuring the rate of evaporation from a free surface, the Fernico tube and reservoir bulb in the above apparatus were replaced by a glass tube, 2.24 cm. in diameter, joined at A in Fig. 1. The smaller tube was filled to within a few centimeters of its top, and measurements were carried out as in Method I. Metal disks attached to the condensing tube (*cf.* Fig. 3) were used to minimize radiation losses from the surface of the liquid. (An attempt to reduce these losses by replacing the liquid air with 15° water had to be abandoned because of incomplete condensation.) Identical experimental results were obtained with the following systems of baffles, connected so as to make heat flow as difficult as possible: 7 nickel disks, 0.013 cm. thick; 3 such disks; and 3 disks with a nickel oxide or a silver surface facing the liquid.

The rates of evaporation measured in this apparatus increased as the level of the material approached A (Fig. 1), indicating that the 2.24-cm. tube was narrow enough to reduce the rate of evaporation to a value below that for a free surface.

A new apparatus (Fig. 3) was then constructed in which the position of the liquid meniscus could be accurately measured with a cathetometer in order to establish the length of narrow tube through which the vapor was effusing. The tube B (diameter 2.133 cm.) extends about 1 cm. into the larger tube, has its top carefully ground level, was sealed in without being distorted, and bears a reference mark to facilitate the cathetometer measurements. The baffle system consists of 3 nickel disks, 0.013 cm. thick.

Method II. (Fig. 3.)—The rate of evaporation from a free surface was measured directly by raising the level of the liquid to the top of B.

Method III. (Fig. 2.)—The rate of effusion of saturated vapor through a circular hole (diameter 0.1078 cm.) in a nickel disk 0.013 cm. thick held in a Fernico seal was measured. The diameter of the hole was measured after the seal had been made by projecting the image of the hole and a millimeter scale on a large screen.

Method IV. (Fig. 4.)—A static method can yield reliable vapor pressure results for substances (*e. g.*, plastics) for which dynamic methods may involve undesired changes in composition during the measurements. The apparatus of Hickman, Hecker and Embree[1] was modified by the addition of the condensing tube C (filled with liquid air) intended to eliminate possible back pressure on the disk D, and by the addition of a platinum resistance heater at 0. One or two watts output by the heater for a few minutes drove any material condensed near 0 back into the boiler; the presence of the condensate did not affect the experimental results, but it did introduce the hazard of having D held to the glass by the surface tension of the liquid. The vapor pressure is measured by turning the entire apparatus through an angle θ that will just suffice to close the orifice. To measure θ, the turning motion was carried through a worm gear to a disk 15.0 cm. in diameter divided on its circumference into 216 divisions, each of which corresponded to a deflection of one minute of arc. Consecutive readings at a given temperature could easily be reproduced to within one minute of arc. The pendulum consists of a duralumin disk D, 0.013 cm. thick, suspended by means of duralumin wire, 0.05 cm. in diame-

ter, from a shaft riding in jeweled bearings. The circular corrugation (dd′, Fig. 4) in the disk serves to stiffen and hold it perfectly flat. The effective weight of the assembled pendulum, carefully determined on an analytical balance, was 0.787 g. The vapor pressure is obviously given by

$$P \text{ (microns)} = \frac{0.787 \sin\theta}{0.00136(1.567)^2\pi} \qquad (1)$$

where the factor 0.00136 converts the pressure from grams per square centimeter into microns, and 1.567 cm. is the radius of the orifice at 0. The results of duplicate measurements on the same materials are given under Method IV, Columns A, B and C in the tables.

Materials.—A colorless sample of tri-*m*-cresyl phosphate was obtained from the Celluloid Corporation, and a slightly yellowish one from the Eastman Kodak Company. Neither sample was treated further.

The tri-*p*-cresyl phosphate was a Celluloid Corporation product melting at 76.4–76.7° (stem correction included). Five recrystallizations from a five-to-one mixture of absolute ethanol and water did not change this melting point, and made only a slight difference in the shape of the cooling curve.

The dibutyl phthalate was purified by vacuum distillation through a 1.25-meter column. The middle fraction, which was used, was colorless, neutral, with the theoretical saponification value, and $n^{20}D$ equal to 1.4933. Further distillation did not change the refractive index.

The dibenzyl sebacate was prepared and carefully purified in this Laboratory by Burnett and Russell.[1a]

The plastics were prepared by weighing out the required quantities of polyvinyl chloride and the Celluloid Corporation tri-*m*-cresyl phosphate, mixing by milling at 100°, and pressing into a thin sheet at 500 lb./sq. in. (33 atm.) for five minutes at 140°. Loss in the milling and pressing operations amounted to 0.2–0.4%. The pressed sheets were cut into strips weighing from 7 to 10 g., on which the measurements were made.

Calculations for the Dynamic Methods.—The number of molecules per second, Z, colliding with (hence entering) a uniform circular tube of radius a is

$$Z = a^2 p N \sqrt{\pi/2RTM} \qquad (2)$$

where p is the pressure; N, R and T have their usual meanings; M is the molecular weight; and c. g. s. units are employed. The experimental results give the rates of effusion, Q, in grams/sec., through tubes of varying length, when the pressure is equal to the vapor pressure of the liquid at one end and virtually zero at the other. To obtain the rate at which matter will leave such a tube, Z must be multiplied by the weight of a molecule and by the probability, W, that a molecule entering the tube will leave it; or

$$Q = WZM/N = Wa^2P\sqrt{M\pi/2RT} \qquad (3)$$

For a hole in an infinitely thin sheet, W is equal

(1a) Burnett and Russell, THIS JOURNAL, **61**, 2246 (1939).

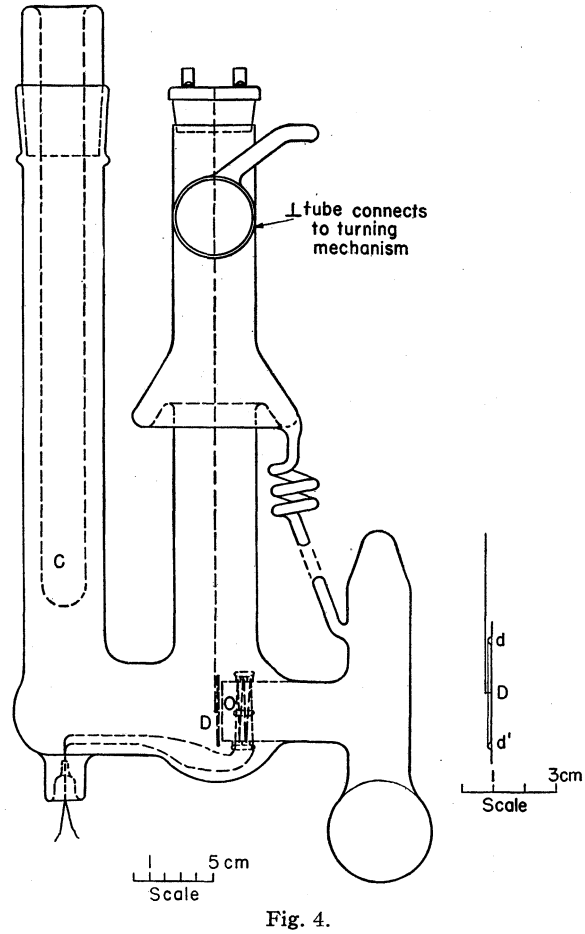


Fig. 4.

to unity; for a cylindrical tube with perfectly diffusing walls of length l such that $l \gg a$, at pressures such that the mean free path is much larger than the diameter of the tube, W equals $8a/3l$. For cylindrical tubes of intermediate length, Clausing[2] gives a table of values of W for various values of l/a, which represent close approximations that he made because he was unsuccessful in deriving an accurate expression for W in terms of known functions. The values of W used in calculating our values were obtained when necessary by interpolating in this table; for example, when $l/a = 8.025$ (Method I), $W = 0.2310$ so that

$$p = \frac{Q}{0.2310\, a^2}\sqrt{\frac{2RT}{\pi M}} \qquad (4)$$

In the actual calculations, $R = 83.15(10^6)$ ergs/degree was used, and the right-hand side of Eq. 4 was multiplied by 0.75 to give the pressures in microns.

For Method I′, W was obtained as for Method I. For Method II, W is obviously unity, and the

(2) Clausing, *Ann. Physik*, **12**, 961 (1932).

TABLE I

THE VAPOR PRESSURE OF TRI-*m*-CRESYL PHOSPHATE

a. Celluloid Corporation Samples

Vapor pressure in microns

	Method I		Method I′		Method II	Method IV		
l/a	8.035	8.035	2.850	1.669				
	A	B				A	B	C
T, °C.	⊙	⊘	⊡	⊠	⊗	△	▽	▷
80.0			0.0459	0.0453	0.0387			
90.0	0.133							
100.2	.346							
109.9		0.925						
110.5	.957							
114.0						1.59	1.56	1.60
119.0						2.42		
120.0		2.36						
120.7	2.37							
124.0						3.69	3.78	
125.9	3.82							
128.8						5.54		
129.0							5.89	5.83
130.0		5.83						
131.0	6.07							
136.2	10.14							

b. Eastman Kodak Company Sample

Temp., °C.	85.2	95.4	105.6	115.8	126.0
p, microns	0.0993	0.250	0.562	1.33	3.36

Method I was used. $l/a = 8.035$.

pressures were calculated on the assumption that the area of the liquid surface was equal to the cross-sectional area of B (Fig. 3). For Method III, W is unity and a is the area of the hole in the nickel disk.

In all these calculations, an accommodation coefficient of unity is assumed.

Results and Discussion

The Pure Substances.—The detailed results for the pure substances are given in Tables I–IV and in Fig. 5, in which the values of Hickman, Hecker and Embree[1] for dibutyl phthalate have also been plotted. The constants derived from these detailed results are given in Table V. With a single exception, there is no systematic departure from the straight lines in Fig. 5 for any one method of measurement on any one sample. The exception, tri-*p*-cresyl phosphate, shows results by method IV that are definitely larger than those by method I; a slight decomposition of the material to give volatile products is one reasonable explanation of this discrepancy. Our failure to check the measurements of Hickman, Hecker and Embree exactly is not surprising in view of the differences which we found in the vapor pressures of the tri-*m*-cresyl phosphates from two different sources.

TABLE II

THE VAPOR PRESSURE OF TRI-*p*-CRESYL PHOSPHATE

Vapor pressure in microns

	Method I	Method IV	
l/a	8.035	A	B
T, °C.	⊙	△	▽
92.0	0.0848		
100.0	.200		
110.0	.490		
119.0		1.35	1.42
123.5			2.11
124.0		2.12	
125.0	1.87		
129.0		3.31	3.36
134.0		5.01	
134.5			5.22
135.0	4.50		
145.0	11.7		

TABLE III

VAPOR PRESSURE OF DIBUTYL PHTHALATE

Vapor pressure in microns

	Method I		Method I′	Method III	Method IV
l/a	8.035	8.035	2.765		
	A	B			
T, °C.	⊙	⊘	⊡	●	△
40.0			0.167		
55.0	1.03	0.816			
59.7					1.78
64.7					2.95
65.0	3.07				
69.7					4.59
70.0	4.51				
74.6					7.36
75.0	8.07			6.78	
85.0	21.6	18.9		18.9	
95.0				45.3	

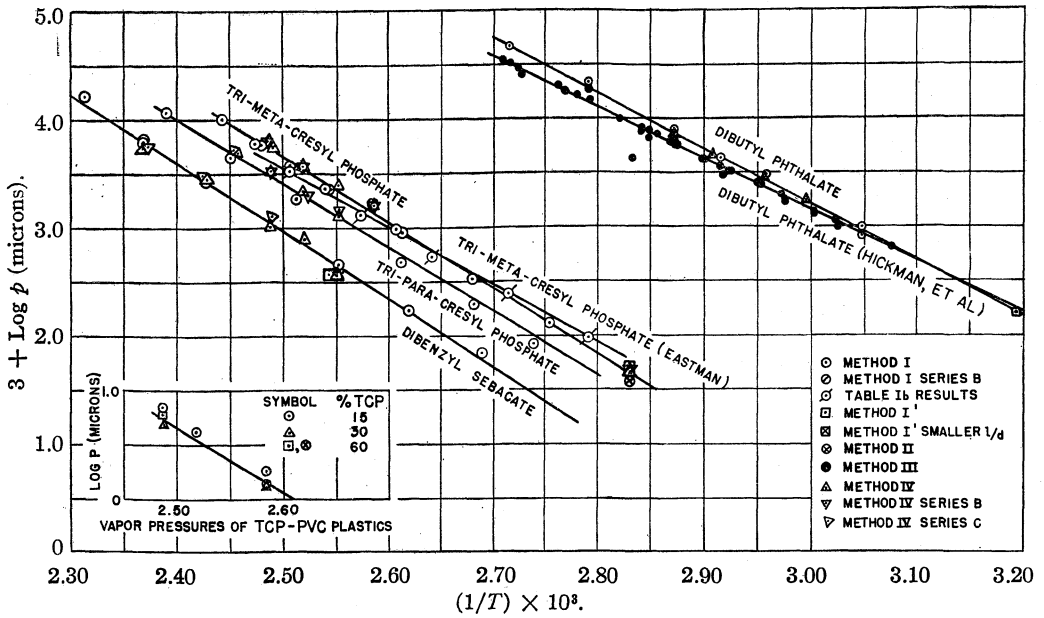


Fig. 5.—Vapor pressures of plasticizers.

TABLE IV

VAPOR PRESSURE OF DIBENZYL SEBACATE

	Vapor pressure in microns				
	Method I		Method I'	Method IV	
l/a	8.035	8.035	2.653		
	A	B		A	B
T, °C.	⊙	⊘	⊡	△	▷
99.0	0.0679				
100.0			0.0552		
109.0	.169				
118.9				0.365	
119.0	.451	0.398			
120.0			.366		
124.0					0.792
129.0	1.05			1.03	1.21
139.0	2.56			2.67	2.75
148.7					5.71
149.1	6.48	5.90		5.69	
159.1	16.6				

TABLE V

DERIVED CONSTANTS FOR THE PURE SUBSTANCES

	A	B	L	Observer or source of material
Tri-*m*-cresyl phosphate	6088	15.886	27,850	Celluloid Corp.
	5373	13.982	24,580	Eastman
Tri-*p*-cresyl phosphate	5926	15.223	27,110	
Dibutyl phthalate	5122	15.589	23,440	Verhoek and Marshall
	4680	14.215	21,400	Hickman, Hecker and Embree
Dibenzyl sebacate	6320	15.775	28,910	

$$\log p \text{ (microns)} = -(A/T) + B \quad L = 4.575\,A.$$

That the *accommodation coefficients* for all four substances are unity is shown by the agreement of the Method I′ results with the others. If a vapor pressure is calculated from a rate of evaporation into a vacuum (Method I′) on the assumption that the accommodation coefficient is unity, this calculated pressure will be less than the true pressure (as measured, for example, by Method III or IV) if a fractional accommodation coefficient exists.[3] Our results indicate that the accommodation coefficients will always be unity for substances of the type studied here.

Although it is true that the vapor pressure calculated from the rate of evaporation from a free surface (Method II) is somewhat lower than the others, this small discrepancy probably does not indicate the existence of a fractional accommodation coefficient. A difference of 1.1° between the temperature of the bath and the temperature of the liquid at the surface of Tube B, Fig. 3, is sufficient to account for the lower vapor pressure obtained by Method II. Since the apparatus is so constructed that the heat lost from the surface by evaporation is not readily replaced, such a temperature difference may well have existed.

The Plastics.—The static vapor pressures obtained by Method IV on three different polyvinyl chloride–tri-*m*-cresyl phosphate plastics are summarized in Table VI and plotted in Fig. 5. The values of θ could not be determined as accurately here as for the pure substances because the disk closing the orifice continued to vibrate. This vibration, which could not be eliminated by prolonged evacuation at the temperatures of the

(3) *Cf.* Langmuir, *Phys. Rev.*, **11**, 329 (1913), or Knudsen, *Ann. Physik*, **47**, 697 (1915).

measurements, might have been caused either by a continued liberation of air occluded in the sample or by the steady production of a volatile decomposition product in small amount (that a slight decomposition did occur was indicated by a gradual darkening of the sample). This explanation gains in plausibility from the fact that the measured vapor pressures for two of the plastics exceed somewhat the vapor pressure of the pure plasticizer.

TABLE VI

VAPOR PRESSURES OF POLYVINYL CHLORIDE–TRI-*m*-CRESYL PHOSPHATE PLASTICS

% polyviny chloride.....	0[a]	40	40	70	85
T, °C.					
114	1.44	1.38	1.68	1.37	1.79
119	2.29				3.17
124	3.59		4.19		4.17
129	5.57		6.02	4.97	7.02

[a] Calculated values (*cf.* Table V).

It seems reasonable to conclude that the vapor pressure of the plasticizer in these plastics is independent of concentration over the range 15–100% plasticizer. More results will be needed with other plasticizers to confirm this conclusion. It is possible that the quantity being measured in these experiments is the vapor pressure of a film of plasticizer on the surface of the plastics. Since the slope of the vapor pressure curve and also its absolute position is the same for the plastics and the pure plasticizer, it may be concluded from this type of experimentation that the heat involved on mixing polyvinyl chloride and tricresyl phosphate is practically zero. To confirm this conclusion it would be desirable to carry out calorimetric experiments on the heat of wetting at elevated temperatures of polyvinyl chloride by several plasticizers.

Summary

The vapor pressures of tri-*m*-cresyl phosphate, tri-*p*-cresyl phosphate, dibutyl phthalate and dibenzyl sebacate in the neighborhood of 100° have been measured by a static and by dynamic methods.

The accommodation coefficients for these liquids are unity.

The vapor pressure of the plasticizer in a polyvinyl chloride–tri-*m*-cresyl phosphate plastic containing at least 15% of the latter appears to be equal to the vapor pressure of the pure plasticizer and is independent of the composition of the plastic.

SCHENECTADY, N. Y. RECEIVED JUNE 21, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY, UNIVERSITY OF MISSOURI, AND THE NEW MEXICO NORMAL UNIVERSITY]

Pied des Monts Uraninite

BY O. B. MUENCH

A fine specimen of uraninite was collected from the Lac Pied des Monts district in Quebec and given to Mr. H. S. Spence,[1] who sent it by way of Dr. A. C. Lane[2] to the writer for an age determination by the lead–uranium method and for the extraction and preservation of the lead for an isotopic determination to be made later by A. O. Nier at Harvard University. This material is of interest since considerable work has been done by Ellsworth[3] on samples from this district. He gives a description of the geological occurrence of minerals in this district, accompanied by a complete chemical analysis and age determination. Another interesting account of the location, with references, is given in *Le Naturaliste Canadien*.[4] Material from this location has been called cleveite[5] by some, but Ellsworth,[3] Berman,[6] and others prefer the term uraninite for this mineral.

The surface of the mineral did not show any indication or sign of secondary uranium minerals. Before beginning the analysis, several autoradiographs were made of various pieces of the specimen on different smoothly ground surfaces. Some sections were cut through the middle and autoradiographs made of these. The prints seem to in-

(1) Mining Engineer, Mines Branch, Department of Mines, Canada.

(2) Chairman of the "Committee on the Measurement of Geologic Time."

(3) Report of the Committee on the Measurement of Geologic Time, 1934; *Am. Min.*, **19**, 421–425 (1934).

(4) Carl Faessler, "La Cote Nord," *Le Naturaliste Canadien*, April, 1932, pp. 100–102.

(5) *J. Can. Min. Inst.*, **7**, 245–256 (1904). Obalski first mentioned the location and found the large crystal from which Ellsworth determined the lead ratio on a small sample.

(6) Dr. Berman of the Harvard Department of Mineralogy in a private communication to Professor A. C. Lane.

dicate a fairly uniform distribution of radioactive material and no visible evidence of leaching.

Analysis

The sample was broken into smaller pieces in a clean iron mortar and then finely powdered in a clean agate mortar to pass a 100-mesh sieve. The precautions necessary to this type of analysis were observed carefully to avoid contamination. Special precautions were taken in this respect with the lead. Pure analytical reagents were used, and these were purified further where the accuracy of the analysis depended upon it.

The sample was decomposed in nitric acid and the silica removed in the usual way. The lead, after separation and purification, was weighed as the sulfate. Recoveries for lead were made on all filtrates and from the silica.

The uranium was determined as the pyrophosphate,[7] which method is described in detail in previous papers.

Four five-gram samples were run for thorium by the iodate method, which also is described in previous papers.[7,8] The very small, hardly weighable residue carried some of the rare earths in the form of oxides as indicated by the pale yellow color.

TABLE I

RESULTS

Lead

Sample, g.	$PbSO_4$, g.	Lead, %
1.0005	0.0975	6.655
1.0024	.0979	6.675
1.0016	.0981	6.689
1.0020	.0978	6.666
1.0000	.0976	6.666
	Average	6.670

Uranium

Sample, g.	$(UO_2)_2P_2O_7$, g.	Uranium, %
0.2025	0.1495	49.22
.2016	.1488	49.23
.2027	.1498	49.29
.2013	.1487	49.27
	Average	49.25

Thorium

Four separate five gram samples quantitatively gave only a slight indication of thorium. Rare earths were present. 0.0% Thorium.

Loss on ignition	12.07%
Loss at 100° for four hours	0.41%

The lead-uranium ratio is 6.67/49.25 = 0.135.

The age of this mineral, calculated from the above figures, and using the logarithmic formula of Holmes,[9] is

$$\frac{\log (U + 0.36Th + 1.155Pb) - \log (U + 0.36Th)}{6.6 \times 10^{-5}} \text{ million years} = 956 \text{ million years.}$$

The lead sulfate from the lead determination was saved and sent to Alfred O. Nier at Harvard University for the isotopic determination. His analysis[10] has direct reference to this paper, and is of special interest in this age determination since it gives the figures for the isotopic composition of the lead which was used in this determination. The following is from his paper, with 206 taken as 100 in the proportion of isotopes

Pb	204	206	207	208
	0.047 ± 5%	100	7.60	1.92 ± 2%

Mass number	Physical atomic weight
206.103 ±0.002	206.078

Ac D/Ra G %	Pb/U	Ra G/U^{238}
6.88	0.1354	0.1233

Age, accordingly in million years: 903 by Ac D/Ra G
882 by Ra G/U^{238}

Calculation from the lead–uranium ratio without taking into consideration the isotopic composition of the lead yields an age of 956 million years.

The results of Nier's isotopic analysis of the lead from this sample indicate that about 4% of the lead is common lead. Correcting the lead percentage for this amount of common lead, changes the lead figure from 6.67 to 6.40%. This correction alters the lead–uranium ratio to 0.130. The corresponding age calculated by the logarithmic formula is 920 million years, which is nearer to Nier's ages determined by different methods.

Nier in his paper[10] has pointed out the fact that uranium rather than lead is usually lost whenever alteration takes place in a uranium mineral, thus making the lead–uranium ratio too high, whereas the age computed from Pb^{207}/Pb^{206} ratio hardly differs from the true age of the mineral.

Acknowledgments.—The author is indebted to the Geological Society of America for financial assistance in part, for this work; to Professor A. C. Lane for his constant inspiration and encouragement; to Mr. H. S. Spence for the mineral; and to the late Dr. Herman Schlundt and the University of Missouri for the generous use of laboratories, chemicals, and other facilities.

(7) Muench, THIS JOURNAL, **59**, 2269 (1937).

(8) Method of Meyer and Speter as given by Hillebrand and Lundell, "Applied Inorganic Analysis," John Wiley and Sons, Inc., New York, N. Y., 1929, p. 420.

(9) A. Holmes, National Research Council, Washington, Bull. 80, 207 (1931).

(10) A. O. Nier, *Phys. Rev.*, **55**, 158–159 (1939).

Summary

The lead–uranium ratio of a uraninite from Lac Pied des Monts, Quebec, was determined as 0.135. The analytical results show 6.67% lead, 49.25% uranium, and a trace of thorium.

An isotopic determination on the lead obtained from this analysis was made by A. O. Nier at Harvard University. With these results available, the age of the Lac Pied des Monts uraninite can now be given with greater assurance and accuracy. Corrections for common lead made from Nier's determination change the percentage to 6.40 and the lead–uranium ratio to 0.130. The age of the mineral, calculated with these corrected figures, is 920 million years and compares favorably with the results calculated from the isotopic determination of the lead from this sample.

Two independent age determinations made by entirely different methods on the same specimen yield results in fairly good agreement.

LAS VEGAS, N. M. RECEIVED MAY 22, 1939

[CONTRIBUTION OF THE DEPARTMENT OF CHEMISTRY OF THE OHIO STATE UNIVERSITY]

The Solubility of Mercuric Halides in Solutions of Potassium Halides. The Character of the Mercuric Halide Complex Ions. Evidence for Polymerization of Mercuric Chloride

BY A. B. GARRETT

The purpose of this paper is to present measurements of the solubility of mercuric halides in halide solutions and to calculate the equilibrium constants for the reactions involved in the formation of the complex mercuric halide ions; the values of these constants should indicate the character of the complex ions of mercury in the solutions studied.

The moderately low solubility of mercuric bromide and mercuric iodide makes possible a fairly direct determination of the character of the complex ions of these mercuric halides by means of solubility measurements. Additional information essential to this determination are these facts: (1) earlier work[1-6] has shown that the mercury halides are only slightly dissociated and (2) their solubility in halide solutions is predominantly specific to the concentration of the halide ion and not to the ionic strength. These facts make it possible to attribute the solubility of mercuric halides in halide solutions mainly to several or to all of the following reactions (using the bromide as an example)[7]

$$HgBr_2(\text{solid}) = HgBr_2(\text{solution}) \quad (1)$$

$$HgBr_2 + Br^- = HgBr_3^- \quad (2)$$

$$HgBr_2 + 2Br^- = HgBr_4^= \quad (3)$$

The data necessary are those in low concentrations where one might reliably expect the limiting law to be applicable. Only a meager amount of such data is available from early work.[1-6]

Early work is at variance with respect to definite conclusions concerning the character of these halide ions. A number of workers[3,8-10] have claimed the formation $HgCl_3^-$, $HgBr_3^-$ or HgI_3^- whereas others[11-13] submit evidence for the $HgI_4^=$ ion. Job[11] claims the presence of $KHgCl_3$, K_2HgBr_4 and K_2HgI_4 in their respective solutions. Sherrill[4] even gives data on the ionization constants for all of these salts, *i. e.*, $KHgI_3$, K_2HgI_4, $KHgBr_3$, K_2HgBr_4, etc. Tananaev and Pilipenko[13] assumed the near 2 to 1 ratio of added potassium iodide to mercuric iodide indicated the formation of $HgI_4^=$ predominantly.

Procedure.—Baker C. P. quality and Mallinckrodt Analytical Reagent mercuric bromide and mercuric iodide were used. For a number of preparations the mercuric bromide was recrystallized from hydrobromic acid solution and heated at 115° for four hours to assure complete removal of any hydrogen bromide. The same procedure was followed with the mercuric iodide but the recrystallization was omitted.

Baker Analytical Reagent potassium bromide and potassium iodide were used.

(1) Thomas, THIS JOURNAL, **61**, 920 (1939). This paper contains a very good bibliography on the mercuric chloride–chloride system.

(2) Herz and Paul, *Z. anorg. Chem.*, **82**, 431 (1913).

(3) Abegg (with Immerwahr and Jander), *Z. Elektrochem.*, **8**, 689 (1902); (with Sherrill) **9**, 550 (1903).

(4) Sherrill, *Z. physik. Chem.*, **43**, 727 (1903).

(5) Le Blanc and Noyes, *ibid.*, **6**, 389 (1890).

(6) Richards and Archibald, *ibid.*, **40**, 385 (1902).

(7) See latter section of this paper for additional equilibria that may exist in the $HgCl_2$–Cl system.

(8) Naude, *Z. physik. Chem.*, **125**, 98 (1927).

(9) Pernot, *Compt. rend.*, **185**, 950 (1927); *Ann. chim.*, [10] **15**, 5 (1931).

(10) Dunningham, *Proc. Chem. Soc.*, **30**, 8 (1914); *J. Chem. Soc.*, **105**, 368 (1914).

(11) Job, *Ann. chim.*, **9**, 113 (1928), from light absorption studies.

(12) Golse, *Compt. rend.*, **190**, 873 (1930), from studies on the equilibrium $AgNO_3 + HgI_2 + KI$.

(13) Tananaev and Pilipenko, *J. Applied Chem.* (U. S. S. R.), **10**, 549 (1937).

All work was done in conductivity water which was boiled free of oxygen, in an atmosphere of nitrogen, and at 25 ± 0.02°. Equilibrium was approached from undersaturation (u) and supersaturation (s). An equilibrium period of three days was established by the close approach of the (u) and (s) values. The data given are averages of these two values.

The samples were analyzed by precipitating the mercury as the sulfide. The halide content was determined by preparing the samples in standard halide solutions.

The *p*H of a number of the samples was measured with a glass electrode.

The Data

The data are given in Tables I to III. All values are expressed in moles per 1000 g. of water.

The water solubility was reinvestigated for the bromide since it is a critical value in the later treatment of the data. During this investigation it was revealed that repeated, careful washing was not enough to remove the impurity of hydrobromic acid. It seems only to be removed by oven drying and heating. The comparison of the data in Table I shows the consistent results obtained by such treatment and agree with values in the literature. Samples not receiving such treatment varied from 1.84×10^{-2} to 2.01×10^{-2} mole per 1000 g. of water.

TABLE I

WATER SOLUBILITY OF MERCURIC BROMIDE

	Moles of $HgBr_2$ per 1000 g. water
Baker C. P.	0.0167^s
Analyzed heated	$.0167^u$
four hours	$.0169^s$
at 115°	$.0171^u$
Average	0.0168_5
Baker C. P. Analyzed	0.0171^s
recrystallized from hydro-	$.0170^u$
bromic acid solution and	$.0170^s$
heated four hours at 115°	$.0170^u$
Average	0.0170
Best value	.0170
Other workers[a]	.0170

[a] Moles and Marquina, *Anales soc. españ. fís. quím.*, **22**, 551 (1924); Sherrill, ref. 4; Jander, ref. 3.

TABLE II

Moles KBr per 1000 g. H_2O	Moles $HgBr_2$ per 1000 g. H_2O	Moles KBr per 1000 g. H_2O	Moles $HgBr_2$ per 1000 g. H_2O
0.003006	1.86×10^{-2}	0.0607	5.85×10^{-2}
.00506	2.05	.0712	6.42
.00506	2.05	.0917	7.64
.00709	2.17	.1022	8.36
.01011	2.44	.155	11.78
.01011	2.32	.319	22.3
.01512	2.63	.417	28.7
.02024	2.95	.642	43.8
.0303	3.71	.868	58.6
.405	4.28	1.006	67.3

TABLE III

Moles per KI per 1000 g. water	Moles of HgI_2 per 1000 g. water
0.00400	1.50×10^{-3}
.01011	3.87×10^{-3}
.01011	3.71×10^{-3}
.0202	8.22×10^{-3}
.0403	1.78×10^{-2}
.0705	3.15×10^{-2}
.1020	4.70×10^{-2}
.3128	1.53×10^{-1}
.539	2.72×10^{-1}
.795	4.09×10^{-1}
1.131	5.86×10^{-1}
1.161	6.10×10^{-1}

Water solubility:
1.3×10^{-4} mole/kg. H_2O Morse, *Z. physik. Chem.*, **41**, 731 (1902).
1.32×10^{-4} mole/kg. H_2O Tananaev and Pilipenko, ref. 13.

Tables IV and V give smooth data taken from a large scale graph. Column 3 of these tables gives the amount of the complex ion present at a given concentration of potassium halide. The value is obtained by assuming that the amount of complex ion equals the total mercury content minus the water solubility (equation 1). Column 4 of Tables IV and V gives the concentration of halide ion in solution calculated on the assumption that

TABLE IV

M_{KBr}	$M_{mercury}$	$M_{complex}$	M_{Br^-}	$K_2 = M_{complex}/M_{Br^-}$
0.000	0.0170			
.001	.0176			
.002	.0183	0.0013	0.0007	1.85
.004	.0196	.0026	.0014	1.85
.006	.0209	.0039	.0021	1.85
.008	.0222	.0052	.0028	1.86
.01	.0235	.0065	.0035	1.86
.03	.03650	.0195	.0105	1.85
.08	.0692	.0522	.0278	1.87
.10	.0825	.0655	.0345	1.89
.3	.213	.196	.104	1.88
.8	.543	.526	.274	1.91
1.0	.672	.655	.345	1.90

TABLE V

M_{KI}	$M_{mercury}$	$M_{complex}$	M_{I^-}	$K_2 = M_{complex}/M_{I^-}$
0.00	1.32×10^{-4}			
.01	3.79×10^{-3}	3.66×10^{-3}	6.34×10^{-3}	0.577
.04	1.65×10^{-2}	1.64×10^{-2}	2.36×10^{-2}	.694
.07	3.05×10^{-2}	3.04×10^{-2}	3.96×10^{-2}	.767
.1	4.60×10^{-2}	4.59×10^{-2}	5.41×10^{-2}	.848
.2	9.60×10^{-2}	9.59×10^{-2}	1.04×10^{-1}	.922
.4	2.00×10^{-1}	2.00×10^{-1}	2.00×10^{-1}	1.00
.6	3.05×10^{-1}	3.05×10^{-1}	2.95×10^{-1}	1.03
.8	4.10×10^{-1}	4.10×10^{-1}	3.90×10^{-1}	1.05
1.0	5.16×10^{-1}	5.16×10^{-1}	4.84×10^{-1}	1.07

the solubility of the mercuric halide can be accounted for by equations (1) and (2) only. Column 5 of Tables IV and V gives the ratio Hg complex/halide ion or in other words the equilibrium constant for equation (2) calculated on the assumption that equations (1) and (2) represent the only reactions taking place. The near constancy of the value of K_2 for the bromide suggests that the $HgBr_3^-$ ion is the main ion formed with the possibility of only a very small amount of the $HgBr_4^=$ ion. However, the value of K_2 for the iodide varies considerably, thus indicating that an additional reaction probably is present, namely, that represented by equation 3.

The calculation of K_2 is made quite accurately from the relationship

$$K_2 = \frac{m_{\text{Hg complex}^-}\gamma_{\text{Hg complex}^-}}{m_{\text{Br}^-}\gamma_{\text{Br}^-}}$$

and upon the reasonable assumption that the ratio $\gamma_{\text{Hg complex}^-}/\gamma_{\text{Br}^-}$ is unity throughout this range of concentrations.

The small variation in the value of K_2 (1.85 to 1.91) for mercuric bromide from 0.002 to 1 molal hardly justifies the calculation of the value of K_3 for reaction (equation(3)). Choosing the value of 1.85 as the most reliable value for K_2 as determined from low concentration measurements the value of ΔF_{298} is -365 cal. for equation (2).[14]

The variation in the value of K_2 for the iodide and the less than 2 to 1 ratio of potassium iodide–mercuric iodide complex indicate the necessity of including equation (3), together with equations (1) and (2), to explain the solubility of mercuric iodide in iodide solutions. The method of Garrett and Howell[15] for the calculation of the dissociation constants for mercuric hydroxide gives the values $K_2 = 0.48$, $\Delta F^\circ_{298} = +430$ cal., $K_3 = 35$ $\Delta F^\circ_{298} = -2100$ cal. for the iodides. This value of K_2 is in agreement with the extrapolation of the values of K_2 given in column 5 of Table V. These values of K_2 and K_3 indicate an appreciable amount of $HgI_4^=$ in solution.

The Mercuric Chloride–Chloride System

WITH ERNEST HOGGE

The mercuric chloride–chloride ion equilibrium has been investigated by Thomas.[1]

It is not easily possible to treat the data of these chlorides exactly due to the high molalities; however, this interesting observation is evident, namely, the concentration of the complex ion stands in almost a 1:1 ratio with the concentration of added chloride ion for reasonable concentrations of hydrochloric acid (to 1 molal) and for all concentrations of other salts (see Table VI). This suggests that equation (2) is sufficient to account for the increased solubility of mercuric chloride and that the most common complex chloride ion of mercuric chloride in all probability has the formula $HgCl_3^-$. The higher ratio of $m_{\text{HgCl}_2\text{ complex}}/m_{\text{added chloride}}$ at high solute concentrations suggests the possibility of the formation of a small amount of $HgCl_4^=$, but, on the other hand, this higher ratio may also be due to changing activity coefficients, which is expected at these high concentrations. It is virtually impossible to treat quantitatively any type of solution at such high concentrations; however, it may be concluded that the data in all the solutes used indicate the formation of $HgCl_3^-$ predominantly.

If it is true that the predominating ion is $HgCl_3^-$, then a quantitative treatment of the data becomes more possible due to the unit or near unit ratio of $\gamma_{HgCl_3^-}/\gamma_{Cl^-}$ in the equilibrium constant of K_2, for equation (2) over a wide range of concentrations. This should make possible a fairly reliable calculation of the value of K_2 from data even at 1 molal of added chloride ion (see Table VI, column 5). It is of interest to point out here the relatively large values of K_2 are indicative of a high ratio of $HgCl_3^-$ ion to free Cl^- ion; they also indicate that any other ion existing in the solution must be of relatively low concentration.

TABLE VI

[Thomas (ref. 1) revised]

m_{Cl}	s_{HgCl_2} in HCl	m_{HgCl_2} complex in HCl	m_{HgCl_2} complex in LiCl	Ratio $HgCl_2$ complex to free chloride ions = K_2	m_{HgCl_2} complex in $CaCl_2$	m_{HgCl_2} complex in $AlCl_3$
0.00	0.2702					
.1	.376	0.106	0.105		0.105	0.103
.2	.481	.211	.205		.208	.201
.3	.586	.316	.300		.303	.298
.5	.795	.525	.491	44	.492	.486
1.0	1.325	1.055	.960	24	.969	.965
2.0	2.420	2.150	1.907	21	1.937	1.926
3.0	3.557	3.287	2.375	23	2.915	2.906
4.0	4.726	4.456	3.864	28	3.894	3.862
5.0	5.901	5.631	4.862	35	4.874	4.774
6.0	7.054	6.784	5.861	42	5.853	
7.0	8.176	7.906	6.850	46		
8.0	9.264	8.994	7.827	45		
9.0	10.309	10.039				

(14) This calculation and that for the iodides do not take into consideration a possibility of polymerization of mercuric bromide or mercuric iodide (see latter section of this paper for a discussion of this possible effect with mercuric chloride). No evidence of this effect in the bromide or iodide has come to our attention.

(15) Garrett and Howell, THIS JOURNAL, **61**, 1730 (1939).

An apparent anomaly still exists in these data at low concentrations of added chloride ion, namely, the data in Table VI show higher (about 5%) mercuric complex concentrations than can be accounted for on the basis of the 1:1 ratio of $HgCl_2:Cl^-$. This is outside the limit of experimental error and is consistent for all the salts used.

A very probable explanation of this apparent anomaly is the fact that a polymerization equilibrium may exist in mercuric chloride solutions. Such an equilibrium would make necessary the consideration of the following additional reactions in interpreting these data

$$xHgCl_2 \rightleftharpoons (HgCl_2)_x \qquad (4)$$

and

$$(HgCl_2)_x + Cl^- \rightleftharpoons (HgCl_2)_xCl^- \qquad (5)$$

That a polymerization equilibrium does exist is supported by other independent evidence, namely, (1) measurements of rise of the boiling point of mercuric chloride solutions[16-19] and (2) freezing point lowering.[20,21] Such evidence is somewhat uncertain as individual cases but all of the evidence taken as a whole points strongly to the validity of this assumption of the existence of at least a small per cent. of polymerized mercuric chloride molecules in solution.

An additional observation that seems to lend further support to this assumption is the fact that the values of K_2 calculated from Thomas'[1] data go through a minimum (see column 5, Table VI) whereas the values of K_2 for similar data for the bromide and iodide vary in the direction that one might reasonably expect if there are no secondary equilibria such as polymerization.

It is obvious that more careful work is necessary on vapor pressure lowering, freezing point lowering, distribution ratios, etc., to verify this assumption of polymerization. However, it would be reasonable to conclude that from the data now at hand the amount of polymerized mercuric chloride molecules need only be in the order of 10% to account for the apparent anomalous behavior of mercuric chloride. This also leads one to the conclusion that the complex ion of mercuric chloride that one expects to predominate is the $HgCl_3^-$ ion but it does not exclude the possibility of smaller amounts of other ions such as $(HgCl_2)_xCl^-$, $HHgCl_4^-$ and $HgCl_4^=$.

It may also be observed that a near 1 to 1 ratio of mercuric chloride to added chloride ion would indicate only a small amount of free chloride ions in solution and thus suggest a highly stable complex ion. Other work pointing to the high stability of these complex ions is the work of LeBlanc and Noyes[21] on the effect of mercuric chloride on the rate of catalysis of methyl acetate with hydrochloric acid and the work of Richards and Archibald[22] on the effect of mercuric chloride on the conductivity of hydrochloric acid. These papers also indicate that the new compounds formed are strong electrolytes. Again one is led to the conclusion that the predominating ion is the $HgCl_3^-$ ion; otherwise one would expect the catalytic activity and the conductivity of the hydrochloric acid to be considerably altered due to the removal of hydrogen ions to form the $HHgCl_4^-$ ion which would be only slightly dissociated in such concentrated solutions.

This conclusion is further supported by the data on these other halides which suggest an appreciable amount of $HgI_4^=$, and only a very small amount (if any) of $HgBr_4^=$. A reasonable prediction would suggest a still smaller amount of $HgCl_4^=$. If this conclusion be justified, then one obtains an approximate value of $K_2 = 20$ from Thomas' data, and a value of $\Delta F^\circ_{298} = -1700$ cal. if one assumes no polymerization at this value of chloride ion concentration. This value indicates a fairly stable complex chloride ion, which is in agreement with other evidence.

Evidence of hydrolysis was obtained in the mercuric bromide–bromide system when it was found that the *p*H of the samples varied from 4.1 for water solubility to 4.8 for the salt samples from $m_{KBr} = 0.01$ to 1.0 molal.

Acknowledgments.—The author is indebted to Mr. James Lemley and Dr. Claude Acker for aid in the experimental part of this paper.

Summary

The solubilities of mercuric bromide and mercuric iodide have been determined in potassium

(16) Kahlenberg, *J. Phys. Chem.*, **5**, 367 (1901), whose data indicate molecular weights from 310 to 423 (theoretical mol. wt. 271).

(17) Beckmann, *Z. physik. Chem.*, **6**, 460 (1890), whose data indicate molecular weights from 275 to 342 except at high dilutions.

(18) Bourion and Rouyer, *Ann. chim.*, **10**, 263 (1928); *Compt. rend.*, **177**, 546 (1923), whose data indicate single and double molecules at 25°. These authors also give references to other evidence of polymerization.

(19) Tourneux, *Bull. soc. chim.*, [5] **1**, 1043 (1934).

(20) Raoult, *Compt. rend.*, **87**, 169 (1878), whose data indicate a molecular weight of 387.

(21) See ref. 5. A brief but significant summary of this work is given by Sherrill, ref. 4, who points out an interpretation of the data in terms of polymerized molecules.

(22) Richards and Archibald, *Z. physik. Chem.*, **40**, 385 (1902).

bromide and potassium iodide solutions. The water solubility of mercuric bromide has been redetermined.

The equilibrium constants for the formation of the complex ions of mercuric halides have been evaluated. These calculations indicate that $HgBr_3^-$, HgI_3^- and $HgI_4^=$ are formed. Earlier work indicated the formation of $HgCl_3^-$ with small amounts of $(HgCl_2)_x$ and $(HgCl_2)_xCl^-$.

The anomalous solubility of mercuric chloride in low concentrations of chloride solutions is accounted for on the basis of polymerization of mercuric chloride. Other evidence is cited to indicate the existence of polymerized mercuric chloride molecules.

A number of different independent arguments are presented to indicate that the chief ion formed in the chloride solutions is the $HgCl_3^-$ ion.

The equilibrium constants and ΔF°_{298} of several of these ions have been evaluated. They have been shown to be in agreement among themselves and with other known data.

The free energy of formation of the various halide ions from mercuric halide and the halide ions is $HgCl_3^-$, $\Delta F^\circ_{298} = -1700$ cal.; $HgBr_3^-$, $\Delta F^\circ_{298} = -365$ cal.; HgI_3^-, $\Delta F^\circ_{298} = +430$ cal.; $HgI_4^=$, $\Delta F^\circ_{298} = -2100$ cal.

COLUMBUS, OHIO RECEIVED JULY 7, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE ETHYL GASOLINE CORPORATION]

The Redistribution Reaction. I. The Random Intermolecular Exchange of Organic Radicals

BY GEORGE CALINGAERT AND HAROLD A. BEATTY

This is the first of a series of papers describing a hitherto unrecognized type of intermolecular exchange of organic radicals. The systematic study of this reaction has yielded simple laws governing its course, and supplies a ready interpretation of the small amount of related data scattered through the literature. The results obtained offer interesting suggestions regarding the behavior of the covalent bond as well as possibilities for new methods of probing into this field. The reaction also constitutes a new tool for the synthesis of several types of organic compounds. This first paper defines the nature of the reaction, using illustrations from the field of organo-metallic compounds, and constitutes a general introduction to subsequent papers which will cover specific phases of the subject.

Introduction.—A wide variety of reactions is known in which atoms or radicals linked by covalent bonds are transferred from one molecule to another through exchange with an atom or radical of another kind. For example, in the Jacobsen reaction, bromobenzene under the influence of aluminum chloride yields a mixture containing benzene and *p*-dibromobenzene, as well as other products. Likewise, under the influence of the same catalyst, toluene is converted into a mixture containing, in addition to toluene itself, benzene and several polymethylated benzenes. Reactions of this type are also known in the field of organo-metallic compounds. Dialkylzinc compounds have long been prepared by heating alkylzinc halides, which are converted into a mixture of the dialkyl compound and the zinc halide, the former being removed as formed, by distillation. A few cases also have been reported where the radicals exchanged were similar instead of dissimilar: for example, the interchange of methyl and ethyl radicals in organo-silicon compounds,[1] of phenyl and tolyl radicals in triarylbismuth compounds[2] and of halogen atoms in ethylene chlorobromide.[3]

Except in the last case, little or no indication has been given of the existence of an equilibrium, and in most cases a considerable amount of side reaction takes place. Also, the conditions used, namely, elevated temperatures or the presence of a powerful catalyst or both, suggest that the reactions are closely related to the irreversible decompositions of the compounds involved.

In the studies which will be reported in the present series of papers, it has been found that by a judicious choice of operating conditions and catalyst, it is possible to bring about an extensive

(1) Dolgov and Volnov, *Zhur. Obshchei Khim.*, Khim. Ser., **1**, 91 (1931).

(2) Challenger and Allpress, *J. Chem. Soc.*, **119**, 913 (1921); Challenger and Ridgway, *ibid.*, **121**, 104 (1922).

(3) Dougherty, THIS JOURNAL, **51**, 576 (1929).

interchange of similar radicals, and of certain similar atoms, between molecules of the same chemical class. In contrast to most of the cases reported above, the present reaction takes place smoothly, without noticeable evolution of energy, and the resultant product is free from the secondary or decomposition products usually found in reactions involving the liberation of functional groups or atoms without substitution. While this reaction has been found to take place quite generally, and with several different classes of compounds, including alkyl halides, esters of organic acids, and organo-metallic compounds, the present general exposition will be based on the last-named compounds, which have proved to be particularly suitable for quantitative study.

The Exchange of Radicals in Organo-Metallic Halides.—As will be shown later, the present reaction is closely related to the interchange between radicals and halogen atoms in organo-metallic halides, and for that reason this type of reaction will be considered first. It is well known that several metallic halides react with organo-metallic compounds in accordance with the general equation

$$R_nM + M'X_{n'} \longrightarrow R_{n-m}MX_m + R_mM'X_{n'-m}$$

the extent to which the reaction takes place depending upon the nature of the metals (or metal), the R group and the halogen involved.[4] In some cases which have been studied more extensively, notably that of the system $R_2Mg + MgX_2$, the existence of a state of equilibrium has been established definitely.[4b]

In a previous report from this Laboratory,[5] it was shown that in the case of ethyllead halides, such a transformation did take place in both directions, between any of the possible stable components of the system, as indicated schematically below

$$R_4Pb \rightleftharpoons R_3PbX \rightleftharpoons R_2PbX_2 \rightleftharpoons [RPbX_3]$$
$$\downarrow \qquad\qquad \downarrow$$
$$R_2 + PbX_2 \qquad RX + PbX_2$$

The study of equilibrium in such a system as this is rendered difficult, if not impossible, by the instability of some of the compounds involved, as indicated above by the vertical arrows; nevertheless the formation of all these compounds in the system has been established with certainty.

It may be inferred from the above that the interchange of organic radicals and halogen atoms in organo-metallic compounds is quite general, and this suggests the use of this reaction to effect the interchange of organic radicals themselves between different molecules.

The first step in the broadening of our knowledge of the reactions in this field consisted in testing the possibility of the occurrence of this interchange between a fully alkylated metal atom and its corresponding monohalide, a case in which the reaction conceivably might not take place, as it does not lead to the formation of any new compound. This interchange was tested with triethyllead chloride and tetraethyllead, the latter compound containing the radioactive isotope of lead, Radium D, as an indicator. It was found that, even at room temperature and without a catalyst or solvent, radioactivity was detected after a short time in the triethyllead chloride, and after one day the lead obtained from both the tetraethyllead and triethyllead chloride showed the same intensity of radioactivity, and continued to do so. This demonstrates the rapid interchange of the chlorine atoms and ethyl radicals in accordance with the equation

$$Et_4Pb^* + Et_3PbCl \rightleftharpoons Et_3Pb^*Cl + Et_4Pb$$

The same reaction was then studied in the case where the alkyl groups present in the tetraalkyllead compounds are different from those present in the chloride: the pair, tetramethyllead plus triethyllead chloride, was used. Here again the reaction took place readily, but a complex mixture was obtained. Careful fractional distillation of the tetraalkyllead portion of the product showed the presence of all the five possible compounds containing either or both methyl and ethyl groups, that is, tetramethyllead, trimethylethyllead, dimethyldiethyllead, methyltriethyllead, and tetraethyllead. The alkyllead halide portion of the product was analyzed separately, and it was likewise shown conclusively that all the four possible trialkyllead chlorides were present. These results are represented by the equation

$$\left.\begin{matrix} Me_4Pb + \\ Et_3PbCl \end{matrix}\right\} \longrightarrow \left\{\begin{matrix} Me_4Pb + Me_3EtPb + Me_2Et_2Pb + \\ \qquad\qquad MeEt_3Pb + Et_4Pb \\ + Me_3PbCl + Me_2EtPbCl + \\ \qquad\qquad MeEt_2PbCl + Et_3PbCl \end{matrix}\right.$$

Equilibrium Interchange of Radicals in Metal Alkyls.—In the next step of this investigation,

(4) For a discussion of this subject, see (a) Challenger, Pritchard and Jinks, *J. Chem. Soc.*, **125**, 864 (1924); (b) Gilman, "Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1938, Vol. I, Chapter 4.

(5) Communication to the Mid-West Regional Meeting of the American Chemical Society, Columbus, Ohio, November, 1937; to be published.

the amount of alkyllead salt was decreased to catalytic quantities, and two different tetraalkyllead compounds were used. Again, extensive interchange of the alkyl groups took place at low temperature, and the product contained all the possible tetraalkyl compounds. Yet in the absence of the catalyst, there was no detectable reaction, even after prolonged heating. This indicated that the presence of the alkyllead salt caused the alkyl groups in tetraalkyllead compounds to become mobile to the extent of migrating from one molecule to another, as represented by the equation

$$R_4Pb + R'_4Pb \longrightarrow R_4Pb + R_3R'Pb + R_2R'_2Pb + RR'_3Pb + R'_4Pb$$

An investigation was then made to determine how general the reaction was for different R radicals and whether it would take place as well with other metals, and by means of other catalysts. It was found, indeed, to be quite general. Numerous tests were made, using two or more different radicals, including methyl, ethyl, *n*-propyl, isopropyl, *s*-butyl, *t*-butyl, phenyl, and *p*-tolyl, bound to one or more metals, including lead, tin, silicon, and mercury. In all cases, interchange took place freely, and ample evidence was found of the formation of all the possible compounds between the R groups and M atoms present. Whenever compounds of two different metals reacted under similar conditions, as a rule they also reacted with one another, again yielding all the possible compounds of both metals. Thus, the equation which expresses the products obtained from two different R groups bound to two different M atoms of different valences, and which illustrates the type of result obtained from all these transformations in general, is

$$R_nM + R'_{n'}M' \xrightarrow{\text{Catalyst}} R_nM + R_{n-1}R'M + R_{n-2}R'_2M + \ldots + RR'_{n-1}M + R'_nM + R_{n'}M' + R_{n'-1}R'M' + R_{n'-2}R'_2M' + \ldots + RR'_{n'-1}M' + R'_{n'}M'$$

Numerous catalysts also were found, most of which consisted, either directly or through secondary reaction, of halides or organic halides of elements susceptible of forming organo-metallic compounds. The activities of the various catalysts differed, and compounds of different metals reacted at different rates, depending on the temperature and on the kind and amount of catalyst. Usually, the reaction time was limited to five hours or less, and the reaction velocity was increased by elevating the temperature to 60–80° or, for some of the heavier R groups or less active catalysts, to 100–180°. To obtain these temperatures, and at the same time to provide stirring and to exclude air, it was convenient to add an inert solvent such as hexane or decalin, and to reflux the mixture. There was no evidence that these solvents participated in any way in the reaction. Experimental information and data on these topics will be presented in detail in a subsequent paper; illustrations of some of the systems tested, including different compounds and catalysts, are given in Tables I and II.

TABLE I

EXAMPLES OF METALS AND RADICALS WHICH DISPLAY INTERCHANGE

Reaction conditions, in general: a total of 0.3 mole organo-metallic compound, 1 g. $AlCl_3$, and 50 ml. hexane, heated to the boiling point, 60–80°, for 5–7 hours.

Metals	Radicals	Halides[a]
$Me_4Pb + Et_4Pb$	$Me_4Pb + Et_4Pb$	$Me_3PbCl + Et_3PbCl$[b]
$Me_4Sn + Et_4Sn$	$Me_3EtPb + MeEt_3Pb$[c]	$Me_2EtPbCl$[b]
$Me_2Hg + Et_2Hg$[c]	Me_2Et_2Pb	$Me_4Pb + Et_3PbBr$
$Et_4Si + Pr_4Si$[d]	Me_3-*i*-$PrPb$	$Me_4Pb + Et_3PbCl$
$Me_4Sn + Et_4Pb$	$Et_4Pb + Pr_4Pb$	$Et_4Pb + Me_3PbBr$
$Et_2Hg + Me_4Pb$	Et_2-*n*-Pr_2Pb	
	Me_2-*i*-Bu_2Pb	
	$Me_4Pb + Ph_4Pb$	
	$Ph_4Pb + (p\text{-tolyl})_4Pb$[e]	
	Me_3-*t*-$BuPb$[f]	

[a] No $AlCl_3$ used. [b] Acetone used as solvent. [c] No solvent used. [d] Temperature 180°. [e] Temperature 100°. [f] Temperature 130°; some decomposition occurred, probably as a result of the instability of the poly-*t*-butyllead compounds.

TABLE II

EXAMPLES OF CATALYSTS

Reaction tested, except as noted, with 0.3 mole mixed $Me_4Pb + Et_4Pb$, 50 ml. hexane or decalin, 1–2 g. catalyst, heated to 80° for five to six hours.

$ZnCl_2$[a,b,c]	Me_2AlCl	Me_3PbI[d,e]
ZnF_2[a]	$Bu_3Al_2I_3$[f]	PCl_3[a]
$HgCl_2$[a]	$ZrCl_4$[a]	$AsCl_3$[a,b]
BF_3 gas	$SnCl_4$[a,b,g]	$BiCl_3$[a]
$AlCl_3$	Et_3SnBr[d]	$FeCl_3$[a]
$AlBr_3$[d]	Et_3PbCl[e]	$PtCl_4$[h]

[a] Temperature 160–175°. [b] Some decomposition occurred. [c] Time 24 hours. [d] Reaction not complete in time allowed. [e] Catalyst 13 g. [f] Catalyst 5 g. [g] Reacted vigorously, forming lead chloride. [h] Temperature 100°.

Characteristics of the Reaction.—In most organic reactions involving the intermolecular transfer or metathetical substitution of radicals, functional groups, or atoms, yields of 80 to 90% of a single product are usually considered excellent, and it is generally accepted that a substan-

tial fraction of the compounds entering the reaction is diverted through competitive side reactions, including decompositions, polymerization, etc. In contrast, the type of reaction described in the present paper shows as one of its distinctive characteristics the essential absence of decomposition or other side reactions. In general, this was evidenced by the fact that there was no observable evolution of gas, or precipitation of metal, or heat of reaction, and that the recovery of the reactants was complete except for normal handling losses. The few exceptions, such as those noted in Tables I and II, could be ascribed to the use of high temperatures and the thermal instability at these temperatures of some of the compounds formed, or to the occurrence of irreversible reactions between the compounds and the catalyst when the latter was present in substantial amount. Quantitative evidence for the absence of side reactions in a typical normal case is given in the third paper of this series.[6]

Moreover, it was found that—after a period of time which depends on the temperature, the catalyst, and the compounds used—the system reached a constant composition which was not changed by further prolonged contact with the catalyst. This final composition is an equilibrium, since it can be reached from any direction, that is, starting with any initial mixture (or mixed-radical compound) which contains altogether the same proportions of each different kind of atom and radical involved. For example, an equimolecular mixture of tetramethyllead and tetraethyllead, or of trimethylethyllead and methyltriethyllead, or the single compound, dimethyldiethyllead, each gives the same final product. Also, these equilibria are entirely unaffected by the usual factors such as solvent, catalyst, or even temperature, and the equilibrium composition is a function only of the mole fraction of the various R and M components present in the system.

In view of this, it seemed logical to make the simplest possible hypothesis as to the nature of the process: to wit, that the interchange occurs *at random.* This was found to be the case: the final composition of any system agrees with that calculated from the laws of probability alone. The distinctive characteristics of this reaction and of the resulting equilibrium—the freedom from side reactions, and the absence of chemical or energy factors affecting this random equilibrium—seem to justify identifying them by new names, and it is proposed to call the reaction the "Redistribution Reaction," and its product a "Random Equilibrium Mixture."

Random Distribution: The Application of the Laws of Probability.—To illustrate the application of the laws of probability to this random distribution of the interchanged radicals or atoms, consider the simple case of a single metal, M, and two organic radicals, A and B, the mole fractions of which are a and b, respectively, where $a + b = 1$. Imagine that all the radicals have been removed from the M atoms, and are to be returned thereto at random. Then the probability that the first valence of M will be satisfied by A is a, and by B, is b; so that the concentrations will be

$$a\mathrm{MA} \quad \text{and} \quad b\mathrm{MB}$$

For the second valence, the same holds, and applies independently to MA and MB, giving, respectively

$$a^2\mathrm{MA_2} + ab\mathrm{MAB} \quad \text{and} \quad ab\mathrm{MAB} + b^2\mathrm{MB_2}$$

or

$$a^2\mathrm{MA_2} + 2ab\mathrm{MAB} + b^2\mathrm{MB_2}$$

Applying the same method of deduction to the more general case of one kind of central atom (or group) M, of valence n, and s different kinds of substituent radicals (or atoms), $\mathrm{R_1}$, $\mathrm{R_2}$, . . ., $\mathrm{R_s}$, whose mole fractions are $r_1, r_2, \ldots, r_s$, respectively, gives as a result that the concentration of any one of the possible compounds, $\mathrm{M(R_1)}_a\mathrm{(R_2)}_b \ldots \mathrm{(R_s)}_j$ (where $a + b + \ldots + j = n$) is equal to

$$\frac{n!\,(r_1)^a(r_2)^b \ldots (r_s)^j}{a!\,b! \ldots j!}$$

and the total number of different $\mathrm{R}_n\mathrm{M}$ compounds is equal to

$$\frac{(n + s - 1)\,!}{n!\,(s - 1)\,!}$$

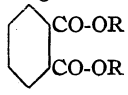
When more than one kind of central atom or group, M, is present, these two general formulas apply independently to each kind of M taken in conjunction with the R groups attached to it.

The above formulas reduce to rather simple forms in the case of systems containing few constituents. Thus, when there is only one central group M of valence n and two different kinds of radicals ($s = 2$), the number of different compounds is equal to $(n + 1)$, and the concentration of each is given by the corresponding term of the binomial expansion of $(r_1 + r_2)^n$. Denoting

(6) Calingaert and Soroos, THIS JOURNAL, **61**, 2758 (1939).

TABLE III

NUMBER, CONCENTRATIONS, AND EXAMPLES OF R_nM COMPOUNDS

Valence of M = n	No. of compds. R_nM	Concentration of R_nM, $R_{n-1}R'M$, ..., R'_nM					Examples of types of compds.
1	2	r	$(1-r)$				$CH_3CO\text{-}OR$; Et-X; R-Na; R-HgCl
2	3	r^2	$2r(1-r)$	$(1-r)^2$			R_2-Hg; R_2-$PbCl_2$; X_2-C_2H_4; 
3	4	r^3	$3r^2(1-r)$	$3r(1-r)^2$	$(1-r)^3$		R_3-Bi; R_3-PbBr
4	5	r^4	$4r^3(1-r)$	$6r^2(1-r)^2$	$4r(1-r)^3$	$(1-r)^4$	R_4-Sn

r_1 by r, and r_2 by $(1-r)$, the corresponding values for valences of M from 1 to 4 are given in Table III, which includes examples of corresponding types of compounds.

From a knowledge of the composition of the original mixture, or from the over-all analysis of the product, the values of the r's are determined, and the expected concentrations in the final mixture can be calculated. As an illustration, the calculated concentrations of all five constituents in the system R_4M containing two kinds of groups, R and R', is shown in Fig. 1, for the whole range from $r = 0$ to $r = 1$.

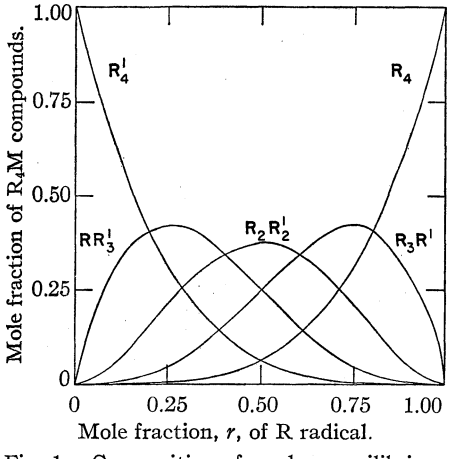


Fig. 1.—Composition of random equilibrium mixtures of the type $(R_nR'_{4-n})M$.

Experimental Confirmation of Random Equilibrium Mixtures.—The experimental data covering many of the systems which underwent the redistribution reaction were tested in this manner, with convincing results. In general, the analytical procedure consisted in washing or extracting the final reaction mixture to remove the catalyst, together with organo-metallic halides if present; the volatile metal alkyls (or other volatile compounds) were then separated by fractional distillation[7]; the less volatile metal aryls were analyzed by freezing-point determinations, and the halides, if any, were identified by methods (which will be described elsewhere) based on solubility and alkylation.

Since these studies in general were regarded as being exploratory in a new field, and it was desired to extend their scope as far as was expedient within the time available, it was advantageous in some cases to carry out the analyses only partially, or semi-quantitatively, to an extent sufficient to show that the redistribution reaction had occurred and that the composition of the product was at least roughly in accord with that estimated for a random equilibrium mixture.

The typical results obtained in most cases are illustrated, for six representative mixtures, by Figs. 2–5. These give the experimental distillation data plotted on a volume percentage basis, in comparison with the ideal distillation curves which were calculated for random equilibrium mixtures of the over-all compositions indicated by the experimental data. It is clear that these typical results show a very satisfactory agreement with the predicted values. The identity in composition shown in Fig. 2 for the prod-

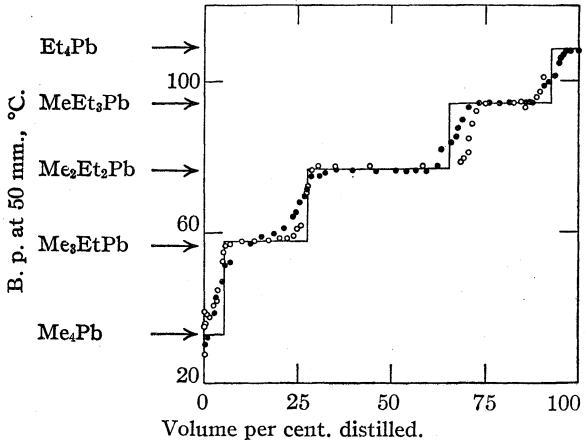


Fig. 2.—Distillation of the reaction product from: ○, Me_3EtPb + $MeEt_3Pb$; ●, Me_4Pb + Et_4Pb. Solid line calculated for random equilibrium mixture having [Me] = 0.50.

(7) The procedure followed and results obtained are described in the second paper of this series, by Calingaert, Beatty and Neal, THIS JOURNAL, **61**, 2755 (1939).

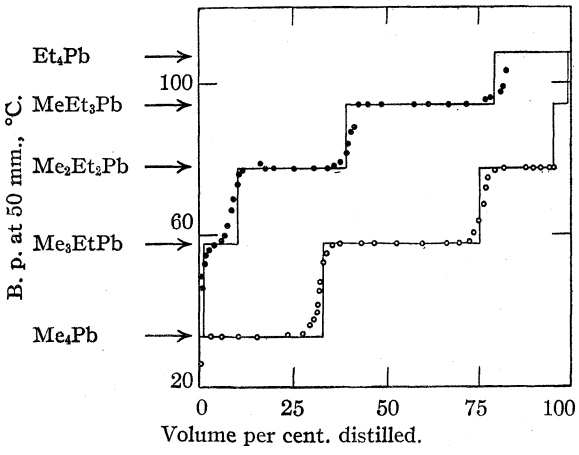


Fig. 3.—Distillation of the reaction product from $Me_4Pb + Et_4Pb$. Solid line calculated for random equilibrium mixture having ○ [Me] = 0.776; ● [Me] = 0.345.

ucts from two entirely different mixtures of the same over-all composition, and the marked difference between this product and those from two similar mixtures of somewhat different over-all composition (shown in Fig. 3) is noteworthy. The distillation shown in Fig. 4, although not

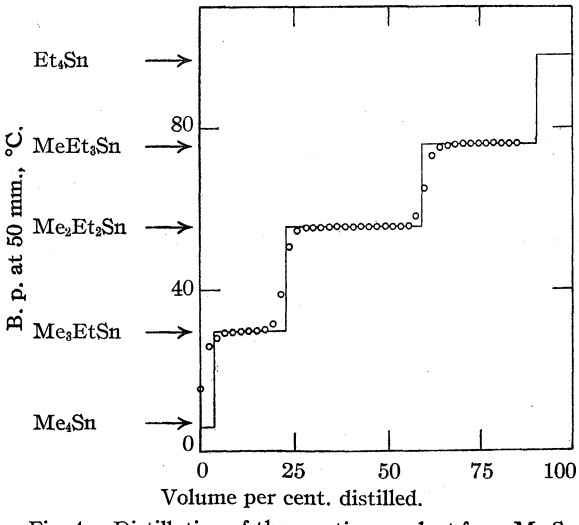


Fig. 4.—Distillation of the reaction product from $Me_4Sn + Et_4Sn$. Solid line calculated for random equilibrium mixture having [Me] = 0.46.

completed, is ample evidence for the agreement with theory in this case. In the particular experiment with two metals illustrated by Fig. 5, the separation and analysis of the various fractions was not rigorous, and as a result the over-all composition was not known with certainty. Hence, the ideal distillation curve is not given, but the results are considered adequate to indicate the presence of all ten possible compounds. As the care and accuracy of the analyses increase the agreement with theory becomes more exact, and is within the experimental error of less than 1%.[7]

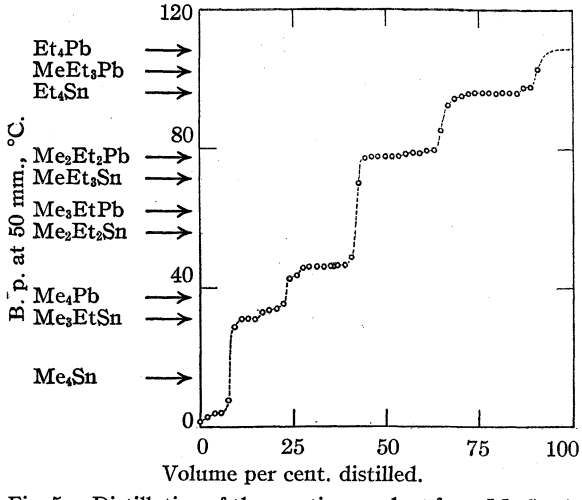


Fig. 5.—Distillation of the reaction product from $Me_4Sn + Et_4Pb$ (experimental curve only).

Discussion.—It is worthy of emphasis that, although organo-metallic compounds have been used for illustration here, the redistribution reaction is not limited to this field. The content of the present paper is designed to serve only as a general presentation of the subject, and subsequent contributions will cover, individually, specific points of interest in both organo-metallic compounds and other fields. Although we are not prepared to consider the scope of this reaction and its implications at this time, a few salient points may be mentioned here.

While the mechanism of the reaction clearly involves atoms and radicals, it is evident, from common knowledge of the conditions under which free atoms or radicals exist, that these are not present as such. Free radicals, of the kinds to be expected here, if liberated in a liquid phase would result in the formation of a variety of secondary products which are totally absent in the present reaction. Dissociation into ionized radicals also appears improbable, especially for the halogen-free alkyls; in accord with this, solvents are not required and, if added, do not appear to influence the reaction proper.

Accordingly, a mechanism involving the formation of molecular complexes or coördination compounds with the catalyst is indicated. The catalysts used are such as can be converted, in the reaction mixture, into the form of organic or

organo-metallic compounds which contain the radicals to be interchanged. Then the possibility is evident for the interchange to occur when the reactants and the catalyst are united together in a complex.

While the molecular activation required to form such complexes might be anticipated as the result of the action of powerful catalysts such as aluminum chloride, it would hardly have been expected with catalysts such as trialkyllead halides. Moreover, in some of the metal aryls at higher temperatures there is a spontaneous interchange of radicals without the presence of any catalyst, suggesting that the catalyst merely accelerates a process, the possible occurrence of which is inherent in the reactants themselves. This argues for a considerably greater flexibility of the covalent bonds in the metal alkyls and aryls than would commonly be assigned to compounds of their structure and chemical stability, and it is not evident how this can be ascribed to the existence of mesomeric or electromeric forms or to a state of resonance.

Information as to the relative mobilities or reactivities of the radicals, and as to the preferential association between different central atoms and radicals, can be obtained in one and the same system, when more than two different radicals or more than one central atom are present. Even when only one central group and two kinds of radicals are employed, the formation of random equilibrium mixtures implies that the energy of formation of the different compounds in each system is a linear function of the molecular weight, and (surprisingly) is not affected by the symmetry (or asymmetry) of the molecules. For example, the energy of formation of one mole each of tetramethyllead and tetraethyllead is equal to that of one mole each of trimethylethyllead and methyltriethyllead.

For studies of reaction kinetics in the liquid phase, catalyzed reactions such as described here, which reach an equilibrium in a measurable time and are free from side reactions and specific solvent effects, are particularly suitable. Also, the occurrence of two or more simultaneous reactions in such systems as R_4M or R_3M permits an internal check on the relative rates of the different reactions, regardless of the absolute rates, and this in turn provides a distinctive method of approach to the determination of the reaction mechanism.

In addition to opening up avenues of theoretical investigation, the redistribution reaction is adaptable as a new method of organic synthesis. As one illustration, metathesis can now be induced directly between similar compounds which are usually inert to one another, such as esters; more broadly, mixed compounds, such as mixed esters of polybasic acids, mixed polyhalides, and mixed organic compounds of polyvalent metals, can be prepared by direct metathetical reactions which may afford a considerable saving of time and material over the classical step-wise methods. A few examples of this type are

$$Me_4Pb + Et_4Pb \longrightarrow 2Me_2Et_2Pb$$
$$MeCOOEt + PrCOOMe \longrightarrow MeCOOMe + PrCOOEt$$
$$2EtCl + C_2H_4Br_2 \longrightarrow 2EtBr + C_2H_4Cl_2$$

Here the arrows indicate a suitable combination of reaction, separation, and re-cycle processes.

Summary

A hitherto unrecognized type of reaction is described, in which all the radicals or atoms of one kind, present in a mixture in which they are linked to one or more central groups or atoms of another kind, are interchanged between all the central groups present. This process, which is termed the "Redistribution Reaction," takes place smoothly at low temperatures in the liquid phase under the influence of a catalyst. The yield is quantitative, and the composition of the resultant mixture can be calculated from that of the reactants on the basis of a random distribution of the interchanged radicals or atoms: this reaction product is therefore termed a "Random Equilibrium Mixture." The reaction presents interesting possibilities for theoretical investigation into the nature and behavior of covalent bonds and the mechanism and kinetics of their reactions; also, the reaction provides novel methods of preparation of various organic compounds.

DETROIT, MICHIGAN RECEIVED JULY 21, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE ETHYL GASOLINE CORPORATION]

The Redistribution Reaction. II. The Analysis of Metal Alkyl Mixtures and the Confirmation of Random Distribution

BY GEORGE CALINGAERT, HAROLD A. BEATTY AND HERBERT R. NEAL

In the previous paper of this series[1] it was stated that the analysis of mixtures of organo-metallic compounds which had undergone the redistribution reaction showed that the composition of the product obtained corresponded to a random distribution of the interchanged radicals. The present paper describes the analytical method used for the volatile metal alkyls, including a test of its accuracy, and gives a quantitative demonstration of this random distribution. The corresponding analytical methods and results obtained for organo-metallic halide mixtures will be given in a subsequent paper.

The Accuracy of Analysis.—From an estimation of the precision of the various analytical observations and of other sources of error, it was concluded that the absolute accuracy obtainable for a mixture of volatile metal alkyls should be close to 1% for each constituent. This conclusion was tested as follows. Two different mixtures of the five methyl and ethyl tetraalkyllead compounds were prepared—one containing about equal amounts of each compound, the other having about the composition of a random equilibrium mixture containing equal proportions of methyl and ethyl radicals. These mixtures were made up by one experimenter, by volume, from the pure individual compounds, and the volumetric summation was checked by comparison of the total net weight with that calculated from the densities of the compounds. The entire mixtures were each analyzed by another experimenter, using the procedure described below. The results, given in Table I, confirm the predicted accuracy, and indicate that the errors are independent of the volatility or concentration of the constituent; the standard deviation between the taken and observed values for the entire group of ten values was 0.6%, and the maximum deviation was 0.7%.

Confirmation of Random Distribution.—Most of the data suitable for comparison with the compositions predicted for random distribution were obtained for mixtures of the methyl and ethyl tetraalkyllead compounds. The data in Table II were selected as the best of a large number of analyses of these mixtures, the basis of the selection being solely the appearance of the plotted distillation curve together with freedom from known unusual sources of error or other complications. Of this group so selected, one analysis was discarded as being statistically out of line with the remainder.

TABLE I

ANALYSIS OF KNOWN MIXTURES

Compound	Volume, ml. Taken	Volume, ml. Found	Volume, % Taken	Volume, % Found	Error
		Test no. 1			
Me_4Pb	13.00	12.3	20.60	19.9	−0.7
Me_3EtPb	12.49	12.7	19.79	20.5	.7
Me_2Et_2Pb	12.00	12.1	19.01	19.6	.6
$MeEt_3Pb$	12.30	12.0	19.49	19.4	− .1
Et_4Pb	13.32	12.7	21.11	20.5	− .6
Total	63.11	61.8			
Weight, g., calcd., 114.04; found, 114.01					
		Test no. 2			
Me_4Pb	2.90	2.5	4.77	4.15	−0.6
Me_3EtPb	14.51	14.8	23.86	24.6	.7
Me_2Et_2Pb	23.80	23.4	39.14	38.85	− .3
$MeEt_3Pb$	15.00	14.5	24.67	24.1	− .6
Et_4Pb	4.60	5.0	7.56	8.3	.7
Total	60.81	60.2			
Weight, g., calcd., 108.96; found, 108.98.					

The mole fraction of methyl and ethyl radicals in the mixture is denoted, respectively, by r and $(1 - r)$. The value of r was, in many cases, not known in advance; accordingly, it was calculated in each case from the result of the analysis by means of the equation

$$r = [Me_4Pb] + 0.75[Me_3EtPb] + 0.5[Me_2Et_2Pb] + 0.25[MeEt_3]Pb$$

where the brackets denote the concentration in mole fraction. The predicted mole fractions of the five tetraalkyllead compounds are

Me_4Pb	Me_3EtPb	Me_2Et_2Pb	$MeEt_3Pb$	Et_4Pb
r^4	$4r^3(1-r)$	$6r^2(1-r)^2$	$4r(1-r)^3$	$(1-r)^4$

Inspection of the differences shown in Table II indicates that, like those in Table I, they are scattered at random and do not appear to be a function of the compounds or of their concentrations or of r, the mole fraction of methyl radicals. Moreover, there is no statistically

(1) Calingaert and Beatty, THIS JOURNAL, 61, 2748 (1939).

TABLE II

ANALYSIS OF RANDOM EQUILIBRIUM MIXTURES FOR METHYL-ETHYLLEAD ALKYLS

	Composition, mole per cent.														
	Me_4Pb			Me_3EtPb			Me_2Et_2Pb			$MeEt_3Pb$			Et_4Pb		
r	Found	Calcd.	Diff.	Found	Calcd.	Diff.	Found	Calcd.	Diff.	Found	Calcd.	Diff.	Found	Calcd.	Diff.
0.205	0.0	0.2	−0.2	2.8	2.7	+0.1	16.1	15.9	+0.2	41.3	41.2	+0.1	39.8	40.0	−0.2
.258	.2	.4	− .2	4.7	5.1	− .4	22.5	22.0	+ .5	43.4	42.2	+1.2	29.2	30.3	−1.1
.325	.8	1.1	− .3	8.7	9.3	− .6	29.5	28.9	+ .6	41.6	40.0	+1.6	19.4	20.7	−1.3
.329	1.5	1.2	+ .3	8.8	9.5	− .7	29.5	29.2	+ .3	40.2	39.8	+0.4	20.0	20.3	−0.3
.340	1.7	1.3	+ .4	9.3	10.4	−1.1	31.1	30.2	+ .9	39.0	39.1	− .1	18.9	19.0	− .1
.463	5.3	4.6	+ .6	20.2	21.3	−1.1	37.6	37.1	+ .5	28.6	28.7	− .1	8.4	8.3	+ .1
.667	19.2	19.8	− .6	40.7	39.5	+1.2	29.1	29.6	− .5	9.8	9.9	− .1	1.2[a]	1.2	0
.737	29.3	29.5	− .2	42.5	42.1	+0.4	22.5	22.5	0	5.2	5.4	− .2	0.5[a]	0.5	0
Mean			− .025			− .275			+ .31			+ .35			− .36
Standard dev.			.44			.85			.54			.72			.66

[a] Estimated from the total of $MeEt_3Pb$ + Et_4Pb.

significant difference between the results given in Tables I and II. It appears, therefore, that the differences in Table II can be ascribed solely to experimental error. In contrast to these small differences are the large effects resulting from a change in the relative proportions of methyl and ethyl radicals, as can be seen by comparing the calculated compositions for different values of r in Table II, or by referring to Fig. 1 in the preceding paper.[1] The confirmation of the randomness of the redistribution, for this system of lead compounds at least, is evident.

TABLE III

ANALYSIS OF RANDOM EQUILIBRIUM MIXTURES FOR OTHER SYSTEMS

The mole fraction of the first of the two radicals cited is denoted by r. The data are given in mole per cent.

Compd.	Found	Calcd.	Diff.
System: Me_4Sn + Et_4Sn; r = 0.459			
Me_4Sn	24.6	4.4	−0.7
Me_3EtSn		20.9	
Me_2Et_2Sn	38.4	37.0	1.4
$MeEt_3Sn$	28.6	29.1	−0.5
Et_4Sn	8.4	8.6	− .2
System: $C_2H_4Cl_2$ + $C_2H_4Br_2$; r = 0.467			
$C_2H_4Cl_2$	23.0	21.8	1.2
C_2H_4ClBr	47.4	49.8	−2.4
$C_2H_4Br_2$	29.6	28.4	1.2
System: Et_4Si + Pr_4Si; r = 0.464			
Et_4Si	4.5	4.6	−0.1
Et_3PrSi	21.3	21.4	− .1
Et_2Pr_2Si	39.6	37.1	2.5
$EtPr_3Si$	24.3	28.6	−4.3
Pr_4Si	10.3	8.3	2.0
System: Me_2Hg + Et_2Hg; r = 0.486			
Me_2Hg	25.5	23.6	1.9
MeEtHg	46.1	50.0	−3.9
Et_2Hg	28.4	26.4	2.0
System: CH_3COOMe + C_3H_7COOEt; [CH_3CO] = 0.50; [OMe] = 0.45[a]			
CH_3COOMe	25.4	22.5	2.9
CH_3COOEt	23.4	27.5	−4.1
C_3H_7COOMe	22.7	22.5	0.2
C_3H_7COOEt	28.5	27.5	1.0

[a] The [OEt] was augmented by the $Al(OEt)_3$ used as catalyst.

Quantitative data for some of the other systems tested are given in Table III. These data were mostly of a somewhat lower order of analytical accuracy than those given above, and it is seen that the deviations from the predicted values are considerably greater. However, the deviations appear to be well scattered and random, and show no statistically significant trends, and it may justifiably be concluded that in these cases also there is no deviation from the random distribution outside of the experimental error in each.

Experimental Method and Procedure.—The relative proportions of the various metal alkyls present in a given mixture were determined by fractional vacuum distillation, after removal of the catalyst and halide salts (if any) by filtration and washing or extraction. Standard distillation practice was followed, with adaptations appropriate to the particular mixtures.

The equipment used, shown schematically in Fig. 1, comprised a small fractionating column, vacuum jacketed and electrically heated; a 100-ml. three-necked distilling flask, fitted with a nitrogen inlet tube and heated with an oil-bath; a still head, fitted with a thermometer, and partial or total condenser; a graduated receiver kept in a transparent Dewar-flask cooling bath; an additional trap kept in a dry-ice-bath; together with a vacuum pump, an adjustable mercury U-tube pressure regulator, manometers for normal and low pressures, a controlled nitrogen supply, and other usual accessory equipment.

The column, 32 cm. long and 14 mm. i. d., was packed with 4.76-mm. ($^3/_{16}$-in.) filed aluminum balls.[2] The still head was designed to reduce the dead space to a minimum, using a partial condenser, but better results were obtained with only a slight increase in hold-up, by using a total con-

(2) This packing is prepared by rubbing the balls between 6-in. (15-cm.) circular flat steel files. It has a fairly low H. E. T. P., a very low hold-up, and high maximum throughput.

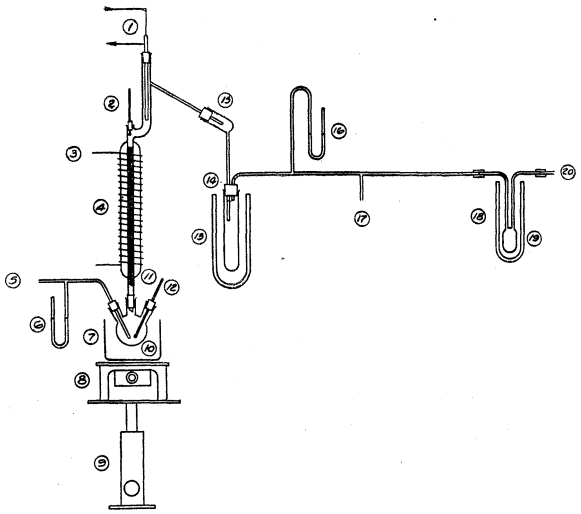


Fig. 1.—Distillation equipment: 1, condenser with regulated water flow; 2, thermometer, range 30–90°; 3, jacket heating wire; 4, evacuated glass jacket; 5, nitrogen inlet; 6, manometer; 7, oil-bath; 8, hot plate; 9, movable platform; 10, 100-ml. flask; 11, 14-mm. i. d. column with 32 cm. of filed aluminum ball packing; 12, thermometer; 13, unsilvered Dewar flask and bath at −30°; 14, 80-ml. graduated receiver; 15, adapter; 16, low-pressure manometer; 17, nitrogen inlet; 18, Dewar flask and bath at −75°; 19, trap; 20, line to pressure regulator, high-pressure manometer, and exhaust.

denser and controlling the delivery of product by the adjustment of a grooved stop-cock. Reflux ratios, and also the correct heating current for the column jacket, were estimated by counting drops. The graduated receiver was kept at about −30° in a trichloroethylene bath with dry-ice. All liquid volumes were corrected to 20° by an arbitrary temperature coefficient of 0.1% per degree. Since the temperature of observation, as well as the true temperature coefficient, was usually almost identical for all the distillate, this arbitrary procedure produced only negligible errors. The pressure was lowered at intervals during the progress of the distillation, and the temperature and level of the heating bath were adjusted, so as to maintain a temperature in the neighborhood of 50–75° at the still head, thus minimizing the thermal decomposition of the higher-boiling metal alkyls. The reflux ratio was maintained at about 5 to 1 over the flat portions of the distillation curves, and was increased to about 10 to 1 at the point of separation between compounds.

The observed temperatures at any given pressure were converted to a common basis of 50 mm. pressure. Inspection of vapor pressure data for the five methyl and ethyl tetraalkyllead compounds, obtained from the literature and in this Laboratory, showed that the vapor pressures are given very accurately by the five equations in Table IV which have a common point of intersection[3] at log P = 4.8566 and $1/(t + 230) = 0.0015097$, where t = °C.

TABLE IV

VAPOR PRESSURES OF LEAD ALKYLS

$\text{Log}_{10} P$ (mm. Hg) $= A - B/(t + 230)$; t = °C.

Compound	A	B	t at 50 mm., °C.
Me_4Pb	6.9381	1378.7	33.2
Me_3EtPb	7.2760	1602.5	57.3
Me_2Et_2Pb	7.5903	1810.7	77.4
$MeEt_3Pb$	7.8768	2000.5	93.8
Et_4Pb	8.1547	2184.6	108.4

The assumption was made that any other similar metal alkyl (or mixture) would have a similar vapor pressure line passing through the same point of intersection. Accordingly a nomogram was constructed to give the temperature at 50 mm. pressure corresponding to any observed pressure and temperature.

The distillation data were plotted to give the volume of distillate corrected to 20° as a function of the temperature corrected to 50 mm. pressure. Good curves usually were obtained and the identity of the distillate over the various flat portions of the curve as a rule was defined beyond question by the nature of the materials taken for the reaction. In these cases the volume of each constituent in the distillate was estimated by dividing the distillation curve into segments at points halfway between the boiling points (at 50 mm.) of the various compounds. While such a method of division is theoretically not strictly accurate, the errors so introduced are very small, and the personal equation is eliminated.

In those cases where the composition of the distillate over each portion of the curve was not unequivocally known (for example, in the product from a mixture of tetramethyltin and tetraethyllead, or in cases where a solvent might also be present), the distillate was taken in separate cuts which were analyzed for the metals present by conventional methods. When most of the charge had been distilled, and no further fractionation was possible, the distillation was stopped, the column allowed to drain, and the volume of residue measured. This volume was taken to consist solely of the highest-boiling constituent, when no other than that one constituent was conceivably present; otherwise, it was taken to comprise all the possible remaining constituents.

From the volumes of the constituents and their known

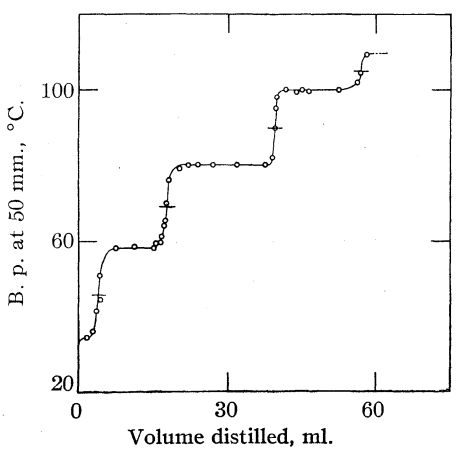


Fig. 2.—Typical distillation curve: —points of division between compounds; ---undistilled residue.

(3) Calingaert and Davis, *Ind. Eng. Chem.*, **17**, 1287 (1925).

densities and molecular weights, the mole fractions of each component of the metal alkyl portion of the product were calculated. In those relatively few cases where two or three components were expected to be present in the residue, a reasonable estimate of each was made; inasmuch as the amounts of these involved were always small and their various molecular volumes did not differ greatly, this procedure introduced no significant uncertainty in computation of the total amount of each kind of metal and alkyl group present.

TABLE V

ANALYSIS OF A TETRAALKYLLEAD MIXTURE

Pressure, mm.	Vapor temp. Obsd.	Vapor temp. Corr. to 50 mm.	Distillate Vol. obsd. at −30°	Distillate Vol. corr. to 20°
60	38.5	34.8	1.5	1.5
	41.6	37.5	3.2	3.3
	45.4	41.8	3.6	3.7
33	40.0	49.0	4.2	4.4
	45.2	54.2	5.0	5.2
	46.5	55.9	5.5	5.7
	47.0	56.1	7.5	7.8
	47.4	56.4	11.0	11.5
32	47.2	57.0	13.0	13.6
	48.5	58.2	15.6	16.3
	53.0	63.0	16.3	17.1
11	36.6	67.0	17.0	17.8
	42.5	73.3	17.3	18.1
	45.5	76.5	19.2	20.1
	46.3	77.2	21.0	22.0
	46.0	77.0	26.0	27.3
	46.0	77.0	33.0	34.6
	46.0	77.0	36.0	37.8
	50.5	81.3	37.8	39.6
5.5	45.0	88.2	38.7	40.6
	49.4	93.0	39.5	41.4
	49.5	93.0	42.0	44.1
	49.5	93.0	44.3	46.5
	50.5	94.0	49.0	51.4
	50.4	94.0	52.6	55.2
	52.5	96.0	54.0	56.7
	54.4	98.0	54.2	56.9
	59.4	103.2	54.5	57.2
4.5	59.0	106.5	56.0	58.8

Compound	Cut points, ml.	Vol., ml.	Millimole	Mole, %
	0			
Solvent	1.5			
Me_4Pb	4.2	2.7	20.1	5.5
Me_3EtPb	17.6	13.4	89.6	24.4
Me_2Et_2Pb	40.5	22.9	138.9	37.8
$MeEt_3Pb$	57.2	16.7	92.6	25.2
Et_4Pb dist.	59.8	5.1	26.1	7.1
Et_4Pb residue	62.3			

[Me] = 0.055 + (0.75 × 0.244) + (0.5 × 0.378) + (0.25 × 0.252) = 0.490.

The observed and derived data and the distillation curve for a typical example of a satisfactory analysis of a mixture of the five methyl and ethyl tetraalkyllead compounds are given in Table V and Fig. 2.

Summary

The procedure used for the analysis of volatile metal alkyl mixtures by distillation is described, and is shown by tests to give results accurate to less than 1% of the total volume.

Analyses of a series of mixtures of methyl and ethyl lead alkyls which have undergone the redistribution reaction show, within this experimental error, exact agreement with the compositions predicted for random equilibrium mixtures; individual analyses for other systems are also in satisfactory accord with prediction.

DETROIT, MICHIGAN RECEIVED JULY 21, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE ETHYL GASOLINE CORPORATION]

The Redistribution Reaction. III. Determination of a Material Balance

BY GEORGE CALINGAERT AND HAROLD SOROOS

The first paper[1] of this series reported, as a distinctive characteristic of the redistribution reaction, its essential freedom from side reactions and decomposition. This was evidenced, for many different systems, by the absence of gas evolution, precipitation, tar formation, or heat of reaction, and by satisfactory recoveries of material. To provide a quantitative measure of this, for one case at least, the present work was undertaken, and consisted in carrying out a representative redistribution reaction in the usual manner, obtaining an accurate material balance, and testing for secondary products.

Such a determination can be made with a high degree of accuracy for a reaction involving tetraalkyllead compounds, since any side reactions will convert the lead to other forms, which can be separated readily from the tetraalkyllead compounds constituting the bulk of the reaction mass. Accordingly, a mixture of tetramethyl- and tetraethyllead was used for this test.

Table I gives the material balance on a lead basis for two tests in which a mixture of the two

(1) Calingaert and Beatty, THIS JOURNAL, **61**, 2748 (1939).

TABLE I

MATERIAL BALANCE WITH ALUMINUM CHLORIDE CATALYST

Input	Test 1 G.	Test 1 Millimoles	Test 1 %	Test 2 G.	Test 2 Millimoles	Test 2 %
Pb as R_4Pb	57.864	279.25	100.00	60.7935	293.39	100.00
$AlCl_3$	0.442	3.32		0.3012	2.26	
Recovery						
Pb as R_4Pb	56.7827	274.04	98.13	60.0334	289.72	98.75
Pb as R_3PbCl	0.7803	3.77	1.35	0.9053	4.37	1.49
Pb as $PbCl_2$	0.0470	0.22	0.08	0.0654	0.31	0.11
Loss (or gain)	+0.2540	+1.22	+0.44	−0.2106	−1.01	−0.35
Total	57.8640	279.25	100.00	60.7935	293.39	100.00

lead alkyls was diluted with hexane and treated with aluminum chloride. The recovery of tetraalkyllead averaged 98.5%; the remaining 1.5% was principally trialkyllead chloride. A trace of lead chloride was found, as was to be expected since this is a normal decomposition product of trialkyllead chlorides. No metallic lead was formed. Aluminum chloride is known to react with tetraalkyllead,[2] and the trialkyllead halide found corresponded approximately to the aluminum chloride taken, in accordance with the equation $AlCl_3 + R_4Pb \rightarrow RAlCl_2 + R_3PbCl$.

These results suggested that the use of alkylaluminum chlorides as catalysts might reduce the formation of the lead salts, and this was found to be so. Table II gives the data for two tests in which the mixture of the two lead alkyls, without solvent, was treated with methylaluminum dichloride and dimethylaluminum chloride, respectively. In order to obtain readily-measurable quantities of the products of the reaction with the catalysts, the amounts of the latter used were very much greater than necessary for complete redistribution. Analyses were made only for the alkyllead chlorides and lead chloride formed; again, there was no metallic lead. The amount of lead thus found in the form of salts equalled only 0.10 and 0.04 mole, respectively, per mole of catalyst. A parallel test using aluminum chloride confirmed the results given in Table I, yielding 1.46 moles of lead chlorides per mole of catalyst.

TABLE II

TETRAALKYLLEAD CONVERTED TO LEAD CHLORIDES BY DIFFERENT ALUMINUM CATALYSTS

Pb input, as R_4Pb, millimoles	Catalyst Compound	Catalyst Millimoles	Pb output, as chlorides, millimoles	Moles Pb chlorides per mole Al
296.41	Me_2AlCl	16.10	0.626	0.039
300.81	$MeAlCl_2$	18.84	1.965	0.104
297.19	$AlCl_3$	3.12	4.540	1.455

(2) Gilman and Apperson, *J. Org. Chem.*, **4**, 162 (1939).

In these three tests, the tetraalkyllead product of the reaction was distilled as described in the preceding paper[3] and the redistribution was found to be complete. In the first tests using aluminum chloride the distillation was omitted, since concurrent experiments showed that the reaction was complete, under the conditions used, with lower concentrations of the catalyst.

It is, therefore, evident that the redistribution reaction is quantitative, apart from such irreversible interaction with the catalyst as may be imposed by the selection of one particular catalyst or another.

Experimental

Determination of a Material Balance.—The determination of a material balance was carried out in the following manner.

Approximately 0.15 mole each of tetramethyl- and tetraethyllead with 40-ml. of *n*-hexane were placed in a glass-stoppered flask and weighed. After a sample was withdrawn for a lead analysis, a small amount of anhydrous aluminum chloride was added and its weight determined. A reflux condenser, the top of which was connected to a dry-ice trap, was attached to the flask and the mixture was refluxed at 80° for four hours. The contents of the trap and condenser were washed into the reaction mixture with 5-ml. of *n*-hexane. The main body of the reaction mixture, containing the tetraalkyllead compounds and dissolved trialkyllead chlorides, was filtered by nitrogen pressure through a sintered-glass filter-stick into a tared flask, using several small portions of *n*-hexane to wash the residue. Samples of the filtrate and the hexane washings were analyzed for lead. An aliquot of the filtrate was extracted with four 25-ml. portions of concentrated ammonia solution to remove the dissolved trialkyllead chlorides, and after filtering the combined extracts through a wet filter paper, the lead content was determined. The residue was washed with five 10-ml. portions of benzene, followed by filtration through the filter-stick to remove the undissolved trialkyllead chlorides, and the lead content of the washings was determined. About 100 ml. of water in small portions was next used to wash the residue free of lead chloride. The lead content of the washings was determined. The flask and filter-stick were finally washed with

(3) Calingaert, Beatty and Neal, THIS JOURNAL, **61**, 2755 (1939).

nitric acid and the lead was determined. The analytical data for the two experiments are given in Table III.

TABLE III

LEAD ANALYSIS

	Input	Pb found, g. Test 1	Test 2
R_4Pb	(Hexane solution)	57.8640	60.7935
	Recovery		
R_4Pb, R_3PbCl	(Hexane solution)	55.5530	58.8735
R_4Pb, R_3PbCl	(Hexane washings)	1.4430	1.5290
R_3PbCl	(NH_3 extraction)	0.2133	0.3691
R_3PbCl	(Benzene washings)	.5670	.5362
$PbCl_2$		.0440	.0639
Residue	(HNO_3 washings)	.0030	.0015

Determination of Lead Chlorides Formed with Different Catalysts.—The determination of the amount of tetraalkyllead compounds converted to alkyllead chlorides and lead chloride using different aluminum catalysts was carried out in the following manner.

To a weighed amount of the catalyst, contained in a 500-ml. 3-necked flask equipped with vapor-proof mechanical stirrer, thermometer, and reflux condenser, the tetraethyllead followed by the tetramethyllead was added slowly from a dropping funnel in the top of the condenser. The flask was cooled in an ice-bath and an atmosphere of nitrogen was maintained within the flask during the addition of the alkyllead compounds. Failure to follow the experimental procedure and precautions outlined above may result in violent decomposition of the tetraalkyllead, especially of the tetramethyllead. The ice-bath was then removed and replaced by an oil-bath; the mixture was stirred and maintained at 80° in an atmosphere of nitrogen for two hours.

The reaction flask was then cooled and the catalyst decomposed by shaking with 100 ml. of distilled water. The aqueous layer, containing alkyllead chlorides and lead chloride, was separated, filtered through a wet filter paper and analyzed for lead. The alkyllead layer was extracted with four 25-ml. portions of concentrated ammonia solution, to remove trialkyllead chlorides. The extracts were combined, filtered through a wet filter paper, and analyzed for lead. The filter papers were finally washed with nitric acid to dissolve any lead residue, and the washings were analyzed for lead.

The alkyllead layers were finally distilled to ascertain the extent of redistribution. The reaction was complete in every case. Table IV gives the analyses of products for lead chlorides.

TABLE IV

LEAD ANALYSIS

Products	Catalyst Me_2AlCl	$MeAlCl_2$	$AlCl_3$
Pb in Aq. layer, g.	0.1296	0.3150	0.9220
Pb in NH_3, g.	.0000	.0926	.0193
Pb in residue, g.	.0000	.0000	.0000
Pb (total), g.	.1296	.4076	.9413

Summary

By determination of an accurate material balance, the redistribution of a mixture of tetramethyl- and tetraethyllead in hexane solution is shown to be quantitative. When aluminum chloride is used as the catalyst, it is found to react irreversibly with the alkyllead compounds, as expected, forming alkyllead chlorides in very small quantities, equivalent to about 1.5 moles per mole of catalyst. When methylaluminum chlorides are used as catalysts, this amount becomes negligible.

DETROIT, MICHIGAN RECEIVED JULY 21, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

The Reaction of the Grignard Reagent with Homophthalic Anhydride

BY CHARLES C. PRICE, FREDERICK M. LEWIS AND MORRIS MEISTER

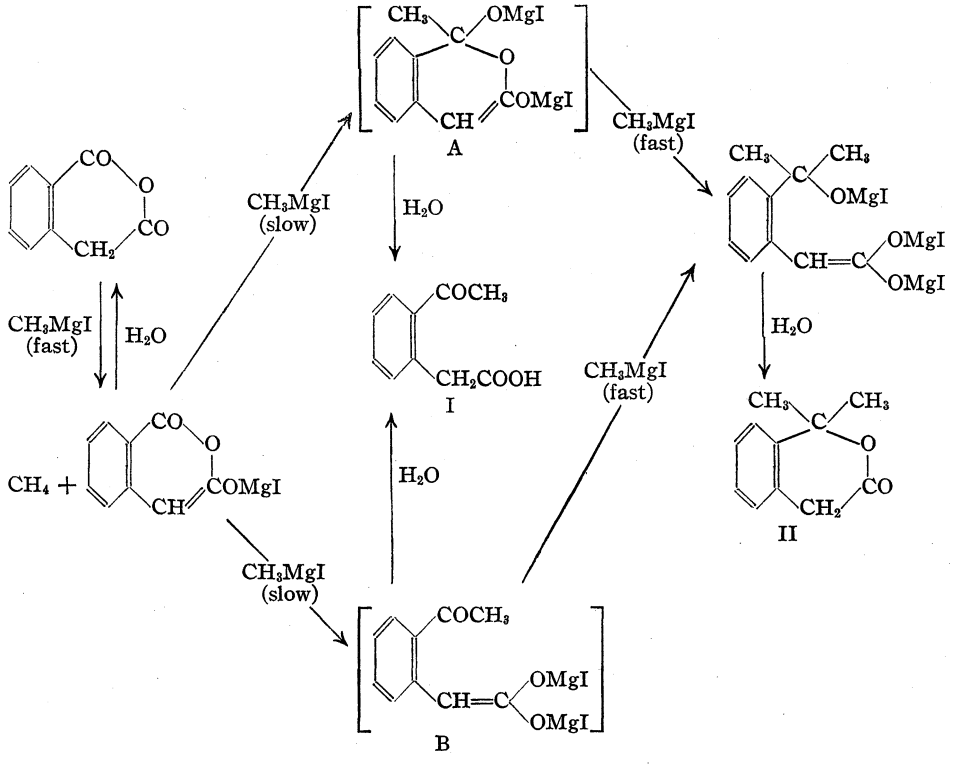
The reaction of methylmagnesium iodide with homophthalic anhydride has been investigated as a possible method for the preparation of the unreported keto acid, *o*-acetylphenylacetic acid (I), which was desired in connection with another investigation.

Bauer and Wolz,[1] in determining the products from the action of an excess of several Grignard reagents on homophthalic anhydride, obtained only the various homophthalides. Since Simonis and Arand and Weizmann, Bergmann and Bergmann[2] have reported keto acids as well as phthalides from phthalic anhydride, the reaction with homophthalic anhydride has been studied under conditions more favorable for the formation of the desired keto acid. However, in spite of using the inverse procedure, *i. e.*, adding the Grignard reagent to a solution of the anhydride, and using just the calculated amount of reagent, one-half of the starting material was converted to dimethylhomophthalide (II), the remainder was recovered unchanged. No *o*-acetylphenylacetic acid was obtained, although in a few cases the recovered homophthalic acid had a low melting point and gave an iodoform test, indicating the possible presence of small amounts of this substance.

(1) Bauer and Wolz, *Arch. Pharm.*, **249**, 454 (1911).

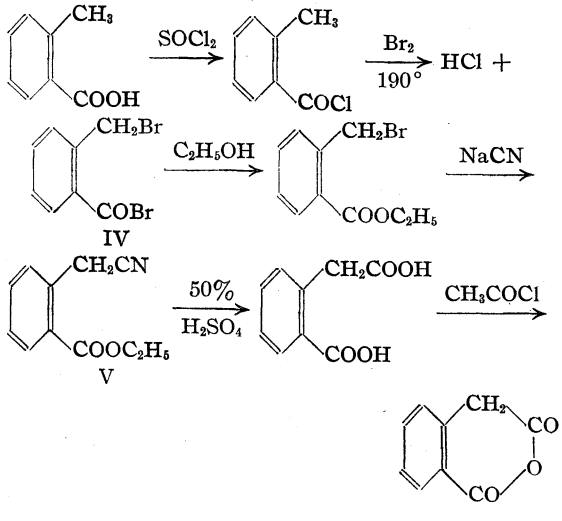
(2) (a) Simonis and Arand, *Ber.*, **42**, 3721 (1909); (b) Weizmann, Bergmann and Bergmann, *J. Chem. Soc.*, 1369 (1935).

Since the anhydride enolizes readily, the first mole of Grignard reagent is converted to methane. The theoretical amount of reagent for the formation of the keto acid is, therefore, two moles. The non-formation of the keto acid by the second mole of reagent under these conditions indicates that the reaction must follow either of the two courses outlined below.

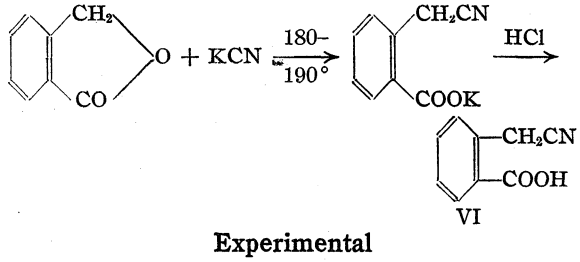


It is the opinion of the authors that the reaction through intermediate A is the more likely.

A procedure for the preparation of homophthalic acid from *o*-toluic acid has been developed. The latter acid is converted to its acid chloride and brominated according to the directions of Davies and Perkin.[3] Treatment with alcohol and sodium cyanide converted the bromo acid bromide (IV) to the nitrile ester (V) of homophthalic acid. Hydrolysis to the acid was accomplished by warming with 50% sulfuric acid. The preparation is relatively simple since the first product isolated is the nitrile-ester and the over-all yield from *o*-toluic acid to homophthalic anhydride is 70–75% of the theoretical.



Another simple preparation, which apparently has been neglected, is that reported by Wislicenus[4] starting from phthalide. The yield of acid nitrile obtained in this Laboratory by this method was as high as 80–85%.



Experimental

o-**Carbethoxyphenylacetonitrile (V).**—*o*-Toluic acid (100 g.) was refluxed for two hours with twice the theoretical

(3) Davies and Perkin, *J. Chem. Soc.*, **121**, 2202 (1922).
(4) Wislicenus, *Ber.*, **17**, 2178 (1884).

quantity of thionyl chloride. After the excess thionyl chloride had been removed by distillation, the acid chloride was heated to 185–195° in an oil-bath and 135 g. of bromine was added slowly (one to two hours) through a separatory funnel the tip of which was below the surface of the reaction mixture. After cooling in an ice-bath, 200–250 cc. of absolute alcohol was added. The alcoholic solution of the bromoester was then poured into a solution of 40 g. of sodium cyanide in 30 cc. of warm water, the mixture refluxed for five hours and then half the alcohol removed by evaporation or distillation.

The ester was extracted with several portions of ether, the ethereal solution washed three times each with water, with sodium bicarbonate and again with water and then dried over sodium sulfate. Evaporation of the ether left a dark brown oil from which 85–90 g. (71–76%) of colorless material was obtained by distillation (16 mm.), b. p. 170–170.5°. This compound had the following properties: d^{20}_{20} 1.1246; $n^{20}D$ 1.5172; M_D calcd., 51.2; M_D found, 50.8. *Anal.* Calcd.: N, 7.4. Found: N, 7.7.

Homophthalic Anhydride.—The hydrolysis of the nitrile and ester groups in the above compound was accomplished readily in over 90% yield by the action of an equal volume of 50% sulfuric acid at 100° for twelve hours. Longer reaction time or higher or lower acid concentration decreased the yield. The reaction mixture was poured over an equal weight of ice and the precipitated acid collected and dried. Conversion to the anhydride was accomplished readily by refluxing a solution of the acid in three times its weight of acetyl chloride for half an hour and precipitating the anhydride with petroleum ether (60–90°). The product was obtained in 90–95% yields and melted at 140–141°.

***o*-Carboxyphenylacetonitrile (VI)**[5] was prepared according to the directions of Wislicenus.[4] A mixture of 40 g. of phthalide and 40 g. of potassium cyanide yielded 35 g. (82%) of crystalline acid nitrile, m. p. 114–115°. Seven grams of phthalide was recovered unchanged.

Experimental Procedure.—A solution of methylmagnesium iodide was prepared by treating 2 g. of magnesium turnings with 4.7 cc. of methyl iodide and 39 cc. of ether for one hour. The solution, under an atmosphere of nitrogen at all times, was transferred to a separatory funnel and added to 5 g. of homophthalic anhydride dissolved in ether in a flask equipped with a mechanical stirrer and a reflux condenser. During the addition of the first half of the reagent, methane was evolved with the formation of a yellow precipitate. The time for the addition of the remaining reagent varied from one to six hours, that of subsequent refluxing from three to six hours, and that of standing at room temperature after refluxing from zero to fifteen hours with no appreciable difference in the products of the reaction.

At the end of the specified time, the reaction mixture was poured into ice and 35 cc. of hydrochloric acid. Unreacted homophthalic anhydride precipitated. It was collected, recrystallized from ether and weighed 1.3–1.8 g., m. p. 140–141°. The ether layer in the first filtrate was washed thoroughly with sodium bicarbonate solution. Addition of acid to this bicarbonate extract precipitated homophthalic acid which was dried and weighed 0.4–0.6 g., m. p. 173–175°. In a few cases the precipitated acid melted low and over a wider range and gave an iodoform test indicating the presence of at least a small amount of *o*-acetylphenylacetic acid. The pure keto acid could not be isolated, however.

The ether solution was next dried and evaporated, leaving a neutral yellow oil and white solid. The solid was collected by filtration, washed with a minimum amount of ether and then recrystallized from ether. The white needle-like crystals were weighed 1.9–2.3 g., m. p. 94–95°. The combined ethereal mother liquors were evaporated and the residual yellow oil weighed 0.6–0.8 g. No pure compound was isolated from this material.

(5) This compound was prepared by Richard G. Rogers.

Summary

The addition of the calculated amount of methylmagnesium iodide to homophthalic anhydride does not lead to the formation of a keto acid. Instead one-half of the starting material is recovered unchanged; the other half is converted to dimethylhomophthalide.

URBANA, ILLINOIS RECEIVED JULY 13, 1939

[CONTRIBUTION FROM THE DERMATOLOGICAL RESEARCH LABORATORIES, DIVISION OF ABBOTT LABORATORIES]

Chemistry and Chemotherapy of 4,4′-Diaminodiphenylsulfone, 4-Amino-4′-hydroxydiphenylsulfone and Related Compounds[1]

BY G. W. RAIZISS, L. W. CLEMENCE, M. SEVERAC AND J. C. MOETSCH

4,4′-Diaminodiphenylsulfone was prepared by Fromm and Wittmann[2] by reduction of the corresponding dinitro compound which they obtained by the oxidation of 4,4′-dinitrodiphenylsulfide. They prepared the latter compound by action of sodium sulfide on *p*-chloronitrobenzene according to Nietzki and Bothof.[3] Our attempts to follow this method had produced an impure product from which the dinitrosulfide could be obtained only in very poor yields, after numerous recrystallizations. This was in accordance with the findings of Kehrmann and Bauer,[4] who showed that the reaction between sodium sulfide and *p*-chloronitrobenzene could produce a mixture of seven compounds.

We prepared the diaminosulfone by oxidation of the 4,4′-diaminodiphenylsulfide (thioaniline), protecting the amino groups by acetylation, and subsequently hydrolyzing. Hoffman[5] had prepared thioaniline by heating aniline, sulfur, and lead oxide (PbO). The yields were not good and the method rather unwieldy. We chose as our starting material 4-nitro-4′-aminodiphenylsulfide which Hodgson and Rosenberg[6] had prepared by reaction of sodium *p*-aminothiophenol and *p*-chloronitrobenzene. Lantz[7] described a two-stage reaction in which an excess of sodium sulfide reacted with *p*-chloronitrobenzene to form sodium *p*-aminothiophenol and without isolating the material another equivalent of *p*-chloronitrobenzene was added to the reaction mixture, the final product was 4-nitro-4′-aminodiphenylsulfide in good yields and fairly pure.

4′-Amino-4′-hydroxydiphenylsulfone was prepared by diazotization of 4-amino-4′-acetylaminodiphenylsulfone and simultaneous deacetylation and replacement of the diazo group by hydroxyl. The 4-amino-4′-acetylamino compound was prepared by reduction of 4-nitro-4′-acetylaminodiphenylsulfone which was obtained by oxidation of the corresponding sulfide.

(1) Presented before Division of Medicinal Chemistry, A. C. S., Baltimore, April 6, 1939.

(2) Fromm and Wittmann, *Ber.*, **41**, 2264 (1908).

(3) Nietzki and Bothof, *ibid.*, **27**, 3261 (1894).

(4) Kehrmann and Bauer, *ibid.*, **29**, 2362 (1896).

(5) Hoffman, *ibid.*, **27**, 2807 (1894).

(6) Hodgson and Rosenberg, *J. Chem. Soc.*, 180 (1930).

(7) French Patent 715,359; English Patent 376,961; U. S. Patent 1,965,776.

Buttle[8] and others[9,10] discovered that 4,4′-diaminodiphenylsulfone had a better curative effect in β-hemolytic streptococcus infection of mice than sulfanilamide. In a recent publication we have shown[11] that diaminodiphenylsulfone and the corresponding sulfide were more toxic for rabbits than sulfanilamide. The diacetyl derivatives of the sulfone and sulfide were, however, considerably less toxic than sulfanilamide. We found that the therapeutic effect of diaminodiphenylsulfone was considerably better than that of sulfanilamide. Therapeutic effects of the sulfide and the diacetyl derivatives of the sulfone and sulfide compared favorably with that of sulfanilamide. 4-Amino-4′-acetylaminodiphenylsulfone, 4-amino-4′-hydroxydiphenylsulfone, 4-acetylamino-4′-hydroxydiphenylsulfone and 4-acetylamino-4′-acetoxydiphenylsulfone were of about the same therapeutic effectiveness in experimental streptococcic infection as sulfanilamide, but they were inferior to diaminodiphenylsulfone.

Experimental Part

Preparation of 4,4′-Diaminodiphenylsulfone

4-Nitro-4′-aminodiphenylsulfide.—The method was essentially that of Lantz: a mixture of 480 g. of sodium sulfide, dissolved in 2000 cc. of water, and 128 g. of *p*-chloronitrobenzene was refluxed for eight hours; 128 g. of *p*-chloronitrobenzene was added and refluxing was continued for fifteen hours. The mixture was steam distilled to remove unchanged *p*-chloronitrobenzene, breaking up lumps which had tendency to form. After cooling the non-volatile portion, the crude orange-yellow crystals were filtered off; yield, 160 g. (80%). The material was recrystallized from alcohol.

4,4′-Diaminodiphenylsulfide (Thioaniline).—To a boiling suspension of 200 g. of nitroaminosulfide in a mixture of 530 cc. of concd. hydrochloric acid and 500 cc. of water, 180 g. of tin turnings was added slowly and after solution was complete, 40 cc. of concd. hydrochloric acid and 22 g. of tin were added. After ten minutes of boiling, 2 g. of "darco" was added, the solution then boiled fifteen minutes longer and filtered hot. After thorough cooling, 40% sodium hydroxide solution was added until strongly alka-

(8) Buttle, *Lancet*, 1331 (1937).

(9) E. Fourneau, J. and MMe. J. Trefouel, F. Nitti, and D. Bovet, *Bull. Acad. Med.*, **118**, 210 (1937).

(10) H. Bauer and S. M. Rosenthal, *Pub. Health Rept.*, **53**, 40 (1938).

(11) G. W. Raiziss, M. Severac, J. C. Moetsch, and L. W. Clemence, *Proc. Soc. Exptl. Biol. Med.*, **39**, 339 (1938).

line, the thick pasty precipitate changing to a gray-colored curd which was filtered and washed with water until washings were neutral to litmus, and drained well. The material was suspended in 1200 cc. of boiling alcohol, 5 g. of "darco" added and refluxed for thirty minutes. The hot, almost colorless filtrate was added to 10 liters of cold water with stirring, precipitating a white, fluffy precipitate which was filtered and dried in vacuum; yield, 140 g. (80%). The product was fairly pure, it was recrystallized further from 50% alcohol.

4,4'-Diacetylaminodiphenylsulfide.—To 140 g. of diaminodiphenylsulfide suspended in 200 cc. of glacial acetic acid, 140 cc. of acetic anhydride was added gradually with stirring, the mixture then refluxed for one hour and poured into 8 liters of ice and water, stirring well to break up lumps. The precipitate was filtered and washed with water until free of acetic acid and dried in vacuum; yield, 190 g. (97%). It was purified by recrystallization from alcohol.

4,4'-Diacetylaminodiphenylsulfone.—One hundred and fifty grams of potassium dichromate was dissolved in 2000 cc. of water and 1400 cc. of concd. sulfuric acid added. After cooling to 15° the mixture was added slowly with stirring to a solution of 100 g. of diacetylaminodiphenylsulfide in 1000 cc. of glacial acetic acid (dissolved by warming, then cooled to 20°). The reaction mixture was kept below 20° by external cooling and, after addition was complete, allowed to stand at room temperature for ninety minutes. It was then poured into 24 liters of ice and water, with stirring; the precipitate was filtered and washed with water until free of acid; yield, 70 g. (63%). It was purified by dissolving 50 g. in a boiling mixture of 1500 cc. of alcohol and 200 cc. of water; after adding 2.5 g. of "darco" and refluxing for thirty minutes, it was filtered hot and added to 6000 cc. of ice water; yield 35 g.

4,4'-Diaminodiphenylsulfone.—A suspension of 100 g. of crude diacetylaminodiphenylsulfone in 360 cc. of concd. hydrochloric acid and 300 cc. of water was heated under reflux for two hours. To the solution which was obtained 4 g. of "darco" was added and heating continued twenty minutes, then filtered and cooled well. Solid sodium carbonate was added with stirring until slightly alkaline to litmus. The precipitate was filtered and washed with water. The crude product, after vacuum drying, weighed 65 g. (87%). It was purified by refluxing in 1000 cc. of 40% alcohol, to which 5 g. of "darco" was added, for thirty minutes, and after filtering through a steam funnel and adding to 1000 cc. of hot water, it was mixed well with 3000 g. of ice; yield, 55–60 g.

Preparation of 4-Amino-4'-hydroxydiphenylsulfone

4-Nitro-4'-acetylaminodiphenylsulfide.—Two hundred and fifty grams of 4-nitro-4'-aminodiphenylsulfide was suspended in 500 cc. of glacial acetic acid and 150 cc. of acetic anhydride added gradually with stirring. The mixture was refluxed for two hours and poured into 7500 cc. of ice water with efficient stirring to break up lumps, then filtered and the crystalline precipitate washed with water until free of acid; yield, 290 g. (98%). It was purified by recrystallization from alcohol.

4-Nitro-4'-acetylaminodiphenylsulfone.—One hundred grams of nitro-acetylaminosulfide was oxidized using the quantities and method described in the case of diacetylaminosulfide; yield, 90 g. (81%). The material was only slightly soluble in hot alcohol and required a large volume for recrystallization.

4-Amino-4'-acetylaminodiphenylsulfone.—A solution of 203 g. of stannous chloride in 600 cc. of alcohol was added to a boiling suspension of 100 g. of the crude nitro compound in 600 cc. of alcohol; the mixture was refluxed for fifteen minutes and a clear solution was obtained. After thorough cooling an excess of 40% sodium hydroxide solution (about 750 cc.) was added, followed by the addition of 10 liters of water, stirring to break up lumps. The precipitate was filtered and washed with water until the washings were neutral, and sucked fairly dry on the funnel; it was then refluxed in 1300 cc. of alcohol for one hour with 5 g. of "darco" added, filtered hot, and the solution diluted with five volumes of ice water. On stirring a crystalline precipitate separated; yield, 60 g. (66%). It was purified by recrystallization from 50% alcohol.

4-Amino-4'-hydroxydiphenylsulfone.—A suspension of 50 g. of aminoacetylamino in 380 cc. of water and 33 cc. of concd. sulfuric acid, was cooled to 0–5°, and diazotized by a solution of 12.5 g. of sodium nitrite in 40 cc. of water. The nitrite solution was added dropwise, with mechanical mixing, in thirty minutes. The mixture was further stirred until a test with starch–iodide paper, which was strongly

TABLE I

COMPOUNDS, PROPERTIES AND ANALYSES

Diphenylsulfide	Appearance	M. p., °C.	Formula	Analyses % N Calcd.	% N Found	% S Calcd.	% S Found
4-Nitro-4'-amino-	Orange-yellow plates	145[a]	$NO_2C_6H_4SC_6H_4NH_2$	11.38	11.17	13.00	12.70
4,4'-Diamino-	Colorless needles	108	$NH_2C_6H_4SC_6H_4NH_2$	12.96	12.93	14.81	14.62
4,4'-Diacetylamino-	Colorless plates	223–224[b]	$CH_3CONHC_6H_4SC_6H_4NHOCCH_3$	9.33	9.22	10.66	10.62
4-Nitro-4'-acetylamino-	Pale yellow needles	198[c]	$NO_2C_6H_4SC_6H_4NHOCCH_3$	9.72	9.48	11.11	10.80
Diphenylsulfone							
4,4'-Diamino-	Almost colorless plates	175[d]	$NH_2C_6H_4SO_2C_6H_4NH_2$	11.29	10.98	12.88	12.99
4,4'-Diacetylamino-	Pale yellow leaflets	285[d]	$CH_3CONHC_6H_4SO_2C_6H_4NHOCCH_3$	8.43	8.18	9.63	9.70
4-Nitro-4'-acetylamino-	Cream colored needles	229–230	$NO_2C_6H_4SO_2C_6H_4NHOCCH_3$	8.75	8.44	10.00	9.74
4-Amino-4'-acetylamino-	Pale yellow leaflets	242–243	$NH_2C_6H_4SO_2C_6H_4NHOCCH_3$	9.65	9.31	11.03	10.74
4-Amino-4'-hydroxy-	Colorless prisms	193–194	$NH_2C_6H_4SO_2C_6H_4OH$	5.62	5.50	12.80	12.69
4-Acetylamino-4'-hydroxy-	Colorless leaflets	274–275	$CH_3CONHC_6H_4SO_2C_6H_4OH$	4.81	4.85	10.99	11.04
4-Acetylamino-4'-acetoxy-	Colorless prisms	171–172	$CH_3CONHC_6H_4SO_2C_6H_4OOCCH_3$	4.20	4.22	9.60	9.90

[a] Kehrmann and Bauer and Lantz reported 143°. [b] Merz and Weith [*Ber.*, **4**, 390(1871)] reported 213–215°, Nietzki and Bothof reported 211°. [c] Kehrmann and Bauer reported 193°. [d] Fromm and Wittmann reported 174° for diamino, 280° for diacetyl.

positive at first, no longer diminished in intensity; it was then added in several portions to a boiling solution of 250 cc. of concd. sulfuric acid and 500 cc. of water, and boiling continued for ninety minutes, under reflux. After cooling, solid sodium carbonate was added until just neutral to litmus and the precipitate filtered, washed with water and suspended in 500 cc. of water containing 4.5 g. of sodium hydroxide. After agitating vigorously, any undissolved material was filtered off, and hydrochloric acid (1:1) added to filtrate until just acid to litmus. The precipitate was purified by crystallization from 1000 cc. of boiling water using 2.5 g. of "darco"; yield, 18–20 g. (42–46%).

4 - Acetylamino - 4' - hydroxydiphenylsulfone.—Twenty-five grams of aminohydroxysulfone was suspended in 125 cc. of ice water and 25 cc. of acetic anhydride gradually added with mechanical mixing. A gummy mass separated, but on further stirring it hardened to a white crystalline precipitate. After stirring one hour, the material was filtered and washed with water, crystallized from 300 cc. of 50% alcohol, using 1 g. of "darco"; yield, 22 g. (76%).

4 - Acetylamino - 4' - acetoxydiphenylsulfone.—Twenty-five grams of aminohydroxysulfone was suspended in 50 cc. of acetic anhydride and 10 drops of concd. sulfuric acid added; the mixture became hot; after boiling under reflux for twenty minutes, the clear solution was cooled and stirred to prevent crystallization to a hard mass, and the crystalline mush added to 500 cc. of water. After adding 40% sodium hydroxide solution until alkaline to litmus, it was filtered and washed well with water, then crystallized from 700 cc. of 50% alcohol using 1 g. of "darco"; yield, 26 g. (78%).

Summary

Chemical properties and methods of preparation of 4,4'-diaminodiphenylsulfone, 4,4'-diaminodiphenylsulfide, 4-amino-4'-hydroxydiphenylsulfone and their acetyl derivatives are described. The diaminodiphenylsulfone is superior, while the aminohydroxydiphenylsulfone and the acetyl derivatives are about equal to sulfanilamide in their therapeutic effect.

PHILADELPHIA, PENNA. RECEIVED JULY 19, 1939

[CONTRIBUTION NO. 383 FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF PITTSBURGH]

Thio Compounds Derived from Aroyl-*o*-benzoic Acids[1]

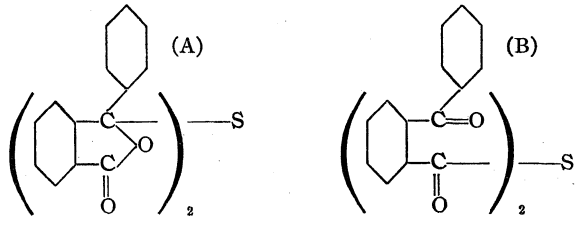
BY JOHN O'BROCHTA AND ALEXANDER LOWY

Introduction

Aroyl-*o*-benzoic acids are of theoretical importance because of their peculiar reactivity to form isomeric derivatives.[2] Blicke and Swisher[3] gave a summary of the evidence for the pseudo and normal forms of these derivatives. A search of the literature revealed no thio compounds of any of the aroyl-*o*-benzoic acids. Hence, a study was undertaken with the object of synthesizing sulfur derivatives of some of these acids, and of investigating their properties. Phosphorus pentasulfide and also hydrogen sulfide were selected as a means for the introduction of sulfur.

A schematic summary of the studies undertaken is given in Chart A. The chart contains the formulas of compounds prepared from *o*-benzoylbenzoic acid. Wherever CH_3 and Cl appear with Roman numerals and arrows on the chart, the analogous types of compounds have also been prepared; these substituents are in the para position.

The mechanism of the reaction of phosphorus pentasulfide upon *o*-benzoylbenzoic acid (I), *p*-toluyl-*o*-benzoic acid (IX) and 4'-chloro-*o*-benzoylbenzoic acid (XIV), to form 3,3'-diphenyldiphthalidyl sulfide (II), 3,3'-di-(*p*-tolyl)-diphthalidyl sulfide (X) and 3,3'-di-(*p*-chlorophenyl)-diphthalidyl sulfide (XV), respectively, shows the pseudo structures of the aroyl benzoic acids. The fact that hydrogen peroxide oxidation gave (I) and phenyl phthalide (VII), along with the molecular weight indication of a dimolecular type, suggested that the sulfur atom may be attached to a (I) and a (VII) fragment. The analysis checked for the following structures for compound (II)



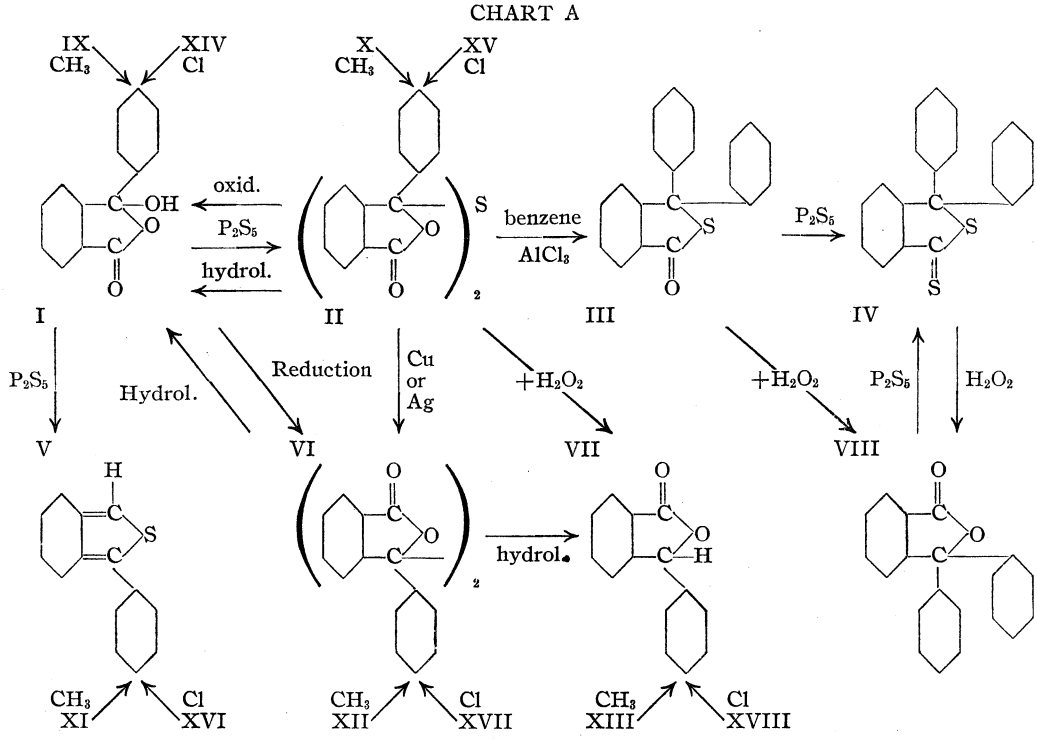
Both structures (A) and (B) could yield *o*-benzoylbenzoic acid by hydrolysis but it was difficult to account for the formation of phenyl phthalide (VII) by hydrogen peroxide oxidation of a compound with the structure of (B). The graphic representation (B) was further eliminated

(1) Abstracted from a Thesis presented by John O'Brochta to the Graduate School in partial fulfilment of the requirements for the Ph.D. degree.

(2) Meyer, *Monatsh.*, **25**, 475 (1904).

(3) Blicke and Swisher, THIS JOURNAL, **56**, 902 (1934).

CHART A



in that normal *o*-benzoylbenzoic acid anhydride has a melting point of only 120°.[4] It did not appear probable that a sulfur atom substitution would raise the m. p. by 127°. Structure (A) was further substantiated by the formation of 3,3′-diphenyldiphthalidyl (VI) from 3,3′-diphenyldiphthalidyl sulfide (II) on reaction with metals. By a different procedure the action of phosphorus pentasulfide on compound (I) produced a compound containing no oxygen. Structure (V) has been proposed for this reaction product. This reaction is analogous to the action of phosphorus pentasulfide on γ-ketonic acids[5] for the formation of thiophene type compounds. *o*-Benzoylbenzoic acid may be looked upon as a γ-ketonic acid. Dufraisse and Daniel[6] already have synthesized a product of this type of structure, namely, α,α′-diphenylisobenzothiophene. The *p*-methyl and *p*-chloro compounds (IX) and (XIV), respectively, behaved in analogous manner in all of the above reactions.

Experimental

3,3′-Diphenyldiphthalidyl Sulfide (II). Preparation (a) from *o*-Benzoylbenzoic Acid (I) and Phosphorus Pentasulfide in Benzene.—Twenty grams of the anhydrous form of (I) was mixed in a three-necked one-liter flask with 20 g. of phosphorus pentasulfide in 700 cc. of dry benzene. The condenser was equipped with a calcium chloride tube. The mixture was refluxed on an oil-bath, with mechanical stirring. Hydrogen sulfide was evolved. At the end of twenty-five hours, the hot mixture was filtered and the solvent distilled with suction. The residual solid was dried at room temperature, triturated in 200 cc. of 3% sodium hydroxide, filtered, washed free of alkali with water and dried. On acidification, the filtrate evolved hydrogen sulfide but no precipitate was formed, showing the absence of any unchanged (I). The alkali-insoluble residue was crystallized four times from xylene, filtered, washed with petroleum ether and dried at 100°; yield 11 g. of white odorless crystals, m. p. 247°. The compound was very soluble in hot cymene and chloroform; fairly soluble in hot benzene, toluene, xylene and glacial acetic acid and insoluble in petroleum ether, cyclohexane and hot or cold aqueous media.

Anal. Calcd. for $C_{28}H_{18}O_4S$: C, 74.65; H, 4.03; S, 7.12; mol. wt., 450. Found: C, 74.60, 74.45; H, 4.00, 4.07; S, 7.07, 6.97; mol. wt., 423, 445.

(b) From (I) and Phosphorus Pentasulfide.—Ten grams of (I) was ground together with 10 g. of phosphorus pentasulfide. The mixture was heated on an oil-bath at 115° (bath temp.) and stirred occasionally. After fifteen minutes of heating, the mass changed to a brick-red color, began to liquefy and hydrogen sulfide was evolved. It gradually formed into a thick gum and finally solidified at the end of one hour of heating. The solid was cooled, pulverized, and extracted with 200 cc. of cold 3% sodium hydroxide solution; 2.5 g. of (I) was recovered upon acidification of the filtrate. The alkali-insoluble fraction was crystallized from 200 cc. of glacial acetic acid. On further recrystallization from xylene, 5 g. of product (II) resulted.

(4) Von Pechmann, *Ber.*, **14**, 1865 (1881).
(5) Kues and Paal, *ibid.*, **19**, 3141 and 555 (1886).
(6) Dufraisse and Daniel, *Bull. soc. chim.*, [5] **4**, 2063 (1937).

The m. p. 247° and a mixed m. p. of 247° checked with the previously prepared (II).

(c) **From the Acid Chloride of (I) and Hydrogen Sulfide.**—Compound (I), 100 g., was converted to the acid chloride by the thionyl chloride method.[7] The resultant thick sirup was dissolved in 400 cc. of dry benzene and dry hydrogen sulfide was passed into the boiling solution. There was an immediate and strong evolution of hydrogen chloride. Hydrogen sulfide was passed through the dry solution until the evolution of hydrogen chloride ceased. A heavy white precipitate formed. After cooling, precipitation was completed by adding 200 cc. of petroleum ether. The resultant solid was filtered and extracted with cold 3% sodium hydroxide solution, filtered, and washed free of alkali. A very small amount of (I) was recovered on acidification. After drying the alkali-insoluble residue, followed by three recrystallizations from xylene, washing with petroleum ether, and drying, 60 g. of a white crystalline product resulted; m. p. 246–247°. A mixed m. p. of the product with compound (II), as prepared by the above phosphorus pentasulfide methods, showed no depression.

Reactions of 3,3′-Diphenyldiphthalidyl Sulfide (II).—Sodium hydroxide fusion[8] gave a positive test for a divalent sulfur atom. Hydrolysis by refluxing with a 5% alcoholic potassium hydroxide solution and subsequent purification yielded compound (I). The sulfur of (II) was eliminated as hydrogen sulfide. Dehydration with sulfuric acid, according to the conditions prescribed for *o*-benzoylbenzoic acid dehydration,[9] gave anthraquinone. Oxidation with chromic or nitric acid in glacial acetic acid resulted in the formation of (I). Oxidation with 30% hydrogen peroxide at 100° in glacial acetic acid yielded (I) and phenyl phthalide (VII), m. p. 115°.[10] Boiling with aqueous-alcoholic lead acetate solution resulted in the elimination of sulfur from (II) with the formation of lead sulfide and (I). Reactions with phenylhydrazine, aniline and phenol yielded compounds which checked for those obtained by the corresponding reactions of these reagents with the acid (I).[11–13]

3,3′-Diphenyldiphthalidyl (VI).—Three grams of 3,3′-diphenyldiphthalidyl sulfide (II) and 6 g. of copper dust were refluxed for three hours in 40 cc. of freshly distilled cymene. A grayish-black precipitate formed. The mixture was filtered hot and the solution deposited a grayish-white solid upon cooling. This was filtered, washed with petroleum ether, and dried. After two recrystallizations from xylene, 2 g. of a white compound (VI) resulted; m. p. 265–266°. The m. p. had to be determined by very slow heating. The mixed m. p. and hydrolytic products, *o*-benzoylbenzoic acid (I) and phenyl phthalide (VII), checked with a purified sample of 3,3′-diphenyldiphthalidyl, prepared according to the method of Eckert and Pollak.[14] This reaction was repeated with thin silver foil and an analogous result was obtained.

(7) Meyer, *Monatsh.*, **22**, 787 (1901).

(8) Mulliken, "Identification of Pure Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1904, Vol. IV, p. 11.

(9) Dougherty and Gleason, THIS JOURNAL, **52**, 1024 (1930).

(10) Beilstein, "Handbuch der organischen Chemie," fourth edition, Band X, System No. 1297, pp. 727, 759.

(11) Meyer, *Monatsh.*, **30**, 481 (1909).

(12) Meyer, *ibid.*, **28**, 1211 (1907).

(13) Von Pechmann, *Ber.*, **13**, 1613 (1880).

(14) Eckert and Pollak, *Monatsh.*, **38**, 16 (1917).

Thiodiphenyl phthalide (III).—Twenty-five grams of 3,3′-diphenyldiphthalidyl sulfide (II) was mixed with 25 g. of anhydrous aluminum chloride in 300 cc. of benzene. The mixture was heated at 75–78° for eighteen hours in analogous manner to the preparation of *o*-benzoylbenzoic acid (I) from phthalic anhydride and benzene. Hydrogen chloride was evolved copiously but only traces of hydrogen sulfide. The reddish-brown mass was cooled, decomposed with cold dilute hydrochloric acid, and was extracted with 200 cc. of benzene. The extract was washed with water and vacuum distilled to dryness; a faintly yellow solid remained. Four recrystallizations from ethanol and a final recrystallization from a 2:1 benzene–petroleum ether solution yielded 6 g. of white crystals (III); m. p. 162°. A mixed m. p. checked with thiodiphenyl phthalide as prepared by Kleibacker.[15] Diphenyl phthalide (VIII)[4] was recovered from the filtrates.

Anal. Calcd. for $C_{20}H_{14}OS$: S, 10.60. Found: S, 10.77; 10.84.

Kleibacker's structure for thiodiphenyl phthalide (III) was concurred by hydrogen peroxide oxidation in acetic acid of (III) to (VIII) and by the conversion with phosphorus pentasulfide of (III) to dithiodiphenyl phthalide (IV).

Anal. Calcd. for $C_{20}H_{14}S_2$: S, 20.14. Found: S, 20.05, 20.08.

Hydrogen peroxide oxidation in acetic acid of (IV) yielded diphenyl phthalide (VIII).

2-Phenyl-3,4-benzothiophene (V).—Fifty grams of (I) was mixed in 600 cc. of xylene in a reflux apparatus equipped with a calcium chloride drying tube. The mixture was heated to boiling on an oil-bath; 50 g. of phosphorus pentasulfide was added, and the mixture refluxed for four hours. Hydrogen sulfide was evolved and a purplish-brown color appeared within an hour. This coloration deepened as the reaction proceeded. The hot solution was filtered; a charry residue and some unchanged phosphorus pentasulfide remained. The xylene solution was steam distilled, leaving a reddish-brown gum which solidified on cooling. It was boiled for two hours with 10 g. of sodium hydroxide in 300 cc. of 80% ethanol. The mixture was cooled and filtered. The filtrate was reddish-brown in color but on acidification it gave only traces of hydrogen sulfide and a slight turbidity; no *o*-benzoylbenzoic acid (I) was recovered. The alcoholic-alkali insoluble residue was washed with water and dried in a vacuum desiccator. The solid was then boiled in 200 cc. of xylene and filtered hot. Upon cooling, the filtrate yielded a reddish-brown solid It was filtered; the residue weighed 7 g. after drying. It was treated again with alcoholic sodium hydroxide and then recrystallized 3 times from xylene. Four grams of reddish-brown needles (V), m. p. 236–237°, was obtained. The combined xylene filtrates were steam distilled and 35 g. of a brownish-red gum remained in the distilling flask. The gum was dried, after which it solidified to a brittle mass. Attempts to crystallize something from it proved unsuccessful. By dissolving the gum in 500 cc. of xylene and refluxing for three hours with 25 g. of phosphorus pentasulfide, as in its original preparation, three more

(15) W. Kleibacker, Ph.D. Thesis, University of Pittsburgh, June, 1938.

TABLE I

No.	Compound	Reagents used	Solvent, cc.	Time, hrs. at b. p. of solvent	Yield, %	M. p., °C.
1	3,3′-Di-(*p*-tolyl)-diphthalidyl sulfide (X)[a]	20 g. (IX), 20 g. P_2S_5	700 benzene	24	30	212
2	3,3′-Di-(*p*-chlorophenyl)-diphthalidyl sulfide (XV)[b]	20 g. (XIV), 20 g. P_2S_5	500 benzene	24	40	232
3	2-(*p*-Tolyl)-3,4-benzothiophene (XI)	50 g. (IX), 50 g. P_2S_5	600 xylene	2.5	8	217
4	2-(*p*-Chlorophenyl)-3,4-benzothiophene (XVI)	8 g. (XIV), 8 g. P_2S_5	200 xylene	5	12	241–42
5	3,3′-Di-(*p*-tolyl)-diphthalidyl (XII)[c]	5 g. (X), 28 g. Ag foil	50 cymene	14	70	247–48
6	3,3′-Di-(*p*-chlorophenyl)-diphthalidyl (XVII)[d]	1 g. (XV), 8 g. Ag foil	75 cymene	6	90	247
7	*p*-Tolylphthalide (XIII)[e]	2.5 g. (X), 2 g. 30% H_2O_2	50 HOAc	3[g]		128
8	*p*-Chlorophenyl phthalide (XVIII)[f]	10 g. (XV), 20 g. 30% H_2O_2	100 HOAc	2[g]	50	124

No.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Sulfur, % Calcd.	Sulfur, % Found	Chlorine, % Calcd.	Chlorine, % Found
1	$C_{30}H_{22}O_4S$	75.29	75.15, 75.37	4.63	4.53, 4.59	6.69	6.52, 6.62		
2	$C_{28}H_{16}O_4SCl_2$					6.17	6.27, 6.18	13.65	13.77, 13.70
3	$C_{15}H_{12}S$	80.31	80.06, 80.28	5.39	5.21, 5.29	14.30	14.31, 14.21		
4	$C_{14}H_9SCl$	68.70	68.31, 68.38	3.71	4.09, 4.06	13.10	12.89, 13.05	14.49	14.60, 14.75
5	$C_{30}H_{22}O_4$								
6	$C_{28}H_{16}O_4Cl_2$								
7	$C_{15}H_{12}O_2$								
8	$C_{14}H_9O_2Cl$	68.70	68.60, 68.42	3.71	3.45, 3.59			14.50	14.42, 14.66

[a] (X) was prepared (60% yield) by the action of hydrogen sulfide on the acid chloride of (IX) as described above for (II). [b] (XV) was prepared (68% yield) by the action of hydrogen sulfide on the acid chloride of (XIV) as described above for (II). [c] Previously prepared by phosphorus–hydriodic acid reduction of (IX), reported by Limaye [*Chem. Zentr.*, **104**, I, 1777 (1933)]. [d] Previously prepared by aluminum–sulfuric acid reduction of (XIV), method described by Eckert and Pollak.[14] [e] Previously prepared by reduction of (IX) with zinc dust and ammonia, Limpricht [*Ann.*, **314**, 251 (1901)]. [f] Converted to (XIV) by chromic anhydride oxidation according to the method described for the oxidation of (VII) to (I), (Beilstein, "Handbuch der organischen Chemie," fourth edition, Band XVII, System No. 2467, p. 361). [g] At 100°.

grams of compound (V) was recovered. The combined products (V), 7 g., were recrystallized from xylene; m. p. 236–237°. 2-Phenyl-3,4-benzothiophene (V) is slightly soluble in cold benzene, toluene, xylene, carbon disulfide and hot glacial acetic acid; very soluble in hot xylene and nitrobenzene; insoluble in hot or cold alcohol, ether, petroleum ether and aqueous media.

Anal. Calcd. for $C_{14}H_{10}S$: C, 79.96; H, 4.79; S, 15.25; mol. wt., 210. Found: C, 80.01, 80.29; H, 4.72, 4.73; S, 15.02, 15.05; mol. wt., 223, 239.

Reactions of 2-Phenyl-3,4-benzothiophene (V).—Sodium hydroxide fusion was carried out according to the method described by Mulliken,[8] except that a steel bomb and five minutes of heating at 340–350° were used. A positive test for a divalent sulfur was obtained. Attempted hydrolysis with alcoholic sodium hydroxide resulted in no change. Stability toward metals: 2 g. of (V) and 8 g. of copper powder were heated in diphenyl at 255–265° for four and one-half hours. Compound (V) was recovered unchanged. Boiling the compound in xylene with an equal weight of metallic sodium or mercuric oxide gave the same result. The isatin thiophene test was negative. Oxidations of (V) in glacial acetic acid with potassium permanganate, hydrogen peroxide, 1:1 nitric acid or chromium anhydride yielded a yellow compound melting at 186°.

In addition to the above compounds, the following homologs and analogs have been prepared and their data given in Table I. The respective oxidation, reduction and hydrolytic products are given in Chart A.

Summary

1. Thio compounds and derivatives of three aroyl-*o*-benzoic acids have been prepared and their properties studied.

2. The following new compounds have been prepared by the reaction of phosphorus pentasulfide in benzene: (a) 3,3′-diphenyldiphthalidyl sulfide (II), (b) 3,3′-di-(*p*-tolyl)-diphthalidyl sulfide (X), (c) 3,3′-di-(*p*-chlorophenyl)-diphthalidyl sulfide (XV). These sulfides were also prepared by the corresponding reactions of the acid chlorides with hydrogen sulfide.

3. The reaction of phosphorus pentasulfide in boiling xylene produced colored sulfur-containing compounds to which a thiophene type structure was ascribed tentatively: (a) 2-phenyl-3,4-benzothiophene (V), (b) 2-(*p*-tolyl)-3,4-benzothiophene (XI), (c) 2-(*p*-chlorophenyl)-3,4-benzothiophene (XVI).

4. A new method of preparation of the following compounds is reported: (a) 3,3′-diphenyldiphthalidyl (VI), (b) 3,3′-di-(*p*-tolyl)-diphthalidyl (XII), (c) 3,3′-di-(*p*-chlorophenyl)-diphthalidyl (XVII).

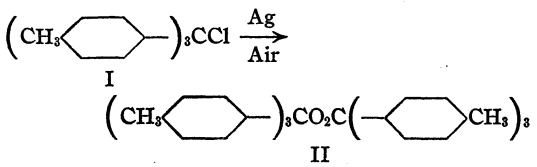
PITTSBURGH, PENNA. RECEIVED JULY 29, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Effect of Substitution on the Dissociation of Hexaarylethanes. VIII.[1] The Disproportionation of Tri-*p*-tolylmethyl

BY C. S. MARVEL, WILLIAM H. RIEGER AND MAX B. MUELLER

Gomberg[2] has found that hexa-*p*-tolylethane does not dissociate reversibly to give a stable triarylmethyl radical as do many hexaarylethanes. The radical is formed when tri-*p*-tolylmethyl chloride (I) is treated with silver as shown by the fact that the expected peroxide (II) is obtained when the reaction is carried out in the presence of air or oxygen. If a benzene solution of the chloride is treated with silver in the absence of oxygen a light orange colored solution is produced but the color fades rapidly. Removal of the solvent at this stage leaves a glassy residue which has never been satisfactorily characterized.



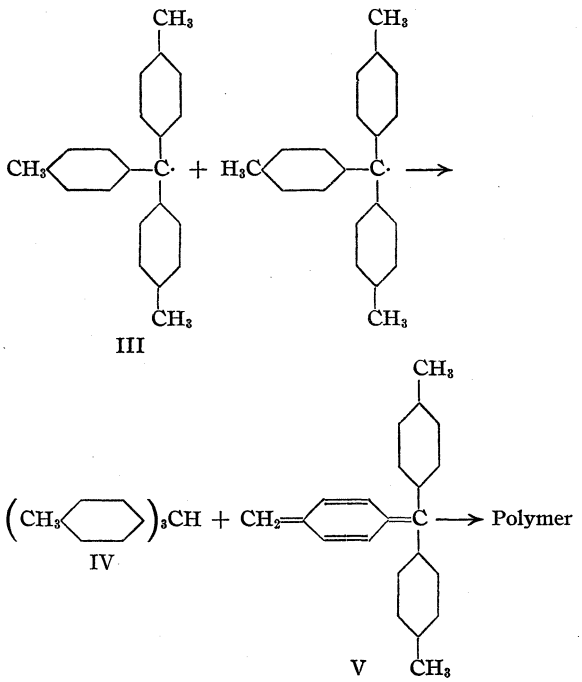
I

II

A further study of hexa-*p*-tolylethane now has been undertaken in connection with the study of the effect of alkyl groups on the dissociation of hexaarylethanes. When tri-*p*-tolylmethyl chloride (I) was purified carefully to remove all traces of moisture and hydrogen chloride before treating it with silver, it was possible to obtain a benzene solution of hexa-*p*-tolylethane which was light orange in color. Magnetic susceptibility[3] measurements showed that this ethane was dissociated to the extent of at least 16%. If the solution was allowed to stand at room temperature (25–30°) for a few hours the color disappeared entirely and magnetic susceptibility measurements showed that no free radical remained.

The solvent was removed from this decolorized solution and the glassy residue described by Gomberg[2] was obtained. By putting this residue in a molecular still[4] and warming it to about 85° under a pressure of 10^{-4} mm., a distillate consisting of pure tri-*p*-tolylmethane (IV) was obtained. The material which did not distill consisted of a brownish-yellow powder soluble in hexane and benzene but almost insoluble in ether. It was obviously polymeric in nature. Attempts to determine a molecular weight by cryoscopic methods gave no satisfactory results.

The identification of tri-*p*-tolylmethane (IV) and a polymeric residue as the products of disproportionation of tri-*p*-tolylmethyl (III) makes



III

IV

V

it possible to suggest a mechanism for the reaction. If one free radical strips a hydrogen atom from one of the *p*-methyl groups of another radical to give tri-*p*-tolylmethane (IV), the dehydrogenated radical can stabilize itself by assuming the quinoid structure (V). This molecule is one of the activated vinyl types and it should be expected to polymerize with ease. Since the polymer is not a pure hydrocarbon, some oxidation must occur during its isolation. The color change from an orange to an almost colorless solution shows that the polymerization must have occurred before the tube was opened to the air.

Confirmation of this explanation of the disproportionation reaction has been obtained. Schlenk and Meyer[5] have found that pyridine will remove

(1) For the seventh communication in this series, see THIS JOURNAL, **61**, 2008 (1939).

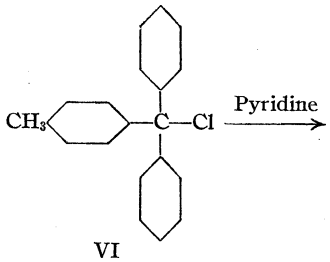
(2) Gomberg, *Ber.*, **37**, 1626 (1904).

(3) (a) Müller, *et al.*, *Ann.*, **520**, 235 (1935); **521**, 89 (1935); (b) Roy and Marvel, THIS JOURNAL, **59**, 2622 (1937).

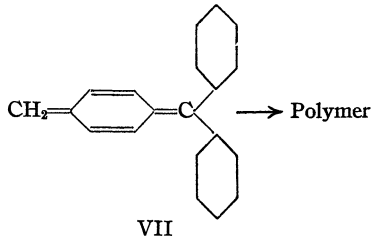
(4) Washburn, *Bur. Standards J. Research*, **2**, 476 (1929).

(5) Schlenk and Meyer, *Ber.*, **52**, 9 (1919).

hydrogen chloride from diphenyl-*p*-tolylmethyl chloride (VI) to give a polymeric product. They postulate a quinoid intermediate (VII) and have actually isolated properly substituted molecules of this type.



VI



VII

Treatment of tri-*p*-tolylmethyl chloride with pyridine in an oxygen-free atmosphere produced a solution which was qualitatively indistinguishable in color from the corresponding free radical solution. When this solution was allowed to stand, the color faded and when the pyridine hydrochloride and excess pyridine were removed a polymeric residue remained. This residue had approximately the same solubilities and carbon and hydrogen content as did the polymer obtained by disproportionation of the free radical. While comparisons of polymers are not completely satisfactory for identification purposes, there seems to be little doubt that these products were the same.

Experimental

Tri-*p*-tolylmethyl Chloride.—The tri-*p*-tolylmethylcarbinol was obtained in 65% yield from *p*-tolylmagnesium bromide and diethyl carbonate.[6] It was converted to the chloride by treating its dry ether solution with dry hydrogen chloride. The chloride was recrystallized from carefully dried ethyl acetate and stored in a desiccator over solid potassium hydroxide under reduced pressure. This product melted at 171–172° (literature[2] gives m. p. at 173°).

Anal. Calcd. for $C_{22}H_{21}Cl$: Cl, 11.08. Found: Cl, 11.10.

Dissociation of Hexa-*p*-tolylethane.—A benzene solution of 1.032 g. of tri-*p*-tolylchloromethane was shaken with 3 g. of molecular silver for ten minutes in the apparatus described previously.[3b] The radical solution was filtered immediately from the silver–silver chloride residue and its magnetic susceptibility was determined. Two more determinations were made at ten-minute intervals. Extrapolation to zero time (see graph) indicates that hexa-*p*-tolylethane is 20% dissociated in 0.05 molar benzene solution. Assuming that the dissociation of hexaarylethanes obeys the mass law, this corresponds to a dissociation of 16% in 0.08 molar benzene solution.

These calculations are based upon the assumption that the reaction between tri-*p*-tolylchloromethane and molecular silver is 80% complete at the end of ten minutes. This assumption is supported by the observation that about 80% of the theoretical amount of oxygen is absorbed in ten minutes by a similarly treated bromobenzene solution of the chloromethane. Since the ethane is so unstable no more satisfactory determination was possible; however, it seemed probable that the assumed concentration is accurate within ±10%. A variation in concentration within these wide limits would cause a maximum variation of only ±2% in the value of the dissociation.

Disproportionation of Radical.—A solution of 2 g. of tri-*p*-tolylmethyl chloride in 150 cc. of dry benzene was frozen in a dry-ice–acetone bath and 0.8 g. of molecular silver was added. The flask was swept out with dry nitrogen, evacuated and sealed. The solution was allowed to warm to room temperature and it took on the characteristic light orange color. The flask was shaken for twenty-four to thirty hours at which time the color had faded to a very light yellow. The flask was opened, the silver recovered by filtration and the solvent removed under reduced pressure. The residual amber colored oil set to a hard glassy solid on cooling to room temperature.

A sample (1.219 g.) of this glassy solid was placed in a molecular still under a pressure of 10^{-4} mm. The bath temperature was maintained at about 85°. The distillate (0.239 g.) was a white solid which melted at 57°. A mixture of this material with an authentic specimen of tri-*p*-tolylmethane showed no depression in melting point.

The residue which did not distill was a light brown powder. It was fairly soluble in benzene and hexane and almost insoluble in ether. Attempts to determine its molecular weight in freezing benzene gave erratic results typical of polymeric materials.

Anal. Found: C, 89.79; H, 7.48.

This analysis shows the carbon and hydrogen ratio is that expected for a polymer of the quinoid type of molecule shown in formula V but there apparently has been added about one atom of oxygen for each quinoid unit. A poly-

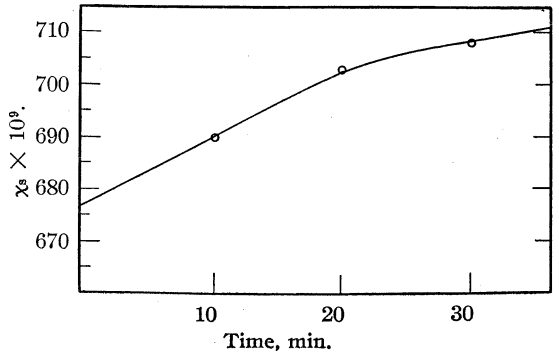


Fig. 1.—Change of magnetic susceptibility (χ_s) of hexa-*p*-tolylethane solution with time.

(6) Copenhaver, Roy and Marvel, THIS JOURNAL, 57, 1311 (1935).

merization of the vinyl type would still leave a conjugated system in each unit which might readily add oxygen.[7]

Preparation of Polymer from Tri-*p*-tolylmethyl Chloride and Pyridine.—A solution of 2.72 g. of tri-*p*-tolylmethyl chloride in 15 cc. of pure dry pyridine was heated under a reflux condenser in an atmosphere of dry nitrogen. The solution became yellow almost at once, then light orange and wine red. In about five minutes the color began to fade and heating was stopped. In about thirty minutes the solution was a yellowish brown and white crystals of pyridine hydrochloride had separated in the cold solution. Some dry ether was added and the pyridine hydrochloride was removed by filtration. The ether and excess pyridine were removed by evaporation under reduced pressure. A yellowish oil remained and on cooling in air it set to a hard, glassy solid. This solid was also soluble in benzene and hexane and almost insoluble in ether.

Anal. Found: C, 87.62, 87.93; H, 7.16; 7.45.

(7) Compare Kogerman, *Trans., 2nd World Power Conf., Berlin*, **8**, 33 (1930); *C. A.*, **25**, 5549 (1931).

Summary

1. Determination of the degree of dissociation of hexa-*p*-tolylethane on a rapidly prepared benzene solution shows it is dissociated to the extent of 16 ± 2% in 0.08 molar solution in benzene at 30°.

2. Tri-*p*-tolylmethyl rapidly undergoes disproportionation in benzene solution to give tri-*p*-tolylmethane and a polymeric material.

3. Removal of hydrogen chloride from tri-*p*-tolylmethyl chloride by the action of pyridine leads to a polymer apparently identical with that obtained by disproportionation of the radical. These facts are used to explain the course of the disproportionation reaction.

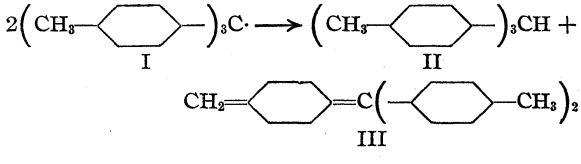
URBANA, ILLINOIS RECEIVED AUGUST 14, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

The Disproportionation of Hexa-*p*-alkylphenylethanes and the Effect of ortho-, meta-, and para-Alkyl Groups on Dissociation of Hexaarylethanes[1]

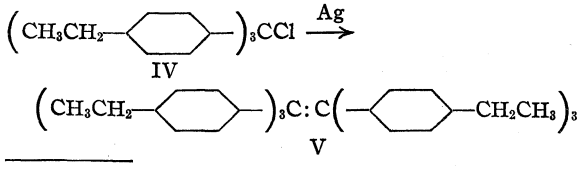
BY C. S. MARVEL, MAX B. MUELLER, CHESTER M. HIMEL AND JULIUS F. KAPLAN

The discovery[1] that tri-*p*-tolylmethyl (I) undergoes rapid disproportionation to yield tri-*p*-tolylmethane and a quinoid residue (III) which rapidly polymerizes, has made it seem probable that groups other than methyl which still have hydrogen on the alpha carbon should likewise cause instability of the radical. Accordingly we



have reinvestigated the series of *p*-alkylphenylethanes which was recently described from this Laboratory.[2]

When tri-*p*-ethylphenylchloromethane (IV) in benzene solution was shaken with molecular silver

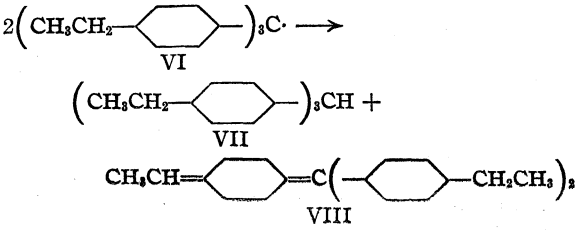


(1) This is the ninth communication on the effect of alkyl groups on the dissociation of hexaarylethanes. For the eighth, see THIS JOURNAL, **61**, 2769 (1939).

(2) (a) Copenhaver, Roy and Marvel, *ibid.*, **57**, 1311 (1935); (b) Roy and Marvel, *ibid.*, **59**, 2622 (1937).

for only fifteen minutes and the magnetic susceptibility of the resulting solution was examined, it was found that the free radical was present to the extent of 17%. On standing there was little change in the color of the solution but the change in magnetic susceptibility showed that the free radical was disappearing very rapidly. The experiments were carried out at higher temperatures (30°) than had been used previously (20°)[2b] and in the present series of tests no radical remained in the solution after twenty-four hours, the time used before for the preparation of the solutions to be studied.

The fact that the color of the solution did not fade appreciably during the disproportionation of the free radical (VI) is of interest. It indicates that in the series above methyl the quinoid hydrocarbon (VIII) produced in the disproportionation does not polymerize. This is to be expected



since substituted vinyl residues having one substituent on each of the carbon atoms rarely polymerize easily. The color of the solution obtained by treating tri-*p*-ethylphenylchloromethane with silver was qualitatively the same as the color of the solution obtained by treating the same chloride with pyridine in the manner used by Schlenk and Meyer[3] to obtain quinoid derivatives related to VIII. The fact that the color does not change to an appreciable extent as the radical changes into a mixture of triarylmethane and the quinoid derivative is evidence in favor of Gomberg's well-known idea that the quinoid ring structure of the radical is the form which contributes the color to the solution.[4]

In addition to the *p*-ethyl derivative, the *p*-*n*-propyl, *p*-isopropyl, *p*-isobutyl and *p*-*s*-butyl derivatives also have been reëxamined.[5] In each case the solution of the hydrocarbon first obtained showed a high free radical content and this disappeared on standing. The rate of disproportionation of the various free radicals was determined by following the change in magnetic susceptibility The order of increasing stability of the various free radicals agreed exactly with the previously reported order of increasing dissociation. The results are plotted in Fig. 1.

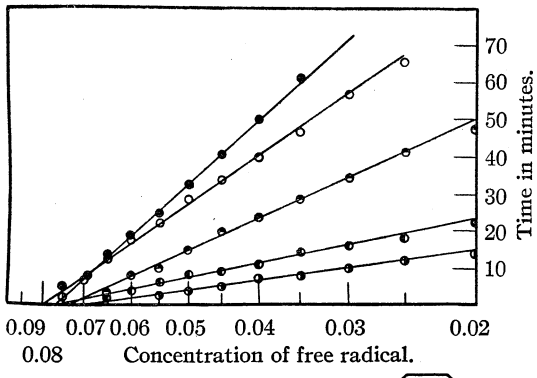


Fig. 1.—Rate of decomposition of (R⟨⟩)$_3$C—: ◑, R = Et; ◐, R = *n*-Pr; ◒, R = *i*-Pr; ○, R = *s*-Bu; ●, R = *i*-Bu.

By use of the data on the rate of disproportionation it was possible to calculate the dissociation of the various ethanes at zero time and thus to obtain fairly accurate estimates of the effects of the various para-alkyl groups on the degree of dissociation. These effects were much more marked than had been anticipated and it is obvious that the size and shape of a para-alkyl group is an important factor in the amount of radical formation in the hexa-*p*-alkylphenylethane series. Table I contains a summary of the new results.

TABLE I

DISSOCIATION OF HEXA-*p*-ALKYLPHENYLETHANES

Alkyl group	Degree of dissociation, %
Ethyl	17 ± 2
n-Propyl	21 ± 2
Isopropyl	26 ± 2
s-Butyl	33 ± 2
Isobutyl	27 ± 2

Certain other observations also contribute evidence to support the above view of the disproportionation of these *p*-alkylphenylethanes. Hexa-*m*-tolylethane[6] was prepared in benzene solution and it was stable more or less indefinitely. The magnetic susceptibility of its solutions did not change over a twenty-four hour period. This stability was expected as meta-quinone structures cannot form. The meta-methyl group was even more effective than the para-methyl group in producing dissociation since hexa-*m*-tolylethane existed to the extent of at least 40% as the free radical. No other crystalline tri-*m*-alkylphenylchloromethane has been obtained, so the effect of other meta-alkyl groups cannot yet be reported.

It might be predicted that an ortho-methyl group also would contribute to the instability of the radical since ortho-quinoid molecules form rather easily. It has not been possible to prepare tri-*o*-tolylchloromethane due apparently to steric factors but *o*-tolyldiphenylchloromethane with silver gave a stable ethane which was dissociated to the extent of 25%. This result showed the very marked effect of introducing more steric hindrance around the central carbon atom of the free radical since one ortho-methyl group was more effective in producing dissociation than were three para-methyl groups. These steric factors must also explain the stability of the ortho-methyl derivative. If it is assumed that a free radical must collide with the methyl group of another radical before a hydrogen atom can be removed it is rather easy to see why the ortho-methyl compound (IX) does not undergo the disproportionation reaction characteristic of the para-series.

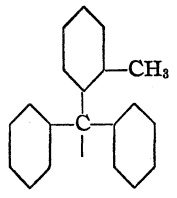
p-*t*-Butylphenyldiphenylchloromethane (X) has been prepared and converted to the correspond-

(3) Schlenk and Meyer, *Ber.*, **52**, 9 (1919).

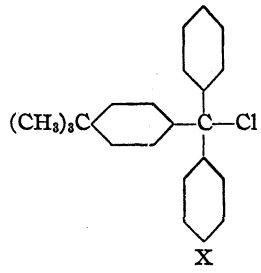
(4) Gomberg, *ibid.*, **40**, 1847 (1907).

(5) The *p*-*n*-butyl derivative will be reported in a later communication.

(6) Brown and Marvel, THIS JOURNAL, **59**, 1175 (1937).



IX



X

ing ethane. Since there are no hydrogen atoms on the alkyl carbon attached to the ring, this compound did not undergo the disproportionation observed with the other *p*-alkyl derivatives. For comparison the mono-*p*-methyl and *p*-isopropyl derivatives were prepared. Both of these radicals showed the disproportionation reaction but both decomposed more slowly than did the corresponding tri-*p*-alkylphenylmethyl radicals. This increased stability was expected as the chance of the radical colliding with an active hydrogen atom is much less in the monosubstituted series than in the trisubstituted series. In Table II are recorded the degrees of dissociation of these dialkylphenyltetraphenylethanes.

TABLE II

DEGREE OF DISSOCIATION OF SOME DIALKYLPHENYLTETRAPHENYLETHANES

Alkyl group	Degree of dissociation, %
p-Methyl	5 ± 1.0
o-Methyl	25 ± 1.0
p-Isopropyl	8–10 ± 1.0
p-*t*-Butyl	8–9 ± 1.0

Thus all the *p*-alkylphenylmethyl radicals which can lose hydrogen from the α-carbon of the para-alkyl group undergo rather rapid disproportionation. When there is no possibility of quinoid structure formation by loss of hydrogen, the radicals are relatively stable as is triphenylmethyl. Alkyl groups in the para-position have a marked effect on increasing the dissociation of hexaphenylethane and the larger groups are more effective than the smaller ones. A meta-methyl group is more effective than a para-methyl group in promoting dissociation. An ortho-methyl group is very effective in this regard. These effects of ortho- and meta-substituents must be due in part to steric factors.

Experimental

Preparation of *p*-*t*-Butylbromobenzene.—This compound was prepared by Schramm[7] by the bromination of *t*-butylbenzene; however, no specific directions for the preparation were given. The following procedure has been found to give satisfactory results. A solution of 80 g. (0.5 mole) of bromine in 67 g. (0.5 mole) of *t*-butyl benzene[8] in a 500-cc. round-bottomed flask connected to a reflux condenser by a ground-glass joint was exposed to sunlight for four days. The initial reaction was rather vigorous and it was necessary to cool the flask in ice for the first four or five hours. When the evolution of hydrogen bromide ceased (four days), the reaction mixture was washed with 10% sodium bisulfite solution, water, 10% sodium carbonate solution and water. The organic layer was separated, dried and distilled through a fourteen-inch (35-cm.) modified Widmer column. A small low boiling fraction consisting chiefly of unreacted *t*-butylbenzene was obtained, but the bulk of the distillate was collected at 230°. The yield was 64 g. which is 60% of the theoretical.

Preparation of *p*-Isopropylphenyldiphenylcarbinol.—The Grignard reagent was prepared from 100 g. of *p*-bromoisopropylbenzene and 12 g. of magnesium in about 200 cc. of anhydrous ether. After the addition of the bromide the mixture was stirred and refluxed for two hours. Then 88 g. of benzophenone in 100 cc. of dry benzene was added and the mixture was stirred and refluxed for an additional three hours. The reaction mixture was decomposed by pouring it into dilute sulfuric acid containing some cracked ice. The organic layer was separated and the ether and benzene removed by distillation. The residue was distilled with steam until no trace of organic material was detectable in the distillate. The carbinol was obtained as a clear glass. No attempt was made to purify it. Instead the impure product was used directly in the preparation of the chloromethane.

Preparation of *p*-*t*-Butylphenyldiphenylcarbinol.—This carbinol was prepared from *p*-*t*-butylbromobenzene by the same procedure used for *p*-isopropylphenyldiphenylcarbinol. Again the impure carbinol was used directly in the preparation of the corresponding chloromethane.

Preparation of Triarylchloromethanes.—The procedures used in the preparation of most of the chloromethanes reported in this communication were those reported by Marvel, Copenhaver and Roy.[2a] It was discovered, however, that chloromethanes which melted above 130° were prepared more easily by dissolving the corresponding impure carbinol in acetyl chloride.[9] The crystalline chloromethane was obtained by concentrating and cooling the solution. The chloromethanes were purified as before by recrystallization from ethyl acetate. The following compounds were prepared in this way: tri-*p*-ethylphenylchloromethane, tri-*p*-isopropylphenylchloromethane, tri-*p*-*s*-butylphenylchloromethane and tri-*p*-isobutylphenylchloromethane.

Analysis of *p*-isopropylphenyldiphenylchloromethane, m. p. 90–91°. Calcd. for $C_{22}H_{21}Cl$: C, 82.37; H, 6.55. Found: C, 83.41; H, 7.06. *Analysis* of *p*-*t*-butylphenyldiphenylchloromethane, m. p. 133–134°. Calcd. for $C_{23}H_{23}Cl$: C, 82.53; H, 6.88. Found: C, 82.53; H, 7.02.

The melting points of the previously known triarylchloromethanes are listed in Table IIA.

(7) Schramm, *Monatsh.*, **9**, 848 (1888).

(8) Huston, Fox and Binder, *J. Org. Chem.*, **3**, 251 (1938).

(9) Gomberg, *Chem. Rev.*, **1**, 91 (1924).

TABLE IIA

Chloromethane	M. p., °C. Found	M. p., °C. Reported
p-Tolyldiphenylchloromethane	99	99[10]
o-Tolyldiphenylchloromethane	135	136–137[10]
Tri-*m*-tolylchloromethane	83–84	84–85[5]
Tri-*p*-ethylphenylchloromethane	156–157	157–158[2a]
Tri-*p*-*n*-propylphenylchloromethane	89–90	90[2a]
Tri-*p*-isopropylphenylchloromethane	166–167	167–168[2a]
Tri-*p*-isobutylphenylchloromethane	134–135	135–136[2a]
Tri-*p*-*s*-butylphenylchloromethane	130–131	132[2a]

Preparation of Peroxides.—Five-thousandths of a mole of the appropriate triarylchloromethane was shaken with three grams of molecular silver for fifteen minutes in the apparatus described previously.[2b] The solution was filtered from the silver–silver chloride, removed from the apparatus and exposed to the air until it was entirely decolorized. The solvent was removed and the residue was purified by several recrystallizations from a mixture of benzene and absolute ethanol.

Analysis of *o*-tolyldiphenylmethyl peroxide, m. p. 148–149°. Calcd. for $C_{40}H_{34}O_2$: C, 87.91; H, 6.23. Found: C, 87.63; H, 6.26. *Analysis* of *p*-isopropylphenyldiphenylmethyl peroxide, m. p. 139–140°. Calcd. for $C_{44}H_{42}O_2$: C, 87.71; H, 6.98. Found: C, 87.59; H, 7.33. *Analysis* of *p*-*t*-butylphenyldiphenylmethyl peroxide, m. p. 156–157°. Calcd. for $C_{46}H_{46}O_2$: C, 87.62; H, 7.30. Found: C, 88.07; H, 7.67.

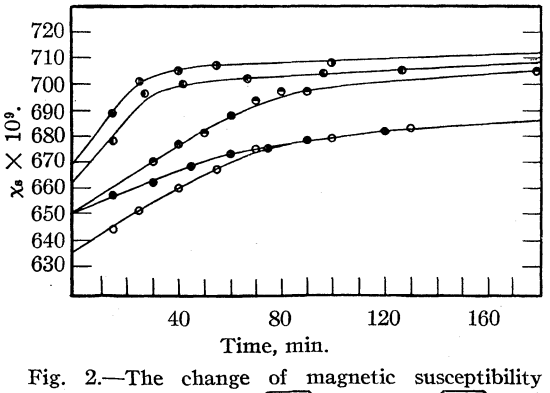


Fig. 2.—The change of magnetic susceptibility (χ_s) of solutions of $(R\langle\bigcirc\rangle)_3C{-}C(\langle\bigcirc\rangle R)_3$, with time: ◑, R = Et; ◐, R = *n*-Pr; ◓, R = *i*-Pr; ○, R = *s*-Bu; ●, R = *i*-Bu.

Preparation of Hexaarylethanes.—Because of the instability of the *hexa-p*-alkylphenylethanes reported in this communication it was necessary to determine the time required for the completion of the reaction between molecular silver and triarylchloromethanes. This was done by measuring the amount of oxygen absorbed by a sample of the chloromethane when it was shaken with molecular silver in the presence of oxygen.[11] The results are tabulated in Table III.

(10) Bistrzycki and Gyr, *Ber.*, **37**, 661, 1250 (1904).

(11) Bachman and Kloetzel, *J. Org. Chem.*, **2**, 356 (1937).

TABLE III

Triarylchloromethane	Time, min.	% oxygen absorbed
p-Tolyldiphenylchloromethane	4	83
	15	84
o-Tolyldiphenylchloromethane	7	90
p-Isopropylphenyldiphenylchloromethane	10	83
	30	96
Tri-*p*-ethylphenylchloromethane	10	80
	15	83
Tri-*p*-*n*-propylphenylchloromethane	10	80
	15	82
Tri-*p*-isopropylphenylchloromethane	8	90
	23	93
Tri-*p*-isobutylphenylchloromethane	15	80
Tri-*p*-*s*-butylphenylchloromethane	3	83
	20	90

The Dissociation of Hexaarylethanes.—The degree of dissociation of the hexaarylethanes studied was measured by the magnetic susceptibility method[12] in the apparatus described previously.[2b] In the case of the hexa-*p*-alkylphenylethanes which decompose rapidly, 0.02 molar solutions of the chloromethanes were shaken with molecular silver for fifteen minutes, filtered and the magnetic susceptibility of the solutions determined immediately. Determinations were then made on the same sample at ten or fifteen minute intervals until the sample showed a constant magnetic susceptibility. By extrapolation from these values the magnetic susceptibility at zero time (*i. e.*, before any decomposition took place) was calculated. These extrapolations are shown in Fig. 2.

In order to calculate the degree of dissociation from these data, it is necessary to know the concentration of the ethane. Since oxygen absorption experiments under similar conditions have shown that the chloromethane is converted to the ethane to the extent of at least 80% in every case, the ethane solution was assumed to be 0.08 ± 0.01 molar. This comparatively large possible variation in concentration, however, causes a maximum uncertainty of only ±2% in the degree of dissociation.

In the case of the more stable ethanes, the chloromethanes were shaken with molecular silver until parallel oxygen absorption experiments indicated that the reaction was complete. The experimental data for all of the ethanes reported are collected in Table IV.

Rate of Decomposition of Hexa-*p*-alkylphenylethanes.—From the values of α listed in Table IV

(12) Müller, *et al.*, *Ann.*, **520**, 235 (1935); **521**, 89 (1935); see also ref. 2b.

TABLE IV

Ethane	$T°$	% ethane	$-\chi_s \times 10^6$	α
Di-*p*-tolyltetraphenylethane	28	4.74	0.695	0.053 ± 0.02
Di-*o*-tolyltetraphenylethane	30	5.85	.632	.267 ± .02
Di-*p*-isopropylphenyltetraphenylethane	28	6.77	.680	.083 ± .02
Di-*p*-*t*-butylphenyltetraphenylethane	29	6.09	.688	.078 ± .02
Hexa-*m*-tolylethane	28	6.47	.594	.400 ± .02
Hexa-*p*-ethylphenylethane	29	6.06	.670	.167 ± .03
Hexa-*p*-*n*-propylphenylethane	29	6.81	.662	.209 ± .03
Hexa-*p*-isopropylphenylethane	28	6.85	.650	.260 ± .03
Hexa-*p*-isobutylphenylethane	29	7.65	.650	.269 ± .03
Hexa-*p*-*s*-butylphenylethane	29	7.66	.635	.330 ± .03

it is possible to calculate the equilibrium constant for the dissociation of any ethane from the equation

$$K = \frac{\alpha^2 w_0}{1 - \alpha}$$

where w_0 = initial concentration of the ethane.

Then from the equation

$$\chi_\rho = \frac{1233}{w_1}\sqrt{K^2 + 4Kw_1} - K$$

where w_1 = the concentration of the ethane, it is possible to calculate the paramagnetic susceptibility due to the free radical for any value of w_1, and from the equation

$$\chi_s = \frac{\chi_d}{M}w_0 + 0.708w_2 - \frac{\rho}{M}w_1$$

where w_2 = the weight fraction of the solvent, the corresponding measured susceptibility of the solution. Using the values of χ_s obtained in this way, the amount of undecomposed ethane present at any given time may be obtained from Fig. 2. When the logarithms of the concentrations so obtained are plotted against time (see Fig. 1) a series of straight lines are obtained indicating that the decomposition is apparently a first order reaction.

Summary

1. Hexa-*p*-alkylphenylethanes in which the alkyl group has a hydrogen atom on the carbon atom attached to the ring have been found to dissociate to free radicals which undergo disproportionation.

2. The degree of dissociation of ethanes in this series has been found to be much higher (17–33%) than was previously thought (2–6%).

3. Ortho- and meta-methyl substituents in hexaphenylethanes have a greater effect on the degree of dissociation than do para-methyl substituents and the ortho- and meta- derivatives give relatively stable radicals.

4. A few di-*p*-alkylphenyltetraphenylethanes have been described. They are more highly dissociated than hexaphenylethane and disproportionate less rapidly than the corresponding hexaalkyl derivatives. In this series the *t*-butyl derivative did not undergo disproportionation.

URBANA, ILLINOIS RECEIVED AUGUST 14, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

The Alleged *cis-trans* Isomerism of alpha- and beta-*p*-Azophenol

BY W. M. LAUER, H. P. KLUG AND S. A. HARRISON[1]

The existence of isomeric forms of *p*-azophenol was reported in 1906 by Willstätter and Benz.[2] One form, designated α, was obtained by coupling *p*-hydroxybenzenediazonium chloride with phenol or preferably by the fusion of *p*-nitrophenol with potassium hydroxide, while the second form, designated β, resulted from the reduction of benzoquinoneazine with phenylhydrazine.[3] An analysis of the evidence at their disposal led these investigators to the view that *cis–trans* isomerism was the most likely basis upon which to account for the existence of isomers in this case. This interpretation also was favored by Hantzsch,[4] who studied the absorption spectra of α- and β-azophenol and their sodium salts. Several years later, Robertson[5] also concluded that this was a case of *cis–trans* isomerism on the basis of a difference in behavior of the two forms, which he observed on bromination and nitration. Thus, he reported that nitration of α-azophenol gave a tetranitro derivative (m. p. 230°), whereas dinitroazophenol (m. p. 240°) was obtained from β-azophenol, and that bromination produced different tetrabromo derivatives (m. p. 250–252°, m. p.

(1) Abstract of Ph.D. Thesis, 1939.

(2) Willstätter and Benz, *Ber.*, **39**, 3492 (1906).

(3) Two additional forms were described in a later publication [Willstätter and Benz, *ibid.*, **40**, 1578 (1907)], which lists the properties of all of the alleged isomers.

(4) Hantzsch, *ibid.*, **43**, 2512 (1910); see also Tuck, *J. Chem. Soc.*, **95**, 1816 (1909).

(5) Robertson, *ibid.*, **103**, 1472 (1913).

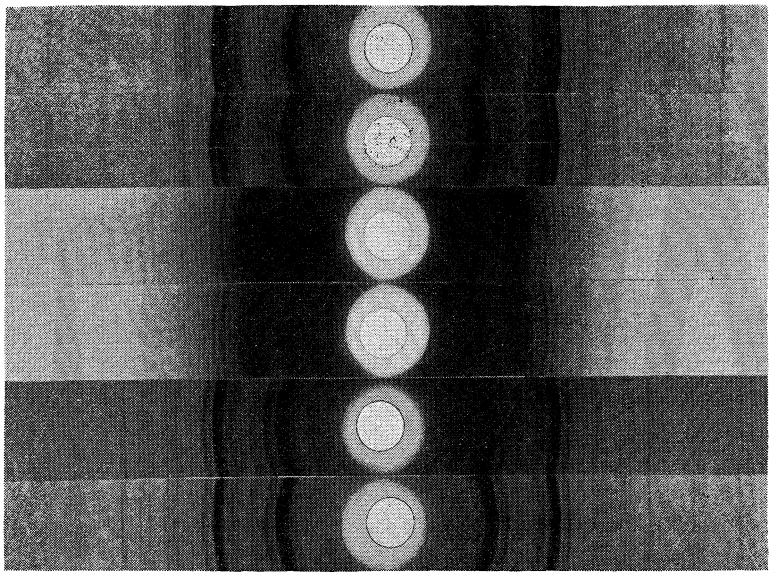


Fig. 1.—Powder photographs of *p*-azophenol.

271°) in the two cases.[6] This difference in behavior was attributed to steric hindrance in the case of the β-azophenol, to which Robertson assigned the *cis* configuration.

An important contribution to this problem was made recently by Dostrovsky and Le Fèvre.[7] They found that the dipole moments of α- and β-azophenol are identical, and consequently it is very improbable that the α- and β- forms are *cis–trans* isomers. Furthermore, in view of the lability of the *cis* form of azobenzene, it appeared unlikely that the *cis* form of azophenol would maintain its configuration when subjected to bromination and nitration. These considerations, together with evidence, which was accumulated in the present work, lead to the conclusion that the alleged isomers, α- and β-azophenol, are in reality identical. Hydrated *p*-azophenol upon dehydration gives the anhydrous compound, which exists in two solid modifications, brick-red and green. The transformation of the brick-red metastable form to the green form is subject to various influences (*e. g.*, impurities) which were not investigated. That the so-called α-azophenol is identical with the azophenol designated as the β-form and produced by the reduction of quinoneazine becomes evident from the following studies.

(6) The use of an excess of bromine and rapid addition of this reagent gave the higher melting tetrabromo derivative with both forms of the azophenol. However, Hunter and Barnes [*J. Chem. Soc.*, 2051 (1928)] also reported a tetrabromo derivative, melting at 252° with decomposition.

(7) Dostrovsky and Le Fèvre, *J. Chem. Soc.*, 535 (1939).

X-Ray Diffraction Studies.—Powder photographs of eight different samples of *p*-azophenol were taken using a camera of approximately 57.4 mm. radius and FeK radiation. The history of each of the eight samples follows: (1) hydrated α-azophenol, purified chromatographically and precipitated from a potassium hydroxide solution by means of carbon dioxide; (2) hydrated β-azophenol, purified by recrystallization from alcohol and precipitation from a potassium hydroxide solution by means of carbon dioxide; (3) anhydrous brick-red modification produced by sublimation of α-azophenol; (4) anhydrous brick-red modification prepared by heating hydrated β-azophenol; (5) anhydrous green α-azophenol obtained by heating hydrated α-azophenol; (6) anhydrous green β-azophenol produced by heating relatively large crystals of the hydrated β-form; (7) hydrated α-azophenol obtained from sample 5 by rehydration; and (8) hydrated β-azophenol obtained from sample 4 by rehydration. All samples were ground in an agate mortar to 200-mesh size before mounting on or in a thin-walled glass capillary tube. The exposures in all cases except 3 and 4 were approximately four hours at 12.5 m. a. and 34 k. v. Samples 3 and 4 were sealed inside a thin-walled glass tube and required exposures of approximately twenty-four hours.

Six of the photographs are reproduced in Fig. 1. They show unequivocally that the hydrated α- and β- varieties, 1 and 2, are in reality the same substance, that the two anhydrous brick-red modi-

fications, 3 and 4, are identical but different from the hydrated or anhydrous green forms, and that the two anhydrous green varieties, 5 and 6, likewise are the same but are different in crystal structure from the anhydrous brick-red forms. Samples 7 and 8 gave patterns identical with those of 1 and 2. The X-ray photographs for each of the pairs correspond not only in the positions but also in the intensities of the lines.

Ebullioscopic Studies.—Since α- and β-azophenol decompose on melting, mixed melting point determinations are of little value as a test for identity in this case. However, a method, developed by Halford,[8] of determining the identity of solids, by measuring the rise in boiling point on the addition of one substance to a saturated solution of the other, proved to be of considerable value. An application of this method showed that the α- and β-forms of *p*-azophenol, as usually prepared and purified, were not pure substances. The pure α-variety could be obtained by chromatographing an ethyl acetate solution, using calcium carbonate as the adsorbent. When this carefully purified α-form was added to a saturated solution of the so-called β-form in ethyl ether only a negligible rise in the boiling point was obtained. The addition of the β-form as ordinarily prepared to a solution saturated with the pure α-form was accompanied by a small rise which was of the same order of magnitude as that obtained by the addition of the β-form to a solution saturated with β-azophenol.

Polarographic Studies.—*p*-Azophenol can be oxidized to quinoneazine, and if α- and β-azophenol are in reality *cis* and *trans* forms, oxidation should take place at different potentials in the two cases. Therefore, dropping mercury electrode studies were carried out. Oxidation was first attempted in a buffer of *p*H 5.75 but it was found that the oxidation potential of *p*-azophenol at this *p*H was above that for mercury. However, both forms could be reduced at this *p*H. Identical cathodic waves were obtained for the α- and β-forms.[9]

It was possible to oxidize *p*-azophenol in a buffer of *p*H 9.2. The anodic waves were identical for the two forms.

Chemical Studies.—The chemical evidence which was cited in favor of isomerism of *p*-azophenol was reëxamined. Several derivatives of α- and β-azophenol were prepared by Willstätter and Benz,[10] but only in the case of the diacetates did they find indication of any difference. Thus, it was reported that the α-azophenol diacetate melted at 198–199°, and that the melting point of β-azophenol diacetate was 192°, but that, upon repeated crystallization, the lower melting diacetate was transformed into the higher melting one. Repetition of these acetylations led only to the higher melting diacetate. Furthermore, the diacetate obtained from the β-azophenol did not depress the melting point of the diacetate derived from the so-called α-form.

The work of Robertson concerning nitration and bromination of α- and β-azophenol also was repeated. Instead of isolating the tetranitro-*p*-azophenol in the case of the α-azophenol, which according to previous work melts at 230° and is the expected product, a dinitro compound (m. p. 235–236°) was obtained from both the α- and β-forms. In order to produce the tetranitro compound it was necessary to use more drastic conditions and the product obtained in this way melted with decomposition at 261–262°. The α-

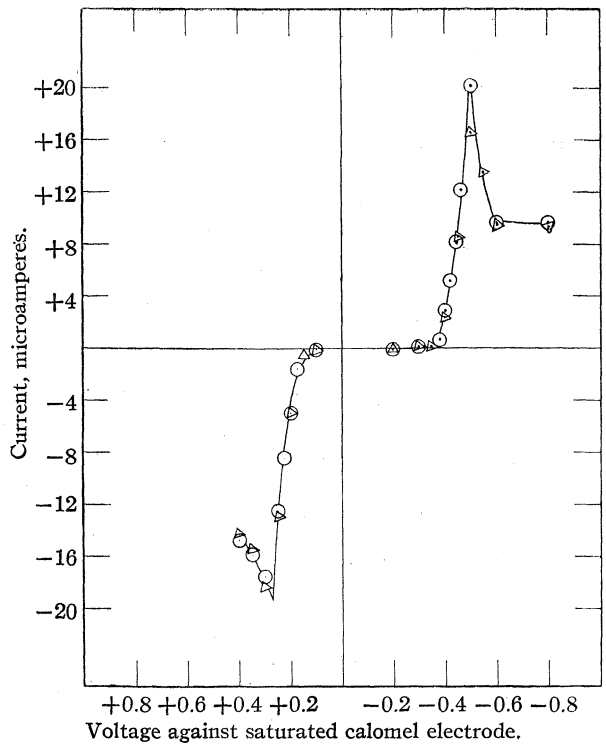


Fig. 2.—Polarographic analysis of α- and β-*p*-azophenol: ⊙, α, *p*H 5.75; △, β, *p*H 5.75; ○, α, *p*H 9.20; △, β, *p*H 9.20.

(8) Halford, THIS JOURNAL, **53**, 2640 (1931).

(9) The presence of maxima precluded an analysis of the reduction process.

(10) Willstätter and Benz, *Ber.*, **40**, 1578 (1907).

and β-azophenols upon bromination also gave only one tetrabromoazophenol, melting at 273–274° with decomposition, in spite of many attempts to obtain the lower melting isomer previously reported.

Experimental

α- and β-azophenol were prepared according to the directions of Willstätter and Benz.

Chromatographic Studies.—Anhydrous (green) α-azophenol (1 g.) was dissolved in ethyl acetate (100 ml.) and the solution passed through a column of precipitated calcium carbonate, 12 cm. long and 1.5 cm. in diameter. The α-azophenol was weakly adsorbed, but could be completely washed through with additional ethyl acetate. As the solution passed through the column a pink zone developed at the top which was not washed down by ethyl acetate. Elution of this zone with methanol gave a small amount of an oily red substance which was not investigated. The ethyl acetate solution of α-azophenol which had passed through the column yielded 0.93 g. of *p*-azophenol, which was crystallized from an aqueous ethanol solution in orange-yellow plates.

One gram of the anhydrous (brick-red) β-azophenol was chromatographed in the same manner. No pink zone was obtained. Crystallization produced β-azophenol in orange-red plates with a blue reflex.

Several mixtures of α- and β-azophenol were chromatographed using different solvents and adsorbents, but no separation was obtained. Likewise attempts to obtain *cis* and *trans* forms by irradiation according to the method which was successfully employed by Cook[11] were fruitless. However, irradiation of *p*-azoanisole in petroleum ether brought about deepening in the color of the solution. When this solution was passed through a column of aluminum oxide, an orange zone of rather strongly adsorbed material appeared at the top of the column. Below this the normal yellow zone of azoanisole was obtained. The orange zone gave a red solid upon elution with ether. Heated to temperatures above 50° it rapidly changed to yellow, the color of ordinary *p*-azoanisole, and melted at 162–164°, the m. p. of ordinary azoanisole. Cook reported a similar behavior in the case of *p*-benzeneazophenetole.

Miscellaneous Observations.—It was noted that the method of separation of β-azophenol from solution had much to do with its appearance. Slow crystallization from an ethanol–water (1:1) solution yielded relatively large crystals which turned green rather than brick-red on heating to 120°. However, if this same material was dissolved in alcohol and rapidly precipitated by the addition of water, the small crystals so produced turned brick-red on heating to 120°, but continued heating transformed this brick-red material to a green product. The time required to bring about the change from brick-red to green varied considerably with different samples.

When pure α-azophenol was precipitated in small crystals from an ethanol–water solution and then heated to 100°, it turned red, but the red material changed to a green within a few minutes. At higher temperatures the change was so rapid that in many cases the hydrated form appeared to go directly to the anhydrous green form.

Sublimation at a pressure of 10^{-2} mm. produced the anhydrous red variety in the case of both α- and β-azophenol. The conversion of this anhydrous red to the anhydrous green modification required only a few seconds at 120°.

Ebullioscopic Studies.—Absolute ether (20 ml.) was used as the solvent in each of the following determinations: (1) boiling point elevation on saturation of ether with pure anhydrous α-azophenol, 0.384°; (2) amounts of pure α-azophenol required for saturation, 0.55 g.; (3) boiling point elevation on the addition of 0.2 g. of anhydrous α-azophenol, prepared and purified in accordance with earlier methods, to solution saturated with α-azophenol, 0.03°; (4) average boiling point elevation on the addition of 0.2 g. of anhydrous β-azophenol to solution saturated with β-azophenol, 0.038°; (5) boiling point elevation on the addition of 0.2 g. of α-azophenol, purified by chromatographing, to solution saturated with α-azophenol, 0.00°; (6) boiling point elevation on the addition of 0.7 g. of pure anhydrous α-azophenol to a solution saturated with β-azophenol, 0.01°; (7) boiling point elevation on addition of 0.42 g. of anhydrous β-azophenol to a solution saturated with anhydrous α-azophenol, 0.09°.

Polarographic Studies.[12]—The set-up used was essentially the same as that described by Kolthoff and Lingane.[13] Measurements were made with reference to a saturated calomel electrode. The α- and β-azophenols were dissolved in the following buffer solutions: (1) a buffer of *p*H 5.75 prepared by combining 200 ml. of 0.999 *N* acetic acid, 100 ml. of 0.982 *N* sodium hydroxide and 300 ml. of absolute alcohol; (2) a buffer of *p*H 9.2 prepared by combining 80.9 ml. of 0.0982 *N* sodium hydroxide, 6.184 g. of boric acid, 209 ml. of conductivity water and 300 ml. of absolute alcohol. To this solution was added 2.5 g. of potassium nitrate to serve as an electrolyte. The molar concentrations of the azophenols were as follows:

	*p*H 5.75	*p*H 9.2
α-Azophenol	1.016×10^{-3}	1.004×10^{-3}
β-Azophenol	1.005×10^{-3}	1.017×10^{-3}

The results are shown in Fig. 2.

Nitration of α- and β-Azophenol.—Following the procedure of Robertson, anhydrous α-azophenol (1.5 g.) was dissolved in glacial acetic acid (75 ml.) by warming. The solution was then cooled until the acetic acid began to crystallize, at which time concd. nitric acid (7 ml.) was added with stirring over a period of fifteen minutes. The reaction mixture was then placed in an ice box overnight. Yellow needle-like crystals (m. p. 230–232°; 0.48 g.) separated. This crude product was extracted twice with hot ethanol and the residue crystallized twice from glacial acetic acid. The dinitro-*p*-azophenol obtained in this manner melted at 235–236°, and yielded a dinitrodibromo-*p*-azophenol (m. p. 281–282°) on bromination.

β-Azophenol (1.5 g.), nitrated in the same manner, yielded 0.46 g. of slightly impure dinitro-*p*-azophenol, which upon purification also melted at 235–236°. A mixed melting point of the two nitration products showed no depression.

(11) Cook, *J. Chem. Soc.*, 878 (1938).

(12) The authors are indebted to Mr. Carl Miller for valuable assistance during these studies.

(13) Kolthoff and Lingane, *Chem. Rev.*, 24, 12 (1939).

Tetranitro-*p*-azophenol (m. p. 261–262°, with dec.) was obtained by slowly adding dinitro-*p*-azophenol (1 g.) to fuming nitric acid (5 ml.), cooled in an ice–salt bath. After stirring for five minutes, the reaction mixture was poured on ice. The crude product (1 g.) was purified by crystallization from glacial acetic acid.

Anal. Calcd. for $C_{12}H_6O_{10}N_6$: C, 36.55; H, 1.52; N, 21.32. Found: C, 36.93; H, 1.73; N, 21.45.

Tetrabromoazophenol (m. p. 273–274°) was obtained in equal yield from both α- and β-azophenol. To a solution of the monohydrate of *p*-azophenol (2 g.) and sodium acetate (3 g.) in glacial acetic acid (130 ml.) was added a solution of bromine (3 g.) in glacial acetic acid (50 ml.). Mechanical stirring was employed during the period (twenty-five minutes) that bromine was added and for thirty minutes thereafter. A dark green precipitate (1.3 g.) was filtered off. After four crystallizations from glacial acetic acid, the tetrabromo derivative melted at 273–274°.

Anal. Calcd. for $C_{12}H_6O_2N_2Br_4$: C, 27.20; H, 1.14. Found: C, 27.04; H, 0.87.

The diacetate (m. p. 263–264°) was prepared in the usual way.

Anal. Calcd. for $C_{16}H_{10}O_4N_2Br_4$: C, 31.27; H, 1.63. Found: C, 31.32; H, 1.73.

The dibenzoate (m. p. 297–298°) was obtained by benzoylation in pyridine with benzoyl chloride.

Anal. Calcd. for $C_{26}H_{14}O_4N_2Br_4$: C, 42.28; H, 1.90. Found: C, 42.12; H, 2.37.

Summary

The recorded evidence for *cis–trans* isomerism in the case of *p*-azophenol has been reëxamined and new findings have been introduced with the result that it may now be concluded that the so-called α- and β-forms of *p*-azophenol are not *cis–trans* isomers. The anhydrous *p*-azophenol does exist in two solid modifications, however.

MINNEAPOLIS, MINN. RECEIVED AUGUST 8, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

The Effect of Nuclear and Side Chain Substitution on the Oxonium Ion Catalyzed Iodination of Acetophenone Derivatives

BY LOIS ZUCKER[1] AND LOUIS P. HAMMETT

Nathan and Watson,[2a] and Evans,[2b] measured the rates of bromination of a number of acetophenone derivatives in acetic acid–water solutions containing hydrochloric acid, and found the effect on the rate of substitution of a methyl group for hydrogen in the side chain much greater than the effect of substitution in the ring. Since the reaction is subject to general acid catalysis,[3] the specific bromination rate in a given medium is the sum of a series of specific catalytic bromination rates, one for each catalyst present, and the effect of a given substitution cannot be expected to be the same for different catalysts. This makes the observed rate in this medium an unnecessarily complicated function of the structure of the ketone,[4] since undissociated acetic acid, hydrogen ion solvated with water (oxonium ion), and hydrogen ion solvated with acetic acid are possible catalysts. A more easily interpretable catalytic system is found in a not too concentrated aqueous solution of a strong monobasic acid, which can contain only one effective catalyst, oxonium ion. Accordingly, we have measured the rates of iodination (equal to the rates of enolization) of some of these ketones, together with that of 2,4,6-trimethylacetophenone (not on the previous list), in 1.388 molar aqueous perchloric acid solution, using a colorimetric technique.

(1) Part of a thesis submitted by Lois Zucker in partial fulfilment of the requirements for the degree of Doctor of Philosophy in the Faculty of Pure Science of Columbia University.

(2) (a) Nathan and Watson, *J. Chem. Soc.*, 217 (1933); (b) Evans, *ibid.*, 785 (1936); see also (c) Evans, Morgan and Watson, *ibid.*, 1167 (1935).

(3) Zucker and Hammett, THIS JOURNAL, **61**, 2785 (1939).

(4) Hammett, *Trans. Faraday Soc.*, **34**, 156 (1938).

Experimental

Apparatus.—The iodinating solution was contained in a closed glass cell shown in Fig. 1, closure being made with a very well fitting ground glass joint, of which the colorimeter plunger forms the stopper. Error introduced by this closure, as far as optical alignment and effective depth of layer are concerned, was within the ordinary precision of matching, ±0.17 mm. under the conditions of a kinetic run. A really well fitting glass joint is also necessary to retain iodine in an aqueous solution containing no iodide over a period of many hours. The double lines indicate brass, the single lines glass. The cell stood directly on a plane glass disk (removable for cleaning) which formed part of the bottom of a flattened cylindrical brass water jacket, of 80 cc. capacity with the cell mounted, which in turn was fastened to the colorimeter platform with a lock nut. Water was circulated from a large thermostat through insulated tubing and the likewise well insulated jacket at the rate of 5 cc. per sec. Temperature in the cell could be maintained at 25.00 ± 0.01°, as checked by thermocouple, even when room temperature was as low as 17°.

The colorimeter was the Klett–Beaver model,[5] with the above-described cell mounted on one side, and on the other side the standard two-cup, two-plunger system for maintaining a constant 5 cm. depth of absorbing layer, with variable contributions from the colorimetric standard and pure water. The fields were viewed through a dense blue filter, Wratten L50; applied to the usual incandescent bulb it supplies a deep blue–violet light representing a fairly narrow spectral band. The filters were placed inside the prism housing immediately over the ends of the plungers.

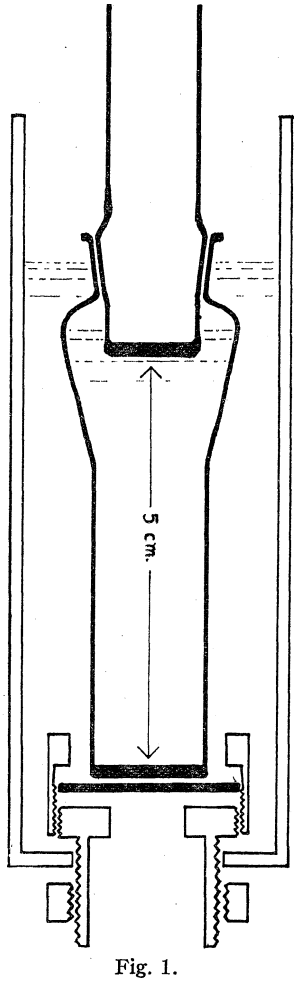


Fig. 1.

Method.—The reaction products, derivatives of phenacyl iodide, are rather insoluble in any aqueous media. The maximum concentration of iodine which can disappear from solution before the appearance of insoluble phenacyl iodide is 17×10^{-5} molar, and some of the substitution products of phenacyl iodide are considerably less soluble. Iodine concentrations used in runs were accordingly of this order of magnitude, so that large relative changes in iodine concentration could be observed; the range of iodine concentrations covered was 30 to 0.5×10^{-5}. The more dilute of these solutions, although hardly distinguishable from water by general illumination, have reasonably strong color when viewed through the blue filter used, since the filter cuts out most of the light not appreciably absorbed by aqueous iodine solutions.

Because of the great instability in an open cup of aqueous iodine solutions containing no iodide, we had to use an artificial colorimetric standard—a dilute (4 mg. per liter) solution of methyl orange in water. Although this solution differs markedly in color from iodine solutions in general illumination, when viewed by the light transmitted by the filter methyl orange and iodine solutions are indistinguishable by eye over the range of concentrations covered.

Beer's law was shown to apply to this system by determining the depth of layer of the standard methyl orange solution necessary to match the same 5-cm. layer of at least eight different iodine solutions covering the range of iodine concentrations used, and made up by adding an excess of sodium iodate or sodium nitrite to a known acidified solution of potassium iodide. Then

$$c_{I_2} = \frac{c_{MeO}\bar{k}_{MeO}}{h_{I_2}\bar{k}_{I_2}} \times h = mh$$

where c_{I_2} and c_{MeO} are the molar concentrations of iodine and methyl orange, $\bar{k}_{I_2}$ and $\bar{k}_{MeO}$ are the effective molecular extinction coefficients of iodine and methyl orange for the spectral region employed,[6] h_{I_2} is the depth of layer of iodine solutions (close to 5 cm.), h the depth of layer of methyl orange solution necessary for match, and m is the slope of the linear plot of c_{I_2} against h.

Under ordinary conditions only one atom of iodine from each iodine molecule is introduced into the ketone, the other being liberated as iodide ion. Because the resultant gradual increase in concentration of the intensely yellow polyiodide ions would cause a change in the color value and intensity of the solution, and because iodide ion undergoes oxidation by dissolved oxygen which is relatively rapid in acid solution, and finally to avoid reversal of the reaction, most of the runs were made in the presence of an oxidizing agent, either sodium nitrite or sodium iodate, which converts iodide to iodine as fast as it is formed. This device is due to Bartlett,[7] who used nitric acid as the oxidizing agent in glacial acetic acid. Then

$$\Delta c_{KH} = f\Delta c_{I_2} = mf\Delta h \qquad (1)$$

where Δc_{KH} is the change in concentration of the ketone as a result of the iodination, Δc_{I_2} and Δh are the corresponding changes in iodine concentration and in colorimeter setting. The factor f has the value 2.5 if the oxidizing agent is iodate, 2 if it is nitrite. Some runs were made with each ketone with nitrite, some with iodate—agreement of the rates is evidence that neither oxidizing agent is interfering with the rate measurement. Good agreement was found for all the ketones except 2,4,6-trimethylacetophenone and isobutyrophenone; in the latter case both oxidizing agents obviously were causing some other reaction, accom-

(5) Beaver, *J. Opt. Soc. Am.*, **18**, 41 (1929).

(6) Kortüm, *Z. angew. Chem.*, **50**, 193 (1937); Müller, *Ind. Eng. Chem., Anal. Ed.*, **31**, 1 (1939).

(7) Bartlett and Vincent, THIS JOURNAL, **55**, 4992 (1933).

panied by the production of a brown color in the case of the iodate, and a precipitate in the case of the nitrite. Runs were made with both these ketones without any oxidizing agent, small portions of the reacting solution being read in the colorimeter at suitable time intervals, immediately after the addition of a slight excess of nitrite. The reverse reaction between iodide ion and phenacyl iodide derivative cannot be neglected if iodide is allowed to accumulate, so that the apparent rate does fall off; nevertheless the initial part of the reaction is not affected appreciably. Isobutyrophenone could be studied only by this method. The rate of iodination of 2,4,6-trimethylacetophenone in the absence of an oxidizing agent was found to be in excellent agreement with the rate in the presence of nitrite; it was therefore concluded that the discrepancy between runs with nitrite and with iodate is in this case due solely to some side reaction with the iodate.

The usual procedure was to weigh a suitable quantity (about 9 cc.) of a solution containing known concentrations of ketone and perchloric acid into the reaction cell, which was equipped with a spare stopper, and bring to temperature in the large thermostat while water was circulated through the water jacket on the colorimeter. About 0.2 cc. of a known aqueous potassium iodide solution was added from a weight pipet, the solution mixed, and left in the thermostat ten minutes longer. The reaction was started by the addition of a small crystal of solid oxidizing agent, the cell was transferred to the colorimeter, and readings were taken. The total time of mixing and transfer from one thermostat to the other was not more than twenty seconds. Time was measured from the instant of addition of oxidizing agent to the nearest one-tenth minute with a stop watch calibrated against an electric clock. This procedure allows a very satisfactory approximation to instantaneous mixing since the ketone concentration, upon which alone the rate depends, is at its correct initial value even before mixing.

For the runs without oxidizing agent each point on the time curve had to be determined on a separate portion of the reacting solution. In the case of 2,4,6-trimethylacetophenone it was most convenient to make up the solution in the colorimeter cell by the rapid addition from a weighing bottle of about 9 cc. of a solution of the ketone in perchloric acid, already at temperature, to about 0.1 cc. (known weight) of an aqueous solution containing potassium iodide and not quite an equivalent of sodium iodate, in the colorimeter cell also at temperature. After a suitable time interval a drop of an aqueous sodium nitrite solution was added, amounting to a slight excess over the concentration necessary to take care of the probable iodide concentration in the reacting solution. Readings were completed within five minutes of this addition.

This procedure applied to isobutyrophenone would have made the reaction cell unavailable for other measurements for weeks; therefore the initial solution was made up in 130-cc. quantities in bottles of about 140-cc. capacity with very well ground glass stoppers, and at suitable intervals a portion of the solution was poured into the dry cell for reading. Experiments showed that with smooth pouring the first portion run into the cell is of the same iodine concentration as that in the bottle before pouring; however, with each opening of the bottle to pour out a portion, the iodine concentration of the solution in the bottle decreases slightly and this effect is the more pronounced the larger is the ratio of gas volume to liquid volume in the bottle. (The vapor pressure of iodine at 25° is 0.311 mm.[8]; these solutions have approximately one-fourth of the saturation concentration.) Only two portions could be taken from each bottle.

Materials.—Aqueous acid iodine solutions prepared from weighed portions of potassium iodide with an excess of either sodium iodate or sodium nitrite, formed the primary colorimetric standards. The sample of potassium iodide used throughout was of C. P. grade. It was dried at 105° and kept in a desiccator. At various times solutions prepared from the standard sample of potassium iodide were compared with solutions nominally of the same iodine concentration prepared from two other samples of potassium iodide of different origins and a sample of sodium iodide, and found to have the same color intensity within the error of the determination. Sodium iodate and sodium nitrite were of C. P. grade. Iodine solutions made up from the same iodide solution with iodate and with nitrite had the proper concentration ratio of 6 to 5.

Methyl orange was of the ordinary commercial grade for indicator use. The sample used appeared not entirely homogeneous with respect to depth of color of various particles. The secondary colorimetric standard was a stock solution of 100 mg. of methyl orange in 1 liter of aqueous solution, from which the working standard was prepared at frequent intervals by a 1 to 25 dilution. The stock solution retained the same iodine equivalence for over a year.

Perchloric acid solutions were made up from 60% reagent grade, ACS specification, and standardized against 0.1 normal sodium hydroxide, the primary standard being Bureau of Standards potassium acid phthalate.

Acetophenone,[9a,b] *p*-methylacetophenone,[9c] 2,4,6-trimethylacetophenone and *p*-bromoacetophenone[9c] previously had been purified carefully. The first three were purified further by fractionating three times *in vacuo;* the *p*-bromoacetophenone was recrystallized once from ethanol–water solution. Propiophenone and *n*-butyrophenone obtained from the Eastman Kodak Company, and isobutyrophenone, made by Friedel–Crafts synthesis from benzene and isobutyryl chloride (Eastman), were recrystallized several times each from purified petroleum ether in an acetone–dry-ice bath, separation between crystals and liquid being effected by an Emig immersion filter. They were then each fractionated three times *in vacuo*. The purified samples all distilled within a temperature range of 0.2°.

(8) "International Critical Tables," Vol. III, p. 201.

(9) (a) Morgan and Lammert, THIS JOURNAL, **46**, 881 (1924); (b) Flexser, Hammett and Dingwall, *ibid.*, **57**, 2103 (1935); (c) Flexser and Hammett, *ibid.*, **60**, 885 (1938).

Ketone	B. p. °C.	Mm.	F. p., °C.	$n^{25.3}$°D
Acetophenone	67	5	19.6–19.65	1.53142
Propiophenone	85	7	18.4–18.5	1.52436
n-Butyrophenone	75	4½	12.65–12.7	1.51741
Isobutyrophenone	97	10	−1.35 to −1.3	1.51480
p-Methylacetophenone	72	4		1.53161
p-Bromoacetophenone			52.2–52.5	
2,4,6-Trimethylacetophenone	105	9		1.51444

Rate Calculations.—The reaction is first order in ketone and independent of iodine concentration, following the equation

$$-dc_{KH}/dt = kc_{KH} = k(c^0_{KH} - \Delta c_{KH})$$

where c^0_{KH} is the initial concentration of ketone. Substitution of equation (1) converts this to

$$-mf\frac{dh}{dt} = mfk\left(\frac{c^0_{KH}}{mf} - \Delta h\right)$$

whose integrated form is

$$\log\left(\frac{c^0_{KH}}{mf} - \Delta h\right) = -\frac{k}{2.303}t + \log\frac{c^0_{KH}}{mf} \quad (2)$$

If only a small fraction of the total ketone present reacts

$$\frac{c^0_{KH}}{mf} >> \Delta h, \text{ and } -h = \frac{kc^0_{KH}}{mf}t - h^0 \quad (3)$$

Since in all runs the change in iodine concentration during the run was limited to $\Delta c_{I_2} = m\Delta h \leq 17 \times 10^{-5}$, equation (3) could be applied to most of these ketones in spite of their small solubility. Equation (2) had to be used only for the most insoluble ketones, *p*-bromoacetophenone, isobutyrophenone, and 2,4,6-trimethylacetophenone.

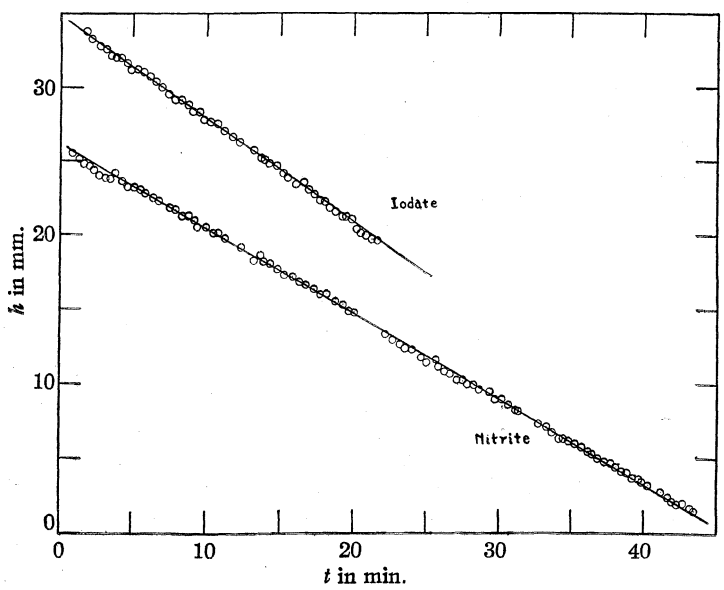


Fig. 2.

In all cases k was calculated from the slope of the line fitted by eye to the appropriate graphical plot of the data. The ketone concentration used in equation (3) was actually the average concentration for the run, which in no case differed from the initial concentration by more than 2%. The value of h^0 necessary for the application of equation (2) could be obtained either by extrapolation of a plot of h against t, or from the known initial iodide concentration of the solution by the application of the formulas

$$h^0 = \frac{c^0_{I_2}}{m} = \frac{c^0_{I^-}}{m(1-1/f)}$$

for solutions made up with excess oxidizing agent, and

$$h^0 = \frac{c^0_{I_2}}{m} = \frac{1}{2m}(c^0_{I^-} - c^0_{NaIO_3})$$

for solutions made up with iodide in excess over iodate, the oxidation being completed later with nitrite. Agreement of h^0 determined in these two ways shows the absence of any appreciable concentration of the enols of these ketones.

Precision.—The error in k calculated by the method outlined using equation (3) depends on the error in m (0.5%), in c^0_{KH} (0.1%) and in the slope of the line fitted to the plotted points by eye. The important factors in the error in slope are the number of points (from 80 to 100 for most of these experiments) and the average deviation of the points from the best line, measured along the h-axis relative to the total length of the h-axis (Δh_{max}). The error in measurement of time can be neglected by comparison with the error in h. To estimate the error for one experiment (the longer run shown in Fig. 2), we have combined the standard deviation of the slope of the line[10] calculated by the least squares technique (0.25%) with a reasonable estimate of the average deviation of the slope of a line fitted by eye from that of the least squares line (0.75%), the resultant figure being 0.8%. The error in the slope for other experiments, for which a least squares line has not been calculated, was obtained from the 0.8% figure in the following way. The

(10) Wright and Hayford, "The Adjustment of Observations," D. Van Nostrand Company, New York, N. Y., 1906, p. 132.

average deviation in h, based on a large series of readings, is 0.17 mm. for h in the range 45–5 mm. The average deviation put on a comparable basis for a series of experiments is $0.17/\Delta h_{max}$. The error in the slope certainly increases with an increase in this figure; we have assumed that the error in the slope is inversely proportional to Δh_{max}, so that the estimated precision of the slope for the shorter run in Fig. 2 is 1.3%. Including the effect of the 0.5% error in m, the precision measures for all the runs using equation (3) range from 1 to 1.4%.

It can be shown that the error due to Δh in the ordinate, log $(c^0_{KH}/mf - \Delta h)$, used in plotting equation (2), relative to the maximum value of that ordinate is

$$\frac{\epsilon_{\Delta h}}{\Delta h_{max} + \frac{\Delta h_{max}}{c^0_{KH}/mf}(1/2\,\Delta h_{max} - \Delta h)}$$

where ϵ represents error in the sense of average deviation. This is not a general equation, but is a valid approximation for all our experiments, since $\Delta h_{max}/(c^0_{KH}/fm)$ (fraction of ketone reacting during the run) was maximally 1/4. This average deviation of points from the line increases with extent of reaction, but even in the most extreme case differs from $\epsilon_{\Delta h}/\Delta h_{max}$ by ±13%. The average deviation is still approximately inversely proportional to Δh_{max}. The situation is illustrated in Fig. 3, which shows plots according to equation (2) of one run with *p*-bromoacetophenone, with $\Delta h_{max} = 15$, $\Delta h_{max}/(c^0_{KH}/fm) = 0.1$, and one run with 2,4,6-trimethylacetophenone, with $\Delta h_{max} = 5.4$, $\Delta h_{max}/(c^0_{KH}/fm) = 0.25$. Precision measures have been calculated for these two ketones in the same way as before, and are 1.5 and 3.6%, respectively. The isobutyrophenone experiments are characterized by considerably greater experimental error, besides having a Δh_{max} of only 6; the assigned precision measure in this case is 6%.

Results

The results are presented in Table I. The iodination of acetophenone is accurately first order in acetophenone with a 7-fold variation in initial concentration, and zero order in iodine,

TABLE I

IODINATION RATES IN 1.388 MOLAR $HClO_4$ AT 25.00°

Ketone	No. of expts.	Av. k (min.$^{-1}$)
Acetophenone	4	0.001104
Propiophenone	3	.000513
n-Butyrophenone	2	.000418
Isobutyrophenone	3	.0000224
p-Methylacetophenone	2	.001305
p-Bromoacetophenone	2	.000850
2,4,6-Trimethylacetophenone	3	.001625

with a 3-fold variation in initial concentration, and an 11-fold variation in iodine concentration during the course of a single run, in all a 22-fold variation in iodine concentration. We did not investigate the dependence of the rate on the concentrations of the reactants for any of the other ketones so fully. Aside from acetophenone, *n*-butyrophenone was the only ketone whose rate was shown to be first order in ketone concentration. The dependence of rate on iodine concentration was shown to be zero order for propiophenone, *p*-methylacetophenone, and *p*-bromoacetophenone. The acid catalyzed iodination of the reaction product, substituted phenacyl iodide, is so slow by comparison with that of the original ketone that it does not take place to any appreciable extent under the experimental conditions. This is so even for 2,4,6-trimethylacetophenone, where the ratio product/reactant reached a maximum value of 1/4.

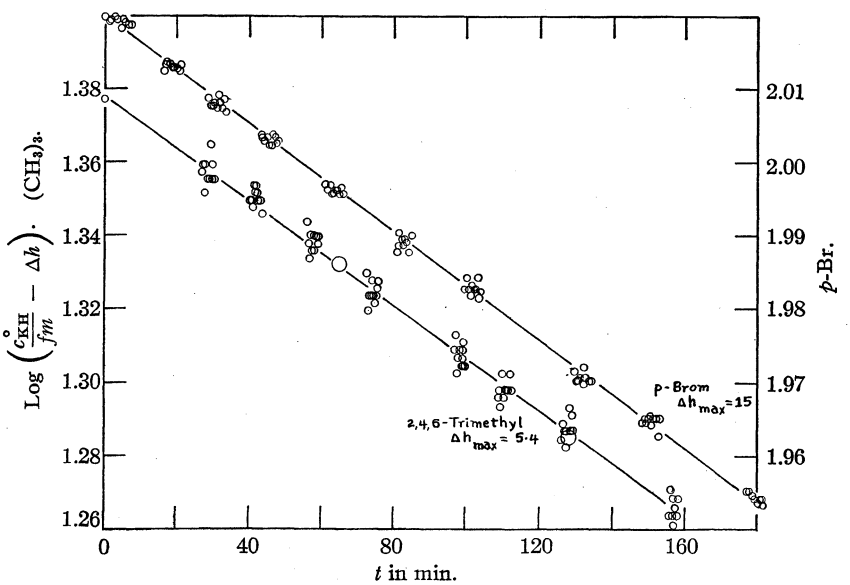


Fig. 3.—o, with oxidizing agent; O, without oxidizing agent.

Rough experiments showed the rates of iodination of these ketones in 0.01 molar perchloric acid to be negligible by comparison with the rates in 1.388 molar perchloric acid, proving the absence of any effective water catalysis. These rates cannot be expected to be identical with those calculated from the specific catalytic constants for the oxonium ion catalyzed reaction in dilute aqueous solution, because of salt effect, but the salt effect should be small, and consequently of approximately equal effect on all the rates. Actually for acetophenone the ratio of the rates in 1.388 molar and 0.210 molar perchloric acid solutions is only 7% greater than the ratio of the molar concentrations of perchloric acid in the two solutions.

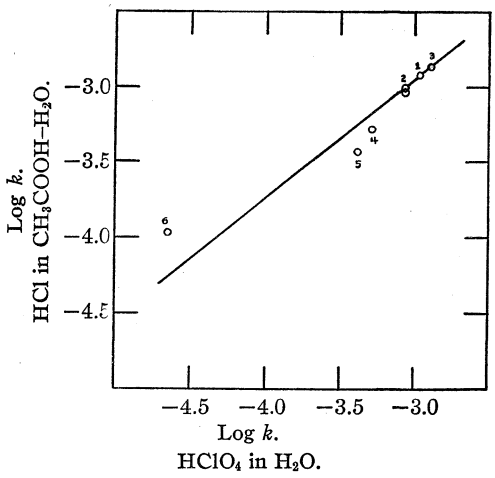


Fig. 4.—1, Acetophenone; 2, *p*-bromoacetophenone; 3, *p*-methylacetophenone; 4, propiophenone; 5, *n*-butyrophenone; 6, isobutyrophenone.

Discussion

Our results are in agreement with the conclusion of the Cardiff workers[2] as to the large effect of substitution on the alpha carbon on the rate of enolization. There is a quantitative difference in the results, whether due to the polycatalytic composition of the acetic acid medium, or to some other medium effect of unknown nature; these differences are presented in the form of a plot of the logarithms of the rates in one medium against those in the other (Fig. 4). If there were no medium effect, the points would all lie on a straight line of unit slope. Medium effects for substitutions not too close to the seat of the reaction usually cause the points to form a straight line of arbitrary slope, with points representing compounds differing by an alpha substitution showing no simple relation to each other.[4]

Previous work on the effect of ortho methyl substitution on the reactions of phenyl ketones[11] shows strong suppression of only those typical ketone reactions which involve addition at the carbon of the carbonyl group. The most probable enolization mechanism involves addition of a proton to the carbonyl oxygen and removal of a proton from the alpha carbon[12]; if the above generalization is correct no steric hindrance of enolization is to be expected with ortho methyl substitution. And in fact ortho methyl substitution increases the rate of enolization, just as *p*-methyl substitution does.

Summary

The rates of iodination of the ketones acetophenone, *p*-bromoacetophenone, *p*-methylacetophenone, 2,4,6-trimethylacetophenone, propiophenone, *n*-butyrophenone and isobutyrophenone in 1.388 molar aqueous perchloric acid, and of acetophenone in 0.210 molar aqueous perchloric acid, have been measured by a colorimetric method. The rates are compared with those reported for some of the same ketones in 75% acetic acid–water solution 0.5 molar to hydrochloric acid. No steric hindrance was found in the iodination of 2,4,6-trimethylacetophenone.

NEW YORK, N. Y. RECEIVED JUNE 24, 1939

(11) Kohler and Baltzly, THIS JOURNAL, **54**, 4015 (1932).
(12) Pedersen, *J. Phys. Chem.*, **38**, 581 (1934).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

The Mechanism of the Acid Catalyzed Enolization of Acetophenone Derivatives

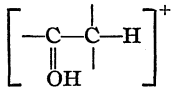
BY LOIS ZUCKER[1] AND LOUIS P. HAMMETT

The rate determining step in the enolization of ketones is probably a proton transfer, one of the two necessary to convert ketone to enol. The mechanism of this reaction when catalyzed by oxonium ion is[2]

$$KH + OH_3^+ \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} IH_2^+ + H_2O$$

$$IH_2^+ + H_2O \xrightarrow{k_2} EH + OH_3^+$$

where KH is the keto form of the ketone, EH is the enol form, and IH_2^+ is the intermediate ion



In this reaction, as in most others subject to acid or base catalysis, more than one proton transfer is involved, and the question as to which of these is the rate determining step is an important one. Its significance is especially emphasized by the recent work of Bonhoeffer[3] on the relative rates of proton and deuteron transfer in the enolization reaction, and of Cohn and Urey[4] in the oxygen exchange of ketones with solvent.

A possible method of attack upon the mechanism problem is based upon the quantitative correlation which must exist between the rate of proton transfer to or from the substrate in a catalyzed reaction, and the acid or base strength of the substrate. The necessity of the correlation follows from the following considerations. A linear relation is quite generally observed between the logarithms of the ionization constants of a series of catalysts and the logarithms of the specific catalytic rate constants for a reaction with a single substrate.[2] All these specific rates are equal to, or proportional to, the specific rates of transfer of a proton either from acidic substrate to basic catalyst, or from acid catalyst to basic substrate.[2] Consequently, the observed linear relation must be based on a more general linear relation between the logarithms of the ionization constants of any series of bases (acids), and the logarithms of the specific rates of transfer of a proton between a given acid (base) and the series of bases (acids). Applying this generalization to the case of variable catalyst–fixed substrate gives the observed relation between rates and strengths of catalysts; applying it to the case of variable substrate–fixed catalyst, allows the prediction of a linear relation between the logarithms of the appropriate basic (acidic) ionization constants of a series of substrates which can undergo the same acid (base) catalyzed reaction, and the logarithms of the specific catalytic rate constants for the reaction with a single catalyst.[5]

Thus for the enolization catalyzed by oxonium ion, as outlined above, the following should be true equations when the ketone is varied

$$\log k_1 = -\alpha \log K_{KH} + \beta \quad (1)$$

$$\log k_2 = \alpha' \log K_{EH} + \beta' \quad (2)$$

where

$$K_{KH} = \frac{a_{H^+}\, a_{KH}}{a_{IH_2^+}}$$

and

$$K_{EH} = \frac{a_{H^+}\, a_{EH}}{a_{IH_2^+}} = K_{KH} K_{\text{Enolization}}$$

and α, β, α', β' are constants for the series of ketones with oxonium ion. If step 1 in the enolization is rate determining, it should be true that

$$\log k = \log k_1 c_{OH_3^+} = -\alpha \log K_{KH} + \beta'' \quad (3)$$

where

$$k = -\frac{1}{c_{KH}} \frac{dc_{KH}}{dt}$$

$c_{OH_3^+}$ is constant for all the ketones, and no other catalyst is present in the solution. If step 2 is rate determining

$$\log k = \log k_2 c_{OH_3^+}/K_{KH} = (\alpha' - 1) \log K_{KH} + \alpha' \log K_{Enol.} + \beta'''$$

and no linear relation is to be expected between log k and log K_{KH}, unless all changes in structure concerned have quantitatively similar effects on both equilibrium constants.

There are some limitations on the applicability of these rate–equilibrium constant relationships concerned with allowable differences in structure of the bases (acids) being compared, which can be

(1) Part of a thesis submitted by Lois Zucker in partial fulfilment of the requirements for the degree of Doctor of Philosophy in the Faculty of Pure Science of Columbia University. The material was presented at the Milwaukee meeting of the American Chemical Society, September, 1938.

(2) Pedersen, *J. Phys. Chem.*, **38**, 581 (1934).

(3) Bonhoeffer, *Trans. Faraday Soc.*, **34**, 252 (1938).

(4) Cohn and Urey, THIS JOURNAL, **60**, 679 (1938).

(5) Pedersen, Dissertation, Copenhagen, 1932; Hammett and Pfluger, THIS JOURNAL, **55**, 4079 (1933); Bell, *Proc. Roy. Soc.* (London), **154**, 414 (1936).

deduced from the results of comparing specific rates obtained for a series of catalysts and the acid (base) strengths of the catalysts. Acids with varying numbers of acidic hydrogens, or their conjugate bases, can be compared only if statistical corrections are applied to their experimentally determined ionization constants.[2] Acids or bases differing largely in structure cannot be compared; substitution on the same atom which carries or can receive the acidic hydrogen,[6] and changes in charge type appear to be such large changes in structure.

Lack of quantitative information about any basic or acidic ionization constants of typical substrates or their conjugate acids or bases, has prevented the practical application of these expectations. Recently, however, a method has been developed for measuring the basic ionization constants of extremely weak bases by the changes in their ultraviolet absorption spectra on ionization in various sulfuric acid–water solutions[7a]; pK's are already available for acetophenone,[7a] *p*-bromoacetophenone[7b] and *p*-methylacetophenone,[7b] and to these we have now added propiophenone, *n*-butyrophenone and isobutyrophenone. The rates of enolization of these ketones, the catalyst being oxonium ion, already have been reported.[8] Equation (1) should apply for all these acetophenone derivatives. They are all monoacid bases, so there is no necessity for statistical corrections. When substrate is fixed and catalyst changed, points for alpha substituted aliphatic carboxylic acids or their ions fall on the same line as points for substituted benzoic acids or their ions[2]; it is therefore very improbable that any of the substitutions involved with these ketones is sufficiently drastic to invalidate equation (1). (This set of ketones would not be suitable for a comparison involving the use of equation (2), because of the substitution on the carbon carrying the acidic hydrogen.) Then if step 1 is rate determining, equation (3) is a true equation and a plot of log k against log K_{KH} should be a straight line. If step 2 is rate determining, equation (3) is not a true equation, because the relative effects of side chain substitution and of ring substitution cannot be expected to be the same on log k_2 as on log K_{KH}; in this case the plot of log k against log K_{KH} will not be a straight line.

The rates actually measured were the rates of iodination of the ketones, which should equal the rates of enolization.[9,2] Before making the comparison between these rates and the base strengths of the ketones, we investigated the nature of the acid catalysis of the iodination of acetophenone, since if general acid catalysis as distinguished from specific hydrogen ion catalysis[2] is not proved definitely, there is the possibility of an iodination mechanism differing fundamentally from that outlined. General acid catalysis has been established for the halogenation of acetone alone among ketones.[10]

Experimental

Materials.—The physical constants and details of purification of the ketones used were given in the preceding paper.[8]

Chloroacetic acid was recrystallized four times from benzene, m. p. 63.0–63.2°; acid titration 99.83% of theoretical.

Method: pK' Measurements.—The method of Flexser, Hammett and Dingwall[7a] was used. In this technique the temperature of the solution was 22 ± 5°; closer temperature control was considered unnecessary because of the very small temperature coefficients characteristic of absorption of ultraviolet and visible light, and of the ionization equilibrium. However, the few cases known with very large temperature coefficients of light absorption, all involve ions.[11] We have measured the absorption of isobutyrophenone in 89.7% sulfuric acid, in which it is nearly completely ionized, at room temperature, and at 45 ± 0.2°. Since the results agreed within the error of measurement, and since the water jacketing is extremely troublesome in the small space available around the absorption cell, all the other measurements reported here were made without temperature control, as previously.

The sodium salicylate treatment[12] of photographic plates for increasing contrast at very short wave lengths was found very useful for determining extinction coefficients from 2100 to 2300 Å.

The "isobestic point" method[7a] of calculating the pK's was used. The use of areas under the curves representing extinction coefficients as a function of wave length, over intervals of 100 Å., gave only slightly better results than the use of the extinction coefficients themselves at wave lengths in the centers of these intervals.

(6) Pfluger, Abstracts of papers presented before the Division of Phys. and Inorg. Chem., Am. Chem. Soc., April, 1939, p. 23; Brönsted and Pedersen, *Z. physik. Chem.*, **108**, 185 (1924); Junell, Dissertation, Uppsala, 1935.

(7) (a) Flexser, Hammett and Dingwall, THIS JOURNAL, **57**, 2103 (1935); (b) Flexser and Hammett, *ibid.*, **60**, 885 (1938).

(8) Zucker and Hammett, *ibid.*, **61**, 2779 (1939).

(9) Lapworth, *J. Chem. Soc.*, **85**, 30 (1904).

(10) (a) Dawson and Carter, *ibid.*, 2282 (1926); Dawson and Spivey, *ibid.*, 2180 (1930); (b) Dawson and Key, *ibid.*, 1239, 1248 (1928); Dawson, Hoskins and Smith, *ibid.*, 1884 (1929); Dawson and Smith, *ibid.*, 2530 (1929); 79 (1930); Dawson and Spivey, *ibid.*, 2612 (1932).

(11) Scheibe, *Z. Elektrochem.*, **35**, 701 (1929); Kortüm, *Z. physik. Chem.*, **B30**, 315 (1935); Mukerji, *J. Phys. Chem.*, **32**, 1834 (1928).

(12) Tien Kui. *Compt. rend.*, **201**, 1348 (1935); Terrien. *ibid.*, **202**, 211 (1935); Tien Kui, *ibid.*, **203**, 1144 (1936); Montague and Ricard, *ibid.*, **202**, 477 (1936).

Rate Measurements.—The reaction was studied by the colorimetric technique previously described.[8] Differences in technique arise from two features of these experiments, the low acidity of the solutions and the necessity for maintaining constant ionic strength. The rate of the oxidation of iodide ion to iodine, produced by potassium iodate in all cases, is too slow in this range of hydrogen ion concentration when only a slight excess of iodate is present. The concentration of potassium iodate necessary to prevent any accumulation of iodide ion could be calculated from the known rate of the iodide–iodate reaction,[13] the hydrogen ion concentration of the solution, and an approximate figure for the rate of the iodination reaction. In all runs except 18, 0.01 molar potassium iodate was more than sufficient; in run 18, with a hydrogen ion concentration of 0.001, the concentration of iodate used was 0.08. Because of the necessity of having known concentrations of potassium iodate it was not possible to start the reaction by the addition of an excess of solid potassium iodate as previously; instead, 0.1 cc. of an aqueous potassium iodide solution was added to a known volume of solution containing known concentrations of ketone, catalyst, potassium iodate, and sodium perchlorate.

The decrease in hydrogen ion concentration due to making up the iodine solution from iodide and iodate, equal to twice the initial iodine concentration (and most usually in the neighborhood of 0.0004) is just appreciable in the most dilute perchloric acid solutions; the calculated hydrogen ion concentration was corrected for this effect wherever necessary. The change in hydrogen ion concentration during a run, equal to half the change in iodine concentration, was negligible for all runs.

The ionic strength was maintained at 0.21 by the addition of the appropriate amount of sodium perchlorate. Buffer mixtures were made up from standard carbonate-free sodium hydroxide solution, and chloroacetic acid solution standardized against the sodium hydroxide. The composition of the buffer mixtures was calculated by the use of the value 0.0025 for the ionization constant of chloroacetic acid.[14]

The identity of the principal reaction product was checked by running a large scale bromination of acetophenone in 0.5 molar hydrochloric acid. The mechanism of the bromination should be identical with that of the iodination, and phenacyl bromide has the advantage over phenacyl iodide of being a solid at room temperature, and quite stable away from contact with the solution from which it is prepared. Bromine was added to five liters of a saturated solution of acetophenone (about 0.045 molar) in 0.5 molar hydrochloric acid, the bromine being at approximately a fifth the concentration of the acetophenone. By the time the solution was colorless (about twenty-four hours), a large portion of the product had come out of solution in well-formed crystals (about 6.5 g.). The melting point of the crystals after thorough washing was 47.5–50°. One recrystallization from petroleum ether brought the melting point to 49–50°.

Rate Calculations.—k, the first order specific rate, could in all cases be obtained from the slope of a plot of colorimeter settings against time, using the simplified form[8] which the integrated rate equation takes if only a few per cent. of the ketone present is allowed to react. The slope of the plot of the various values of k for perchloric acid solutions against concentration of perchloric acid is the specific catalytic constant for oxonium ion. The results in the buffer solutions were fitted to the equation

$$k - k_{OH_3^+} c_{OH_3^+} = k_{HC} c_{HC} + k_{C^-} c_{C^-}$$

by the method of least squares, using the value of $k_{OH_3^+}$ determined in perchloric acid solutions. HC refers to chloroacetic acid, C^- to chloroacetate ion.

(13) "International Critical Tables," Vol. VII, p. 149.

(14) Randall and Failey, *Chem. Rev.*, **4**, 291 (1927).

Results

The results of the rate measurements are presented in Table I. The calculated k's were obtained by the use of the specific catalytic constants listed. Water catalysis is too small to measure. The effect of chloroacetate ion is small: only in experiment 18 does the calculated contribution of the chloroacetate catalysis amount to more than 4% of the total rate. While further iodination of the initial product, phenacyl iodide, by means of the acid catalyzed mechanism is so slow as to be negligible with these high constant acetophenone concentrations, iodine substitution very much favors further iodination by the basic mechanism.[15] The effect of a basic catalyst consequently is determined by a competition between the reaction with acetophenone, the reaction with ω-iodoacetophenone, with maximally one-fiftieth the con-

TABLE I

RATES OF IODINATION IN PERCHLORIC ACID SOLUTIONS AND IN BUFFER MIXTURES AT 25.00°

Expt.	Stoichiometric concentrations HClO₄	NaOH	HC	$k \times 10^4$ (min.$^{-1}$) Obsd.	Calcd.
1	0.1916			1.410	1.423
2	.2076			1.597	1.550
3	.2108			1.548	1.572
9	.2004			1.491	1.490
10	.1037			0.773	0.772
11	.0502			.372	.374
12		0.1284	1.028	.465	.466
13		.1940	0.679	.245	.243
14		.1840	1.472	.625	.624
15	.0494			.367	.368
17		.0705	0.564	.296	.297
18		.1273	.1820	.0356	.0363

Least squares constants in units of $\left(\text{min.} \frac{\text{mol}}{\text{liter}}\right)^{-1}$:

k_{HC}	0.388×10^{-4}
k_{C^-}	$.06 \times 10^{-4}$
$k_{OH_3^+}$	7.45×10^{-4}

(15) Hughes, Watson and Yates, *J. Chem. Soc.*, 3318 (1931); Watson and Yates, *ibid.*, 1207 (1932); Pedersen, *J. Phys. Chem.*, **38**, 601, 999 (1934).

TABLE II

EXTINCTION COEFFICIENTS AND BASE STRENGTH OF PROPIOPHENONE

	% H_2SO_4								
λ	0	62.4	69.9	73.7	75.3	77.5	79.8	88.2	95.8
3800		(2)	(7)	13	18	32	48	100	178
3700		(4)	20	48	75	122	164	330	460
3600		9	60	150	210	330	460	790	1050
3500		19	126	330	450	670	960	1450	1700
3400		42	230	550	760	1100	1440	2020	2250
3300		86	380	780	1070	1470	1880	2390	2550
3200		178	560	1080	1480	2000	2460	3200	3520
3100	110	460	1150	2240	2930	4400	5800	8700	10300
3000	290	1060	2730	5800	7400	11000	14000	19800	21500
2900	810	1890	4370	7800	9600	13600	16100	19800	19900
2800	1140	2430	4900	7600	8700	11400	12200	11400	10500
2700	1330	4100	6100	6900	7500	7600	7400	5200	4150
2600	4070	8600	8900	7600	7100	6100	4800	1900	1270
2500	10500	10800	9200	7000	5800	4700	2800	690	400
2400	11000	8200	6000	4200	3200	2500	1500	460	410
2300	6000	3650	2360	1700	1240	1000	780	500	630
2200	2130	1350	1450	1450	1900	2350	3000	3000	3500
H_0		−4.58	−5.52	−6.01	−6.21	−6.46	−6.79	−8.00	−8.84
pK'			−6.28	−6.29	−6.32	−6.25	−6.25		
			±0.05	±0.06	±0.05	±0.03	±0.06		

Average value of pK' −6.28 ± 0.06. Isobestic point, λ 2680, ext. coeff. 7300. Reference curves, 62.4%, 88.2%.

TABLE III

EXTINCTION COEFFICIENTS AND BASE STRENGTH OF *n*-BUTYROPHENONE

	% H_2SO_4					
λ	64	73.5	75.2	76.6	78.1	89.7
3800		(15)	25	32	40	109
3700		60	88	123	149	450
3600		190	270	350	430	980
3500	(6)	420	580	700	870	1570
3400	20	700	950	1100	1300	2300
3300	85	1040	1320	1530	1770	2580
3200	185	1430	1800	2100	2410	3610
3100	450	3070	3970	4700	5500	10100
3000	1070	7200	9400	10800	13400	21100
2900	1900	9800	12200	13600	15100	18800
2800	2420	9000	9900	10700	11200	10200
2700	4100	7700	7500	7300	7000	4370
2600	8600	7500	6200	5500	4680	1590
2500	11200	6200	5000	3960	2980	800
2400	8300	3600	2870	2270	1710	780
2300	3650	1480	1220	1050	940	960
2200	1500	2210	2500		3000	
H_0		−5.99	−6.19	−6.36	−6.54	
pK'		−6.21	−6.22	−6.23	−6.20	
		±0.07	±0.06	±0.07	±0.08	

Average value of pK' −6.21 ± 0.06. Isobestic point, λ 2710, ext. coeff. 7650. Reference curves, 64%, 89.7%.

centration of the acetophenone but with a much higher specific reaction rate, and the reaction with ω,ω-diiodoacetophenone, maximum concentration unknown, but with a still very much higher specific reaction rate. Any appreciable amount of secondary iodination should produce curvature in the time curves (although possibly too small a curvature to be apparent), and a definite lack of constancy of the apparent specific catalytic rates with varying buffer concentration. Neither of these effects appeared in the results. The calculated k_C- is probably not a correct value for the specific catalytic constant for the introduction of the first iodine, but the whole effect of chloroacetate ion is so small that the calculated k_{HC} is undoubtedly quite good. The reaction is certainly subject to general acid catalysis.

The results of the absorption measurements are presented in Tables II–IV. Figures in parentheses are somewhat less reliable than the others. Methyl substitution in the side chain is much more effective in changing the base strength than it is in changing the absorption spectra of the ketone and its conjugate acid formed by the addition of a proton to the oxygen. The spectra of these ketones are practically identical with that of acetophenone within the error of measurement,[7a] (average deviation of the extinction coefficient from the mean 5%). Comparison of the spectra of the conjugate acids cannot be made so directly because data are not available for all the compounds in the same highly acid medium, and there is a medium effect on the absorption distinct from the effect of changing acidity on the ionization equilibrium[7a]; however, specific differences between the spectra of the conjugate acids of the various ketones are certainly small. Alpha

TABLE IV

EXTINCTION COEFFICIENTS AND BASE STRENGTH OF ISOBUTYROPHENONE

	% H_2SO_4											
λ	0	65	69.7	73.6	75.3	77.4	78.6	79.6	81.5	83.0	89.7	96
3800				(8)	(12)	(23)	(40)	48	73	89	145	178
3700			(6)	(28)	46	88	130	155	230	268	440	540
3600			(19)	77	115	220	298	385	540	600	930	1110
3500		(6)	46	150	223	435	580	710	990	1090	1570	1760
3400		(22)	81	247	367	610	810	1080	1400	1530	2100	2290
3300	62	59	143	400	520	820	1130	1450	1850	1970	2600	2760
3200	91	149	298	650	830	1280	1710	2200	2820	3050	4000	4500
3100	140	405	760	1600	2000	3300	4230	5250	7500	8300	11500	13350
3000	310	920	1630	3510	4110	6800	9300	10700	13500	15100	20300	21000
2900	840	1610	2660	4650	5600	8300	10000	11800	13800	14600	16900	18400
2800	1120	2140	3200	4970	5600	6800	8200	8600	9900	9200	9500	8700
2700	1400	3950	5300	6400	6500	6600	6500	6400	6100	4900	3850	3480
2600	4800	8400	9200	9600	8600	7000	6700	5900	4770	3350	1500	1120
2500	10500	10400	10000	9600	8100	6200	5800	4570	3550	2230	750	550
2400	10200	7800	7200	5800	4440	3730	3290	2830	2050	1390	600	620
2300	5200	3400	2910	2380	1910	1570	1400	1280	1100	880	760	950
2200	(1730)	(1350)	(1490)	(1650)	(1620)	(1870)	(2200)	(2800)	(2960)		(3650)	(3650)
H_0			−5.50	−6.00	−6.20	−6.45	−6.61	−6.76	−7.07	−7.32	−8.15	
pK'				−6.76	−6.79	−6.68	−6.69	−6.67	−6.65	−6.74		
				±0.07	±0.06	±0.04	±0.03	±0.06	±0.08	±0.07		

Average value of pK' −6.72 ± 0.07. Isobestic point, λ 2710, ext. coeff. 6500. Reference curves, 65%, 89.7%.

methyl substitution definitely reduces the base strength—compare acetophenone, with a pK' of −6.03,[7a] with the figures for propiophenone and isobutyrophenone. The difference between the pK's of propiophenone and *n*-butyrophenone is within the error of measurement.

Discussion

The comparison of the rates of enolization of these ketones with their base strengths is shown in Fig. 1; the rectangle about each point indicates the precision measures of the two measurements. There is obviously no simple functional relationship between the two sets of data, so that step 1 cannot be exclusively rate determining. Other possibilities which must be considered are (a) step 2 is rate determining, (b) steps 1 and 2 both affect the rate, (c) the enolization is a one step, termolecular reaction rather than two separate bimolecular reactions. Pedersen[2] objects to c, because product terms of the type $kc_{HA}c_{A^-}$ should be of much greater magnitude than terms kc_{HA} or kc_{A^-} in the rate equation. This is definitely not the case, although some of Dawson's experiments[10a] may be interpreted to indicate the presence of small product terms.

Both an acid and a base are necessary for any of these mechanisms. Mechanism c was rejected because both the acid and the base appear in the rate determining step and should therefore appear in the rate equation. But it would seem that mechanism b as well as mechanism c, should call for first order specific rates varying with the concentrations of two catalysts; the concentrations of one acid and one basic catalyst are certainly concerned in rate determining processes, and, in general, if more than one catalyst is present, catalyst pairs which are not conjugate are no less probable than catalyst pairs which are conjugate.

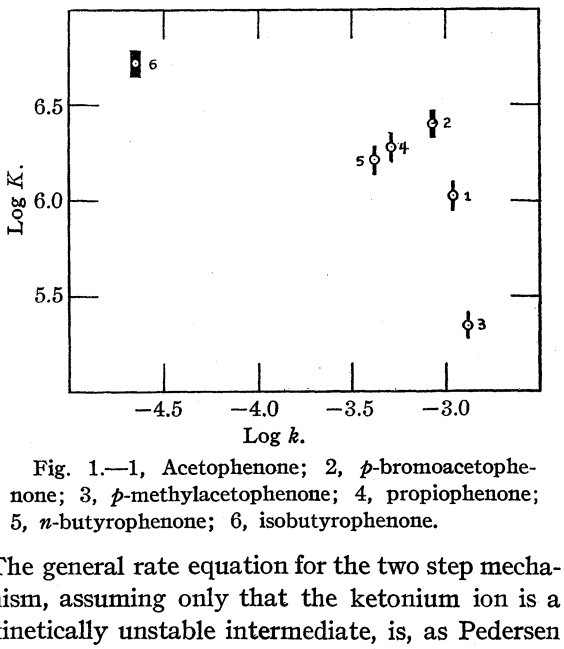


Fig. 1.—1, Acetophenone; 2, *p*-bromoacetophenone; 3, *p*-methylacetophenone; 4, propiophenone; 5, *n*-butyrophenone; 6, isobutyrophenone.

The general rate equation for the two step mechanism, assuming only that the ketonium ion is a kinetically unstable intermediate, is, as Pedersen has shown[2]

$$-\frac{1}{c_{KH}}\frac{dc_{KH}}{dt} = k = \frac{\Sigma k_{1BH^+}c_{BH^+}\Sigma k_{2B}c_B}{\Sigma k_{2B}c_B + \Sigma k_{-1B}c_B} = \frac{\Sigma k_{1BH^+}c_{BH^+}}{1 + \frac{\Sigma k_{-1B}c_B}{\Sigma k_{2B}c_B}}$$

where BH^+ represents any acid, B any base, and summation is to be taken over all acids and bases in the solution. These designations are not intended to specify the charge type of the acids and bases. Let

$$F = \frac{\Sigma k_{-1B}c_B}{\Sigma k_{2B}c_B}$$

When $F << 1$, step 1 is rate determining and $k = \Sigma k_{1BH^+}c_{BH^+}$; when $F >> 1$, step 2 is rate determining, and since

$$k_{1BH^+}c_{BH^+} = c_{H^+}k_{-1B}c_B/K_{KH} \qquad (4)$$

for every acid-base pair present, k reduces to

$$\sum \frac{k_{2B}K_{BH^+}c_{BH^+}}{K_{KH}},$$

which is in the proper experimental form. When $F \sim 1$, we have mechanism b, and it is usually assumed that k reduces to the observed form because F is independent of the relative concentrations of the various catalysts, and hence a constant. This would be true in general only if

$$\frac{k_{2B}}{k_{-1B}} = \frac{k_{2C}}{k_{-1C}} = \frac{k_{2D}}{k_{-1D}} = \cdots \qquad (I)$$

for all bases which might be present, but this is highly improbable. Application of the log–log relation between rates and equilibrium constants for protolytic reactions yields the following:

$$\log k_{-1B} = \alpha \log K_B + \beta$$
$$\log k_{2B} = \alpha' \log K_B + \beta'$$
$$k_{-1B} = bk_{2B}(K_B)^{(\alpha-\alpha')}$$
$$F = \frac{b\Sigma K_B{}^{(\alpha-\alpha')}k_{2B}c_B}{\Sigma k_{2B}c_B}$$

The requirement (I) and the constancy of F with changing relative catalyst concentrations are equivalent to the requirement that $\alpha = \alpha'$, *i. e.*, that the linear relation between the logarithms of the ionization constants of a series of bases and the logarithms of the rates of acceptance of one proton of the dibasic acid $[RC(OH)CH_3]^+$ shall have the same slope as that for the same set of bases and the other proton of the dibasic acid, the one hydrogen being bound to carbon, the other to oxygen. This is definitely not the case for the entirely equivalent example of two monobasic acids even for much smaller differences in structure. A statement equivalent to requirement (I), and one which is manifestly incorrect, is this: the log–log relations between rates and base strengths of a given series of catalysts should have the same slope for all general base catalyzed reactions.

In special cases F can still be constant; it is constant if there is only one catalyst present, or if only one base out of several present is effective in steps 2 and -1. That is, F is constant only if it is true for all the solutions studied that

$$k_{-1B}c_B >> k_{-1C}c_C + k_{-1D}c_D + \cdots$$
$$k_{2B}c_B >> k_{2C}c_C + k_{D2}c_D + \cdots$$

But equation (4), which applies whether there is equilibrium in step 1 or not, shows that the first inequality is identical with

$$k_{1BH^+}c_{BH^+} >> k_{1CH^+}c_{CH^+} + k_{1DH^+}c_{DH^+} + \cdots$$

If F is constant for these reasons, then

$$k = \frac{k_{1BH^+}c_{BH^+}}{1 + \frac{k_{-1B}}{k_{2B}}}$$

In other words, if F is constant with varying relative concentrations of two or more catalysts, it is because a single acid–base pair is causing practically all the reaction, and no other catalyst is very effective, either as acid in step 1, or as base in steps 2 and -1. Conversely, if it is possible to detect large catalytic effects of two or more catalysts present in the same solution, and to calculate specific catalytic constants for each which are truly constant as the relative concentrations are varied, then mechanism b, with neither step solely rate determining, can be rejected. In the particular case in question, the acid catalyzed enolization of acetophenone, the ratio of the contributions of chloroacetic acid and oxonium ion to the rate ranges from 1.5 to 4 in the buffer solutions, and is of course 0 in the perchloric acid solutions.

Since we have eliminated all other suggested mechanisms, it seems highly probable that mechanism a, in which step 2 is rate determining, is the correct one. The same conclusion is a necessary corollary of the mechanism proposed by Cohn and Urey[4] for the isotopic oxygen exchange between acetone and water. Thus two independent types of evidence strongly support both the proposed mechanism for the enolization and the proposed mechanism for the oxygen exchange reaction.

Summary

The basic ionization constants of propiophenone, *n*-butyrophenone and isobutyrophenone have been measured.

The iodination of acetophenone exhibits a general acid catalysis.

Direct evidence is offered to show that the proton removal is the rate determining step in the acid catalyzed enolization of ketones.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

Kinetics of the Iodination of Acetophenone in Sulfuric and Perchloric Acid Solutions

BY LOIS ZUCKER[1] AND LOUIS P. HAMMETT

The acidity function H_0[2] for sulfuric acid–water solutions (and for aqueous solutions of some other strong acids) combines in one functional representation all effects of continuing increase in acid concentration on the ionization equilibria of electrically neutral monoacid bases. These effects are presumably two—the result of increasing the acidity *per se*, and the result of changing the thermodynamic nature of the medium. There is also excellent correlation between the rates of some acid catalyzed reactions in increasingly acid solutions, and the acidity function for these solutions[2,3] and consequently between the effects of increasing acid concentration on the rates of these acid catalyzed reactions, and on the ionization equilibria of electrically neutral monoacid bases. This is simply explained in terms of the transition state theory of reaction velocity if the equilibrium between reactants and activated complex, whose position determines the rate of the reaction, is or approximates an ionization equilibrium of the correct charge type.

On the other hand, the bromination of *m*-nitroacetophenone in moderately concentrated solutions of sulfuric acid in acetic acid–water mixtures shows no such correlation of rate with acidity function.[4] This might be a property of the acetic acid medium or it might be a characteristic property of the enolization reaction. We have therefore studied the rate of iodination of acetophenone in sulfuric acid–water and perchloric acid–water solutions.

Experimental

Rate Measurements.—The colorimetric method used was that previously described.[5]

The color of iodine in sulfuric acid solutions changes in hue from brown in the most dilute solutions to rose in 95% solution, and the effective extinction coefficient for the blue-violet light used slowly decreases. The change becomes perceptible with 46% sulfuric acid solution; for 46 and 51% solutions a pinker colorimetric standard is necessary to get a good match, and is supplied conveniently by an aqueous solution of methyl orange of the same concentration as that used for more dilute acid solutions, but buffered at *p*H 3.8 with 0.05 molar acetate buffer. The effective extinction coefficient of the iodine decreases by about 2% from 39.5 to 45.9% sulfuric acid, and by another 3% from 45.9 to 51% sulfuric acid. No hue which can be obtained from methyl orange at any reasonable acidity is sufficiently like that of iodine in 66% sulfuric acid solution with light of the spectral composition used to allow precise matching. The one experiment in 66% sulfuric acid was very crudely done by measuring the times at which the reacting solution matched, to the eye, various standard iodine solutions all in bottles of closely similar shape and color.

Both potassium iodate and sodium nitrite were satisfactory oxidizing agents for the more dilute acid solutions, up to and including 25% sulfuric acid. Potassium iodate could not be used in 39.5% sulfuric acid; iodine solutions made up from potassium iodide and excess potassium iodate increase steadily in depth of color for several minutes after mixing, although the iodine production should be practically instantaneous. If a large excess of potassium iodate is present, the color then decreases slowly over a period of days to weeks. In 70% sulfuric acid an iodine solution saturated with potassium iodate takes only a few days for complete decolorization. These two phenomena (production of more intense color, and decolorization) are instantaneous in 95% sulfuric acid with suitable relative concentrations of iodine and potassium iodate and are ascribed by Masson, *et al.*,[6] to the formation of stabilized ions on the oxidative level of I^+ (dark brown) and I^{+++} (colorless), respectively. One or both of these ions seems to be kinetically active in 39.5% sulfuric acid. No difficulties were observed with sodium nitrite which was used exclusively for all the sulfuric acid solutions more concentrated than 25%. The innocuousness of this oxidizing agent could not be tested by comparing results obtained with it with those obtained with some other agent, because no other suitable oxidizing agent was found. Nor could rates in the presence of

(1) Part of a thesis submitted by Lois Zucker in partial fulfilment of the requirements for the degree of Doctor of Philosophy in the Faculty of Pure Science of Columbia University.

(2) Hammett and Deyrup, THIS JOURNAL, **54**, 272 (1932); Hammett and Paul, *ibid.*, **56**, 827 (1934).

(3) Hammett and Paul, *ibid.*, **56**, 830 (1934); Hammett, *Chem. Rev.*, **16**, 67 (1935).

(4) Paul and Hammett, THIS JOURNAL, **58**, 2182 (1936).

(5) Zucker and Hammett, *ibid.*, **61**, 2779 (1939).

(6) (a) Masson and Race, *J. Chem. Soc.*, 1718 (1937); (b) Masson and Hanby, *ibid.*, 1699 (1938); (c) Masson and Argument, *ibid.*, 1702 (1938); (d) Masson, *ibid.*, 1708 (1938).

nitrite be compared with rates without any oxidizing agent, because the rate of the reverse reaction between phenacyl iodide and iodide ion increases rapidly with acidity; iodination in 39.5% sulfuric acid will hardly proceed at all without an oxidizing agent. The concentration of sodium nitrite used was approximately that necessary to cause the initial oxidation of iodide to iodine, and to take care of all the iodide which might be formed during the reaction, assuming nitrite and iodide equivalent on a molar basis. Since 1 mole of nitrite will oxidize somewhat more than 1 mole of iodide, this procedure left some factor of safety.[7] In 39.5% sulfuric acid, good agreement was obtained among the specific rates determined under these conditions over a 13-fold variation in acetophenone concentration, and a 700-fold variation in iodine concentration. The first effect of increasing the nitrite concentration was to cause some reversal of the reaction, probably due to replacement of iodide by nitrite in the phenacyl iodide. This reversal was only detected in the presence of two to three times the concentration of nitrite ordinarily used, and then only when over 30% of the ketone had reacted; the effect was most definitely observed in 51% sulfuric acid, where the reaction came to an almost complete stop after 35% of the ketone had reacted, and the iodine concentration was brought back almost to its initial value by the addition of about twenty times the usual concentration of sodium nitrite. Since the nitrite reaction causing reversal appears to increase with increasing acidity, the experiment in 66% sulfuric acid solution may be considerably in error on this account.

Because of the speed of the reaction in the stronger acid solutions, rather low initial ketone concentrations were necessary, with a large fraction of the ketone reacting. One experiment in 19% sulfuric acid showed that the introduction of a second iodine into the molecule does not become apparent until 55% of the acetophenone has reacted. (The ratio of the rate of introduction of the second iodine to that of the first is 0.033 in 19% sulfuric acid.) It was assumed that the ratio of the rates of introduction of the first and second iodines does not decrease with increasing acidity, and that it was perfectly safe to allow up to 40% of the acetophenone to react.

The procedure described previously[5] was used for all runs except those in 30% and more concentrated sulfuric acid. In these solvents oxidation of iodide to iodine by dissolved oxygen or by sulfuric acid itself,[8] is so fast that appreciable oxidation may take place in the fifteen minutes allowed for the solution to come to thermostat temperature, causing the iodination reaction to start prematurely. For these more concentrated solutions, the following procedure was used. A known solution of iodine in sulfuric acid was prepared in a tube of about 35-cc. capacity, with a well-fitting ground-glass stopper, by adding 25 cc. of sulfuric acid solvent from a pipet (recalibrated for each solvent) to a weighed out quantity of a known aqueous potassium iodide solution. Solid sodium nitrite (amounting to from 0.5 to 5 mg. weighed out on an analytical balance) was added, the solution stirred thoroughly, but smoothly without bubble formation, and the tube stoppered with the stirring rod inside. The ground-glass joint was kept dry. About 9 cc. of a known solution of acetophenone in the same sulfuric acid solvent was weighed in a small weighing bottle. The two solutions were brought to temperature in the large thermostat. The reaction was started by rapidly pouring the contents of the small weighing bottle into the tube, shaking thoroughly, and pouring about 9 cc. of the resulting solution into the dry reaction cell, which previously had been mounted on the colorimeter with water at 25.00 ± 0.01° circulating through the water jacket. The small weighing bottle wet with the acetophenone solution was put in a large stoppered weighing bottle and weighed at leisure. The addition of the ketone solution to the iodine solution took not more than one-tenth minute. The solutions were out of a thermostat for a total of about one minute. The first reading could be taken about two minutes after mixing.

The solubility of the reaction product, phenacyl iodide, is fortunately greater (up to 3 times) under the experimental conditions in the highly acid solutions than it is in more dilute solutions.

Although iodide ion is unstable in 95% sulfuric acid, and the equilibrium concentration of iodide which can exist in such a solution is certainly very small, the iodination reaction is highly reversible in 95% sulfuric acid. In a solution saturated with iodine (*ca.* 0.0001 molar)[6d] and 0.01 molar in acetophenone, iodination did not proceed noticeably, as measured by diminution of color perceptible to the eye, over a period of a month at room temperature. That no other reaction had intervened to prevent the iodination was shown from the following: iodine could be extracted from the solution with petroleum ether and tested for by contact with an aqueous starch–iodide solution. The acetophenone was liberated from its salt by dilution with water; the resulting solution was colorless, smelled of acetophenone, and took up freshly added iodine at approximately the correct rate (within 20%) for the acidity of the solution. A partly reacted system reverts to acetophenone in 95% sulfuric acid; phenacyl iodide, prepared in 40% sulfuric acid, was transferred first to petroleum ether solution, together with all the unreacted acetophenone but without the hydrogen iodide, and then from the petroleum ether to 95% sulfuric acid; after thirty-six hours the 95% sulfuric acid solution had approximately the full color of the iodine originally added to the 40% solution. The petroleum ether had been purified by repeated washing with 95% sulfuric acid over a period of a month, until no further color formation took place overnight with a fresh portion of sulfuric acid, followed by several distillations alternately from 95% sulfuric acid and solid sodium hydroxide. The stabilizing effect of 95% sulfuric acid on iodine at the oxidative level of I^{+}[6d] must mean that there is an I^{+} acceptor in this solvent, which may also be able to accept I^{+} from phenacyl iodide, or its conjugate acid, causing reversal of the iodination reaction.

The iodination is not catalyzed by the light source of the colorimeter in 40% sulfuric acid, since good agreement was found for duplicate runs, one with the light on throughout the run, the other with the light off except for one minute at the end of the run (after thirty minutes) when five readings were made.

(7) Gmelins "Handbuch der anorganischen Chemie," 1933, Vol. VIII, p. 336.

(8) Smith and Mayer, THIS JOURNAL, **46**, 75 (1924).

Materials.—The purification and physical constants of the materials used were described in a previous paper.[5]

Results

Kinetic Formulation.—In dilute aqueous solutions the rate of halogenation of ketones has with one exception been found independent of the concentration of the halogen and first order in ketone, which is interpreted to mean that the rate is determined by a relatively slow enolization, the enol reacting with halogen as fast as it is formed. The exception[9] is chlorination in highly alkaline solution, in which the rate is first order in chlorinating agent (hypochlorite ion) as well as in ketone. The usual state of affairs is just reversed, and there is a rapid formation of enol or enolate ion, followed by a slow rate-determining reaction between enol or enolate ion and hypochlorite ion. A simple first order formulation fits our results in perchloric acid solutions up to and including 20%, and in sulfuric acid solutions up to and including 15%. In 51% sulfuric acid the reaction is second order. There are two possible explanations for the change in order. One is that the rate of enolization increases so rapidly that it first becomes comparable with, and finally very much greater than, the rate of iodination of the enol, so that the second step becomes rate determining. This is like the situation found by Bartlett, except that the same halogenating agent is involved in the second order as in the first order reaction. Or, perhaps the rose colored modification of iodine which begins to appear in the more concentrated acid solutions can directly iodinate the ketone without the necessity of a preliminary enolization. If this is the explanation, the order of the reaction in 51% sulfuric acid means that the direct iodination has completely supplanted iodination through the enol. For the mechanism

$$\mathrm{KH} \underset{k_{-\mathrm{E}}}{\overset{k_{\mathrm{E}}}{\rightleftarrows}} \mathrm{EH}$$

$$\mathrm{EH} + \mathrm{I_2} \xrightarrow{k_{\mathrm{I}}} \text{products}$$

making no assumptions as to the relative rates of the two steps, we have the following three equations connecting the unknowns c_{KH}, c_{EH} and $c_{\mathrm{prod.}}$, where c is concentration

$$c^0_{\mathrm{KH}} = c_{\mathrm{KH}} + c_{\mathrm{EH}} + c_{\mathrm{prod.}}$$
$$2\Delta c_{\mathrm{I_2}} = c_{\mathrm{prod.}}$$
$$k_{\mathrm{E}} c_{\mathrm{KH}} = k_{-\mathrm{E}} c_{\mathrm{EH}} + k_{\mathrm{I}} c_{\mathrm{I_2}} c_{\mathrm{EH}}$$

c^0_{KH} is the initial concentration of ketone. The factor 2 enters the second equation because of the presence of the sodium nitrite. The last equation represents the assumption that EH is a kinetically "unstable" intermediate.[10] Substitution in the rate equation

$$-2\frac{dc_{\mathrm{I_2}}}{dt} = k_{\mathrm{I}} c_{\mathrm{EH}} c_{\mathrm{I_2}}$$

leads to

$$-2\frac{dc_{\mathrm{I_2}}}{dt} = \frac{k_{\mathrm{E}}(c^0_{\mathrm{KH}} - 2\Delta c_{\mathrm{I_2}})c_{\mathrm{I_2}}}{k_{-\mathrm{E}}/k_{\mathrm{I}} + c_{\mathrm{I_2}}} \qquad (1)$$

Integrating, and substituting the equation

$$2m\Delta h \equiv 2\Delta c_{\mathrm{I_2}} = \Delta c_{\mathrm{KH}}$$

where h is the colorimeter setting, we get

$$(1 - B/A)\log\frac{c^0_{\mathrm{KH}}/2m}{c^0_{\mathrm{KH}}/2m - \Delta h} + B/A \log\frac{h^0}{h} = k_{\mathrm{E}}t/2.303 \qquad (2)$$

$$B = k_{-\mathrm{E}}/mk_{\mathrm{I}} \qquad A = c^0_{\mathrm{KH}}/2m - h^0$$

For the second possibility, which includes the additional reaction

$$\mathrm{KH} + \mathrm{I_2} \xrightarrow{k_{\mathrm{D}}} \text{prod.}$$

and the additional assumption that $k_{\mathrm{I}}c_{\mathrm{I_2}} \gg k_{-\mathrm{E}}$ (*i. e.*, the rate of enolization is rate determining for that part of the iodination which still goes through the enol), the differential equation is

$$-2\frac{dc_{\mathrm{I_2}}}{dt} = k_{\mathrm{D}}(c^0_{\mathrm{KH}} - 2\Delta c_{\mathrm{I_2}})(k_{\mathrm{E}}/k_{\mathrm{D}} + c_{\mathrm{I_2}}) \qquad (3)$$

The important difference between the two differential equations lies in this, that according to equation (1) the apparent order of the reaction with respect to iodine increases during the reaction, while according to equation (3) the apparent order decreases during the reaction; any reaction involving a sufficiently large change in iodine concentration cannot possibly be fitted by both these equations. The integrated form of equation (3) is very unsuccessful when applied to experiments in 39.5% sulfuric acid, in which the iodine concentration was varied more than 100-fold during the reaction; a value of $k_{\mathrm{D}}/k_{\mathrm{E}}$ suitable for the high initial iodine concentrations is much too large for the low iodine concentrations near the end of the reaction.

The lowest curve in Fig. 1 is a plot of the left side of equation (2) against time, for six experiments in 39.5% sulfuric acid. The value of B used to calculate the ordinate is 11; this was selected by trial and error, using the two criteria of freedom from curvature of the plot for a single experiment, and quality of agreement of the slopes

(9) Bartlett, THIS JOURNAL, **56**, 967 (1934); Bartlett and Vincent, *ibid.*, **57**, 1596 (1935).

(10) Skrabal, *Monatsh.*, **64**, 289 (1934).

of the plots of different experiments. Initial acetophenone concentration in these six runs ranged from 814 to 50.6 × 10^{-5} molar, initial iodine concentration from 49.4 to 7.24 × 10^{-5} molar, and the total range of iodine concentration covered was from 49.4 to 0.07 × 10^{-5} molar. The agreement of the data with equation (2) shows that the first explanation for the dependence of the rate on iodine concentration is the correct one.

Rate Calculations.—All the results in 30 to 51% sulfuric acid were fitted to equation (2), one

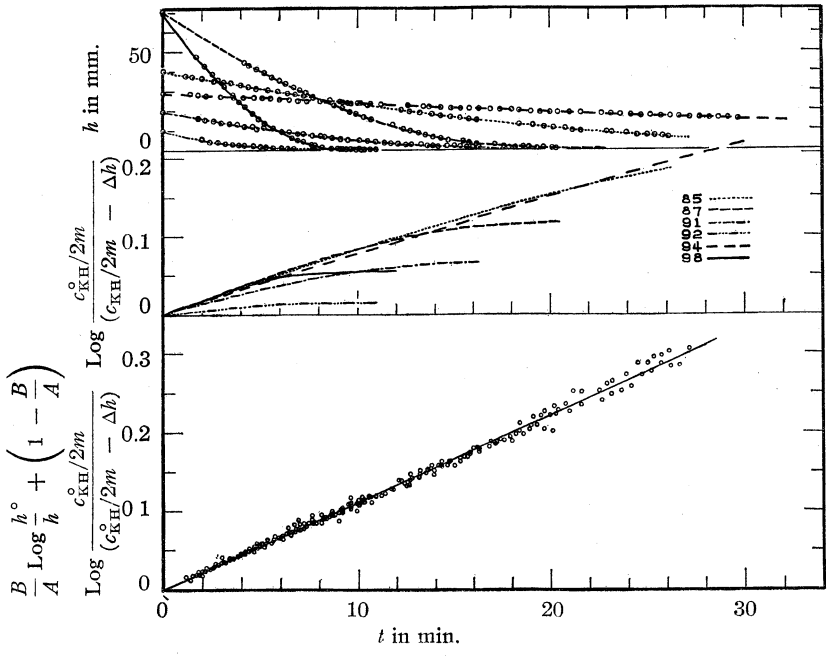


Fig. 1.

of the two unknowns in the equation being determined by trial and error in the manner described, the other calculated from the slope of the resulting plot. For each experiment the two quantities k_E and $K_E k_I$ were calculated, making use of the equation

$$K_E k_I = \frac{k_E}{k_{-E}} \frac{k_{-E}}{mB} = \frac{k_E}{mB}$$

In the more dilute acid solutions in which the rate is dependent on iodine concentration, it was possible to work with such high initial ketone concentrations that $c^0_{KH}/mf \gg \Delta h$ (f has the value 2 for nitrite oxidation, 2.5 for iodate oxidation) and equation (2) could be simplified to

$$h - \frac{Bc^0_{KH}/2m}{A - B} \ln \frac{h^0}{h} = \frac{Ac^0_{KH}/2m}{A - B} k_E t + h^0 \quad (4)$$

This equation requires much less computation than equation (2). The two equations corresponding to equations (2) and (4) for runs showing no dependence of rate on iodine concentration already have been derived,[5] or can be derived from equations (2) and (4), for $k_I \gg k_{-E}$. They are listed below for purposes of reference.

$$\log[c^0_{KH}/mf - \Delta h] = -\frac{k_E}{2.303} t + \log c^0_{KH}/mf \quad (5)$$

$$h = -\frac{c^0_{KH}}{mf} k_E t + h^0 \quad (6)$$

where

$$c^0_{KH}/mf \gg \Delta h$$

The average specific rates k_E and $K_E k_I$ for the various acid concentrations are presented in Table I. Acid concentrations of multiplicates were usually not quite identical; for averaging, the rates were all calculated to the same acid concentration, assuming the rate linear in the acid concentration. The number of experiments run with sodium nitrite is tabulated under the heading N and the number with potassium or sodium iodate under I. The precision of rates calculated by equations (5) and (6) already has been discussed[5]; where there are several multiplicates, the average deviation from the mean is well within the assigned precision measure in all cases. The tabulated $P.\ M.$ in per cent. was calculated by dividing the estimated average deviation from the mean by the square root of the number of experiments. Where k_E has little influence in determining the rate of the over-all reaction (46, 51% sulfuric acid), a considerable range of values of k_E will allow linear plots with very little variation in the value of $K_E k_I$, and the reverse is true when the reaction is nearly zero order in iodine. This range has been indicated in Table I. The difference between the best value and one end of this range is a maximum deviation rather than an average deviation, and is not strictly comparable with the precision measures tabulated for other runs. The experimental error certainly increases with increasing acidity. The increasing speed of the reaction reduces the number of readings which

TABLE I

RATES IN PERCHLORIC ACID SOLUTIONS AT 25.00°

% $HClO_4$	No. of expts. I	N	k_E (min.$^{-1}$)	P. M. for k_E %	$K_E k_I$ (min. mol./liter)$^{-1}$
2.091	5		0.0001565[a]	0.5	
3.523	1		.000270	1.0	
7.16	2		.000571	0.7	
10.50	1	3	.000874	.5	
13.00	4		.001104[a]	.5	
20.40	1	1	.001983	.7	>1350
24.90	1	2	.00276	1.0	<5000
30.20	1	3	.00394	2.0	<3000

[a] Taken from ref. 5.

RATES IN SULFURIC ACID SOLUTIONS AT 25.00°

% H_2SO_4	No. of expts. I	N	k_E (min.$^{-1}$)	P. M. for k_E %	$K_E k_I$ (min. mol./liter)$^{-1}$
0.520	1		0.0000650	1.0	
1.069	1		.0001344	1.0	
1.586	1		.0001870	1.0	
2.100	1		.000278	1.0	
4.122	1		.000539	1.0	
5.185	1		.000755	1.0	
7.49	1		.001132	1.0	
9.90	7		.001750	0.5	>1220
13.71	1		.00280	1.0	
15.22	2		.00331	2.0	
19.00	5	3	.00521	0.4	<5000
24.40	2	1	.00856	1.0	<1950
30.78		2	.01438	2.5	570 ± 130
35.40		3	.0213 ± 0.001		420 ± 100
39.50		10	.0258 ± .004		325 ± 60
45.9		2	.051 ± .015		120 ± 10
51.0		4	>.05		62 ± 2
66		1			(4)

can be made, and increases the importance of the error in measuring time. The method of mixing which must be used for the reactions in 30 to 51% sulfuric acid introduces further error because the time of mixing is of appreciable duration compared to the total reaction time (one- to two-tenths minute compared with six minutes or more), and during this time ketone concentration is higher than the calculated initial ketone concentration. Since equations (2) and (4) contain the absolute value of h, rather than only terms in Δh, the ever-present possibility of spoiling the optical balance of the colorimeter in mounting the cell at the beginning of the reaction supplies another source of error. Large errors caused by this trouble were avoided by rejecting all runs in which the calculated h^0 did not lie on a smooth extrapolation of the observed h's. It is necessary to include very low colorimeter settings to get sufficiently large changes in iodine concentration. The absolute error for settings below 5 mm. increases steadily above the 0.17 mm. found for settings from 45–5 mm., and of course the percentage error in h becomes very large.

Effect of Increasing Acidity on $K_E k_I$.—Values of $K_E k_I$ in sulfuric and perchloric acid solutions of the same concentration are equal, within the rather large error of measurement, and decrease steadily with increasing acidity. The mechanism of enol iodination is probably[11]

$$EH + I_2 \underset{}{\overset{k_I}{\rightleftharpoons}} EHI^+ + I^-$$
$$EHI^+ + B \rightleftharpoons KI + BH^+$$

Our experimental conditions were such that the reversal of the first step was suppressed, and k_I is simply the forward rate of the reaction between enol and iodine. The decrease in this rate can only be attributed to a medium effect of whose nature we are ignorant. The change in the color of the iodine–solvent complex with increasing acid concentration may be connected with a decrease in efficiency as a donor of I^+.

Effect of Increasing Acidity on k_E.—The probable mechanism of the enolization is[12]

$$KH + H^+ \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} IH_2^+ \text{ equilibrium}$$
$$IH_2^+ + B^z \xrightarrow{k_2} EH + BH^{(z+1)} \text{ rate determining step}$$

z represents the charge on the base B. By the Brönsted rate equation

$$\frac{dc_{EH}}{dt} = \sum_{B^z} k_{2B^z} c_{IH_2^+} c_{B^z} \frac{f_{IH_2^+} f_{B^z}}{f_{[X^+]^*}}$$

where f is activity coefficient, $[X^+]^*$ is the activated complex $[IH^+_2 \cdot B^z]^*$, and summation is to be taken over all bases in the solution. Then

$$k_E = \frac{1}{c_{KH}} \frac{dc_{EH}}{dt} = \sum_{B^z} k_{2B^z} \frac{c_{IH_2^+}}{c_{KH}} c_{B^z} \frac{f_{IH_2^+} f_{B^z}}{f_{[X^+]^*}} \quad (7)$$

$c_{IH_2^+}/c_{KH}$ increases with increasing acidity according to the equations

$$\frac{c_{IH_2^+}}{c_{KH}} = \frac{a_{H^+} f_{KH}}{K_{KH} f_{IH_2^+}} = \frac{K_{BH^{(z+1)}} a_{BH^{(z+1)}} f_{KH}}{K_{KH} a_{B^z} f_{IH_2^+}} = \frac{h_0}{K_{KH}}$$

where h_0 is the negative antilogarithm of the acidity function H_0[2]. Substituting the last pair of equalities in equation (7), we arrive at the following pair of equations

$$k_E = \frac{1}{K_{KH}} \left[k_{2H_2O} c_{OH_3^+} \frac{f_{KH} f_{OH_3^+}}{f_{[X^+]^*}} + K_{HSO_4^-} k_{2SO_4^-} c_{HSO_4^-} \frac{f_{KH} f_{HSO_4^-}}{f_{(X^-)^*}} + \ldots \right] \quad (8)$$

$$k_E = \frac{1}{K_{KH}} \left[k_{2H_2O} h_0 a_{H_2O} \frac{f_{IH_2^+}}{f_{[X^+]^*}} + k_{2SO_4^-} h_0 a_{SO_4^-} \frac{f_{IH_2^+}}{f_{[X^-]^*}} + \ldots \right] \quad (9)$$

(11) Bartlett and Tarbell, THIS JOURNAL, **58**, 466 (1936).

(12) Zucker and Hammett, *ibid.*, **61**, 2785 (1939); Cohn and Urey, *ibid.*, **60**, 679 (1938).

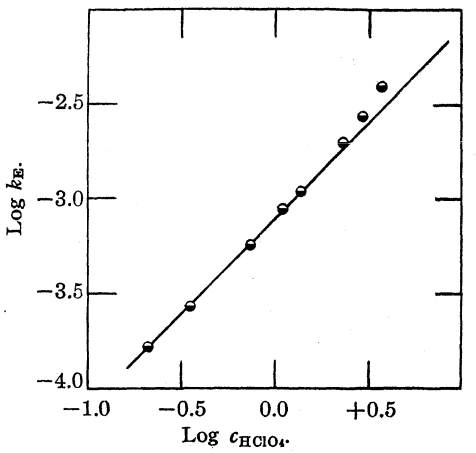


Fig. 2.

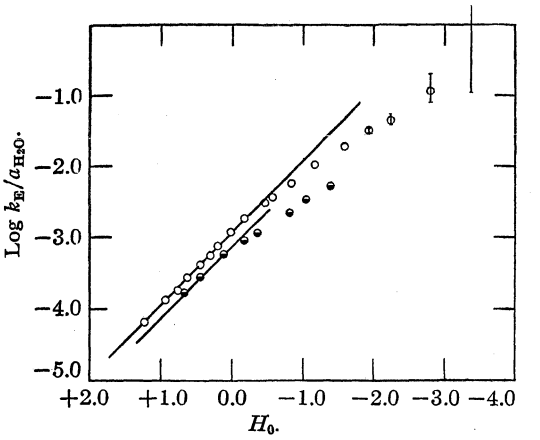


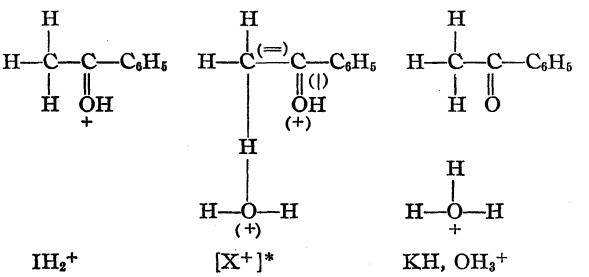
Fig. 3.—●, Expts. in $HClO_4$; ○, expts. in H_2SO_4.

The first term in each equation represents acid catalysis by oxonium ion; the second term represents acid catalysis by bisulfate ion, and vanishes in the case of perchloric acid solutions; other terms which may enter the summation for both acids are those corresponding to catalysis by molecular acid, or by the acid conjugate to molecular acid. Bisulfate ion catalysis is very important in the sulfuric acid solutions, which therefore offer a more complicated case; this is shown by the fact that the specific rate in any sulfuric acid solution is always considerably larger than that in the perchloric acid solution of the same weight per cent., even though the two solutions are nearly identical in H_0 as well as in molarity, molality or mole fraction of any other catalyst present.

In dilute aqueous solutions the concentration of each catalyst can be determined independently; consequently the quantities of the form

$$k_{2B^z}\frac{f_{KH}f_{BH^{(z+1)}}}{f_{[X^{(z+1)}]^*}}$$

in equation (8) can be determined, and have been found to show a very small dependence upon the ionic strength of the medium. This is because the long range or coulombic forces which determine the activity coefficients under these conditions depend almost entirely upon the ionic charge; $f_{BH^{(z+1)}}$ therefore cancels $f_{[X^{(z+1)}]^*}$ since their charges are identical, and f_{KH} is nearly independent of medium. A similar argument would lead one to expect a cancellation of the $f_{IH_2^+}/f_{[X^+]^*}$ factor in the first term of equation (9). In more concentrated solutions in which the highly specific short range forces are important, one cannot predict any cancellation with certainty. Yet the data for the enolization in perchloric acid show a satisfactory proportionality to $c_{OH_3^+}$, and none to $h_0a_{H_2O}$. This is shown in Figs. 2 and 3 in which log k_E is plotted against log $c_{OH_3^+}$ and log k_E/a_{H_2O}[13] is plotted against log h_0, respectively. Proportionality requires a linear plot of unit slope. In terms of equations (8) and (9) this means that $f_{KH}f_{OH_3^+}/f_{[X^+]^*}$ is constant in this range of media while $f_{IH_2^+}/f_{[X^+]^*}$ is not. There must therefore be a fairly exact and complete cancellation of this type of medium effect in the one ratio which cannot take place in the other. If actual structures are compared, it is obvious that any



effect of the medium change specifically on the H–O–H part of $[X^+]^*$ which causes a change in the activity coefficient of $[X^+]^*$, cannot possibly be counterbalanced by any corresponding change in the activity coefficient of IH_2^+, whereas there might be a similar change in the activity coefficient of the oxonium ion. If one can generalize from this case, it must be possible to factor the activity coefficient, at least roughly, into one factor due to charge and another for each of the several parts of the molecule.

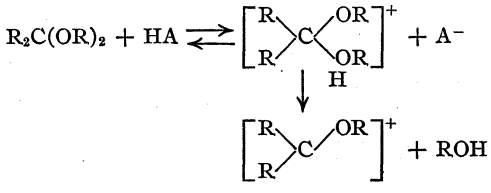
The relative degree of dependence on changing acid concentration of the two types of activity coefficient ratio involved in the comparison of

(13) Values of a_{H_2O} obtained from Pearce and Nelson, THIS JOURNAL, **55**, 3075 (1933).

rates with the two acidity measures may throw some light on the detailed nature of the rate-determining step of any acid-catalyzed reaction. There are three possibilities: (a) the rate determining step is a proton transfer as it is in the enolization; (b) it involves a water molecule in some other way than as a base, as in the following possible mechanism for the acid catalyzed hydration of an olefin

$$R_2C{=}CR_2 + HA \rightleftharpoons [R_2CH{-}CR_2]^+ + A^-$$
$$[R_2CH{-}CR_2]^+ + H_2O \longrightarrow [R_2CH{-}CR_2OH_2]^+, \text{ etc.}$$

(c) it involves a spontaneous cleavage or other change of the conjugate acid of the substrate, as is possible in the acetal hydrolysis



In case (a) equations similar in form to (8) and (9) can always be derived; if the first rather than the second proton transfer is rate determining, k_1 is substituted for k_2/K_S, and $[X^+]^*$ is $[S{\cdot}OH_3^+]^*$ instead of $[SH^+{\cdot}OH_2]^*$, where S is substrate. All such reactions are subject to general acid catalysis. In case (b) the proper equations are the first terms only of the series in (8) and (9). The only possible catalyst is oxonium ion, no matter what the solvent. In case (c) we have the following pair of equations

$$-\frac{1}{c_S}\frac{dc_S}{dt} = k_a = \frac{k}{K_S}\frac{c_{OH_3^+}}{a_{H_2O}}\frac{f_S f_{OH_3^+}}{f_{[SH^+]^*}} = \frac{k}{K_S}h_0\frac{f_{SH^+}}{f_{[SH^+]^*}}$$

This type can show catalysis by the solvated proton only; in water the catalyst is oxonium ion, in 100% sulfuric acid it is $H_3SO_4^+$, etc. The last two types are usually not differentiated and are called together specific hydrogen ion catalysis; however, only the last is a true specific hydrogen ion catalysis in all solvents and the other might be called specific oxonium ion catalysis.

If general acid catalysis can be demonstrated for a reaction, it must have a mechanism of the first type. A reaction for which only oxonium ion catalysis can be demonstrated in aqueous solutions may belong in any one of the three classes. But if the reaction is in either of the first two classes, the activated complex contains a molecule of water, $f_S f_{OH_3^+}/f_{[SHOH_2^+]^*}$ should be more independent of changing acidity than $f_{SH^+}/f_{[SHOH_2^+]^*}$, and $c_{OH_3^+}$ should be a better measure of acidity than h_0. And if the reaction is in the third class, $f_{SH^+}/f_{[SH^+]^*}$ should be more independent of changing medium than $f_S f_{OH_3^+}/f_{[SH^+]^*}$, and h_0 should be a better measure of acidity than $c_{OH_3^+}$. In order to apply this criterion it is necessary to know the rates in solutions in which h_0 can be measured,[2] and in which $c_{OH_3^+}$ is known—*i. e.*, aqueous perchloric, hydrochloric or nitric acids. It is also necessary to carry the rate measurements into a region where h_0 and $c_{OH_3^+}$ are different. h_0 equals $c_{OH_3^+}$ for all these acids within the error of measurement of h_0 up to about 1 molar acid; it is only in more concentrated acid that h_0 becomes greater than $c_{OH_3^+}$, and not before about 1.5 molar acid that a very marked and rapidly increasing divergence sets in. By this criterion the hydrolyses of sucrose and of cyanamide belong to the third class, while that of ethyl acetate has not been studied in sufficiently acid solutions to make an unambiguous determination possible.[3]

Nachod[14] observed a decrease in the apparent equilibrium constant for the enolization of acetyl acetone with increasing concentration of hydrochloric acid in methanol solution. He suggested by way of explanation the formation of a coördination compound between ketone and acid, $R_2C{=}O{-}H{-}A$. If such a reaction took place with acetophenone in the solutions in which the iodination was studied, both k_E and $K_E k_I$ as defined could be expected to have a different dependence on the acidity of the solution than that previously derived, assuming no coördination. However, there are several reasons why this is unlikely. Hydrogen bonding of the sort suggested should cause any equilibrium constant involving the ketone, calculated for the total apparent ketone concentration, to vary with changing acidity; the effect should appear in the basic ionization constant as well as in the enolization constant, yet the ionization constant of acetophenone is independent of acidity over the entire region of ionization (55–86% sulfuric acid).[15] Coördination should cause the solubility of a ketone to increase with increasing acidity; actually the solubility of acetophenone decreases with increasing concentration of sulfuric acid and of perchloric acid, at least up to 1 molar solutions. And, finally, the phenomenon observed by Nachod cannot be of

(14) Nachod, *Z. physik. Chem.*, **A182**, 193 (1938).
(15) Flexser, Hammett and Dingwall, *ibid.*, **57**, 2103 (1935).

very widespread occurrence among ketones, because the enolization constant of acetoacetic ester (which is much more closely related structurally to the ketones studied by Nachod than is acetophenone), has been calculated from kinetic data for hydrochloric acid solutions from 0 to 0.370 molar,[16] and the values show no trend with increasing acidity.

Summary

The iodination of acetophenone has been studied in 2 to 30% aqueous perchloric acid solutions, and in 0.5 to 66% aqueous sulfuric acid solutions. The rate is determined by the rate of enolization of acetophenone in the more dilute acid solutions, and by the rate of reaction of the enol with iodine in 51% and more concentrated sulfuric acid solutions; at intermediate acidities these two rates are of comparable magnitudes.

Even in the simplest case, in aqueous perchloric acid solutions, the enolization rate is not proportional to h_0, but is proportional over a considerable range to $c_{OH_3^+}$. Reactions whose rates are directly proportional to h_0, when this is varied widely, are probably examples of specific hydrogen ion catalysis, and not of general acid catalysis.

(16) Pedersen, *J. Phys. Chem.*, **57**, 751 (1934).

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[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

Molecular Rotation and Polymorphism in the *t*-Butyl Halides

BY WILLIAM O. BAKER AND CHARLES P. SMYTH

A variety of roughly spherical molecules from methane to camphor is found to possess rotational freedom in the solid state, as well as polymorphic transitions at temperatures below which such freedom is generally lost.[1,2] The lower isomeric alkyl halides provide opportunity for studying the effect of structure on crystal form and molecular freedom in simple polar lattices by dielectric and optical measurements.[3,4] The tertiary butyl halides are the most symmetrical members of this series, and, despite their considerable dipole moments resulting from the dissimilar groups, they behave as spherical molecules in such a kinetic process as viscous flow.[3] Also, electron diffraction results on *t*-butyl chloride[5] indicate no appreciable distortion of the usual tetrahedral arrangement. The data of the present report on these compounds also may be compared with similar studies on the hydrogen halides.[6–9]

Preparation and Purification of Materials.—The final purification of the chloride and bromide was fractionation in an 80 × 2 cm. Pyrex glass column, packed with beads, wrapped, and jacketed. It had a still head equipped for reflux ratio control. Temperatures were measured by short-range Anschütz type thermometers previously calibrated by the Bureau of Standards. The *t*-butyl iodide sample finally was distilled through a shorter Vigreux-type column under reduced pressure. Refractive indices were obtained from a Pulfrich refractometer. Immediately upon distillation the samples were frozen and kept in the dark until the dielectric measurements were begun.

***t*-Butyl Chloride.**—The compound was prepared by the method of "Organic Syntheses,"[10] from *t*-butyl alcohol and hydrochloric acid. The usual precautions of neutralization and washing were followed by prolonged drying over calcium chloride. The product was twice fractionally distilled; b. p. 50.60°; f. p. −24.6°; $n^{20.0}D$ 1.38470. Material recrystallized from its own melt gave the same constants. Recent literature values give b. p. 51.0°,[11] and the refractive index noted above lies between the reported values 1.38528[12] and 1.3839.[13]

***t*-Butyl Bromide.**—As with the chloride, this compound was distilled from a mixture having the proportions of one mole of *t*-butyl alcohol and two moles of constant-boiling hydrobromic acid. After washing, it was dried for several days over anhydrous calcium bromide, and was thrice fractionated. Successive middle fractions had the same refractive index: b. p. 73.2°, f. p. −17.7°, $n^{20.0}D$ 1.42757. A separately prepared lot gave the same refractive index, and boiled at 73.3°. The best literature values include: b. p. 73.25°,[11] $n^{20}D$ 1.4275–1.4277.[14]

***t*-Butyl Iodide.**—The Eastman Kodak Co. product was distilled repeatedly under reduced pressure after thorough drying. Even though the best fractions came over colorless and were at once frozen, a light straw color always

(1) Smyth, *Chem. Rev.*, **19**, 329 (1936).
(2) Eucken, *Z. Elektrochem.*, **45**, 126 (1939).
(3) Baker and Smyth, THIS JOURNAL, **61**, 1695 (1939).
(4) Baker and Smyth, *ibid.*, **61**, 2063 (1939).
(5) Beach and Stevenson, *ibid.*, **60**, 475 (1938).
(6) Smyth and Hitchcock, *ibid.*, **55**, 1830 (1933).
(7) Hettner and Pohlman, *Z. Physik*, **108**, 45 (1937).
(8) Damkohler, *Ann. Physik*, **31**, 76 (1938).
(9) Kruis and Kaischew, *Z. physik. Chem.*, **B41**, 427 (1939).
(10) Gilman, "Organic Syntheses," John Wiley and Sons, Inc., New York, N. Y., 1928, Vol. VIII, p. 50.
(11) Timmermans and Delcourt, *J. chim. phys.*, **31**, 85 (1934).
(12) Smyth and Dornte, THIS JOURNAL, **53**, 545 (1931).
(13) Kistiakowsky and Stauffer, *ibid.*, **59**, 165 (1937).
(14) Kharasch and Potts, *ibid.*, **58**, 57 (1936).

developed in them, as was noted by Parts[15] also. However, if the samples were shaken with 1 cc. of pure mercury per 15 cc. of iodide, the sample became perfectly clear and could be distilled and preserved so. Indeed, liquid thus treated could be exposed to daylight for two days without noticeable discoloration, which suggests that minute traces of the decomposition products markedly accelerate the reaction. No reliable constants for this compound seem to be available in the literature. The melting point here found is −38.2°.

Experimental Method and Apparatus

The dielectric measurements were made with a shielded capacitance bridge coupled to a General Radio Company low frequency variable oscillator and vacuum tube amplifier, and operated in the general fashion previously described.[6,16] The dielectric constant determinations for *t*-butyl bromide near and through the melting point were made at 520 kilocycles frequency with a heterodyne beat apparatus. Residual inductances introduced by the cell, which would cause its apparent capacity as measured by the bridge to vary with frequency, were found to be negligible by a calculation following a recently suggested scheme.[17]

All temperature measurements were made with a platinum resistance thermometer. Temperature control was by a metal block–Dewar tube assembly[16,18] of high heat capacity into which liquid air could be injected and evaporated at desired rates. Precautions were taken to ensure temperature equilibrium during runs, and to free the samples from gas bubbles by evacuation and slow, repeated freezing.

The compounds were examined from the liquid to low temperature crystalline states with a polarizing microscope, the arrangement in Fig. 1 being employed. Such optical examinations previously have been found useful in conjunction with other dielectric investigations,[19] and have been employed also by Kruis and Clusius to supplement X-ray data on hydrides.[20,21] In Fig. 1, T is an unsilvered Pyrex Dewar tube 11 cm. long by 3 cm. in diameter. It is held by clips on the microscope stage between the polarizer P and object lenses M. A low power lens gives adequate magnification, but for shorter focal distances an indentation in the side of T would permit closer approach of M to the drop of sample which rests on a glass slide S. The slide S is supported by a slotted cork section C at one end and by the stopper B at the other. It also rests on a glass tube A, through which liquid air may be injected in desired amounts to cool the sample through the freezing and transition points. I is a tube through which the sample is introduced, while V is a vent. Through V also may be passed the wires of a thermal element that may be sealed on the under side of S below the sample, and used to measure the temperatures of solidification, fusion and transition, although accurate determinations are unlikely in the simple system shown. Observations with rising temperature are made by allowing the system to warm slowly, as the unsilvered Dewar permits. Under humid conditions, drying tubes are provided to prevent entrance and condensation of water vapor. Observations are conveniently made at least as low as liquid air temperatures. Such a scheme would seem to be of general use not only in preliminary investigations of solid state transitions, but also in rather striking visual demonstrations of transitions that are often found to cause large thermal, dielectric and density effects. The interpretation is by the usual polarizing microscope theory.[22]

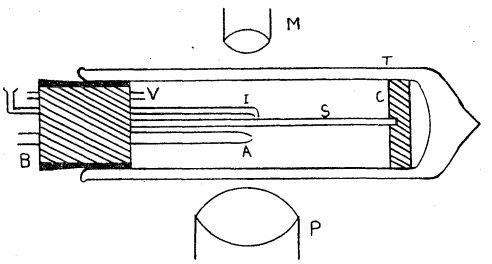


Fig. 1.—Vacuum-jacketed cell for use with polarizing microscope.

Experimental Results

The dielectric constants ϵ and specific conductances k(ohm^{-1} cm.$^{-1}$) are listed in Table I with appropriate temperatures and frequencies. The readings were made in the time sequence 50, 5, 0.5 kc., so that when the dielectric constant was falling rapidly and isothermally at a freezing or transition point, the smaller number of dipoles left free to orient when the 0.5 kc. reading was made as compared to that present an instant before when the higher frequency readings were made caused the actual dielectric constant values to be higher at the higher frequency. The specific conductance values near the melting points and in the liquid probably contain some d. c. conductivity contribution. Both preliminary runs and duplicate measurements have been omitted for the sake of brevity.

Discussion of Results

The cooling curve for *t*-butyl chloride in Fig. 2 reveals a previously unreported thermal transition at −53.8° whose latent heat considerably exceeds that of fusion. The variation of the dielectric constant with temperature is seen from Fig. 3 to resemble that of hydrogen chloride.[6,7] The portions of the curves obtained on cooling, however, slope downward with decreasing temperature while detailed results on the cooling behavior of hydrogen chloride are not available for comparison.

(15) Parts, *Z. physik. Chem.*, **B7**, 327 (1930).
(16) Smyth and Hitchcock, THIS JOURNAL, **54**, 4631 (1932).
(17) Miller, *ibid.*, **60**, 42 (1938).
(18) Cone, Denison and Kemp, *ibid.*, **53**, 1278 (1931).
(19) Baker and Smyth, *ibid.*, **60**, 1229 (1938).
(20) Kruis and Clusius, *Physik. Z.*, **38**, 510 (1937).
(21) Kruis and Kaischew, *Z. physik. Chem.*, **B41**, 427 (1939).
(22) Hartshorne and Stuart, "Crystals and the Polarizing Microscope," Edward Arnold and Co., London, 1934.

TABLE I

DIELECTRIC CONSTANTS AND SPECIFIC CONDUCTANCES

t, °C.	Kc. 50	Kc. 5	Kc. 0.5	ϵ 50	$k \times 10^{10}$ 5	$k \times 10^{10}$ 0.5
			t-C_4H_9Cl, Cooling			
8.0	10.54			1280		
3.8		10.77			1120	
3.3			11.78			1200
2.7	10.74	11.16	11.70	1260	1240	1240
1.8	10.84			1260		
− 6.2	11.36			1350		
− 8.4	11.53			1370		
− 9.2	11.57		11.61	1380		1350
− 9.6	11.59			1380		
−10.1	11.61			1400		
−10.4	11.67			1390		
−13.3	11.88			1300		
−15.1	11.91			1280		
−16.8	12.03			1280		
−20.1	12.34			1280		
−20.5	12.37			1280		
−21.8	12.45			1280		
−22.3	12.49			1280		
−23.2	12.70			1250		
−24.6	14.28			21.4		
−29.2	13.89			19.6		
−31.6	13.79			17.7		
−33.0	13.68			17.7		
−35.0		13.69	13.77		3.5	1.6
−37.0	13.57	13.64	13.85	15.9	3.1	1.3
−38.6	13.57	13.68	13.89	14.2	3.0	1.3
−41.2	13.51	13.55	13.80	14.2	2.4	1.0
−46.3	13.39			8.9		
−49.1		13.40			1.7	
−51.3			13.52			0.8
−54.0	8.47	5.61	2.71	8.9	1.2	1.0
−53.8	4.03			14.2		
−53.8	2.51	2.55	2.65	5.3	2.8	1.2
−53.8	2.46	2.50	2.54	5.3	2.7	1.2
−56.2	2.45	2.48	2.52	4.0	1.6	0.9
−60.0			2.52			.6
−66.6	2.41	2.43	2.47	3.5	1.0	.4
			Warming			
−69.3	2.53	2.56	2.58	0.1	0.1	0.1
−66.0	2.55	2.57	2.60	.1	.1	.1
−62.8	2.57	2.58	2.62	.1	.1	.1
−59.6	2.58	2.60	2.64	.1	.1	.1
−56.9	2.60	2.63		.1	.7	
−55.8			2.68			.6
−53.8	2.63	2.67	2.83	.1	.6	.5
−53.5	3.08	5.36	9.45			
−53.4	14.94			26.6		
−53.4	15.02			26.6		
−52.9	15.07			26.6		
−52.2	14.97			26.6		
−51.2	14.95			26.6		
−48.4	14.89			26.6		
−46.8	14.82			45.2		
−43.3		14.72	14.77		1.2	0.5
−39.4	14.55	14.54	14.62	45.2	1.2	.6
−36.0	14.38	14.40	14.50	45.2	1.6	.6
−34.0	14.32	14.34	14.44	45.2	1.8	.6
−29.5	14.18	14.20	14.32	38.5	1.7	0.7
−26.1	14.16	14.43	14.47	40.2	2.6	1.8
−25.4	14.08			35.2		
			t-C_4H_9Br, Cooling			
−28.3	13.81	14.09	14.38	83.4	13.0	7.2
−30.7	13.83	14.11	14.37	81.8	12.5	6.9
−32.0	13.85	14.13	14.36	83.4	12.1	6.8
−35.6	13.86	14.13	14.35	102.8	11.7	6.0
−39.3	13.91	14.16	14.34	102.8	10.3	5.3
−41.9	13.95	14.20	14.37	117.4	9.7	5.0
−44.9	14.04	14.28		122.2	9.1	
−41.6			12.89			5.3
−42.0	12.42			120.6		
−43.7		12.69	12.88		9.9	5.0
−45.5	12.45	12.70	12.90	137.9	6.2	4.5
−48.4	12.50	12.75	12.91	176.3	9.2	4.0
−65.5	13.00	13.03	13.05	88.2	5.0	2.4
−65.7		12.15	10.20		5.0	2.4
−65.9	8.54	5.07	3.33	52.0	10.6	6.9
−66.0	2.88	2.91	3.04	26.6	9.6	5.3
−72.1	2.75	2.81		21.4	7.6	
−75.3			2.91			4.6
−83.7	2.65	2.70	2.80	17.7	4.4	3.5
			Warming			
−118.5	2.42	2.42	2.40	1.4		
−106.5	2.50	2.51	2.51	1.5		
−100.2	2.61	2.62	2.62	1.5		
−70.7	2.69	2.79	2.98	14.2	5.4	3.6
−68.1	2.71	2.84	3.08	17.7	7.1	5.0
−65.8	2.74	2.88	3.20	19.6	9.2	6.3
−64.5	2.79	2.97	3.25	23.1	8.4	5.8
−64.5	2.94	3.09	3.35	19.6	7.4	4.5
−64.4	3.24	3.41	3.70	17.7	5.3	3.3
−64.3	5.01	6.67	8.96	17.7	5.9	3.2
−64.2	11.79	11.97	12.07	23.1	6.0	3.3
−64.1	11.86	12.03	12.15	23.1	6.2	3.5
−63.6	11.88	12.06	12.17	23.1	6.5	3.5
−59.7	11.89	12.07	12.22	24.9	7.1	3.8
−55.4	11.90	12.10	12.27	28.3	7.6	4.2
−43.8	11.99	12.20	12.42	31.8	9.4	5.3
−42.4	11.99	12.23	12.44	33.5	9.6	5.3
−41.3	12.14	12.70	13.42	35.2	10.5	5.3
−41.4	13.54	14.28	14.48	35.2	9.2	5.0
−41.4	14.09	14.33	14.51	35.2	9.2	5.1
−41.1	14.12	14.35	14.54	35.2	9.4	5.3
−38.4	14.13	14.36	14.56	35.2	9.9	5.6
−25.8	14.17	14.45	14.74	45.2	14.2	8.6
−25.0	15.03	16.06	17.41	162.0	41.5	23.6
−24.3	15.05	16.20	17.76	177.2	48.5	29.0
−23.6	15.11	16.66	18.28	219.5	65.0	37.3
−22.7	15.15	17.02	19.12	309.2	78.4	50.1
−21.1	15.26	18.89	21.87	523.3	139.4	99.2

Kc. 520 t, °C.	ϵ	Kc. 520 t, °C.	ϵ	Kc. 520 t, °C.	ϵ
		Warming			
−23.6	14.11	−18.7	13.87	−17.7	13.16
−22.7	14.11	−18.5	13.79	−17.6	12.62
−21.8	14.07	−18.4	13.73	−17.5	12.52
−21.0	14.03	−18.3	13.63	−16.9	12.48
−20.5	14.02	−18.1	13.56	−15.9	12.43
−20.0	14.02	−17.9	13.54	−14.7	12.37
−19.3	13.99	−17.8	13.53		

TABLE I (*Concluded*)

Kc. / t, °C.	50	5	0.5	50	5	0.5
		ε			$k \times 10^{10}$	
		t-C_4H_9I. Warming				
−184.3	2.58	2.57	2.58	3.5	0.6	0.6
−149.7	2.60	2.60	2.65	3.5	.7	.5
−141.4	2.64	2.65	2.70	7.1	1.4	1.0
−120.2	2.67	2.67	2.72	5.3	1.7	1.5
−107.0	2.68	2.68	2.87	8.9	4.7	3.7
− 87.9	2.72	2.86	3.61	28.3	17.5	12.6
− 83.0	2.73	2.96	4.08	38.5	25.0	16.5
− 79.2	2.74	3.74	7.50	122.2	75.5	41.0
− 72.6	2.80	4.45	9.01	200.0	112.8	66.0
− 68.4	2.88	4.91	9.24	258	142.0	87.7
− 62.2	3.13	5.40		347	268	
− 59.2	3.25	5.70		428	258	
− 55.3	3.47	6.21		512	348	
− 52.9	3.65	6.52		669	430	
− 50.7	3.83	6.82		802	534	
− 45.6	4.20			1333		
− 44.0	4.67			1586		
− 43.3	4.73			1685		
− 40.9	3.12			2220		
− 39.4	5.81			2718		
− 39.2	6.25			2880		
− 39.1	6.36			2890		
− 39.1	6.45			2900		
− 39.0	6.62			2920		
− 38.9	6.90			2940		
− 38.8	7.12			2940		
− 38.2	10.13			2790		
− 38.2	10.50			2800		
− 38.2	11.22			2440		
− 38.2	11.09			2420		
− 38.1	11.12			2873		
− 38.0	11.04			2870		
− 38.0	10.99			2870		
− 34.3	10.61			2020		
− 33.7	10.61			1881		
− 33.4	10.47			1840		
− 32.6	10.45			1780		
− 32.2	10.44			1770		

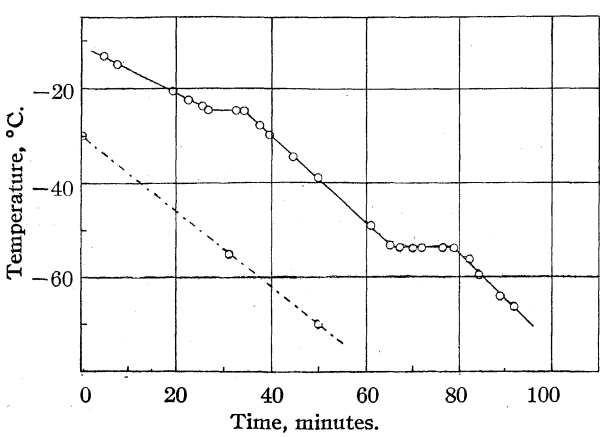


Fig. 2.—Temperature–time curve (cooling) for *t*-butyl chloride.

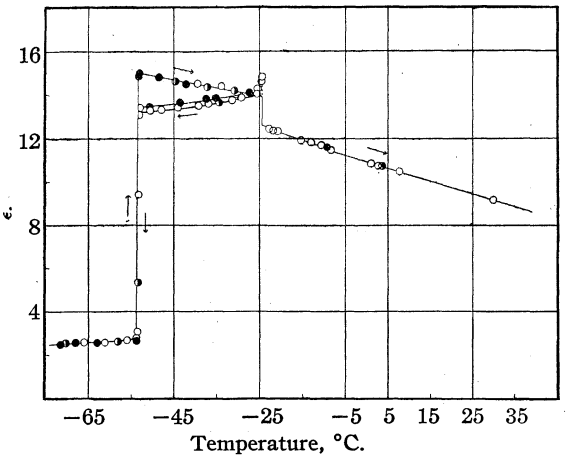


Fig. 3.—Temperature dependence of the dielectric constant of *t*-butyl chloride. (Hollow circles represent values at 50 kc., half-filled circles values at 5 kc., and filled circles values at 0.5 kc.)

The highest temperature point in the liquid on Fig. 3 was obtained independently[12] in a dipole moment study. On solidification the dielectric constant rises because of increase in density, shows a low sharp peak, presumably because of a small Maxwell–Wagner interfacial polarization, and then gradually declines with a small but definite dispersion. At the transition temperature, the dielectric constant drops sharply to a value near to the square of the refractive index, with disappearance of dispersion. The transition is shown by the polarizing microscope to be an enantiotropic transformation from a high temperature cubic to a low temperature form of lower symmetry. The abrupt lattice change into an anisotropic packing arrangement would follow from a coöperative interlocking of the dipoles when they had reached a sufficiently low temperature to lose most of their librational energy. Such a sharp interaction is indicated by Fig. 4, where the curve denoting the lower ϵ'' values in the region of −53.8° rises steeply to a maximum just at the temperature of the transition. Hence, a rapid and widespread interference to orientation is introduced by a loss maximum, so narrow that it is only a straight line for 50 kc. at the peak. Then the dipoles are immobilized in the low temperature crystal form.

The dielectric constant curve obtained with rising temperature, shown by arrows on Fig. 3, exhibits a sharp ascent at the transition, which is unaccompanied by thermal hysteresis, to a value which declines on further warming, as expected from the Debye relation. If the co-

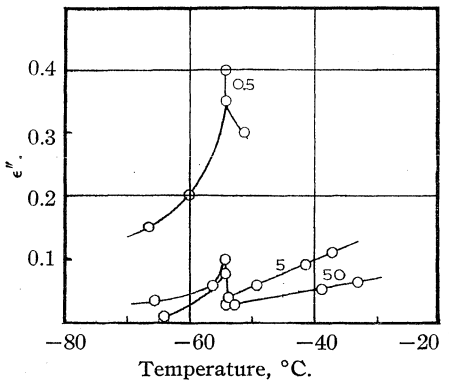


Fig. 4.—Temperature dependence of the imaginary part ϵ'' of the dielectric constant of *t*-butyl chloride.

operative[23] loosening of the molecules at the transition on warming is strong enough to give immediately the maximum orientational freedom of the cubic lattice, whereas, on cooling, a decrease in the molecular disorder probably existing immediately after solidification gradually reduces this freedom, the observed difference in the warming and cooling curves would be accounted for. Microscopic examination revealed qualitatively a considerable density increase on cooling through the transition.

Figure 5 contains the thermal arrests marking the two polymorphic transitions found for *t*-butyl bromide. The higher temperature transition, henceforth called I, is attended by supercooling but comparison of the heating and cooling curves, together with the dielectric results, indicates that it occurs without thermal hysteresis at −41.4°.

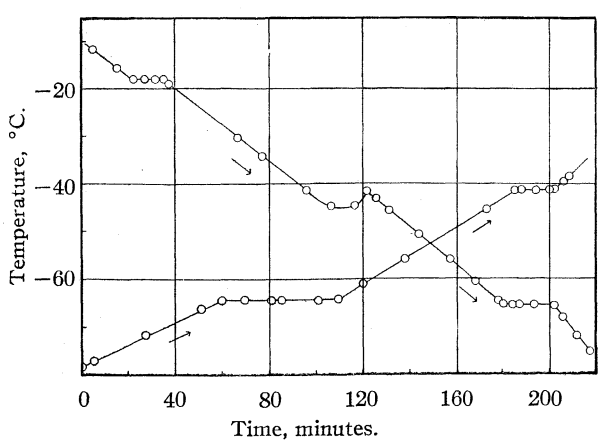


Fig. 5.—Temperature–time curves for *t*-butyl bromide.

The lower transition II shows no supercooling but occurs abruptly at −65.8° on cooling, and at −64.2° on warming. Evidently from Fig. 5 the heat of fusion is less than the heat of transition II, and much less than the sum of the heats of the two transitions.

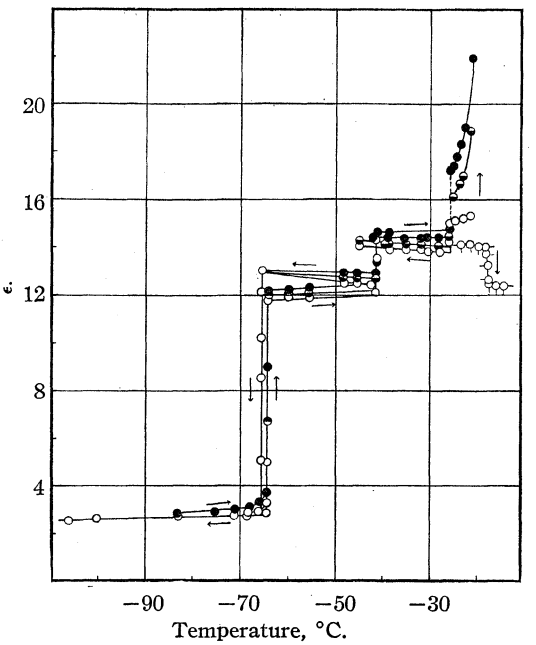


Fig. 6.—Temperature dependence of the dielectric constant of *t*-butyl bromide. (Hollow circles represent values at 50 kc., half-filled circles values at 5 kc., and filled circles values at 0.5 kc.)

An enhanced dispersion in the same frequency range results from replacement of a chlorine atom by the larger, more polarizable bromine, as demonstrated by Fig. 6. In some parts of the graphed data points at the three frequencies would have been superposed, so but one point was indicated, for example, the point immediately above transition II, on cooling. The data for the lower frequencies begin somewhat below the freezing point, for, just after solidification, bridge balancing became uncertain and large apparent dielectric constant values were obtained, probably because of interfacial polarization. This effect has been found by Yager and Morgan[24] for several camphor derivatives, and by White and Morgan[25] for ethylene cyanide, all of which possess rotational freedom in the solid. The effect here does not exceed a maximum apparent specific conductance of 5×10^{-8} ohm^{-1} cm.$^{-1}$, whereas they report values greater than 10^{-6} ohm^{-1} cm.$^{-1}$. The values obtained at 520 kilocycles with a

(23) "Coöperative" is here and elsewhere taken from the usage of Fowler, "Statistical Mechanics," Cambridge University Press, Cambridge, England, 2d ed., 1936, Chap. 21.

(24) Yager and Morgan, THIS JOURNAL, **57**, 2071 (1935).

(25) White and Morgan, *J. Chem. Phys.*, **5**, 655 (1937).

heterodyne beat apparatus are shown through the melting point by the tagged circles.

The supercooling at transition I is expressed on the dielectric graph by an exact continuation of the curves for the highest temperature solid form some 3° below −41.4°. Suddenly, the values revert back on just these lines, as far as could be determined experimentally, and the dielectric constant drops sharply at the transition to a new set of curves, which show diminishing dispersion with decreasing temperature. At −65.8°, a transition like that in *t*-butyl chloride occurs. However, below this point for a short temperature interval there is still dispersion, apparent in the data but too slight to be evident in Fig. 6. As with the chloride, a sharp rise in ϵ'' marks the interaction introduced by transition II.

On warming, a slight rotational pre-melting, consonant with the suggestion of coöperative lattice loosening with rising temperature noted for *t*-butyl chloride, is followed by the onset of rotation, now at −64.2°. This slight rotational freedom below a transition seems comparable to the pre-melting previously noted for many molecular lattices.[19] The latter behavior has been confirmed by X-ray and thermal analyses of highly purified hydrocarbons,[26] and has been given theoretical interpretation and justification by Frank's recent order–disorder treatment of melting.[27] It would seem that in a treatment of arrangement in terms of rotational disorder and of the corresponding lattice energy change dependent on the degree of such disorder, a transition state just below the observed transition temperature like that proposed by Frank just below the melting point would account for the experimental data.

The apparent 1.6° hysteresis in the temperatures of transition resembles the 1.1° difference in the case of the analogous transition in hydrogen sulfide,[28] the longer interval in ethylene cyanide,[25] and the less sharply defined hystereses in camphor and its derivatives.[24] The same hystereses are found in thermal measurements, and were thus discovered at the rotational transitions of methane and deuterated methane.[29]

Pressure studies by Clusius and Weigand[30] on the hydrogen sulfide transition reveal that it is accompanied by a volume change of about 7.6%, and by a mean lattice separation change so small that it might remain undetected in X-ray photographs. However, easily obtainable pressures with hydrogen gas broadened the hysteresis range, and the hysteresis area was found to be smaller in deuterium sulfide. Hence, apparent hysteresis in these transitions would seem to be sensitively affected by changes in structure and environment. The apparent temperature of the monotropic transition in ethyl stearate was found to depend on the temperature gradient to which the sample was exposed.[19] This result was confirmed for other similar long chain compounds.[31] It provides evidence for the idea that critical fluctuations in ΔF and ΔS must occur for the progression of spontaneous solid transformations. This concept has been elaborated by Ubbelohde.[32] The activation entropies for rotation of even simple molecules in the solid state have been found to be very high.[33] Therefore, it is possible that the *t*-butyl bromide hysteresis occurs because, in order that transformation may be induced, the substance must be cooled slightly below the true equilibrium point to produce an enhanced thermodynamic potential. Then, the material may lose heat to the environment so readily that the temperature of the sample never rises to the equilibrium value, despite the relatively large latent heat. This agrees with the observation that the sample could be cooled under a larger gradient and made to lose heat so rapidly that the transition appeared to occur at −67.2°. However, the process at −65.8° as shown by Figs. 5 and 6 is not an ordinary supercooling like that at transition I.

A macroscopic potential, or tension, in the crystal mass produced by the transition has been suggested by Frank[34,35] as the possible cause of hysteresis. The rate of temperature change as the transition is approached should strongly influence the hysteresis, it would seem. Further limitations on this idea have been noted by Eucken.[36]

An explanation applicable to certain examples of hysteresis is suggested by the dielectric and thermal results on *n*-amyl bromide,[3] and by the X-ray studies of Wallerant on camphor.[37] The

(26) Ubbelohde, *Trans. Faraday Soc.*, **34**, 282, 292 (1938).
(27) Frank, *Proc. Roy. Soc.* (London), **170**, 182 (1939).
(28) Smyth and Hitchcock, THIS JOURNAL, **56**, 1084 (1934).
(29) Kruis, Popp and Clusius, *Z. Elektrochem.*, **43**, 664 (1937).
(30) Clusius and Weigand, *ibid.*, **44**, 674 (1938).
(31) Vold and Vold, THIS JOURNAL, **61**, 808 (1939).
(32) Ubbelohde, *Trans. Faraday Soc.*, **33**, 1203 (1937).
(33) Baker and Smyth, *J. Chem. Phys.*, **7**, 574 (1939).
(34) Frank and Wurtz, *Naturwissenschaften*, **26**, 687 (1938).
(35) Frank, *Z. Elektrochem.*, **45**, 150 (1939).
(36) Eucken, *ibid.*, **45**, 150 (1939).
(37) Wallerant, *Compt. rend.*, **158**, 597 (1914).

latter found that, besides the cubic form existing above the transition, three less symmetrical classes occur at successively lower temperatures. Monotropic transitions below a rotational transition would produce the same effect on it as that of the *n*-amyl bromide transition in raising the melting point several degrees above the freezing point. A careful thermal and X-ray analysis of other substances showing hysteresis might establish such low temperature polymorphism.

Examination with the polarizing microscope showed *t*-butyl bromide to form a translucent, isotropic, definitely crystalline lattice on solidification, which was transformed enantiotropically at transition II to or from an opaque, birefringent, anisotropic lattice. Transition I was accompanied by no change in the cubic form, but, apparently, by a contraction on cooling and an expansion on warming. This is indicated by the migration of the Beeke line across the sample as it transforms. In a homogeneous medium, differences in refractive index, detected under the polarizing microscope by brightness variations with a constant source, result from density differences. At the vertical junction between a more dense phase B and a less dense one A, $n_B > n_A$, where n is the refractive index. The rays which pass from A to the denser medium B are bent toward the normal to the junction within B. Rays passing from B toward the junction which impinge within the critical angle are totally reflected and emerge on the B side. The result of these combined effects is to illuminate more brightly the B side of the junction. Here the junction is the interface between the transformed and untransformed material, and, at the transition point, a darkish line is seen to move across the sample. It is concluded that I is an enantiotropic lattice change shown by Fig. 5 to possess a latent heat and accompanied by a density shift which does not destroy the cubic arrangement.

The supercooling at transition I, shown on Figs. 5 and 6, is like that frequently observed at solid–liquid transitions. Thermal measurements on phosphine disclosed a low temperature rotational transition and an intermediate one,[38] analogous to those of *t*-butyl bromide. The intermediate transition in phosphine also shows supercooling, whereas the lower one, which presumably marks the end of librational freedom, does not, in agreement with the *t*-butyl bromide results. The dielectric data provide a possible interpretation of the general property of supercooling in some polymorphic transitions, and its absence in others. Figure 5 indicates a much smaller latent heat for transition I than for transition II. The difference between the entropy changes at the two points is also large. A metastable condition of the solid phase which is stable above the temperature of transition I induced by cooling it somewhat below the transition temperature will be under a relatively small thermodynamic potential tending to force the transformation. Further, Fig. 6 indicates by the relatively small decrease in dielectric constant at transition I only a slight loss in orientational freedom of the dipoles. Hence, on cooling, the thermal agitation of the molecules which, at a given instant, have undergone the transition, will make them poor ordering centers for the coöperative formation of the lower temperature stable form. On the other hand, transition II, and, presumably also, as a dielectric study should reveal, the lowest transition in phosphine, marks the loss of most of the rotational molecular freedom. The molecules cease to exhibit nearly spherically symmetrical force fields, and become so definitely oriented that a rearrangement occurs, resulting in the formation of an anisotropic lattice. These effects are evidenced by the loss of orientational polarization seen in Fig. 6, and the large latent heat of the transition indicated in Fig. 5. The same causes account for the absence of supercooling at the transition in *t*-butyl chloride. Such considerations would seem generally adaptable to thermal studies of polymorphism in molecular and some ionic lattices. They are consonant with other ideas on the importance of orientation in supercooling.[4]

Figure 7 indicates the expected result that the least symmetrical most polarizable molecule of the series, t-C_4H_9I, interacts in the solid so strongly that it can rotate only with difficulty above the transition point $-79.4°$. This hindrance effects the pronounced dispersion seen on the graph, but the dielectric loss, proportional to the tabulated apparent specific conductance, contains a considerable d. c. conductance contribution from impurities which could not be removed. The critical frequency of the rotating dipoles is probably near 50 kc., as the dielectric constant values for this frequency rise from nearly the square of the refractive index, only shortly below the

(38) Clusius and Frank, *Z. physik. Chem.*, **34B**, 405 (1936).

melting point −38.2°. Sufficiently high frequencies might convert the chloride and bromide curves to ones resembling the iodide.

Examination with the polarizing microscope revealed an apparently anisotropic lattice above the transition, which was replaced by one of much stronger birefringence below it. Suspected impurities make uncertain a definite assignment of non-cubic class to the high temperature form.

The melting behavior of *t*-butyl iodide is in agreement with the theory of melting point variation in isomeric and otherwise similar substances previously proposed.[3] Its gain of librational freedom postpones the melting point to 234.9°K., 65.3° higher than *n*-butyl iodide, m. p. 169.6°K., and 55.3° higher than *i*-butyl iodide, m. p. 179.6° K., and 65.8° higher than *s*-butyl iodide, m. p. 169.1°K.

The present results show the variation in intermolecular action of nearly spherical molecules produced when atoms of gradually increasing size and polarizability are successively substituted as one of four groups about a central atom, the other three groups remaining unchanged. As noted previously,[3,4] the orientational interaction is found to be very sensitive to structure. A further method of studying the possible coupling is to dilute the dipoles in the solid state, preferably by solid solution formation with a similar, non-polar substance. A preliminary microscopic examination of a 50% by volume mixture of *t*-butyl chloride and carbon tetrachloride revealed that, as would be expected, the transition was made less sharp, and was displaced to lower temperatures, and that the whole solid formed an isotropic high temperature system, which would be anticipated from the known high temperature cubic form of carbon tetrachloride. However, partial melting was found to occur sharply and uniformly, leaving a skeleton-like isotropic lattice which itself melted sharply a few degrees higher. Dielectric measurements on such a system might show a complex behavior because of the coexistence of phases.

The discovery of rotational freedom in the solid forms of these simple molecules suggests

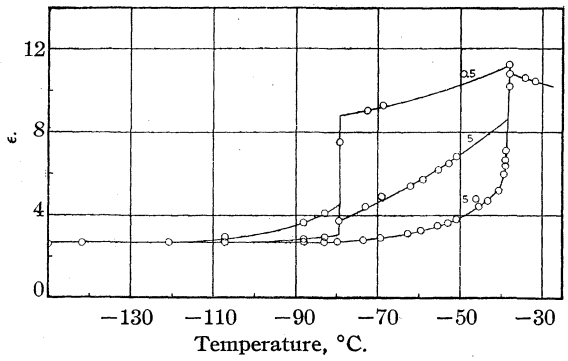


Fig. 7.—Temperature dependence of the dielectric constant of *t*-butyl iodide.

experiments to discover its effect on other physical properties. That is, the form of the solid above the transition might differ significantly from that below it in temperature coefficient of thermal conductivity, diffusion, solution rate and sublimation vapor pressure. If these processes were thus connected with rotation or non-rotation, information on their mechanism would be gained.

Summary

Polymorphism has been found and studied by means of thermal, optical and dielectric measurements in *t*-butyl chloride, bromide and iodide. Dispersion, hysteresis and supercooling effects have been interpreted in terms of possible molecular processes. Solid state transitions of the first kind are attended by supercooling when a relatively small free energy difference obtains between the metastable and the stable phases below the transition. The dielectric results indicate that this supercooling may be a function of the ordering ability of the molecules in the stable form. Rotational "premelting" before a solid state transition is analogous to the premelting found in solids near the melting point. Results with the polarizing microscope establish a correlation of lattice symmetry with molecular rotational freedom, and, conversely, the isotropic lattices previously found for many organic molecules above polymorphic transitions are associated with the development of rotational freedom at such transitions.

PRINCETON, NEW JERSEY RECEIVED JUNE 27, 1939

[CONTRIBUTION NO. 228 FROM THE WOODS HOLE OCEANOGRAPHIC INSTITUTION]

The Helium–Neon Content of Sea Water and its Relation to the Oxygen Content[1]

BY NORRIS W. RAKESTRAW, CLIFFORD E. HERRICK, JR.,[2] AND WM. D. URRY

One of the most widely discussed topics in the field of oceanography at the present time is the cause and significance of the "oxygen minimum zone." The vertical distribution of oxygen in the deeper parts of the ocean shows a minimum concentration at a depth which varies with the location, generally between 200 and 1000 meters. This minimum may be very pronounced, as in parts of the Pacific where there is virtually no oxygen. In the Atlantic the minimum zone is seldom less than 30% saturated, and in the far north and south there is sometimes no minimum.

Some time ago there were reported analyses of the helium–neon content of sea water,[3] the outstanding feature of which was an apparent minimum of the helium–neon mixture coinciding with the oxygen minimum in the same water. The significance of this was discussed briefly and some possible explanations suggested. All of these explanations, however, are in rather serious conflict with other oceanographic evidence. In view of this, as well as the limited number of observations made at that time, we have undertaken to repeat the work, on water from a variety of different locations, and with certain improvements in the analytical method.

The details of the technique are described in the references in the earlier paper, but briefly it consists of boiling the dissolved gas out of the water sample under reduced pressure, adsorption on charcoal at the temperature of liquid air, and measurement of the non-adsorbable residue (helium and a constant fraction of the neon) by means of a McLeod gage. High vacuum technique is used throughout, and great care must be exercised in flushing out the line with pure electrolytic oxygen, removing traces of hydrogen by repeatedly passing over hot palladium.

Slight modifications in the original method consisted of increasing the size of the water sample to about 300 ml., an addition to the line to permit flushing the gas out of the boiling flask by means of oxygen, instead of depending entirely upon water vapor, and a graphic method of calculating results from the McLeod gage readings.

Because of the extremely small size of the gas sample measured (less than 10^{-5} ml.) a capillary of about 0.1 mm. diameter must be used in the McLeod gage. To eliminate the effect of capillary depression upon the mercury level a series of readings was taken for each measurement, at different pressures. When these are plotted graphically the slope obtained is a measure of the volume of gas trapped. This practice largely overcame the great variability in capillary depression which was observed from time to time. It was impossible to determine a constant factor for a given tube. Electrodeless discharge in the capillary, for the purpose of testing the residual gas for hydrogen, was found to change the glass surface so much as to make the tube practically useless.[4]

Water samples were collected in the routine manner at sea, by means of reversing water bottles, and stored in glass citrate bottles, completely filled, to prevent exposure to the air. A method of doing this has been described.[5] From these the water was introduced into the boiler by direct mercury displacement, with only momentary and non-turbulent exposure to the air, a major improvement over the earlier method of pouring from the storage bottle.

The oxygen determinations were made by the routine Winkler method, on shipboard, immediately after collecting the samples.

The results are given in Table I. The five stations chosen present a complete array of conditions, in regard to the oxygen minimum. Four are in the Atlantic and one in the Pacific, the latter being almost entirely depleted of oxygen at a depth of about 600 meters. One of the Atlantic stations, 3113, is in the Sargasso Sea, south of the Gulf Stream; two others somewhat to the north. The oxygen minimum at these three varies from 200 to 900 meters. The last station, 2822CG, shows no oxygen minimum whatever.

In none of these is there any consistent relation between the oxygen and the helium–neon content, nor indeed any regular variation in the latter. We can only conclude that the earlier results, based upon a few observations at only two stations, were in some way fortuitous.

We were also unable to notice any significant difference between the solubility of the helium–neon mixture in sea water at 6 and at 23°, or in normal sea water diluted to half its original salinity, the figures obtained in these three respective cases being 16.9, 16.4, and 17.6.

Although the results obtained from the water of the Pacific are higher than all the others, we do not think this represents a real difference. These determinations were made several months after the others, with a different McLeod capillary and a number of other conditions altered. Nevertheless, although they probably cannot be compared

(1) This work was made possible by a grant from the Elizabeth Thompson Science Fund.

(2) Present address: Department of Chemistry, University of Rochester.

(3) Urry, THIS JOURNAL, **57**, 657 (1935).

(4) In the earlier work a spectroscopic examination was regularly made, by means of an electrodeless discharge in the capillary, after the measurements had been taken. This necessitated a frequent change of capillary.

(5) Rakestraw and Emmel, *Ind. Eng. Chem., Anal. Ed.*, **9**, 344 (1937).

TABLE I

	Depth, meters	Temp., °C.	Oxygen ml./l.	He–Ne ml./l. × 10^{-5}
	0	18.28	5.15	18.5
	5	18.31	5.15	14.1
Station 3025	25	17.97	5.05	15.2
35°-55′N	62	17.93	5.17	15.2
67°-39′W	166	17.92	5.15	15.2
Apr. 7, 1938	333	17.63	4.90	15.6
	622	15.62	4.10	15.9
	912	9.55	3.60	15.9
	1772	3.86	5.88	16.5
	2959	3.16	6.15	17.8
	0	...	4.92	13.5
	24	20.78		16.3
	47	17.78	4.80	15.9
Station 3105	95	14.68	4.10	16.6
39°-20′N	189	14.27	4.58	17.4
70°-32′W	284	12.16	3.40	16.6
July 14, 1938	378	9.10	3.21	15.4
	474	6.83	4.07	15.4
	568	5.41	4.78	15.6
	663	4.76		15.2
	717	4.47	5.59	15.9
	986	4.04	5.98	17.2
	1702	3.46	6.10	14.8
	0	26.14	4.75	13.3
	21	25.81	4.76	13.1
	85	14.85	3.99	15.0
Station 3113	171	9.18	3.14	14.3
37°-01′N	260	7.03	3.94	
74°-21′W	389	5.55	4.73	12.4
Aug. 2, 1938	435	4.88	5.25	13.9
	555	4.55	5.54	15.4
	722	4.19	5.84	
	1055	3.80	6.14	17.9
	1388	3.55	6.24	12.8
	95	3.54	6.64	15.4
Station 2822CG	286	3.28	6.63	16.1
57°-25′N	531	3.22	6.67	15.0
48°-47′W	898	3.18	6.68	15.6
July 26, 1938	1953	3.26	6.58	14.8
	3072	2.46	6.30	14.8
	10	16.39	5.66	17.3
Pacific station	25	14.67	5.93	20.5
32°-34′N	74	10.75	3.91	16.8
117°-28′W	199	8.83	2.11	16.9
Nov. 9, 1938	298	7.98	1.25	16.9
	503	6.11	0.32	16.8
	607	5.41	.26	18.9
	808	4.48	.48	16.8
	979	4.07	.49	17.3
	1121	3.69	.69	16.9

with those from the other stations, they clearly indicate a regular and consistent distribution at this particular station. This view is confirmed by the fact that at this stage two samples of sea water saturated with air at 23 and 24° showed helium–neon contents of 19.1 and 18.7, respectively, higher than the solubility measurements made earlier.

Occasionally, in the earlier part of this work, a determination yielded an impossibly low result, compared with a duplicate. This was sometimes the case even with water saturated with air. Although we never located the reason for this with complete certainty, it seemed to be connected with the process of letting the gas into the adsorption line from the boiling flask. After every movement at this point had been standardized, and especially after provision had been made for washing the gas into the line with excess oxygen, no trouble of this sort was experienced. It is possible that this was the cause of the two or three unusually low values in the previous investigation, leading to the assumption of a helium–neon minimum.

Summary

A repetition of earlier work, under more suitable and representative conditions, shows the sea to be practically saturated with helium and neon at all depths, with no evidence of any depth of minimum concentration, and hence no relation to the depth of oxygen minimum.

RECEIVED AUGUST 17, 1939

[CONTRIBUTION NO. 175 FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING OF THE UNIVERSITY OF TEXAS]

Partial Vapor Pressures of Aqueous Ethylamine Solutions

BY B. P. DAILEY WITH W. A. FELSING

Object of the Investigation.—In a previous paper[1] there were reported the partial vapor pressures of methylamine solutions, the investigation being one of a series dealing with the possible uses of these amines as refrigerating fluids in the absorption type of refrigerating units. The ethylamines have been suggested by Taylor[2] for use in such systems and Mehl[3] has investigated some of the pertinent properties of monoethylamine for the same purpose.

In this investigation it was decided to determine experimentally the partial vapor pressures of aqueous solutions of the ethylamines in order to aid in evaluating these substances as refrigerants. The data obtained were used to calculate the free energy decrease attending the solution of these amines in water.

Previous Investigations.—The literature records but few determinations of the partial vapor pressures of ethylamine solutions. Lattey[4] cites values for two concentrations at 2° intervals from 6 to 50°, which values were calculated from total pressure determinations. Doyer[5] gives one value at 60° for both mono- and diethylamine.

Method of the Investigation.—The method used was the dynamic, air-saturation method previously described.[1] The complete apparatus, as described there, was used in this investigation.

The amine solutions were prepared by dissolving in cold distilled water of conductivity grade either the gaseous or liquid amines. They were generated from repurified C. P. Eastman Kodak Co. hydrochlorides by the action of concentrated potassium hydroxide solution. Standard **acid** and **base** solutions were prepared with the usual precautions for highest accuracy. Weight burets were used throughout; the indicator was methyl red.

The Results Attained.—The partial vapor pressures were calculated by the procedure described[1]; five to six acceptable determinations were made at each concentration, the mean of which is reported in the table. The results are believed to be accurate to better than ±0.02 mm.

TABLE I

PARTIAL PRESSURES OF ETHYLAMINE SOLUTIONS AT 25°

Concn. C (moles/1000 g. H_2O)	Pressure, p, mm.	p/C (obsd.)	Best "K"
	Monoethylamine		
0.2529	1.97	7.789	
.5410	4.27	7.893	
1.0867	8.84	8.134	
2.2602	17.78	7.866	7.86
	Diethylamine		
0.2228	3.79	17.010	
.3926	6.28	15.995	
.8585	13.73	15.993	
1.8142	29.58	16.304	16.25
	Triethylamine		
0.0550	4.72	85.818	
.0919	8.84	96.191	
.2654	25.55	96.269	
.3330	31.43	94.384	95.00

The best "K" was obtained by plotting the pressure as a function of the molarity; a straight line reproduces well the observed data over the range of concentrations investigated.

The partial vapor pressures of the amine solutions at exactly 1 molar are calculated to be 7.86 mm. for the mono-, 16.25 mm. for the di-, and 95.0 mm. for the triethylamine. With the aid of these data, the following free energy values were calculated for the reaction: Amine (760 mm.) = Amine (1 M) + ($-\Delta F$). The values of $-\Delta F$ were found to be 2709 cal./mole for the mono-, 2278 cal./mole for the di-, and 1232 cal./mole for the triethylamine.

Mehl[3] has given vapor pressure relations for the three liquid amines; from these the vapor pressures at 25° were found to be 1059 mm. for the mono-, 235 mm. for the di- and 78.5 mm. for the triethylamine. From these values the free energy decrease attending the change: Amine (p, mm.) = Amine (760 mm.) was calculated and combined with the preceding free energy values to yield the free energy decrease attending the change: Amine (liquid) = Amine (1 M) + ($-\Delta F$). The results obtained for ($-\Delta F$) were

(1) Felsing and Phillips, THIS JOURNAL, **58**, 1973 (1936).
(2) Taylor, *J. Am. Soc. Refrig. Eng.*, **17**, 136 (1929).
(3) Mehl, *Beihefte Z. ges. Kälte-Ind.*, Reihe 1, Heft 3, 7 (1933).
(4) Lattey, *J. Chem. Soc.*, **91**, 1959 (1909).
(5) Doyer, *Z. physik. Chem.*, **6**, 481 (1890).

2905 cal./mole for the mono-, 1583 cal./mole for the di-, and −103 cal./mole for the triethylamine.

Summary

1. The partial vapor pressures of aqueous solutions of mono-, di- and triethylamine have been determined at 25° over a range of concentration of approximately 0.05 to 2.2 *M*.

2. The free energy decreases attending the change: Amine (liquid) = Amine (1 *M*) have been evaluated from the observed data.

AUSTIN, TEXAS RECEIVED JULY 20, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

Infrared Absorption Studies. VIII. Hydrazoic Acid

BY A. M. BUSWELL, G. W. MCMILLAN, W. H. RODEBUSH AND F. T. WALL

In the study of the tendency of hydrogen compounds of nitrogen to form hydrogen bonds, our attention was attracted to hydrogen azide. This compound has interested inorganic chemists for many years but because of its dangerously explosive character it has remained a substance little known. Dr. L. F. Audrieth[1] of this Laboratory kindly furnished us with the material for, and advice concerning, the preparation of the pure substance and we wish to acknowledge our indebtedness to him.

Hydrazoic acid has about the same strength as acetic acid and readily forms salts. The molecule is supposed to involve a resonance between the two structures

$$N{=}N{=}N{-}H \text{ and } N{\equiv}N{-}N{-}H$$

while the ion has the possibility of at least one more resonance structure thus accounting to some extent for the acid strength. The azide group is known to be linear but the hydrogen must be attached at an angle with the azide group. Hydrogen azide is much more soluble in ether than in water, the distribution ratio being 7:1. This peculiar behavior would seem to require some explanation since acetic acid shows no such surprising behavior.

Experimental.—The prism spectrometer used in this work has been described previously.[2]

The hydrogen azide was generated by dropping concentrated sulfuric acid on the dry potassium salt. Since the vapor as well as the pure liquid is very explosive, the substance was prepared in carbon tetrachloride solution.

The salt was immersed in carbon tetrachloride which had been prepared from the technical material by chlorination and subsequent fractional distillation. A calculated amount of concentrated sulfuric acid was added slowly from a dropping funnel. A trap of methanol was set up beyond the generator to prevent diffusion of hydrogen azide into the laboratory. It was regarded as advisable to use a generator flask whose volume was some three to four times that of the solution it contained. After generation the solution was carefully decanted from the sulfuric acid layer into tubes and sealed until used. In this way solutions of the order of 0.1 molar could be obtained anhydrous with a minimum of handling. The entire operation was performed behind screens.

Careful tests showed that sulfuric acid did not dissolve in the carbon tetrachloride in sufficient amounts to produce any noticeable absorption in the infrared. The solution prepared in this way from the pure salt was evidently free from any appreciable contamination by impurities.

Deuterium azide was prepared by shaking the carbon tetrachloride solution of hydrogen azide with 99% D_2O. This resulted in a 75–80% conversion. Excess water and D_2O was removed with calcium chloride.

Results.—In the drawings the molal absorption coefficient (so-called) is plotted against wave number. This coefficient is defined by the expression

$$\frac{1}{cd} \log \frac{I_0}{I}$$

where c is the concentration (moles per liter of solution), d is the cell thickness in centimeters and I and I_0 the galvanometer deflections obtained through equal paths in solution and pure solvent, respectively. Since the control of concentrations was difficult the accuracy of the calculated coefficients is not good and it was not always possible to maintain constant values for cd.

Three frequencies are always observed in hydrogen azide which remain unchanged in intensity as long as cd is maintained constant. One of these occurs at 4.75 μ and is also found in deuterium azide and phenyl azide (Fig. 1). This is evidently the linear N–N–N vibration which already has been assigned to the 4.8 μ absorption

(1) For an excellent review of the literature concerning hydrogen azide see L. F. Audrieth, *Chem. Rev.*, **15**, 169 (1934).

(2) A. M. Buswell, Victor Dietz and W. H. Rodebush, *J. Chem. Phys.*, **5**, 501 (1937).

in lead azide by Sutherland and Penney.[3] The frequency of this vibration would decrease slightly with increasing weight of the attached group. In the case of the isostere molecule NNO the absorption for this vibration is found at 4.5 μ.[3]

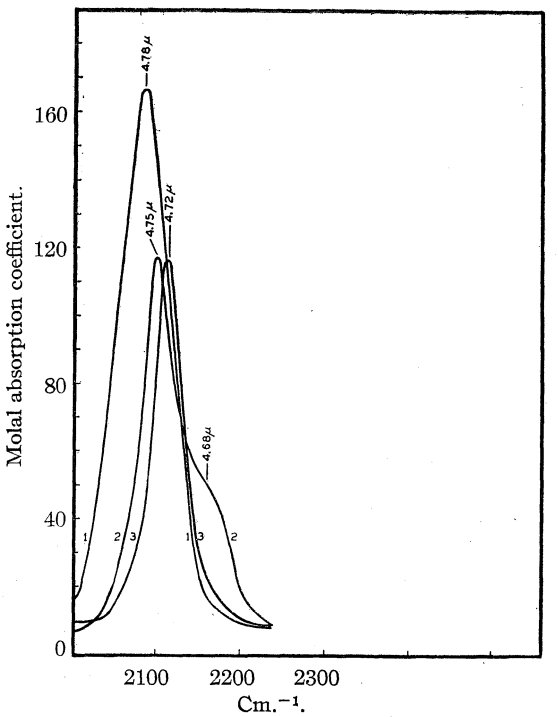


Fig. 1.—Absorption due to the azide group: (1) 0.035 molal phenyl azide in 0.3251 cm. cell; (2) 0.035 molal deuterium azide in 0.3251 cm. cell; (3) 0.035 molal hydrogen azide in 0.3251 cm. cell.

The absorption at 3.03 μ (Fig. 2) is evidently the unbonded N–H vibration. This frequency is lower than any other observed frequency of hydrogen in a N–H compound and might according to deductions previously drawn indicate a very high acidity. It must be remembered, however, that hydrogen azide is as a whole not a linear molecule since the hydrogen must lie at a considerable angle with the nitrogen group. For this reason the normal mode of vibration will not consist of a pure valence or stretching frequency but will be compounded with the much lower bending frequency. The acid strength, therefore, while greater than that of an acid amide is not as much greater as would be indicated by a shift of 0.15 μ in wave length.

The absorption at 4.35 μ must be attributed to an unbonded hydrogen frequency since it is un-

(3) G. B. B. M. Sutherland and W. C. Penney, *Proc. Roy. Soc.* (London), **A156**, 678 (1936).

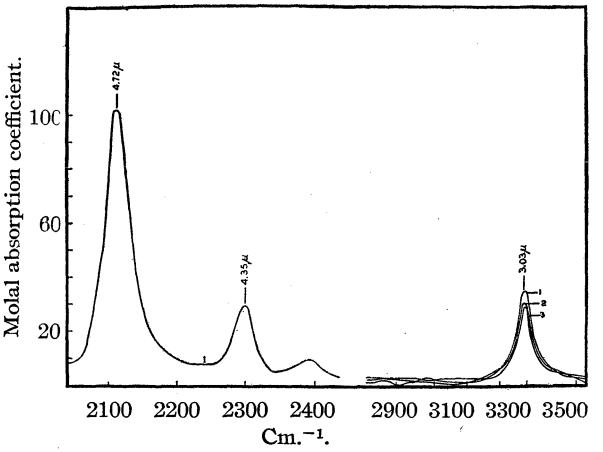


Fig. 2.—Hydrogen azide: (1) 0.34 molal in 0.3251 cm. cell; (2) 0.045 molal in 2.53 cm. cell; (3) 0.0012 molal in 10.2 cm. cell.

affected by anything except deuteration. As already has been said the non-linear character of the hydrogen azide molecule must lead to a mixing of the stretching and bending frequencies in the normal modes of vibration. In the case of chloroform absorption in this region was interpreted as an overtone of the bending frequency.[4]

It was hoped that hydrogen azide would furnish a good example of N–H → N bonding, but the acid does not show any evidence of association. This is perhaps not surprising since it contains no basic or amide nitrogen to act as donor. On the other hand, it is too strong an acid to form hydrogen bonded complexes with amines. Salt formation and precipitation result instead.

N–H → O bonding is of course to be expected and since ether has been found to be one of the best molecules for forming complexes of this type with an active hydrogen, we can be sure that the unusual solubility in ether is to be accounted for in this manner. However, we are confronted here with difficulty that because of the unusually low hydrogen frequency the rule of Venkateswaran[5] predicts that the N–H → O bonded frequency will lie under the ordinary C–H frequencies. Consequently the exact determination of the form and frequency of the hydrogen bond absorption is not possible. In Fig. 3 the curves show a marked increase in absorption in the C–H region when hydrogen azide is present and absorption at 3.19 which must have something to do with the formation of the ether complex since it is not

(4) A. M. Buswell, W. H. Rodebush and M. F. Roy, THIS JOURNAL, **60**, 2528 (1938).

(5) C. S. Venkateswaran, *Proc. Ind. Acad.*, **7**, 13 (1938).

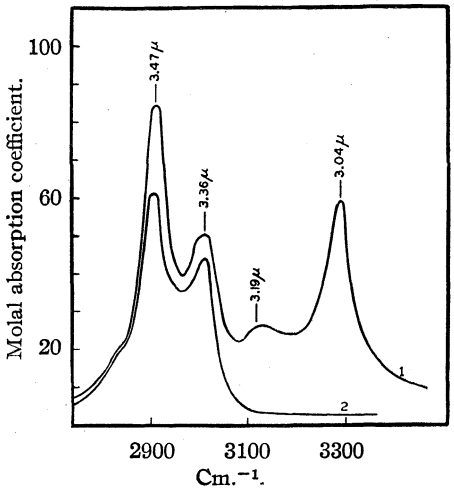


Fig. 3.—(1) 0.12 molal hydrogen azide and 0.05 molal ether in 0.325 cm. cell; (2) 0.05 molal ether in 0.325 cm. cell.

present for either constituent alone. Even more positive evidence of the formation of a complex is furnished by solutions of hydrogen azide in carbon tetrachloride saturated with water (Fig. 4). The solubility of water in carbon tetrachloride is always small but it is perhaps doubled in a dilute solution of hydrogen azide. There is evidence here both for the bonding of hydrogen azide to water and of water to hydrogen azide (or to itself). This may appear surprising in view of the low solubility of hydrogen azide in water as compared to ether but we interpret this fact as being due to the great amount of bonding between water molecules themselves in liquid water. In this figure only the logarithm absorption log I_0/I is plotted since it was not possible to determine concentrations exactly.

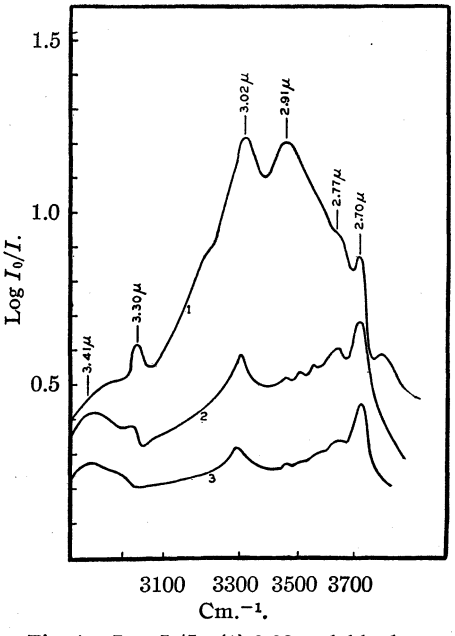


Fig. 4.—Log I_0/I: (1) 0.02 molal hydrogen azide saturated with water in 0.3251 cm. cell; (2) 0.01 molal hydrogen azide; water one-half of saturated concentration 0.640 cm. cell; (3) 0.005 molal hydrogen azide; water one-fourth of saturation concentration in 1.26 cm. cell.

Deuterium Azide.—In Fig. 5 are shown absorption curves for deuterium azide. In no case was the deuterium azide pure but always some unconverted hydrogen azide was present. Curve (1), however, may be taken as the characteristic absorption of deuterium azide. Here the deuterium frequency is found at 4.07 μ, which is about what one would calculate from the 3.03 μ frequency of hydrogen azide. (The absorption at 4.35 μ already has been shown to be characteristic of the hydrogen compound.)

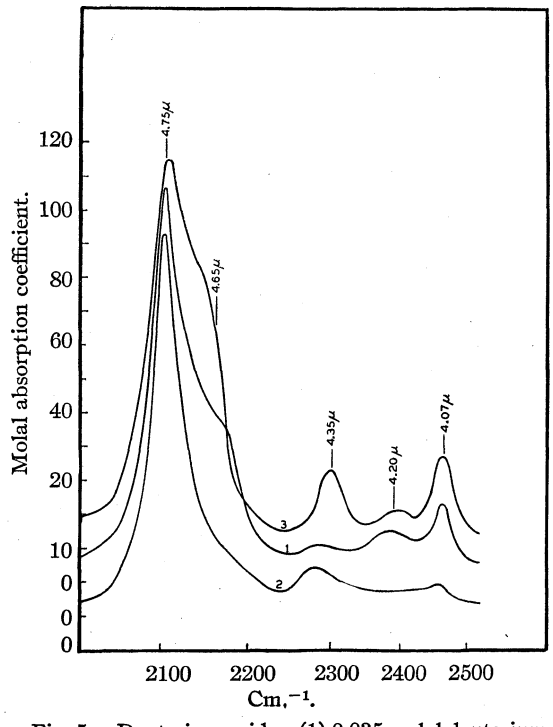


Fig. 5.—Deuterium azide: (1) 0.035 molal deuterium azide; (2) the same solution after exchange with water; (3) deuterium azide made with 85% deuterium azide.

Finally it will be noted that an absorption exists near 4.63 μ which is nearly obliterated by the N–N–N frequency which must be characteristic of the deuterium azide. This absorption suggests bonding when compared with a 3.30 μ ab-

sorption found for hydrogen azide when water was present. Since there is not enough water present to give this much absorption, one might be led to suspect N–D → N bonding as a result of association of the deuterium azide molecules. This in turn would imply that deuterium shows a stronger tendency toward bonding than hydrogen. This inference appears to be justified by a comparison of the physical properties of deuterium oxide with ordinary water.

It is evident that the hydrogen azide molecule shows a very interesting characteristic with considerable deviation from the normal behavior of hydrogen compounds. The only explanation for this behavior that we can offer is that the hydrogen is attached to a nitrogen which is part of a rigid linear group, the bond being predominantly of double bond character. There is no lack of evidence for the peculiar rigidity of the double bonded nitrogen atom. It is highly desirable that a sufficient number of frequencies be measured to make certain the assignment to the various modes of motion in order to get a clear understanding of the behavior of the hydrogen azide molecule.

The authors wish to acknowledge their indebtedness to the Rockefeller Foundation for funds which enabled them to conduct this research.

Summary

A number of frequencies have been observed for hydrogen and deuterium azides and some examples of hydrogen bonding by these molecules are shown. Certain peculiarities in the hydrogen frequencies are attributed to the non-linear character of the hydrogen azide molecule.

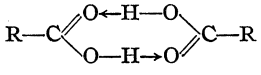
URBANA, ILLINOIS RECEIVED AUGUST 3, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Infrared Absorption Spectra of Some Carboxylic Acids and of Dibenzoylmethane and Related Molecules

BY F. T. WALL AND W. F. CLAUSSEN

Of the various molecules capable of undergoing association through hydrogen bond formation, the carboxylic acids in particular show the effect to a considerable extent. This association, which was predicted by Latimer and Rodebush[1] and first demonstrated in the case of formic acid vapor by Pauling and Brockway,[2] leads to dimers in the case of monocarboxylic acids, with the following general structure



(1)

Evidence for hydrogen bond formation can be provided in numerous ways, but one of the most convenient methods involves infrared absorption measurements. Following the pioneer work of Wulf[3] and others, considerable research has been carried out in this way. Among these investigations have been numerous studies on the infrared absorption of carboxylic acids under various conditions.[4] Those acids which have been investigated most thoroughly are formic, acetic and benzoic, both ordinary and deuterated. In this paper there will be reported results for deutero-acetic, deutero-benzoic, ordinary and deutero-propionic acids, as well as for two dibasic acids, azelaic and diethylmalonic.

The studies were all made for carbon tetrachloride solutions of the substances at room temperature. Heavy acetic acid was investigated previously (in the vapor state) by Herman and Hofstadter,[4] but with lower dispersion than employed here. Heavy benzoic acid was studied by Buswell, Rodebush and Roy,[4] but their results were not quite complete, as mentioned in an earlier note.[5]

In addition to the carboxylic acids mentioned, dibenzoylmethane, diphenylmethane and benzil have been subjects for study in this research. Dibenzoylmethane was investigated by Wulf, *et al.*,[3] in the 1.5 μ region and by Buswell, Rodebush and Roy[6] in the 3 μ region. Their results were not in agreement, however, so it was felt desirable to

(1) W. M. Latimer and W. H. Rodebush, THIS JOURNAL, **42**, 1432 (1920).

(2) L. Pauling and L. O. Brockway, *Proc. Natl. Acad. Sci. U. S.*, **20**, 336 (1934).

(3) Hilbert, Wulf, Hendricks and Liddel, THIS JOURNAL, **58**, 548 (1936).

(4) Gillette and Daniels, THIS JOURNAL, **58**, 1139 (1936); Badger and Bauer, *J. Chem. Phys.*, **5**, 839 (1937); Davis and Sutherland, *Nature*, **141**, 372 (1938); Buswell, Rodebush and Roy, THIS JOURNAL, **60**, 2239 (1938); Bonner and Hofstadter, *J. Chem. Phys.*, **6**, 531 (1938); Herman and Hofstadter, *ibid.*, **6**, 534 (1938); R. Hofstadter, *ibid.*, **6**, 540 (1938).

(5) F. T. Wall, *J. Chem. Phys.*, **7**, 87 (1939).

(6) Buswell, Rodebush and Roy, THIS JOURNAL, **59**, 1767 (1937).

repeat the study and to publish the absorption curves. The curves for diphenylmethane and benzil are included to assist in the interpretation of the dibenzoylmethane absorption although diphenylmethane was more carefully investigated by Fox and Martin and by Wall and McMillan previously.[7]

Preparation of Substances.—The deutero-acetic and -propionic acids were prepared by treating the corresponding purified anhydrides with equimolar amounts of heavy water. Deutero-benzoic acid was prepared by heating benzoyl chloride with an excess of heavy water. The excess heavy water and the deuterium chloride which formed were then removed by pumping.

Dibenzoylmethane, diphenylmethane, benzil and the dibasic acids mentioned were obtained from the stock rooms of the organic chemistry division. They were purified carefully by recrystallizing from alcohol.

Experimental

The infrared absorption measurements were made on carbon tetrachloride solutions of the substances. The technique employed has been described previously.[4d] In the case of the deutero-acids, it was necessary to take precautions to prevent the solution from coming in contact with the air, else exchange takes place with the water vapor of the air. After the absorption of a deutero-acid was measured, however, a small amount of light water was added to the solution to bring about an exchange. After the exchange had occurred, the same solutions were run again, in order to get the absorption curve for the ordinary acid, which could be compared with previous direct measurements. In this way a check could be obtained on the materials and the interpretation of the results was facilitated.

Since we were interested primarily in hydrogen or deuterium bonding, only a limited region of the spectrum was studied. The range investigated was from 2.8 to 4.9 μ, which covers the absorption due to OH and OD bonds.

TABLE I

Substance	Wave lengths of maxima, μ					
Acetic acid (deutero)		4.42		4.71	4.87	
Acetic acid (ordinary)[a]	2.82	3.30	3.39	3.71	3.78	3.89
Benzoic acid (deutero)		4.46		4.65	4.87	
Benzoic acid (ordinary)[a]		3.29	3.45	3.74	3.91	
Propionic acid (deutero)		4.40		4.72	4.85	
Propionic acid (ordinary)[a]	2.82	3.33		3.60	3.79	3.87
Diethylmalonic acid	2.82	3.23	3.33	3.44	3.77	
Azelaic acid	2.82	3.26	3.38	3.46	3.71	

[a] Obtained by exchange from deutero compound.

TABLE II

Substance	Wave length of maxima, μ			
Dibenzoylmethane		3.24[a]		3.82
Diphenylmethane		3.27[a]	3.42	3.51
Benzil	2.98	3.24[a]	3.44	

[a] Unresolved aromatic C–H absorption. For more detail in case of diphenylmethane see ref. 7.

(7) Fox and Martin, *Proc. Roy. Soc.* (London), **9**, 167, 257 (1938); Wall and McMillan, THIS JOURNAL, **61**, 1053 (1939).

Discussion of Results

The infrared absorption curves are shown in Figs. 1–5. In each case log I_0/I is plotted against wave length where I_0/I is the ratio of the intensity of light transmitted by pure solvent to that of the solution. The positions of the maxima are tabulated in Tables I and II. Although the curves for the ordinary acids were those obtained after exchanging the heavy acid with light water, they

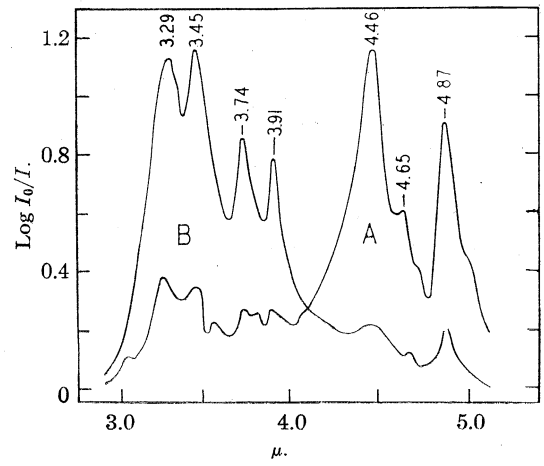


Fig. 1.—Infrared absorption curves: A, 0.032 M deuterobenzoic acid in 0.325-cm. cell; B, benzoic acid obtained by exchange from A.

are in excellent agreement with curves obtained directly from the pure substances. In the case of propionic acid the curves obtained by the two methods were so similar, the positions of maxima being in agreement to 0.01 μ, that it was not felt necessary to publish the directly obtained curve for ordinary propionic acid, although it had been run.

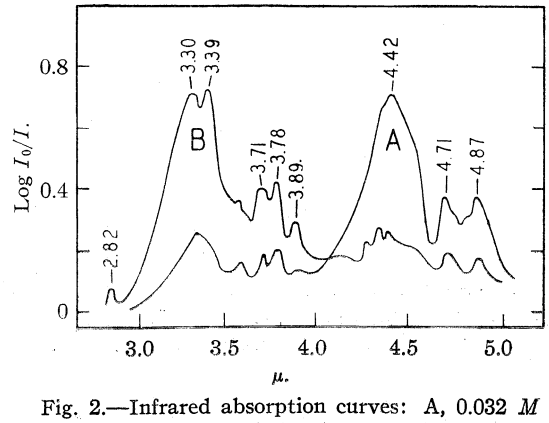


Fig. 2.—Infrared absorption curves: A, 0.032 M deuteroacetic acid in 0.325-cm. cell; B, acetic acid obtained by exchange from A.

It is apparent at a glance that considerable similarity exists between the absorption curves for

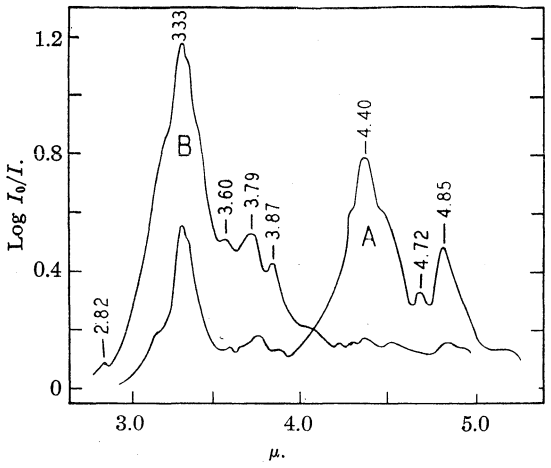


Fig. 3.—Infrared absorption curves: A, 0.04 *M* deuteropropionic acid in 0.325-cm. cell; B, propionic acid obtained by exchange from A (this curve is the same as that obtained by starting with pure ordinary acid).

acetic, benzoic and propionic acids, both heavy and light. This can be attributed to the common linkage indicated by (1). The most noticeable difference is the extra height of the 3.33 μ peak of propionic acid. This is due to the fact that the fundamental CH and OH absorptions overlap as suggested by Buswell, Dietz and Rodebush.[8] Since propionic acid has an extra CH_2 group, and accordingly has its methyl groups bent off to destroy much of the symmetry present in the acetic acid dimer, its CH absorption will be increased.

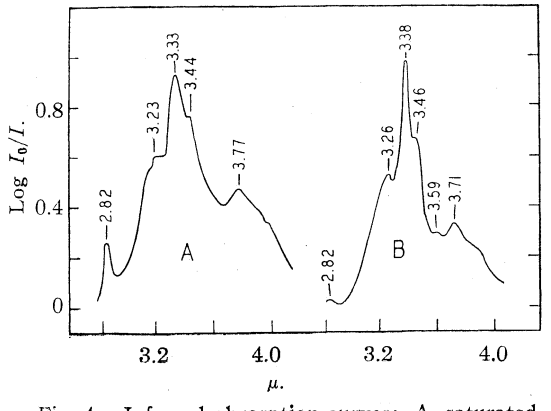


Fig. 4.—Infrared absorption curves: A, saturated solution of diethylmalonic acid in 10.18-cm. cell; B, saturated solution of azelaic acid in 10.18-cm. cell.

Although an exact interpretation of the results is difficult, the following conclusions can be arrived at from examination of the curves. For the three acids, acetic, propionic and benzoic, the absorption between 3.2 and 4.0 μ (aside from the CH mentioned above) is due principally to the hydrogens of the hydrogen bonds. This follows because of the fact that deuteration cuts down the absorption to such a great extent.

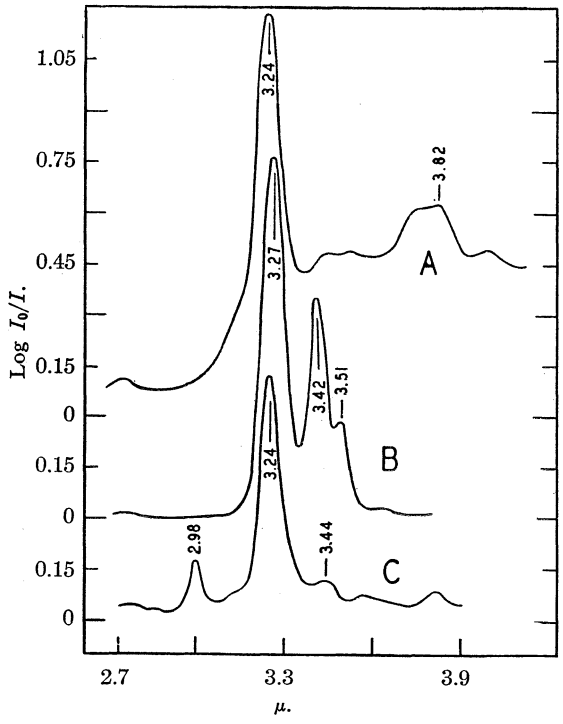


Fig. 5.—Infrared absorption curves, all 0.016 *M* in 2.53-cm. cell: A, dibenzoylmethane; B, diphenylmethane; C, benzil.

The four peaks of benzoic acid can be regarded as two doublets, each split as a result of some internal effects. These internal effects may arise from the double minima in the potential energy system. Upon deuteration the mean wave lengths of the doublets are shifted by a factor of about 1.3, which is close to the square root of the reduced mass ratio for hydrogen and deuterium vibrating against an oxygen atom. In addition a small intermediate peak appears, which is difficult to explain. The deutero compound does not show the well-defined double splitting, which fact might be expected from mass considerations if the splitting were due to the double minima.

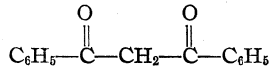
Although acetic and propionic acids do not give curves identical with that for benzoic acid, they doubtless behave much as benzoic acid does. The biggest difference between the various deutero curves is found in the relatively high intermediate absorption at 4.71 μ for deuteroacetic acid. In

(8) Buswell, Dietz and Rodebush, *J. Chem. Phys.*, **5**, 84, 501 (1937).

any case, the absorption between 4.3 and 4.9 μ can be attributed to deuterium bonds.

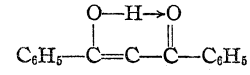
The lower dibasic acids were quite insoluble in carbon tetrachloride, but diethylmalonic and azelaic acids were sufficiently soluble to get the curves shown in Fig. 4. These curves are quite similar to the one for propionic acid. The abnormal heights of the 3.33 and 3.38 μ maxima are due, as for propionic acid, to the superposition of CH absorption upon that for the hydrogen bonds. The dibasic acids offer the possibility of forming monomolecular hydrogen bonded rings as well as dimers or even polymers. Unfortunately the data are not sufficient to tell precisely what is taking place, except that considerable hydrogen bonding does occur.

From the formulas for dibenzoylmethane ($C_6H_5COCH_2COC_6H_5$), diphenylmethane ($C_6H_5CH_2C_6H_5$) and benzil ($C_6H_5COCOC_6H_5$), one would expect certain similarities in their absorption spectra. All three compounds give the characteristic aromatic CH absorption in the neighborhood of 3.24 μ. The aliphatic CH absorption for diphenylmethane is easily accounted for,[7] but the broad absorption of the dibenzoylmethane near 3.8 μ needs some other explanation. It is evident that the aliphatic hydrogens of the conventional structure



(2)

have undergone some change. A plausible explanation is that advanced by Hilbert, Wulf, Hendricks and Liddel,[3] who suggested enolization followed by hydrogen bonding to give the structure



(3)

Since no fundamental OH absorption is observed, the hydrogen bonding of the enol must be complete. Benzil, on the other hand, cannot enolize and accordingly does not show the same absorption.

The authors are indebted to Professors W. H. Rodebush and A. M. Buswell for helpful suggestions and criticism.

Summary

The infrared absorption spectra for ordinary and deuterated acetic, benzoic and propionic acid have been investigated in the "hydrogen bond" region and the results interpreted on the basis of their structures. Likewise the absorption for diethylmalonic and azelaic acids has been studied and discussed. Infrared absorption measurements for dibenzoylmethane (and related molecules) suggest that dibenzoylmethane undergoes enolization followed by hydrogen bonding.

URBANA, ILLINOIS RECEIVED AUGUST 7, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

The Structure of Monocrotaline, the Alkaloid in *Crotalaria Spectabilis* and *Crotalaria Retusa*. I

BY ROGER ADAMS AND E. F. ROGERS

Crotalaria is a genus of leguminous plants, many species of which are commonly used in the southern part of the United States as soil-enriching legumes. *Crotalaria spectabilis* is perhaps the most important. Like many species of *Crotalaria* it is toxic and its toxicity has been shown to be due to an alkaloid monocrotaline.[1a] The same alkaloid has now been found also in the seed of the *Crotalaria retusa*.[1b]

(1) (a) Neal, Rusoff and Ahmann, THIS JOURNAL, **57**, 2560 (1935). (b) Greshoff, *Ber.*, **23**, 3537 (1890). The *Crotalaria spectabilis* strain grown in Florida and southern Georgia is toxic to chickens and larger animals. On the other hand, in South Carolina the seed of the early strain of *Crotalaria spectabilis* is non-toxic to blackbirds and partridge. Whether these birds are resistant to the alkaloid or whether the strain as grown in South Carolina contains no alkaloid or a different non-toxic alkaloid is now being studied.

Neal, Rusoff and Ahmann[1a] extracted monocrotaline from crushed seed by means of aqueous ammonia and reported a tentative formula of $C_{16}H_{26}O_6N$. The extraction proceeded much more smoothly, however, and the yields were improved several fold if ethanol was used as a solvent. A careful analysis of pure monocrotaline, its hydrochloride and methiodide revealed the molecular formula to be not that previously suggested but $C_{16}H_{23}O_6N$. Such a formula resembles closely those of the *Senecio*, *Heliotropium* and *Trichodesma* alkaloids, characteristic for which is alkaline hydrolysis to an acid and an alkanolamine. Hydrolysis of monocrotaline confirmed this supposition for cleavage yielded a basic product

which proved to be retronecine, the base obtained by hydrolysis of several of the *Senecio* alkaloids and an acid, $C_7H_{12}O_3$, monocrotic acid.

$$C_{16}H_{23}O_6N + H_2O(BaO_2H_2) \longrightarrow C_8H_{13}O_2N + C_7H_{12}O_3 + [CO_2]$$

From the above equation, it is obvious that carbon dioxide has been lost in the reaction due, presumably, to decomposition of the acid present in the monocrotaline.

Another mode of cleavage[2] successful on analogous alkaloids has been by hydrogenolysis. In those alkaloids previously studied which gave retronecine on hydrolysis, reduction gave retronecanol which has one less hydroxyl than retronecine and no olefin linkage. The acid part of the molecule unless containing an olefin linkage remained unaffected. Monocrotaline was readily reduced to retronecanol and an acid which will be designated as monocrotalic acid since it is presumably the acid present in the form of an ester in the alkaloid.

$$C_{16}H_{23}O_6N + 2H_2 \longrightarrow C_8H_{15}ON + C_8H_{12}O_5$$

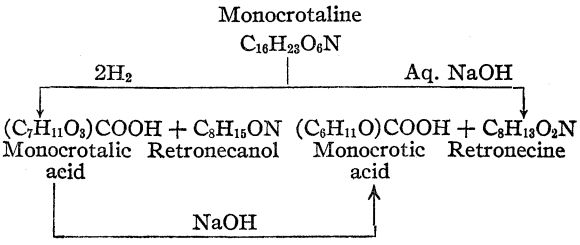
A mixed melting point of retronecine from monocrotaline with authentic retronecine, kindly furnished by Dr. R. H. F. Manske, gave no depression. A table showing the properties of retronecine and retronecanol from monocrotaline in comparison with those of the bases isolated from other sources is given below.

TABLE I

CONSTANTS ON ALKANOLAMINES FROM MONOCROTALINE

Alkanolamine	M. p., ° C.	Rot. $[\alpha]_D$	Alkanolamines from monocrotaline M. p.	Rot.	Solvent for rotation
Retronecine[2b]	121–122	+50.2	121	+49.3	Ethanol
Retronecine hydrochloride[2b]	161	−16.0	161–162	−15.4	Ethanol
Retronecine diac. picrate[2b]	146		146		
Retronecanol[3]	98–99 (92–93)		95–96	−91.1	Ethanol
Retronecanol hydrochloride			210		
Retronecanol methiodide[2b]			193	−52.8	Methanol
Retronecanol picrate	208 (211)		210		

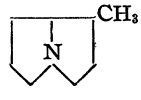
Monocrotalic acid is optically active. Direct titration indicates it to be monobasic but by addition of excess alkali and back titration, a higher neutral equivalent is found, strongly indicating the presence of a lactone linkage. It forms a *p*-bromophenacyl ester. By heating monocrotalic acid with alkali, decomposition occurs and a liquid monobasic acid, $C_7H_{12}O_3$, monocrotic acid, results. This acid is identical with that obtained by alkaline hydrolysis of the original alkaloid. It is optically inactive, monobasic, and forms a *p*-bromophenacyl ester. The transformations just discussed may be tabulated



The structure of the $C_6H_{10}O$ residue in monocrotic acid is now being studied.

The acid portions of the *Senecio*, *Heliotropium*, and *Trichodesma* alkaloids have received very limited examination. The facts that are known about them, however, lead us to believe that it is doubtful whether they are so dissimilar in constitution as expressed by a reviewer of the work in this field.[4] The acids are unknown in structure except *dl*-lactic acid, which is probably a degradation product of the acid occurring in the alkaloid trichodesmine, and angelic acid which is possibly a degradation product of the acid occurring in the alkaloid lasiocarpine.

The knowledge of the most commonly occurring base, retronecine, or the other very closely related bases is still limited. Menshikov[2a,5] has established the probable structure of the nucleus present in these bases as a methylpyrrolizidine



but no evidence is as yet available which will place the hydroxyls and olefin linkage.

A large number of alkaloids with different acids and identical or very similar bases has been shown to occur in four genera of plants, the *Senecio*, *Trichodesma*, *Heliotropium* and recently *Erechtites* to which must now be added a fifth genus, the *Crotalaria*. The relationship between the alkaloids now known is shown in the following table.

(2) (a) Menshikov, *Ber.*, **68**, 1051 (1935); (b) Barger, Seshadri, Watt and Yabuta, *J. Chem. Soc.*, 11 (1935).

(3) (a) Menshikov and Rubinstein, *Ber.*, **68**, 2039 (1935); (b) Konovalova and Orekhov, *Bull. soc. chim.*, [5] **4**, 1285 (1937).

(4) Haworth, *Ann. Reports Chem. Soc. London*, 329 (1938).

(5) Menshikov and co-workers, *Ber.*, **65**, 974 (1932); **66**, 875 (1933); **68**, 1555 (1935); **69**, 1799, 1802 (1936); *J. Gen. Chem. (U. R. S. S.)*, **7**, 1632 (1937); *Bull. Acad. Sci. (U. R. S. S.) Classe Sci. Math. Ser. Chim.*, **5**, 1035 (1937).

TABLE II

KNOWN ALKALOIDS OF THE ACID-ALKANOLAMINE TYPE

	Alkaloid	Alkanolamines	Acid
Crotalaria			
spectabilis[1a]	Monocrotaline, $C_{16}H_{23}O_6N$	Retronecine, $C_8H_{13}O_2N$	Monocrotalic, $C_8H_{12}O_5$
retusa[1b]	Monocrotaline, $C_{16}H_{23}O_6N$	Retronecine, $C_8H_{13}O_2N$	Monocrotalic, $C_8H_{12}O_5$
Trichodesma incanum[3a]	Trichodesmine, $C_{18}H_{27}O_6N$	Retronecine	*dl*-Lactic and isobutyl methyl ketone
Senecio			
cineraria[6]	Jacobine, $C_{18}H_{25}O_6N$	Retronecine	Jaconecic, $C_{10}H_{16}O_6$
jacobaea[6a,7]	Jacobine, $C_{18}H_{25}O_6N$	Retronecine	Jaconecic, $C_{10}H_{16}O_6$
	Jaconine, $C_{18}H_{25}O_8N$	.....	.....
	Jacodine, $C_{18}H_{25}O_5N$	.....	.....
aquaticus[6b]	Jacodine, $C_{18}H_{25}O_5N$	.....	.....
vulgaris[8]	Senecine, ...	.....	.....
	Senecionine, $C_{18}H_{25}O_5N$	Retronecine	Senecic, $C_{10}H_{14}O_4$
viscosus[8b]	Senecionine, $C_{18}H_{25}O_5N$	Retronecine	Senecic, $C_{10}H_{14}O_4$
aureus[6a,7a,13,14]	Senecionine, $C_{18}H_{25}O_5N$	Retronecine	Senecic, $C_{10}H_{14}O_4$
squalidus[8b]	Senecionine, $C_{18}H_{25}O_5N$	Retronecine	Senecic, $C_{10}H_{14}O_4$
	Squalidine, $C_{18}H_{25}O_5N$	Retronecine	Squalinecic, $C_{10}H_{14}O_4$ or $C_{10}H_{18}O_5$
stenocephalus[9]	Seneciphylline, $C_{18}H_{23}O_5N$	Retronecine	Seneciphyllic, $C_{10}H_{14}O_5$
platyphyllus[9,10]	Seneciphylline, $C_{18}H_{23}O_5N$	Retronecine	Seneciphyllic, $C_{10}H_{14}O_5$
	Platyphylline, $C_{18}H_{25}O_5N$	Platynecine, $C_8H_{15}O_2N$	Platynecic, $C_{10}H_{14}O_4$
retrorsus[2b,7a]	Retrorsine, $C_{18}H_{25}O_6N$	Retronecine	Retronecic, $C_{10}H_{16}O_6$
glaberrimus[6b]	Retrorsine, $C_{18}H_{25}O_6N$	Retronecine	Retronecic, $C_{10}H_{16}O_6$
venosus[6b]	Retrorsine, $C_{18}H_{25}O_6N$	Retronecine	Retronecic, $C_{10}H_{16}O_6$
isatideus[6b]	Retrorsine, $C_{18}H_{25}O_6N$	Retronecine	Retronecic, $C_{10}H_{16}O_6$
	Isatidine, $C_{18}H_{25}O_7N$	Isatinecine, $C_8H_{13}O_3N$	Isatinecic, $C_{10}H_{16}O_6$
erucifolius[6b]	....., $C_{18}H_{27}O_5N$	.....	.....
palustris[6b]	....., $C_{18}H_{27}O_5N$	.....	.....
latifolius[2b,11]	Senecifoline, $C_{18}H_{27}O_8N$	(Senecifolinine, $C_8H_{11}O_2N$)?	Senecifolic, $C_{10}H_{16}O_6$
	Senecifolidine, $C_{18}H_{25}O_7N$	.....	.....
mikanoides[8a]	Mikanoidine, $C_{21}H_{29}O_6N$	(Mikanecine, $C_8H_{15}O_2N$)?	Mikanecic acid, $C_{13}H_{16}O_5$
Heliotropium			
lasiocarpum[2a,5,12]	Heliotrine, $C_{16}H_{27}O_5N$	Heliotridine, $C_8H_{13}O_2N$	Heliotrinic, $C_8H_{16}O_4$
	Lasiocarpine, $C_{21}H_{33}O_7N$	Heliotridine, $C_8H_{13}O_2N$	Lasiocarpinic, $C_8H_{16}O_5$ and angelic

Experimental

Extraction of Monocrotaline from *Crotalaria spectabilis*.—Two kilograms of Florida grown *Crotalaria spectabilis* seed ground to 16-mesh was extracted continuously for seventy-two hours with 95% ethanol. The green-black solution was acidified to congo paper with citric acid, the solvent removed *in vacuo*, and the residue taken up in 400 cc. of water. The suspended fat was extracted with successive portions of ether until the ether extracts were colorless, then with two 100-cc. portions of chloroform. The aqueous solution was now treated with 200 cc. of chloroform and saturated aqueous sodium carbonate solution added with shaking, until the solution was distinctly alkaline to litmus. The color of the solution during this operation changes from a dull yellow-brown to a golden-yellow. The alkaloid was then extracted with two additional portions of 200 cc. and three portions of 100 cc. of chloroform. The combined chloroform extracts were evaporated to dryness *in vacuo* and the crude alkaloid obtained as a yellowish-white crystalline mass. It was purified by two crystallizations from absolute ethanol: white prisms, m. p., 197–198° (corr.) with decomposition; yield, 65 g. (3.2%).

Anal. Calcd. for $C_{16}H_{23}O_6N$: C, 59.06; H, 7.12; N, 4.30. Found: C, 59.14, 59.16; H, 7.05, 7.17; N, 4.42, 4.36.

Rotation. 0.5054 g. made up to 10 cc. in chloroform at 26°. α_D −5.54; *l*, 2; $[\alpha]^{26}D$ −54.7°.

The alkaloid does not react with nitrous acid. Methylimide and methoxyl determinations were negative.

No evidence indicating the presence of any other alkaloid could be secured either by fractional crystallization from absolute ethanol or fractional neutralization and extraction of a hydrochloric acid solution of the alkaloid.

Monocrotaline Hydrochloride.—The base was dissolved in ethanol and neutralized to congo paper with dilute hydrochloric acid. The solution was then evaporated to dryness, the hydrochloride taken up in the minimum

(6) (a) Barger and Blackie, *J. Chem. Soc.*, 584 (1937); (b) Blackie, *Pharm. J.*, **138**, 102 (1937).

(7) (a) Manske, *Can. J. Research*, **5**, 651 (1931); (b) Hosking and Brandt, *New Zealand J. Sci. Tech.*, **17**, 638 (1936).

(8) (a) Manske, *Can. J. Research*, **14**, 6 (1936); (b) Barger and Blackie, *J. Chem. Soc.*, 743 (1936); (c) Grandval and Lajoux, *Compt. rend.*, **120**, 1120 (1895); *Bull. soc. chim.*, [3] **13**, 942 (1895).

(9) Konovalova and Orekhov, *ibid.*, [5] **4**, 2037 (1937).

(10) Orekhov and Tiedebel, *Ber.*, **68**, 650 (1935); Orekhov, Konovalova and Tiedebel, *ibid.*, **68**, 1886 (1935).

(11) Watt, *J. Chem. Soc.*, **95**, 466 (1909).

(12) Menshikov and Shdanovich, *Ber.*, **69**, 1110 (1936).

(13) Manske, *Can. J. Research*, **17B**, 1 (1939).

(14) Manske, *ibid.*, **17B**, 8 (1939).

amount of hot methanol and ether added to turbidity. On cooling, the product crystallized: white prisms, m. p. 184° (corr.) with decomposition.

Anal. Calcd. for $C_{16}H_{23}O_6N\cdot HCl$: C, 53.11; H, 6.69; Cl, 9.79. Found: C, 53.22; H, 6.69; Cl, 9.87.

Rotation. 1.30 g. made up to 25 cc. in water at 28°. α_D −4.00; *l*, 2; $[\alpha]^{28}D$ −38.4°.

Monocrotaline Methiodide.—To a solution of 1 g. of monocrotaline in 10 cc. of chloroform and 1 cc. of methanol was added 2 cc. of methyl iodide. The oily methiodide which separated crystallized on cooling. Recrystallization from methanol–chloroform gave white prisms, m. p. 205° (corr.) with decomposition.

Anal. (Dried *in vacuo*.) Calcd. for $C_{16}H_{23}O_6N\cdot CH_3I$: C, 43.69; H, 5.61; I, 27.16. Found: C, 43.62; H, 5.54; I, 27.02. (Undried.) Calcd. for $C_{16}H_{23}O_6N\cdot CH_3I\cdot 3CH_3OH$: CH_3OH, 17.07. Found: CH_3OH, 17.11.

Rotation. (Dried sample.) 0.310 g. made up to 10 cc. in methanol at 28°. α_D +1.45; *l*, 2; $[\alpha]^{28}D$ +23.4°.

Extraction of Monocrotaline from *Crotalaria retusa*.—Extraction of 200 g. of *Crotalaria retusa* seed by the procedure described above for isolation of monocrotaline from *Crotalaria spectabilis* gave 3.77 g. (1.89%) of product, recrystallized from absolute ethanol. It proved to be monocrotaline as shown by m. p. 197–198° with decomposition, and rotation, as well as by the melting points of the hydrochloride, 185°, and of the methiodide, 205°.

Anal. (Base.) Calcd. for $C_{16}H_{23}O_6N$: C, 59.06; H, 7.12; N, 4.30. Found: C, 58.89; H, 7.05; N, 4.20.

Rotation. 1.05 g. made up to 25 cc. in chloroform at 28°. α_D −4.68; *l*, 2; $[\alpha]^{28}D$ −55.7°.

Anal. (Hydrochloride.) Calcd. for $C_{16}H_{23}O_6N\cdot HCl$: Cl, 9.79. Found: Cl, 9.80. (Methiodide.) Calcd. for $C_{16}H_{23}O_6N\cdot CH_3I$: I, 27.16. Found: I, 26.89.

Alkaline Hydrolysis of Monocrotaline

A. Monocrotic Acid, $C_7H_{12}O_3$.—A mixture of 20 g. of monocrotaline and 40 g. of barium hydroxide octahydrate in 250 cc. of water was refluxed for one hour. After cooling, the solution was saturated with carbon dioxide and the barium carbonate filtered. The filtrate was made just acid to congo and then submitted to continuous extraction with ether for twelve hours. The ether extract was dried over anhydrous sodium sulfate, the ether removed, and the residue distilled *in vacuo*. A second distillation gave a pure product, b. p. 145–146° (18 mm.); $n^{17.5}D$ 1.4449; d^{26}_4 1.072; yield, 4.2 g. (48%).

Anal. Calcd. for $C_7H_{12}O_3$: C, 58.31; H, 8.39: Found: C, 58.26; H, 8.37.

The neutral equivalent of this product always ran from 5–7% high for a monobasic acid. Undoubtedly this was due to presence of a few per cent. of anhydro compound formed during the distillation. The compound shows no optical rotation.

***p*-Bromophenacyl Ester of Monocrotic Acid.**—This was prepared from monocrotic acid by the usual procedure. It was purified from aqueous ethanol: white needles, m. p. 78°.

Anal. Calcd. for $C_{15}H_{17}O_4Br$: C, 52.79; H, 5.02. Found: C, 53.0; H, 5.25.

B. Base Hydrochloride, $C_8H_{13}O_2N\cdot HCl$.—The aqueous solution obtained after ether extraction of the acid just described was evaporated *in vacuo* to dryness. The sirup thus obtained was dissolved in about 100 cc. of absolute ethanol, and the solvent removed by evaporation. A crystalline mass thus resulted which was extracted with three 30-cc. portions of boiling absolute ethanol to free from barium salts. The combined ethanolic extracts were concentrated to about 20 cc. and allowed to cool. The salt separated and the filtrate yielded an additional amount by addition of a little ether. It was recrystallized from absolute ethanol: white prisms, m. p. 161–162° (corr.); yield, 10.3 g. (87%).

Anal. Calcd. for $C_8H_{13}O_2N\cdot HCl$: C, 50.11; H, 7.36 Cl, 18.51. Found: C, 50.43; H, 7.22; Cl, 18.77.

Rotation. 1.20 g. made up to 25 cc. in ethanol at 25°. α_D −1.48; *l*, 2; $[\alpha]^{25}D$ −15.4°.

Retronecine Base.—A solution of the base hydrochloride in water was treated with one equivalent of *N* aqueous sodium hydroxide. It was then evaporated to dryness *in vacuo*. The oily residue was extracted with hot dry acetone, from which, after concentration and cooling, the crystalline base separated; purified from dry acetone: white irregular prisms, m. p. 121°. A mixed melting point with an authentic sample kindly furnished by Dr. R. H. F. Manske of the National Research Council of Canada, Ottawa, showed no depression.

Anal. Calcd. for $C_8H_{13}O_2N$: C, 61.91; H, 8.44. Found: C, 61.80; H, 8.46.

Rotation. 1.3316 g. made up to 25 cc. in ethanol at 28°. α_D +5.25; *l*, 2; $[\alpha]^{28}D$ +49.3°.

Diacetylretronecine Picrate.—The base was acetylated according to the directions of Barger[2b] for retronecine and the picrate formed by his procedure: yellow prisms, m. p. 146° (corr.).

Anal. (Dried at 100°.) Calcd. for $C_8H_{11}O_2N(OCCH_3)_2\cdot C_6H_3O_7N_3$: N, 11.95: Found: N, 11.5.

Hydrogenolysis of Monocrotaline

Monocrotalic Acid, $C_8H_{12}O_5$.—A solution of 10.8 g. of monocrotaline in a mixture of 10 cc. of glacial acetic acid and 40 cc. of ethanol was hydrogenated at 2–3 atm. with 0.1 g. of platinum oxide catalyst. In about five hours two moles of hydrogen had been absorbed and the reduction was complete. The solution was filtered from the catalyst and evaporated *in vacuo*. The remaining sirup was taken up in 34 cc. of *N* hydrochloric acid and the aqueous solution thus obtained extracted continuously with ether for twenty-four hours. The ether solution was dried over anhydrous sodium sulfate, the solvent removed *in vacuo*, and the crystalline acid thus obtained was purified by recrystallization from acetone–petroleum ether (b. p. 30–60°): white plates, m. p. 181–182° (corr.).

Anal. Calcd. for $C_8H_{12}O_5$: C, 51.06; H, 6.43; neut. equiv., 188. Found: C, 51.06, 51.11; H, 6.43, 6.34; neut. equiv., 190.

Rotation. 1.1734 g. made up to 25 cc. in water at 28°. α_D −0.50; *l*, 2; $[\alpha]^{28}D$ −5.33.

If excess alkali is used in the determination of the neutral equivalent followed by back titration, values corresponding to between one and two carboxyls are obtained.

p-Bromophenacyl Ester of Monocrotalic Acid.—This was prepared by refluxing 0.68 g. of monocrotalic acid, exactly neutralized with alkali, with 1 g. of *p*-bromophenacyl bromide in 50% ethanol for five hours. The product was purified from ethanol: white crystals, m. p. 162–163° (corr.); yield, 0.47 g. (34%).

Anal. Calcd. for $C_{16}H_{17}O_6Br$: C, 49.87; H, 4.42. Found: C, 49.66; H, 4.46.

Rotation. 0.142 g. made up to 3.74 cc. in ethanol at 30.5°. α_D −1.07; *l*, 2; $[\alpha]^{30.5}D$ −14.1°.

Retronecanol, $C_8H_{15}ON$.—After extraction with ether of the acid just described, the aqueous solution was clarified with norite, filtered and made strongly alkaline with sodium hydroxide. It was then extracted with five 50-cc. portions of ether. The ether extracts were dried with anhydrous sodium carbonate and the ether removed *in vacuo*. The oily basic residue quickly solidified. It was best purified by distillation, 140° (30 mm.): white crystals, m. p. 95–96°.

Anal. Calcd. for $C_8H_{15}ON$: C, 68.04; H, 10.70; N, 9.91. Found: C, 67.90; H, 10.50; N, 10.09.

Rotation. 1.524 g. made up to 25 cc. in ethanol at 28°. α_D −11.0; *l*, 2; $[\alpha]^{28}D$ −91.1°.

Retronecanol Hydrochloride.—This product was prepared from retronecanol in the same manner as described for retronecine hydrochloride: white prisms from methanol–ether, m. p. 210° (corr.) with decomposition.

Anal. Calcd. for $C_8H_{15}ON \cdot HCl$: C, 54.03; H, 9.07. Found: C, 54.14; H, 9.14.

Retronecanol Methiodide.—This product was prepared by treating a dry ether solution of the base with the calculated amount of methyl iodide. It was purified from methanol–ether: white plates, m. p. 193° (corr.) with decomposition.

Anal. (Dried at 100°.) Calcd. for $C_8H_{15}ON \cdot CH_3I$: I, 44.88. Found: I, 45.22.

Rotation. 0.473 g. made up to 10 cc. in methanol at 27°. α_D −5.00; *l*, 2; $[\alpha]^{27}D$ −52.8.

Retronecanol Picrate.—The picrate was prepared in aqueous solution and was purified from water: thin yellow plates, m. p. 210° (corr.).

Anal. Calcd. for $C_8H_{15}ON \cdot C_6H_3O_7N_3$: N, 15.13. Found: N, 14.93.

Alkaline Degradation of Monocrotalic Acid to Monocrotic Acid.—A mixture of 5 g. of monocrotalic acid and 30 cc. of 10% aqueous sodium hydroxide was heated under reflux for one hour. The solution was then acidified and extracted rapidly with ether. After drying the ether solution over anhydrous sodium sulfate, the solvent was removed and the product distilled, b. p. 145–147° (20 mm.), d^{26}_4 1.072; $n^{19}D$ 1.4480.

Anal. Calcd. for $C_7H_{12}O_3$: C, 58.31; H, 8.39. Found: C, 58.66; H, 8.39.

The acid gave a *p*-bromophenacyl ester, m. p. 78°, identical with that from monocrotic acid obtained directly from the monocrotaline.

Summary

The alkaloid, monocrotaline, is extracted by ethanol in good yields from *Crotalaria spectabilis* or *Crotalaria retusa*. It has the formula $C_{16}H_{23}O_6N$ and resembles the alkaloids occurring in various species of *Senecio, Heliotropium, Trichodesma* and *Erechtites*.

Monocrotaline undergoes alkaline hydrolysis to retronecine, $C_8H_{13}O_2N$, and an optically inactive, monobasic acid, $C_7H_{12}O_3$, called monocrotic acid. By hydrogenolysis monocrotaline gives retronecanol, $C_8H_{15}ON$, and an acid designated as monocrotalic acid, $C_8H_{12}O_5$.

It has been shown that monocrotalic acid is optically active, monobasic, and upon treatment with alkali gives the optically inactive acid, monocrotic acid, $C_7H_{12}O_3$, obtained by alkaline hydrolysis of the alkaloid.

URBANA, ILLINOIS RECEIVED JULY 20, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Structure of Monocrotaline. II. Monocrotic Acid Obtained by Alkaline Hydrolysis of the Alkaloid[1]

BY ROGER ADAMS, E. F. ROGERS AND F. J. SPRULES[2]

By alkaline hydrolysis of monocrotaline, the alkaloid present in the seed of the *Crotalaria spectabilis* and *Crotolaria retusa*, there were obtained retronecine and an acid, $C_7H_{12}O_3$, called monocrotic acid.

$$C_{16}H_{23}O_6N + H_2O(BaO_2H_2) \longrightarrow \underset{\text{Retronecine}}{C_8H_{13}O_3N} + \underset{\text{Monocrotic acid}}{C_7H_{12}O_3} + [CO_2]$$

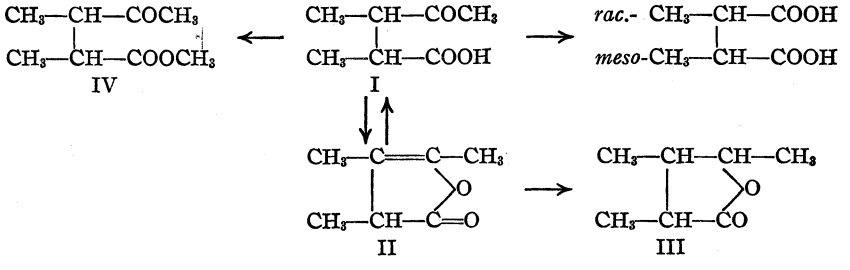
The same acid resulted when monocrotalic acid, $C_8H_{12}O_5$, obtained by hydrogenolysis of monocrotaline, was treated with aqueous alkali.

Monocrotic acid is optically inactive. It is monobasic and forms a monomethyl ester with diazomethane. The character of the third oxygen was determined by condensation of the methyl ester with dinitrophenylhydrazine. A hydrazone was formed in 85% yield and, since the ester shows no reducing action with Tollens' reagent or Feh-

(1) For previous paper see, Adams and Rogers, THIS JOURNAL, **61**, 2815 (1939).

(2) An abstract of a portion of a thesis submitted in partial fulfilment of the requirements for the Degree of Doctor of Philosophy.

ling's solution, the presence of a ketone group was assumed. The action of iodine and alkali on the acid gave iodoform, thus indicating a CH_3CO- group. Oxidation with sodium hypobromite resulted in a mixture of two products which proved to be *meso* and racemic α,α'-dimethylsuccinic acids, identified by comparison with authentic samples. Certain derivatives also were compared and shown to be identical. On the basis of these data the structural formula of monocrotic acid may be postulated as α,β-dimethyllevulinic acid (I).



Monocrotic acid (I) on heating at atmospheric pressure loses water to give a neutral substance, $C_7H_{10}O_2$, which is reconverted to the acid by hydrolysis. Undoubtedly this is a lactone (II), and its formation may be explained by the loss of water between the enol form of the ketone group and the carboxyl, a reaction characteristic of γ-ketonic acids. Moreover, the lactone (II) was shown to be unsaturated by catalytic reduction to the saturated lactone (III). The lactone (II) also gave a positive test with Legal's reagent and Tollens' reagent, which is characteristic of β,γ-unsaturated γ-lactones.[3]

The formation of approximately an equal mixture of *meso* and racemic α,α'-dimethylsuccinic acids by hypobromite oxidation may be due to rearrangements taking place during the reaction, or it may be due to the fact that diastereoisomers exist in the monocrotic acid which cannot be separated by distillation. The former possibility is favored, since methyl monocrotate gives an 85% yield of pure dinitrophenylhydrazone. The clarification of this point must await synthesis.

Experimental

Methyl Monocrotate.—Pure monocrotic acid[1] was treated in ether solution with excess diazomethane, b. p. 94–96° (18 mm.); $n^{25}D$ 1.4273: $d^{25.5}_4$ 0.9968; yield 90%.

Anal. Calcd. for $C_8H_{14}O_3$: C, 60.75; H, 8.93. Found: C, 60.63; H, 8.77.

(3) Jacobs and Hoffman, *J. Biol. Chem.*, **61**, 333 (1925).

Esterification of monocrotic acid with methanol and sulfuric acid gave the same product in somewhat lower yields.

Methyl Monocrotate 2,4-Dinitrophenylhydrazone.—A mixture of 2 cc. of methyl monocrotate and 2.64 g. of 2,4-dinitrophenylhydrazine in 100 cc. of methanol was heated to boiling, 1 cc. of concentrated hydrochloric acid was added and the solution, after five minutes of refluxing, was allowed to cool. The orange crystals which separated were pure and the melting point did not change by recrystallization; m. p. 95–96°; yield, 3.63 g. (85%).

Anal. Calcd. for $C_{14}H_{18}O_6N_4$: C, 49.70; H, 5.36. Found: C, 49.42; H, 5.31.

Iodoform Reaction and Hypobromite Oxidation of Monocrotic Acid

***Meso* and Racemic α,α'-Dimethylsuccinic Acids.**—From 1 g. of monocrotic acid dissolved in 13 cc. of 10% aqueous sodium hydroxide and treated with 35 cc. of a solution containing 10 g. of iodine and 20 g. of potassium iodide per 80 cc. of water, 0.157 g. of iodoform was isolated, m. p. 119°.

A solution of 5 g. of monocrotic acid in 30 cc. of water was made slightly alkaline with potassium hydroxide and cooled to 0°. A potassium hypobromite solution prepared by dissolving 18 g. of potassium hydroxide and 10 g. of bromine in 225 cc. of water was then added dropwise. The reaction mixture was stirred vigorously and maintained at 0° during the addition. After one and one-half hours at 0°, the solution was allowed to warm to room temperature, then concentrated to half its volume, acidified and extracted with ether. Upon evaporation of the ether, 4.6 g. of a yellow oily solid was obtained. This was dissolved in boiling water, treated with norite, then concentrated to 20 cc. and cooled. This caused 1.75 g. of an acid to separate which, after further purification from water, formed white crystals, m. p., 203–204° (the exact value depending upon the rate of heating). This compound gave no depression in a mixed melting point determination with authentic *meso*-α,α'-dimethylsuccinic acid.

Anal. Calcd. for $C_6H_{10}O_4$: C, 49.31; H, 6.90. Found: C, 49.33; H, 6.81.

The mother liquors from the isolation of the *meso* α,α'-dimethylsuccinic acid gave on concentration to 5 cc. 1.29 g. of acid which, on purification by crystallization from benzene, melted at 121–122.5°. This compound gave no depression in a mixed melting point determination with racemic α,α'-dimethylsuccinic acid.

Anal. Calcd. for $C_6H_{10}O_4$: C, 49.30; H, 6.90. Found: C, 49.50; H, 7.03.

These two products were converted to their half anilides by the method of Auwers[4] and compared with synthetic half anilides of *meso* and racemic α,α'-dimethylsuccinic acids. From 203° melting acid was obtained a half anilide, m. p. 169–170°, and from the 121° melting acid, a half anilide, m. p. 135–136°.

Anal. (Half-anilide, m. p. 169–170°.) Calcd. for $C_{12}H_{15}O_3N$: C, 65.15; H, 6.84; N, 6.34. Found: C, 65.14; H, 7.09. (Half anilide, m. p. 135–136°.) Found: N, 6.29.

p-Bromophenacyl Ester of Acid, M. P. 203°.—This was made by the usual procedure. It was purified from ethanol and gave white needles, m. p. 155–156°. The *p*-bromophenacyl ester of authentic *meso*-α,α'-dimethylsuccinic acid gave the same product.

Anal. Calcd. for $C_{22}H_{20}O_6Br_2$: C, 48.93; H, 3.73. Found: C, 48.78; H, 3.66.

Anhydride of Acid, M. P. 121°.—This was prepared according to the procedure of Bone and Sprankling.[5] It was purified by crystallization from dry ether, m. p. 88°. It proved to be racemic α,α'-dimethylsuccinic anhydride.

Anal. Calcd. for $C_6H_8O_3$: C, 56.25; H, 6.25. Found: C, 55.58; H, 6.39.

Dehydration of Monocrotic Acid to a Lactone; α,β,γ-Trimethylangelicalactone.—In a distillation apparatus 5 g. of monocrotic acid was heated to 240–250° at atmospheric pressure. At this temperature a colorless neutral liquid distilled. The product was taken up in ether, the ether solution washed with aqueous sodium bicarbonate and dried. The product boiled at 121° (20 mm.); $n^{19}D$ 1.4665; $n^{29}D$ 1.4640; d^{29}_4 1.024.

Anal. Calcd. for $C_7H_{10}O_2$: C, 66.66; H, 7.94; M_D 33.95. Found: C, 66.09; H, 7.90; M_D 33.55.

This compound decolorizes permanganate, gives a positive test with Tollens' reagent and with sodium nitroprusside (Legal's test). These latter two tests were performed according to the procedure recommended by Jacobs and Hoffman.

A solution of 5 g. of the lactone in 20 cc. of 10% ethanolic potassium hydroxide was refluxed for one hour. It was then neutralized with hydrochloric acid to litmus and the ethanol evaporated *in vacuo*. The residue was taken up in water, ether was added and hydrochloric acid also. Continuous extraction took up the acid: colorless liquid, 145–147° (20 mm.), which was identical with the acid from which the lactone was formed.

Anal. Calcd. for $C_7H_{12}O_3$: C, 58.31; H, 8.79. Found: C, 58.40; H, 8.40.

Hydrogenation of Lactone: α,β-Dimethyl-γ-valeroactone.—A solution of 10 g. of the lactone just described n 100 cc. of ether was hydrogenated under 2000-lb. (133 atm.) pressure at 120° in the presence of 2 g. of Raney nickel. Reduction was complete in three hours; yield, 9.8 g. The product boiled at 106–107° (20 mm.); $n^{19}D$ 1.4382; $n^{29}D$ 1.4348; d^{27}_4 0.987.

Anal. Calcd. for $C_7H_{12}O_2$: C, 65.62; H, 9.44; M_D 34.02. Found: C, 65.28; H, 9.62; M_D 33.84.

The same product resulted when methyl monocrotate was hydrogenated under similar conditions except that reduction was carried on for seven hours.

Anal. Found: C, 65.18; H, 9.39.

Summary

Monocrotic acid, $C_7H_{12}O_3$, was obtained from the alkaloid monocrotaline by alkaline hydrolysis or by the action of alkali on monocrotalic acid.

It is optically inactive, monobasic and forms a monomethyl ester by the action of diazomethane. The methyl ester gives a dinitrophenylhydrazone indicating the presence of a ketone group. The acid is oxidized by sodium hypobromite to *meso* and racemic α,α'-dimethylsuccinic acid.

Monocrotic acid dehydrates on heating to a neutral lactone which can be hydrolyzed to the acid. The lactone gives the color reactions characteristic for β,γ-unsaturated lactones.

It is concluded, therefore, that monocrotic acid is α,β-dimethyllevulinic acid.

URBANA, ILLINOIS RECEIVED AUGUST 14, 1939

(4) Auwers, Oswald and Thorpe, *Ann.*, **285**, 226 (1895).

(5) Bone and Sprankling, *J. Chem. Soc.*, **75**, 861 (1899).

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

The Structure of Monocrotaline. III. Monocrotalic Acid[1]

BY ROGER ADAMS, E. F. ROGERS AND R. S. LONG[2]

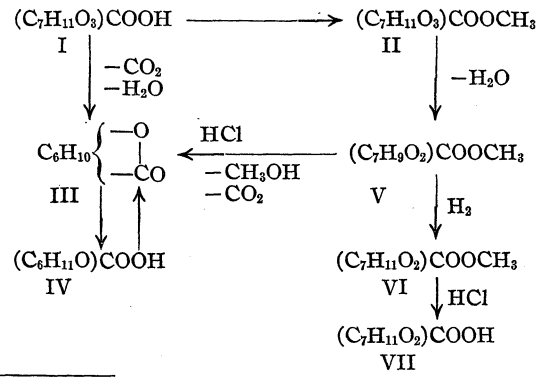
On catalytic hydrogenation of monocrotaline, two moles of hydrogen are absorbed with formation of an alkanolamine, retronecanol, and an optically active acid, $C_8H_{12}O_5$, called monocrotalic acid.[3]

$$C_{16}H_{23}O_6N + 2H_2 \longrightarrow \underset{\text{Retronecanol}}{C_8H_{15}ON} + \underset{\text{Monocrotalic acid}}{C_8H_{12}O_5}$$

Monocrotalic acid (I) contains one carboxyl group. On back titration of the acid from excess alkali, the presence of a lactone group is indicated. The acid gives a crystalline monomethyl ester (II) with diazomethane which shows one active hydrogen by a Zerewitinoff determination. Esterification of the acid with methanol and sulfuric acid was unsuccessful and only a very poor yield of ester was obtained with methanol saturated with hydrogen chloride.

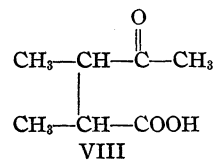
The acid decomposes on heating past its melting point to give an optically inactive neutral compound, $C_7H_{10}O_2$ (III or IX), which is identical with α,β,γ-trimethylangelicalactone obtained by dehydration of monocrotic acid, $C_7H_{12}O_3$ (IV or VIII).

The same lactone can be obtained by a two-step procedure which clarifies the reaction. Methyl monocrotalate (II) on heating *in vacuo* loses water to give an unsaturated ester $(C_7H_9O_2)$-$COOCH_3$ (V), together with a small amount of lactone (III). This ester reduces acid permanganate and can be hydrogenated under high pressure to a dihydro ester (VI) which in turn may be hydrolyzed to a crystalline lactonic acid, $(C_7H_{11}O_2)COOH$ (VII). The unsaturated ester (V) on hydrolysis with concentrated hydrochloric acid, yields the same lactone, $C_7H_{10}O_2$ (III), which is obtained by thermal decomposition of monocrotalic acid. It is obvious then that upon heating monocrotalic acid two reactions occur, dehydration and decarboxylation. These reactions just discussed are shown in tabular form.

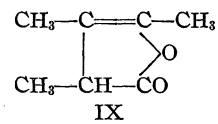


The above observations show that monocrotalic acid contains a lactone group which, while stable to heat and strong acid, cleaves readily with alkali to give an unstable, easily decarboxylated acid which could not be isolated. The ease of dehydration of monocrotalic acid and especially of its methyl ester is best explained by the presence of a tertiary hydroxyl group.

It has been demonstrated[1] that the acid obtained by alkaline hydrolysis of monocrotalic acid is α,β-dimethyllevulinic acid (VIII).

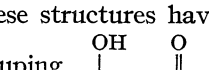


VIII



IX

Since IV has the structural formula VIII, it follows that the corresponding lactone (III) must be α,β,γ-trimethylangelicalactone (IX) which was obtained by the dry distillation of monocrotalic acid (I). Three structures of monocrotalic acid (I) may be considered, XI, XII and XIII.

Structures XIV, XV and XVI would then represent, respectively, the anhydromonocrotalate (V). All three of these structures have as a common feature the grouping 

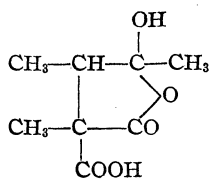
which explains the smooth formation of a keto acid on breaking the lactone ring. The structures differ in the position given the free carboxyl group.

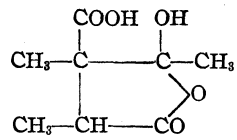
Structure XIII appears unlikely due to the fact that monocrotalic acid is esterified with acid and methanol only with great difficulty. This is indicative of a tertiary carboxyl. Structure XIII should not decarboxylate as readily on heating as was actually observed. Moreover, methyl anhydromonocrotalate does not give a Legal test al-

(1) For previous paper see Adams, Rogers and Sprules, THIS JOURNAL, **61**, 2819 (1939).

(2) An abstract of a thesis submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy in chemistry.

(3) Adams and Rogers, THIS JOURNAL, **61**, 2815 (1939).


XI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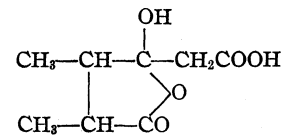
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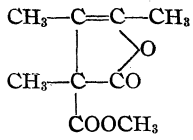
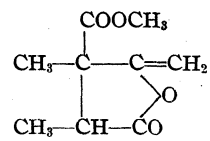
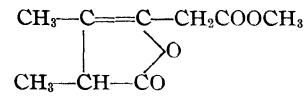
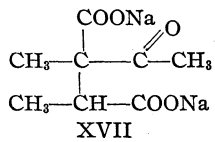

XIV


XV


XVI

though the unsaturated ester (XVI) derived from an acid of structure XIII should do so, since this test is specific for β,γ-unsaturated γ-lactones containing a free hydrogen in the α-position.[4] On the basis of this evidence, structure XIII may be excluded.

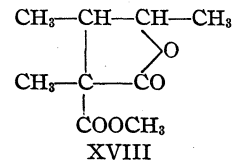
The degradation of monocrotalic acid (I) with alkali goes smoothly and quantitatively to monocrotic acid (VIII).[3] This reaction proceeds equally well whether dilute or concentrated alkali is used. Unquestionably the first step in the degradation is the formation of the salt of the tautomeric keto acid. Thus, XII would be converted to XVII, which is a β-ketonic acid. A difference

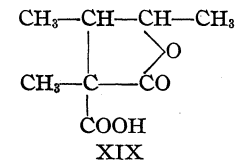

XVII

in the decarboxylation products should result whether diluted or concentrated alkali is used, for the former should give a ketone splitting to a levulinic acid derivative, whereas the latter should give at least partially an acid splitting with formation of a α,α'-dimethylsuccinic acid. None of the latter product could be isolated.

Methyl anhydromonocrotalate can be reduced catalytically only under high pressure. This fact is better reconciled with a substituted angelicalactone of formula XIV rather than XV. It is concluded, therefore, that formula XI represents the most likely structure for monocrotalic acid, namely, α-carboxy-α,β-dimethyl-γ-hydroxy-γ-valerolactone. It explains also the presence of one active hydrogen in methyl monocrotalate.

On this basis, the other degradation products would have the structures: hydrogenated methyl anhydromonocrotalate (XVIII) and its acid hydrolysis product (XIX).


XVIII


XIX

Monocrotalic acid and all of its derivatives in which the carboxyl group is intact are optically active, whereas the lactone obtained from monocrotalic acid or its derivatives is inactive due probably to its ease of enolization.

Experimental

Methyl Monocrotalate.—To a suspension of 5 g. of monocrotalic acid[3] in 30 cc. of chloroform was added slowly with stirring an ether solution of diazomethane until a slight excess was present as evidenced by a yellow color in the solution. The temperature was not allowed to rise above 10°. Evaporation of the ether and chloroform under diminished pressure left an oil which crystallized rapidly. The product was purified by recrystallization from ether: white crystals, m. p. 79–80° (corr.); yield, 5.17 g. (97%).

Anal. Calcd. for $C_9H_{14}O_5$: C, 53.47; H, 6.93. Found: C, 53.87; H, 7.09.

Rotation. 0.502 g. made up to 10 cc. at 30° in absolute ethanol. α_D −1.63; *l*, 2; $[\alpha]^{30}D$ −16.24°.

A Zerewitinoff determination showed 1.18 active hydrogens.

Heat Decomposition of Monocrotalic Acid: α,β,γ-Trimethylangelicalactone.—In a small modified Claisen distilling flask immersed in a Woods' metal bath was placed 15 g. of pure monocrotalic acid. Heat was applied and, at a bath temperature of 200°, the evolution of carbon dioxide and water was apparent. When this had ceased the bath was cooled and the residue distilled: colorless liquid, b. p. 82–83° (1 mm.); d^{29}_4 1.024; $n^{20}D$ 1.4664; yield, 8.6 g. (86%).

Anal. Calcd. for $C_7H_{10}O_2$: C, 66.67; H, 7.94. Found: C, 66.45; H, 8.04.

(4) Jacobs and Hoffman, *J. Biol. Chem.*, **61**, 333 (1925).

Methyl Anhydromonocrotalate.—In a small modified Claisen distilling flask 15 g. of methyl monocrotalate was heated at 200–210° until the evolution of water was complete. Fractionation of the residue gave 4.5 g. of material, b. p. 100–115° (3 mm.), and 7.5 g. of pure methyl anhydromonocrotalate, b. p. 115–116° (3 mm.); $n^{20}D$ 1.4700; d^{32}_4 1.131.

Anal. Calcd. for $C_9H_{12}O_4$: C, 58.70; H, 6.52. Found: C, 58.83; H, 6.82.

Rotation. (Pure liquid at 30°) αD +58.22; *l*, 2; $[\alpha]^{30}D$ +25.74.

A second fractionation of the low boiling portion gave 1.8 g. of low boiling material and 1.7 g. of pure methyl anhydromonocrotalate. Further purification of the low boiling material from this distillation gave 0.5 g. of pure α,β,γ-trimethylangelicalactone identical with that obtained directly from monocrotalic acid, b. p. 92° (3 mm.); $n^{20}D$ 1.4658.

Anal. Calcd. for $C_7H_{10}O_2$: C, 66.67; H, 7.94. Found: C, 66.10; H, 8.02.

Hydrogenation of Methyl Anhydromonocrotalate and α,β,γ-Trimethylangelicalactone: α-Carbomethoxy-α,β-dimethyl-γ-valerolactone and α,β-Dimethyl-γ-valerolactone.—Unfractionated methyl anhydromonocrotalate (9 g.) containing α,β,γ-trimethylangelicalactone was dissolved in 70 cc. of ether and hydrogenated at 2200 pounds (167 atm.) and 125° using Raney nickel as the catalyst. The theoretical amount of hydrogen was absorbed and the residue, after removal of the ether, was carefully fractionated; yield, 0.8 g. of α,β-dimethyl-γ-valerolactone, b. p. 67–69° (2 mm.); $n^{20}D$ 1.4382; d^{29}_4 0.987, and 6.0 g. of hydrogenated methyl anhydromonocrotalate, b. p. 115–117° (1 mm.); $n^{20}D$ 1.4510; d^{28}_4 0.996.

Anal. (α,β-Dimethyl-γ-valerolactone.) Calcd. for $C_7H_{12}O_2$: C, 65.63; H, 9.38. Found: C, 65.43; H, 9.57. (Hydrogenated methyl anhydromonocrotalate.) Calcd. for $C_9H_{14}O_4$: C, 58.06; H, 7.53. Found: C, 58.09; H, 7.70.

Rotation. (Pure liquid at 29°) αD +11.15; *l*, 2; $[\alpha]^{29}D$ +5.60.

When pure methyl anhydromonocrotalate was hydrogenated under similar conditions, a pure reduced product was obtained with constants identical with those just described.

Hydrolysis of Dihydromethyl Anhydromonocrotalate: α-Carboxy-α,β-dimethyl-γ-valerolactone.—A mixture of 4.6 g. of dihydromethyl anhydromonocrotalate and 20 cc. of concentrated hydrochloric acid was refluxed for five hours. Evaporation of the water under reduced pressure left 2.7 g. (63%) of crude acid which after purification by recrystallization from benzene gave 2.5 g. of pure acid: white crystals, m. p. 131–132° (corr.).

Anal. Calcd. for $C_8H_{12}O_4$: C, 55.81; H, 6.98. Found: C, 55.57; H, 6.98.

Rotation. 0.303 g. made up to 10 cc. of absolute ethanol at 30°. αD +0.23; *l*, 2; $[\alpha]^{30}D$ +3.80°.

The *p*-bromophenacyl ester was prepared from 0.1 g. of the acid and an equivalent amount of *p*-bromophenacyl bromide according to the standard procedure. Purified from ethanol it formed white crystals, m. p. 142–143° (corr.); yield, 0.12 g. (57%).

Anal. Calcd. for $C_{16}H_{17}O_5Br$: C, 52.03; H, 4.61. Found: C, 52.33; H, 4.91.

Rotation. 0.2315 g. made up to 5 cc. in acetone at 29°. αD −0.36; *l*, 2; $[\alpha]^{29}D$ −3.89°.

Hydrolysis of Methyl Anhydromonocrotalate: α,β,γ-Trimethylangelicalactone.—A solution of 6 g. of methyl anhydromonocrotalate in 10 cc. of concentrated hydrochloric acid was refluxed for eight hours. The oil which separated was extracted with ether and the ether solution was dried over anhydrous sodium sulfate. The product was pure, inactive α,β,γ-trimethylangelicalactone, b. p. 90–92° (3 mm.); $n^{20}D$ 1.4659 identical with that obtained directly from monocrotalic acid by heat decomposition.

Anal. Calcd. for $C_7H_{10}O_2$: C, 66.67; H, 7.94. Found: C, 65.97; H, 8.23.

Summary

Monocrotalic acid, obtained by hydrogenolysis of monocrotaline, has been shown to be monobasic with the carboxy group tertiary, and to contain a lactone grouping. It decomposes when heated to lose water and carbon dioxide with formation of α,β,γ-trimethylangelicalactone. It was possible to form this same lactone by heat decomposition of methyl monocrotalate and hydrolysis of the resulting methyl anhydromonocrotalate.

The discussion of the possible structure for monocrotalic acid is given with the conclusion that it is optically active α-carboxy-α,β-dimethyl-γ-hydroxy-γ-valerolactone.

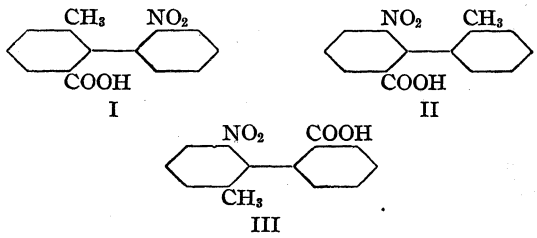
URBANA, ILLINOIS RECEIVED AUGUST 14, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Stereochemistry of Biphenyls. XLVIII. A Comparison of the Racemization Rates of Three Isomeric 2,2′,6-Nitro-, Carboxy-, Methyl-biphenyls[1]

BY ROGER ADAMS AND J. B. HALE[2]

A previous study of various easily racemized biphenyls[3] has demonstrated that various substituents in positions other than the 2,2′,6,6′ materially affect the rate of racemization of the active molecules. A study now has been made of the three possible isomeric 2,2′,6-trisubstituted biphenyls (I, II and III) in which the substituents are methyl, nitro and carboxyl groups.



If, in these three compounds, the two phenyl groups are assumed to be rigidly coaxial and the distance between the rings essentially constant, it might be anticipated that the relative rates of racemization would be dependent primarily upon the blocking effect of the two smaller interfering groups present in the 2,2′-positions. Previous study of various substituted biphenyls as well as X-ray data indicate that semiquantitatively the size of the groups is in the following order: nitro > methyl > carboxyl. Accepting these facts, compounds II and III should be of essentially the same stability (CH_3, COOH collision) and both of these should be less stable than compound I (COOH, NO_2 collision).

The actual experimental results failed to conform to this postulation. It was found that compound II was the least stable, compound I more stable, and compound III the most stable. The half-life periods of these three compounds (Table I) were sufficiently different to eliminate the possibility of experimental error.

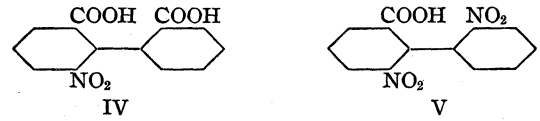
The solvent used in the racemization experiments affects the rate. In Table I acetic acid and *n*-butanol, two solvents which boil within a degree of each other, are compared.

(1) For previous paper see Adams and Finger, THIS JOURNAL, **61**, 2182 (1939).

(2) An abstract of a thesis submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy in chemistry.

(3) Kuhn and Albrecht, *Ann.*, **455**, 272; **458**, 221 (1927); Chien and Adams, THIS JOURNAL, **56**, 1787 (1934); Hanford and Adams, *ibid.*, **57**, 1592 (1935); Yuan and Adams, *ibid.*, **54**, 2996, 4434 (1932).

A comparison of two other 2,2′,6-trisubstituted biphenyls also has been made, namely, 6-nitrodiphenic acid (IV) and 2,2′-dinitro-6-carboxybiphenyl (V). As deduced merely from the size of groups, compounds IV and V (COOH, NO_2 collision) should have essentially the same stability. Experimental results indicated that compound IV was more stable in *n*-butanol, less stable in acetic acid, and far less stable in aqueous sodium hydroxide than compound V (Table I).



The conclusion to be drawn from these data is that the relative positions of the different groups to each other is a factor in the rate of racemization of the molecules.

Experimental

2-Methyl-6-nitro-2′-carboxybiphenyl.—The data used in the tables on this compound were those previously described by Stoughton and Adams.[4]

2-Carboxy-6-nitro-2′-methylbiphenyl.—A mixture of 20 g. of methyl 3-nitro-2-bromobenzoate and 34 g. of *o*-iodotoluene in a three-necked flask with reflux condenser and stirrer was heated in a metal bath at 225° (bath temp.). Over a period of one hour, 40 g. of copper powder was added with stirring. The bath temperature was then raised to 230° for thirty minutes. After cooling, the reaction mixture was extracted with three 100-cc. portions of hot ethanol. These filtered extracts were mixed with 400 cc. of 5% aqueous sodium hydroxide and refluxed for eight hours. The solution was then boiled for an additional two hours to remove a large proportion of the ethanol. Upon cooling, an oil separated which was chiefly the excess of *o*-iodotoluene. The aqueous solution was removed, treated with norit, filtered, and acidified with concentrated hydrochloric acid. An oil separated which soon solidified. This crude material was extracted with hot benzene in which the 2-nitro-6-carboxy-2′-methylbiphenyl was soluble, and the 6,6′-dinitrodiphenic acid practically insoluble. The benzene solution was extracted with dilute aqueous sodium hydroxide and the aqueous solution acidified with hydrochloric acid.

The product was purified by several recrystallizations from dilute ethanol: white crystals, m. p. 162–163°; yield, 3 g. (15%).

(4) The data given for compound III are those of Stoughton and Adams, *ibid.*, **52**, 5263 (1930), and were observed at a temperature of 20°.

TABLE I

Compound	Solvent	Sample in g. made up to cc.	α_D $l = 2$	$[\alpha]^{25}D$	Av. K	Half-life period, min.
I	C_2H_5OH	0.1 (15 cc.)	+1.01	+ 75.7	.....	..
	CH_3COOH	.1 (20 cc.)	+0.49	+ 49.5	0.00028	1075
	n-C_4H_9OH	.1 (20 cc.)	+ .73	+ 73	.00033	913
II	C_2H_5OH	.0464 (15 cc.)	+ .38	+ 61.5	.....	..
	CH_3COOH	.1 (25 cc.)	− .52	− 65	.00168	179
	n-C_4H_9OH	.1 (25 cc.)	− .59	− 73.8	.0018	166
III[4]	C_2H_5OH	.095 (25 cc.)	− .52	− 68.4	.....	..
	CH_3COOH	.0840 (15 cc.)	− .97	− 86.6	.00015	2007
	n-C_4H_9OH	.0583 (15 cc.)	− .56	− 72.0	.00115	2510
IV	C_2H_5OH	.05 (15 cc.)	+ .26	+ 3.90	.....	..
	CH_3COOH	.1 (20 cc.)	− .84	− 84	.0033	91, 90
	n-C_4H_9OH	.195 (20 cc.)	− .53	− 27.2	.0030	101, 107
	NaOH (0.1 N)	.05 (25 cc.)	+1.17	+293	.066	4.6
V	C_2H_5OH	.10 (15 cc.)	+2.69	+201.5	.00015	2000
	CH_3COOH	.07 (25 cc.)	+1.13	+202	.0024	125, 120
	n-C_4H_9OH	.07 (25 cc.)	+1.22	+218	.0033	91, 86
	NaOH (0.1 N)	.2 (25 cc.)	−1.49	− 93.0	.0033	91

Anal. Calcd. for $C_{14}H_{11}O_4N$: C, 65.4; H, 4.28; N, 5.45. Found: C, 65.38; H, 4.1; N, 5.41.

Resolution of 2-Methyl-6-nitro-2′-carboxybiphenyl.—To a boiling solution of 3.28 g. of 2-nitro-6-carboxy-2′-methylbiphenyl in 500 cc. of 60% ethanol was added 4.13 g. of quinine. After standing overnight 3.8 g. of crystals separated which were purified by crystallization three times from 200 cc. of hot 50% ethanol. The salt thus obtained gave a constant rotation and weighed 1.7 g. Before drying, the product had a melting point of 135–140° and after drying, 168–171°.

Rotation (dry l salt). 0.05 g. made up to 15 cc. in chloroform at 25°. α_D −0.89°; $l = 2$; $[\alpha]^{25}D$ −133.5°.

Anal. Calcd. for $C_{34}H_{35}O_6N_3$: N, 7.22. Found: N, 7.53.

Rotation (solvated l salt) 0.05 g. made up to 15 cc. in chloroform at 25°. α_D −0.83°; $l = 2$; $[\alpha]^{25}D$ −124.2°.

On cooling the original mother liquor from the less soluble salt, a small crop of crystals separated which were discarded. The alcohol solution was then allowed to evaporate until the more soluble salt separated. This was purified by three crystallizations from 100 cc. of hot 30% ethanol. The precaution was taken during the first two crystallizations to discard the first third of the salt which separated. The final product gave a constant rotation, m. p. 118–123° before drying and 128–131° after drying.

Anal. (dry d-salt) Calcd. for $C_{34}H_{35}O_6N_3$: N, 7.22. Found: N, 7.12.

Rotation (solvated d-salt) 0.10 g. made up to 15 cc. in chloroform at 25°. α_D −1.40°; $l = 2$; $[\alpha]^{25}D$ −105°.

The solvation of these salts appeared not to be constant so that the rotations of the solvated salts are not significant.

d- and l-2-Nitro-6-carboxy-2′-methylbiphenyl.—A suspension of 2 g. of the less soluble salt in 10 cc. of water was cooled in an ice-bath and treated with 10 cc. of cold dilute hydrochloric acid. After stirring for a few minutes the mixture was extracted with ether and the ether extracts washed several times with dilute hydrochloric acid and then with water. The ether solution was then treated with 10 cc. of dilute sodium hydroxide and the aqueous alkaline extract acidified in the cold with hydrochloric acid. The l-form of the product separated and was recrystallized from dilute ethanol: white crystals, m. p. 153–155°.

Rotation. (l-acid) 0.10 g. made up to 25 cc. in ethanol at 25°. α_D −0.52; $l = 2$; $[\alpha]^{25}D$ −65°.

The d-acid was obtained in a similar manner and had a melting point of 153–156°.

Rotation. (d-acid) 0.0464 g. made up to 15 cc. in ethanol at 25°. α_D +0.38°; $l = 2$; $[\alpha]^{25}D$ +61.5°.

2-Methyl-6-carboxy-2′-nitrobiphenyl.—*m*-Toluic acid was nitrated to 2-nitro-3-methylbenzoic acid according to the method of Findeklee.[5a] This was esterified[5b] and then reduced by means of stannous chloride and hydrochloric acid[6] to the amine. The amino group was replaced by iodine[7] to give methyl 2-iodo-3-methylbenzoate.

A mixture of 24 g. of methyl 2-iodo-3-methylbenzoate and 60 g. of *o*-iodonitrobenzene was heated in a metal bath with stirring at 230°. Copper-bronze powder (65 g.) was added at such a rate that the temperature of the reaction mixture never rose above 245°. The bath temperature was then raised to 250° and maintained at that temperature for fifteen minutes. After cooling, the reaction mixture was extracted with 300 cc. of hot ethanol, filtered, and refluxed for eight hours with 400 cc. of 5% aqueous sodium hydroxide. The reaction mixture was then boiled for two hours and the ethanol allowed to distill. Upon cooling, a brown semi-solid mass separated and was filtered. The solution was treated with norit, filtered, and acidified with dilute hydrochloric acid. The yellow oil which separated soon solidified. The product thus obtained was dissolved in 200 cc. of hot benzene, filtered, and the desired acid extracted with aqueous sodium hydroxide. After acidification the crude 2-methyl-6-car-

(5) (a) Findeklee, *Ber.*, **38**, 3553 (1905); (b) Jurgens, *ibid.*, **40**, 4409 (1907).

(6) Müller, *ibid.*, **42**, 423 (1909).

(7) Mayer, *ibid.*, **44**, 2298 (1911).

boxy-2′-nitrobiphenyl was filtered and crystallized several times from 80% ethanol: yellowish white crystals, m. p. 157°; yield, 12 g. (50%).

Anal. Calcd. for $C_{14}H_{11}O_4N$: N, 5.45; neut. equiv., 257. Found: N, 5.55; neut. equiv., 260.

Resolution of 2-Methyl-6-carboxy-2′-nitrobiphenyl.—A solution of 3 g. of 2-methyl-6-carboxy-2′-nitrobiphenyl in 20 cc. of boiling methanol was mixed with a boiling solution of 5.43 g. of anhydrous brucine in 50 cc. of methanol. After standing for three hours, 5 g. of salt deposited. After three recrystallizations from 50 cc. of methanol a constant rotation was obtained: white crystals, m. p. 165–167°.

Rotation. 0.05 g. made up to 15 cc. in chloroform at 25°. α_D +0.32; $l = 2$; $[\alpha]^{25}D$ +48°.

Anal. Calcd. for $C_{37}H_{37}N_3O_6$: N, 6.97. Found: N, 7.02.

Upon cooling the mother liquor, 2.4 g. of salt separated. This was dissolved in 40 cc. of methanol and cooled slowly. The first portion of crystals was discarded and finally 1.6 g. of salt was collected. Recrystallization of this from methanol did not change the melting point or the rotation: white crystals, m. p. 153–160°.

Rotation. 0.05 g. made up to 15 cc. in chloroform at 25°. α_D −0.34; $l = 2$; $[\alpha]^{25}D$ −51°.

Anal. Calcd. for $C_{37}H_{37}N_3O_6$: N, 6.97. Found: N, 6.86.

***d*- and *l*-2-Methyl-6-carboxy-2′-nitrobiphenyl.**—The active acids were formed as previously described for the active 2-carboxy-6-nitro-2′-nitrobiphenyls. The active acids were purified by recrystallization from dilute ethanol, *d*-acid m. p. 179–181°, *l*-acid m. p. 175–179°.

Rotation. (*d*-acid) 0.05 g. made up to 15 cc. in chloroform, α_D +0.49; $l = 2$; $[\alpha]^{25}D$ +73.5°. (*l*-acid) 0.0485 g. made up to 15 cc. in chloroform. α_D −0.47; $l = 2$; $[\alpha]^{25}D$ −72.6°.

6-Nitrodiphenic Acid.—This was prepared and resolved according to the method of Bell and Robinson[8] using morphine.

Rotation. (less soluble salt) 0.1 g. made up to 15 cc. in pyridine at 25°. α_D −1.04; $l = 2$; $[\alpha]^{25}D$ −78°.

The active acids were liberated from the salt in the way previously described and were purified by dissolving in dilute aqueous ammonia and precipitating with dilute hydrochloric acid.

Rotation. *d*-acid (from less soluble salt) 0.05 g. made up to 15 cc. in ethanol at 25°. α_D +0.26; $l = 2$; $[\alpha]^{25}D$ +39.0°; α_{5461} +0.44; $l = 2$; $[\alpha]^{20}_{5461}$ +66.0°. *l*-acid (from soluble salt) 0.05 g. made up to 15 cc. in ethanol at 25°. α_D −0.25; $l = 2$; $[\alpha]^{25}D$ −37.5°.

2,2′-Dinitro-6-carboxybiphenyl.—A mixture of 20 g. of methyl-3-nitro-2-bromobenzoate and 34 g. of *o*-iodonitrobenzene was heated in a metal bath at 220°. Copper-bronze powder (40 g.) was then added at such a rate that the temperature of the reaction mixture did not exceed 225°. The bath temperature was raised to 225° for a period of thirty minutes. After cooling the reaction mixture was extracted with three 100-cc. portions of hot ethanol, the filtered extracts added to 400 cc. of 5% aqueous sodium hydroxide and the mixture refluxed for eight hours. The reaction mixture was then boiled for about two hours to remove most of the alcohol. On cooling a dark solid mass separated and was filtered. The solution was treated with norit and acidified with concentrated hydrochloric acid to congo red. A crude oil separated which soon solidified. This was extracted with hot benzene in which the by-product of dinitrobiphenyl is practically insoluble. The benzene solution was then extracted with dilute aqueous sodium hydroxide and upon acidification crude 2,2′-dinitro-6-carboxybiphenyl separated. It was purified by crystallization from dilute acetic acid: m. p. 164°; yield, 6 g. (30%).

Anal. Calcd. for $C_{13}H_8O_6N_2$: C, 54.1; H, 2.78; N, 9.72; neut. equiv., 288. Found: C, 53.97; H, 2.89; N, 10.0; neut. equiv., 283.

Resolution of 2,2′-Dinitro-6-carboxybiphenyl.—To a warm solution of 4 g. of 2,2′-dinitro-6-carboxybiphenyl in 800 cc. of 75% ethanol was added with stirring 4.5 g. of quinine. After standing overnight approximately half of the salt separated. It was purified by crystallization twice from 400 cc. of 50% ethanol. The salt then had a constant rotation, m. p. 156–191°. After drying the melting point was 195–197°.

Rotation. (dry *d*-salt) 0.05 g. made up to 15 cc. in chloroform. α_D +0.35; $l = 2$; $[\alpha]^{25}D$ +52.5°.

Evaporation of the mother liquor from the less soluble salt resulted in the separation of an oil which after standing for a few days gradually solidified. The solid was thoroughly pulverized and allowed to stand in 200 cc. of ethanol with occasional stirring. The solution was filtered and upon evaporation of the solvent the salt obtained solidified rapidly: m. p. 121–125°; yield, 2.5 g.

Rotation. (more soluble salt) 0.1 g. made up to 15 cc. in chloroform at 25°. α_D −3.16; $l = 2$; $[\alpha]^{25}D$ −238°.

Anal. Calcd. for $C_{33}H_{32}O_8N_4$: N, 9.15. Found: N, 8.96.

***d*- and *l*-2,2′-Dinitro-6-carboxybiphenyl.**—The active acids were liberated from the salts in the manner previously described. The active acids were obtained as oils which solidified upon standing in a vacuum desiccator overnight. They were recrystallized from dilute acetic acid; m. p. of *d*-acid from the less soluble salt was 135–137°; the *l*-acid 127–130°.

Rotation. (*d*-acid) 0.10 g. made up to 15 cc. in ethanol at 25°. α_D +2.69; $l = 2$; $[\alpha]^{25}D$ +201.5°. (*l*-acid) 0.05 g. made up to 15 cc. in ethanol at 25°. α_D −1.33; $l = 2$; $[\alpha]^{25}D$ −199.5°.

Summary

The preparation of 2-methyl-6-carboxy-2′-nitrobiphenyl, 2-nitro-6-carboxy-2′-methylbiphenyl, and 2-methyl-6-nitro-2′-carboxybiphenyl is described. They were resolved and the rates of racemization compared. The half-life periods do not correspond to what might be anticipated merely from the relative size of the groups as deduced from X-ray data or from the rates of racemization of previously studied biphenyls. The

(8) Bell and Robinson, *J. Chem. Soc.*, 1695 (1927).

relative positions of the groups have a marked effect on the stability of the molecule. The rate of racemization is modified by the solvent used.

A comparison of the rates of racemization of optically active 6-nitrodiphenic acid with optically active 2,2′-dinitro-6-carboxybiphenyl also has been made. The latter is the more stable.

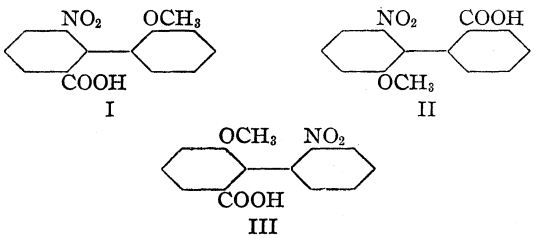
URBANA, ILLINOIS RECEIVED JULY 24, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Stereochemistry of Biphenyls. XLIX. Comparison of the Racemization Rates of the 2,2′,6-Nitro-, Carboxy- and Methoxy-biphenyls[1]

BY ROGER ADAMS AND G. C. FINGER[2]

In the previous paper the relative stabilities of biphenyls containing nitro, methyl and carboxyl in the three possible combinations in the 2,2′,6-positions were described. Another similar series has been prepared now in which the nitro, methoxyl and carboxyl groups occupy the three possible positions in biphenyl.



Based upon the expectations from the relative size of the groups, compounds I and II (CH_3O, COOH collision) should have essentially the same stability and compound III should be more stable. Experimentally compound I proved to be very unstable while compounds II and III were much more stable. The value of the half-life period obtained for compound II is possibly unreliable due to the fact that the formation of the salt and the decomposition to the active acid was abnormal, and the yields of the acid were poor. It is likely, therefore, that the half-life period is more in error than usual.

The variation in stability of these molecules is concordant with the results described in the previous paper[1] in which the methyl group was present in place of the methoxyl.

Experimental

2-Methoxy-6-carboxy-2′-nitrobiphenyl.—The 1-methoxy-2-iodo-3-carbomethoxybenzene was prepared by the method of Stanley, McMahon and Adams.[3]

In a large Pyrex test-tube a mixture of 5 g. of 1-methoxy-2-iodo-3-carbomethoxybenzene, 4.3 g. of *o*-iodonitrobenzene and 10 g. of copper-bronze powder was heated under reflux in an oil-bath for two hours at 200°. The reaction mixture was extracted with acetone, the acetone solution refluxed with norit, and the solvent concentrated to small volume.

The crude material, which separated, was refluxed for eighteen hours with a mixture of 2 g. of sodium hydroxide and 8 g. of sodium carbonate in 350 cc. of water and 50 cc. of ethanol. The saponification mixture was filtered from the alkali-insoluble 2,2′-dinitrobiphenyl. The alkaline filtrate was diluted to 1500 cc. and acidified with dilute sulfuric acid to precipitate the product. The crude material which amounted to about 5 g. was crystallized from 80% ethanol, from which it formed white needles, m. p. 234–236°.

Anal. Calcd. for $C_{14}H_{11}O_5$: C, 61.53; H, 4.03; N,

TABLE I

RACEMIZATION OF ACTIVE ACIDS

Compound	Wt. in g. made up to 10 cc. in abs. ethanol	Minutes before initial reading	Initial α_D (l = 1) t = 27°	Final α_D	Calcd. for zero time α_D	Calcd. for zero time $[\alpha]_D$	Final α_D	Av. K[a]	Av. dev. K	Half-life period, min.
I	0.0557	7	+0.21	0.0	+0.33	+ 59.4	0.0	0.02936	±0.00081	10.2[b]
II	.0430	31	− .50	.0	−0.55	−127.9	.0	.001364	± .000048	219[c]
III	.0473	120	− .76	.0	−1.01	−213.3	.0	.00111	± .00006	271

[a] The K value was calculated by the formula $K = \frac{1}{t} \log \frac{\alpha 0 - \alpha f}{\alpha t - \alpha f}$. [b] Stoughton and Adams first prepared this active acid [THIS JOURNAL, **54**, 4406 (1932)] and reported 9.4 minutes; Li and Adams found 12.2 minutes [Li and Adams, *ibid.* **57**, 1565 (1935)]. [c] *l*-Acid from hydrochloric acid hydrolysis gave 288 minutes.

(1) For previous paper see Adams and Hale, THIS JOURNAL, **61**, 2825 (1939).

(2) An abstract of a thesis submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy in chemistry.

(3) Stanley, McMahon and Adams, THIS JOURNAL, **55**, 708 (1933).

5.16; neut. equiv., 273. Found: C, 61.58; H, 4.1; N, 5.24; neut. equiv., 269, 273.

Resolution of 2-Methoxy-6-carboxy-2'-nitrobiphenyl.—To a warm solution of 0.72 g. of 2-methoxy-6-carboxy-2'-nitrobiphenyl in 35 cc. of ethanol was added a solution of 1.05 g. of anhydrous brucine in 50 cc. of ethanol. The mixture was allowed to stand in the ice box for two days. The brucine salt separated as white powdery crystals; m. p. 222–225°, yield 0.92 g.

Anal. Calcd. for $C_{37}H_{37}N_3O_9$: C, 66.54; H, 5.59. Found: C, 66.30; H, 5.54.

Mutarotation. 0.1060 g. of brucine salt was made up to 20 cc. in dry chloroform. α_D (after six minutes) −0.49; $l = 2$; $[\alpha]^{27}D$ −47.1°.

The rotation was read at first every two minutes then every ten and finally every hour until seven hundred forty-five minutes had elapsed: α_D −0.16; $[\alpha]^{27}D$ −15.1°. The half-life period calculated on the basis of a monomolecular reaction is 99 ± 11 min.

***l*-2-Methoxy-6-carboxy-2'-nitrobiphenyl.**—A mixture of 0.4 g. of brucine salt and 25 cc. of dilute hydrochloric acid (1:1) was kept in an ice-bath and shaken occasionally over a period of an hour. The mixture was filtered rapidly and washed with a small amount of ice-cold water. The precipitate was again treated with 25 cc. of dilute acid and allowed to stand overnight at 0°. The active acid was washed with ice-cold dilute hydrochloric acid and water until completely free from brucine and chloride ion. The acid weighed 0.14 g. and had a melting point of 229–232°.

2-Methoxy-6-nitro-2'-carboxybiphenyl

1-Methoxy-2-chloro-3-nitrobenzene.—The 2-chloro-3-nitrophenol was made by the method of Erp[4] and esterified by the method described below.

To a hot solution of 39 g. of 2-chloro-3-nitrophenol in 250 cc. of hot xylene was added slowly with rapid stirring 40 g. of finely powdered anhydrous potassium carbonate. The red phenol salt separated and in some instances it was necessary to add more xylene to facilitate the agitation. To this mixture was now added 30 cc. of dimethyl sulfate at such a rate that the reaction mixture boiled rather vigorously. After continued stirring and refluxing for an hour, the mixture was treated with a little dilute sodium hydroxide and then steam distilled. After all the xylene had come over, the distillation was stopped and the residual material cooled. The crude 1-methoxy-2-chloro-3-nitrobenzene solidified, yield, 39 g. (92%). It was purified from 40% ethanol and formed white flake-like crystals, m. p. 93–94°. Erp reported m. p. 94°.

A mixture of 14 g. of 1-methoxy-2-chloro-3-nitrobenzene and 20 g. of methyl *o*-iodobenzoate was heated in an oil-bath to 255°. The temperature was raised gradually to 275° over a period of one hour and during this period 32 g. of copper-bronze powder was added in about 5-g. quantities at regular intervals. The mixture was stirred rapidly during the addition. After the addition was completed, the temperature was raised to 280° for about five to ten minutes and then allowed to drop.

The reaction product was refluxed with ethanol for two hours, the solvent decanted and the residual material again extracted for several hours with fresh ethanol.

After evaporation of the solvent, a black semi-solid mass was obtained weighing 13 g. This was refluxed for ten to twelve hours with a mixture of 5 g. of sodium hydroxide, 10 g. of sodium carbonate, 50 cc. of ethanol and 200 cc. of water. After cooling, the mixture was filtered and the insoluble residue separated from the alkaline solution. It proved to be 2,2'-dimethoxy-6,6'-dinitrobiphenyl. The alkaline solution was refluxed with norit for two hours, then filtered and acidified with dilute hydrochloric acid. The precipitated product was extracted with ether, the ether solution dried over anhydrous magnesium sulfate and the solvent evaporated. The product thus obtained which appeared to be a mixture of a solid and a very viscous oil was heated with successive portions of 25 cc. of benzene, the extracts were combined and allowed to cool. Diphenic acid separated. The benzene was evaporated gradually and intermittently cooled. When a volume of about 20 cc. had been reached, crude 2-methoxy-6-nitro-2'-carboxybiphenyl separated and by further evaporation of the filtrate a second crop could be obtained. The product was purified by recrystallization from 50% methanol: pale cream colored crystals, m. p. 196–198°; yield, 1.5 g.

Anal. Calcd. for $C_{14}H_{11}NO_5$: C, 61.53; H, 4.03; N, 5.16; neut. equiv., 273. Found: C, 61.76; H, 4.02; N, 5.24; neut. equiv., 271, 272.

2,2'-Dimethoxy-6,6-dinitrobiphenyl.—The alkali-insoluble material obtained in the condensation of 1-methoxy-2-chloro-3-nitrobenzene and methyl *o*-iodobenzoate was purified by crystallization from ethanol in the presence of norit. It formed yellow crystals.

The same product was prepared by heating a mixture of 5 g. of 1-methoxy-2-chloro-3-nitrobenzene in 30 g. of anhydrous nitrobenzene at 180° and adding gradually with stirring 5 g. of copper-bronze powder. The reaction mixture was then maintained at a temperature of 200–210° for five hours, cooled and filtered. The copper residue was extracted carefully with acetone.

The nitrobenzene solution and acetone extracts were subjected to steam distillation, whereupon the solvent was removed as well as some of the unreacted chloro compound. The crude residual product was filtered and dissolved in acetone. This solution was then heated with norit, filtered, and evaporated on a steam cone. Upon treatment of this residue with 50 cc. of hot ethanol, the oily material went into solution and yellow crystals of the 2,2'-dimethoxy-6,6'-dinitrobiphenyl remained undissolved; yield 2.8 g. from ethanol, m. p. 226–228°. The compound can also be purified very satisfactorily from hot glacial acetic acid.

Anal. Calcd. for $C_{14}H_{12}O_6N_2$: N, 9.2. Found: N, 9.13.

Resolution of 2-Methoxy-6-nitro-2'-carboxybiphenyl.—To a warm solution of 0.72 g. of 2-methoxy-6-nitro-2'-carboxybiphenyl in 25 cc. of absolute ethanol was added a warm solution of 1.05 g. of brucine in 50 cc. of absolute ethanol. After filtration, the mixture was allowed to stand at 0° for thirty hours. Yellow needle-like crystals separated; yield, 0.83 g. A second crop could be obtained by allowing the mother liquor to stand at 0° for several days.

(4) Erp, *J. prakt. Chem.*, **127**, 20 (1930).

The product was purified by dissolving 0.91 g. in 40 cc. of hot absolute ethanol and allowing to stand at 0° for thirty hours. Cream colored crystals were thus obtained.

The melting point of the brucine salt showed unusual irregularity, some samples partially melting around 70°, others at 80 or 90°. The decomposition points ranged from 108–125°.

The brucine salt had practically a zero rotation and no mutarotation was observed over a period of several hours. In spite of this, active acid was obtained from the salt by hydrolysis. Although the salt was well crystallized, the analyses did not indicate absolute purity.

l-2-Methoxy-6-nitro-2′-carboxybiphenyl

A. Hydrolysis with Acid.—The brucine salt was hydrolyzed with dilute hydrochloric acid (1:1) as described previously for 2-methoxy-6-carboxy-2′-nitrobiphenyl. An exceedingly low yield of active acid resulted.

B. Hydrolysis with Dilute Sodium Hydroxide.—At 0° 0.1 g. of brucine salt was shaken with 15 cc. of aqueous 10% sodium hydroxide for one hour. Extraction with chloroform served to remove the brucine. After filtering the alkaline solution, it was acidified with dilute hydrochloric acid (1:1) at 0°. The *l*-acid separated but, as it was too fine for filtrations, it was extracted with ether. The solvent was evaporated at a low temperature and the residue dried in a vacuum desiccator at room temperature; weight, 0.022 g., m. p. 195–199°.

Anal. Calcd. for $C_{13}H_{11}O_5N$: N, 5.16. Found: N, 5.10.

Summary

The following compounds have been prepared: 2-methoxy-6-carboxy-2′-nitrobiphenyl, 2-nitro-6-carboxy-2′-methoxybiphenyl, and 2-methoxy-6-nitro-2′-carboxybiphenyl. The 2-nitro-6-carboxy-2′-methoxybiphenyl proved to be unstable and the least stable of the three. The other two were relatively stable compounds. A more exact comparison of the stability of the latter two was impossible due to the fact that the purity of one of them appeared to be questionable.

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[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Synthesis in the 1,2,3,4-Tetrahydroquinoline Series

BY WILLIAM S. EMERSON AND J. W. DAVIS

The N-alkyl-1,2,3,4-tetrahydroquinolines represent an interesting and but little studied group of compounds. Very few containing alkyl groups in the benzene ring have ever been prepared, much less, thoroughly examined.

These compounds can be prepared readily from the corresponding quinolines either by reduction of the quinoline methiodides[1] or by first reducing the quinolines and then treating the tetrahydro compounds with methyl iodide.[1,2] In examining the second method we were surprised to find that 1,2,3,4-tetrahydroquinolines vary markedly in their stability and reactivity. This paper reports the great differences in these respects between 2,6- and 2,8-dimethyl-1,2,3,4-tetrahydroquinoline.

While the 2,8-compound is relatively stable, forming a well defined picrate and zinc chloride–hydrochloric acid double salt, the corresponding derivatives of the 2,6-compound are unstable, decomposing when attempts are made to crystallize them. In the case of the picrate, 2,6-dimethylquinoline picrate subsequently was isolated from the filtrate. The 2,6-compound also reacted much more violently with methyl iodide than the 2,8-compound. On the other hand, the N-methyl derivative of 2,6-dimethyl-1,2,3,4-tetrahydroquinoline was found to be stable and normal in its reactions.

Reduction studies of alkyl and aryl quinolines[3] showed that 2,6-dimethylquinoline was reduced readily with nickel and hydrogen at 105°. At the same pressure three monomethylquinolines were reduced at 120°, while a temperature of at least 150° was required in all other cases. 2-Methylquinoline could be reduced at temperatures as low as 110°, but the reaction proceeded more smoothly at 150°. Since this type of hydrogenation is reversible, it is interesting that the tetrahydroquinoline which we have found to be unstable was prepared at the lowest temperature in these reduction studies.

Experimental

2,8-Dimethylquinoline was prepared by the method of Doebner and v. Miller; b. p. 245–255°; $n^{20}D$ 1.5955; d^{20}_4 1.036; M_D calcd. 51.73; M_D found 51.60. Its identity was checked by means of the picrate, m. p. 177–179° (180°).[4]

(1) Möller, *Ann.*, **242**, 313 (1887).

(2) Doebner and v. Miller, *Ber.*, **16**, 2464 (1883).

(3) Von Braun, Petzold and Seemann, *ibid.*, **55**, 3779 (1922); v. Braun, Gmelin and Schultheiss, *ibid.*, **56**, 1338 (1923); v. Braun, Petzold and Schultheiss, *ibid.*, **56**, 1347 (1923); v. Braun, Gmelin and Petzold, *ibid.*, **57**, 382 (1924).

(4) Eibner, *ibid.*, **34**, 2450 (1901).

The zinc chloride–hydrochloric acid double salt was prepared by mixing one part of the base with two parts of a solution of 13.6 g. of zinc chloride in 20 cc. of concentrated hydrochloric acid and 10 cc. of glacial acetic acid. After filtration from the reaction mixture the white needles were recrystallized from glacial acetic acid. They were filtered and washed free of acid with ether, m. p. 270° dec. This is a modification of Craig's procedure[5] for preparing the zinci-hydrochloride of methyldiphenylamine.

Anal. Calcd. for 2 $2C_{11}H_{11}N \cdot 2HCl \cdot ZnCl_2$: Cl, 27.2. Found: Cl, 26.9.

2,8-Dimethyl-1,2,3,4-tetrahydroquinoline was prepared by dissolving 39 g. of 2,8-dimethylquinoline in 100 cc. of water and 200 cc. of concentrated hydrochloric acid and refluxing the resulting solution for fifteen hours with an excess of tin.[2] The product was isolated by making the mixture alkaline with sodium hydroxide and distilling with steam. After the distillate was extracted with ether, the ether solution dried over sodium hydroxide and the ether distilled, the base distilled at 250–255°: yield 27.9 g. or 69%; $n^{20}D$ 1.5610; d^{20}_4 1.000; M_D calcd. 51.90; M_D found 52.24. The picrate crystallized from alcohol in yellow needles, m. p. 159.5–161.0°.

Anal. Calcd. for $C_{17}H_{18}O_7N_4$: C, 52.3; H, 4.62. Found: C, 52.3; H, 4.62.

The zinc chloride–hydrochloric acid double salt melted at 270° with decomposition. A mixed melting point determination with the zinc chloride–hydrochloric acid double salt of 2,8-dimethylquinoline showed a depression of fifteen degrees.

Anal. Calcd. for $2C_{11}H_{15}N \cdot 2HCl \cdot ZnCl_2$: Cl, 26.7. Found: Cl, 26.5.

The benzoyl derivative, prepared by the Schotten–Baumann method, crystallized from aqueous alcohol in white plates, m. p. 118.5–120°.

Anal. Calcd. for $C_{18}H_{19}ON$: N, 5.28. Found: N, 5.42.

1,2,8-Trimethyl-1,2,3,4-tetrahydroquinoline hydriodide was prepared by allowing a mixture of 20 g. of 2,8-dimethyl-1,2,3,4-tetrahydroquinoline and 17.6 g. of methyl iodide to stand for sixteen hours. The white crystals were recrystallized from absolute alcohol; yield 26.5 g. or 70%, m. p. 154.5–155.5°.

Anal. Calcd. for $C_{12}H_{18}NI$: I, 41.9. Found: I, 42.0.

1,2,8-Trimethyl-1,2,3,4-tetrahydroquinoline was prepared by dissolving 20 g. of 1,2,8-trimethyl-1,2,3,4-tetrahydroquinoline hydriodide in 20 cc. of water and adding 30 cc. of 10% sodium hydroxide. The oil so formed was extracted with ether and the ether solution dried over potassium hydroxide. After the ether had been distilled, the product was distilled at 21 mm., b. p. 130°: yield 10.2 g. or 88%; $n^{20}D$ 1.5450; d^{20}_4 0.9826; M_D calcd. 57.30; M_D found 56.43.

The picrate was crystallized from alcohol, m. p. 177–178°. A mixed melting point determination with the picrate of 2,8-dimethylquinoline (m. p. 177–179°) showed a depression of twenty-seven degrees.

Anal. Calcd. for $C_{18}H_{22}O_7N_4$: N, 13.88. Found: N, 14.04.

(5) Craig, THIS JOURNAL, **55**, 3723 (1933).

The zinc chloride–hydrochloric acid double salt was also prepared as white crystals, m. p. 213–214°.

Anal. Calcd. for $2C_{12}H_{17}N \cdot 2HCl \cdot ZnCl_2$: Cl, 25.4. Found: Cl, 25.4.

The hydriodide was prepared by mixing equal volumes of the base and hydriodic acid of sp. gr. 1.50. After crystallization had been induced by adding ethyl acetate, the product was filtered and crystallized from absolute alcohol to give white crystals, m. p. 155–157°. A mixed melting point determination with a sample prepared by treating 2,8-dimethyl-1,2,3,4-tetrahydroquinoline with methyl iodide (m. p. 154.5–155.5°) gave 155–157°.

2,6-Dimethylquinoline was prepared by the method of Doebner and v. Miller[2]; b. p. 255–265°; m. p. 60°.

The picrate was crystallized from alcohol in yellow needles, m. p. 186–187°. Doebner[6] gives 178° as the melting point of this compound.

Anal. Calcd. for $C_{17}H_{14}O_7N_4$: N, 14.51. Found: N, 14.45.

The zinc chloride–hydrochloric acid double salt was prepared as white crystals, m. p. 211.5–213°.

Anal. Calcd. for $2C_{11}H_{11}N \cdot 2HCl \cdot ZnCl_2$: Cl, 27.1. Found: Cl, 27.1.

2,6-Dimethylquinoline methiodide was prepared by warming equimolar quantities of methyl iodide and 2,6-dimethylquinoline. It crystallized from absolute alcohol in yellow crystals, m. p. 239–240° (236–237°,[7] 246–247°[8]).

2,6-Dimethyl-1,2,3,4-tetrahydroquinoline was prepared by reducing 52 g. of 2,6-dimethylquinoline with tin and hydrochloric acid using the same procedure as for 2,8-dimethyl-1,2,3,4-tetrahydroquinoline. In this way 37.3 g. (70%) of product was obtained; b. p. 142–149° (25 mm.).

To a solution of 6 g. of this crude product in a mixture of 10 cc. of concentrated hydrochloric acid and 30 cc. of water was added 3 g. of sodium nitrite. After the oil which separated had been extracted with ether, the ether was evaporated in the cold and the residue added with cooling to 15 g. of stannous chloride and 75 cc. of concentrated hydrochloric acid. This mixture was allowed to stand for one-half hour before being heated on the steam-bath for fifteen minutes. It was then diluted with water and made basic with sodium hydroxide. The oil which volatilized on steam distillation was extracted from the distillate with ether. After drying over potassium hydroxide, the ether was distilled and then the product was distilled at 24 mm.; b. p. 147–149°; yield 2.5 g.

The benzoyl derivative prepared by the Schotten–Baumann method and crystallized from aqueous alcohol melted at 104–105° (103–105°).[9]

The zinc chloride–hydrochloric acid double salt melted at 187–195° after one crystallization from acetic acid.

The picrate when first prepared melted at 126–128°. After one crystallization from alcohol it melted at 150–155°. Another raised it to 165–169°. In both cases the solution turned red on heating, and, while the color disappeared on cooling, it reappeared after the filtrate had stood for one hour. (This red color was not encountered

(6) Doebner, *Ber.*, **33**, 677 (1900).
(7) Möller, *Ann.*, **242**, 300 (1887).
(8) Lund and Wise, *Ind. Eng. Chem.*, **11**, 458 (1919).
(9) Pope and Rich, *J. Chem. Soc.*, **75**, 1093 (1899).

in recrystallizing the picrate of 2,8-dimethyl-1,2,3,4-tetrahydroquinoline and filtrates from this recrystallization were yellow after standing for thirty days.)

When the deep red filtrate from the recrystallization of the picrate of 2,6-dimethyl-1,2,3,4-tetrahydroquinoline was allowed to stand for thirty days, orange crystals separated. They were recrystallized from alcohol, m. p. 185–186°; mixed m. p. with the picrate of 2,6-dimethylquinoline (m. p. 186–187°) 186–187°. No crystals separated from the orange filtrate from the recrystallization of the picrate of 2,8-dimethyl-1,2,3,4-tetrahydroquinoline.

1,2,6-Trimethyl-1,2,3,4-tetrahydroquinoline hydriodide was prepared by mixing 17.6 g. of methyl iodide and 20.6 g. of the crude tetrahydroquinoline. So vigorous a reaction immediately took place that the mixture boiled violently. The resulting sticky red product was crystallized from alcohol giving 24 g. of a mixture of yellow and white crystals. Two crystallizations from water dissolved the yellow crystals to leave the white crystals, m. p. 187–188.5°. A mixed melting point of these with the hydriodide of 1,2,6-trimethyl-1,2,3,4-tetrahydroquinoline prepared below (m. p. 187.5–188.5°) was 187–188°.

1,2,6-Trimethyl-1,2,3,4-tetrahydroquinoline was prepared by refluxing 22 g. of 1,2,6-trimethylquinoline hydriodide with excess tin and hydrochloric acid for seven hours. The product obtained as in preceding preparations weighed 8.3 g. (64%); b. p. 145° (20 mm.); $n^{20}D$ 1.5611; d^{20}_4 0.9906; M_D calcd. 57.29; M_D found 57.31.

The hydriodide prepared by mixing equal volumes of the base and hydriodic acid of sp. gr. 1.50 crystallized from water in white crystals, m. p. 187.5–188.5°.

Anal. Calcd. for $C_{12}H_{18}NI$: I, 41.8. Found: I, 41.8.

The picrate after four crystallizations from alcohol appeared as yellow crystals, m. p. 141–142°.

Anal. Calcd. for $C_{18}H_{22}O_7N_4$: N, 13.88. Found: N, 13.76.

Summary

2,6-Dimethyl-1,2,3,4-tetrahydroquinoline has been found to be very much more unstable and reactive than 2,8-dimethyl-1,2,3,4-tetrahydroquinoline. Its N-methyl derivative, however, is stable. Eleven new compounds in the 2,6- and 2,8-dimethylquinoline series have been prepared and characterized.

URBANA, ILLINOIS RECEIVED JULY 28, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

Osage Orange Pigments. II. Isolation of a New Pigment, Pomiferin[1]

BY M. L. WOLFROM, F. L. BENTON, A. S. GREGORY, W. W. HESS, J. E. MAHAN AND P. W. MORGAN

The isolation of a new yellow pigment from the fruit of the osage orange (*Maclura pomifera* Raf.) has been reported previously[2] from this Laboratory. The name osajin was assigned to the substance and the data reported were shown to be in harmony with a provisional formula of $C_{25}H_{22}O_3(OH)_2$.

Osajin melts at 189°[3]. In the preparation of further material from the natural source it was found that material of this same melting point could be prepared which, however, depressed the melting point of highly purified samples of osajin that melted at the same point. Further investigation showed that two yellow pigments were present, the original osajin of melting point 189° and a second of melting point 200.5°. The name pomiferin is suggested for this second product. The data so far obtained for pomiferin and its derivatives indicate a probable formula of $C_{25}H_{21}O_3(OH)_3$, thus differing from osajin by the presence of one additional oxygen atom combined as an hydroxyl group. We now find that the substance described by us[2] as osajic acid di-*p*-toluenesulfonate was actually pomiferin di-*p*-toluenesulfonate (m. p. 148°) of high purity. The correct *p*-toluenesulfonate derivative of osajin has been prepared and has been found to be a mono-*p*-toluenesulfonate (m. p. 152°) crystallizing in beautiful, lustrous plates of a golden yellow color. We have also established the melting point of osajin diacetate as 164°. Other than this, the properties of osajin (m. p. 189°), osajin monoacetate (m. p. 159°), and of osajin diacetate (m. p. 164°) have been found correct as previously reported.

We also postulated the probable presence of a lactone group in osajin. We now believe that no lactone group is present but that the consumption of one equivalent of alkali by osajin is due to the presence of an acidic phenolic group, such as is present in gossypol and in other naturally occurring phenolic structures.

Pomiferin has been characterized by a number of derivatives. It forms a diacetate and a triacetate, a dimethyl ether and a trimethyl ether, and also a dimethyl ether monoacetate.

Both osajin and pomiferin are isomerized to

(1) Presented before the Division of Organic Chemistry at the 97th Meeting of the American Chemical Society, Baltimore, Maryland.

(2) E. D. Walter, M. L. Wolfrom and W. W. Hess, THIS JOURNAL, **60**, 574 (1938).

(3) All melting points herein reported are uncorrected.

high melting, colorless products by the action of sulfuric acid in glacial acetic acid. These substances have been designated iso-osajin and iso-pomiferin, respectively. Iso-osajin gives no phenolic ferric chloride test, while iso-pomiferin does. Pomiferin di-*p*-toluenesulfonate, which initially gives a phenolic ferric chloride test and possesses a slight tinge of yellow color, is isomerized under these same conditions to a colorless isomer which no longer gives a phenolic test with ferric chloride and which is identical with the product obtained by the reaction of the isomerized pomiferin with *p*-toluenesulfonyl chloride. It would thus appear that a phenolic or enolic group is concerned in this isomerization.

The relationship of the various derivatives of osajin and pomiferin described in this paper are given in Fig. 1.

Further work on these two pigments of the fruit of the osage orange is in progress in this Laboratory.

Experimental

Isolation and Properties of a Second Pigment (Pomiferin) from the Osage Orange.—The ground and dried meal of the whole, ripe fruit of the osage orange tree (*Maclura pomifera* Raf.) was extracted with petroleum ether and ether as described previously.[2] The ether-soluble material was recrystallized repeatedly from xylene until material of melting point 200.5° was obtained. This material was unchanged in melting point on further recrystallization from xylene, benzene or ethanol. The crystals were of a yellow color and were of a deeper tinge than osajin. The substance was slightly less soluble than osajin in the same organic solvents. The properties of the substance were similar to those of osajin and it exhibited the same general behavior with chemical reagents as described previously for osajin.[2] It also showed the same evidence of possessing phenolic rather than carboxylic acidity, as described below for osajin.

Both osajin and pomiferin give only yellow colorations with pyroboroacetate in acetic anhydride and with alcoholic nickel acetate.

Anal.[4] Calcd. for $C_{25}H_{24}O_6$: C, 71.42; H, 5.75; mol. wt., 420.4; Found: C, 71.47, 71.36; H, 5.90, 5.90; mol. wt. (Rast), 388, 361.

The mother liquor material from the pomiferin isolation was repeatedly recrystallized from ethanol and yielded the previously described osajin[2] of melting point 189°.

Evidence of Phenolic Nature of Osajin Acidity.—Osajin (1 g.), dissolved in 50 cc. of ether, was placed in a 200-cc. separatory funnel and the air displaced with methane (natural gas). The top of the funnel was connected to the outlet of a 60-cc. separatory funnel containing 20 cc. of a 10% sodium hydroxide solution. As the sodium hydroxide was allowed to drop, with shaking, into the ether solution of osajin, the yellow color in the ether layer gradually disappeared and the aqueous hydroxide layer became the characteristic greenish-yellow color of alkaline osajin. After the ether layer had become completely colorless, the upper funnel was removed and a stream of carbon dioxide was passed into the funnel containing the two layers. The color in the aqueous layer disappeared completely and the yellow color of osajin returned to the ether layer. Osajin was recovered on evaporation of the ether layer.

Pomiferin exhibited the same behavior when subjected to the identical treatment described above for osajin.

Osajin Mono-*p*-toluenesulfonate.—Osajin (1 g.) was dissolved in 10 cc. of dry pyridine and treated with a solution of *p*-toluenesulfonyl chloride (4 g.) in 15 cc. of dry pyridine. The solution stood at room temperature for eighteen hours and was then poured into 400 cc. of ice and water. The resultant gum hardened readily on standing at ice-box temperature for a few hours. It was removed by filtration, washed with water and recrystallized from absolute ethanol. Pure material was obtained on several recrystallizations from absolute ethanol; m. p. 152°, unchanged on further recrystallizations from either absolute ethanol or xylene–methanol. The substance crystallized as lustrous plates of a golden yellow color and gave a green coloration, in alcoholic solution, with ferric chloride.

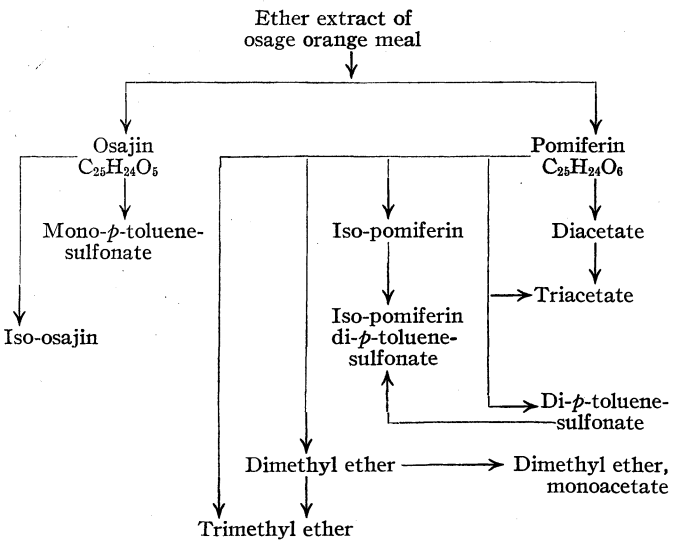


Fig. 1.

Anal. Calcd. for $C_{25}H_{23}O_4(OSO_2C_6H_4CH_3)$: C, 68.79; H, 5.41; S, 5.73; mol. wt., 558.5. Found: C, 68.84, 68.83; H, 5.42, 5.40; S, 5.79; mol. wt. (Rast), 584, 531.

Iso-osajin.—Osajin (5 g.) was dissolved in 75 cc. of boiling glacial acetic acid and 3 cc. of concentrated sulfuric acid added dropwise to the hot solution. The resulting dark orange solution was allowed to stand overnight at room temperature, after which an equal volume of water

(4) All combustion analyses herein reported were made by Dr. Ing. A. Schoeller, Berlin.

was added. The thick, curdy mass which separated crystallized on standing at ice-box temperature for an hour. The light yellow crystals were separated by filtration and washed several times with water; yield 4.1 g., m. p. 200–201°. Concentration of the mother liquors under reduced pressure yielded additional material; 0.56 g., m. p. 139°; total yield, 4.66 g. Recrystallization from absolute ethanol yielded pure colorless crystals, m. p. 285° (dec.).[5]

Iso-osajin is more difficultly soluble in organic solvents than osajin. An alcoholic solution of the substance shows no coloration with ferric chloride; it reduces Fehling's solution and, in pyridine solution, reduces Tollens' reagent. Iso-osajin was recovered unchanged when treated with an alcoholic solution of hydroxylamine acetate (refluxed for ten minutes and allowed to stand overnight). Iso-osajin is insoluble in cold 20% potassium hydroxide, but dissolves on boiling to give a greenish-yellow solution from which the substance can be recovered unchanged by acidification. The addition of a few drops of concentrated sulfuric acid to a solution of iso-osajin in glacial acetic acid gave only a deep yellow coloration. A negative test for sulfur was obtained by sodium fusion methods and by the Parr bomb. Iso-osajin also can be prepared by using an equivalent amount of concentrated hydrochloric acid in place of the sulfuric acid.

Anal. Calcd. for $C_{25}H_{24}O_5$: C, 74.25; H, 5.98; mol. wt., 404.4. Found: C, 74.24, 74.33; H, 6.00, 5.88; mol. wt. (Rast), 396, 361, 364.

Pomiferin Di-*p*-toluenesulfonate.—Pomiferin (2 g.) was treated as described for the prepartion of osajin mono-*p*-toluenesulfonate[2]; yield 2.9 g., m. p. 148°. This substance was identical (mixed m. p. unchanged) with the product of m. p. 148° previously described[2] as osajic acid di-*p*-toluenesulfonate.

Anal.[2] Calcd. for $C_{25}H_{22}O_4(OSO_2C_6H_4CH_3)_2$: C, 64.3; H, 4.98; S, 8.80; mol. wt., 728.8. Found: C, 64.4; H, 5.08; S, 8.75; mol. wt. (Rast), 680.

Iso-pomiferin.—Pomiferin was isomerized with sulfuric acid in glacial acetic acid as described for the preparation of iso-osajin and was purified by recrystallization from absolute ethanol; m. p. 265°.[5] The substance formed colorless needles and gave a green coloration with ferric chloride, changing to violet on the addition of ammonium hydroxide. It reduces Fehling's solution and, in pyridine solution, reduces Tollens' reagent. In cold 20% potassium hydroxide it turns yellow but does not dissolve; upon boiling, brownish yellow flocs form and the solution becomes dark yellow. Concentrated sulfuric acid added to a glacial acetic acid solution of the substance produces only a deep yellow color.

Anal. Calcd. for $C_{25}H_{24}O_6$: C, 71.42; H, 5.75; mol. wt., 420.4. Found: C, 71.53, 71.53; H, 5.69, 5.83; mol. wt. (Rast), 423, 399.

Iso-pomiferin Di-*p*-toluenesulfonate.—Pomiferin di-*p*-toluenesulfonate (1 g.) was isomerized with sulfuric acid in glacial acetic acid as described for the preparation of iso-osajin and the product was purified by recrystallization from alcohol followed by recrystallization from xylene by the addition of methanol; yield 0.72 g., m. p. 194°.

(5) Taken on a modified Berl–Kullman block as described by F. W. Bergstrom, *Ind. Eng. Chem., Anal. Ed.*, **9**, 340 (1937).

An alcoholic solution of the product shows no coloration with ferric chloride and does not reduce Fehling's solution or Tollens' reagent. A few drops of concentrated sulfuric acid added to a glacial acetic acid solution of the substance impart a very light yellow color. The compound was recovered unchanged after refluxing with acetic anhydride and sodium acetate for two hours.

Iso-pomiferin di-*p*-toluenesulfonate was also prepared by treating iso-pomiferin in pyridine solution with a pyridine solution of *p*-toluenesulfonyl chloride. The identity of the products was established by melting point and mixed melting point.

Anal. Calcd. for $C_{25}H_{22}O_4(OSO_2C_6H_4CH_3)_2$: C, 64.3; H, 4.98; S, 8.80; mol. wt., 728.6. Found: C, 64.1, 64.0; H, 5.11, 5.11; S, 8.55; mol. wt. (Rast), 645, 633.

Pomiferin Diacetate.—Pomiferin (1 g.) was dissolved in 12 cc. of pyridine and 24 cc. of acetic anhydride and placed in the ice-box overnight. This solution was poured into water and the crude material which separated was crystallized from methanol by the addition of water. The crystals were in the form of bright yellow plates; yield 1 g., m. p. 134.5°. Recrystallization from benzene and petroleum ether gave long, radiating needles. The melting point was not raised by recrystallization from benzene or ethanol.

The reactions and solubilities of this compound are similar to those of the monoacetate of osajin previously described.[2] The substance gave a green coloration, in alcoholic solution, with ferric chloride. Yellow crystals, m. p. 198.5°, were recovered after treatment of the compound with sodium hydroxide at ice-box temperature for three hours followed by acidification. The saponification was carried out in an atmosphere of nitrogen. A mixed melting point with pomiferin and this product showed no depression.

Anal. Calcd. for $C_{25}H_{22}O_4(OCOCH_3)_2$: C, 69.03; H, 5.59; saponification equivalent, 252.3 (3.96 cc. of 0.1 *N* NaOH per 100 mg.); mol. wt., 504.5. Found: C, 69.02, 69.22; H, 5.61, 5.57; saponification equivalent (Freudenberg method[6]), 255, 258 (3.93 cc. and 3.88 cc. of 0.1 *N* NaOH per 100 mg.); mol. wt. (Rast), 430.

Iso-pomiferin was recovered from the Freudenberg acetyl analyses and identified by melting point and mixed melting point. Pomiferin subjected to the conditions of this analysis yielded iso-pomiferin and no volatile esters.

Pomiferin Triacetate.—Pomiferin (1 g.) was refluxed for three hours with 75 cc. of acetic anhydride and 6 g. of fused sodium acetate. The mixture was poured into water and kept overnight at ice-box temperature. The crystalline material was removed by filtration; yield 1.2 g., m. p. 154°, unchanged on recrystallization from alcohol or from benzene by the addition of petroleum ether. The substance crystallized as colorless needles and gave no coloration, in alcoholic solution, with ferric chloride. Its solubilities and other reactions were much like those of osajin diacetate.

This compound also was prepared by treating pomiferin diacetate in the same manner.

Anal. Calcd. for $C_{25}H_{21}O_3(OCOCH_3)_3$: C, 68.1; H, 5.53; saponification equivalent, 182.2 (5.49 cc. of 0.1 *N* NaOH per 100 mg.); mol. wt., 546.6. Found: C, 68.07,

(6) K. Freudenberg and M. Harder, *Ann.*, **433**, 230 (1923).

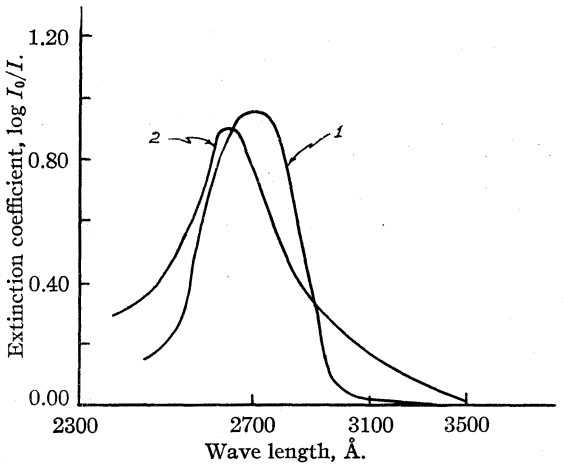


Fig. 2.—Curve 1—Absorption spectra of osajin: maximum at 2730 Å.; solvent, absolute ethyl alcohol; concentration 0.00166 g. /100 cc. Cell 0.4 cm. Curve 2—Absorption spectra of iso-osajin: maximum at 2660 Å.; solvent, absolute ethyl alcohol; concentration 0.00142 g./100 cc. Cell, 0.4 cm.

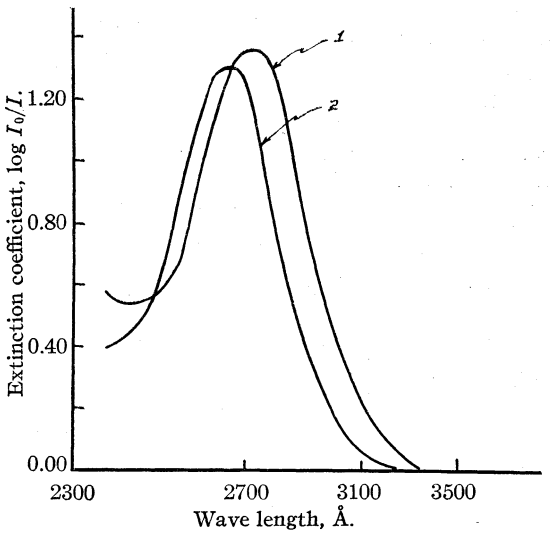


Fig. 3.—Curve 1—Absorption spectra of pomiferin: maximum at 2750 Å.; solvent, absolute ethyl alcohol; concentration 0.00303 g./100 cc.; cell 0.4 cm. Curve 2—Absorption spectra of iso-pomiferin: maximum at 2680 Å.; solvent, absolute ethyl alcohol; concentration, 0.00289 g./100 cc.; cell, 0.4 cm.

68.08; H, 5.59, 5.57; saponification equivalent (Freudenberg method,[6] 190, 191 (5.26 cc. and 5.25 cc. of 0.1 *N* NaOH per 100 mg.); mol. wt. (Rast), 540, 570.

Iso-pomiferin was recovered from the Freudenberg acetyl analyses and identified by melting point and mixed melting point.

Osajin acetylated as above yielded the previously described[2] diacetate, m. p. 164°.

Pomiferin Dimethyl Ether.—Pomiferin (1 g.) was methylated in 45 cc. of methyl alcohol under an atmosphere of nitrogen, by first adding a solution of 2.5 g. of potassium hydroxide in 40 cc. of methanol, cooling the mixture to 0° and, finally, adding 18 cc. of dimethyl sulfate with vigorous shaking of the mixture. The mixture was allowed to stand for an hour and was then poured into ice and water, filtered, and thrice recrystallized from ethanol; yield 1.1 g., m. p. 132°.

The substance crystallizes in fluffy masses of light yellow needles and is soluble in the common organic solvents. An alcoholic solution of the substance gives a green coloration with ferric chloride, but no violet coloration on the further addition of ammonia. In glacial acetic acid solution, it gives an orange coloration on the addition of sulfuric acid. It does not reduce Fehling's solution or Tollens' reagent (in pyridine solution). In carbon tetrachloride solution it shows bromine and iodine absorption. It is insoluble in hot aqueous solutions of sodium carbonate and potassium hydroxide. The substance shows no loss in weight on heating at 125–130° for several hours over phosphorus pentoxide under reduced pressure.

Anal. Calcd. for $C_{25}H_{22}O_4(OCH_3)_2$: C, 72.3; H, 6.29; OCH_3, 13.8; mol. wt., 448.4. Found: C, 72.2; H, 6.33; OCH_3, 13.6; mol. wt. (Rast), 428, 387.

The compound gives no positive saponification value even when heated at 90° with alcoholic sodium hydroxide for several hours.

Pomiferin Dimethyl Ether Monoacetate.—Pomiferin dimethyl ether (0.4 g.) was treated with 2 g. of anhydrous sodium acetate and 20 cc. of acetic anhydride and the mixture refluxed for three hours. The mixture was poured into ice and water, allowed to stand overnight and the product removed by filtration; yield, 0.43 g. Pure material was obtained on recrystallization from ethanol; m. p. 128–129°.

The substance crystallized as a fluffy mass of white needles. When dissolved in alcohol, it gives no coloration on the addition of ferric chloride. In glacial acetic acid solution, it gives a light yellow coloration on treatment with sulfuric acid. It gives no positive tests with Fehling's solution or Tollens' reagent (in pyridine). It is insoluble in aqueous sodium hydroxide.

Anal. Calcd. for $C_{25}H_{21}O_3(OCH_3)_2(OCOCH_3)$: C, 71.00; H, 6.16; sap. equiv., 490.4 (2.04 cc. of 0.1 *N* NaOH per 100 mg.); mol. wt., 490.4. Found: C, 71.16, 70.96; H, 6.14, 6.19; sap. equiv. (Freudenberg method,[6] 472, 483 (2.12 cc. and 2.07 cc. of 0.1 *N* NaOH per 100 mg.); mol. wt. (Rast), 458, 454.

Pomiferin Trimethyl Ether.—Pomiferin (2 g.) was dissolved in 130 cc. of acetone under reflux and to this solution, maintained at the boiling point, was added 24 cc. of dimethyl sulfate followed by six alternate portions of 6 cc. each of dimethyl sulfate and 8 cc. of 50% aqueous potassium hydroxide, all added as rapidly as possible. The solution was refluxed for two hours, during which time a white precipitate of potassium methyl sulfate separated, leaving a clear yellow solution. The mixture was cooled to room temperature, poured into one liter of ice and water and the excess methyl sulfate just neutralized with 10% potassium hydroxide. The white crystalline product which separated was removed by filtration and washed with water; yield 2.3 g., m. p. 120–125°. Pure material was obtained on recrystallization from ethanol; m. p. 139.5°, unchanged on further recrystallization. The substance was unchanged in weight on heating

at 110° for several hours over phosphorus pentoxide under reduced pressure.

An alcoholic solution of the product shows no coloration with ferric chloride and it does not reduce Fehling's solution. A chloroform solution of the substance absorbs bromine and it shows a yellow coloration in acetic acid on the addition of a few drops of sulfuric acid. The product was recovered unchanged after refluxing with acetic anhydride and sodium acetate for two hours. It was not affected by cold 20% potassium hydroxide but dissolved slowly on boiling to produce a light yellow solution.

Anal. Calcd. for $C_{25}H_{21}O_3(OCH_3)_3$: C, 72.7; H, 6.57; OCH_3, 20.1; mol. wt., 462.4. Found: C, 72.9; H, 6.69; OCH_3, 20.06; mol. wt. (Rast), 420, 437.

The same product was obtained by application of the same methylation procedure to pomiferin dimethyl ether. The identity of the products was established by melting point and mixed melting point.

Absorption Spectra.[7]—The absorption spectra of osajin, iso-osajin, pomiferin and iso-pomiferin were observed in absolute ethanol. The data are shown in Fig. 2 and Fig. 3. A single band spectrum was obtained for each compound.

Acknowledgment is gratefully made to the National Youth Administration for assistance rendered in this investigation.

Summary

1. A second yellow pigment has been isolated from the fruit of the osage orange tree (*Maclura pomifera* Raf.). The name pomiferin is assigned to this substance and it is shown that the experimental data so far obtained harmonize with a provisional formula of $C_{25}H_{24}O_6$.

2. The basicity of osajin is shown to be more in harmony with an acidic phenolic structure than with a lactone structure.

3. The substance previously described as osajic acid di-*p*-toluenesulfonate[2] is shown to be pomiferin di-*p*-toluenesulfonate.

4. Osajin forms a mono-*p*-toluenesulfonate (m. p. 152°).

5. The melting point of osajin diacetate is established as 164°.

6. A diacetate, triacetate, dimethyl ether, trimethyl ether, and dimethyl ether monoacetate of pomiferin have been prepared.

7. Both osajin and pomiferin are isomerized by sulfuric acid–glacial acetic acid mixtures to high-melting, colorless, crystalline substances.

8. Pomiferin di-*p*-toluenesulfonate is isomerized under the same conditions and the product is identical with the reaction product formed between iso-pomiferin and *p*-toluenesulfonyl chloride.

9. The absorption spectra of osajin, iso-osajin, pomiferin and iso-pomiferin have been observed.

COLUMBUS, OHIO RECEIVED AUGUST 9, 1939

(7) The absorption spectra measurements were made by Miss J. Appleton of this Laboratory, according to the method described in Brode, "Chemical Spectroscopy," John Wiley and Sons, Inc., New York, N. Y., 1939, p. 273.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

Dibenzofuran. XIII. Orientation and Substituted Amines[1]

BY HENRY GILMAN, PAUL T. PARKER, JAMES C. BAILIE AND GEORGE E. BROWN

Introduction

Incidental to the determination of structure of substituted amines, it is now shown that the generalizations on orientation postulated previously[2] are adequate for the predominant products which result from polysubstitution of the dibenzofuran nucleus.

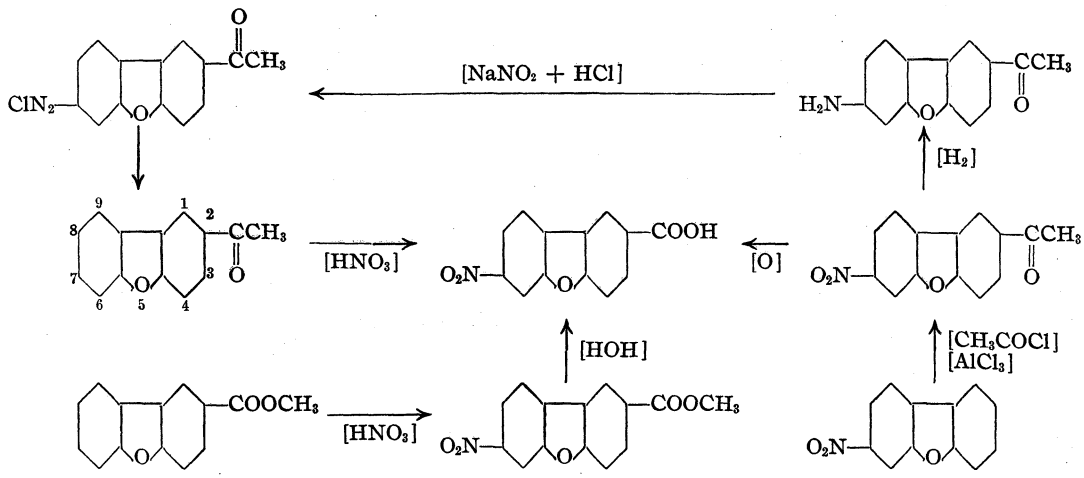
Nitration.—Nitration of a monosubstituted dibenzofuran having a strongly meta-orienting group proceeded heteronuclearly and the entering nitro group went largely to the 7-position, and the 8-position was involved only to a subordinate extent. The nitro acid obtained from nitration of 2-acetyldibenzofuran was identical with that obtained from nitration of methyl 2-dibenzofurancarboxylate. The same acid resulted by oxidation of the acetyl-3-nitrodibenzofuran prepared by a Friedel–Crafts reaction with 3-nitrodibenzofuran.

The chief nitro ester obtained by nitration of methyl 3-dibenzofurancarboxylate was methyl 2-nitro-7-dibenzofurancarboxylate. The position of the nitro group was shown by hydrolysis to a nitro acid which on decarboxylation yielded 2-nitrodibenzofuran.

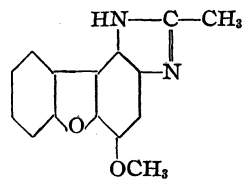
Nitration of 1-acetamino-4-methoxydibenzofuran took place homonuclearly, as might have been predicted, and the nitro group was directed ortho to the acetamino group. The structure of

(1) Paper XII, THIS JOURNAL, **61**, 1371 (1939).

(2) Gilman, Brown, Bywater and Kirkpatrick, *ibid.*, **56**, 2473 (1934); Gilman, Van Ess and Hayes, *ibid.*, **61**, 643 (1939). See, also, Cullinane, *J. Chem. Soc.*, 2365 (1932).



the 1-acetamino-2-nitro-4-methoxydibenzofuran was established by reduction and cyclization to a methoxy-imidazole. Incidentally, it was shown



that the nitro group did not go ortho to the methoxy group, for the replacement of the original acetamino group by hydrogen gave a nitro-4-methoxydibenzofuran unlike the known 3-nitro-4-methoxydibenzofuran.[3]

The nitration product of 1-bromo-4-methoxydibenzofuran was shown to be 1-bromo-3-nitro-4-methoxydibenzofuran, for debromination and reduction gave a quantitative yield of the known 3-amino-4-methoxydibenzofuran.[3]

Nitration of 2-acetyl-7-acetaminodibenzofuran must have introduced a nitro group ortho to the acetamino group because reduction and cyclization gave an acetyl-imidazole. The nitro group undoubtedly entered the 8-position rather than the 6-position, for there is no case of direct nuclear substitution (other than metalation) into the 4- or the 6-position.[4]

Nitration of 4-bromo- and 4-iododibenzofuran would be expected to go heteronuclearly to a predominant extent, for nitration of 2-bromodibenzofuran gave 2-bromo-7-nitrodibenzofuran.[5] Furthermore, the nitrobromo compound obtained by nitration of 3-bromodibenzofuran[5] has now been shown to be 3-bromo-7-nitrodibenzofuran because catalytic reduction replaced the bromine by hydrogen and reduced the nitro group to give 3-aminodibenzofuran. A similar reduction of the nitro-4-iododibenzofuran did not reduce the nitro group appreciably, and the chief product was 3-nitrodibenzofuran.

Bromination and Thiocyanogenation.—Bromination of ethyl 2-dibenzofurancarboxylate gave ethyl 2-bromo-8-dibenzofurancarboxylate. This structure followed from the fact that the bromo acid obtained by hydrolysis of the bromo ester was identical with the bromo acid obtained by oxidation of the Friedel–Crafts acetylation product of 2-bromodibenzofuran.

Thiocyanogenation of 3-aminodibenzofuran introduced the thiocyanogen group either into the 2- or the 4-position because the aminothiocyanogen compound could be rearranged to a thiazole. The thiocyanogen group undoubtedly entered the 2-position. Thiocyanogenation is like halogenation, and it is known that bromination of 3-acetaminodibenzofuran gives 2-bromo-3-acetaminodibenzofuran.[5] In addition, we already have mentioned the improbability of direct substitution into a 4- or 6-position.

Friedel–Crafts Reactions.—Diacetylation of dibenzofuran[6] and acetylation of 2-acetyldibenzofuran gave 2,8-diacetyldibenzofuran, identified by oxidation to the corresponding dibasic acid. Acetylation of methyl 4-dibenzofurancarboxylate gave methyl 2-acetyl-6-dibenzofurancarboxylate, the structure of which was established by hydrolysis and then decarboxylation to yield 2-acetyldi-

(3) Gilman, Jacoby and Swislowsky, THIS JOURNAL, **61**, 954 (1939).

(4) In the preparation of pyridodibenzofurans by the Skraup synthesis with 3-aminodibenzofuran, one of the isomers involves a ring closure in the 4-position. See Mosettig and Robinson, *ibid.*, **57**, 902 (1935), and Kirkpatrick and Parker, *ibid.*, **57**, 1123 (1935). It is understood that a suitable accumulation of groups might force a direct nuclear substitution to the 4- or 6-position.

(5) Gilman, Brown, Bywater and Kirkpatrick, *ibid.*, **56**, 2473 (1934).

(6) Borsche and Schacke, *Ber.*, **56**, 2498 (1923).

benzofuran, and by making the reasonable assumption that heteronuclear substitution occurs when a strongly meta-orienting group is present. This assumption has great validity because bromine, which has a less marked heteronuclear orientation effect than a carbomethoxy group, directs acylation heteronuclearly. For example, acetylation of 2-bromodibenzofuran gave 2-acetyl-8-bromodibenzofuran, the structure of which was established by oxidation to a 2-bromodibenzofurancarboxylic acid, which on debromination yielded 2-dibenzofurancarboxylic acid.

Acetylation of 2,8-dibromodibenzofuran gave 2,8-dibromo-3-acetyldibenzofuran. The structure of this product was proved by debromination and then oxidation of the resulting 3-acetyldibenzofuran to the known 3-dibenzofurancarboxylic acid.

Other Friedel–Crafts reactions have been mentioned in the discussion of nitration, and the Experimental Part describes additional reactions of this kind leading to amino derivatives of the brazan and other types. A miscellany of reactions other than those concerned with direct nuclear substitution are also contained in the Experimental Part.

Experimental Part

Nuclear Substitutions of 4-Derivatives

1-Bromo-4-methoxydibenzofuran.—A solution of 27.5 g. (0.17 mole) of bromine in 170 cc. of acetic acid was added in several portions to a solution of 34 g. (0.17 mole) of 4-methoxydibenzofuran in 340 cc. of acetic acid at room temperature with shaking. Decolorization was immediate. After standing overnight the product was thrown out of solution by diluting with water. Crystallization from ethanol gave 42 g. (88%) of material melting at 96–97°. A second recrystallization gave the pure product melting at 97–97.5° which showed no depression in melting point when mixed with an authentic specimen prepared by the methylation of 1-bromo-4-hydroxydibenzofuran.[7]

4-Methoxy-1-dibenzofurancarboxylic Acid.—The Grignard reagent prepared from 5 g. (0.018 mole) of 1-bromo-4-methoxydibenzofuran and 0.5 g. (0.02 g. atom) of magnesium in a mixture of 25 cc. of ether and 10 cc. of benzene was carbonated in the customary manner. A yield of 2.7 g. (62%) of the pure compound (crystallization from ethanol) was obtained melting at 279–280° with decomposition.

Anal. Calcd. for $C_{14}H_{10}O_4$: C, 69.40; H, 4.13. Found: C, 69.67 and 69.00; H, 4.61 and 4.90.

1-β-Hydroxyethyl-4-methoxydibenzofuran.—To an ice-cold solution of the Grignard reagent prepared from 22.2 g. (0.08 mole) of 1-bromo-4-methoxydibenzofuran was added 8.0 g. (0.18 mole) of ethylene oxide. The solution was allowed to warm to room temperature and then refluxed for one hour. After standing overnight, most of the ether was distilled off and replaced by dry benzene, and refluxing was continued for one hour. The resulting mixture was hydrolyzed by ice and 30% sulfuric acid, and the benzene layer was washed with sodium carbonate solution, dried and distilled under reduced pressure. The material, 11.5 g. (59%), distilled between 195–206° (2 mm.). Recrystallization from petroleum ether (b. p., 60–68°) gave crystals melting at 96–96.5°.

Anal. Calcd. for $C_{15}H_{14}O_3$: C, 74.35; H, 5.83. Found: C, 74.42; H, 6.03.

1-β-Diethylaminoethyl-4-methoxydibenzofuran Hydrochloride.—Dry hydrogen bromide was bubbled through 8.8 g. (0.028 mole) of molten 1-β-hydroxyethyl-4-methoxydibenzofuran for two and one-half hours at 100°. After washing with water and recrystallizing twice from ethanol, the product weighed 2.0 g. and melted at 91–91.5°. The 1-β-bromoethyl-4-methoxydibenzofuran was mixed with 2.0 g. (0.016 mole) of diethylamine and 2 cc. of ethanol and heated for six hours at 100°. When cool the reaction product was treated with 5% sodium hydroxide solution and extracted with ether. The ether solution was evaporated and the residue warmed to drive off the excess diethylamine. Saturating an ether solution of the residual oil with dry hydrogen chloride precipitated the salt which was purified by recrystallizing from an acetone–ether mixture. The yield was 1.5 g. (68%) of hydrochloride melting at 187° with decomposition.

Anal. Calcd. for $C_{19}H_{24}O_2NCl$: N, 4.20. Found: N, 4.26 and 4.43.

1-Acetyl-4-methoxydibenzofuran.—A Friedel–Crafts reaction was effected with 10 g. (0.05 mole) of 4-methoxydibenzofuran in 50 cc. of carbon disulfide, 6.8 g. (0.05 mole) of aluminum chloride and 4.0 g. (0.05 mole) of acetyl chloride. One recrystallization of the crude material from ethanol gave 8.0 g. (66%) of product melting at 132–133°. A second recrystallization raised the melting point to 134–134.5°.

Anal. Calcd. for $C_{15}H_{12}O_3$: C, 74.97; H, 5.04. Found: C, 74.66 and 75.30; H, 5.42 and 5.39.

Oxidation of 1 g. (0.004 mole) of the 1-acetyl-4-methoxydibenzofuran in 130 cc. of water containing 2 g. of sodium hydroxide with 3 g. (0.019 mole) of potassium permanganate gave a 90% yield of 4-methoxy-1-dibenzofurancarboxylic acid (mixed m. p.).

The oxime of 1-acetyl-4-methoxydibenzofuran was obtained in an 88% yield, and melted at 176–177.5° after crystallization from ethanol.

Anal. Calcd. for $C_{15}H_{13}O_3N$: N, 5.49. Found: N, 5.44.

Beckmann Rearrangement of the Oxime from 1-Acetyl-4-methoxydibenzofuran.—The rearrangement was effected in 95% yield by treating a suspension of the oxime in benzene with phosphorus pentachloride. The resulting **1-acetamino-4-methoxydibenzofuran** melted at 222–223° after crystallization from ethanol.

Anal. Calcd. for $C_{15}H_{13}O_3N$: N, 5.49. Found: N, 5.43 and 5.47.

Refluxing a solution of 2 g. (0.008 mole) of the 1-acetamino-4-methoxydibenzofuran in 200 cc. of 95% ethanol with 50 cc. of concd. hydrochloric acid gave a 91% yield

(7) Gilman and Van Ess, THIS JOURNAL, **61**, 1365 (1939).

of 1-amino-4-methoxydibenzofuran hydrochloride. The free base melting at 103–104° showed no depression in melting point with the 1-amino-4-methoxydibenzofuran obtained by reduction of 1-nitro-4-methoxydibenzofuran.[3]

1-Acetamino-2-nitro-4-methoxydibenzofuran.—Nitration of 0.8 g. (0.003 mole) of 1-acetamino-4-methoxydibenzofuran in glacial acetic acid with 1 cc. of fuming nitric acid gave a 74% yield of the nitro compound which melted at 244° after recrystallization from acetic acid.

Anal. Calcd. for $C_{15}H_{12}O_5N_2$: N, 9.33. Found: N, 9.30 and 9.69.

The acetamino compound was hydrolyzed in essentially quantitative yield by refluxing with concd. hydrochloric acid in ethanol. The **1-amino-2-nitro-4-methoxydibenzofuran** melted at 206–207° after crystallization from toluene.

Anal. Calcd. for $C_{13}H_{10}O_4N_2$: N, 10.85. Found: N, 10.36 and 10.70.

2-Nitro-4-methoxydibenzofuran.—The 1-amino-2-nitro-4-methoxydibenzofuran could not be diazotized by usual procedures; however, diazotization was effected in essential accordance with the directions of De Milt and Van Zandt.[8]

A mixture of 15 cc. of concd. sulfuric acid and 7.5 cc. of water was cooled to 5° in an ice-bath. Six-tenths of a gram (0.009 mole) of sodium nitrite was added and the mixture was warmed gently on the steam-bath until a clear solution resulted. This solution was cooled to 5–10° and a solution of 0.6 g. (0.0023 mole) of the 1-amino-2-nitro-4-methoxydibenzofuran in 12 cc. of pyridine was added dropwise over a period of forty-five minutes with continuous shaking. The temperature was maintained below 10° at all times. Following the addition of the pyridine solution the mixture was allowed to stand at this temperature for one-half hour and then stirred into 50 g. of ice. To remove the excess of nitrous acid, 0.6 g. of urea was added and the mixture stirred until foaming had ceased. Fifteen cc. of ethanol was added and the clear solution was refluxed for five minutes on the hot plate. When cool, the red-brown precipitate was recrystallized repeatedly from methanol, and there resulted a 35% yield of the 2-nitro-4-methoxydibenzofuran as light yellow, feathery needles melting at 185–186°.

Anal. Calcd. for $C_{13}H_9O_4N$: N, 5.76. Found: N, 5.72 and 5.66.

2-Amino-4-methoxydibenzofuran.—A suspension of 0.1 g. of the 2-nitro-4-methoxydibenzofuran in 25 cc. of ethanol was reduced at room temperature under forty-five pounds (4 atm.) gage pressure of hydrogen using Raney nickel as a catalyst. The amine was obtained in fine, slightly colored crystals melting at 127–127.5° after crystallization from ethanol.

Anal. Calcd. for $C_{13}H_{11}O_2N$: N, 6.57. Found: N, 6.74.

3-Dibenzofurylurea.—A solution of 9.15 g. (0.05 mole) of 3-aminodibenzofuran and 6.0 g. (0.057 mole) of nitrourea in 150 cc. of ethanol was allowed to stand at room temperature. A pearly, crystalline precipitate of pure 3-dibenzofurylurea had settled at the end of two days, weighing 7.5 g. (66.5% yield). In a capillary tube the material shows signs of softening at 215–220°, but does not melt up to 325°. On a nickel block the substance melts and resolidifies immediately at 222–223°.

Anal. Calcd. for $C_{13}H_{10}O_2N_2$: N, 12.38. Found: N 12.65 and 12.52.

Buck and Ferry[9] have observed that ethanol is a better medium than water for the reaction between amines and nitrourea.

4-Bromodibenzofuran.—An ether solution of 4-dibenzofuryllithium was prepared by metalating 42 g. (0.25 mole) of dibenzofuran with *n*-butyllithium. To the cooled solution was admitted a slow stream of bromine vapor obtained by bubbling nitrogen through 40 g. (0.25 mole) of bromine. The yield of 4-bromodibenzofuran melting at 70–71° was 40.5%.

Anal. Calcd. for $C_{12}H_7OBr$: Br, 25.05. Found: Br, 25.19.

4-Bromo-7-nitrodibenzofuran.—An acetic acid solution of 4-bromodibenzofuran was nitrated by fuming nitric acid to give 4-bromo-7-nitrodibenzofuran which melted at 205° after crystallization from acetic acid.

Anal. Calcd. for $C_{12}H_6O_3NBr$: N, 4.79. Found: N, 5.10 and 5.18. The residues are being examined for isomers.

4-Iodo-7-nitrodibenzofuran.—To a solution of 10 g. (0.034 mole) of 4-iododibenzofuran in 50 cc. of glacial acetic acid was added 8 cc. of fuming nitric acid, and the mixture was warmed and stirred for three hours. The yellow 4-iodo-7-nitrodibenzofuran was obtained in 32.4% yield, and melted at 223° after crystallization from acetic acid.

Anal. Calcd. for $C_{12}H_6O_3NI$: N, 4.13. Found: N, 4.13 and 4.14.

Reduction of 4-Iodo-7-nitrodibenzofuran and 3-Bromo-7-nitrodibenzofuran.—An absolute ethanol solution of 0.25 g. of 4-iodo-7-nitrodibenzofuran was reduced in essential accordance with the directions of Busch and Stöve[10] using the palladium catalyst and shaking for one and one half hours under a 15-pound gage pressure of hydrogen. A 32% yield of 3-nitrodibenzofuran (mixed m. p.) was obtained.

Under corresponding conditions, 3-bromo-7-nitrodibenzofuran[5] gave a 40% yield of 3-aminodibenzofuran (mixed m. p.).

Methyl 2-Acetyl-6-dibenzofurancarboxylate.—To a suspension of 13.5 g. (0.06 mole) of methyl 4-dibenzofurancarboxylate and 10.6 g. (0.08 mole) of aluminum chloride in 100 cc. of carbon disulfide was added 4.7 g. (0.06 mole) of acetyl chloride. After refluxing for eight hours and then allowing to stand overnight, there was obtained 2.5 g. (15.5%) of methyl 2-acetyl-6-dibenzofurancarboxylate which melted at 174–175° subsequent to recrystallization from ethanol. In addition there was recovered 9.6 g. of the initial ester.

Anal. Calcd. for $C_{16}H_{12}O_4$: C, 71.64; H, 4.48. Found: C, 71.47 and 71.38; H, 4.65 and 4.56.

Hydrolysis of the acetyl ester by heating with 20% sodium hydroxide gave 2-acetyl-6-dibenzofurancarboxylic acid, which when crystallized from dilute ethanol melted

(8) De Milt and Van Zandt, THIS JOURNAL, **58**, 2044 (1936).

(9) Buck and Ferry, *ibid.*, **58**, 854 (1936).

(10) Busch and Stöve, *Ber.*, **49**, 1063 (1916).

at 262–265°. This acetyl acid was decarboxylated by heating with copper bronze and quinoline for one-half hour at 235–240° to give 2-acetyldibenzofuran (mixed m. p.).

Nuclear Substitutions of 3-Derivatives

2-Acetyl-7-nitrodibenzofuran.—A Friedel–Crafts reaction was carried out with a suspension of 56 g. (0.26 mole) of 3-nitrodibenzofuran in 400 cc. of nitrobenzene, 53 g. (0.40 mole) of powdered aluminum chloride, and 33 g. (0.42 mole) of acetyl chloride. Subsequent to hydrolysis the aqueous layer was decanted from the resulting gelatinous precipitate and nearly all of the nitrobenzene was removed by steam distillation. Complete removal of the solvent was effected by shaking the residue with methanol, filtering, and washing the material with an additional small quantity of methanol. The crude product weighed 62 g. (93.5%) and melted at 208–210°. Crystallization from acetic acid gave the pure compound melting at 212–213°.

Anal. Calcd. for $C_{14}H_9O_4N$: N, 5.49. Found: N, 5.58 and 5.62.

When carbon disulfide was used as the medium, the 3-nitrodibenzofuran was recovered unchanged after heating for eight hours.

2-Acetyl-7-aminodibenzofuran.—If the nitro compound used in this preparation was washed with dilute ammonium hydroxide and thoroughly dried, it was hydrogenated easily with Raney nickel catalyst. Twenty grams (0.079 mole) of 2-acetyl-7-nitrodibenzofuran suspended in 150 cc. of absolute ethanol was reduced with hydrogen at steam temperature under forty-five pounds gage pressure using approximately 10 cc. of an alcoholic suspension of Raney nickel catalyst. Reduction required about an hour and gave practically a quantitative yield of the crude amine melting at 156°. After recrystallization from ethanol the 2-acetyl-7-aminodibenzofuran melted at 158–159°.

Anal. Calcd. for $C_{14}H_{11}O_2N$: N, 6.22. Found: N, 6.26 and 6.54.

2-Acetyl-7-acetaminodibenzofuran and Its Oxime.—A nearly quantitative yield of the crude monoacetamino compound was obtained, at room temperature, by adding 8.7 g. (0.08 mole) of acetic anhydride to a well-stirred solution of 15.3 g. (0.068 mole) of the 2-acetyl-7-aminodibenzofuran in 150 cc. of acetic acid diluted with 35 cc. of water. The acetamino compound, which precipitated immediately, was recrystallized from ethanol and finally from benzene to yield cotton-like needles melting at 203°.

Anal. Calcd. for $C_{16}H_{13}O_3N$: N, 5.24. Found: N, 5.32.

A portion of this compound was converted to the oxime to make certain that reduction of the ketone group had not occurred in the preceding hydrogenation. A solution of 0.5 g. of potassium hydroxide in 5 cc. of water was added to a solution of 1.35 g. (0.005 mole) of the 2-acetyl-7-acetaminodibenzofuran and 0.5 g. (0.007 mole) of hydroxylamine hydrochloride in 75 cc. of ethanol. After four and one-half hours of refluxing the solution was poured into water and the precipitate filtered off. Crystallization from ethanol gave a 64% yield of colorless crystals of **1-acetyl-7-acetaminodibenzofuran oxime** melting at 203°. A mixed melting point with the starting material was 176–178°.

Anal. Calcd. for $C_{16}H_{14}O_3N_2$: N, 9.92. Found: N, 9.92.

Replacement of Amino Group in 2-Acetyl-7-aminodibenzofuran by Hydrogen.—The acetyl-amino compound was diazotized, and by customary procedures, using ethanol, the diazonium group was replaced by hydrogen. The resulting 2-acetyldibenzofuran was identified by mixed melting point.

Oxidation of 2-Acetyl-7-nitrodibenzofuran.—A solution of 16 g. of the acetyl-nitro compound in 150 cc. of acetic acid was oxidized by heating for three hours with 80 g. of chromic acid in 150 cc. of acetic acid. The resulting 3-nitro-7-dibenzofurancarboxylic acid, purified through the sodium salt, was obtained in a yield of 11.5 g. (72%) and was observed to soften at 295° and decompose at 300°.

Anal. Calcd. for $C_{13}H_7O_5N$: N, 5.45; neut. equiv., 256. Found: N, 5.53 and 5.51; neut. equiv., 251 and 252.

The following oxidizing agents were not satisfactory: acid or neutral potassium permanganate, bromine, sodium dichromate and sulfuric acid, and "Perchloron" (70% calcium hypochlorite).

Nitration of Methyl 3-Dibenzofurancarboxylate.—The 3-dibenzofurancarboxylic acid (m. p. 270°) was prepared in an 84% yield by carbonation of 3-dibenzofurylmagnesium bromide. Esterification by methanol and hydrogen chloride gave a quantitative yield of methyl 3-dibenzofurancarboxylate.

Nitration of 6 g. (0.0265 mole) of methyl 3-dibenzofurancarboxylate by a mixture of 32.5 cc. of concd. nitric acid and 5 cc. of fuming nitric acid gave 2.5 g. (34.8%) of **methyl 2-nitro-7-dibenzofurancarboxylate** which melted at 235–236° after recrystallization from acetic acid.

Anal. Calcd. for $C_{14}H_9O_5N$: N, 5.17. Found: N, 5.28 and 5.13.

In addition to some unaltered ester, there was isolated another nitro ester which melted at 202–203° and which was probably **methyl 3-nitro-7-dibenzofurancarboxylate.**

Hydrolysis of the methyl 2-nitro-7-dibenzofurancarboxylate by heating with a mixture of acetic and hydrochloric acids gave **2-nitro-7-dibenzofurancarboxylic acid** which did not melt at 330°. This nitro acid was decarboxylated, by heating with quinoline and copper, to yield 2-nitrodibenzofuran (mixed m. p.).

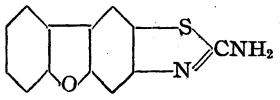
3-Amino-2-dibenzofurylthiocyanate.—Five grams (0.027 mole) of 3-aminodibenzofuran and 8.5 g. (0.11 mole) of ammonium thiocyanate were dissolved in 400 cc. of 95% acetic acid and cooled to 1–3°. A solution of 4.3 g. of bromine in 25 cc. of acetic acid was then added dropwise over a period of fifteen minutes to the vigorously stirred mixture. Despite the addition of 100 cc. more of 95% acetic acid a complete solution could not be maintained at this temperature. The crude material was recrystallized from hot ethanol to yield 2.8 g. (43%) of slightly crude 3-amino-2-dibenzofurylthiocyanate. Further recrystallization gave the pure product melting at 175° with immediate resolidification.

Anal. Calcd. for $C_{13}H_8OSN_2$: N, 11.66. Found: N, 11.88 and 11.62.

The compound gave the characteristic yellow precipitate always formed when an alkaline lead tartrate solution is

added to an ethanolic solution of a thiocyanate.[11] Rearrangement had not taken place to the thiazole, for the thiazole compound (described below) gave a white precipitate under corresponding conditions.

2 - Aminobenzofuro[2,3-*f*]benzothiazole.—A rearrangement of the 3-amino-2-dibenzofurylthiocyanate to the thiazole compound was effected by refluxing an ethanolic



solution with hydrochloric acid for one-half hour. A quantitative yield of the crude compound was obtained which was recrystallized several times from benzene to give the pure product melting at 268–269°.

Anal. Calcd. for $C_{13}H_8OSN_2$: N, 11.66. Found: N, 11.64 and 11.62.

The hydrochloride, precipitated from an ether solution of the base by dry hydrogen chloride, decomposed above 300°.

Nuclear Substitutions of 2-Derivatives

2,8-Diacetyldibenzofuran.—This diacetyl derivative was prepared by Friedel–Crafts reactions starting with either dibenzofuran or 2-acetyldibenzofuran. To a solution of 67.2 g. (0.4 mole) of dibenzofuran and 80 g. (0.6 mole) of aluminum chloride in 200 cc. of carbon disulfide was added 31.4 g. (0.4 mole) of acetyl chloride. The reaction products were fractionated under reduced pressure. The yield of pure 2-acetyldibenzofuran ranged from 46 to 57%, and the yield of 2,8-diacetyldibenzofuran was about 8%. With acetic anhydride, the yield of diacetyl compound increased somewhat at the expense of the monoacetyl compound. Nitrobenzene appeared less satisfactory as a medium, for the yield of monoacetyl compound was 40% and the mixture was worked up with greater difficulty.

Under essentially corresponding conditions, 18 g. (0.086 mole) of 2-acetyldibenzofuran, 22.8 g. (0.17 mole) of aluminum chloride, 7.3 g. (0.09 mole) of acetyl chloride and 100 cc. of carbon disulfide yielded 7 g. (32%) of 2,8-diacetyldibenzofuran. The diacetyl compound melted in all cases at 160° and not at 140° as reported previously.[6] The identity of our diacetyl compound was established by oxidation to 2,8-dibenzofurandicarboxylic acid. Incidentally this dibasic acid was also synthesized in a low yield by carbonation of the di-Grignard reagent prepared from 2,8-dibromodibenzofuran. It was, however, best prepared by carbonation of the dilithium compound obtained by interaction of *n*-butyllithium and 2,8-dibromodibenzofuran. Metalation of 2,8-dibromodibenzofuran by means of phenylcalcium iodide, and then carbonation yielded 2,8-dibromo-4,6-dibenzofurandicarboxylic acid.[12]

The oxime of 2-acetyldibenzofuran was obtained in a 97% yield, and melted after crystallization from ethanol at 139–140°.

Oxidation of 10 g. (0.03 mole) of 2-acetyldibenzofuran by an alkaline solution of "Perchloron" gave a 97% yield of 2-dibenzofurancarboxylic acid melting at 236–242°. Recrystallization from ethanol raised the melting point to 247–248°. The procedure described was less satisfactory when larger quantities of reactants were used. 2-Acetyldibenzofuran was first oxidized to 2-dibenzofurancarboxylic acid by means of calcium hypochlorite.[13]

2,8-Dibromo-3-acetyldibenzofuran.—From reaction between 22.8 g. (0.07 mole) of 2,8-dibromodibenzofuran, 13.3 g. (0.1 mole) of aluminum chloride and 5.5 g. (0.07 mole) of acetyl chloride in 150 cc. of carbon disulfide was obtained 10 g. (35%) of 2,8-dibromo-3-acetyldibenzofuran melting at 157–157.5° after crystallization from acetic acid.

Anal. Calcd. for $C_{14}H_8O_2Br_2$: Br, 43.48. Found: Br, 43.67 and 43.72.

The structure of the dibromo-acetyl compound was established by first replacing the bromines by hydrogen (palladium–calcium carbonate catalyst) to get a relatively pure 3-acetyldibenzofuran which melted at 120–122° after crystallization from ethanol; and then oxidizing the acetyl compound by alkaline permanganate to 3-dibenzofurancarboxylic acid, which was compared with an authentic specimen.

Nitration of 2-Acetyldibenzofuran.—The nitro-acetyl compound obtained by earlier workers[6] was not isolated by us; instead, a nitro acid was obtained which melted at 290°.

Methyl 3-Nitro-8-dibenzofurancarboxylate.—A 95% yield of methyl 2-dibenzofurancarboxylate, melting at 73–74° after crystallization from petroleum ether (b. p. 60–68°), was obtained by the rapid addition of hydrogen chloride to a heated suspension of 2-dibenzofurancarboxylic acid in methanol. When the ester was nitrated in essential accordance with the directions described recently[14] for the nitration of methyl 4-dibenzofurancarboxylate, one of the products isolated melted at 239–240°.

Acetylation of 2-Bromodibenzofuran.—A 32% yield of 2-bromo-8-acetyldibenzofuran distilling at 205° (4 mm.) was obtained by a Friedel–Crafts reaction between 2-bromodibenzofuran and acetyl chloride in carbon disulfide. Oxidation of the bromo-acetyl compound by means of hypochlorite gave 2-bromo-8-dibenzofurancarboxylic acid melting at 328°. Debromination of the bromo acid by means of hydrogen and the palladium–calcium carbonate catalyst gave 2-dibenzofurancarboxylic acid (mixed m. p.).

Ethyl 2-Bromo-8-dibenzofurancarboxylate.—Ethyl 2-dibenzofurancarboxylate, prepared by the addition of absolute ethanol to the reaction mixture of 2-dibenzofurancarboxylic acid and thionyl chloride, melted at 54°. To 5 g. (0.02 mole) of this ester in 30 cc. of glacial acetic acid was added 3.33 g. (0.02 mole) of bromine. The mixture was heated for eight hours at 70° and finally for four hours at 115° before bromine vapors ceased refluxing. A part of the product was 2-bromo-8-dibenzofurancarboxylic acid. The main fraction (28% yield) was ethyl 2-bromo-8-dibenzofurancarboxylate which melted at 130°.

Anal. Calcd. for $C_{15}H_{11}O_3Br$: Br, 32.36. Found: Br, 32.53 and 32.40.

The ester was hydrolyzed quantitatively, by refluxing with a mixture of acetic and concd. hydrochloric acids, to 2-bromo-8-dibenzofurancarboxylic acid which melted with decomposition at 328°.

Neutralization equivalent. Calcd. for $C_{13}H_7O_3Br$: 291.

(11) Soderbach, *Ann.*, **443**, 156 (1925).

(12) Studies by R. E. Dickey.

(13) Mayer and Krieger, *Ber.*, **55**, 1659 (1922).

(14) Gilman, Van Ess and Hayes, THIS JOURNAL, **61**, 643 (1939).

Found: 290. A comparison of this bromo acid with that obtained from the Friedel-Crafts reaction with 2-bromodibenzofuran showed them to be the same.

1-Bromo-3-nitro-4-methoxydibenzofuran and its Reduction to 3-Amino-4-methoxydibenzofuran.—A mixture of 10 g. (0.036 mole) of 1-bromo-4-methoxydibenzofuran, 10 cc. of fuming nitric acid (sp. gr. 1.50) and 75 cc. of glacial acetic acid was heated with stirring for one and one-half hours at 90–95°. The yield of 1-bromo-3-nitro-4-methoxydibenzofuran, melting at 160–161°, was 47.5%. The acetic acid filtrate from the nitration contains the initial compound which can be recovered readily and used in a second nitration.

Anal. Calcd. for $C_{13}H_8O_4NBr$: N, 4.35. Found: N, 4.31.

When an ethanolic solution of the bromonitromethoxy compound was reduced using the palladium–calcium carbonate catalyst, there resulted a quantitative yield of 3-amino-4-methoxydibenzofuran (mixed m. p.).

1-Bromo-3-amino-4-methoxydibenzofuran.— Reduction of an acetic acid solution of the bromonitromethoxy compound by stannous chloride and hydrochloric acid gave a practically quantitative yield of 1-bromo-3-amino-4-methoxydibenzofuran which melted at 135–136° after crystallization from ethanol.

Anal. Calcd. for $C_{13}H_{10}O_2NBr$: N, 4.79. Found: N, 4.95.

1-Bromo-3-acetamino-4-methoxydibenzofuran prepared by acetylation of the corresponding amine melted at 178–179° after crystallization from ethanol.

Anal. Calcd. for $C_{15}H_{12}O_3NBr$: N, 4.19. Found: N, 4.50.

Brazan Derivatives

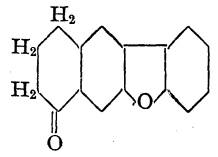
β-[2-Dibenzofuroyl]-propionic Acid.—This compound was originally prepared by Mayer and Krieger[13,15] but the method by which it was obtained was not described. The following procedure is based on the one used by Fieser and Hershberg[16] for the Friedel–Crafts reaction of succinic anhydride with phenol ethers.

Dibenzofuran, 84.0 g. (0.5 mole), and succinic anhydride, 55.0 g. (0.55 mole), were suspended in a mixture of 400 cc. of tetrachloroethane and 200 cc. of nitrobenzene. With the temperature of the mixture held at 0–5°, 147.0 g. (1.1 moles) of powdered aluminum chloride was added in small portions with vigorous stirring. Subsequent to hydrolysis and steam distillation, the residue was filtered and extracted several times with hot sodium carbonate solution. The combined filtrates were acidified with dilute hydrochloric acid and the dried precipitate recrystallized from ethyl acetate to give 111 g. (83%) of the purified compound which melted at 185–186° in agreement with the value reported by Mayer and Krieger.[13]

β-[2-Dibenzofuryl]-*n*-butyric Acid.—For the reduction of the dibenzofuroylpropionic acid, the modified Clemmensen method reported by Martin[17] was employed.

Fifty-five grams of β-[2-dibenzofuroyl]propionic acid was suspended in a mixture of 100 cc. of toluene, 75 cc. of water and 175 cc. of concd. hydrochloric acid, and refluxed for twenty-five hours with 100 g. of amalgamated zinc. Three additional 50-cc. portions of concd. hydrochloric acid were added at approximately six-hour intervals. Crystallization from petroleum ether (b. p. 80–100°) gave 43.6 g. (83%) of the pure compound melting at 112–113°, in agreement with the melting point reported.[13]

7 - Keto - 7,8,9,10 - tetrahydrobenzo[*b*]naphtho[2,3-*d*]-furan.—Five grams (0.02 mole) of β-[2-dibenzofuryl]-*n*-



butyric acid was stirred into 100 g. of 88% sulfuric acid and the mixture allowed to stand at room temperature for fifteen minutes. The resulting deep red solution was poured on ice and the dilute acid decanted from the precipitate. The crude material was washed by decantation and warmed with 50 cc. of 10% sodium carbonate solution. The insoluble product was filtered off and recrystallized from ethanol to give 2.0 g. (45%) of pure compound melting at 137°.

Anal. Calcd. for $C_{16}H_{12}O_2$: C, 81.32; H, 5.12. Found: C, 81.53; H, 5.56.

Using sulfuric acid as the cyclizing agent none of the isomeric keto compound was isolated.[18] Later, Robinson and Mosettig[15] used phosphoric acid as the condensing agent and obtained a 3–4% yield of the isomer, and also established the structure of the 137° compound by conversion to brazan (benzo[*b*]naphtho[2,3-*d*]furan).

The **oxime of 7-keto-7,8,9,10-tetrahydrobenzo[*b*]-naphtho[2,3-*d*]furan,** obtained in 85% yield, melted at 212–213° after crystallization from ethanol.

Anal. Calcd. for $C_{16}H_{13}O_2N$: N, 5.58. Found: N, 5.48.

7 - Amino - 7,8,9,10 - tetrahydrobenzo[*b*]naphtho[2,3-*d*]furan Hydrochloride.—Fifty grams of freshly prepared 2% sodium amalgam was added in small portions to a well-stirred solution of 1.7 g. (0.007 mole) of the oxime of 7-keto-7,8,9,10-tetrahydrobenzo[*b*]naphtho[2,3-*d*]furan in 65 cc. of absolute ethanol at a temperature of 55–60°. The solution was constantly maintained slightly acid by the dropwise addition of acetic acid. When reduction was complete the solution was decanted away from the mercury into several times its volume of water. The solution was made acid to litmus with acetic acid and extracted once with ether. The ether extract was discarded and the aqueous layer was made alkaline with dilute sodium hydroxide solution and extracted twice with ether. The ether extracts were dried, and dry hydrogen chloride passed into the solution. The amine hydrochloride was obtained in a 54% yield and melted at 266–267° after crystallization from an ethanol–ether mixture.

Anal. Calcd. for $C_{16}H_{16}ONCl$: N, 5.12. Found: N, 4.95 and 5.23.

7-Keto - 8 - dimethylaminomethyl - 7,8,9,10 - tetrahydrobenzo[*b*]naphtho[2,3-*d*]furan Hydrochloride.—The

(15) See, also, Robinson and Mosettig, THIS JOURNAL, **61**, 1148 (1939).

(16) Fieser and Hershberg, *ibid.*, **58**, 2314 (1936).

(17) Martin, *ibid.*, **58**, 1438 (1936).

(18) Parker, *Iowa State Coll. J. Sci.*, **12**, 148 (1937) [*C. A.*, **32**, 2937 (1938)].

method of Mannich and Braun,[19] as modified by Burger and Mosettig,[20] for the preparation of amino ketones was used in this synthesis.

A suspension of 2.4 g. (0.01 mole) of the 7-keto-7,8,9,10-tetrahydrobenzo[*b*]naphtho[2,3-*d*]furan, 1.0 g. (0.012 mole) of dimethylamine hydrochloride and 0.9 g. (0.03 mole) of trioxymethylene in 25 cc. of amyl alcohol was refluxed for five minutes. The hydrochloride was purified by carefully reprecipitating it several times from an absolute ethanolic hydrogen chloride solution with ether. The salt formed lustrous prisms melting at 185–186°. The yield of pure compound was 0.45 g. (14.3%).

Anal. Calcd. for $C_{18}H_{18}O_2NCl$: N, 4.43. Found: N, 4.39.

A repetition of this procedure with a longer time of refluxing gave no improvement in the yield.

Lateral Amino Derivatives

2-α-Aminoethyldibenzofuran Hydrochloride.—Interaction of 10.5 g. (0.05 mole) of 2-acetyldibenzofuran, 20 g. of ammonium formate and 5 cc. of acetic acid gave 2-α-aminoethyldibenzofuran hydrochloride which melted at 222–223° after crystallization from an acetone–ethanol mixture.

Anal. Calcd. for $C_{14}H_{13}ONCl$: N, 5.66. Found: N, 5.57 and 5.92.

2-α-Diethylaminoethyldibenzofuran Picrate.—Methyl-2-dibenzofurylcarbinol was prepared from 2-dibenzofurylmagnesium bromide and acetaldehyde.[21] The corresponding bromide, prepared by means of dry hydrogen bromide, was treated with diethylamine to give the highly hygroscopic diethylamino salt. The picrate of the amine melted at 173–174° after crystallization from aqueous acetone.

Anal. Calcd. for $C_{24}H_{24}O_8N_4$: N, 11.29. Found: N, 11.45.

2-β-Dimethylaminopropionyldibenzofuran.—A mixture of 20.0 g. (0.095 mole) of 2-acetyldibenzofuran, 7.8 g. (0.096 mole) of dimethylamine hydrochloride and 3.0 g. (0.096 mole) of trioxymethylene suspended in 40 cc. of absolute ethanol was heated on the steam-bath for twelve hours. When cool the precipitate was filtered off and the filtrate evaporated. The combined residues were shaken with ether to remove unchanged 2-acetyldibenzofuran. The ether-insoluble crude 2-β-dimethylaminopropionyldibenzofuran hydrochloride weighing 21.4 g. (74%) was purified by recrystallizing from ethanol to give crystals melting at 194–195°. The free base, obtained by adding dilute ammonium hydroxide to an aqueous solution of the salt, was recrystallized from petroleum ether (b. p. 60–68°) and melted at 88–89°.

Anal. Calcd. for $C_{17}H_{17}O_2N$: N, 5.24. Found: N, 5.30.

3-Ethylaminodibenzofuran Hydrochloride.—The experiments in this section provide a new physical constant[22] as well as some reactions of this compound. A mixture of 9.15 g. (0.05 mole) of 3-aminodibenzofuran and 10.5 g. (0.0525 mole) of ethyl *p*-toluenesulfonate was heated at 175–185° for one hour. After treatment with ammonium hydroxide and then with hydrogen chloride, the amine hydrochloride (3.5 g.) (33%) was found to melt at 228–229° with decomposition. Crystallization was from ethanol.

Anal. Calcd. for $C_{14}H_{14}ONCl$: N, 5.66. Found: N, 5.67.

The hydrochloride and sodium acetate in an ether–water medium gave a colorless oil which solidified to crystals melting at 69–70°.

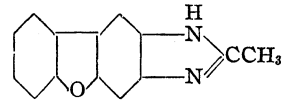
The **3-ethylnitrosoaminodibenzofuran** (prepared from the hydrochloride, sodium nitrite and dilute hydrochloric acid) crystallized from ethanol as bright orange crystals melting at 136–137°.

Anal. Calcd. for $C_{14}H_{12}O_2N_2$: N, 11.66. Found: N, 11.12.

Reduction of the nitrosoamine with stannous chloride and concd. hydrochloric acid gave the 3-ethylaminodibenzofuran hydrochloride (mixed m. p.).

Imidazoles

2-Methyl-1-benzofuro[2,3-*f*]benzimidazole.—3-Aminodibenzofuran was monoacetylated by adding 12 g. (0.12



mole) of acetic anhydride to a solution of 20 g. (0.11 mole) of 3-aminodibenzofuran in a mixture of 150 cc. of acetic acid and 200 cc. of water at a temperature between 40 and 50° with vigorous stirring. The thick, heavy precipitate which resulted in a few seconds was poured into water and filtered off to give a 97% yield of material suitable for nitration.

Nitration was effected by adding 3.5 cc. of fuming nitric acid (sp. gr. 1.50) to a solution of 10 g. (0.04 mole) of 3-acetaminodibenzofuran in 60 cc. of glacial acetic acid at 85–90°. The 2-nitro-3-acetaminodibenzofuran separated almost at once. The mixture was poured into an excess of water and filtered. Crystallization of the crude product from acetic acid yielded 9.2 g. (76%) of light yellow crystals melting at 196°.

To a hot solution of 2.0 g. (0.0074 mole) of 2-nitro-3-acetaminodibenzofuran in 25 cc. of acetic acid was cautiously added in several portions with shaking a solution of 8.0 g. (0.035 mole) of hydrated stannous chloride in 8.0 cc. of concd. hydrochloric acid and the solution heated for a few minutes. The crude imidazole was purified through its hydrochloride by recrystallizing from dilute hydrochloric acid. The hydrochloride (melting above 335°) was converted to the free base which melts at 270°, and was obtained in a yield of 0.9 g. (55%).[23]

Anal. Calcd. for $C_{14}H_{10}ON_2$: N, 12.61. Found: N, 12.79 and 12.87.

2-Methyl-5-methoxy-1-benzofuro[3,2-*e*]benzimidazole.—To a hot solution of 3.0 g. (0.01 mole) of 1-

(19) Mannich and Braun, *Ber.*, **53**, 1874 (1920).

(20) Burger and Mosettig, THIS JOURNAL, **58**, 1570 (1936).

(21) This compound was prepared earlier by Mosettig and Robinson, *ibid.*, **57**, 2186 (1935), by the catalytic hydrogenation of 2-acetyldibenzofuran.

(22) Kirkpatrick and Parker, *ibid.*, **57**, 1123 (1935).

(23) Weidenhagen and Weeden, *Ber.*, **71**, 2347 (1938), have reported a melting point of 264.5° for the free base and a decomposition point at about 278° for the hydrochloride.

acetamino-2-nitro-4-methoxydibenzofuran in 75 cc. of glacial acetic acid was added in several portions a solution of 12.5 g. (0.055 mole) of hydrated stannous chloride in 13.5 cc. of concd. hydrochloric acid. The mixture was then refluxed for five and one-half hours on the hot-plate. After diluting with 200 cc. of water the solution was made alkaline with 33% sodium hydroxide solution and the precipitate filtered off. The crude material was purified by boiling its methanol solution with Norite and saturating the cooled solution with dry hydrogen chloride. The hydrochloride precipitated in fine needles melting at 306–307° with decomposition. From the hydrochloride was obtained the free base in a yield of 1.8 g. (72.5%), melting at 222–222.5°.

Anal. Calcd. for $C_{15}H_{12}O_2N_2$: N, 11.10. Found: N, 10.95 and 11.16.

2 - Methyl - 8 - acetyl - 1 - benzofuro[2,3-*f*]benzimidazole.—First, **2-acetyl-7-acetamino - 8 - nitrodibenzofuran** was prepared. A solution of 5.4 g. (0.02 mole) of 2-acetyl-7-acetaminodibenzofuran in 120 cc. of glacial acetic acid was heated on the steam-bath with stirring, and 6 cc. of fuming nitric acid (sp. gr. 1.50) was added in one portion. The practically pure material thus obtained weighed 4.0 g. (64%) and melted at 269–270°. Crystallization from acetic acid raised the melting point to 270–271°.

Anal. Calcd. for $C_{16}H_{12}O_5N_2$: N, 8.97. Found: N, 9.19 and 9.00.

Four grams (0.013 mole) of 2-acetyl-7-acetamino-8-nitrodibenzofuran was suspended in 80 cc. of ethanol and reduced with hydrogen at 100° for one-half hour under a gage pressure of forty-five pounds using Raney nickel catalyst. The crude 2-acetyl-7-acetamino-8-aminodibenzofuran was refluxed one hour with 50 cc. of glacial acetic acid. The crude imidazole was obtained by diluting the acetic acid solution with water and making alkaline with ammonium hydroxide. The product was dissolved in hot methanol, boiled with Norite, and the solution saturated with dry hydrogen chloride. The pure hydrochloride precipitated in fine needles melting with decomposition at about 325°. From the hydrochloride was obtained the free base melting at 298° in a yield of 2.3 g. (55%).

Anal. Calcd. for $C_{16}H_{12}O_2N_2$: N, 10.59. Found: N, 10.73 and 10.96.

4-Dibenzofuryl Derivatives

1-(4-Dibenzofuryl)-isoquinoline.—This compound was prepared in essential accordance with the directions of Ziegler and Zeiser[24] for 1-*n*-butylisoquinoline, and the method is being extended to other dibenzofurylnitrogen heterocycles.

A solution of *n*-butyllithium prepared from 27.4 g. (0.2 mole) of *n*-butyl bromide and 2.8 g. (0.4 g. atom) of lithium in 300 cc. of ether was refluxed with 30 g. (0.18 mole) of dibenzofuran under a nitrogen atmosphere for four and one-half hours. The resulting solution of 4-dibenzofuryllithium was cooled to 0–5° in an ice-bath and 19.3 g. (0.15 mole) of isoquinoline in 50 cc. of dry ether was added with stirring. Subsequent to hydrolysis and treatment with ammonium hydroxide, several recrystallizations from ethanol gave 5.0 g. (a 11.3% yield based on isoquinoline) of the free base melting at 137–138°.

Anal. Calcd. for $C_{21}H_{13}ON$: N, 4.74. Found: N, 4.83 and 4.82.

The hydrochloride is immediately hydrolyzed in water.

4-Dibenzofurylacetamide.—This synthesis was based on the general procedures of Arndt and Eistert.[25] 4-Dibenzofurancarboxylic acid chloride was prepared by treating the acid with thionyl chloride in the usual manner. A more convenient purification was effected, however, by recrystallizing the acid chloride from petroleum ether (b. p. 60–68°).

To a diazomethane solution in ether, prepared from 50 g. (0.485 mole) of nitrosomethylurea was added 25 g. (0.11 mole) of 4-dibenzofurancarboxylic acid chloride in several portions. The crude diazomethyl 4-dibenzofuryl ketone was obtained in a quantitative yield, and a portion recrystallized once from petroleum ether (b. p. 60–68°) melted at 72–75°. This material was used directly in the following procedure.

Conversion of the diazo compound to the 4-dibenzofurylacetamide is accomplished in a better yield if too large a run is not made. A solution of 5.0 g. (0.02 mole) of the diazomethyl 4-dibenzofuryl ketone in 100 cc. of dioxane was heated on the steam-bath, and 25 cc. of concd. ammonium hydroxide was added followed by 5 cc. of a 10% solution of silver nitrate. The precipitated crude 4-dibenzofurylacetamide was obtained in a 67% yield. Recrystallization from ethanol gave the pure compound melting at 211–212°.

Anal. Calcd. for $C_{14}H_{11}O_2N$: N, 6.22. Found: N, 6.10 and 5.98.

4-Dibenzofurylacetic Acid.—Five grams (0.022 mole) of the 4-dibenzofurylacetamide suspended in 150 cc. of 15% sodium hydroxide solution was refluxed for five hours. Acidification of the solution with dilute hydrochloric acid precipitated the crude 4-dibenzofurylacetic acid in an 82% yield, which melted at 213.5–214.5° after crystallization from ethanol.

Anal. Calcd. for $C_{14}H_{10}O_3$: C, 74.31; H, 4.46. Found: C, 74.57; H, 4.66.

3,4 - Dimethoxy - α - (4 - dibenzofurylacetamino) - acetophenone.—Two grams (0.009 mole) of 4-dibenzofurylacetic acid and 10 cc. of thionyl chloride were gently refluxed together for three hours. The excess thionyl chloride was removed under reduced pressure and the residual oil dissolved in petroleum ether (b. p. 60–68°) and filtered to remove a slight amount of insoluble residue. Evaporation of the petroleum ether left the 4-dibenzofurylacetyl chloride as a viscous oil which was dissolved in 95 cc. of ether and added to 20 cc. of an aqueous solution of 1.5 g. (0.0065 mole) of 3,4-dimethoxy-α-aminoacetophenone hydrochloride.[26] A solution of 2.5 g. of potassium hydroxide in 15 cc. of water was added, and the mixture shaken for ten minutes and allowed to stand overnight. The emulsion which had formed was filtered, leaving a residue of 2.6 g. of the crude amide. Acidification of the

(24) Ziegler and Zeiser, *Ann.*, **485**, 174 (1931).

(25) Arndt and Eistert, *Ber.*, **68**, 200 (1935).

(26) Prepared according to the procedure of Pictet and Gams, *ibid.*, **42**, 2943 (1909).

filtrate yielded 0.3 g. of crude 4-dibenzofurylacetic acid. The crude amide was recrystallized from benzene to yield 1.5 g. (57% yield based on amine) of the pure amide melting at 186–187°.

Anal. Calcd. for $C_{24}H_{21}O_5N$: N, 3.47. Found: N, 3.71 and 3.72.

3,4 - Dimethoxy - α - (4 - dibenzofuroylamino) - acetophenone.—The reaction between 0.1 g. of 4-dibenzofurancarboxylic acid chloride and 0.1 g. of 3,4-dimethoxy-α-aminoacetophenone hydrochloride was carried out by the same procedure as that just given. The product was recrystallized from ethanol and melted at 178–179°.

Anal. Calcd. for $C_{23}H_{19}O_5N$: N, 3.71. Found: N, 3.68.

Acknowledgment.—The authors are grateful to H. B. Willis for assistance.

Summary

Experiments are described concerning the preparation and proof of structure of some substituted amines and other derivatives of dibenzofuran. The generalizations on orientation postulated previously have been shown to be adequate for the predominant products which result from polysubstitution of the dibenzofuran nucleus.

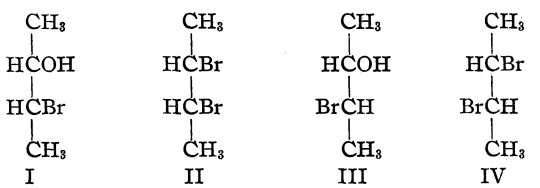
AMES, IOWA RECEIVED JUNE 26, 1939

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, No. 724]

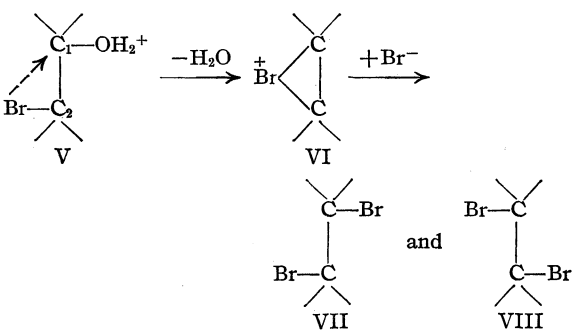
The Loss of Optical Activity in the Reaction of the Optically Active *erythro-* and *threo*-3-Bromo-2-butanols with Hydrobromic Acid

BY S. WINSTEIN[1] AND H. J. LUCAS

Recently it was shown[2] that *dl-erythro*-3-bromo-2-butanol I is converted into *meso*-2,3-dibromobutane II, and *dl-threo*-3-bromo-2-butanol III, is converted into *dl*-2,3-dibromobutane IV, by the action of fuming hydrobromic acid, with complete retention of configuration.[3,4]



In order to account for this unusual behavior, it was assumed that the replacement of the hydroxyl group by the bromine atom took place by a mechanism involving attack by the bromine atom on the adjacent carbon atom of the bromohydrin. This bromine atom, simultaneously with the removal of the OH_2^+ group V (which is formed from the OH group and a proton), forms a bond with the carbon atom on the face away from the OH_2^+ group, thus leading to the formation of the positively charged cyclic intermediate, VI,[5] of Roberts and Kimball[6] which then reacts with bromide ion to produce the two possible dibromides VII and VIII.



On the basis of this mechanism two inversions take place, for the formation of the intermediate, VI, is accompanied by an inversion of carbon atom C_1, and the reaction of this with bromide ion is accompanied by a second inversion. If VII is the product, C_1 is inverted twice, while if VIII is the product C_1 and C_2 are each inverted once. This explains the formation of *meso*-2,3-dibromobutane from the *erythro*-bromohydrin, and of *dl*-2,3-dibromobutane from the *threo*-bromohydrin. In fact, each of the active forms of the *threo*-bromohydrin is predicted by this mechanism to give *dl*-2,3-dibromobutane, since VII and VIII would be formed in equal amounts.

It was pointed out that this feature could be used as a test for the mechanism by starting

(1) At present National Research Fellow in Chemistry at Harvard University.

(2) Winstein and Lucas, THIS JOURNAL, **61**, 1576 (1939).

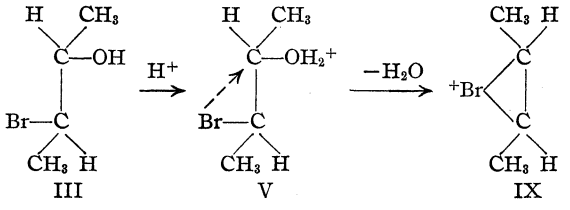
(3) Only one of the two antipodes of the *dl*-compounds is shown.

(4) By retention of configuration in these cases is meant merely that an *erythro*-bromohydrin gives rise to a *meso*-dibromide and a *threo*-bromohydrin to a *dl*-dibromide. Strictly speaking, configuration is not retained.

(5) We propose to call the simplest ion having this structure, ethylenebromonium ion.

(6) Roberts and Kimball, THIS JOURNAL, **59**, 947 (1937).

with optically active *threo*-bromohydrin III. The predicted loss in activity in going from an active *threo*-bromohydrin to an inactive dibromide may be better understood perhaps by noting that the cyclic intermediate IX has the internally compensated *cis* configuration, and thus can give rise to only inactive products.



It has now been found that both the *erythro*- and *threo*-bromobutanols in the active form give rise to inactive dibromides. Moreover, optically active acetates of these two bromobutanols also give rise to inactive dibromides. The conversion was carried out with optically active forms of both the *erythro*- and *threo*-bromohydrins so as to make the test of the proposed mechanism free of any doubt that might be cast on it by questioning the assignment of configurations to the 3-bromo-2-butanols or the 2,3-dibromobutanes.

Optically active bromobutanols and acetates were obtained by partial acetylation of the bromohydrins with acetic anhydride in carbon tetrachloride containing brucine, according to the method which Wegler[7] used in other cases. The *dl-erythro*-3-bromo-2-butanol gave rise to a (+)-*erythro*-3-bromo-2-butanol and a (−)-*erythro*-3-acetoxy-2-bromobutane, while the *dl-threo*-3-bromo-2-butanol gave rise to a (−)-*threo*-3-bromo-2-butanol and a (−)-*threo*-3-acetoxy-2-bromobutane. The resolution to be expected from the method employed is of course quite incomplete.

TABLE I

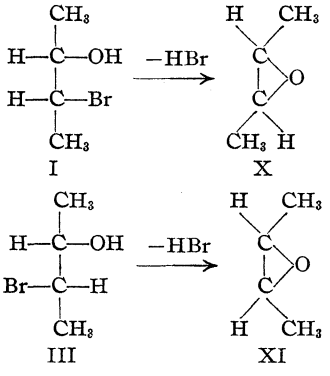
SUMMARY OF THE OPTICAL ROTATION DATA

	Substance	Config.	α_D (1 dcm.)
1	3-Bromo-2-butanol	*erythro*	+1.91 ± 0.02°
2	2-Acetoxy-3-bromobutane	*erythro*	−3.01 ± .03
3	2,3-Dibromobutane from 1	*meso*	0.00 ± .02
4	2,3-Dibromobutane from 2	*meso*	0.01 ± .02
5	2,3-Epoxybutane from 1	*trans*	+4.37 ± .01
6	3-Bromo-2-butanol	*threo*	−1.17 ± .02
7	3-Bromo-2-butanol	*threo*	−1.04 ± .01
8	2-Acetoxy-3-bromobutane	*threo*	−0.31 ± .01
9	2,3-Dibromobutane from 6	*dl*	.00 ± .01
10	2,3-Dibromobutane from 7	*dl*	.00 ± .02
11	2,3-Dibromobutane from 8	*dl*	.00 ± .01
12	2,3-Epoxybutane from 7	*cis*	.01 ± .01

(7) Wegler, *Ann.*, **506**, 77 (1933).

The optical rotations of these compounds, as well as optical data on the oxides and dibromides, are given in Table I.

To make certain that the optical activity in the case of the (−)-*threo*-bromohydrin was not due largely to the presence of a quite small amount of an optically active *erythro* isomer, which would give optically inactive dibromobutane, some of the active *erythro*- and *threo*-bromohydrins were converted to oxides. One would expect active *erythro*-3-bromo-2-butanol I to yield an active *trans*-2,3-epoxybutane X, and active *threo*-3-bromo-2-butanol III to yield inactive internally compensated *cis*-2,3-epoxybutane XI since one inversion accompanies the formation of the oxide ring.[2]



The active bromobutanols behaved as expected on conversion to oxides. It was found that the *trans* oxide from (+)-*erythro*-3-bromo-2-butanol has a (+) rotation while the *cis* oxide from (−)-*threo*-3-bromo-2-butanol was inactive (Table I). Thus, the active *threo*-bromohydrin was not contaminated with appreciable amounts of an active *erythro*-bromohydrin.

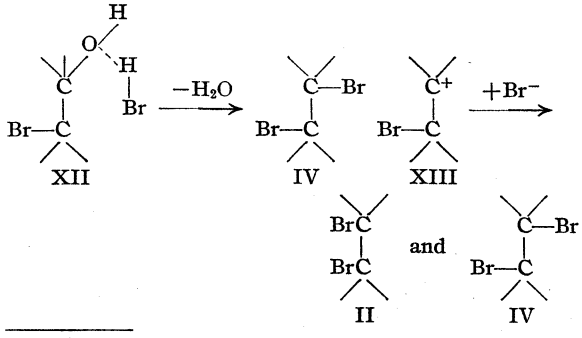
The inactivity of the dibromide from the active *threo*-3-bromo-2-butanol (Table I) hardly can be explained on the basis of a low specific rotation for a *d*- or *l*-2,3-dibromobutane.[8] It seems quite unlikely that the rotation to be expected from (+)- or (−)-2,3-dibromobutane would be smaller than the rotation of (−)-*threo*-3-bromo-2-butanol by a factor of approximately 50 or 100, and thus be within experimental error of zero. Thus it must be that (−)-*threo*-3-bromo-2-butanol gives *dl*-2,3-dibromobutane. This definitely confirms

(8) In many cases, the optical activity of an alcohol is comparable to or less than that of the corresponding halide; see for example, Kenyon, Phillips and Pittman, *J. Chem. Soc.*, 1072 (1935); Levene and Rothen, *J. Biol. Chem.*, **127**, 237 (1939); Hughes, Ingold and Masterman, *J. Chem. Soc.*, 1196 (1937); Hughes, Ingold and Scott, *ibid.*, 1201 (1937); Cowdrey, Hughes and Ingold, *ibid.*, 1208 (1937); Stevens and McNiven, THIS JOURNAL, **61**, 1295 (1939).

the proposed mechanism, which involves the formation of 1,2-dimethylethylenebromonium ion, VI.

It is evident from Table I that the active bromoacetates behave as the bromohydrins do, to give inactive dibromides. This is to be expected since the bromoacetates presumably are converted to the dibromides by way of the bromohydrins.[9] It must be recognized that the butylenebromonium ion can react with water, as well as with bromide ion. The reaction with water, in the case of the *cis* ion, will give rise to *dl-threo*-3-bromo-2-butanol. Here then is a way for the active *threo*-bromohydrin to become inactive. It is probable, however, that the positive ion reacts practically exclusively with bromide ion in the present reaction medium. This statement is based upon the observations that the corresponding oxide is converted almost quantitatively to bromohydrin,[2] not glycol in concentrated hydrobromic acid, and that in bromine additions to double-bonded compounds, in which bromonium ions[10] are intermediates,[2,6,11] bromide ion competes much better than solvent molecules.

Other Possible Mechanisms.—The results obtained show that two other possible mechanisms, which have been proposed for the conversion of monohydric alcohols to bromides, are not operative here. One such mechanism is the internal, cyclic reaction of a bromohydrin–hydrogen bromide complex.[12] This type of reaction which seems to occur in some cases[8] cannot be operative here, otherwise the dibromide IV, resulting from optically active *threo*-3-bromo-2-butanol XII, would possess optical activity.



Another such mechanism is the dissociation[12] of the bromohydrin–proton complex, V, to give a halogen substituted carbonium ion XIII, with subsequent reaction of this ion with bromide ion. In the case of both the active *erythro-* and active *threo*-bromohydrins, this would lead to the production of a mixture of the *meso*-dibromide II and an active dibromide IV, unless one postulates that the configuration of the carbonium ion is stabilized in the pyramidal form. If it is possible for the configuration to be so stabilized, then the resulting dibromide from the active *threo*-bromohydrin would possess optical activity. Thus the carbonium ion mechanism, which has been postulated in other cases[12] but which has been the subject of considerable discussion recently,[13] definitely is not operative in the case of these 3-bromo-2-butanols.

While it might turn out to be useful to think that the chief "driving force"[14] of the reaction of formation of the butylenebromonium ion VI is the tendency for the $-OH_2^+$ group to be dissociated off as a water molecule, nevertheless we must not regard XIII as an intermediate. The bond between bromine and carbon is formed essentially simultaneously with the dissociation of the $-OH_2^+$ group from the rest of the molecule.

Other Changes Involving Halonium Ions.—In addition to the reactions of bromohydrins with acids and of bromine and bromine-donating substances with ethylenic compounds, as discussed previously,[2] there must be other situations in which bromonium ions are intermediates. This would be expected when there is a tendency to remove one group in a molecule in which there is a bromine substituent able to attack the back face of the carbon atom losing the group. Thus, for example, the production of *cis*-1,2-diacetoxycyclohexane from the action of silver acetate on 1,2-dibromocyclohexane in acetic acid does not necessarily indicate that the 1,2-dibromocyclohexane is the *cis* isomer.[15] We prefer the explanation that an odd number of inversions are involved in the transformation to the diacetate and that 1,2-dibromocyclohexane has the *trans* configuration. It seems plausible that the bromonium ion is produced by the action of a silver ion[14,16] simultaneously with the attack by the bromine

(9) Winstein and Lucas, THIS JOURNAL, **61**, 1581 (1939).

(10) Pfeiffer and co-workers have isolated and formulated salts which bear a formal resemblance to our bromonium salts, such as $\{[(CH_3)_2NC_6H_4]_2CCHBr\}^+ ClO_4^-$ [see Pfeiffer and Wizinger, *Ann.*, **461**, 132 (1928)] and $[(C_6H_5C_6H_4)_2CCHBr]^+Br_3^-$ [see Pfeiffer and Schneider, *J. prakt. Chem.*, **129**, 129 (1931)].

(11) (a) Bartlett and Tarbell, THIS JOURNAL, **58**, 466 (1936); (b) Read and Williams, *J. Chem. Soc.*, **117**, 359 (1920); (c) Ingold, *Chem. Rev.*, **15**, 225 (1934).

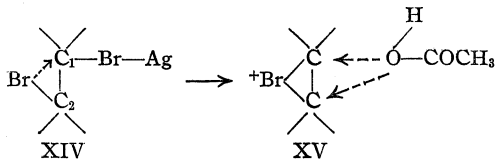
(12) Cowdrey, Hughes, Ingold, Masterman and Scott, *J. Chem. Soc.*, 1252 (1937).

(13) (a) Winstein, THIS JOURNAL, **61**, 1635 (1939); (b) Bartlett, *ibid.*, **61**, 1630 (1939). See these articles for further references.

(14) Roberts and Hammett, *ibid.*, **59**, 1063 (1937).

(15) Rothstein, *Ann. chim.*, **14**, 461 (1930).

(16) See Hughes, Ingold and Masterman, *J. Chem. Soc.*, 1236 (1937); Cowdrey, Hughes and Ingold, *ibid.*, 1243 (1937).



XIV XV

atom of carbon atom C_2 as shown by XIV and that this ion reacts with solvent as shown by XV. An inversion at the replacement of the second bromine atom by acetate would result in there being three inversions in the whole transformation. It seems plausible that presently the steric course of reactions of dihalides, halohydrins, etc., will be better understood when it is realized to what extent bromonium ions and hitherto unknown compounds of a similar sort play a part.

Besides bromonium ions there may be chloronium and iodonium ions of similar structure.

Experimental

Materials.—The *dl-erythro*-3-bromo-2-butanol was prepared from the pure *trans*-2,3-epoxybutane and the *dl-threo*-3-bromo-2-butanol from both pure *cis*-2,3-epoxybutane or *cis*-2-butene according to directions previously given.[2]

Merck brucine was employed and the acetic anhydride was purified by fractionation.

Partial Resolution of *erythro*-3-Bromo-2-butanol and Conversion to 2,3-Dibromobutane.—In 500 ml. of pure carbon tetrachloride was dissolved with heating 50 g. of brucine, then 50 ml. of *dl-erythro*-3-bromo-2-butanol and 22 ml. of acetic anhydride were added in turn and the reaction mixture was refluxed for two hours. After the reaction mixture was cool, it was washed first with dilute hydrochloric acid and then sodium carbonate solution. The mixture was dried over potassium carbonate, most of the carbon tetrachloride was distilled off through a 15-cm. column of glass helices at about 40°, and the residue was fractionated through a 40-cm. Weston[17] column. There was obtained 38 ml. of distillate, 12 ml. being essentially pure bromohydrin, b. p. (13 mm.) 53.1–53.7°, $n^{25}D$ 1.4762 and 19 ml. being pure acetoxybromobutane, b. p. (13 mm.) 67.0–67.2°, $n^{25}D$ 1.4488. Intermediate fractions made up the remainder of the material. The rotation αD (1 dcm.) of the bromohydrin was 1.91° and of the acetate −3.01°. Half of the bromohydrin sample was converted to oxide as previously described,[2] the oxide exhibiting αD (1 dcm.) +4.37°. The oxide and bromohydrin were dissolved in fuming hydrobromic acid, the dibromide b. p. (50 mm.) 73.2°, $n^{25}D$ 1.5090, possessing αD (1 dcm.) 0.00°. The acetate similarly gave rise to dibromide b. p. (50 mm.) 73.2°, $n^{25}D$ 1.5090 which possessed αD (1 dcm.) 0.00°. The intermediate fractions also were converted to dibromide. The combined and redistilled dibromobutane from the bromohydrin and oxide, acetoxybromobutane, and the intermediate fractions, b. p. (50 mm.) 73.3°, $n^{25}D$ 1.5091 possessed a dielectric constant[2,18] of 6.208. This indicates a few % of *dl*-dibromobutane in the *meso*-dibromide. Some stereomutation from *erythro* to *threo* apparently takes place during the procedure for partial resolution of the bromohydrin.

Partial Resolution of *threo*-3-Bromo-2-butanol and Conversion to 2,3-Dibromobutane.—From the treatment of 44 ml. of *threo*-3-bromo-2-butanol with 44 g. of brucine and 22 ml. of acetic anhydride in 440 ml. of carbon tetrachloride as described above in the case of the *erythro*-bromohydrin and subsequent washing, drying and distillation was obtained 39 ml. of distillate, 8 ml. being quite pure bromohydrin, b. p. (13 mm.) 50.0–50.8°, $n^{25}D$ 1.4757, 13 ml. being quite pure acetoxybromobutane, b. p. (13 mm.) 69.6°, $n^{25}D$ 1.4491, the rest of the material consisting of intermediate fractions. The bromohydrin exhibited αD (1 dcm.) −1.17° while the acetoxybromobutane possessed αD (1 dcm.) −0.31°. The bromohydrin, acetoxybromobutane and the combined intermediate fractions were converted to dibromobutanes in the usual way. The dibromobutane b. p. (50 mm.) 76.1° from the bromohydrin exhibited αD (1 dcm.) 0.00°, that from the intermediate fractions, b. p. (50 mm.) 76.0° possessed αD (1 dcm.) 0.00°, and the dibromide b. p. (50 mm.) 76.2° from the bromohydrin acetate yielded αD (1 dcm.) 0.00°. The combined and redistilled dibromobutane b. p. (50 mm.) 75.9–76.2°, $n^{25}D$ 1.5121, possessed a dielectric constant of 5.797. Here, too, a little stereomutation must have been involved in the procedure for the partial resolution of the bromohydrin.

When 46 ml. of *threo*-3-bromo-2-butanol was partially resolved with the aid of 46 g. of brucine, 20 ml. of acetic anhydride and 500 ml. of carbon tetrachloride and distillation was carried out, 10 ml. of bromohydrin fraction b. p. (13 mm.) 50.2–50.7°, $n^{25}D$ 1.4749, αD (1 dcm.) −1.04° was obtained. Three ml. of this bromohydrin yielded an oxide having αD (1 dcm.) 0.01°. The remainder of the bromohydrin yielded a dibromide, b. p. (50 mm.) 76.3°, $n^{25}D$ 1.5121, which showed αD (1 dcm.) 0.00°.

In Table I the indicated possible errors in the optical rotations are the sum of the mean deviations for a set of readings on the zero point and a set of readings on the substance in question. For the readings a Zeiss 0.01° instrument and a small capacity 1-dcm. tube were employed.

Summary

There is complete loss of optical activity when active *erythro*- or *threo*-3-bromo-2-butanol is converted to 2,3-dibromobutane. This confirms the mechanism previously proposed in connection with the conversion of *dl-erythro*- and *dl-threo*-3-bromo-2-butanol to *meso*- and *dl*-2,3-dibromobutane, respectively. The mechanism consists of the production of a butylenebromonium ion, and the subsequent reaction of this ion with bromide ion, two inversions occurring in the transformation. Other possible mechanisms for the transformation of bromohydrin to dibromide are discussed and rejected.

RECEIVED AUGUST 9, 1939

(17) Weston, *Ind. Eng. Chem., Anal. Ed.*, **5**, 179 (1933).

(18) Winstein and Wood, unpublished work.

[CONTRIBUTION FROM THE BAKER LABORATORY OF CHEMISTRY, CORNELL UNIVERSITY]

Structures of Complex Fluorides. Potassium Hexafluogermanate and Ammonium Hexafluogermanate

BY J. L. HOARD AND W. B. VINCENT

Among compounds of type formula R_2MX_6, in which R = K, NH_4; M = Si, Ge, Sn, Ti, Zr, Mn, only the fluosilicates have been prepared in crystalline modifications possessing the familiar fluorite-like arrangement of R^+ and $MX_6^=$ ions known as the ammonium chloroplatinate structural type.[1] Most of these complex fluorides crystallize in the hexagonal system with crystal habits and axial ratios which suggest a general isomorphism within the group. In the present paper we report the determination by means of X-rays of the atomic arrangement which exists within crystals of ammonium and potassium fluogermanates. The structure of these compounds proves to be of the same general type as that of the hexagonal modification of ammonium fluosilicate, which has been studied by Gossner and Kraus.[2]

Using filtered CuK α radiation complete sets of oscillation photographs were prepared from small, well-formed crystals of both compounds. In each case the symmetry of the patterns obtained from carefully oriented specimens is that of $D_3^d - \bar{3}\,m$. The fundamental lattice is hexagonal with the following values of the lattice constants, accurate to within 0.01 Å.: ammonium fluogermanate, $a = 5.85$, $c = 4.775$ Å., $c/a = 0.816$; potassium fluogermanate, $a = 5.62$, $c = 4.65$ Å., $c/a = 0.827$. Groth[3] gives $c/a = 1.6078$ for the potassium salt as derived from goniometric measurements.

For one stoichiometric molecule within the unit cell the calculated densities are 2.60 g./cc. for the ammonium salt and 3.43 g./cc. for the potassium compound; approximate experimental values determined by the pycnometer method are, respectively, 2.64 g./cc. and 3.32 g./cc.

Symmetry planes belong to the form {11·0} rather than to {10·0}. Since, moreover, all classes of reflections are observed, the possible space groups are limited to $C_{3v}^1 - C3\,m$, $D_3^2 - C32$, and $D_{3d}^3 - C\bar{3}\,m$. The actual atomic arrangement is found to possess the complete symmetry of D_{3d}^3, and we shall base our description of the structure upon this space group.

Using the standard notation,[4] we place Ge in (a): 000; 2K or $2NH_4$ in 2(d): $^1/_3$, $^2/_3$, u; $^2/_3$, $^1/_3$, $\bar{u}$; 6F in 6(i): $x\bar{x}z$; x, $2x$, z; $2\bar{x}$, $\bar{x}$, z; $\bar{x}x\bar{z}$; $\bar{x}$, $2x$, $\bar{z}$; $2x$, x, $\bar{z}$ of D_{3d}^3. The values of these atomic coördinates as derived from the diffraction data are as follows: ammonium fluogermanate, $u = 0.695$, $x = 0.143$, $z = 0.214$; potassium fluogermanate, $u = 0.700$, $x = 0.148$, $z = 0.220$. Table I contains a comparison of observed with calculated reflection amplitudes for several types of reflections. The agreement is seen to be very good; details of the calculations follow.

TABLE I

AMMONIUM FLUOGERMANATE $\sqrt{I}$			POTASSIUM FLUOGERMANATE $\sqrt{I}$	
Calcd.[a]	Obsd.	(hkl)	Calcd.[a]	Obsd.
106	105	10·0	76	62
93	90	00·1	76	67
80	90	10·1	106	95
73	90	10·$\bar{1}$	47	57
1	0	20·0	− 17	16
− 43	32	00·2	− 67	63
− 34	26	20·1	− 51	51
111	90	20·$\bar{1}$	134	114
12	12	10·2	5	6
43	45	10·$\bar{2}$	64	63
47	37	20·2	68	57
73	64	20·$\bar{2}$	65	51
14	23	30·0	44	51
12	18	00·3	29	36
1	0	30·1	1	0
47	26	30·$\bar{1}$	36	36
18	15	10·3	10	4
17	15	10·$\bar{3}$	25	14
22	22	30·2	13	12
38	22	30·$\bar{2}$	22	10
57	37	20·3	57	36
7	10	20·$\bar{3}$	− 10	0
9	6	40·0	1	0
41	26	40·1	57	51
1	0	40·$\bar{1}$	− 12	9
40	26	00·4	45	36
34	26	10·4	43	44
17	13	10·$\bar{4}$	4	0
38	23	30·3	49	18

(1) R. W. G. Wyckoff, "The Structure of Crystals," Chemical Catalog Co., New York, N. Y., 2d ed., 1931, p. 304.

(2) B. Gossner and O. Kraus, *Z. Krist.*, **88**, 223 (1934).

(3) P. Groth, "Chemische Krystallographie," Engelmann, Leipzig, 1906, Erster Teil, p. 486.

(4) "Internationale Tabellen zur Bestimmung von Kristallstrukturen," Gebrüder Borntraeger, Berlin, 1935, Erster Band, Gruppentheoretische Tafeln, p. 258.

TABLE I (*Concluded*)

$\sqrt{I}$ Calcd.[a]	$\sqrt{I}$ Obsd.	(*hkl*)	$\sqrt{I}$ Calcd.[a]	$\sqrt{I}$ Obsd.
20	13	30·$\bar{3}$	32	16
33	20	40·2	31	17
27	13	40·$\bar{2}$	39	18
22	19	20·4	5	5
2	3	20·$\bar{4}$	12	11
6	1	50·0	2	0
9	10	40·3	− 7	0
29	18	40·$\bar{3}$	31	17
30	13	50·1	17	15
6	0	50·$\bar{1}$	19	9
22	15	30·4	21	14
7	10	30·$\bar{4}$	12	14
26	15	00·5	12	20
22	20	10·5	24	28
27	20	10·$\bar{5}$	28	32
29	20	50·2	37	32
16	10	50·$\bar{2}$	12	11
6	10	20·5	9	16
14	10	20·$\bar{5}$	22	22
6	6	40·4	13	14
12	14	40·$\bar{4}$	1	8
10	6	50·3	9	12
18	15	50·$\bar{3}$	8	12
20	20	60·0	32	24
3	1	30·5	− 4	0
7	10	30·$\bar{5}$	2	0
8	12	60·1	9	8
10	12	60·$\bar{1}$	7	8
10	10	00·6	10	24
54	62	11·0	79	108
36	44	11·1	24	26
20	20	21·0	16	18
34	42	11·2	23	18
47	32	21·1	32	30
21	22	21·$\bar{1}$	50	58
51	42	21·2	61	60
28	22	21·$\bar{2}$	23	20
30	26	31·0	21	20
40	30	11·3	51	45
34	20	31·1	45	54
22	22	31·$\bar{1}$	14	18
18	11	21·3	16	12
29	24	21·$\bar{3}$	13	8
18	11	31·2	13	12
23	20	31·$\bar{2}$	36	24
19	14	11·4	20	22
21	14	41·0	32	24
9	0	41·1	5	0
26	16	41·$\bar{1}$	19	6
12	7	31·3	2	0
18	10	31·$\bar{3}$	18	16
5	0	21·4	− 6	0
24	22	21·$\bar{4}$	34	28
13	6	41·2	4	0
20	14	41·$\bar{2}$	8	7
9	6	51·0	5	0
18	12	31·4	27	30
13	10	31·$\bar{4}$	1	0
23	14	41·3	32	30
13	14	41·$\bar{3}$	23	25
8	9	11·5	− 5	0
11	12	51·1	5	7
16	12	51·$\bar{1}$	25	25
14	16	21·5	21	32
11	14	21·$\bar{5}$	16	20
19	12	51·2	28	30
16	12	51·$\bar{2}$	13	10
7	14	41·4	22	28
10	24	41·$\bar{4}$	16	25
14	16	51·3		
10	14	51·$\bar{3}$		
15	16	31·5		
13	24	31·$\bar{5}$		

[a] Temperature factor and absorption correction not included.

The intensities of reflections appearing on photographs taken from hexagonal tablets, of diameter about 0.25 and 0.50 mm., respectively, for potassium and ammonium fluogermanate, were visually estimated by comparison with an intensity scale prepared for this purpose; the observed amplitudes of Table I are proportional to the square roots of these data. Theoretical amplitudes were calculated by means of the formula

$$I = \text{Constant}\left(\frac{1+\cos^2 2\theta}{2\sin 2\theta}\right)^{1/2} S$$

in which the structure factor is

$$S = f_{Ge} + 2f_N \cos 2\pi\left(\frac{h+2k}{3} + lu\right) + 2f_F\,[\cos 2\pi\,(hx - kx + lz) + \cos 2\pi\,(hx + 2kx + lz) + \cos 2\pi\,(2hx - kx + lz)]$$

The atomic f-values of Pauling and Sherman[5] are used throughout this paper.

As a matter of fact, the calculated amplitudes are but little altered by introducing small variations from the coördinates of fluorine and ammonium listed above. The parameter values given are essentially those derived from approximate Fourier projections of relative electron density on (1$\bar{2}$·0) using experimental (*h*0*l*) data. The reflection amplitudes used in calculating these projections were taken proportional to the square roots of the quantities obtained after correction of the estimated intensities by the Lorentz and polarization factor. The formula required in making the projection is

$$\rho(x,z) = \Sigma_h \Sigma_l \, F_{(h0l)} \cos 2\pi(hx + lz)$$

The method of Lipson and Beevers[6] was used in making the summations.

The resulting simple projections of relative electron density need not be reproduced here since their important features can be described in

(5) L. Pauling and J. Sherman, *Z. Krist.*, **81**, 1 (1932).
(6) Lipson and Beevers, *Phys. Soc. London*, **48**, 772 (1936).

few words. Excepting that potassium shows up more prominently than does ammonium, the contour maps are very similar for the two compounds. The values of the fluorine parameters as read from the peak arising from the superposition of two fluorine atoms on the projection are for ammonium fluogermanate $x = 0.147$, $z = 0.205$; for potassium fluogermanate $x = 0.148$, $z = 0.215$. The corresponding Ge–F separations in the almost regular octahedral GeF_6 groups are, respectively, 1.77 and 1.755 Å. Neither the ammonium nor the potassium peak is completely resolved from that of a single fluorine atom in each plot but it is possible, nevertheless, to determine the atomic positions with a fair degree of accuracy. It is probable that $u_K = 0.700$ is reliable to within a few thousandths, and that $u_N = 0.695$ is not in error by more than 0.015.

We see that the parameter values derived from the Fourier analyses of the (*h*0*l*) data are very nearly those used in calculating the reflection amplitudes of Table I. In the latter case we have assumed the complex anions to be regular octahedra with Ge–F = 1.77 Å.

An additional Fourier projection of relative electron density on (00·1) using experimental (*hk*·0) reflection amplitudes was made for ammonium fluogermanate. Peaks for germanium at 00; for ammonium at $^1/_3$, $^2/_3$ and $^2/_3$, $^1/_3$; and for fluorine at x, $2x$, etc., with $x = 0.150$ are observed. The value of the fluorine parameter is slightly larger than that obtained from the analysis of the (*h*0*l*) data. The Fourier data do not indicate completely regular complex anions for either compound: in ammonium fluogermanate the octahedron appears to be slightly flattened perpendicular to the unique axis; in potassium fluogermanate the octahedron appears to be slightly elongated along this axis. Within the accuracy of the data, however, we may conclude that both compounds contain practically regular octahedral GeF_6 groups with Ge–F = 1.77 Å.

The experimental Ge–F separation, 1.77 Å., may be compared with the sum of the "univalent" ionic radii[7] corrected for the actual ionic charges, 1.74 Å., with the sum of the "normal valence" radii,[8] 1.86 Å., and with the quite approximate value, 1.8 Å., derived from the X-ray study of the cubic cesium fluogermanate.[9] The more appropriate "octahedral" radius of germanium is probably somewhat larger than the "normal valence" or "tetrahedral" value. In the light of numerous electron diffraction data dealing with gaseous fluorides, however, we might well expect the Ge–F separation to be appreciably smaller than the sum of the covalent radii.

The parameter data used in calculating the reflection amplitudes of Table I lead to a regular GeF_6 group with Ge–F = 1.77 Å., F–F = 2.51 Å. Between adjacent anions, F–F = 3.11 Å. $(K–F)_1 = 2.84$ Å. (six of these), $(K–F)_2 = 2.86$ Å. (3), $(K–F)_3 = 3.01$ Å. (3), $(NH_4–F)_1 = 2.97$ Å. (6), $(NH_4–F)_2 = 3.00$ Å. (3), $(NH_4–F)_3 = 3.14$ Å. (3). We may accept the conclusion that three of the twelve potassium–fluorine separations are appreciably larger than the others; this is very probably true for the ammonium–fluorine separations as well. The coördination number of the univalent cation is then nine, although the approximation to coördination number twelve is not bad.

Drawings of the structure of potassium fluogermanate are shown in Fig. 1. The atomic arrangement can be described qualitatively as based on hexagonal closest-packing of fluorine and potassium atoms, from which, however, there are very considerable distortions. With the cubic ammonium chloroplatinate arrangement, fluorine and potassium atom would be in approximate cubic closest-packing, potassium being required by symmetry to possess twelve equidistant neighbors. These relations have been pointed out previously in the case of the dimorphous ammonium fluosilicate by Gossner and Kraus.[2] These authors have suggested approximate values for the parameters of ammonium and fluorine in the hexagonal modification of ammonium fluosilicate which lead to nine ammonium–fluorine separations of about 2.92 Å. as compared with about 2.98 Å. in the present work on the fluogermanate.

The hexagonal or low temperature modification of ammonium fluosilicate has a density about 7% larger than that of the cubic or high temperature form. As mentioned previously, the fluogermanates have been prepared only with the hexagonal structure.

Qualitatively, it appears that a considerable degree of ionic character in the M–F bonds of the complex would favor the assumption of the hexagonal rather than the cubic structure. This conclusion could be checked by calculating

(7) L. Pauling, THIS JOURNAL, **49**, 769 (1927).
(8) L. Pauling and M. L. Huggins, *Z. Krist.*, **87**, 205 (1934).
(9) R. W. G. Wyckoff and J. H. Muller, *Am. J. Sci.*, **13**, 347 (1927).

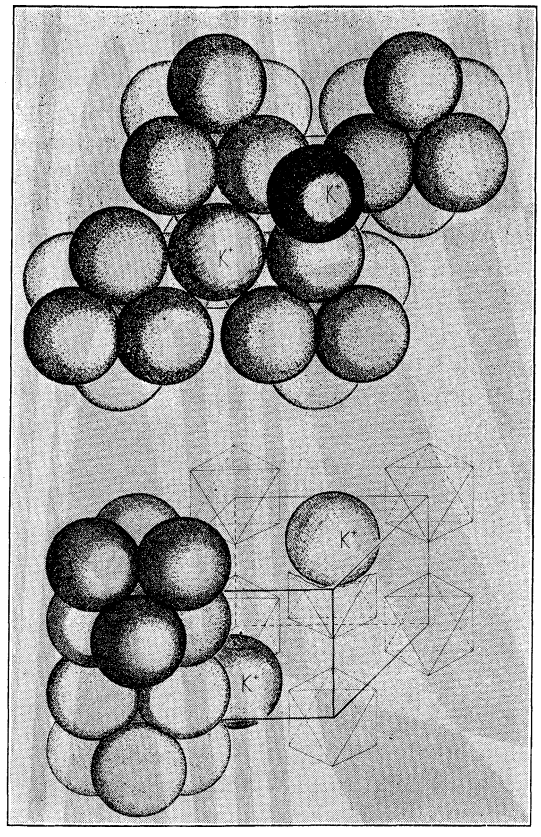


Fig. 1a.—Packing drawing along the hexagonal axis of the structure of potassium fluogermanate (upper). Fig. 1b.—View of the structure along the normal to (011) (lower).

the difference of potential energy between the two structural types for various distributions of charge over the anion, assuming an equal contribution of covalent binding to the M–F bond in both structures. With absorption of thermal energy the more symmetrical cubic structure becomes relatively more stable, although it is not possible at present to set up the partition functions required for quantitative calculations. Only complex fluorides have been prepared with the hexagonal structural type.

We have found that crystals of rubidium fluogermanate prepared at ordinary temperatures possess neither of the structures discussed above. Although hexagonal, the unit cell of this compound contains two stoichiometric molecules with the approximate axial lengths $a = 5.96$ Å., $c = 9.72$ Å. Our diffraction data are incomplete as yet, but the values of the lattice constants suggest that the structure is one in which rubidium ion has accurately a coördination number of twelve.

Although it appears certain that a system of fixed hydrogen bridges does not exist in ammonium fluogermanate, it is probable, nevertheless, that the interactions of hydrogen with fluorine are larger than would be the case for any structural type in which ammonium would have twelve equidistant neighbors. In ammonium fluogermanate it is reasonable to suppose that the ammonium ion is oriented so that three protons lie nearly in the plane of the six fluorine atoms which are about 2.97 Å. from each nitrogen atom. In the absence of any effect of this kind we would expect ammonium and rubidium fluogermanates to be isomorphous.

Summary

It is deduced from X-ray data that crystals of the isomorphous ammonium and potassium fluogermanates possess one-molecule hexagonal units of structure with $a = 5.85$ Å., $c = 4.775$ Å. and $a = 5.62$ Å., $c = 4.65$ Å., respectively, space-group D_{3d}^3–$C3\ m$. The structure is an aggregate of univalent cations (K^+, NH_4^+) and nearly regular octahedral anions (GeF_6^{-4}) with Ge–F = 1.77 Å. Each cation is surrounded by nine nearly equidistant fluorine atoms and three others at somewhat greater distances. This structure has been found only in the case of complex fluorides, for which at ordinary temperatures it is usually preferred to the cubic ammonium chloroplatinate structural type.

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[CONTRIBUTION FROM THE BAKER LABORATORY OF CHEMISTRY, CORNELL UNIVERSITY]

The Structure of Potassium Molybdocyanide Dihydrate. The Configuration of the Molybdenum Octocyanide Group

BY J. L. HOARD AND H. H. NORDSIECK

Potassium molybdocyanide dihydrate, $K_4Mo(CN)_8 \cdot 2H_2O$, is one of the more familiar examples of the class of compounds containing discrete coördination groups in which eight atoms or radicals are bound to a common central atom. The configuration of a molecule or complex ion of formula MX_8 has not been established with certainty in any single case heretofore, although the cube and the square Archimedean antiprism have been regarded as geometrically plausible possibilities. In the present paper we describe an X-ray study of potassium molybdocyanide dihydrate from which we have succeeded in deducing the complete atomic arrangement existing within the crystal. We shall show that the actual configuration of the molybdenum octocyanide ion, $Mo(CN)_8^{-4}$, is of a less obvious but apparently at least as satisfactory a type as either the cube or the antiprism.

The potassium molybdocyanide dihydrate used in this work was prepared and analyzed by Professor H. H. Willard and Dr. R. C. Thielke,[1] who very kindly supplied us with samples of two different preparations. The color of the crystals varied from a nearly pure yellow to an orange yellow depending, apparently, on their size and habit; the lighter colored preparation was made up of particularly thin leaflets. The crystals belong to the orthorhombic system,[2] being tabular on (100). When examined with a polarizing microscope they exhibit the required parallel extinction.

Using Cu–Kα radiation complete sets of fifteen degree oscillation photographs were prepared with each of the three crystallographic axes in turn as the rotation axis. The reflections were recorded on film in a cylindrical camera of 5 cm. radius, the positions of the knife edges corresponding to $2 \sin \theta = 1.990$. For the photographs with b and c vertical, it was possible to cut and grind the crystals into cylindrical form; the specimens used in these two cases were very nearly 0.10 mm. in diameter and about 0.50 mm. long. For the case of a vertical it was not feasible to prepare an entirely satisfactory specimen because of the habit and the cleavage properties of the crystals. Photographs taken with a specimen approximately $0.28 \times 0.60 \times 0.70$ mm. in size afforded diffraction data which proved to be very useful even though the estimated intensities were necessarily quite approximate.

As required by the orthorhombic system, the X-ray photographs exhibit the complete symmetry of the point group $D_2^h - mmm$. The lattice constants are $a = 16.55$ Å., $b = 11.70$ Å., $c = 8.68$ Å., $a:b:c = 0.7073:1:0.3709$. Goniometric measurements[2] give $a:b:c = 0.7028:1:0.3711$. Using these lattice constants to construct reciprocal lattice plots, it was possible to index all reflections appearing upon our photographs.[3]

Examination of the data demonstrates the regular and complete absence of $\{hk0\}$ reflections with h odd, and $\{0kl\}$ reflection with $k + l$ odd. These data render it almost certain that the space group[4] is either $D_{2h}^{16} - pnma$ or $C_{2v}^{9} - pna$. (The sequence of axes chosen on the basis of the crystallographic data happens to be the same as that used in the International Tables in describing these space groups.) The crystallographic data quoted by Rosenheim[2] assign the crystals to the point group D_2^h, and we assume accordingly the isomorphous space group D_{2h}^{16}. All later developments support this choice.

The space group requires that the unit cell contain 4, 8, 12, . . . $4n$ molecules of $K_4Mo(CN)_8 \cdot 2H_2O$. An approximate experimental determination of the density by the pycnometer method resulted in $d = 1.94$ g./cc.; the calculated density with four stoichiometric molecules per unit cell is 1.964 g./cc. We are required then to place 4Mo, 16K, 32C, 32N, and $8H_2O$ within the unit cell.

During indexing the relative intensities of all $\{hk0\}$, $\{h0l\}$, and $\{0kl\}$ reflections (appearing on the equators of photographs taken with c, b, and a, respectively, as rotation axes) were carefully estimated by visual comparison with an intensity

(1) H. H. Willard and R. C. Thielke, THIS JOURNAL, **57**, 2609 (1935).

(2) A. Rosenheim, *Z. anorg. Chem.*, **54**, 97 (1907).

(3) *Cf.* J. D. Bernal, *Proc. Roy. Soc.* (London), **A113**, 117 (1926).

(4) "Internationale Tabellen zur Bestimmung von Kristallstrukturen," Gebrüder Borntraeger, Berlin, 1935, Erster Band, Gruppentheoretische Tafeln.

scale prepared for this purpose. To obtain the important $\{hk0\}$ and $\{h0l\}$ data each of the authors independently went through the entire experimental procedure of photographing (different) specimens, indexing the reflections, and estimating the relative intensities. Using cylindrical specimens very nearly 0.10 mm. in diameter, the resulting photographs were exceptionally clear.

Comparison of the independently derived $\{hk0\}$ data disclosed that the intensities estimated by the senior author showed a larger spread in magnitudes by a factor of about two in going from reflections with small $\sin\theta$ to those with large $\sin\theta$. The two sets of data for $(h0l)$ reflections were in rather closer agreement. For each set of reflections mean intensities were computed, and these were divided by the Lorentz and polarization factor to obtain values of $|F_{(hkl)}|^2$. The $(hk0)$ and the $(h0l)$ reflections were not corrected for absorption of X-rays in the irradiated specimens. Approximate absorption corrections were required in the case of the $(0kl)$ data. Questions having to do with the self-consistency and probable accuracy of our data are considered in greater detail later in this paper.

Following methods which were employed to determine the structures of potassium heptafluocolumbate and potassium heptafluotantalate,[5] we use the $|F_{(hkl)}|^2$ data to make Patterson projections upon each of the three axial planes in order to place approximately molybdenum and potassium atoms within the unit cell. A knowledge of the positions of molybdenum and potassium suffices to determine the signs of the more important reflection amplitudes required in making approximate Fourier projections of relative electron density upon the axial planes. Refinement of these projections by a process of successive approximations leads ultimately to a complete structural determination.

The formula required for computing the Patterson projection on (010) is

$$P(X,Z) = \Sigma h \Sigma l \mid F_{(h0l)} \mid^2 \cos 2\pi(hX + lZ)$$

Similar expressions apply to the calculations of the projections on (100) and (001). The actual summations were carried out by the method of Lipson and Beevers[6] using a set of the Lipson and Beevers strips. Collected data from the three projections are given in Table I.

Remembering that coördinates of maxima on the Patterson plot represent components of interatomic distances in the projections on (010) of the contents of the actual unit structure, four molybdenum atoms placed in the centers of symmetry[4]—either 4(a) or 4(b) of D_{2h}^{16}—would require very large maxima at $X = 1/2$, $Z = 1/2$. This is not observed. The remaining possibility for molybdenum is 4(c); x, $1/4$, z; $\bar{x}$, $3/4$, $\bar{z}$; $1/2 - x$, $3/4$, $1/2 + z$; $1/2 + x$, $1/4$, $1/2 - z$. These would lead to maxima on the Patterson plot at the following values of X, Z: $\pm 2x$, $\pm 2z$; $\pm(1/2 - 2x)$, $1/2$; $1/2$, $\pm(1/2 - 2z)$; 0, 0. Large peaks (Table I) are observed at 0.28, 0.20; 0.22, $1/2$; $1/2$, 0.30, in addition to the identity maximum at 0,0. Upon solution we obtain $x = \pm 0.14$, $z = \pm 0.10$, of which the positive values may be chosen arbitrarily provided that a consistent selection of positions for other atoms be made thereafter.

The next most prominent set of peaks on the projection are in general to be associated with molybdenum–potassium separations. A large peak comparable in magnitude with those associated with molybdenum–molybdenum separations is observed at $X = 0$, $Z = 0.375$. This peak is most reasonably interpreted as involving potassium in the general positions 8(d): xyz; $1/2 + x, 1/2 - y, 1/2 - z$; $\bar{x}, 1/2 + y, \bar{z}$; $1/2 - x, \bar{y}, 1/2 + z$; $\bar{x}, \bar{y}, \bar{z}$; $1/2 - x, 1/2 + y, 1/2 + z$; $x, 1/2 - y, z$; $1/2 + x, y, 1/2 - z$, since these atoms superimpose in pairs on any (010) projection. Maxima are expected then at $X = 0.14 \pm x$, $Z = 0.10 \pm z$. Upon solution we find for K_I the values $x = 0.14$, $z = 0.475$ or 0.725 of which the latter value is shown later to be roughly correct. This peak, in fact, involves also several other atomic separations and the z parameter of K_I turns out to be about 0.690. On the basis of $x = 0.14$, $z = 0.725$ for K_I three other molybdenum–potassium maxima are expected at 0.28, 0.18; 0.22, 0.075; 0.50, 0.29. These may be supposed to contribute to the observed peaks at 0.28, 0.20; 0.20, 0.14; 0.50, 0.30. These comparisons are improved on the average by using $z = 0.69$ for K_I.

Indications of the positions of other potassium atoms on this projection are quite indefinite. It turns out later that another structurally different type of potassium atom has very nearly identical x and z coördinates as molybdenum and contributes to the set of peaks first discussed.

The Patterson projection on (001) possesses a plane of symmetry at $X = 1/4$ since only even

(5) J. L. Hoard, THIS JOURNAL, **61**, 1252 (1939).
(6) Lipson and Beevers, *Phys. Soc. London*, **48**, 772 (1936).

values of h are permitted for ($hk0$) reflections. With molybdenum placed in 4(c) we expect maxima at $\pm 2x$, $1/2$; $\pm(2x - 1/2)$, $1/2$; 0, 0; $1/2$, 0. Large peaks (Table I) are observed at 0.28, $1/2$; 0.22, $1/2$; 0, 0; $1/2$, 0, the symmetry of the plot causing two Mo–Mo separations to be included in the identity peak. These data lead to molybdenum parameters of $x = 0.14$, $y = 1/4$.

With potassium in the general positions, Mo–K_I maxima are expected at $\pm(x - 0.14)$, $\pm(y - 1/4)$; $\pm(x + 0.36)$, $\pm(y - 1/4)$; $\pm(x + 0.14)$, $\pm(y + 1/4)$; $\pm(x - 0.36)$, $\pm(y + 1/4)$. Using the large peaks at $X = 0$ (or $1/2$), $Y = 0.20$ and $X = 0.22$ (or 0.28), $Y = 0.30$, we obtain $x = 0.14$, $y = 0.05$ (or 0.45) for K_I, the alternative values for y referring to a pair of equivalent atoms related one to the other through the symmetry plane of the unit cell at $y = 1/4$.

It is possible to associate the peaks observed at $X = 0$ (or $1/2$), $Y = 1/2$ and $X = 0.22$ (or 0.28), $Y = 0$ with Mo–K separations involving four potassium atoms in 4(c). Maxima are then expected at $\pm(0.14 - x)$, 0; $\pm(0.14 + x)$, $1/2$; $\pm(0.36 - x)$, $1/2$; $\pm(0.36 + x)$, 0. Approximate parameter values for K_{II} are then $x = 0.36$ (or 0.86), $y = 1/4$, the alternative values for x referring to two equivalent atoms related through the screw axis lying in the plane $y = 1/4$.

Since there is no indication that the centers of symmetry 4(a) or 4(b) are occupied, the remaining four potassium atoms must be placed in 4(c) also. Peaks observed at $X = 0.18$ (or 0.32), $Y = 0$ and $X = 0.10$ (or 0.40), $Y = 1/2$ are interpreted in terms of Mo–K_{III} separations, the atomic coördinates of K_{III} being then $x = -0.04$ (or 0.46), $y = 1/4$.

The projection on (100) possesses a center of symmetry at $Y = 1/4$, $Z = 1/4$ in addition to the usual one at the origin. Four molybdenum atoms placed in 4(c) should lead to large maxima at 0, $\pm(1/2 - 2z)$; $1/2$, $\pm 2z$; $1/2$, $1/2$; 0, 0. These are observed (Table I) at 0, 0.30; $1/2$, 0.20; $1/2$, $1/2$; 0, 0, all atoms contributing, of course, to the identity peak. As anticipated, these data lead to $y = 1/4$, $z = 0.10$.

The peaks observed at 0.30, 0.21; 0.30, 0.09; 0.20, 0.41; 0.20, 0.29 are interpreted as arising from Mo–K_I separations, such maxima being expected at $\pm(y + 1/4)$, $\pm(z + 0.10)$; $\pm(y + 1/4)$ $\pm(z + 0.40)$; $\pm(1/4 - y)$, $\pm(z - 0.10)$; $\pm(1/4 - y)$, $\pm(z - 0.40)$. These data lead to $y = 0.05$ (or 0.45), $z = 0.69$ (or 0.81), the alternative values for z referring to equivalent atoms related through the screw axis mentioned above.

With potassium in 4(c) Mo–K maxima are expected at 0, $\pm(z - 0.10)$; $1/2$, $\pm(z + 0.10)$; $1/2$, $\pm(z + 0.40)$; 0, $\pm(z - 0.40)$. The peaks observed at 0, $1/2$; $1/2$, 0.30; $1/2$, 0; 0, 0.20 lead to $y = 1/4$, $z = 0.60$ (or 0.90) as coördinates of K_{II}.

The peaks observed at 0, 0.40; $1/2$, 0.40; $1/2$, 0.10; 0, 0.10 are associated with Mo–K_{III} separations, yielding $y = 1/4$, $z = 0.50$ (or 0) for K_{III}.

By considering simultaneously the results derived from the three projections, we get for Mo, $x = 0.14$, $y = 1/4$, $z = 0.10$; for K_I, $x = 0.14$, $y = 0.05$ (or 0.45), $z = 0.69$. Since we obtained no information about the positions of K_{II} and K_{III} from the (010) projection we have in each case two possible non-equivalent combinations of x and z coördinates for $y = 1/4$. The correct combinations turn out to be for K_{II}, $x = 0.36$, $y = 1/4$, $z = 0.60$ (or $x = 0.86$, $y = 1/4$, $z = 0.90$); for K_{III}, $x = -0.04$, $y = 1/4$, $z = 0.50$ (or $x = 0.46$, $y = 1/4$, $z = 0$). Some information on this point was derived from Patterson–Harker[7] summations, which will not be described here.

Table I lists the approximate values of the parameters of molybdenum and potassium together with the coördinates of the observed peaks on the projections from which the parameter data were derived. The brief account of the treatment accorded the Patterson data which we have presented is in some respects quite incomplete, and is probably somewhat misleading with regard to the apparent simplicity of the interpretations. We doubt, however, that we could have arrived at the approximate positions of potassium atoms in a reasonable period of time by any purely trial and error process.

In order to make a Fourier projection of relative electron density on any axial plane of potassium molybdocyanide dihydrate, for instance on (001), a double sum of the following type must be calculated.

$$\rho(x,y) = \Sigma h \Sigma k F_{(hk0)} \cos 2\pi(hx + ky)$$

The relative magnitudes of the $F_{(hk0)}$ are given by the square roots of the $|F_{(hk0)}|^2$ which were used in the computation of the Patterson projection. The signs to be attached to the more important reflection amplitudes can be computed on the basis of the approximate molybdenum and potassium positions of Table I. The pertinent

(7) D. Harker, *J. Chem. Phys.*, **4**, 381 (1936).

structure factors for the general position of D_{2h}^{16} are

$$S_{(hk0)} = 8\,\Sigma_i f_i \cos 2\pi\, hx_i \cos 2\pi\, ky_i,\ k \text{ even}$$
$$S_{(hk0)} = -8\,\Sigma_i f_i \sin 2\pi\, hx_i \sin 2\pi\, ky_i,\ k \text{ odd}$$
$$S_{(h0l)} = 8\,\Sigma_i f_i \cos 2\pi\, hx_i \cos 2\pi\, lz_i,\ h + l \text{ even}$$
$$S_{(h0l)} = -8\,\Sigma_i f_i \sin 2\pi\, hx_i \sin 2\pi\, lz_i,\ h + l \text{ odd}$$

TABLE I

APPROXIMATE PARAMETERS DEDUCED FROM PATTERSON DATA

	Approximate parameters			Peak from which parameters are derived		
Atom	x	y	z	X	Y	Z
Mo	0.14		0.10	0.28		0.20
				.22		.50
				.50		.30
Mo	.14	1/4		.28	0.50	
				.22	.50	
Mo		1/4	.10		0	.30
					.50	.20
K$_I$	.14		.725	0		.375
				.28		.20
	.14		.70	.20		.14
				.50		.30
K$_I$	.14	0.05		0	.20	
				.50	.20	
				.22	.30	
				.28	.30	
K$_I$		0.05	.69		.30	.21
					.30	.09
					.20	.41
					.20	.29
K$_{II}$	.36	1/4		0	.50	
				.50	.50	
				.22	0	
				.28	0	
K$_{II}$		1/4	.60		0	.50
					.50	.30
					.50	0
					0	.20
K$_{III}$	.96	1/4		.18	0	
				.32	0	
				.10	.50	
				.40	.50	
K$_{III}$		1/4	.50		0	.40
					.50	.40
					.50	.10
					0	.10

The atomic f-values of Pauling and Sherman[8] are used throughout this paper.

Table II gives the relative reflection amplitudes for $(hk0)$ and $(h0l)$ reflections. It was possible to assign correctly about 85% of the phases for the first projections, those for which the sign seemed seriously in doubt being omitted.

The actual projections were calculated by the method of Lipson and Beevers.[6] For the (001) projection $\rho\,(x,y) = A(x,0) + \sum_k A(x,k) \cos 2\pi\, ky - \sum_k B(x,k) \sin 2\pi\, ky$, in which $A(x,0) = F_{(000)} + 2\sum_h F_{(h00)} \cos 2\pi\, hx$, $A\,(x,k) = 2F_{(0k0)} + 4\sum_h F_{(hk0)} \cos 2\pi\, hx$, and $B(x,k) = 4\sum_h F_{(hk0)} \sin 2\pi\, hx$. Since $F_{(\bar{h}k0)} = F_{(hk0)}$ for k even, and $F_{(\bar{h}k0)} = -F_{(hk0)}$ for k odd, the A-series includes only reflections with k even, the B-series only those with k odd. Expressions of a similar kind apply to the (010) projection.

From the first incomplete Fourier projections it was possible not only to conclude that an essentially correct assignment of positions to molybdenum and potassium had been derived from the Patterson data but also to secure more accurate values of their atomic coördinates for use in subsequent calculations. In addition, certain minor peaks which appeared were indicative of the positions of carbon, nitrogen, and oxygen atoms.

Some of these minor peaks were immediately interpretable as cyanide groups linearly attached to molybdenum atoms with approximately the interatomic separations calculated from the "Tables of Covalent Radii"[9] (using the "trigonal prism" radius of molybdenum). These separations are 2.14 Å. for Mo–C, 1.15 Å. for C–N (triple bond), and therefore 3.29 Å. for Mo–N. On the basis both of theory and of many experimental data the bond angle Mo—C≡N is expected to be 180°.

During the course of attempts to use the molybdenum and potassium positions as a framework into which to fit various geometrically plausible configurations for the $Mo(CN)_8$ complex which would be compatible with the indications of carbon and nitrogen positions given by the projections, the following possibilities for placing eight cyanide groups about a central molybdenum atom were excluded quite definitely: (a) the configuration outlined (exactly or approximately) by the vertices of a cube; (b) the configuration outlined by the corners of an (approximately) square Archimedean antiprism; and (c) the configuration outlined by the vertices of a figure derived from a trigonal prism by adding two extra cyanide groups along normals to two of the rectangular faces. All of these possibilities, moreover, could be excluded also by arguments based on considerations of interatomic distances, since in every case one or more improbably small N–N separations between adjacent anions were encountered.

(8) L. Pauling and J. Sherman, *Z. Krist.*, **81**, 1 (1932).

(9) L. Pauling and M. L. Huggins, *ibid.*, **87**, 205 (1934).

TABLE II

COMPARISON OF CALCULATED WITH OBSERVED RELATIVE REFLECTION AMPLITUDES FOR (*hk*0) AND (*h*0*l*) REFLECTIONS[a]

(*hkl*)	$F_{(hkl)}$ Obsd.	Calcd.	(*hkl*)	$F_{(hkl)}$ Obsd.	Calcd.	(*hkl*)	$F_{(hkl)}$ Obsd.	Calcd.	(*hkl*)	$F_{(hkl)}$ Obsd.	Calcd.	(*hkl*)	$F_{(hkl)}$ Obsd.	Calcd.
200	5	7	14·2·0	6	− 12	16·9·0	10	25	306	0	12	17·0·1	0	7
210	28	44	2·10·0	0	6	20·3·0	0	− 6	904	0	12	808	0	3
020	44	− 72	14·3·0	8	29	18·7·0	6	− 20	705	11	− 48	209	0	0
220	8	− 13	12·6·0	10	37	6·14·0	2	− 11	406	8	28	11·0·7	0	− 1
400	46	−107	4·10·0	20	80	12·12·0	8	− 16	12·0·1	0	9	13·0·6	0	− 1
410	12	− 21	890	6	30	14·11·0	4	8	805	0	− 3	309	5	− 10
230	6	− 21	14·4·0	16	42	20·5·0	0	− 4	11·0·3	0	− 5	17·0·2	7	42
420	4	− 3	10·8·0	10	− 44	18·8·0	12	− 14	506	3	− 25	409	1	− 10
040	76	167	6·10·0	10	− 35				10·0·4	0	− 5	908	3	− 6
430	6	− 17	12·7·0	0	− 18	101	9	25	12·0·2	12	− 20	15·0·5	7	− 31
600	48	85	14·5·0	0	− 7	201	4	15	606	0	− 1	16·0·4	1	− 13
240	16	− 32	2·11·0	14	− 24	301	29	− 50	905	8	30	509	3	− 10
610	24	− 55	16·0·0	0	− 1	002	10	30	13·0·1	0	5	12·0·7	7	20
620	0	7	16·1·0	16	41	102	28	93	12·0·3	7	− 29	17·0·3	0	− 1
440	36	− 78	4·11·0	6	17	202	1	− 5	107	7	− 25	14·0·6	4	− 1
250	24	40	10·9·0	6	25	401	3	15	706	5	18	609	0	1
630	16	29	8·10·0	12	− 50	302	9	25	11·0·4	6	14	18·0·1	1	5
800	28	79	16·2·0	4	− 24	501	7	7	207	10	− 52	10·0·8	0	5
810	10	17	14·6·0	8	− 39	402	24	− 51	13·0·2	13	− 48	18·0·2	2	− 4
450	22	− 28	12·8·0	12	− 45	103	5	− 20	307	0	4	709	7	27
640	16	41	16·3·0	10	− 29	203	39	122	10·0·5	0	− 3	16·0·5	0	9
060	64	−137	6·11·0	6	20	502	26	− 58	407	5	− 7	13·0·7	0	1
820	20	− 42	0·12·0	16	51	601	9	− 27	806	4	− 12	17·0·4	11	20
260	0	− 15	16·4·0	0	13	303	39	− 98	14·0·1	12	− 29	11·0·8	4	15
830	10	26	2·12·0	0	12	403	18	− 52	507	0	− 22	15·0·6	0	1
650	32	− 75	14·7·0	8	26	602	3	− 4	13·0·3	11	31	809	0	7
460	24	44	10·10·0	14	45	701	10	29	12.0.4	3	32	18·0·3	3	12
840	20	61	4·12·0	0	− 3	503	4	− 35	906	0	7	0·0·10	15	47
10·0·0	40	− 83	8·11·0	0	− 3	004	1	− 15	11·0·5	19	75	1·0·10	3	− 16
10·1·0	6	17	12·9·0	8	− 33	104	1	4	14·0·2	0	− 14	2·0·10	0	− 3
270	6	− 15	16·5·0	16	44	204	5	14	607	9	42	19·0·1	9	− 20
660	14	− 36	6·12·0	0	7	702	9	24	707	0	− 6	3·0·10	0	9
10·2·0	24	48	18·0·0	16	− 37	304	0	− 7	13·0·4	0	8	909	1	14
850	14	32	14·8·0	6	20	801	8	− 19	14·0·3	0	− 12	14·0·7	0	3
470	0	0	18·1·0	0	6	603	31	− 80	15·0·1	14	47	12·0·8	0	− 6
10·3·0	14	− 30	16·6·0	0	− 10	404	20	43	10·0·6	3	− 18	4·0·10	8	− 30
080	24	72	18·2·0	16	37	802	4	− 21	008	2	− 18	19·0·2	9	− 12
10·4·0	26	− 62	2·13·0	0	10	703	11	27	108	3	− 12	17·0·5	5	25
280	0	1	18·3·0	6	− 32	504	0	0	208	2	8	18·0·4	3	− 3
670	8	20	10·11·0	6	− 9	901	0	− 5	12·0·5	4	− 14	5·0·10	0	12
860	28	− 65	12·10·0	8	34	105	16	− 29	308	5	− 5	16·0·6	6	− 17
12·0·0	16	− 45	8·12·0	6	23	205	9	29	15·0·2	3	16	10·0·9	0	− 3
480	6	− 19	4·13·0	0	0	604	4	13	807	18	− 30	6·0·10	8	− 17
12·1·0	16	− 41	16·7·0	0	− 5	902	21	64	408	0	7	19·0·3	0	− 5
10·5·0	0	10	18·4·0	14	− 40	803	16	44	11·0·6	0	− 10	13·0·8	7	18
12·2·0	20	59	14·9·0	6	− 15	305	25	47	14·0·4	7	− 13	20·0·1	5	− 10
12·3·0	4	− 14	18·5·0	0	0	10·0·1	9	9	508	14	50	11·0·9	5	− 14
870	6	28	6·13·0	8	− 24	405	11	− 34	907	0	6	20·0·2	1	− 9
680	2	8	16·8·0	0	− 14	704	0	− 2	15·0·3	1	15	17·0·6	5	− 7
290	14	52	10·12·0	4	− 15	903	0	− 3	13·0·5	6	− 20	19·0·4	0	5
10·6·0	20	47	12·11·0	0	8	505	0	15	16·0·1	5	− 10	8·0·10	7	22
12·4·0	14	− 42	0·14·0	12	− 54	10·0·2	0	− 1	608	4	− 14	14·0·8	0	− 2
490	0	− 15	2·14·0	0	5	804	10	− 13	16·0·2	0	5	16·0·7	3	− 11
880	8	47	14·10·0	10	− 52	11·0·1	6	− 15	12·0·6	0	8	20·0·3	6	− 12
12·5·0	20	− 70	20·0·0	0	2	605	9	− 33	10·0·7	5	− 35	12·0·9	0	− 4
14·0·0	16	36	18·6·0	10	25	006	3	− 15	708	2	9	1·0·11	2	3
14·1·0	4	− 24	20·1·0	8	− 16	106	6	35	15·0·4	1	− 6	19·0·5	2	8
690	12	− 49	8·13·0	0	− 8	10·0·3	12	40	14·0·5	0	− 6	15·0·8	0	− 4
10·7·0	0	− 12	4·14·0	10	28	206	1	13	16·0·3	13	34	21·0·2	3	− 9
0·10·0	44	−130	20·2·0	4	13	11·0·2	6	− 18	109	5	8	3·0·11	3	− 7

[a] Exclusive of reflections incompatible with the symmetry of the space group.

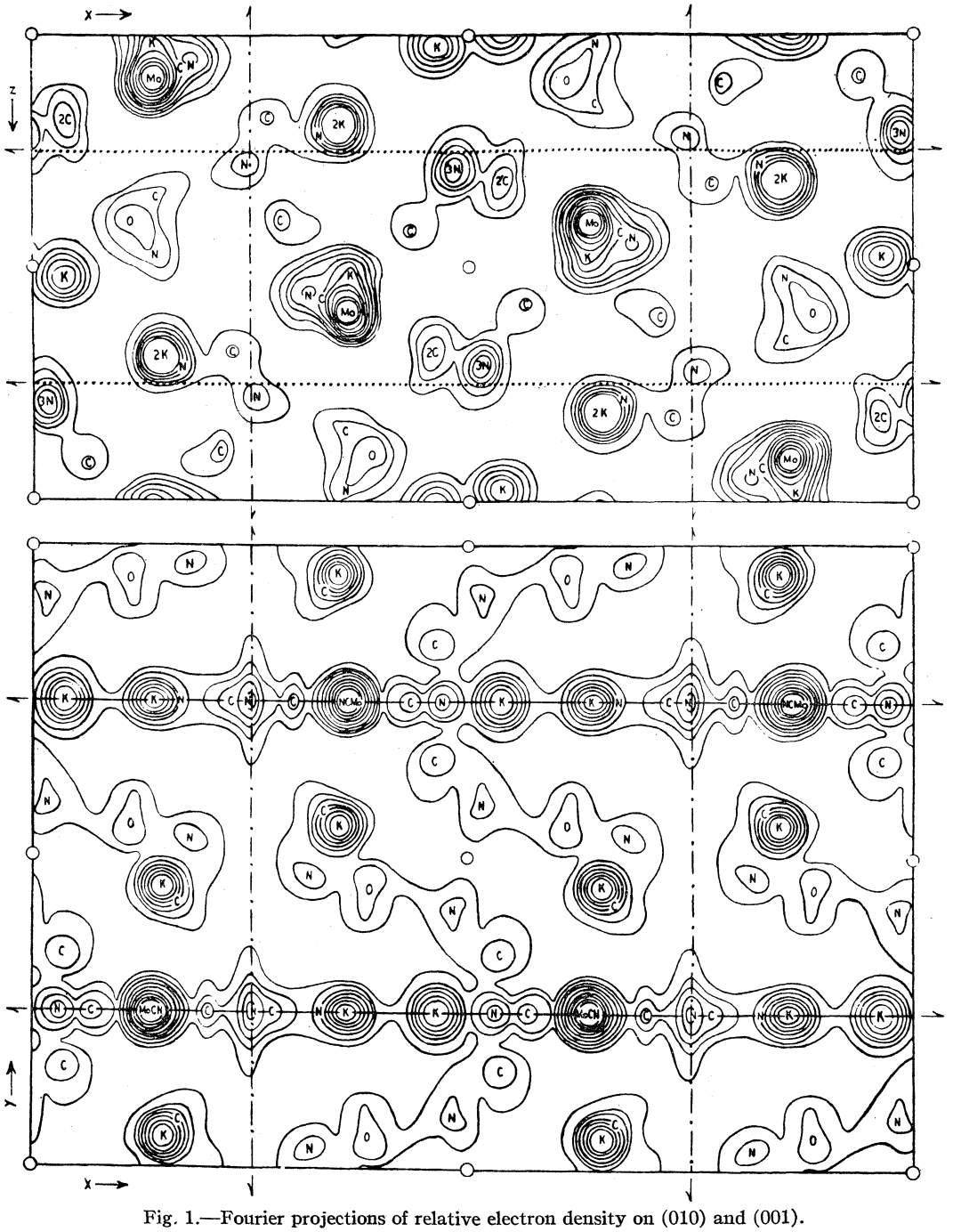

Fig. 1.—Fourier projections of relative electron density on (010) and (001).

The complete structure of potassium molybdocyanide dihydrate (Fig. 2) was gotten as a direct interpretation of the final Fourier projections (Fig. 1) of relative electron density on (001) and (010), without the use of any preconceived notions as to the geometric form of the complex. To obtain the projections in the final form of Fig. 1 it was necessary to recalculate each set of data several times, taking advantage in each calculation of the more nearly complete phase data resulting from the previous approximation.

The peaks on the contour maps of Fig. 1 are marked with the symbols of the atoms whose projections they represent. The atomic positions given by the Fourier analyses are shown still more clearly and completely in Fig. 2, in which diagram-

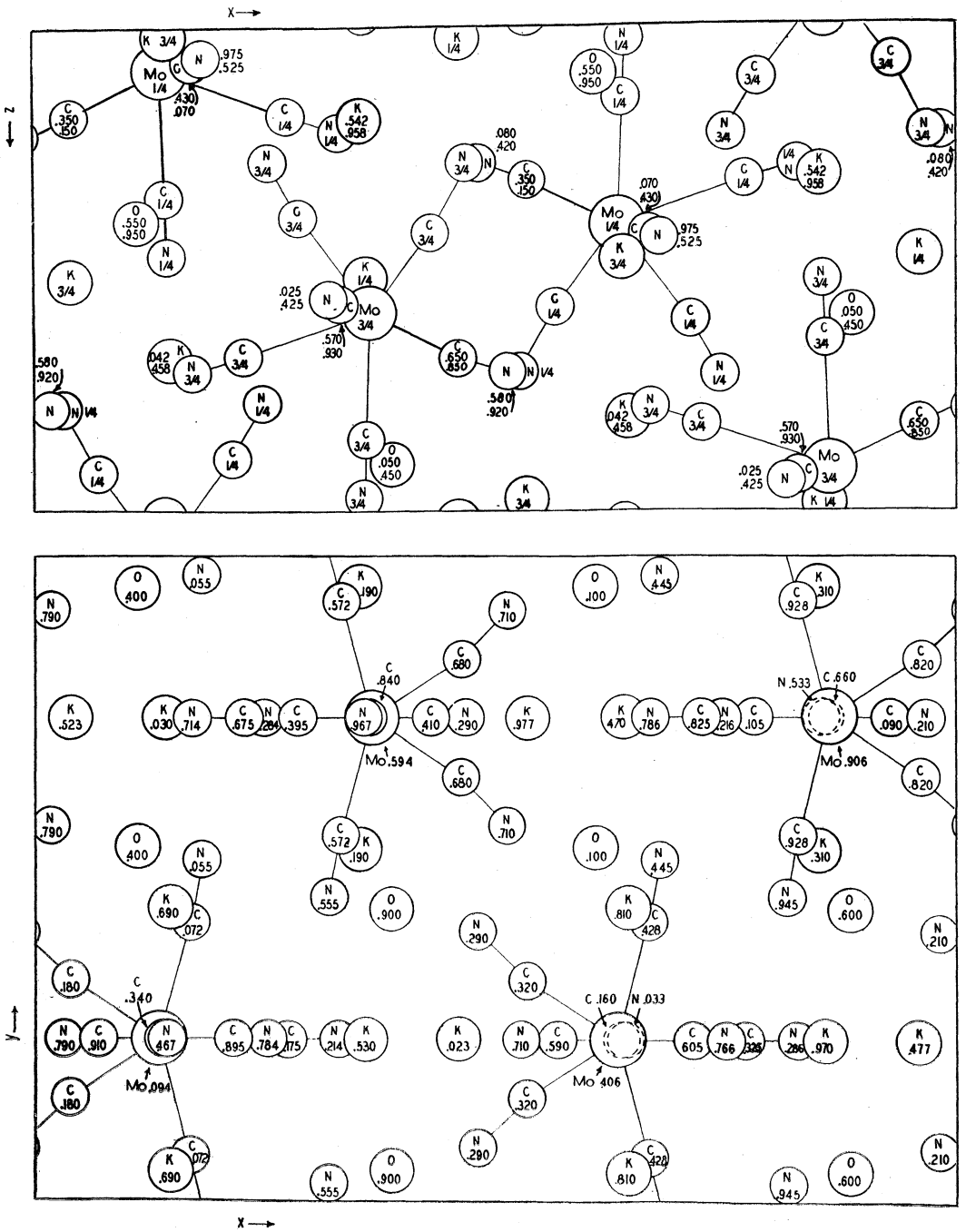

Fig. 2.—Diagrammatic projections of the unit of structure on (010) and (001). The distance of each atom above the plane of projection is indicated.

matic projections of the unit of structure on (010) and (001) are reproduced. Parameter data for all atoms (except hydrogen) as derived from these projections are listed in Table III. The positions of molybdenum and potassium given by the Fourier projections are appreciably different from the approximate values derived from the Patterson data.

A brief critical discussion of the Fourier plots and of the data used in their calculation is appropriate. For those peaks which are completely resolved on the projections the contour lines are nearly circular for the most part, the principal exceptions being oxygen and one type of nitrogen (N_I) on the (001) map. The especial

TABLE III

PARAMETER DATA FOR POTASSIUM MOLYBDOCYANIDE DIHYDRATE

Atom	Atomic coördinates x	y	z
Mo	0.135	1/4	0.094
K_I	.147	0.042	.690
K_{II}	.363	1/4	.530
K_{III}	− .037	1/4	.477
C_I	.036	0.150	.180
C_{II}	.168	0.070	.072
C_{III}	.059	1/4	− .090
C_{IV}	.214	1/4	− .105
C_V	.264	1/4	.175
C_{VI}	.140	1/4	.340
N_I	− .009	0.080	.210
N_{II}	.181	−0.025	.055
N_{III}	.015	1/4	− .210
N_{IV}	.256	1/4	− .216
N_V	.325	1/4	.214
N_{VI}	.140	1/4	.467
O	.110	−0.050	.400

prominence of the molybdenum peaks is not fully indicated in Fig. 1, since it was not practicable to maintain the density interval characteristic of the rest of the plot in drawing in the contour lines of high density on these peaks.

The maximum relative electron density observed for carbon or nitrogen on the (001) projection is appreciably greater for an atom situated in one of the densely populated symmetry planes than for a chemically similar atom in the general position. When similarly situated, however, the densities of peaks due to structurally non-equivalent, but chemically identical, atoms are seen to be nearly equal.

Nitrogen peaks, for the most part, are observed to be larger than those of similarly situated carbon atoms. Otherwise stated, we may conclude from the relative values of the peak densities that carbon rather than nitrogen of the cyanide group is bonded to molybdenum.

There are on each plot several cases of partial superposition of two or more peaks. By considering the two projections simultaneously and taking into account the observed asymmetry of the peaks, there prove to be no difficulties of interpretation, and a reasonable estimate can be gotten for every parameter value.

A comparison of corresponding values of the x-parameters as read from the two plots furnishes a partial test of the internal consistency of the Fourier data. We find virtually identical values for molybdenum and potassium and, at most, slight variations for less prominent atoms. In general, however, we should expect both projections to furnish more accurate values of the x-parameters than of the variable parameters along the other axes.

A comparison of calculated with observed relative reflection amplitudes for ($hk0$) and ($h0l$) reflections is given in Table II. The observed amplitudes are those used in the calculation of the Fourier projections. The calculated amplitudes contain no temperature factor and are, therefore, just the corresponding structure factors. The agreement is quite satisfactory on the whole, but seems to be slightly better for ($hk0$) than for ($h0l$) reflections.

Considering that the effects of thermal agitation are included in the experimental amplitudes, their values seem to be *relatively* somewhat large for the larger values of the scattering angle. Correction of these amplitudes for absorption in the crystal would result in some improvement in this respect, since for the specimens used the relative correction factor varies from 1.0 for the amplitude of smallest sin θ to about 0.9 for that of largest sin θ. The experimental amplitudes do fall off so rapidly with increasing angle of scattering that it is probable that slightly large values for them at large sin θ are of less significance in limiting the precision of the Fourier projections than are the errors in estimating intensities of the strong reflections appearing at small sin θ.

On the average, the amplitude data seem to be satisfactory. Each Fourier series, moreover, contains an unusually large number of terms. The satisfactory character of the results is to be understood in terms of these factors.

We have made also an approximate Fourier projection of relative electron density on (100), using the ($0kl$) amplitudes for which the phases could be assigned readily on the basis of the parameter values resulting from the first Fourier projections on (010) and (001). This incomplete contour map proved to be quite useful during the early stages of refining the (010) and (001) projections. Since the irregular shape and comparatively large size of the specimen used made the absorption corrections on the ($0kl$) data subject to considerable uncertainty, and since, moreover, but few of the minor peaks in which we are mainly interested at this stage are completely resolved on the (100) projection, we have not attempted to put these Fourier data into final

form. While not giving accurate values for the parameters of carbon, nitrogen, and oxygen, the (100) projection constitutes a satisfactory check upon our general conclusions about the structure.

Diagrammatic projections of the structure on (010) and (001) are shown in Fig. 2 and a drawing of the complex $Mo(CN)_8$ group is shown in Fig. 3. Table IV contains interatomic distances as calculated from the parameter data of Table II.

TABLE IV

INTERATOMIC DISTANCES IN POTASSIUM MOLYBDOCYANIDE DIHYDRATE

Atom pair	Separation, Å.	Atom pair	Separation, Å.
	Inside the anion		
$Mo-C_I(2)$	2.14	$C_I-N_I(2)$	1.13
$Mo-C_{II}(2)$	2.17	$C_{II}-N_{II}(2)$	1.14
$Mo-C_{III}$	2.04	$C_{III}-N_{III}$	1.27
$Mo-C_{IV}$	2.16	$C_{IV}-N_{IV}$	1.18
$Mo-C_V$	2.24	C_V-N_V	1.07
$Mo-C_{VI}$	2.14	$C_{VI}-N_{VI}$	1.11
C_I-C_I	2.34	N_I-N_I	3.98
$C_I-C_{II}(2)$	2.55	$N_I-N_{II}(2)$	3.64
$C_I-C_{III}(2)$	2.56	$N_I-N_{III}(2)$	4.17
$C_I-C_{VI}(2)$	2.51	$N_I-N_{VI}(2)$	3.88
$C_{II}-C_{III}(2)$	3.10	$N_{II}-N_{III}(2)$	4.68
$C_{II}-C_{IV}(2)$	2.74	$N_{II}-N_{IV}(2)$	4.06
$C_{II}-C_V(2)$	2.79	$N_{II}-N_V(2)$	4.24
$C_{II}-C_{VI}(2)$	3.18	$N_{II}-N_{VI}(2)$	4.82
$C_{III}-C_{IV}$	2.57	$N_{III}-N_{IV}$	3.99
$C_{IV}-C_V$	2.56	$N_{IV}-N_V$	3.91
C_V-C_{VI}	2.50	N_V-N_{VI}	3.78
	Outside the anion		
K_I-N_I	2.83	$K_{II}-N_I(2)$	3.58
$(K_I-N_{II})_1$	3.33	$K_{II}-N_{II}(2)$	2.74
$(K_I-N_{II})_2$	3.06	$K_{II}-N_{III}$	2.96
K_I-N_{III}	3.36	$K_{II}-N_{IV}$	2.83
K_I-N_{IV}	3.14	$K_{II}-N_V$	2.82
K_I-N_V	3.43	$K_{III}-N_I(2)$	3.09
K_I-N_{VI}	3.12	$K_{III}-N_{III}$	2.85
K_I-O	2.82	$K_{III}-N_V$	2.82
K_I-C_{III}	3.42	$K_{III}-N_{VI}$	2.90
K_I-C_{IV}	3.21	$K_{III}-O$	2.83
$O-N_I$	2.99	$K_{III}-C_I(2)$	3.08
$O-N_{II}$	3.30	$O-N_V$	3.74
$O-N_{IV}$	3.25	$O-N_{VI}$	3.54

Molybdenum–carbon separations lie between 2.04 and 2.24 Å., the average being 2.15 Å. The sum of the covalent radii,[9] using the "trigonal prism" radius for molybdenum, is 2.14 Å. The carbon–nitrogen separations are between 1.07 and 1.27 Å., the average being 1.15 Å., just the "triple bond" value. The average molybdenum–nitrogen separation is 3.29 Å., and the individual Mo—C≡N chains are practically linear throughout. The carbon–carbon separations of adjacent pairs of

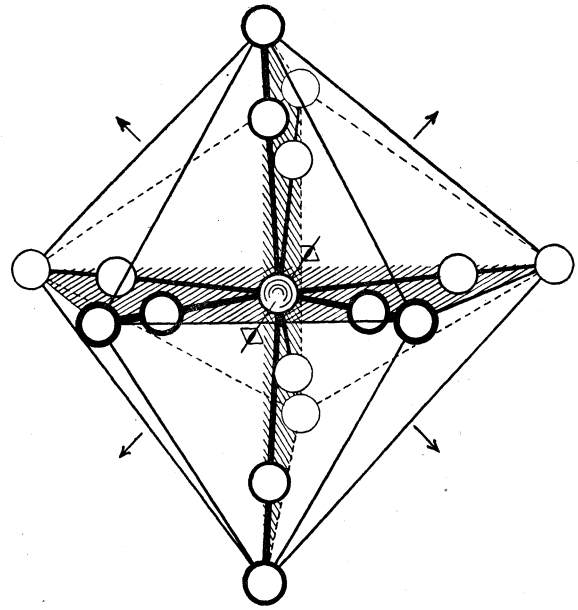

Fig. 3.—The configuration of the idealized molybdenum octocyanide group of symmetry D_{2}^{d}.

atoms within the complex vary between 2.34 and 3.18 Å. The separations may be divided empirically into two types: four longer distances, averaging 3.14 Å., and fourteen shorter distances, averaging 2.59 Å. The corresponding nitrogen–nitrogen separations lie between 3.64 and 4.82 Å., the average of the four longer distances being 4.75 Å., and of the fourteen shorter distances 3.98 Å.

The potassium ion in the general position K_I is surrounded by a rather irregular coördination figure consisting of seven nitrogen, one oxygen, and two carbon atoms, at distances ranging from 2.82 Å. (K_I–O) to 3.43 Å. Each potassium ion of the second kind, K_{II}, has five close neighbors at positions approximating to the vertices of a trigonal bipyramid, the average K–N separation being 2.82 Å. There are two additional nitrogen atoms about 3.58 Å. from each potassium of this kind. The coördination group of the third type of potassium ion consists of an oxygen atom at a distance of 2.83 Å., two carbon atoms at 3.08 Å., and five nitrogen atoms at an average distance of 2.95 Å.

There is no evidence for the existence of a definite hydrogen bridge between nitrogen of a cyanide group and oxygen of the water molecule, since the smallest O–N separation is about 2.99 Å.

The closest distance of approach between two nitrogen atoms of adjacent complexes is in no case less than 3.25 Å.

The complex anion, $Mo(CN)_8^{-4}$, which is shown to exist within crystals of potassium molybdocyanide dihydrate, is required by the space group to possess only a plane of symmetry. A study of the structure shows, however, that the configuration departs but little from the symmetry of the point group $D_2^d-\bar{4}2m$, that is, a fourfold axis of rotary inversion with two mutually perpendicular two-fold axes and two diagonal planes of symmetry. The $Mo(CN)_8$ polyhedron is a duodecahedron with eight vertices and triangular faces. It can be described as the figure outlined by the vertices of two interpenetrating bisphenoids oriented in the same way as the positive and negative tetrahedra of a cube; as compared with these regular tetrahedra one bisphenoid is considerably elongated, and the other is much flattened along the unique axis.

The symmetry of D_2^d divides the eighteen nitrogen–nitrogen (or carbon–carbon) separations of the complex into four structurally distinct types. Corresponding to the empirical distinction already noted it is convenient to divide these distances into but two classes. Assuming linear Mo—C≡N chains with Mo–C = 2.15 Å., C≡N = 1.15 Å., we calculate the separations listed in Table V for the idealized $Mo(CN)_8$ group of symmetry D_2^d. We see at once that there are no significant differences between these calculated distances and the corresponding experimentally determined average values.

TABLE V

DIMENSIONAL COMPARISON OF VARIOUS ANION CONFIGURATIONS

(Mo–N = 3.30 Å.)

Configuration	Separation, Å. C–C	N–N
Experimental $Mo(CN)_8$		
Four longer distances (av.)	3.14	4.75
Fourteen shorter distances (av.)	2.59	3.98
Idealized $Mo(CN)_8$		
Four longer distances	3.09	4.75
Fourteen shorter distances	2.58	3.96
Cube—twelve distances	2.48	3.81
Antiprism—sixteen distances	2.62	4.01

Table V contains also nitrogen–nitrogen and carbon–carbon separations for the cube and the square Archimedean antiprism as calculated for linear Mo—C≡N chains with Mo–N = 3.30 Å. No quantum mechanical treatment of the directional characteristics of quadrivalent molybdenum forming eight bonds has been reported, but the configuration established for the $Mo(CN)_8$ group in this paper seems to compare very favorably with either the cube or the antiprism from a stereochemical point of view. The repulsive potential energy arising from the interpenetration of the closed valence shells of adjacent coördinated atoms in the $Mo(CN)_8$ type of complex is certainly smaller than in the cube, and is not much different from that in the antiprism.

Crystals of potassium tungstocyanide dihydrate, $K_4W(CN)_8\cdot 2H_2O$, and potassium molybdocyanide dihydrate are almost surely isomorphous, and the $W(CN)_8^{-4}$ ion probably has the configuration established for the $Mo(CN)_8$ group. This configuration is also a reasonable one for the TaF_8^{-3} ion in crystals of sodium fluotantalate, Na_3TaF_8, and for the osmium octofluoride molecule, for which the osmium–fluorine distance is known from electron diffraction studies.[10]

It has been pointed out to us by Professor Linus Pauling that the arrangement of eight oxygen atoms around zirconium in zircon,[11] $ZrSiO_4$, is similar to that of the eight cyanide radicals around molybdenum in potassium molybdocyanide dihydrate. In zircon each oxygen atom is at once a part of two such ZrO_8 groups and one tetrahedral SiO_4 group. Other crystals having the zircon type of structure include yttrium phosphate, yttrium vanadate, and calcium chromate.

Subtracting the carbon "single bond" radius,[9] 0.77 Å., from the experimental molybdenum–carbon separation, 2.15 Å., we get 1.38 Å. for the radius of quadrivalent molybdenum form-eight bonds.

Summary

It is shown from X-ray data that the orthorhombic unit cell in crystals of potassium molybdocyanide dihydrate contains four molecules with $a_0 = 16.55$ Å., $b_0 = 11.70$ Å., $c_0 = 8.68$ Å., space-group D_{2h}^{16}–*Pnma*. Patterson projections on the three axial planes together with Patterson–Harker summations calculated from visually estimated intensity data were used to obtain approximate coördinates for molybdenum and potassium (Table I). These data were sufficient to determine the phases of the more important (*hk*0) and (*h*0*l*) reflection amplitudes (Table II) so that incomplete Fourier projections on (001) and (010) could be calculated. Recalculation and refine-

(10) J. Braune and S. Knoke, *Naturwissenschaften*, **21**, 349 (1933).

(11) R. W. G. Wyckoff, "The Structure of Crystals," Chemical Catalog Co., New York, 2d ed., 1931, pp. 286–287, 326.

ment of these projections by familiar methods of successive approximations lead to the complete determination of the structure (Figs. 1 and 2). The parameter data of Table III account satisfactorily for the intensities of X-ray reflections (Table II) and lead to generally reasonable interatomic distances (Table IV).

The structure (Fig. 2) is an aggregate of K^+ ions, $Mo(CN)_8^{-4}$ ions, and water molecules. The configuration of the $Mo(CN)_8$ group (Fig. 3) seems to be stereochemically very reasonable. The $Mo(CN)_8$ polyhedron is a duodecahedron with eight vertices and triangular faces. Although required by the space group to possess only a plane of symmetry, the complex ion in the crystal approximates to the symmetry of the point group D_2^d-$\bar{4}2m$.

ITHACA, N. Y. RECEIVED JULY 20, 1939

[CONTRIBUTION FROM THE GEOPHYSICAL LABORATORY, CARNEGIE INSTITUTION OF WASHINGTON]

Phase Equilibrium Relations in the System, Na_2SiO_3–Li_2SiO_3–SiO_2*

BY F. C. KRACEK

The work described in this paper concerns itself with the general equilibrium relations at one atmosphere pressure in the system Na_2SiO_3–Li_2SiO_3–SiO_2, and comprises the experimental determination of the temperatures at which the various crystalline phases are in equilibrium with one another, and with melts of the appropriate composition. The crystallization relations are comparatively simple, being only slightly complicated by the occurrence of solid solutions arising from a partial mutual replacement of sodium and lithium in the silicate compounds. Only one ternary compound is present in the system. This is $NaLiSiO_3$, formed by replacement of Li for Na in Na_2SiO_3; it is the Li-rich limit of the solid solution series $(Na_2,NaLi)SiO_3$. The other silicates in the system, Li_2SiO_3, $Na_2Si_2O_5$, and $Li_2Si_2O_5$, all form solid solutions of only limited extent.

Experimental Methods

The methods of study were in all respects similar to those already made familiar through the publications of this Laboratory on phase equilibrium relations. The liquidus and other significant temperatures were determined by quenching combined with microscopic examination,[1] except in compositions high in lithium metasilicate which crystallize too rapidly for the quenching technique to be effective. In such cases the temperatures were established by heating curve thermal analysis for the liquidus, and by both heating and cooling curve methods in studying transition phenomena.[2]

Homogeneous glasses of the various compositions in the system were prepared from purified silica, used in the form of cristobalite derived from powdered quartz heated at 1500°, and from reagent grade lithium carbonate and sodium carbonate. Analyses proved the reagents all to be of high purity.[3] The preparations were made up quantitatively from the thoroughly dried reagents, special care being taken to avoid losses, either mechanical, or by volatilization. Losses by volatilization were negligible except in the lithium metasilicate region of the system, where they approached 0.1% of the weight of the preparation. They were almost entirely of lithium, and could be compensated for by small additions of lithium carbonate to the original mixture. The fusions were made in platinum crucibles. To avoid attack on the crucibles by the corrosive melts of the easily fusible carbonate mixtures, it is necessary to exclude oxygen during the initial stages of the heating, until the reaction of the melt with the silica has absorbed most of the free alkali present. This was done by heating the mixtures in covered crucibles over carefully controlled Méker burners (the more convenient initial sintering of the mixtures by heating in electric furnaces always resulted in bad attack on the crucibles), the temperature being kept at the point of incipient fusion until most of the carbon dioxide was driven off. The final heatings were

* Presented before the Division of Physical and Inorganic Chemistry at the 98th meeting of the American Chemical Society, Boston, Mass., September, 1939.

(1) E. S. Shepherd, G. A. Rankin, and F. E. Wright, *Am. J. Sci.*, **28**, 293 (1909).

(2) F. C. Kracek, N. L. Bowen and G. W. Morey, *J. Phys. Chem.*, **41**, 1183 (1937).

(3) See F. C. Kracek, THIS JOURNAL, **61**, 2157 (1939), for analyses of reagents and further experimental details.

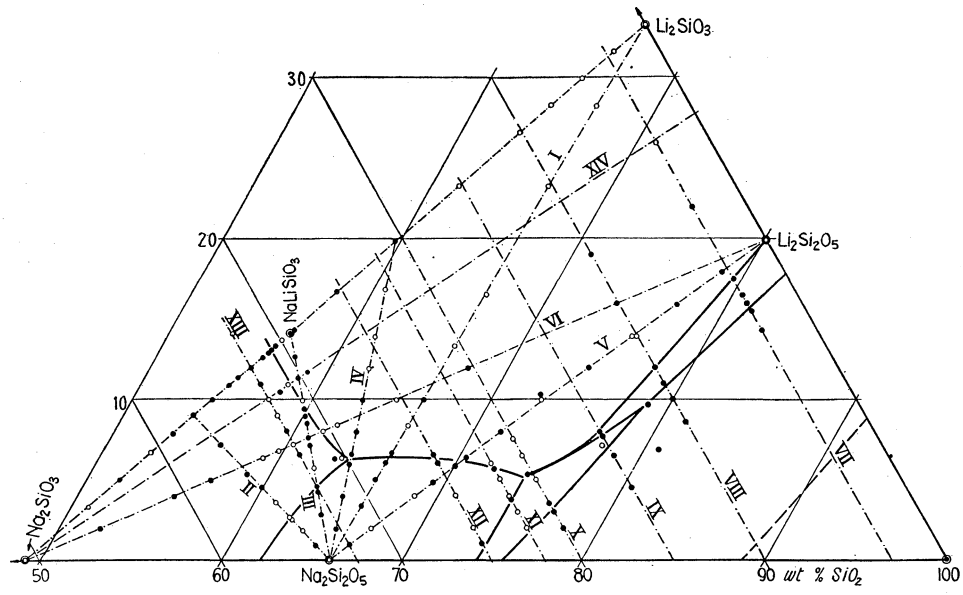

Fig. 1.—Ternary diagram of the system, Na_2SiO_3–Li_2SiO_3–SiO_2, showing the equilibrium fields at the liquidus, and location of the experimental points. Black dots represent compositions for which refractive indices of glasses are included in Table I.

made in electric furnaces in the usual manner, keeping the temperature as low as possible, consistent with complete displacement of the carbon dioxide. The more alkali-rich glasses were crystallized several times during the process, to drive off the carbon dioxide at lower temperatures, and thus to avoid losses by volatilization. The safe maximum temperatures, at which losses are negligible, are roughly, 1100° in the metasilicate, and 1300° in the disilicate regions of the system.

The temperatures were measured by means of platinum against platinum–10% rhodium thermoelements, using a shielded Feussner potentiometer system. The readings of the calibrated thermoelements were converted into temperatures on the Day and Sosman gas thermometer scale with the help of standard tables.[4]

The temperatures of the quenching furnaces were controlled automatically with a precision of ±0.3 to ±0.5°. The time of the individual runs, several of which are needed for each determination by the quenching method, varied from one hour to several days, depending upon the speed with which equilibrium is reached in the different regions of the system. This is most rapid for the metasilicates, and slowest for quartz at the Na_2O–SiO_2 side-line. The rate of dissolution of quartz increases rapidly with even small additions of lithium and, within the system, the reactivities of quartz and tridymite are sufficiently high to permit their mutual conversion (quartz $\rightleftarrows$ tridymite) near the inversion temperature in about twenty-four hours. This has made it possible to redetermine the inversion temperature with somewhat less uncertainty than before.

In presenting the experimental results below, certain minor revisions of previously published data are made. Such revisions are primarily based on very frequent recalibrations of the thermoelements, combined with a general improvement both in apparatus and technique (see ref. 2). Particular attention was given to the attainment of equilibrium in the charges. This is especially important in the cases of the more sluggish reactions, such as the mutual conversion of quartz and tridymite, and the various eutectic meltings, where certain phases tend to persist above the reaction temperatures for considerable periods of time. The measured limits of uncertainty of each determination are given by means of a ± bracket, or by quoting the measured temperature limits, as the case may be.

Experimental Results

The distribution of the compositions studied in the ternary system is represented in Fig. 1, which also shows the boundary curves between the fields. The experimental points are located mainly along certain sections across the ternary

(4) L. H. Adams, "International Critical Tables," Vol. I, 1925, p. 57.

system, chosen so as to present a net of points which would allow for easy interpolation in deriving the liquidus surfaces for the various primary phases. These sections are numbered in the figure by Roman numerals to correspond with the numbering of the sections in Table I. This table contains the experimentally determined temperatures for the various phase reactions. The temperatures given are the nearest determined temperatures, above, and below, the transformation point in question—in other words, the phase reaction temperature lies between the values given. Most of the measurements represent determinations of the liquidus temperatures; at appropriate places in the table, however, temperatures for other phase reactions,

TABLE I

RESULTS OF EQUILIBRIUM MEASUREMENTS IN THE SYSTEM, Na_2SiO_3–Li_2SiO_3–SiO_2

No.	Wt. % B	Na_2O	Li_2O	SiO_2	Measured limits Liquidus temp. °C. Below	Above	Cryst. phases	Refr. index quenched glass
			I. Binary Section: A = $Na_2Si_2O_5$; B = Li_2SiO_3					
31	10.0	30.61	3.31	66.08	790	792	$Na_2Si_2O_5$	1.513
32	15.0	28.94	4.98	66.08	743	746	$Na_2Si_2O_5$	1.517
33	18.0	27.92	5.98	66.10	719	720	$Na_2Si_2O_5$	1.521
					709	710	$Na_2Si_2O_5$ + Li_2SiO_3 binary eutectic	
34	20.0	27.23	6.64	66.12	721	727	Li_2SiO_3	1.521
35	25.0	25.53	8.30	66.17	794	795	Li_2SiO_3	...
36	30.0	23.80	9.95	66.25	850	852	Li_2SiO_3	1.527
37	40.0	20.38	13.23	66.39	941	942	Li_2SiO_3	...
38	50.0	17.00	16.50	66.50	1011	1015	Li_2SiO_3	...
39	70.0	10.2	23.2	66.6	1111 h[a]		Li_2SiO_3	...
40	85.0	5.1	28.2	66.7	1164 h[a]		Li_2SiO_3	...
			II. Ternary Section: A = $Na_2Si_2O_5$; B = (theor.) $Na_4Li_2Si_3O_9$					
41	10.0	34.35	0.89	64.76	845	846	$Na_2Si_2O_5$	1.509
42	20.0	34.65	1.79	63.56	814	816	$Na_2Si_2O_5$	...
43	28.0	34.90	2.50	62.60	789	790	$Na_2Si_2O_5$	...
					781	782	$Na_2Si_2O_5$ + $(Na_2,NaLi)SiO_3$	
44	30.0	34.94	2.60	62.46	788	790	$(Na_2,NaLi)SiO_3$	
45	40.0	35.25	3.58	61.17	814	818	$(Na_2,NaLi)SiO_3$	...
46	50.0	35.58	4.47	59.95	841	842	$(Na_2,NaLi)SiO_3$	1.521
47	60.0	35.89	5.36	58.75	860	862	$(Na_2,NaLi)SiO_3$	1.523
48	80.0	36.50	7.15	56.34	891	893	$(Na_2,NaLi)SiO_3$	1.527
(5)	100.0	37.11	8.94	53.95	906	907	$(Na_2,NaLi)SiO_3$	1.528
			III. Ternary Section: A = $Na_2Si_2O_5$; B = $NaLiSiO_3$					
51	20.0	33.08	2.82	64.10	796	800	$Na_2Si_2O_5$	1.514
52	30.0	32.60	4.23	63.17	748	755	$Na_2Si_2O_5$	1.517
53	32.0	32.49	4.51	63.00	742	743	$(Na_2,NaLi)SiO_3$	1.519
					696	698	Ternary eutectic E_1	
54	40.0	32.12	5.64	62.24	755	758	$(Na_2,NaLi)SiO_3$	...
55	50.0	31.64	7.05	61.31	769	772	$(Na_2,NaLi)SiO_3$	1.525
56	60.0	31.15	8.45	60.40	789	790	$(Na_2,NaLi)SiO_3$	1.528
57	63.0	31.02	8.88	60.10	796	797	$(Na_2,NaLi)SiO_3$	1.531
58	66.0	30.87	9.30	59.83	803	805	Li_2SiO_3	>1.530
59	70.0	30.68	9.87	59.45	812	813	Li_2SiO_3	...
60	80.0	30.20	11.28	58.52	838	841	Li_2SiO_3	>1.530
61	90	29.7	12.6	57.7	860	862	Li_2SiO_3	1.535
(16)	100.0	29.23	14.06	56.71	872	873	Li_2SiO_3	1.538
			IV. Ternary Section: A = $Na_2Si_2O_5$; B = (theor.) $Na_2Li_4Si_3O_9$					
71	10.0	32.69	1.98	65.33	823	825	$Na_2Si_2O_5$	1.511
72	20.0	31.32	3.95	64.73	770	772	$Na_2Si_2O_5$	1.516
73	30.0	29.95	5.93	64.12	708	709	$Na_2Si_2O_5$	1.521
74	33.0	29.59	6.53	63.88	711	712	Li_2SiO_3	1.523
					696	697	Ternary eutectic E_1	
75	40.0	28.64	7.91	63.45	774	778	Li_2SiO_3	1.525

TABLE I (*Continued*)

No.	Wt. % B	Na_2O	Li_2O	SiO_2	Measured limits Liquidus temp. °C. Below	Above	Cryst. phases	Refr. index quenched glass
76	50.0	27.28	9.89	62.83	844	847	Li_2SiO_3	1.529
77	60.0	25.94	11.87	62.19	889	893	Li_2SiO_3	...
78	70.0	24.59	13.85	61.56	927	933	Li_2SiO_3	...
79	85	22.5	16.8	60.7	977	981	Li_2SiO_3	...
(21)	100	20.5	19.8	59.7		1001[b]	Li_2SiO_3	
			V. Ternary Section: A = $Na_2Si_2O_5$; B = $Li_2Si_2O_5$					
81	5.0	32.29	0.99	66.71	845	846	$Na_2Si_2O_5$	1.507
82	10.0	30.64	1.99	67.37	816	818	$Na_2Si_2O_5$	1.509
83	20.0	27.23	3.98	68.79	758	762	$Na_2Si_2O_5$	...
84	24.0	25.87	4.78	69.35	735	736	$Na_2Si_2O_5$	1.513
85	29.2	24.11	5.81	70.08	701	702	$Na_2Si_2O_5$	1.515
					692	694	$Na_2Si_2O_5 + Li_2SiO_3$	
86	32.0	23.15	6.37	70.48	711	712	Li_2SiO_3	1.515
					692	695	$Na_2Si_2O_5 + Li_2SiO_3$	
87	40.0	20.43	7.97	71.61	780	782	Li_2SiO_3	1.518
88	50	17.19	9.94	72.87	849	851	Li_2SiO_3	...
89	60.0	13.62	11.95	74.43	908	912	Li_2SiO_3	1.526
90	70.0	10.20	13.93	75.87	954	956	Li_2SiO_3	...
91	80.0	6.81	15.92	77.28	986	989	Li_2SiO_3	1.530
92	90.0	3.41	17.90	78.69	1012	1014	Li_2SiO_3	1.532
...	100.0	...	19.92	80.08		1034[c]	Li_2SiO_3	...
			VI. Ternary Section: A = Na_2SiO_3; B = $Li_2Si_2O_5$					
101	10.0	45.70	1.99	52.31	1032	1037	$(Na_2,NaLi)SiO_3$	1.519
102	20.0	40.62	3.98	55.40	956	958	$(Na_2,NaLi)SiO_3$	1.523
103	25.0	38.10	4.98	56.92	906	908	$(Na_2,NaLi)SiO_3$	1.523
104	32.0	34.54	6.37	59.09	838	840	$(Na_2,NaLi)SiO_3$	...
105	34.0	33.52	6.77	59.70	819	821	$(Na_2,NaLi)SiO_3$	...
106	36.0	32.49	7.14	60.37	800	803	$(Na_2,NaLi)SiO_3$	...
107	38.0	31.48	7.57	60.95	777	783	$(Na_2,NaLi)SiO_3$	>1.525
108	40.0	30.45	7.92	61.62	762	764	Li_2SiO_3	...
109	42.0	29.45	8.34	62.21	780	783	Li_2SiO_3	...
110	50.0	25.36	9.91	64.73	848	850	Li_2SiO_3	...
111	60	20.26	11.88	67.86	911	913	Li_2SiO_3	1.528
112	80.0	10.14	15.90	73.96	996	998	Li_2SiO_3	1.532
			VII. Ternary Section at 3.0% Na_2O					
121	..	2.99	14.30	82.71	1088	1092	Tridymite	1.519
122	..	2.99	15.46	81.55	999	1001	Tridymite + $Li_2Si_2O_5$	...
					1012	1019	Tridymite	1.524
123	..	3.00	15.96	81.04	1002	1004	$Li_2Si_2O_5$	...
124	..	2.99	16.46	80.55	1004	1005	$Li_2Si_2O_5$	1.528
125	..	2.99	17.46	79.55	1003	1106	Li_2SiO_3	...
126	..	2.99	21.94	75.06	1089	1091	Li_2SiO_3	1.543
127	..	3.00	25.95	71.05		1146h	Li_2SiO_3	...
			VIII. Ternary Section at 10.0% Na_2O					
131	..	9.97	8.59	81.44	1075	1079	Tridymite	1.509
132	..	10.00	10.00	80.00	954	958	Tridymite	...
133	..	10.00	11.01	78.99	906	908	$Li_2Si_2O_5$	1.518
134	..	9.98	11.97	78.05	914	916	$Li_2Si_2O_5$	1.521
135	..	9.98	18.96	71.06	1054	1056	Li_2SiO_3	1.539
			IX. Ternary Section at 15.0% Na_2O					
141	..	15.00	4.51	80.49	1075	1080	Tridymite	1.501
142	..	14.98	6.49	78.52	904	910	Tridymite	1.510
143	..	14.98	7.69	77.33	805	811	Quartz	1.513
					795	799	Quartz + $Li_2Si_2O_5$	
144	..	14.99	7.99	77.02	802	804	Li_2SiO_3, ($Li_2Si_2O_5$)	1.515

TABLE I (*Continued*)

No.	Wt. % B	Na_2O	Li_2O	SiO_2	Measured limits Liquidus temp. °C. Below	Above	Cryst. phases	Refr. index quenched glass
				X. Ternary Section at 20.0% Na_2O				
151	..	19.97	2.00	78.03	974	980	Tridymite	1.498
152	..	20.0	3.0	77.0	871	874	Tridymite	1.502
153	..	19.98	3.50	76.52	829	833	Quartz	1.506
154	..	19.98	5.00	75.02	688	692	Quartz	...
					642	645	Quartz + $Na_2Si_2O_5$	
					636	638	Ternary eutectic E_2	
155	..	20.28	5.30	74.42	660	663	Li_2SiO_3	1.509
					637	639	Ternary eutectic E_2	
156	..	20.00	6.49	73.51	708	709	Li_2SiO_3	...
157	..	20.00	10.00	70.00	854	856	Li_2SiO_3	...
				XI. Ternary Section at 22.0% Na_2O				
161	..	21.99	2.00	76.01	827	831	Quartz	...
162	..	21.96	3.00	75.04	739	747	Quartz	...
163	..	22.00	3.70	74.30	686	688	Quartz + $Na_2Si_2O_5$	1.507
					686	689	$Na_2Si_2O_5$	...
164	..	21.95	3.99	74.05	684	686	$Na_2Si_2O_5$	...
165	..	21.96	5.00	73.04	677	680	$Na_2Si_2O_5$	...
166	..	22.00	5.59	72.41	675	676	$Na_2Si_2O_5$	>1.510
167	..	21.99	5.98	72.03	688	689	Li_2SiO_3	...
				XII. Ternary Section at 25% Na_2O				
171	..	25.00	1.00	74.00	766	767	$Na_2Si_2O_5$	1.501
172	..	24.99	2.00	73.01	762	764	$Na_2Si_2O_5$	...
173	..	24.99	4.00	71.01	735	737	$Na_2Si_2O_5$	...
174	..	25.00	6.00	69.00	707	711	$Na_2Si_2O_5$	1.517
175	..	25.00	6.50	68.50	714	716	Li_2SiO_3	1.519
				XIII. Ternary Section at 32.5% Na_2O				
181	..	32.50	6.50	61.00	780	782	$(Na_2,NaLi)SiO_3$	1.524
182	..	32.47	7.98	59.55	812	816	$(Na_2,NaLi)SiO_3$	1.528
183	..	32.47	8.99	58.54	828	831	$(Na_2,NaLi)SiO_3$	...
184	..	32.46	9.96	57.58	841	843	$(Na_2,NaLi)SiO_3$	>1.530
185	..	32.40	10.93	56.67	847	849	$(Na_2,NaLi)SiO_3$	...
(9)	..	32.48	11.92	55.60	851	853	$(Na_2,NaLi)SiO_3$	...
186	..	32.45	14.02	53.53	834	842	$(Na_2,NaLi)SiO_3$	...
					836h		$(Na_2,NaLi)SiO_3$	...
				XIV. Miscellaneous Ternary Section from Na_2SiO_3 through Composition 60[d]				
(184)	36.00	32.46	9.96	57.58	841	843	$(Na_2,NaLi)SiO_3$	>1.530
191	37.50	31.75	10.43	57.82	832	834	$(Na_2,NaLi)SiO_3$	1.532
192	39.00	30.98	10.85	58.17	830	832	$(Na_2,NaLi)SiO_3$	...
(60)	40.53	30.20	11.28	58.52	838	841	Li_2SiO_3	>1.530
193	42.00	29.46	11.68	58.86	854	855	Li_2SiO_3	1.534
				XV. Miscellaneous Compositions				
201	..	30.60	6.29	63.11	701	703	Li_2SiO_3 + $(Na_2,NaLi)SiO_3$	
					719	720	$(Na_2,NaLi)SiO_3$	1.523
202	..	30.20	6.30	63.50	696	697	Ternary eutectic E_1	
					699	700	$(Na_2,NaLi)SiO_3$ + Li_2SiO_3	
					707	708	$(Na_2,NaLi)SiO_3$	
203	..	17.03	10.32	72.66	863	864	Li_2SiO_3	1.523
204	..	15.29	7.14	77.57	828	837	Quartz	...
205	..	11.49	9.68	78.83	869	870	Tridymite	1.514
					868	869	$Li_2Si_2O_5$ + tridymite	
206	..	12.35	6.86	80.78	1052	1058	Tridymite	1.506

[a] "h" denotes determination by heating curve analysis. [b] Interpolated from data on Na_2SiO_3–Li_2SiO_3. [c] From data on Li_2SiO_3–SiO_2. [d] B = 27.82% Li_2O, 72.18% SiO_2. > = more than.

TABLE I (*Concluded*)
Polymorphous Transitions in $Na_2Si_2O_5$

Composition, wt. % Na_2O	Li_2O	SiO_2	Transition temp.[e] av., °C. I–II	II–III	Remarks
34.05	...	65.95	706.8	677.0	Pure $Na_2Si_2O_5$
37.5	...	62.5	708.7	677.1	Excess Na_2O
35.8	...	64.2	705.9	678.1	Excess Na_2O
31.7	...	68.3	707.4	678.4	Excess SiO_2
31.0	...	69.0	707.7	677.8	Excess SiO_2
27.0	...	73.0	707.6	677.2	Excess SiO_2
30.61	3.31	66.08	699.5	687.7	90% $Na_2Si_2O_5$ + 10% Li_2SiO_3
28.94	4.98	66.08	698.1	688.5	85% $Na_2Si_2O_5$ + 15% Li_2SiO_3
30.64	1.99	67.37	698.6	688.1	90% $Na_2Si_2O_5$ + 10% $Li_2Si_2O_5$
		Polymorphous Transitions in $Li_2Si_2O_5$			
...	19.92	80.08	(960)h[f]	936.6	Pure Li_2SiO_3
...	22.1	77.9	....	935.4	Excess Li_2O
...	17.7	82.3	(960)h[f]	937.2	Excess SiO_2
	12.6	87.4	....	935.5	Excess SiO_2
3.0	17.5	79.5	....	929.5	
3.4	17.9	79.7	....	929.8	90% $Li_2Si_2O_5$ + 10% $Na_2Si_2O_5$

[e] For method of deducing the average transition temperature see Fig. 3. [f] Faint arrest on first heating only.

mainly eutectics, are given, in connection with the composition for which they were determined. The coördinates of the invariant points for the pressure of one atmosphere are collected in Table III.

The Binary Systems on the Side Lines

Before proceeding to a discussion of the relations brought out in the ternary system, it is necessary to describe the fundamental binary systems on the sides of the triangle, Na_2SiO_3–Li_2SiO_3–SiO_2. It will be noted that one of these, Na_2SiO_3–Li_2SiO_3, is a binary section across the larger triangle, Na_2O–Li_2O–SiO_2.

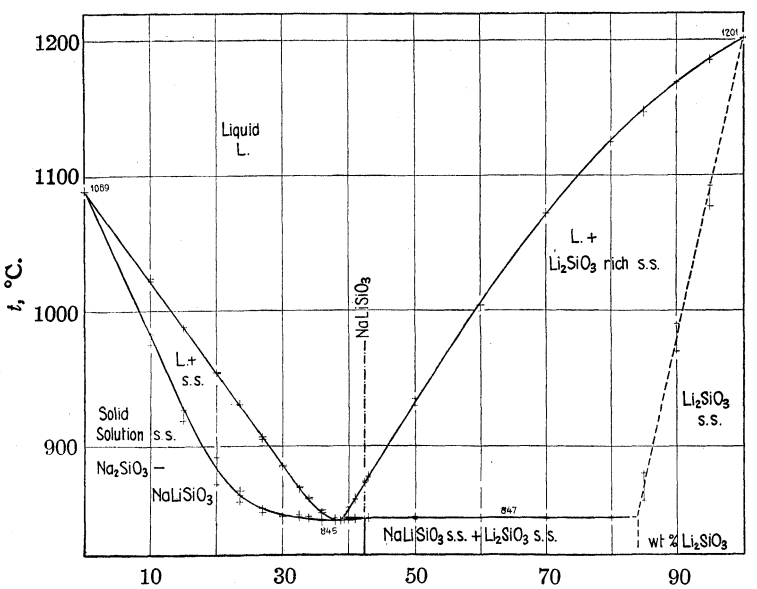

Fig. 2.—The binary system, Na_2SiO_3–Li_2SiO_3. Reprinted from Ref. 3.

1. The System, Na_2SiO_3–Li_2SiO_3.—The data on this system have been published recently.[3] This system is of special interest in that sodium metasilicate crystals are capable of exchanging sodium for lithium in solid solution until the composition sodium lithium (1,1) metasilicate is reached. Lithium metasilicate, on the other hand, takes up only a minor proportion of sodium into its lattice. The compound sodium lithium (1,1) metasilicate melts incongruently at 847°, yielding a liquid of 39.3 wt. per cent. lithium metasilicate, and the sodium-bearing lithium metasilicate crystals. The solid solution series, $(Na_2,NaLi)SiO_3$, has a minimum on its liquidus at 845°, 38.5 wt. per cent. lithium metasilicate (binary compositions). The equilibrium relations are illustrated in Fig. 2 (see also Fig. 2 of ref. 3).

2. The System, Na_2SiO_3–SiO_2.—This system has been studied by Morey and Bowen,[5] and by Kracek[6] who extended the investigation to include the orthosilicate, Na_4SiO_4.

(a) **Polymorphism of Sodium Disilicate.**—Measurements, supplementing those earlier made by Kracek,[6] of thermal arrests in the sodium disilicate region with the improved apparatus now in use (see ref. 2) were made

(5) G. W. Morey and N. L. Bowen, *J. Phys. Chem.*, **28**, 1167 (1924).

(6) F. C. Kracek, *ibid.*, **34**, 1583 (1930).

on pure sodium disilicate (65.95% silicon dioxide), on two preparations toward sodium metasilicate, at 62.5 and 64.2% silicon dioxide, and on three preparations toward silicon dioxide, at 68.3, 69.0, and 73.0% silicon dioxide. Each of these preparations yielded two arrests, one at 678°, the other at 707° (average temperatures), as illustrated in Figs. 3 and 4. The heat effects are relatively small, probably of the order of 2 cal./g. for the 678° arrest, and 1 cal./g. for the 707° arrest. The 707° arrest had escaped detection previously in preparations containing excess silicon dioxide. An arrest, not included in Fig. 4, previously recorded at 768° in silicon dioxide-rich preparations only, is again recorded in the same region, both of temperature and composition, and probably is due to eutectic melting of small amounts of tridymite and cristobalite present.

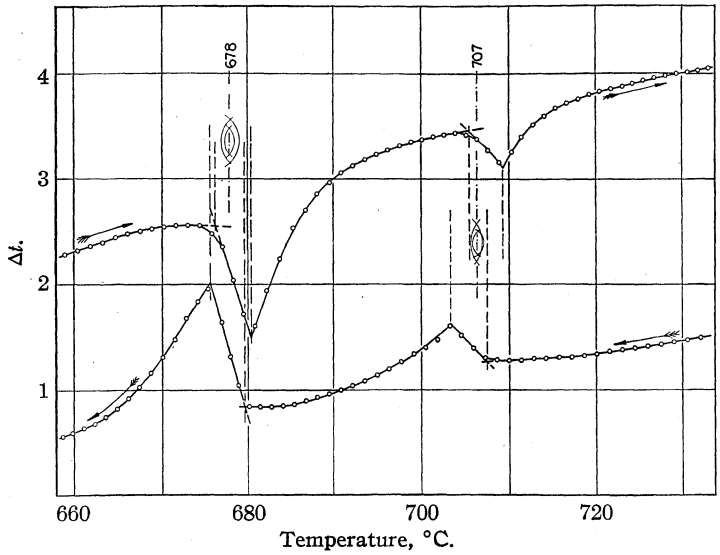

Fig. 3.—Typical differential heating and cooling curves of phase transitions in $Na_2Si_2O_5$, giving geometrical construction for deducing the average transition temperatures.

These measurements lead to the conclusion that sodium disilicate is trimorphous with inversions located at atmospheric pressure at the average temperatures of 678 and 707°. Presence of lithium silicates influences these temperatures, as stated at a later point in the paper (see Figs. 8 and 9).

(b) **The $Na_2Si_2O_5$–Quartz Eutectic.**—The determination of the $Na_2Si_2O_5$–quartz eutectic by heating curves is inexact, yielding an arrest which is spread rather indefinitely over the temperature interval from about 788 to nearly 800°. To verify the location of this eutectic, we have heated completely crystalline preparations of 74.8 and 76.0% silicon dioxide at various temperatures, and quenched. When heated for two days at 786°, the preparations remained powdery. At 788° they sintered to porous lumps, with little or no glass evident under the microscope. At 790° there was much glass, in which were imbedded sharply faceted quartz crystals, and larger eroded quartz grains, with very little unevenly scattered remnants of sodium disilicate crystals. The eutectic temperature is accordingly 789 ± 1°. The quartz liquidus on the 74.8% silicon dioxide preparation (compare Kracek's earlier preparation 571, 74.81% silicon dioxide, 838°) was found by similar procedure to be 822 ± 4°. The intersection of the liquidus curves for sodium disilicate and quartz, at the newly determined eutectic temperature of 789°, is located at 74.2 ± 0.3% silicon dioxide. The former values for the eutectic were 793°, and 73.4% (Morey and Bowen) and 73.9% (Kracek) silicon dioxide.

(c) **The Na_2SiO_3–$Na_2Si_2O_5$ Eutectic.**—Precrystallized preparations of 61.5 and 62.5% silicon

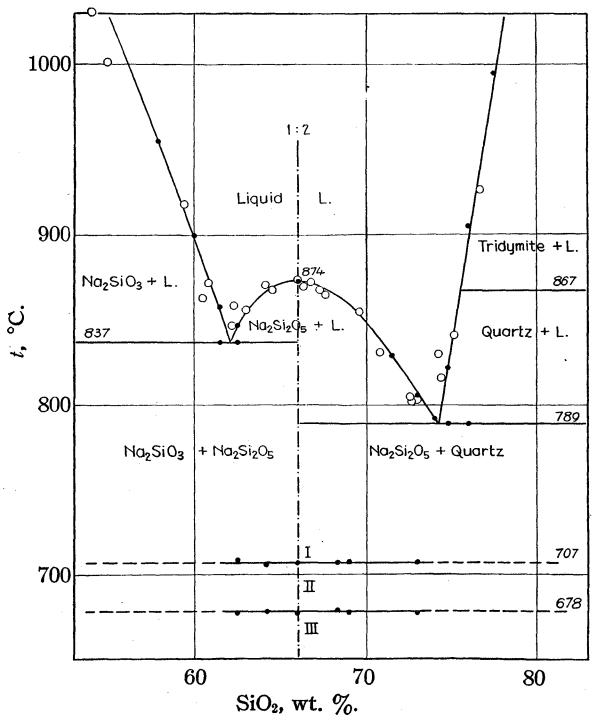

Fig. 4.—The disilicate region of the system, Na_2SiO_3–SiO_2: open circles by Morey and Bowen,[5] and Bowen, Schairer and Willems (unpublished); black dots, Kracek.

dioxide remained unsintered at 836°, and contained much glass at 838°. If 837 ± 1° is taken as the eutectic temperature, the eutectic composition is 62.1 ± 0.2% silicon dioxide. The former values were 840°, 60.8% silicon dioxide (Morey and Bowen), and 846°, 62.1% silicon dioxide (Kracek).

(d) **The Cristobalite Liquidus.**—The liquidus temperatures published earlier by the writer[7] for cristobalite in the system, Na_2O–SiO_2, are slightly higher than those determined in the present work. The high values in the earlier determinations can be ascribed only to the existence of a temperature gradient in the quenching furnace then used. The newly determined values are: 1532 ± 5° at 91.5, 1580 ± 3° at 95.0, and 1628 ± 3° at 97.5% silicon dioxide.

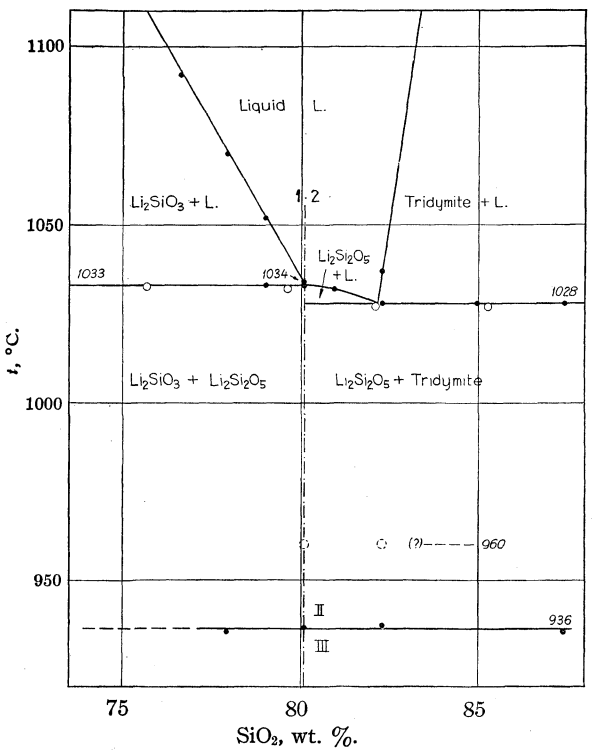

Fig. 5.—The disilicate region of the system, Li_2SiO_3–SiO_2: open circles, Jaeger and van Klooster; black dots and dotted circles, Kracek.

The revisions discussed above have been incorporated in Fig. 4, which represents the phase relations in the system, Na_2SiO_3–SiO_2, for the region in the neighborhood of sodium disilicate.

3. The System, Li_2SiO_3–SiO_2.—The equilibrium relations in this system were studied by Jaeger and van Klooster[8] and by Kracek,[7,9] among others.

(a) **The Cristobalite Liquidus.**—A redetermination was made of the liquidus temperatures for cristobalite as the primary phase. It was found that the published temperatures[7] in this system also are slightly high; the new values are 1508 ± 4° at 92.5, 1561 ± 3° at 95.0, and 1605 ± 3° at 97.0% silicon dioxide.

(b) **Polymorphism of Lithium Disilicate.**—To verify the former[9] thermal analysis measurements in the lithium disilicate region of the system, we have made new determinations on crystallized preparations of 77.9, 80.08 ($Li_2Si_2O_5$), 82.3, and 87.4% silicon dioxide. A small arrest, with a thermal effect of 1 to 2 cal./g. in pure lithium disilicate, was found in all the preparations, at the average temperature of 936°. This arrest has the characteristics associated with typical polymorphic inversions, with hysteresis.

The very small irregularity in differential temperature, formerly noted at 960°, could not be reproduced with certainty. It was noted once, but only during the first heating, in the 80.08 and 82.3% silicon dioxide preparations. It did not reappear during subsequent heat treatments, or in any of the other preparations; hence, its significance remains unexplained.

Addition of sodium silicates to lithium disilicate lowers the 936° inversion to 930° (see the section, $Na_2Si_2O_5$–$Li_2Si_2O_5$).

The phase relations in the neighborhood of lithium disilicate for the system Li_2SiO_3–SiO_2 are illustrated in Fig. 5.

The Ternary System

The only ternary compound in the system is sodium lithium (1,1) metasilicate. This compound is an end-member of the $(Na_2,NaLi)SiO_3$ series of solid solutions, and has no separate field of its own in the ternary system. Hence, the primary phases at the liquidus are the $(Na_2,NaLi)SiO_3$ solid solutions, Li_2SiO_3, $Na_2Si_2O_5$, $Li_2Si_2O_5$, and silica in its three major modifications. The compounds Li_2SiO_3, $Li_2Si_2O_5$, and $Na_2Si_2O_5$ all form limited series of solid solutions with small mutual replacements of lithium and sodium.

Only one section within the system, namely, $Na_2Si_2O_5$–Li_2SiO_3, is binary at the liquidus; the other possible binary section, $Na_2Si_2O_5$–$Li_2Si_2O_5$,

(7) F. C. Kracek, THIS JOURNAL, 52, 1436 (1930).

(8) F. M. Jaeger and H. S. van Klooster, *Proc. Amst. Acad. Sci.*, 16, 857 (1914).

(9) F. C. Kracek, *J. Phys. Chem.*, 34, 2641 (1930).

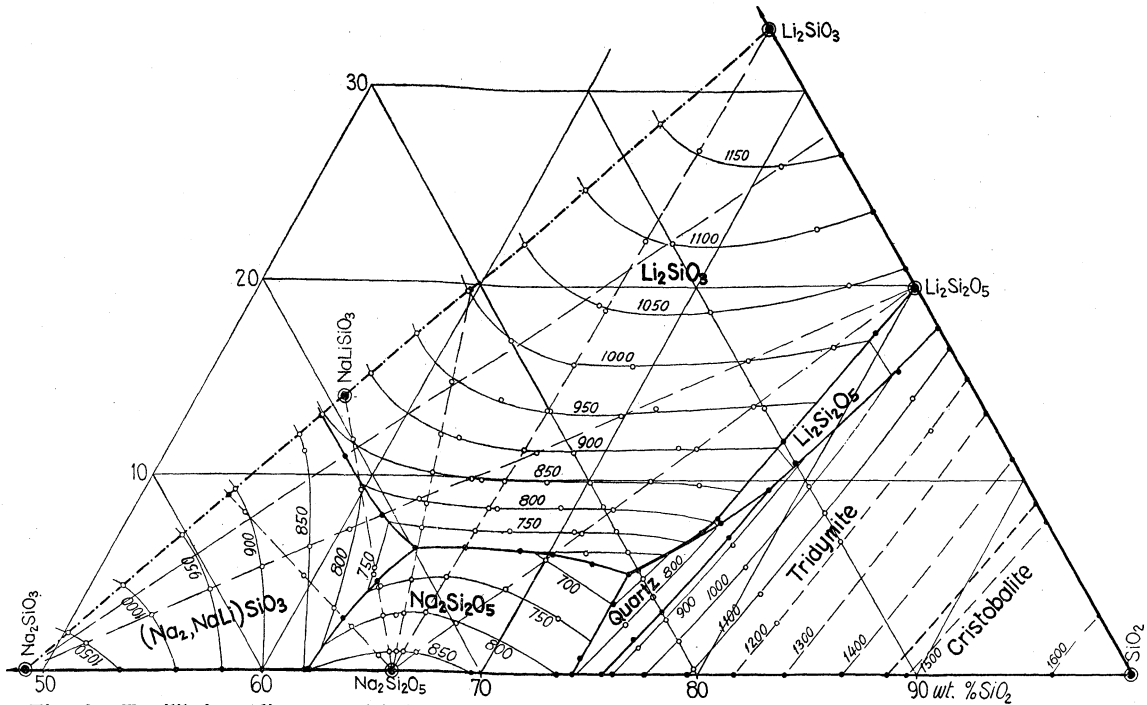

Fig. 6.—Equilibrium diagram with isotherms, of the system, Na_2SiO_3–Li_2SiO_3–SiO_2. Open circles represent interpolated temperatures corresponding to the various isotherms. Black dots give the location of boundary curves as measured or deduced by interpolation from the data on the various cross-sections in the system.

is partly ternary at the liquidus; this is due to the incongruent melting relations of lithium disilicate.

Method of Interpolation in Deriving Isotherms.—The data for each of the sections I to VI across the system, as indicated in Fig. 1, were plotted on a sufficiently large scale to allow for interpolation with a precision of ±0.5°. The compositions corresponding to even temperatures at 50° intervals were then read off from the graphs, and plotted in the ternary system, as indicated in Fig. 6 by the open circles.

Cross interpolation was employed for the remaining sections, VII to XIV. For this purpose the temperatures of intersection of these sections with the sections I to VI were read off from the above graphs, and were then plotted, together with the data for preparations on the individual sections, as indicated in Fig. 7, the abscissa being progressively shifted so as to bring the metasilicate composition for each of the sections VII to XIII upon the vertical line at the left of the diagram. This was done by adding to the lithium oxide content for each section the quantity

$$\%\ Li_2O\ \text{added} = \%\ Na_2O\ \text{along the section} \times \frac{Li_2O\ \text{in}\ Li_2SiO_3}{Na_2O\ \text{in}\ Na_2SiO_3} = 0.6541 \times \%\ Na_2O\ \text{along the section}$$

The resulting figure, Fig. 7, represents a *t*–*x* (temperature–composition) projection of a part of the system upon the plane of the side system, Li_2SiO_3–SiO_2. To avoid confusion in the diagram, only sections up to 25% sodium oxide are represented. The sections I, V, and VI, appear as curved dotted lines, with the interpolated loci of the intersections marked by crosses. Other *t*–*x* projections of the system were constructed to facilitate cross-interpolations in regions not covered by Fig. 7. The data so obtained are plotted in Fig. 6.

The Boundary Curves.—The coördinates of the boundary curves between the various primary phases, as deduced by interpolation from the graphs, or directly from the experimental data, are given in Table II. The boundary curves meet at the invariant points, which are collected for reference in Table III.

1. The System, $Na_2Si_2O_5$–Li_2SiO_3.—The relations in this system are illustrated in Fig. 8. The system is simply eutectoid; both the end-members are present in limited solid solution. The extent of the solid solution in lithium metasilicate is approximately the same as in the system Na_2SiO_3–Li_2SiO_3, as judged from the values of the refractive indices of the crystals. The solid solution

TABLE II

COÖRDINATES OF THE BOUNDARY CURVES IN THE SYSTEM Na_2SiO_3–Li_2SiO_3–SiO_2

Section no. and identification		Wt. % Na_2O	Wt. % Li_2O	Wt. % SiO_2	t, °C.
	A. Boundary between $(Na_2,NaLi)SiO_3$ and $Na_2Si_2O_5$ (s. s.)[a]				
...	Na_2SiO_3–$Na_2Si_2O_5$	37.9	..	62.1	837 ± 1
II	$Na_2Si_2O_5$–$(Na_4Li_2Si_3O_9)$[b]	35.0	2.7	62.3	782
III	$Na_2Si_2O_5$–$NaLiSiO_3$	32.5	4.5	63.0	741
XIII	32.5% Na_2O	32.5	4.6	62.9	741
...	30.0% Na_2O	30.0	6.30	63.7	700
...	Ternary eutectic E_1	29.9	6.2	63.9	697 ± 3
	B. Boundary between $(Na_2,NaLi)SiO_3$ and Li_2SiO_3 (s. s.)				
...	Na_2SiO_3–Li_2SiO_3	30.8	13.1	56.1	847 ± 1
XIV	Na_2SiO_3–72.19% SiO_2 on Li_2SiO_3–SiO_2	30.7	11.0	58.3	831
III	$Na_2Si_2O_5$–$NaLiSiO_3$	30.8	9.5	59.7	799
VI	Na_2SiO_3–$Li_2Si_2O_5$	30.6	7.9	61.5	759
...	30.0% Na_2O	30.0	6.4	63.6	700
...	Ternary eutectic E_1	29.9	6.2	63.9	697 ± 3
	C. Boundary between $Na_2Si_2O_5$ (s. s.) and Li_2SiO_3 (s. s.)				
...	Ternary eutectic E_1	29.9	6.2	63.9	697 ± 3
IV	$Na_2Si_2O_5$–$(Na_2Li_4Si_3O_9)$	29.7	6.3	64.0	698
I	$Na_2Si_2O_5$–Li_2SiO_3, eutectic	27.5	6.4	66.1	709 ± 3
XII	25.0% Na_2O	25.0	6.3	68.7	705
V	$Na_2Si_2O_5$–$Li_2Si_2O_5$	23.7	6.0	70.3	693
XI	22.0% Na_2O	22.0	5.7	72.3	674
...	Quint. point Q_1	20.5	5.2	74.3	641 ± 3
	D. Boundary between $Na_2Si_2O_5$ (s. s.) and $Li_2Si_2O_5$ (s. s.)				
...	Quint. point Q_1	20.5	5.2	74.3	641 ± 3
...	Ternary eutectic E_2	20.5	5.1	74.4	637 ± 3
	F. Boundary between $Na_2Si_2O_5$ (s. s.) and Quartz				
...	$Na_2Si_2O_5$–SiO_2	25.8	...	74.2	789 ± 1
XII	25.0% Na_2O	25.0	0.8	74.2	770
XI	22.0% Na_2O	22.0	3.6	74.4	688
...	Ternary eutectic E_2	20.5	5.1	74.4	637 ± 3
	G. Boundary between Li_2SiO_3 (s. s.) and $Li_2Si_2O_5$ (s. s.)				
...	Quint. point Q_1	20.5	5.2	74.3	641 ± 3
X	20.0% Na_2O	20.0	5.4	74.6	660
IX	15.0% Na_2O	15.0	8.0	77.0	803
VIII	10.0% Na_2O	10.0	12.0	78.0	915
VII	3.0% Na_2O	3.0	17.6	79.4	1008
...	Li_2SiO_3–SiO_2	..	19.9	80.1	1033 ± 1
	H. Boundary between $Li_2Si_2O_5$ (s. s.) and Tridymite				
...	$Li_2Si_2O_5$–SiO_2	...	17.8	82.2	1028 ± 1
VII	3.0% Na_2O	3.0	15.7	81.3	1001
VIII	10.0% Na_2O	10.0	10.8	79.2	904
...	Quint. point Q_2	11.9	9.5	78.6	867 ± 3
	K. Boundary between $Li_2Si_2O_5$ (s. s.) and Quartz				
...	Quint. point Q_2	11.9	9.5	78.6	867 ± 3
IX	15.0% Na_2O	15.0	7.8	77.2	801
X	20.0% Na_2O	20.0	5.3	74.7	657
...	Ternary eutectic E_2	20.5	5.1	74.4	637 ± 3
	L. Boundary for Inversion of Quartz to Tridymite				
...	Na_2SiO_3–SiO_2	24.5	...	75.5	867 ± 3
XI	22.0% Na_2O	22.0	1.8	76.2	867
X	20.0% Na_2O	20.0	3.1	76.9	867
IX	15.0% Na_2O	15.0	7.0	78.0	867
...	Quint. point Q_2	11.9	9.5	78.6	867

[a] (s. s.) = solid solutions. [b] Formula in parentheses signifies a theoretical compound.

TABLE III

INVARIANT POINTS FOR THE PRESSURE OF ONE ATMOSPHERE IN THE SYSTEM Na_2SiO_3–Li_2SiO_3–SiO_2

Phases	Type	Na_2O	Li_2O	SiO_2	t, °C.
Na_2SiO_3	Melting	50.79	...	49.21	1089 ± 1
$Na_2Si_2O_5$	Melting	34.04	...	65.96	874 ± 3
Li_2SiO_3	Melting	...	33.22	66.78	1201 ± 1
$Li_2Si_2O_5$	Peritectic	...	19.9	80.1	1033 ± 1
	Liquidus	...	19.92	80.08	1034 ± 1
$NaLiSiO_3$ and Li_2SiO_3	Peritectic	30.82	13.05	56.13	847 ± 1
$(Na_2,NaLi)SiO_3$	Minimum	31.25	12.79	55.96	845 ± 1
Na_2SiO_3 and $Na_2Si_2O_5$	Eutectic (binary)	37.9	...	62.1	837 ± 1
$Na_2Si_2O_5$ and quartz	Eutectic (binary)	25.8	...	74.2	789 ± 1
$Li_2Si_2O_5$ and tridymite	Eutectic (binary)	...	17.8	82.2	1028 ± 1
$Na_2Si_2O_5$ and Li_2SiO_3	Eutectic (binary)	27.5	6.4	66.1	709 ± 3
$(Na_2,NaLi)SiO_3$, Li_2SiO_3, and $Na_2Si_2O_5$	Eutectic (ternary) E_1	29.9	6.2	63.9	697 ± 3
$Na_2Si_2O_5$, $Li_2Si_2O_5$, and quartz	Eutectic (ternary) E_2	20.5	5.1	74.4	637 ± 3
$Na_2Si_2O_5$, $Li_2Si_2O_5$, and Li_2SiO_3	Peritectic limit, Q_1	20.5	5.2	74.3	641 ± 3
$Li_2Si_2O_5$, quartz, and tridymite	Inversion point, Q_2	11.9	9.5	78.6	867 ± 3
Quartz and tridymite	Inversion	...	...	100.0	867 ± 3
$Na_2Si_2O_5$ I and $Na_2Si_2O_5$ II	Inversion	34.04	...	69.56	707 ± 3
$Na_2Si_2O_5$ I and $Na_2Si_2O_5$ II in solid solutions	Inversion	...	...	...	699 ± 3
$Na_2Si_2O_5$ II and $Na_2Si_2O_5$ III	Inversion	34.04	...	65.96	678 ± 3
$Na_2Si_2O_5$ II and $Na_2Si_2O_5$ III in solid solutions	Inversion	...	...	...	688 ± 3
$Li_2Si_2O_5$ II and $Li_2Si_2O_5$ III	Inversion	...	19.92	80.08	936 ± 3
$Li_2Si_2O_5$ II and $Li_2Si_2O_5$ III in solid solutions	Inversion	...	...	...	930 ± 3

in sodium disilicate is approximately 5 ± 3% lithium metasilicate, as indicated in the diagram; the 678° transition in sodium disilicate is raised to 688°, while the 707° transition is lowered to 699°, as measured by thermal analysis on preparations 31 and 32 (see Table I). The binary eutectic is at 709 ± 3°, 19.20% lithium metasilicate in the binary system (6.38% lithium oxide, 27.50% sodium oxide, 66.12% silicon dioxide in ternary compositions).

2. The Section, $Na_2Si_2O_5$–$Li_2Si_2O_5$.—The phase relations along this section are only partly binary at the liquidus. Lithium disilicate melts incongruently at 1033 ± 1°, the primary phase at the liquidus, 1034 ± 1°, being lithium metasilicate. Additions of sodium disilicate to lithium disilicate lower the peritectic temperature more rapidly than the liquidus, as shown in Fig. 9, so that lithium metasilicate continues to be the primary phase down to the boundary with sodium disilicate, 693°. Beyond this boundary the liquidus relations are binary, sodium disilicate being the primary phase, but the sub-liquidus relations remain ternary to 641 ± 3°, at which temperature the last of the lith-

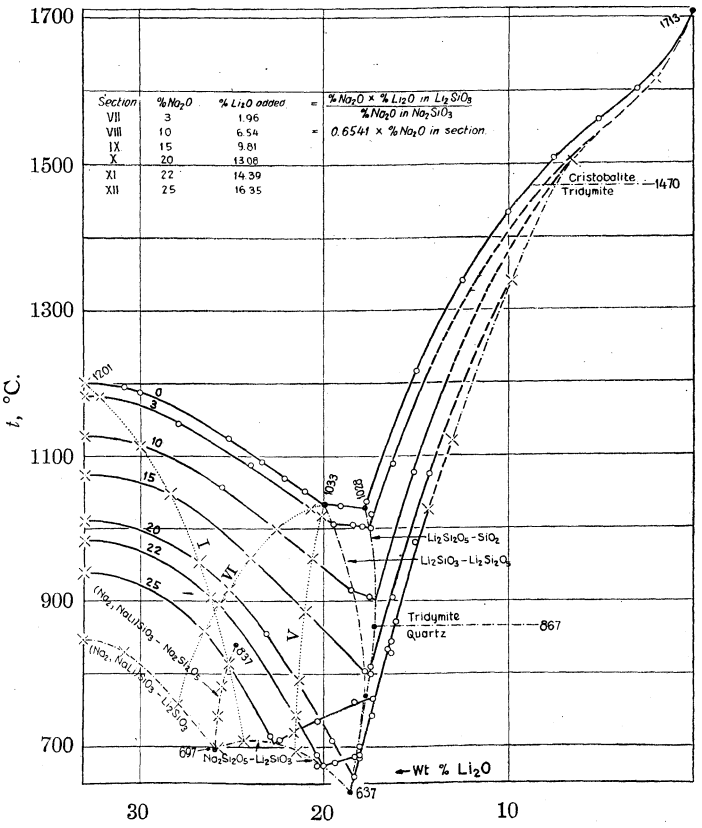

Fig. 7.—Temperature–composition projection of part of the system upon the t–x plane of the system, Li_2SiO_3–SiO_2. Open dots are experimental points. Crosses give intersections of the sections VII to XIII with sections I, V and VI. Dot and dash curves represent phase boundaries, and black circles, intersections of phase boundaries.

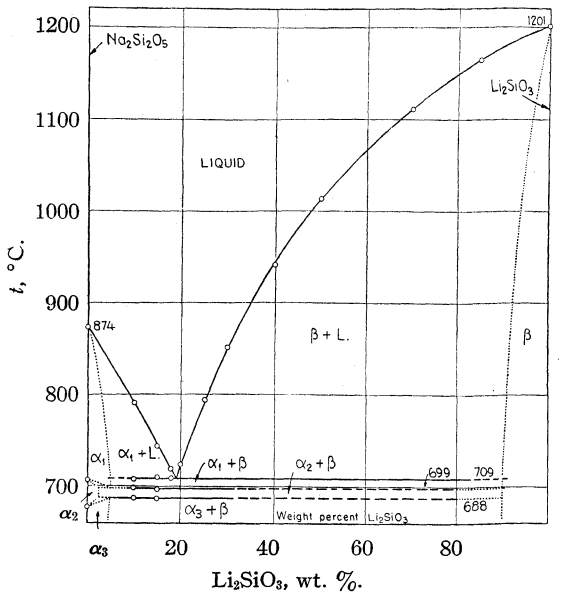

Fig. 8.—The binary system, $Na_2Si_2O_5$–Li_2SiO_3. Solid solution relations, as estimated, are indicated by dotted lines.

ium metasilicate crystals, and liquid, disappear.

The solid solution relations for sodium disilicate and lithium disilicate are indicated in Fig. 9 by dotted lines, the extent in either constituent being estimated to be 5 ± 3% of the other, as based on measurements of the transition temperatures. As already mentioned in discussing the binary system, $Na_2Si_2O_5$–Li_2SiO_3, additions of lithium silicates to sodium disilicate lower the 707° inversion to 699°, and raise the 678° inversion to 688°. On the other hand, the 936° inversion in lithium disilicate is lowered by additions of sodium disilicate to 930°.

The Quartz–Tridymite Inversion.—The temperature of this sluggish, but reversible, transformation is given by Fenner as 870 ± 10°, from measurements made in the presence of sodium tungstate, Na_2WO_4, as flux.[10] Many other substances, such as phosphorus pentoxide, lithium carbonate, potassium carbonate, sodium carbonate, and tungsten trioxide, have been suggested as fluxing agents for accelerating the inversions in silica. Among these, only lithium carbonate holds, *a priori*, any promise of being a more efficient "catalyst" than the sodium tungstate used by Fenner. Van Nieuwenburg[11] reports the conversion of quartz to tridymite in the presence of 1% of lithium carbonate, but he apparently has made no effort to measure the equilibrium temperature closer than about ±30°. Since carbon dioxide is displaced rapidly from such mixtures, the action depends on the speed of reaction between the quartz and the small quantity of crystalline lithium disilicate formed. Fluxing action becomes important only above 1028° (see Fig. 4). For this reason, additions of lithium carbonate to quartz are actually less efficient than those of sodium tungstate in promoting the inversion to tridymite (unpublished experiments by the writer). However, since lithium ions, presumably because of their small dimensions, tend to act as efficient devitrifying agents, it is reasonable to suppose that the inversion would be accelerated by lithium-bearing melts, fluid below the inversion temperature. Compositions in the present system, in the silica field, with liquidus temperatures above 900° fulfil this requirement, and it was

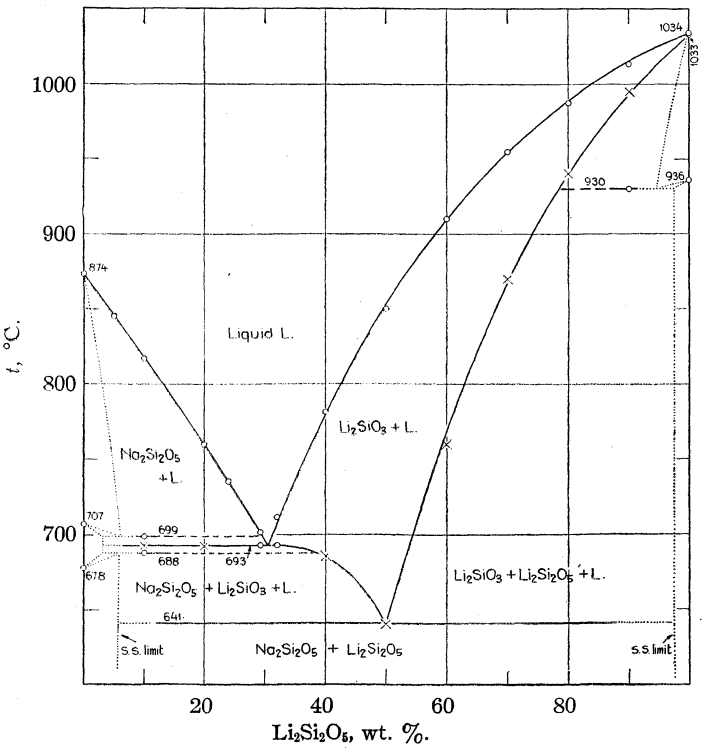

Fig. 9.—The ternary section, $Na_2Si_2O_5$–$Li_2Si_2O_5$. Binary at the liquidus of $Na_2Si_2O_5$, and below 641°. Estimated solid solution relations are indicated by dotted lines.

(10) C. N. Fenner, *Am. J. Sci.* **36**, 331 (1913).

(11) C. J. van Nieuwenburg, *Rec. trav. chim. de Pays-Bas*, **48**, 402 (1929); summary.

found that the most suitable were those whose liquidus lies in the range between 900 and 1000°. The melts of compositions still richer in silicon dioxide tend to be too viscous to act efficiently as fluxes. In the region mentioned (see Fig. 6) quartz is converted into tridymite almost completely (only the larger grains remaining undissolved, but rounded) in twenty-four hours at 869°, and in forty-eight hours at 868°. In the reverse direction, tridymite is converted into sharply faceted crystallites of quartz in twenty-four hours at 866°, and in less than twenty-four hours at 865°. Similar conversions were obtained with all the following compositions: nos. 131, 132, 141, 142, 151, 152. It is concluded that the inversion temperature at one atmosphere pressure is 867 ± 3°, as measured by thermoelements calibrated at the sodium chloride (800.4°) and gold (1062.6°) points. This confirms Fenner's temperature of 870 ± 10°. The temperature 867° is used in presenting the experimental results of this paper.

The liquidus fields of the various primary crystalline phases are smooth sheets pointing down to two ternary eutectics E_1 and E_2 (Table III).

Eutectic E_1 represents the junction of the boundaries between the fields of Li_2SiO_3, $Na_2Si_2O_5$ and $(Na_2,NaLi)SiO_3$, at 697 ± 3°. Of these boundaries, the one between Li_2SiO_3 and $(Na_2,NaLi)SiO_3$ has some theoretical interest. Within the triangle, Na_2SiO_3–$Na_2Si_2O_5$–$NaLiSiO_3$, this boundary is a peritectic (reaction) curve and represents the lowering of the incongruent melting point of sodium lithium (1,1) metasilicate (847° in the pure compound) with the changing compositions of the melts in equilibrium with the crystals. There is no eutectic, but only a minimum on the liquidus of the solid solutions $(Na_2,NaLi)SiO_3$ in the binary system, Na_2SiO_3–Li_2SiO_3 (see also Fig. 2 of ref. 3). As the boundary curve crosses the join, $Na_2Si_2O_5$–$NaLiSiO_3$, this minimum coincides with the curve, which then takes on the character of a eutectoid trough, within the larger triangle, Na_2SiO_3–$Na_2Si_2O_5$–Li_2SiO_3, and finally ends at the ternary eutectic.

The boundary between sodium disilicate and lithium metasilicate, beginning at the ternary eutectic E_1, 697°, rises to the temperature of the binary eutectic between these two compounds, 709 ± 3°, and then descends to the quintuple point Q_1, 641 ± 3°, which is the lowest temperature on the peritectic curve for the incongruent melting relations between lithium disilicate and lithium metasilicate. The ternary eutectic E_2, at 637 ± 3°, practically coincides with the quintuple point Q_1; similarly, the two boundary curves, one between lithium disilicate and lithium metasilicate, the other between lithium disilicate and quartz, lie very close to each other for a considerable portion of their lengths. However, they cannot coincide, since the ternary eutectic E_2 is located within the triangle, $Na_2Si_2O_5$–$Li_2Si_2O_5$–SiO_2, so that the eutectic relations demand that lithium disilicate, and not lithium metasilicate, be one of the eutectic constituents. This will be made clear also by a study of the crystallization relations in Figs. 6 and 9.[11a]

Refractive Indices of the Glasses

Each preparation studied in the course of this work was obtained in the form of a homogeneous glass. A measurement was made of the refractive index of the glass of each composition represented by a black dot in Fig. 1. These measurements were made on crushed, quenched glasses only, by the immersion method, and are estimated to be accurate to ±0.003. The measured values are recorded in Table I, and values along several of the ternary sections in the system are plotted in Fig. 10. This figure also includes published values for Li_2O–SiO_2 glasses,[9] and an interpolated curve for annealed Na_2O–SiO_2 glasses.[12,13]

Cocrystallization of Sodium and Lithium Compounds in Solid Solutions.—Mutual replacement of sodium and lithium plays a sufficiently important part in the crystalline phases of this system (see Figs. 2, 8, 9) to make it desirable to inquire into the general problem of solid solution formation between other sodium and lithium compounds, particularly since it appears to be held by some writers that no such solid solutions have been established[14] for these and other pairs of compounds with cations of the helium and neon-like structures. This view is based on a consideration of the ionic radii, and the differences between the structures of the cations.

(11a) The principles involved in this and the immediately preceding paragraph are discussed in standard books on heterogeneous equilibria, *e. g.*, Rudolf Vogel, "Die heterogenen Gleichgewichte," Akademische Verlagsgesellschaft m. b. H., Leipizig, 1937, pp. 410 *et seq.*

(12) C. A. Faick and A. N. Finn, *Bur. Standards J. Research*, **6**, 993 (1931).

(13) G. W. Morey and H. E. Merwin, *J. Optical Soc. Am.*, **22**, 632 (1932).

(14) See H. G. Grimm and H. Wolff in "Handb. der Physik," **24**, part 2, Verlag von Julius Springer, Berlin, 1933, p. 1097, Table 78.

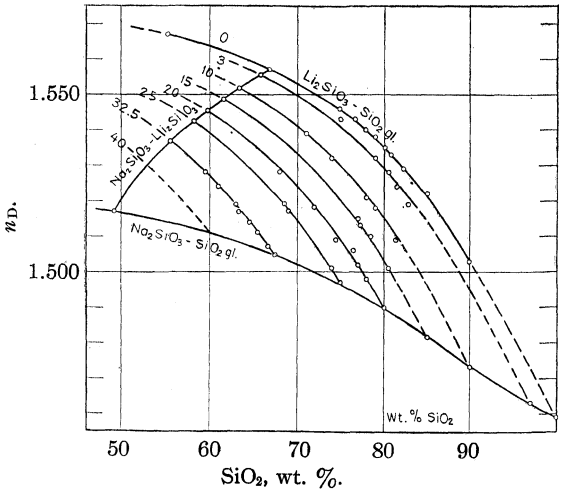

Fig. 10.—Refractive indices of quenched glasses in the system, Na_2SiO_3–Li_2SiO_3–SiO_2. Numbers identifying the curves denote percentage content of Na_2O. The curve for Na_2SiO_3–SiO_2 interpolated from data of Faick and Finn, and of Morey and Merwin, on annealed glasses.

Sodium and lithium compounds probably present the only exception to the rule, and, for that reason, a discussion of the known experimental data is desirable at this point.

The existence of solid solutions in systems of sodium and lithium compounds having the same anion is quite general. The following systems have been studied: LiCl–NaCl,[15] LiBr–NaBr,[16] Li_3AlF_6–Na_3AlF_6,[17] $LiNO_3$–$NaNO_3$,[18] Li_2SO_4–Na_2SO_4,[19] $LiBO_2$–$NaBO_2$,[20] Li_2CO_3–Na_2CO_3,[21] Li_2MoO_4–Na_2MoO_4,[22] Li_2WO_4–Na_2WO_4.[22] The experimental data are indecisive or insufficient for the nitrates, borates, carbonates, molybdates, and tungstates; in all the other cases, considerable miscibility is found at the liquidus, the chlorides, bromides, and the fluoaluminates forming continuous series with a minimum, while the sulfates present two series with an intermediate compound, analogous in principle to the system Na_2SiO_3–Li_2SiO_3[3] (Fig. 2). On the basis of lattice dimensions, it is probable that the iodides also would present a complete series of solid solutions. In the chlorides unmixing occurs below the critical temperature, 270–300°, 58 mole per cent. lithium chloride, the minimum on the liquidus being 553°, 72 mole per cent. lithium chloride; the fluorides may thus be expected to yield continuous solid solutions with unmixing very near the minimum on the liquidus, or actually above it, that is, two series with eutectoid relations. The carbonates, molybdates and tungstates are especially interesting. The sodium compounds are all three, at least partially, miscible with sodium sulfate; among the corresponding lithium compounds only the carbonate is known to be miscible with lithium sulfate; the tungstate and molybdate have not yet been investigated, and crystal structure information is also lacking. It is highly probable that miscibilities analogous to those in the sodium compounds will be found, and that, consequently, small amounts of solid solution will be found also, by sufficiently sensitive methods, in the corresponding systems of lithium and sodium compounds. The data on these systems, as they stand, are decidedly insufficient to deny the existence of such small amounts of solid solutions as exist between crystalline sodium and lithium disilicates (Fig. 9); on the other hand, it is certain that the miscibility, if it exists, must be very limited.

One further case requires consideration. The minerals jadeite ($NaAlSi_2O_6$) and spodumene ($LiAlSi_2O_6$) are found by crystal structure methods to be isomorphous with diopside ($CaMgSi_2O_6$).[23] The symmetry is that of the monoclinic pyroxenes, of which diopside is the type, but the spodumene structure is somewhat distorted by the substitution LiAl for CaMg, allowing the Si–O chains to pack somewhat closer together. It is to be expected, therefore, that spodumene will be only partially miscible with the other pyroxenes.

Summary

The phase equilibrium relations in the system, Na_2SiO_3–Li_2SiO_3–SiO_2 are described in this paper. The work was carried out by the method of quenching supplemented by thermal analysis.

There is one ternary compound, $NaLiSiO_3$, which is an end-member of the solid solution series $(Na_2,NaLi)SiO_3$. It melts incongruently at 847°. At the liquidus in the system, the pri-

(15) S. Zemczuzny and F. Rambach, *Z. anorg. Chem.*, **65**, 403 (1910); W. Schaeffer, *Neues Jahrb. Mineral. Geol.*, Beilage Bd., **43**, 145 (1920).

(16) Kellner, *Z. anorg. Chem.*, **99**, 137 (1917).

(17) P. Drossbach, *Z. Elektrochem.*, **42**, 65 (1936).

(18) Thermal data by H. R. Carveth, *J. Phys. Chem.*, **2**, 209 (1898); calculations by P. de Cesaris, *Atti accad. Lincei*, **20-I**, 749 (1911).

(19) R. Nacken, *Neues Jahrb. Mineral. Geol.*, Beilage Bd., **24**, 1 (1907).

(20) H. S. van Klooster, *Z. anorg. Chem.*, **69**, 122 (1911).

(21) W. Eitel and W. Skaliks, *Z. anorg. allgem. Chem.*, **183**, 263 (1929).

(22) F. Hoermann, *ibid.*, **177**, 145 (1928).

(23) B. E. Warren and J. Biscoe, *Z. Krist.*, **80**, 391 (1931).

mary phases are $(Na_2,NaLi)SiO_3$ solid solutions, Li_2SiO_3, $Na_2Si_2O_5$ and $Li_2Si_2O_5$, all three of which form solid solutions of limited extent, and the three modifications of silicon dioxide, namely, quartz, tridymite, and cristobalite. The liquidus fields meet at two ternary eutectics: one at 697°, with $(Na_2,NaLi)SiO_3$, Li_2SiO_3 and $Na_2Si_2O_5$, the other at 637°, with $Li_2Si_2O_5$, $Na_2Si_2O_5$ and quartz as the eutectic constituents. $Li_2Si_2O_5$ melts incongruently throughout its region of existence in the system, the reaction temperature descending from 1033° in the binary system, Li_2SiO_3–SiO_2, to 641°, the peritectic end-point in the ternary system, with $Li_2Si_2O_5$, Li_2SiO_3, $Na_2Si_2O_5$ and liquid in coexistence.

The inversion temperature of quartz and tridymite has been redetermined. The temperature of 870 ± 10°, given by Fenner in 1913, is confirmed, the value obtained being 867 ± 3°.

Refractive indices of glasses of various compositions in the system were measured.

A discussion of solid solution relationships of sodium and lithium compounds in general is given, with particular reference to the theoretical aspects of the subject.

Minor revisions of the phase relations in the systems, Na_2SiO_3–SiO_2 and Li_2SiO_3–SiO_2, particularly with respect to the polymorphic behavior of $Na_2Si_2O_5$ and $Li_2Si_2O_5$, are presented.

WASHINGTON, D. C. RECEIVED AUGUST 2, 1939

[CONTRIBUTION FROM THE GEOPHYSICAL LABORATORY, CARNEGIE INSTITUTION OF WASHINGTON]

Pressure–Volume–Temperature Relations in Solutions. III. Some Thermodynamic Properties of Mixtures of Aniline and Nitrobenzene

BY R. E. GIBSON AND O. H. LOEFFLER

A few months ago we noted[1] that the absorption of light by mixtures of aniline and nitrobenzene was strongly influenced by pressure changes. In investigating this effect we thought it desirable to examine thoroughly the volume changes which take place when these two liquids are mixed in different proportions at different pressures and temperatures. Furthermore, we have noticed in the pure liquids[2] that, whereas the internal pressure $(\partial E/\partial V)_T$ varies with temperature at constant volume, another quantity, P_A, computed from the P–V–T data is independent of temperature at constant volume and is expressible as a'/V^n. We have tentatively identified P_A as the attractive internal pressure of the liquid. In this paper we shall give data from which the volumes of aniline–nitrobenzene mixtures may be determined at all concentrations, between 25 and 85° and between 1 and 1000 bars, and we shall examine the behavior of P_A in these solutions.

Experimental Results

The solutions were all made up independently from weighed amounts of samples of aniline and nitrobenzene purified to a degree which already has been described.[2] The specific volumes of these solutions were determined at 25.00° in 55-ml. U-tube pycnometers, and the thermal expansions were measured[3] at 10° intervals from 25 to 85° in a weight dilatometer of 18 ml. capacity made of vitreous silica.

The volumes of the solutions were expressed as functions of the temperature by empirical equations of the form

$$v = v_{55} + a(t - 55) + b(t - 55)^2 + c(t - 55)^3 \quad (1)$$

We already have published for the pure components such equations whose coefficients we may call a_1^0, a_2^0, b_1^0, b_2^0, etc. From them we computed[4] $\Delta_T v_1^0$ and $\Delta_T v_2^0$ at each temperature, using 55° as the base temperature, and thence the quantity $\Delta_T v - (x_1\Delta_T v_1^0 + x_2\Delta_T v_2^0) \equiv \delta_T$. This function measures the departures of the thermal expansions

(1) R. E. Gibson and O. H. Loeffler, *J. Phys. Chem.*, **43**, 207 (1939).

(2) R. E. Gibson and O. H. Loeffler, THIS JOURNAL, **61**, 2515 (1939).

(3) For details of the procedure in these measurements the reader is referred to the second paper of this series (ref. 2).

(4) The symbols used here are as follows. The subscripts 1 and 2 refer to nitrobenzene and aniline in solution, respectively, the superscript 0 implies the pure components, and symbols without subscripts refer to the solutions. The weight and mole fractions are given by x and X, respectively, $R_2 = X_2/X_1$, and v and V mean the specific and molal volumes. For a solution $V = v/(x_1/M_1 + x_2/M_2)$, M being the molecular weight. Φ is the apparent molal volume of a component. Δv and ΔV are the volume changes on mixing per gram and per mole of solution. All volumes are given in milliliters.

The pressure in kilobars is given by P, the temperature by t (centigrade scale) or T (absolute), and the total energy by E. Δ_T and Δ_P denote the finite changes with temperature and pressure, respectively, of the quantities to which they are prefixed. $k = -\Delta_P v/v_P = 0$. $z_1 = 1/(1 + R_2V_2^0/V_1^0)$, $z_2 = (1 - z_1)$ are the volume fractions of the components.

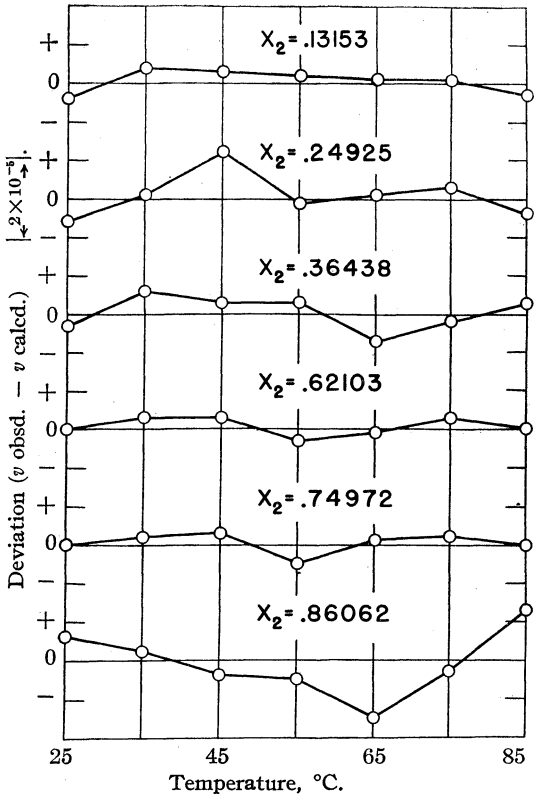

Fig. 1.—Deviations of the values of the specific volumes of aniline–nitrobenzene solutions as calculated from equation (1) from the observed ones at different temperatures.

from the ideal law of mixtures, and it may be represented accurately by the relation

$$\delta_T = l + m(t - 55) \qquad (2)$$

In these solutions $(x_1 \Delta_T v_1^0 + x_2 \Delta_T v_2^0)$ is always numerically greater than $\Delta_T v$. The coefficients l and m were determined by a simplified method of least squares.[5] It will be seen that the coefficients in equation (1) were therefore obtainable from the following relations

$$a = x_1 a_1^0 + x_2 a_2^0 + m; \qquad b = x_1 b_1^0 + x_2 b_2^0$$
$$c = x_1 c_1^0 + x_2 c_2^0 \qquad v_{55} = v_{\text{obsd.}} + l$$

The coefficients a, b, c, and m are given in Table I and the deviation curves in Fig. 1 indicate how well the equations fit the data. It is of interest to note that the coefficients of the second and third powers of the temperature are found directly from the simple law of mixtures.

The compressions of the solutions from 1 to 500 and from 1 to 1000 bars were measured in exactly the same way as those of the pure components[2] and the relative volume changes were expressed as functions of the pressure by the Tait equation

$$k = C \log [(B + P)/(B + P_0)] \qquad (3)$$

where C has the same value as for aniline and nitrobenzene, *viz.*, 0.21591 at all temperatures. The constant B was determined at each temperature from the compressions to 1000 bars. The compressions to 500 bars computed by the appropriate Tait equation always agreed with the observed ones within experimental error. The compressions were measured at 25, 45, 65, and 85°, and the constant B was expressed as a function of the temperature by equations of the type

$$B = B_{25} + \alpha(t - 25) + \beta(t - 25)^2 \qquad (4)$$

which were fitted to the data at 25, 45, and 85°. In Table II we give the values of B_{25}, α and β for the various solutions together with the differences between the observed and calculated values of B at 65° as an illustration of the fit of the empirical equations.

(5) See Ostwald–Luther, "Physikochemischer Messungen," 4th ed., Akademische Verlagsgesellschaft, Leipzig, 1925, p. 39.

TABLE I

COEFFICIENTS IN THE EQUATIONS REPRESENTING THE SPECIFIC VOLUMES OF ANILINE–NITROBENZENE MIXTURES AS FUNCTIONS OF THE TEMPERATURE (EQUATION 1)

The last column gives the value of the principal coefficient in equation (2).

Weight fraction of aniline x_2	Mole fraction of aniline X_2	v_{55}	$10^4 a$	$10^7 b$	$10^9 c$	$10^4 m$
0.0000	0.0000	0.855751_5	7.274_4	6.931_1	1.528_8	
.13153	.16684	$.877160_0$	7.465_5	7.241_1	1.601_1	−0.0193
.24925	.30506	$.895974_4$	7.643_3	7.519_9	1.666_6	− .0303
.36438	.43117	$.914104_4$	7.819_3	7.791_1	1.730_0	− .0382
.49517[a]	.56461	$.934311_1$	8.025_5	8.100_0	1.802_2	− .0413
.62103	.68422	$.953399_0$[b]	8.218_8	8.398_8	1.873_3	− .0501
.74972	.79842	$.972652_2$	8.425_5	8.701_1	1.944_4	− .0483
.86062	.89088	$.988850_3$	8.615_5	8.963_3	2.006_6	− .0358
1.0000	1.0000	1.008746_3	8.874_4	9.292_2	2.083_3	

[a] The thermal expansions of this solution were measured only to 65°, and the compressions only at 25°. [b] Mean of two entirely independent determinations.

TABLE II

COEFFICIENTS IN EQUATION (4) REPRESENTING THE CONSTANT B IN THE TAIT EQUATION AS A FUNCTION OF TEMPERATURE

x_2	B_{25} (kilobars)	$10^3\alpha$	$10^5\beta$	$10^3 B$ (obsd. − calcd.) at 65°
0.0000	1.8652	9.62	1.48	+0.2
.13153	1.8740	9.83	1.72	− .2
.24925	1.8843	9.96	1.86	+2.7
.36438	1.8975	10.08	1.97	+1.2
.62103	1.9320	10.09	1.64	−1.1
.74972	1.9536	10.21	1.62	−3.6
.86062	1.9768	10.48	1.82	+1.6
1.0000	2.0066	10.81	1.99	−0.3

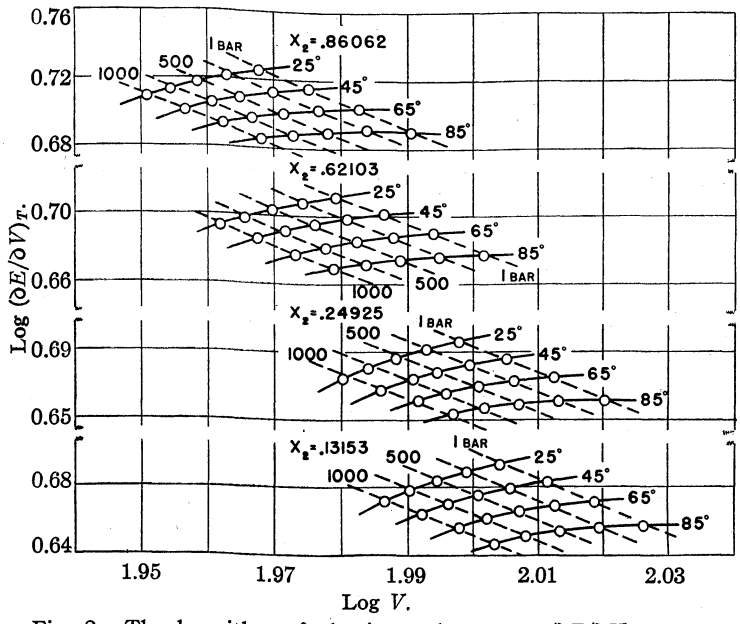

Fig. 2.—The logarithm of the internal pressure $(\partial E/\partial V)_T$ of some aniline–nitrobenzene solutions as a function of the logarithm of the molal volume. Note the different curves for the different temperatures.

The Internal Pressures $(\partial E/\partial V)_T$ and Related Quantities

From equations (1) and (3) the expansion coefficients $(\partial v/\partial T)_P$ and the compressibilities were computed at different pressures and temperatures[6] and hence the coefficients $(\partial P/\partial T)_V$ and $(\partial E/\partial V)_T$ were calculated readily for each solution at 25, 45, 65, and 85°, and at 1, 250, 500, 750, and 1000 bars. The curves of $(\partial E/\partial V)_T$ vs. V, or of $(\partial P/\partial T)_V$ vs. V, for the solutions resembled those for the pure liquids in all major respects[2]; in particular, $(\partial E/\partial V)_T$ decreased with rise of temperature at constant volume. A sample of our results illustrating this temperature effect is given in Fig. 2 where log $(\partial E/\partial V)_T$ is plotted against log V for several solutions.

Applying the method of analysis that we developed for the pure liquids to the results for the solutions,[2] we computed the quantity $(T(\partial P/\partial T)_V + B) = P_A$ which we have interpreted as the attractive internal pressure set up by the intermolecular forces, $(B + P)$ being assumed to be a measure of the repulsive pressure. In Fig. 3 we have plotted log P_A vs. log V for all the solutions including the end members, and in order to facilitate a comparison of Figs. 2 and 3, we have used the same scale in both diagrams. It will be seen that in Fig. 3 the points for the different temperatures all fall on the same straight line for each solution and that the lines for the different solutions all have the same slopes. Over the region we have studied we may, therefore, write

$$P_A = a'/V^{2.737} \qquad (5)$$

2.737 being the constant slope of the lines in Fig. 3. The constants a' were determined from the data and average values are given in Table III. It should be noted that the points at 65 and 85° for nitrobenzene lie on a line which is slightly below that drawn through the points for the lower temperatures. We are not certain that this deviation is a real one and that it does not arise in the equations used for computing the derivatives; but it is significant that the same deviations are found in the solutions rich in nitrobenzene and gradually vanish as the concentration of aniline increases.

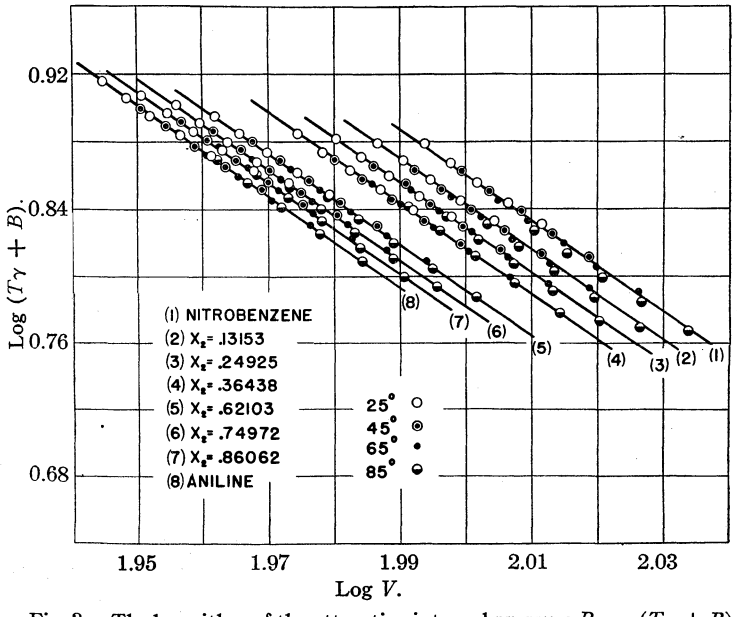

Fig. 3.—The logarithm of the attractive internal pressure $P_A = (T\gamma + B)$ of aniline–nitrobenzene solutions as a function of the logarithm of the molal volume. Note that the points for different temperatures fall on the same line for each solution. The scale in this diagram is the same as in Fig. 2. γ represents the coefficient $(\partial P/\partial T)_V$.

(6) For details of these calculations, see ref. 2.

TABLE III

THE GENERALIZED FRACTION y_1, AND A COMPARISON OF THE VALUES OF a' DETERMINED DIRECTLY FOR EACH SOLUTION (EQUATION 5) AND THE VALUES OF a' COMPUTED FROM EQUATION (9)

x_2	y_1	$10^6a'$ (obsd.)	$10^6a'$ (calcd.)	$\Delta v \times 10^5$ at 25°
0.0000	1.0000	2.163		
.13153	0.90398	2.071	2.079	134
.24925	.81114	2.004	2.010	218
.36438	.71325	1.947	1.950	272
.62103	.46527	1.840	1.841	279
.74972	.32250	1.797	1.796	235
.86062	.18761	1.766	1.764	155
1.0000	.0000	1.730		

The Variation of P_A with Concentration

We shall now attempt to calculate P_A and a' for the solutions from a knowledge of the properties of the pure components. If V is the volume of 1 mole of solution,[4] V^0 the volume of the corresponding amounts of the components (*i. e.*, the ideal molal volume of the solution) and if P_A is the observed attractive pressure in the solution, then P_A^0, the attractive pressure of the solution at volume V^0, is given by

$$P_A^0(V^0)^{2.737} = P_A V^{2.737} = a' \qquad (6)$$

If, furthermore, we suppose the attractive pressures set up between like molecules in the solution to be the same as in the pure liquids, *viz.*, P_{11} for nitrobenzene and P_{22} for aniline, and call the attractive pressure between the unlike molecules P_{12}, we may write

$$P_A^0 = y_1^2P_{11} + y_2^2P_{22} + 2y_1y_2P_{12} \qquad (7)$$

where y_1 and y_2 are concentration functions that indicate the probabilities of significant interactions between the molecules,[7] and are defined as $y_1 = 1/(1 + R_2U_2/U_1)$ and $y_2 = (1 - y_1)$. The parameter U_2/U_1 may be regarded as an empirical constant which is equal to unity when y is the mole fraction and is V_2^0/V_1^0 when y is the volume fraction.

When the mole fractions or the volume fractions were used in equation (7) no results of any special interest were found, and the computed values of P_{12} varied with concentration. We, therefore, assumed[8] that P_{12} was equal to a constant, *viz.*, $(P_{11}P_{22})^{\frac{1}{2}}$, and, using the relation

$$P_A^0 = (y_1P_{11}^{\frac{1}{2}} + y_2P_{22}^{\frac{1}{2}})^2 \qquad (8)$$

we computed U_2/U_1 from our results at 25° and 1 bar and found it to be practically independent of concentration having the average value 0.5263.[9]

Combining equations (5), (6), and (8) we get equation (9)

$$a' = \left\{y_1a_{11}^{\frac{1}{2}}\left(\frac{V^0}{V_1^0}\right)^{1.368} + y_2a_{22}^{\frac{1}{2}}\left(\frac{V^0}{V_2^0}\right)^{1.368}\right\}^2 \qquad (9)$$

which should enable us to calculate a' for any solution in terms of the constants a_{11}, a_{22}, V_1^0, and V_2^0 for the pure liquids, the *ideal* molal volume of the solution and the fraction y_1 which contains the disposable constant U_2/U_1. In Table III we list values of y_1 computed on the assumption that $U_2/U_1 = 0.5304$ (the reason for the choice of this figure, which differs slightly from that given above, will appear under the discussion of the volume change on mixing) together with the values of a' obtained directly from our data for the solutions and values of a' computed from equation (9) when the volumes at 25° and 1 bar were used. The agreement between these two series of figures indicates that equation (9) does give an adequate representation of a' as a function of concentration. Moreover, V^0/V_1^0 changes very little with pressure and temperature, the extreme variation over the range we have studied being less than 0.4%. We may, therefore, conclude that y_1, y_2 and hence U_2/U_1 are independent of pressure and temperature within the limits of accuracy of our results.

The Volume Changes on Mixing

The changes in volume which occur when the components are mixed in different proportions at different pressures and temperatures may be expressed conveniently in terms of the apparent

(7) This treatment, which partly follows that proposed by Scatchard [*Chem. Rev.*, **8**, 321 (1931)], does not limit y_1 and y_2 to the volume fractions based on the volumes of the liquids under ordinary conditions. We also wish to point out that our method of analysis implies that P_A depends chiefly on the mean distance between the molecules and is not greatly influenced by their distribution in the liquid, whereas the repulsive internal pressure depends strongly on the distribution of the molecules in the liquid. This seems plausible because the attractive forces between the molecules vary much less rapidly with distance than do the repulsive forces.

(8) See G. Scatchard, *Trans. Faraday Soc.*, **33**, 162 (1937); S. E. Wood, THIS JOURNAL, **59**, 1511 (1937); J. H. Hildebrand and J. M. Carter, *ibid.*, **54**, 3599 (1932).

(9) In terms of the principle of independent surface or group action [I. Langmuir, *Colloid Symposium Monograph*, **III**, 48 (1925); J. A. V. Butler, D. W. Thomson, and W. H. MacLennan, *J. Chem. Soc.*, 674 (1933)] y_1 and y_2 may be regarded as the volume fractions of the active groups in the nitrobenzene and aniline molecules. An examination of the parachors of benzene, nitrobenzene, and aniline suggests that the molal volume of the NH_2 group is approximately one-half that of the NO_2 group (Landolt-Börnstein, "Tabellen," Erganzungsband II(a), p. 178). Roughly the same result is obtained if one compares the molal volumes of benzene, nitrobenzene, and aniline under pressures where the liquids have the same compressibilities (ref. 1). There is, therefore, some justification for associating y_1 and y_2 with the volume fractions of the NO_2 and NH_2 groups in the solutions.

volumes of one of the components. It will be recalled that if

$$\Delta V = V - (X_1V_1^0 + X_2V_2^0) \text{ then } \Delta V = X_2(\Phi_2 - V_2^0)$$

In the aniline–nitrobenzene system an expansion occurs when the components are mixed, $(\Phi_2 - V_2^0)$ being always positive. Increase of pressure and of temperature both diminish $(\Phi_2 - V_2^0)$, an observation to which special attention is drawn.

A clue to the origin of these volume changes may be obtained from an examination of the effect of temperature on the volume changes on mixing when the volumes of the unmixed components are kept constant. In Fig. 4 we have plotted ΔV against V^0 for various solutions. It will be seen that at constant volume, and presumably constant attractive pressure, ΔV decreases quite rapidly as the temperature rises, and that this decrease is roughly proportional to ΔV itself. Having in mind the interpretation we gave of similar changes in the $(\partial E/\partial V)_T$–$V$ curves, we suggest the following explanation of this decrease of ΔV with rise of temperature at constant V. We assume that the change with temperature in the randomness of the distribution of the molecules in a liquid is proportional to the order already existing in the liquid, and that in a solution of aniline in nitrobenzene the molecular distribution is more random than in the pure liquids at the same temperature (the increase in disorder determining to some extent the volume change on mixing). We should, therefore, expect that a given rise of temperature would have a greater disordering effect on the unmixed liquids than on the solution, and that at high temperatures the change in randomness on mixing should approach zero, and the volume change on mixing should decrease accordingly. The change of $(B + P)$ with temperature at constant volume has been associated[2] with the change in the repulsive pressure due to increase in the randomness of the molecular distribution. Our data show that $(B + P)_V$ increases more rapidly with temperature for the pure liquids than for the solutions.

In a recent paper[1] we attempted to express Δv in terms of the net internal (or repulsive) pressures B' of the solutions and B_1 and B_2 of the pure components by the relation

$$\Delta v/C(x_1v_1^0 + x_2v_2^0) - (z_1 \log B_1 + z_2 \log B_2) = \log B' \quad (10)$$

It was assumed that, on forming the solution at atmospheric pressure, the pure components first expanded or contracted until their repulsive pressures came to the common value B' and then mixed without further change. We indicated also that the values of $\log B'$ computed from the observed values of Δv by means of equation (10) were *smaller* than the observed values of $\log B'$. As equation (10) represents the volume change on mixing on the assumption that mixing introduces no change in the distribution of the molecules, it is suggested that the discrepancy between the observed and calculated values of B' is due to an increase in randomness on mixing. In other words, on the formation of the actual solution a given volume increase (Δv) results in a smaller decrease in $\log B'$ than would be expected if no increase in randomness accompanied the mixing of the components. It is of interest to note that the values of B' computed by equation (10) approach the observed ones more closely as the temperature is raised. These effects are small but they contribute qualitatively to the evidence correlating an increase in the randomness of the molecular distribution with an increase in the

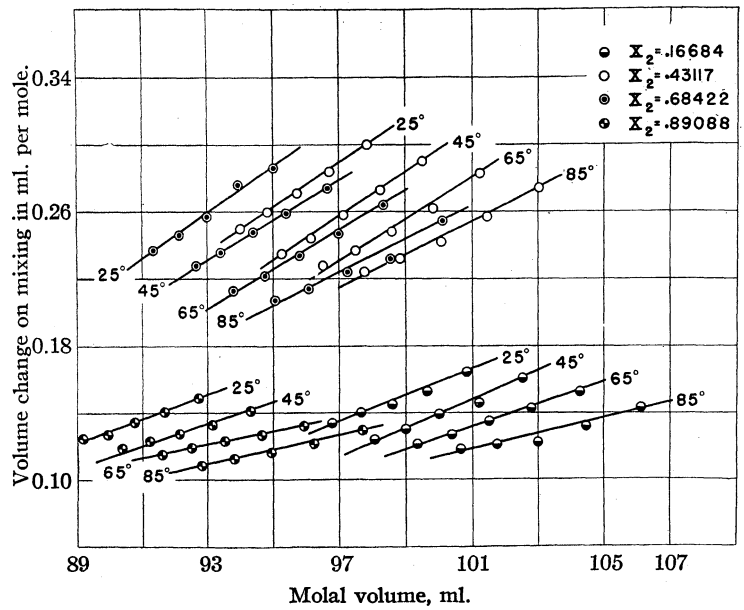

Fig. 4.—The volume changes on mixing per mole of solution in four solutions of aniline in nitrobenzene as functions of the volume at different temperatures.

quantity B' or $(B + P)$ which we have tentatively identified as the repulsive internal pressure of the liquid or solution.

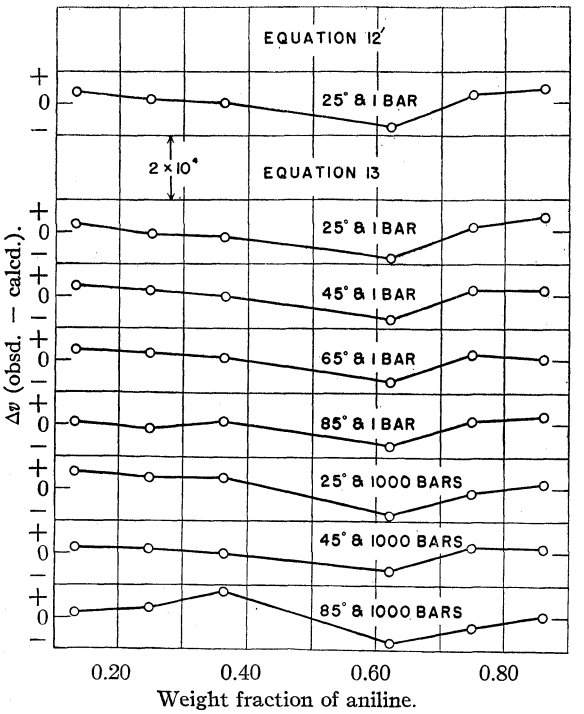

Fig. 5.—Deviations of the values of the volume change on mixing in aniline–nitrobenzene solutions as computed from equation (12′) or (13) from the observed values at different pressures, temperatures and concentrations.

In order to represent the volume changes on mixing as functions of the composition of the solutions, we used equations of the type[10]

$$\Delta V/(X_1V_1^0 + X_2V_2^0) = pz_1z_2(1 + qz_2^3) \quad (11)$$

where z_1 and z_2 are the volume fractions, to represent our data. At 25° with $p = 0.01230$ and $q = 0.341$, equation (11) reproduced the results quite well, the average deviation and the largest deviation corresponding to errors of 1.6 and 3 × 10^{-5}, respectively, in the specific volume. Equally satisfactory fits were obtained at the other temperatures and pressures. The term qz_2^3 in equation (11) shows that the curve of $\Delta V/(X_1V_1^0 + X_2V_2^0)$ vs. z_1 is unsymmetrical, the maximum lying between $z_1 = 0.5$ and $z_1 = 0$. As this asymmetry is found in the effect of concentration on the absorption of light and on the attractive internal pressures of mixtures of nitrobenzene and aniline, it is of interest to examine equations which express the dependence of ΔV on concentration in terms of the general fractions y_1 and y_2. It should also be remarked that the usefulness of equation (11) is diminished somewhat by the fact that z_1, z_2, p, and q all vary with temperature and pressure.

A trial of equation (12) (or its equivalent form equation 12′) which is analogous to equation (11) showed that it gave a good but not altogether satisfactory representation of our data.[11]

$$\Delta V/(X_1U_1 + X_2U_2) = Ky_1y_2 \quad (12)$$

$$(\Phi_2 - V_2^0) = ky_1 = k/(1 + R_2U_2/U_1) \quad (12')$$

The constants k and U_2/U_1 in equation (12′) determined from the data by the method of least squares[12] are given in Table IV and the differences between the observed and calculated values of Δv at 25° and 1 bar are plotted in Fig. 5. The largest deviation corresponds to an error of -7×10^{-5} in Δv. The deviation curves for the results at the other temperatures and pressures are the same as the curve we have given in Fig. 5 within an error of 2×10^{-5} in Δv. In order to give an idea of the numerical value of Δv we have recorded Δv at 25° and 1 bar in the last column of Table III. The parameter U_2/U_1 as obtained from equation (12) varies greatly with temperature and is considerably larger than we found from the attractive pressure equation. In view of our discussion of the effect of change in molecular distribution on the volume change on mixing, of the complicated nature of this quantity, and of the fact that the compressibility of the solution is an important factor in determining the volume

TABLE IV

THE CONSTANTS k AND U_2/U_1 AS OBTAINED BY THE METHOD OF LEAST SQUARES FROM EQUATION (12′) REPRESENTING THE VOLUME CHANGE ON MIXING AS A FUNCTION OF THE GENERALIZED VOLUME FRACTIONS AT DIFFERENT PRESSURES AND TEMPERATURES

t, °C.	P (bars)	k	U_2/U_1	Average Δv (obsd. − calcd.) × 10^5
25	1	1.0428	0.6600	3.3
45	1	1.0297	.6922	2.8
65	1	1.0077	.7164	2.2
85	1	0.9826	.7299	2.4
25	1000	.8694	.6625	3.0
45	1000	.8023	.6265	2.4
65	1000	.7854	.6535	3.8
85	1000	.7649	.6746	3.0

(10) G. Scatchard, S. E. Wood and J. M. Mochel, *J. Phys. Chem.*, **43**, 122 (1939).

(11) From equation (12) it may be seen that $(V_2 - V_2^0) = ky_1^2$, V_2 being the partial molal volume. The analogy with Hildebrand's equation for regular solutions is evident [THIS JOURNAL, **51**, 78 (1929)]. Furthermore, as $y_1 = 1/(1 + R_2U_2/U_1)$, this is the same type of equation that was proposed by van Laar [*Z. physik. Chem.*, **72**, 723 (1910)].

(12) We are indebted to Dr. W. Edwards Deming of the U. S. Department of Agriculture for valuable suggestions concerning these calculations.

change on mixing,[13] it seemed legitimate to regard equation (12) as too simple to be of much physical significance and to examine the behavior of U_2/U_1 in some empirical equations.

The parameters k_1 and U_2/U_1 in equation (13) were evaluated by a least squares method at 25, 45, 65, and 85° both at 1 and 1000 bars.

$$(\Phi_2 - V_2^0) = Vk_1y_1/\log (B' + P) \qquad (13)$$

The results are given in the third and fourth columns of Table V. Although U_2/U_1 obtained in this way is very sensitive to small fluctuations in the specific volume–concentration data, the values we obtained were practically constant over the whole temperature range at 1 bar, and varied no more at 1000 bars than might be expected from the greater uncertainty of the experimental data at the higher pressures. The average value of U_2/U_1 at 1 bar, which was found to be 0.5304, was assumed to be a constant characteristic of the liquid mixture and independent of the pressure, temperature, and concentration. From it we computed the values of y_1 given in Table III. In the fifth column of Table V we give the average values of k_1 consistent with $U_2/U_1 = 0.5304$; and in Fig. 5 we have plotted the differences between the observed values of Δv and those computed from equation (13) with these adjusted values of y_1 and k_1. The deviation curves for the different pressures and temperatures being very much alike, we have given only a few examples. These curves indicate that equation (13) does not represent the volume change on mixing as well as might be desired; indeed, the deviations are only slightly smaller than those given by equation (12′). There is always a deviation of approximately -7×10^{-5} in Δv in the 62% solution. Experimental checks have failed to show that there is any reason to suspect the original data and, as this point occurs near the middle of the concentration range, its importance cannot be minimized. However, the simplicity of equation (13) together with the fact that it yields a value of U_2/U_1 which not only is independent of temperature, pressure, and concentration but also is the same as appears in the equations relating the attractive internal pressures and the optical absorption coefficients[14] to the compositions of the solutions, gives the equation a significance which justifies further study of its applicability.

TABLE V

THE CONSTANTS k_1 AND U_2/U_1 IN EQUATION (13) AS OBTAINED BY THE METHOD OF LEAST SQUARES AT DIFFERENT TEMPERATURES AND PRESSURES. IN THE LAST COLUMN ARE GIVEN AVERAGE VALUES OF k_1 CONSISTENT WITH A VALUE OF U_2/U_1 INDEPENDENT OF PRESSURE AND TEMPERATURE

t, °C.	P (bars)	U_2/U_1	$k_1 \times 10^3$	$k_1 \times 10^3$ ($U_2/U_1 = 0.5304$)
25	1	0.5207	2.744	2.780
45	1	.5346	2.201	2.199
65	1	.5405	1.668	1.657
85	1	.5258	1.152	1.162
25	1000	.5609	4.033	3.940
45	1000	.5308	3.444	3.454
65	1000	.5530	3.095	3.055
85	1000	.5755	2.766	2.669

The quantity $-(\Delta_P\Phi_2 - \Delta_P V_2^0)$ which is a measure of the departures of the compressions (from 1 to 1000 bars) from the ideal law of mixtures is always positive in nitrobenzene–aniline solutions. This is an example of a case where the solutions are more compressible than the pure components and therein it differs from aniline–benzene or aniline–chlorobenzene mixtures. As far as we can tell from our data $-(\Delta_P\Phi_2 - \Delta_P V_2^0)$ for each solution is independent of the temperature; and although $-(\Delta_P\Phi_2 - \Delta_P V_2^0)$ may be calculated satisfactorily from a simple modification of equation (13), we may say that for interpolation purposes the equation $-(\Delta_P\Phi_2 - \Delta_P V_2^0) = 0.1899\ x_1$ gives a simple and adequate expression of the compression data at all temperatures.

The fact that when aniline and nitrobenzene are mixed only a small amount of heat is absorbed and an expansion occurs, together with the fact that this expansion diminishes as the temperature rises, is contributory evidence against compound formation in the ordinary sense of the term and the volume relations are such that on any simple hypothesis we must consider that if a compound were formed in these solutions, it would be destroyed by rise of pressure.

Summary

We have measured the specific volumes at 25°, the thermal expansions at 10° intervals between 25 and 85°, and the compressions to various pressures up to 1000 bars at 25, 45, 65, and 85° of six solutions of aniline in nitrobenzene covering the whole range of concentration. These data have been represented by suitable equations from which the volumes, the thermal expansibilities

(13) R. E. Gibson, THIS JOURNAL, 59, 1521 (1937).

(14) Unpublished results obtained in this Laboratory.

and the compressibilities may be computed at any pressure and temperature within the range of our observations.

Our data enable us to compute $(\partial P/\partial T)_V$, $(\partial E/\partial V)_T$ and the volume changes on mixing for the various solutions, and to examine the variation of these quantities when the temperature is changed at constant volume. In the light of the results of this analysis, we suggest a correlation between the effect of temperature and of mixing on the molecular distribution in the liquids on the one hand and the internal pressures and the volume changes on mixing on the other.

The attractive pressures of the solutions were calculated in the same way as those of the pure liquids and were reproduced by the formula $P_A = a'/V^{2.737}$. An equation was developed whereby the constants a' for the solutions were represented as a function of the concentration in terms of constants for the pure components and the generalized volume fractions y_1 and y_2 which contain an empirical constant, U_2/U_1.

Although the volume changes on mixing were well represented as functions of the ordinary volume fractions of the components by equations of a conventional type, we also examined several equations expressing this quantity in terms of significant properties of the solutions and the fractions y_1 and y_2. These equations reproduced the volume changes on mixing fairly well. One of them had the form of the equations developed for regular solutions and another gave a value of the empirical constant, U_2/U_1, which was independent of temperature and pressure and was approximately equal to the corresponding constant obtained from the attractive pressure–composition equation.

WASHINGTON, D. C. RECEIVED JULY 19, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF PHYSICAL CHEMISTRY, HARVARD MEDICAL SCHOOL]

Serum Albumin. I. The Preparation and Properties of Crystalline Horse Serum Albumin of Constant Solubility

BY T. L. McMEEKIN

Since the crystallization of serum albumin by Gürber in 1894,[1] many investigators have doubted its homogeneity. Fractional crystallization from salt solutions has yielded products that vary widely in solubility,[2] chemical composition,[3,4] and dielectric properties.[5] Despite this evidence of inhomogeneity, the recognition and separation of constituent proteins has proved difficult. Perhaps the most important advance in its purification was the separation of carbohydrate-containing globulins[6] from the albumin fraction and the recognition that serum albumin does not contain carbohydrate.[3,4]

Serum albumin has been reported to be homogeneous in respect to size[7] and electrophoretic mobility.[8] Ultracentrifugal studies have shown it to have a molecular weight of 67,500,[7] independent of *p*H between 4 and 9. In solutions more acid than *p*H 4 it was decomposed into smaller molecules, the process being found to be reversible.

This paper first describes our present procedure for the separation of the serum proteins and the preparation of crystalline carbohydrate-free serum albumin homogeneous with respect to electrophoresis at neutral reactions.[9] This highly purified serum albumin can be separated further into two crystalline fractions differing in chemical composition and electrophoretic mobility in acid but not in neutral solution.[9] The separation of serum albumin into two fractions is based on the discovery made in this Laboratory by J. D. Ferry,[10] that a salt-free concentrated solution of serum albumin crystallizes when brought to *p*H 4.0 with sulfuric acid.[11] The solubility of the

(1) Gürber, *Würzburger physiol. med. Ges.*, **113** (1894).
(2) Sörensen, *Compt. rend. trav. Lab. Carlsberg*, **18**, No. 5, 1 (1930).
(3) Sörensen and Haugaard, *ibid.*, **19**, No. 12 (1933).
(4) Hewitt, *Biochem. J.*, **30**, 2229 (1936).
(5) Ferry and Oncley, THIS JOURNAL, **60**, 1123 (1938).
(6) Hewitt, *Biochem. J.*, **32**, 26 (1938).
(7) Svedberg and Sjogren, THIS JOURNAL, **50**, 3318 (1928); **52**, 2855 (1930).
(8) Tiselius, *Biochem. J.*, **31**, 1464 (1937).
(9) I am indebted to Dr. John A. Luetscher, Jr., for these measurements. See also the second paper in this series, THIS JOURNAL, **61**, 2888 (1939).
(10) Reported by Ferry to the Division of Biological Chemistry at the 96th meeting of the American Chemical Society, Milwaukee, Wis., September 7, 1938.
(11) Piettre, *Compt. rend. Acad. Sci.*, **188**, 463 (1929), reports that among other proteins serum albumin crystallizes from aqueous solution following removal of globulin with acetone, and of acetone by evaporation over sulfuric acid *in vacuo*.

albumin sulfate, and of the regenerated protein, has been found to be essentially independent of the amount of saturating body and certain of its properties have been investigated and are reported.

Fractionation of Serum Proteins.—The proteins of serum were divided into three fractions depending on solubility in salt as a preliminary to further purification. These were: (a) the fraction insoluble in 1.6 *M* ammonium sulfate (0.4 saturated); (b) that soluble in 1.6 *M* but insoluble in 2.1 *M* ammonium sulfate; and (c) that soluble in 2.1 *M* ammonium sulfate but insoluble in 2.8 *M* ammonium sulfate. These fractions were stored in closed containers at 4°.

Fresh serum[12] was diluted with an equal volume of water and the calculated amount of ammonium sulfate (either in the form of a solid or solution) to make the solution 1.6 molar was placed in a cellophane membrane and rotated until equilibrium with the salt had been reached on both sides of the membrane (Fig. 1), usually within forty-eight hours. The precipitate was allowed to settle and the supernatant solution siphoned off. Protein precipitated in this manner was granular, resulting in better separations than when precipitation was more rapid. Because of the granular nature of the precipitates, filtration was carried out on a Büchner funnel, using Schleicher and Schull No. 575 hardened filter paper. The resulting filter cake was washed free from mother liquor.

The filtrate was brought to 2.1 molar ammonium sulfate by adding the calculated quantity of solid ammonium sulfate in a membrane and rotating until equilibrium was reached. After removing the precipitate in the usual manner the filtrate was brought to 2.8 *M* ammonium sulfate by equilibrating with the calculated amount of solid ammonium sulfate in a cellophane membrane. The protein fraction that was soluble in 2.1 molar and insoluble in 2.8 molar ammonium sulfate contains serum albumin as well as many other substances. The yield from each liter of serum was approximately 20 g. of protein soluble in 2.1 *M* and insoluble in 2.8 *M* ammonium sulfate. No acid was added during this separation.

The fraction precipitated per liter of serum between 2.1 and 2.8 molar ammonium sulfate, was dissolved in 80 cc. of water and diluted to 800 cc. with 1.6 molar ammonium sulfate and the *p*H adjusted to 6.4. The solution was then equilibrated at 2.1 molar ammonium sulfate in a membrane. The globulin precipitate was removed and the filtrate was brought to 2.4 molar ammonium sulfate again by equilibrating in a membrane. The precipitate formed was largely crystalline and was removed by filtration. It contained about 10 g. of protein and was the starting material for further purification of albumin.

The precipitate insoluble in 2.4 *M* ammonium sulfate was dissolved in the smallest possible quantity of water, forming practically a sirup and the *p*H adjusted to 5.5. A saturated ammonium sulfate solution was added from a pipet with stirring until near the point of precipitation. On allowing the clear solution to stand overnight turbidity developed and well-shaped, large, long, hexagonal crystals of serum albumin separated.

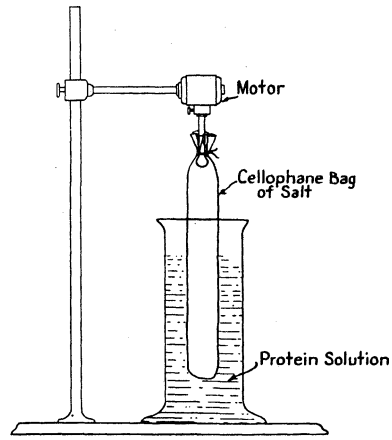

Fig. 1.—Diagram of the apparatus used for adding reagents to protein solutions.

The crystals were removed by centrifugation. Small amounts of globulin did not settle on centrifugation and were thus separated from the crystals. After centrifugation, the crystals were filtered on a Büchner funnel and washed with 2.0 *M* ammonium sulfate. Two further recrystallizations in this manner were usually found adequate for the removal of carbohydrate. Further quantities of carbohydrate-free crystalline albumin were prepared from the supernatant liquors by diluting with 1.6 *M* ammonium sulfate so that the protein concentration was about 1–2% and then gradually adding ammonium sulfate, 0.1 or 0.2 mole greater in concentration than the protein solution, through a rotating membrane.

The crystalline fractions were collected and recrystallized from concentrated solution. The yield of carbohydrate-free albumin as tested for by the Orcin method following the procedure of M. Sörensen and Haugaard[3] has thus far not been greater than 3 g. per liter of original serum.

The proteins soluble in 2.4 *M* ammonium sulfate at *p*H 6.4 and insoluble at 2.8 *M* ammonium sulfate contain besides serum albumin, a considerable amount of globulin, as has been shown by Hewitt,[6] most of the pigments of serum, and choline esterase.[13] Haemocuprein, the copper-containing albumin,[14] was crystallized from this fraction with ammonium sulfate.

Solubility in Ammonium Sulfate of Carbohydrate-free Crystalline Serum Albumin.—The solubility of serum albumin in ammonium sulfate even after repeated recrystallization from this solvent has been shown by Sörensen[2] to depend largely upon the amount of saturating body with which it is in equilibrium, increasing with increase in the total protein in the system. This phenomenon might be expected if more than one protein component were present; that is to say, if the protein had not been

(12) We are indebted to the Massachusetts Antitoxin Laboratory for the horse serum albumin employed in these investigations. In several preparations of the albumin fraction, large amounts of the filtrate from *anti*-pneumococcus serum were employed from which the immune proteins had been removed by 1.6 *M* ammonium sulfate.

(13) McMeekin, *J. Biol. Chem.*, **128**, LXVI (1939).

(14) Mann and Keilin, *Proc. Roy. Soc.* (London), **B126**, 303 (1938).

isolated as a chemical individual, and is characteristic also of other proteins.[15] Mellanby[16] demonstrated that for the serum globulins that he studied a definite ratio obtained between solubility and the amount of total protein in the system. A comparable relation obtained for the various serum proteinsstudied by Sörensen[2,17] and for our repeatedly recrystallized carbohydrate-free serum albumin even after exhaustive fractionation with ammonium sulfate, as is demonstrated by the measurements in Table I of solubility in 1.8 *M* ammonium sulfate at *p*H 4.9. The solubility measurements were made by the method previously described.[18] Not only was the solubility of the albumin greater the greater the amount of saturating body in the system but it diminished at each equilibration of approximately twenty-four hours with fresh aliquots of solvent.

TABLE I

SOLUBILITY OF CARBOHYDRATE-FREE MIXED SERUM ALBUMINS IN 1.8 *M* AMMONIUM SULFATE AT *p*H 4.9 AND 25°

No. of equilibrations of one day each	Vol. of solvent, cc.	Soly., g./liter Solute A 0.37 g. protein	Soly., g./liter Solute B 1.85 g. protein	Solubility A / Solubility B
2	40	0.287	0.802	2.8
3	40	.132	.335	2.5
4	40	.072	.195	2.7

Further Fractionation of Carbohydrate-free Crystalline Serum Albumin.—The procedure of J. D. Ferry for "crystallization of a fraction of horse serum albumin from salt-free solution"[10] was followed next. A salt-free solution of purified albumin containing 26 g. of protein in 260 cc. was brought cautiously to *p*H 4.0 by adding 0.1 normal sulfuric acid (approximately 0.00025 mole of acid being required for each gram of protein) and then concentrated in a negative pressure dialyzing apparatus[19] at 4°. When the protein concentration reached about 25% the solution was brought to room temperature. Crystallization began within an hour and was allowed to continue for four hours. The crystals were removed by centrifugation and washed three times, each time with a volume of water equal to the volume of the precipitate. The supernatant liquor was again concentrated at 4° and a second and third crop of crystals removed. Crystallization was continued until no further separation occurred. The first crop of crystals generally amounted to 10 g. of protein, the second to 3 g. and the third to 0.3 g., leaving 12.5 g. of protein dissolved in solution under these conditions. Thus, about one-half of the original serum albumin was converted into water insoluble crystalline material.

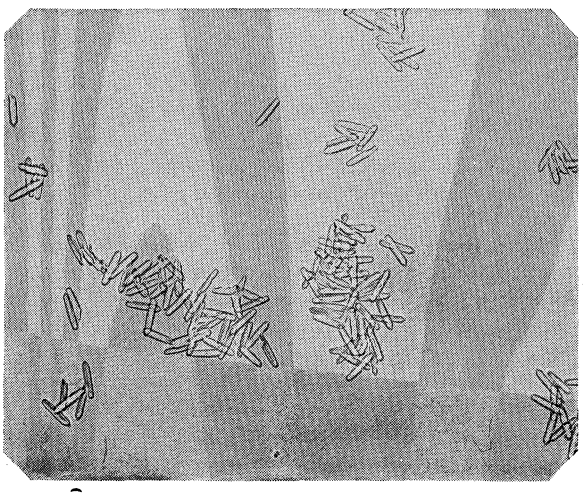

Fig. 2.—Microphotograph of serum albumin sulfate crystallized from water.

Properties of Serum Albumin Crystallized from Water at *p*H 4.0.—The serum albumin sulfate had the same crystal form of hexagonal prisms with pointed ends as the serum albumin from which it was derived. A solution obtained by repeated extraction of the crystals always had a *p*H of 4.0 ± 0.05 and gave a test for sulfate ions indicating that the substance was an albumin sulfate. For complete removal of sulfate, precipitation with barium or electrodialysis was required. After the removal of sulfate by electrodialysis, the solution had a *p*H close to that of the solution from which the albumin sulfate was prepared, indicating that the isolectric points of the several proteins were not sensibly different and close to *p*H 4.8.

The nitrogen factor of the albumin crystallized as sulfate was appreciably higher than that of the carbohydrate-free crystalline serum albumin from which it was derived. The latter carbohydrate-free unfractionated serum albumin was estimated to contain 16.1% nitrogen by macro-Kjeldahl and 16.2% nitrogen by Nesslerization. These results are in good agreement with the older values, but are higher than some recent reports. Abderhalden[20] found the nitrogen content of serum albumin to be 15.89, while Hewitt[4] reports from 14.1 to 14.4%, and Adair and Robinson[21] 15.6% nitrogen.

The isoelectric albumin prepared from the crystalline sulfate was found to contain 16.8% nitrogen by the Kjeldahl method. Protein concentration was determined by evaporation to constant weight of the salt-free solution at the isoelectric point in an oven at 105°, and also by weighing the dried coagulated protein. The results from the two methods were in good agreement.

(15) Steinhardt, *J. Biol. Chem.*, **129**, 135 (1939).
(16) Mellanby, *J. Physiol.*, **33**, 338 (1905–1906).
(17) S. P. L. Sörensen, and M. Sörensen, *Compt. rend. trav. Lab. Carlsberg*, **19**, No. 11, 1 (1933).
(18) Cohn, McMeekin, Edsall and Weare, THIS JOURNAL, **56**, 2270 (1934).
(19) Sörensen, *Compt. rend. trav. Lab. Carlsberg*, **12**, 26 (1917).
(20) Abderhalden, *Z. physiol. Chem.*, **37**, 495 (1903).
(21) Adair and Robinson, *Biochem J.*, **24**, 993 (1930).

Tryptophan has been present in the purest preparations of serum albumin but to a very small extent and it therefore seemed important to determine the amount of this amino acid in our preparations both before and after crystallization of the albumin sulfate. For this purpose Lugg's modification[22] of the Folin–Ciocalteu–Marenzi[23] method was used and a tryptophan content of 0.53% estimated for the albumin both before and after crystallization as a sulfate. This value is in good agreement with that of Folin and Marenzi[23] and is approximately double the value reported by Hewitt.[4,24]

The albumin sulfate was electrophoretically homogeneous at *p*H 7.4, but still showed a small quantity of a second component at *p*H 4.0. Its solubility in water at 4° was very high but at room temperature only moderate. The data in Table II illustrate its solubility in water at 25°. The *p*H was 4.0 ± 0.02 and the solvent was saturated with toluene.

TABLE II

SOLUBILITY OF CRYSTALLINE SERUM ALBUMIN SULFATE AT *p*H 4.0 AND 25°

No. of equilibrations of one day each	Vol. of solvent, cc.	Soly., g./liter: Solute A 0.6 g. protein	Solute B 3.0 g. protein
1	5	31.7	49.3
2	5	29.1	46.4
3	5	34.4	47.5
4	5	14.2[a]	45.0
5	5		43.9
6	5		41.4
			26.0[a]

[a] The solute protein was largely denatured at this stage as was shown by absence of crystalline form and almost complete insolubility in water.

Analysis for the sulfate ion in these crystals yielded the result that each gram of the protein was combined with 0.00035 equivalent of sulfate, a value considerably in excess of the amount of sulfate, 0.00026 equivalent per gram, necessary to titrate the albumin from the isoelectric point to a *p*H 3.95.

The sulfate ion was removed from albumin sulfate by dialysis and electrodialysis and the protein again crystallized from ammonium sulfate. The solubility of these crystals at 25° was determined in a 1.47 *M* ammonium sulfate solution, and the results are given in Table III. Although

TABLE III

SOLUBILITY IN 1.47 *M* AMMONIUM SULFATE OF ALBUMIN ISOLATED BY CRYSTALLIZATION AS SULFATE AT *p*H 4.0 AND 25°

No. of equilibrations of one day each	Vol. of solvent, cc.	Soly., g./liter[a]: Solute A 0.2 g. protein	Solute B 1.0 g. protein
2	40	0.62	(1.03)
3	40	.54	0.50
4	40	.80	.54
5	40	(1.07)	.57
6	40		.49

[a] The *p*H of the filtrate was determined each day. For the more dilute series it always remained 4.8 ± 0.04 and for the more concentrated series 4.63 ± 0.03. In subsequent experiments it should be possible to control the *p*H in these unbuffered solutions even more carefully.

there is some drift from day to day in these unbuffered solutions, there is no evidence of increase in solubility with increase in saturating body or of decrease in solubility with increase in the number of days during which the saturating body was equilibrated with fresh aliquots of solvent. The extent of the purification achieved by crystallization as the albumin sulfate is perhaps best demonstrated by a comparison of Table III with Table I. The results reported in Tables II and III indicate that at least one component of the serum albumin system has been separated as a chemical individual. Further studies both of its composition and properties are being undertaken and will be reported subsequently.

I am indebted to Professor Edwin J. Cohn for his suggestions and advice throughout this investigation.

Summary

1. Carbohydrate-free crystalline serum albumin has been separated into two fractions by crystallizing the sulfates from water.

2. The solubility in salt solution of the protein regenerated from the insoluble albumin sulfate was found to be essentially independent of the amount of protein in the system, and of the volume of solvent with which it was equilibrated, suggesting that this albumin component had been separated as a chemical individual.

3. The percentage of nitrogen in this serum albumin was found to be higher, tyrosine lower, and tryptophan the same as in unfractionated carbohydrate-free crystalline serum albumin.

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(22) Lugg, *Biochem. J.*, **31**, 1422 (1937).

(23) Folin and Ciocalteu, *J. Biol. Chem.*, **73**, 627 (1927); Folin and Marenzi, *J. Biol. Chem.*, **83**, 89 (1929).

(24) Preliminary results on the tyrosine content of the albumin sulfate suggest that it is appreciably lower than that of the material from which it was derived but not by a sufficient amount to account for the differences in nitrogen percentage.

[CONTRIBUTION FROM THE DEPARTMENTS OF PHYSICAL CHEMISTRY AND MEDICINE, HARVARD MEDICAL SCHOOL, AND THE MEDICAL CLINIC OF THE PETER BENT BRIGHAM HOSPITAL]

Serum Albumin. II. Identification of More than One Albumin in Horse and Human Serum by Electrophoretic Mobility in Acid Solution

BY JOHN A. LUETSCHER, JR.

The albumins of serum have constituted a problem of importance both for protein chemistry and clinical medicine. The serum albumins of the horse are readily crystallizable, and those of man have been crystallized, though with greater difficulty.[1,2] The beautifully crystalline albumin of normal horse serum has, however, been shown not to consist of a single chemical individual, as judged by solubility,[3] although it appears to be homogeneous as to molecular weight as judged by the ultracentrifuge,[4] and to migrate with uniform velocity in the electric field at neutral reaction.[5]

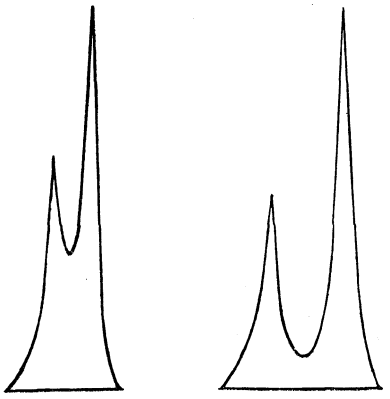

Fig. 1.—Schlieren diagrams (diaphragm level against distance moved) of electrophoresis at *p*H 4.0 and ionic strength 0.02 of (a) horse serum albumin, and (b) normal human serum albumin. Area under each peak is proportional to concentration of that component.

In the preceding paper,[6] McMeekin has succeeded in purifying crystalline serum albumin so as to yield at least one component of constant solubility. This was accomplished by "crystallization of horse serum albumin from salt-free solution" following an observation of J. D. Ferry.[7] The crystallization as an albumin sulfate was carried out at *p*H 4.0 and 25°. The serum albumin so fractionated previously had been crystallized repeatedly so as to free it from carbohydrate and had a single electrophoretic mobility in the Tiselius apparatus at neutral reactions where it has been studied as a function of *p*H, ionic strength, and protein concentration.

It seemed important to investigate the electrophoretic mobility of horse serum albumin at the *p*H at which Ferry and McMeekin have demonstrated that a portion of the albumin can be crystallized as the sulfate. Measurements were therefore undertaken on the same carbohydrate-free crystalline albumin that served as starting material for McMeekin's investigations[6] and which migrated in the electric field with uniform mobility at a great variety of ionic strengths at neutral reactions. When studied in acetate buffers at *p*H 4.0 of ionic strength 0.02, however, two boundaries were clearly visible, as represented in Fig. 1a. Migration was followed by the Toepler–Schlieren method,[8] ordinates and abscissas representing diaphragm level and distance moved. The amount of protein is proportional to the area under the curves. The albumin mobilities were 6.80 and 6.44 $\times 10^{-5}$ cm.^{2}/volt-sec., respectively, about 60% of the protein moving at the faster, 40% at the slower, rate. The protein in this solution, which thus revealed two boundaries when studied at *p*H 4.0, subsequently migrated with a single boundary at *p*H 7.4 of the same mobility as before.

When normal human serum albumin was investigated under precisely the same conditions, two boundaries were also clearly distinguishable, as represented in Fig. 1b. The mobilities of the two human serum albumin components at *p*H 4.0 and $\Gamma/2$ 0.02 were 7.25 and 5.95 $\times 10^{-5}$ cm.^{2}/volt-sec., respectively. The component of greater mobility of human serum albumin therefore moves appreciably faster as a cation than the faster component of horse serum albumin, and the slower component of human serum albumin more slowly than the slower component of horse serum albumin under these conditions. The

(1) Adair and Taylor, *Nature*, **135**, 307 (1935).
(2) Kendall, personal communication.
(3) Sörensen, *Compt. rend. trav. Lab. Carlsberg*, **18**, No. 5 (1930).
(4) Svedberg and Sjogren, THIS JOURNAL, **50**, 3318 (1928).
(5) Tiselius, *Biochem. J.*, **31**, 1464 (1937).
(6) McMeekin, THIS JOURNAL, **61**, 2884 (1939).
(7) Reported by Ferry to the Division of Biological Chemistry at the 96th meeting of the American Chemical Society, Milwaukee, September 7, 1938.
(8) An automatic camera for producing these diagrams has been described by Longsworth, THIS JOURNAL, **61**, 529 (1939).

separation achieved between the components of human serum albumin during electrophoresis is thus by far the greater, as is indicated by the greater separation of the peaks in Fig. 1b than in 1a. The protein migrating with the greater mobility represented approximately 67% and that with the slower mobility 33% of the albumin. Although there is approximately the same proportion of components in horse and man, the difference between the mobilities is sufficient to render practicable electrophoretic separation under these or closely similar conditions, at least in the case of the human protein. Human serum albumin, as in the case of the horse, migrates uniformly at neutral reactions.

Although the loss of serum proteins into the urine in certain diseases involves not only the albumin, but also the globulin fractions, the albumin molecules are generally lost in larger amount. It seemed desirable to investigate the albumin components of blood and urine from patients with certain types of kidney and liver disease. In the nephrotic syndrome, where large amounts of serum albumin are known to be lost and where the concentration of globulins (especially the α- and β-fractions of Tiselius) and fibrinogen in blood is increased, the albumin both in the blood and the urine has been investigated under the same conditions as that of normal human serum albumin, namely, in acetate buffers at *p*H 4.0, and found to be divisible into two components. Unlike normal human albumin, however, the component of slower mobility has been found to be present in larger amount (Fig. 2b). Since the ratio of components appears to be the same in both urine and blood, this abnormality cannot be considered as due to urinary excretion but rather to a difference in protein production. The total amount of albumin is much reduced in these cases, as is indicated by comparing the shaded area under the curves, representing the albumins of nephrotic syndrome, with the area under the outline curve of the normal serum. Taking average concentrations of the normal components, respectively, as 1.3 and 2.7 g. per hundred cc., the concentration of the slower component would be reduced to one-sixth but of the faster component almost to one-thirtieth that of the normal. It follows that the production of the slower component is less affected than that of the faster. It was the urinary albumin from a similar case that had "a dielectric constant increment of 0.5 per gram per liter, higher than any thus far obtained for crystallized horse serum albumin, and a mean relaxation time in dilute solution of 0.2×10^{-6} seconds,"[9] close to that observed for horse serum albumin.[10]

The above condition may be contrasted with that of the blood and urine of patients in the non-edematous end-stage of nephritis. Then the blood proteins approximate the normal picture, both as to the albumins and the globulins, although there would appear in the cases thus far investigated to be very little loss of the slower and a somewhat greater loss of the faster moving component (Fig. 2a).

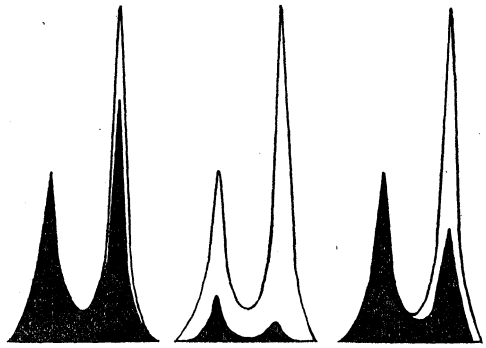

Fig. 2.—Schlieren diagrams of electrophoresis of pathological human albumins compared in each case with the normal picture. Concentrations of components in normal serum are 1.3 and 2.7 g. %; in terminal nephritis (a), 1.2 and 1.9; in nephrotic syndrome (b), 0.24 and 0.10; and in cirrhosis (c), 1.3 and 0.9 g. %, respectively. Ratio of albumins in urine was same as in serum.

In cirrhosis with ascites, where the principal factor in the lowering of plasma proteins is probably a failure of production, the albumin fraction may be much lowered, and in such cases the ratio of albumin components at *p*H 4.0 resembles that of the nephrotic syndrome, with the slower component predominating (Fig. 2c). Indeed, in cases thus far investigated no, or very slight, diminution in the concentration of the slower moving albumin has been detected, whereas the fast moving component has been reduced to one-third of the normal level. The role of the albumins which readily can be distinguished by electrophoresis at *p*H 4.0 is clearly different. That the difference in composition is not due to a gradual change in part of the albumin under

(9) Friend, Ferry and Oncley, *J. Biol. Chem.*, **123**, Proc. XXXIX (1938).

(10) Ferry and Oncley, THIS JOURNAL, **60**, 1123 (1938).

these conditions has been demonstrated by studying electrophoretic mobility of human serum albumin soon after equilibration with acetate buffer and again after a period of some days at 4° when no alteration in the electrophoretic mobility of either component or in the ratio of the components was detected.[11]

The separation and characterization not only of the albumin but also of the various globulin components of normal and pathological sera[12] are being investigated further.

Summary

1. Although crystalline serum albumin has been demonstrated to consist of more than one chemical individual, it has been reported to migrate with uniform velocity both during ultracentrifugation and electrophoresis at neutral reactions.

2. At *p*H 4.0, where a fraction of horse serum albumin crystallizes as a sulfate, the protein exhibits two boundaries in the Tiselius electrophoresis apparatus, which migrate, respectively, with mobilities of 6.80 and 6.44 × 10^{-5} cm.²/volt-sec. in acetate buffers of *p*H 4.0 and Γ/2 0.02.

3. Human serum albumin also consists of at least two components, migrating with velocities of 7.25 and 5.95 × 10^{-5} cm.²/volt-sec., respectively, under the above conditions.

4. In normal sera, the faster moving component constitutes nearly two-thirds of the albumin, but in certain pathological conditions in man, both serum and urinary albumins show a greater diminution of the faster component, leaving the slower component preponderant.

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(11) Several of the pathological specimens were made available through the kindness of Dr. Allan M. Butler of the Children's Hospital, Boston, Mass.

(12) Studies of this kind have been reported by Stenhagen, *Biochem. J.*, **32**, 714 (1938); Blix, *Z. exptl. Med.*, **105**, 595 (1939); MacInnes and Longsworth, *Science*, **89**, 438 (1939).

[CONTRIBUTION FROM THE LABORATORIES OF THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH]

The Synthesis of Certain Substituted Quinolines and 5,6-Benzoquinolines

BY R. GORDON GOULD, JR., AND WALTER A. JACOBS

The synthesis of ergoline (I) and of several of its mono- and dimethyl derivatives by the sodium reduction of 3′-amino-5,6-benzoquinoline-7-carboxylic acid lactam and of the corresponding methyl derivatives already has been reported.[1] Although the yields were only about 5 to 10%, the method appeared to be of fairly general application to the alkyl derivatives. When, however, a free or esterified carboxyl group was present in the pyridine ring, the isolation of a crystalline ergoline derivative became extremely difficult. The preparation of ergoline-7-carboxylic acid in a yield of about 1% and in still somewhat impure condition already has been reported,[2] but all attempts to prepare the isomeric ergoline-8-carboxylic acid have given only amorphous products. This plan of attack on the problem of the synthesis of dihydrolysergic acid has therefore not been so promising as had been anticipated.

In the course of this work several new methods of synthesis of certain quinoline and benzoquinoline derivatives were developed, which are the subject of the present paper.

Conrad and Limpach[3] first prepared 4-hydroxyquinaldine (II) by condensation of aniline with acetoacetic ester at room temperature followed by cyclization at 250°, and Limpach[4] forty-four years later improved the yield from about 30 to 90–95% by the use of mineral oil as a diluent in the cyclization step.

This method of synthesis has now been found to be sufficiently general to be applicable not only to substituted anilines and β-naphthylamines, but also has been extended to the synthesis of 4-hydroxyquinoline-3-carboxylic acids (III) by the use of ethoxymethylenemalonic ester and of 4-hydroxyquinaldine-3-carboxylic acids (IV) by the use of acetylmalonic ester.

As examples, aniline condensed with ethoxymethylenemalonic ester to give anilidomethylenemalonic ester, as reported by Claisen.[5] Cyclization of the latter in mineral oil gave the previously known[6] 4-hydroxyquinoline-3-carboxylic acid (III).

$$C_6H_5NH_2 + C_2H_5OCH{=}C(COOR)_2 \longrightarrow C_6H_5NHCH{=}C(COOR)_2$$

(1) W. A. Jacobs and R. G. Gould, *J. Biol. Chem.*, **120**, 141 (1937).

(2) W. A. Jacobs and R. G. Gould, *ibid.*, **126**, 67 (1938).

(3) M. Conrad and L. Limpach, *Ber.*, **20**, 944 (1887).

(4) L. Limpach, *ibid.*, **64**, 969 (1931).

(5) L. Claisen, *Ann.*, **297**, 77 (1897).

(6) R. Camps, *Ber.*, **34**, 2714 (1901).

Aniline condensed with acetylmalonic ester and the resulting intermediate alkylidene derivative was cyclized in mineral oil. The resulting ester after saponification proved to be the previously known 4-hydroxyquinaldine-3-carboxylic acid[7] (IV).

$$C_6H_5NH_2 + CH_3COCH(COOR)_2 \longrightarrow C_6H_5NHC(CH_3){=}C(COOR)_2$$

In the case of acetoacetic ester and of ethoxymethylenemalonic ester, the condensation to the intermediate alkylidene derivatives went smoothly and apparently in only one sense, with all of the amines used, but acetylmalonic ester was found to give poorer yields of the alkylidene derivatives because of competing side reactions. With aniline, a yield of about 30% of acetanilide and of about 70% of the normal anilidomethylmethylenemalonic ester was obtained.

The condensation of acetylmalonic ester with 3-aminonaphthostyril gave another type of abnormal product which was possibly the result of the condensation of an ester linkage rather than that of the carbonyl group, with the amino group, thus

$$(C_{11}H_6ON)NH_2 + CH_3COCH(COOR)_2 \longrightarrow (C_{11}H_6ON)NHCO\underset{\displaystyle COOR}{\underset{|}{C}}HCOCH_3$$

The alkylidene derivatives which resulted from the normal condensation of the three esters used with amines cyclized smoothly at 250°, and gave in each case the quinoline derivative. In the case of acetoacetic ester, this was a 4-hydroxyquinaldine or benzoquinaldine derivative, and in the cases of ethoxymethylenemalonic ester and acetylmalonic ester the products were derivatives of 4-hydroxyquinoline or benzoquinoline-3-carboxylic acids.

In addition to the examples already cited, the following new substances were prepared by the two steps of condensation, *viz.*, formation of the intermediate alkylidene derivative and subsequent cyclization to the quinoline or benzoquinoline. Acetoacetic ester and 3-amino-1-naphthoic acid (or its ester) gave **4-hydroxy-5,6-benzoquinaldine-7-carboxylic acid** (or its ester) (V). 3-Aminonaphthostyril and acetoacetic ester gave **3′ - amino - 4 - hydroxy - 5,6 - benzoquinaldine-7-carboxylic acid lactam** (VI).

Ethoxymethylenemalonic ester and 3-amino-1-naphthoic acid gave **4-hydroxy-5,6-benzoquinoline-3,7-dicarboxylic acid** (VII), and the same ester with 3-aminonaphthostyril gave **3′-amino-4 - hydroxy - 5,6 - benzoquinoline - 3,7 - dicarboxylic acid lactam** (VIII).

Since in the attempt to prepare **3′-amino-4-hydroxy - 5,6 - benzoquinaldine - 3,7 - dicarboxylic acid lactam** (IX) from 3-aminonaphthostyril and acetylmalonic ester the reaction proceeded abnormally, this substance was obtained instead by the following series of reactions. 4-Hydroxy - 5,6 - benzoquinaldine - 7 - carboxylic acid (V), when condensed with carbon tetrachloride and potassium hydroxide by the Reimer–Tiemann reaction, gave **4-hydroxy-5,6-benzoquinaldine-3,7-dicarboxylic acid** (X). This dibasic acid was characterized also as the **monomethyl ester,** the **dimethyl ester,** and as the **4-methoxy dimethyl ester.** Nitration of the hydroxy dibasic acid gave a mixture of mononitro derivatives which was directly reduced as such. After treatment of the reduction product with acid, 3′-amino-4-hydroxy-5,6-benzoquinaldine-3,7-dicarboxylic acid lactam (IX) was isolated as well as a simultaneously formed free amino derivative which did not lactamize. The latter was possibly **6′-amino-4-hydroxy-5,6-benzoquinaldine-3,7-dicarboxylic acid** (XI).

Several examples have been reported of the oxidation by selenium dioxide of the 2- or 4-methyl group in pyridine or quinoline derivatives to a carboxyl group[8] and of the 2-methyl group in 5,6 - benzoquinaldine - 7 - carboxylic acid.[2] The presence of a 4-hydroxy group appears to block this type of oxidation, however, since none of the 4-hydroxy-5,6-benzoquinaldine derivatives described above were oxidized by selenium dioxide under the conditions usually employed.

The 4-hydroxyl group similarly appeared to block the catalytic hydrogenation of the nitrogen ring of such substances to the tetrahydro derivatives. Ruzicka and Fornasir[9] reported that 4-hydroxypyridine could not be hydrogenated catalytically under ordinary conditions of temperature and pressure and our experience with 4-hydroxyquinoline and -benzoquinoline derivatives appears to confirm this. Also in the case of 3′ - amino - 4 - hydroxy - 5,6 - benzoquinoline-3,7-dicarboxylic acid lactam (VIII), reduction with amalgamated zinc and acetic acid appeared to stop at the dihydro stage, with the formation

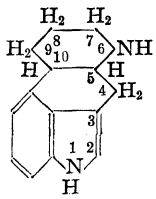
(7) M. Conrad and L. Limpach, *Ber.*, **21**, 1975 (1888).

(8) M. Henze, *Ber.*, **67**, 750 (1934); see also ref. 2.

(9) L. Ruzicka and V. Fornasir, *Helv. Chim. Acta*, **3**, 807 (1920).

of **3′-amino-4-keto-1,2,3,4-tetrahydro-5,6-benzoquinoline-3,7-dicarboxylic acid lactam (XII).**

A few substituted 5,6-benzoquinoline-4-carboxylic acids were prepared by the application of the condensation of aromatic amines with pyruvic acid and aldehydes.[10] With formaldehyde, only complex dimolecular products were obtained, but with acetaldehyde the reaction went smoothly although the yields were poor. 3-Amino-1-naphthoic methyl ester gave **7-carbomethoxy-5,6-benzoquinaldine-4-carboxylic acid (XIII)** which after saponification and oxidation with selenium dioxide yielded **5,6-benzoquinoline-2,4,7-tricarboxylic acid (XIV).** Attempts to prepare lactam derivatives from both the dibasic and tribasic acids by successive nitration and reduction were unsuccessful. Nitration in the 3′ position was apparently not favored.



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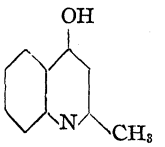

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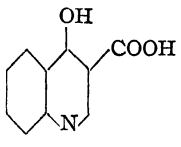

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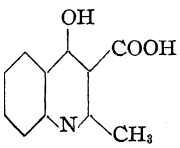

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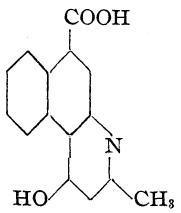

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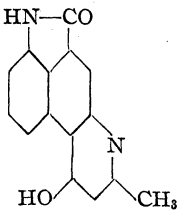

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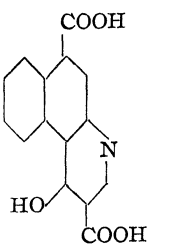

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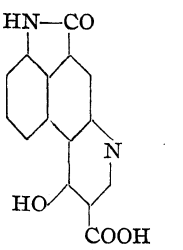

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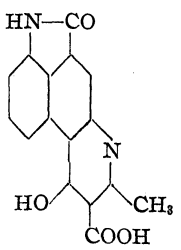

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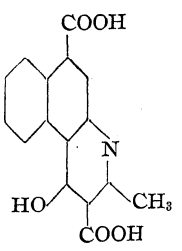

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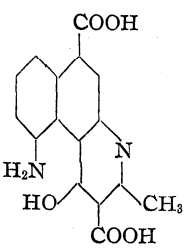

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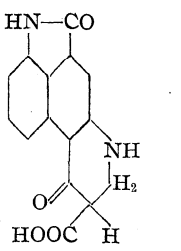

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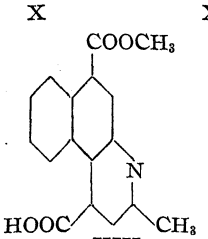

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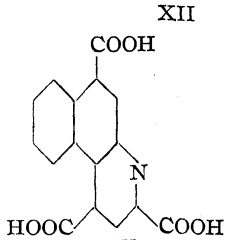

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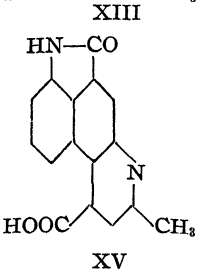

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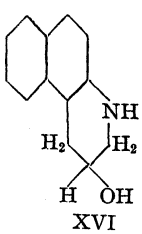

XVI

3-Aminonaphthostyril on condensation with pyruvic acid and acetaldehyde gave **3′-amino-5,6-benzoquinaldine-4,7-dicarboxylic acid lactam (XV)** in poor yield.

Finally, the method developed for the preparation of 3-hydroxy-1,2,3,4-tetrahydro-7,8-benzoquinoline derivatives by the condensation of epichlorohydrin with α-naphthylamine derivatives[11] was tried with several β-naphthylamine derivatives. It was found that β-naphthylamine gave **3-hydroxy-1,2,3,4-tetrahydro-5,6-benzoquinoline (XVI),** but 3-aminonaphthostyril yielded an anomalous product, the nature of which has not been determined.

Experimental

For the preparation of alkylidene derivatives, except where otherwise stated, the condensations with acetoacetic ester and acetylmalonic ester were carried out at room temperature and with ethoxymethylenemalonic ester by heating on the steam-bath. In some cases methyl or ethyl alcohol was used as a solvent. The cyclizations of the alkylidene derivatives were carried out in 10–30 parts of mineral oil at 250–265°, in an atmosphere of dry nitrogen, and with good mechanical stirring. The substance was added in small portions and heating was continued for about fifteen minutes. After cooling, the mixture was treated with the appropriate solvent and the crystalline product was collected.

(3-Naphthyl-1-carboxylic Acid)-β-aminocrotonic Ethyl Ester.—Twenty grams of 3-amino-1-naphthoic acid and 20 g. of acetoacetic ester condensed readily in methyl alcoholic solution. After removal of the solvent *in vacuo* the crystalline product was collected with a cold ether–petroleum ether mixture. The yield was almost quantitative. For analysis it was recrystallized from ether and formed rosets of needles which melted at 157–158°.

Anal. Calcd. for $C_{17}H_{17}O_4N$: C, 68.19; H, 5.73. Found: C, 68.08; H, 5.40.

(10) E. A. Robinson and M. T. Bogert, *J. Org. Chem.*, **1**, 65 (1936–1937).

(11) I. G. Farb. Akt. Ges., French Patent 799,322 (*Chem. Zentr.*, **107**, II, 2020 (1936); Swiss Patent 186,845 (*Chem. Zentr.*, **108**, I, 4024 (1937)).

4-Hydroxy-5,6-benzoquinaldine-7-carboxylic Acid (V).—Cyclization gave an almost quantitative yield of the benzoquinoline derivative. It was purified by recrystallization from 1% hydrochloric acid solution as the hydrochloride which separated as needles.

Anal. Calcd. for $C_{15}H_{11}O_3N \cdot HCl$: C, 62.16; H, 4.18. Found: C, 61.96; H, 4.40.

After liberation from the salt, the substance was obtained as a microcrystalline powder which did not melt below 360°.

Anal. Calcd. for $C_{15}H_{11}O_3N$: C, 71.10; H, 4.38. Found: C, 70.87, 71.34; H, 4.81, 4.50.

The Methyl Ester.—Treatment with boiling methyl alcohol and hydrogen chloride gave the ester, which after recrystallization melted at 295–296° with decomposition.

Anal. Calcd. for $C_{16}H_{13}O_3N$: C, 71.88; H, 4.91. Found: C, 71.74; H, 5.01.

The Ethyl Ester.—The ester was obtained with absolute alcohol and sulfuric acid and formed lustrous leaflets from alcohol, which melted at 295–297°.

Anal. Calcd. for $C_{17}H_{15}O_3N$: C, 72.56; H, 5.38. Found: C, 72.78; H, 5.32.

N-(3-Naphthostyryl)-β-aminocrotonic Ethyl Ester.—Two and one-half grams of 3-aminonaphthostyril was refluxed with an excess of acetoacetic ester in alcohol solution for several hours. The condensation product was collected in a yield of 3.2 g. After recrystallization from alcohol, it melted at 180–182°.

Anal. Calcd. for $C_{17}H_{16}O_3N_2$: C, 68.88; H, 5.44. Found: C, 68.65; H, 5.28.

4-Hydroxy-3′-amino-5,6-benzoquinaldine-7-carboxylic Acid Lactam (VI).—The above aminocrotonic ester was cyclized in mineral oil at 250° and the product was purified through the sparingly soluble hydrochloride which formed needles from dilute hydrochloric acid solution.

Anal. Calcd. for $C_{15}H_{11}O_2N_2Cl$: C, 62.81; H, 3.87. Found: C, 62.96; H, 3.51.

The free hydroxy lactam was insoluble in ammonia and very sparingly soluble in hot pyridine or dilute pyridine. It did not melt below 360°.

Anal. Calcd. for $C_{15}H_{10}O_2N_2$: C, 71.97; H, 4.03. Found: C, 71.49; H, 4.41.

4-Hydroxyquinaldine-3-carboxylic Ethyl Ester.—Ten and one-tenth grams of acetylmalonic ester[12] and 4.7 g. of aniline were allowed to stand at room temperature for three days. Acetanilide separated and was collected in a yield corresponding to about 30% of the aniline used. The filtrate was cyclized in mineral oil, and the product collected with ether. After recrystallization from alcohol, the substance melted at 104–107°.

Anal. Calcd. for $C_{13}H_{13}O_3N$: C, 67.50; H, 5.67. Found: C, 66.97; H, 5.46.

4-Hydroxyquinaldine-3-carboxylic Acid (IV).—Saponification gave the free acid which melted at 245–247° with decomposition. Camps[6] gave 247–248° with decomposition.

Anal. Calcd. for $C_{11}H_9O_3N$: C, 65.00; H, 4.47. Found: C, 65.20; H, 4.38.

(12) H. Lund, *Ber.*, **67**, 937 (1934).

α-Carbethoxyacetoacetyl-3-aminonaphthostyril.—One and eight-tenths grams of 3-aminonaphthostyril and 4 g. of acetylmalonic ester were allowed to stand at room temperature for several months. After recrystallization from alcohol, the substance melted at 268–270° with decomposition.

Anal. Calcd. for $C_{18}H_{16}O_5N_2$: C, 63.50; H, 4.71. Found: C, 63.19; H, 4.65.

4-Hydroxyquinoline-3-carboxylic Acid (III).—One gram of anilidomethylenemalonic ester[5] was cyclized in mineral oil and the crystalline product was collected in a yield of about 60%. Acidification of the aqueous alkaline solution gave long needles which melted at 267–268°. Camps[6] gave 266–267°.

Anal. Calcd. for $C_{10}H_7O_3N$: C, 63.47; H, 3.72. Found: C, 63.60; H, 3.79.

N-(3-Naphthyl-1-carbomethoxy)-β-amino-α-carbethoxyacrylic Ethyl Ester.—One gram of 3-amino-1-naphthoic methyl ester and 1.08 g. of ethoxymethylenemalonic ester[13] were heated for fifteen minutes at 100°. On cooling, a crystalline cake formed which was recrystallized from ether. It formed voluminous long needles melting at 89–90°.

Anal. Calcd. for $C_{20}H_{21}O_6N$: C, 64.66; H, 5.70. Found: C, 64.99; H, 5.62.

4-Hydroxy-5,6-benzoquinoline-3,7-dicarboxylic Acid (VII).—One gram of the above alkylidene derivative at 250° gave 0.73 g. of cyclization product. This monomethyl ester was saponified by heating in dilute sodium hydroxide and the dibasic acid was recrystallized from sodium acetate solution as the beautifully crystalline monosodium salt. It was then isolated as the free acid which did not melt below 360°.

Anal. Calcd. for $C_{15}H_9O_5N$: C, 63.59; H, 3.22. Found: C, 63.91; H, 3.37.

N-(3-Naphthostyryl)-β-amino-α-carbethoxyacrylic Ethyl Ester.—To 104.6 g. of 3-aminonaphthostyril dissolved in 185 cc. of boiling alcohol was added 6 g. of ethoxymethylenemalonic ester, and the solution was refluxed for one hour. The crystalline product was collected in about 75% yield. With material recovered from the mother liquor, the yield was almost the theoretical.

The substance formed light yellow needles from alcohol which melted at 231–232°.

Anal. Calcd. for $C_{19}H_{18}O_5N_2$: C, 64.38; H, 5.12. Found: C, 64.85; H, 5.10.

4-Hydroxy-3′-amino-5,6-benzoquinoline-3,7-dicarboxylic Acid Lactam (VIII).—Six and three-tenths grams of the above substance on cyclization gave an almost quantitative yield of the benzoquinoline derivative. Purification was effected by boiling in 5% sodium hydroxide solution for one hour in order to open the lactam group. After treatment with norite, the clear light yellow solution was made strongly acid to congo red with hydrochloric acid and brought to a boil. The lactam acid formed microscopic needles which did not melt below 360°.

It is soluble in dilute sodium bicarbonate on warming and in dilute piperidine. It forms a sparingly soluble sodium

(13) L. Claisen, *Ann.*, **297**, 76 (1897); H. L. Wheeler and C. O. Johns, *Am. Chem. J.*, **40**, 238 (1908).

salt in more concentrated alkaline solutions, and it is not appreciably soluble in the ordinary organic solvents.

Anal. Calcd. for $C_{15}H_8O_4N_2$: C, 64.27; H, 2.88; N, 10.00. Found: C, 64.01, 64.23; H, 3.09, 3.05; N, 10.20.

The free amino dibasic acid formed a dark red gelatinous precipitate.

3′ - Amino - 4 - hydroxy - 2,3 - dihydro - 5,6 - benzoquinoline-3,7-dicarboxylic Acid Lactam (XII).—The 3′-amino-4-hydroxy-5,6-benzoquinoline-3,7-dicarboxylic acid lactam was suspended in acetic acid and refluxed for about five hours with an excess of amalgamated zinc shot. The supernatant suspension was decanted from the excess zinc and was then collected. It was purified by reprecipitation from a dilute pyridine solution by addition of acetic acid, and did not melt below 350°.

Anal. Calcd. for $C_{15}H_{12}O_4N_2$: C, 63.81; H, 3.57. Found: C, 63.92; H, 3.84.

4 - Hydroxy - 5,6 - benzoquinaldine - 3,7 - dicarboxylic Acid (X).—To 11 g. of 4-hydroxy-5,6-benzoquinaldine-7-carboxylic acid (V) were added 60 cc. of 50% potassium hydroxide, 5 cc. of carbon tetrachloride, about 1 g. of copper powder, and a few cc. of alcohol, and the mixture was refluxed for twenty-four hours. It was then diluted with 5 volumes of water and filtered. The clear, dark-colored filtrate was made just acid to congo red by the addition of hydrochloric acid and then enough excess hydrochloric acid was added to bring the concentration to 1%. After bringing to a boil, the undissolved material was collected. It was again boiled in 200 cc. of 1% hydrochloric acid and collected hot. The insoluble material consisted of the dibasic acid. Unchanged monobasic acid was recovered from the combined filtrates. The yields of dibasic and recovered monobasic acids were respectively 3 g. and 6 g.

The dicarboxylic acid was purified by the following steps: extraction with hot alcohol (in which it is insoluble); recrystallization as the salt from sodium acetate solution; as the nitrate from nitric acid (1.4); and finally from dilute pyridine. It formed leaflets which did not melt below 360°.

Anal. Calcd. for $C_{16}H_{11}O_5N$: C, 64.63; H, 3.73. Found: C, 64.44, 64.57; H, 3.39, 3.74.

A **monomethyl ester** of undetermined identity was obtained by esterification with boiling methyl alcoholic hydrogen chloride. The hydrochloride crystallized from the boiling solution. The free ester, after recrystallization from aqueous pyridine, melted at 290–295°, with decomposition.

Anal. Calcd. for $C_{17}H_{13}O_5N$: C, 65.57; H, 4.21. Found: C, 65.56; H. 4.33.

The **dimethyl ester** was obtained from the dibasic acid in poor yield with methyl alcohol and sulfuric acid. When recrystallized from methyl alcohol it melted at 239–240°.

Anal. Calcd. for $C_{18}H_{15}O_5N$: C, 66.43; H, 4.65. Found: C, 66.72; H, 5.06.

4 - Methoxy - 5,6 - benzoquinaldine - 3,7 - dicarboxylic Dimethyl Ester.—This substance resulted from treatment of a methyl alcoholic suspension of the dibasic acid with diazomethane. It formed long colorless needles from ether or methyl alcohol, which melted at 142–144°.

Anal. Calcd. for $C_{19}H_{17}O_5N$: C, 67.23; H, 5.05. Found: C, 67.19; H, 5.17.

3′ - Nitro - 4 - hydroxy - 5,6 - benzoquinaldine - 3,7 - dicarboxylic Acid.—The preceding dicarboxylic acid was nitrated with fuming nitric acid (1.58). The material which separated on dilution was a mixture of isomeric mononitro derivatives, and was used directly for the following reduction without attempting a separation.

Anal. Calcd. for $C_{16}H_{10}O_7N_2$: C, 56.12; H, 2.95. Found: C, 55.63; H, 3.03.

3′ - Amino - 4 - hydroxy - 5,6 - benzoquinaldine - 3,7 - dicarboxylic Acid Lactam (IX).—The previously described method[1,2] with ferrous hydroxide was used for the reduction of the preceding substance. The crude product was collected after acidification to congo red and boiling for a short time. This material was found on analysis to consist approximately of 30% of the lactam of the 3′-amino derivative and 70% of an isomeric aminodicarboxylic acid, which did not lactamize. The mixture was separated by trituration with half saturated sodium bicarbonate solution at 60° which appeared to dissolve mainly the amino dicarboxylic acid. The lactam acid was purified by recrystallization as the sodium salt from sodium carbonate solution. After liberation from the salt, the lactam acid formed an orange-yellow microcrystalline powder, which did not melt below 360°.

Anal. Calcd. for $C_{16}H_{10}O_4N_2$: C, 65.28; H, 3.43; N, 9.53. Found: C, 65.39; H, 3.61; N, 9.70.

(?) - Amino - 4 - hydroxy - 5,6 - benzoquinaldine - 3,7-dicarboxylic Acid (XI).—The above sodium bicarbonate solution on acidification yielded the by-product which was obtained colorless after purification by repeated recrystallization as the hydrochloride from dilute hydrochloric acid. The free amino acid was obtained as a microcrystalline powder which did not melt below 360°.

Anal. Calcd. for $C_{16}H_{12}O_5N_2$: C, 61.51; H, 3.88. Found: C, 61.12; H, 4.22.

7 - Carbomethoxy - 5,6 - benzoquinaldine - 4 - carboxylic Acid (XIII).—Four grams of 3-amino-1-naphthoic methyl ester, 0.88 g. of pyruvic acid, and 0.88 g. of acetaldehyde were dissolved in 50 cc. of alcohol and the mixture was refluxed for four to five hours. A yield of 0.7 g. of the product crystallized on cooling; 0.2 g. more was obtained from the mother liquor.

The acid formed aggregates of fine white needles from a mixture of pyridine and alcohol, which melted at 265–266°, with decomposition.

Anal. Calcd. for $C_{17}H_{13}O_4N$: C, 69.13; H, 4.44. Found: C, 69.46; H, 4.56.

Saponification of the above monomethyl ester gave the **dibasic acid** as a colorless microcrystalline powder which melted at 298–299°, with decomposition.

Anal. Calcd. for $C_{16}H_{11}O_4N$: C, 68.30; H, 3.95. Found: C, 68.08; H, 3.82.

7 - Carbomethoxy - 5,6 - benzoquinoline - 2,4 - dicarboxylic Acid.—The previous monomethyl ester was oxidized with excess selenium dioxide in pyridine solution. The resulting product was recrystallized from a mixture of pyridine and methyl alcohol from which it separated as diamond-shaped prisms. It melted at 199–200° with decomposition and contained pyridine of crystallization which was not removed by heating to 100° *in vacuo*.

Anal. Calcd. for $C_{17}H_{11}O_6N \cdot C_5H_5N$: C, 65.32; H, 3.99. Found: C, 65.22; H, 4.01.

Saponification of the above oxidation product yielded **5,6-benzoquinoline-2,4,7-tricarboxylic acid (XIV)**, which melted at 285–286° with decomposition.

Anal. Calcd. for $C_{16}H_9O_6N$: C, 61.72; H, 2.92. Found: C, 61.81; H, 3.19.

3′ - Amino - 5,6 - benzoquinaldine - 4,7 - dicarboxylic Acid Lactam (XV).—Three and sixty-eight hundredths grams of 3-aminonaphthostyril, 0.88 g. of acetaldehyde, and 0.88 g. of pyruvic acid dissolved in 200 cc. of alcohol were refluxed for four hours. After concentration a yellow crystalline precipitate was obtained, which was purified from non-acidic material and was finally obtained in a yield of 0.5 g. It melted at 340–342° with decomposition.

Anal. Calcd. for $C_{16}H_{10}O_3N_2$: C, 69.04; H, 3.62. Found: C, 69.04; H, 3.40.

3-Hydroxy-1,2,3,4-tetrahydro-5,6-benzoquinoline (XVI).—β-Naphthylamine was condensed with an equimolecular amount of epichlorohydrin by the method recently developed for α-naphthylamine derivatives,[11] and the resulting product was purified as the hydrochloride, from dilute hydrochloric acid.

Anal. Calcd. for $C_{13}H_{14}ONCl$: C, 66.22; H, 5.99. Found: C, 66.41; H, 5.95.

The free base after recrystallization melted at 82–83°.

Anal. Calcd. for $C_{13}H_{13}ON$: C, 78.35; H, 6.58. Found: C, 78.65; H, 6.95.

Summary

1. A convenient method of synthesis of certain 4-hydroxyquinoline and 4-hydroxy-5,6-benzoquinoline derivatives has been found in the condensation of aniline and β-naphthylamine derivatives with acetylmalonic ester or ethoxymethylenemalonic ester followed by cyclization at 250°.

2. The method of Conrad and Limpach for the synthesis of 4-hydroxyquinaldine from acetoacetic ester and aniline has been extended to include certain substituted β-naphthylamines.

3. The introduction of a carboxyl group in position 3 of 4-hydroxy-5,6-benzoquinaldine-7-carboxylic acid was accomplished by means of the Reimer–Tiemann reaction.

4. Epichlorohydrin on condensation with β-naphthylamine gave 3-hydroxy-1,2,3,4-tetrahydro-5,6-benzoquinoline.

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[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Cleavage of Quaternary Ammonium Salts by Sodium Sulfide. II

BY H. R. SNYDER AND J. C. SPECK

In an earlier communication[1] it was shown that benzyldimethylphenylammonium chloride (I) is cleaved readily by aqueous sodium sulfide to yield benzyl sulfide and dimethylaniline. A number of other salts containing sulfur in its lower valences were also found to be effective cleaving agents. The reaction is of the same type as that observed in the splitting of thiamin[2] (vitamin B_1) with sodium bisulfite, in which a group similar to benzyl is detached from a quaternary nitrogen atom.

$$2[C_6H_5CH_2N(CH_3)_2C_6H_5]^+Cl^- + Na_2S \longrightarrow (C_6H_5CH_2)_2S + 2C_6H_5N(CH_3)_2 + 2NaCl$$

It now has been found that the groups other than benzyl attached to the nitrogen atom play an important part in the cleavage. For instance, benzyltrimethylammonium chloride was completely unaffected under conditions which brought about rapid decomposition of benzyldimethylphenylammonium chloride. That this difference is not due merely to the weight of the phenyl group was shown by the fact that benzylcyclohexyldiethylammonium chloride also resisted the action of aqueous sodium sulfide. Phenyltrimethylammonium iodide, and tetra-*n*-butylammonium iodide also failed to undergo cleavage. Even the presence of two benzyl groups on the nitrogen atom does not produce an activation similar to that in benzyldimethylphenylammonium chloride, since dibenzyldiethylammonium iodide was only very slightly cleaved. Benzylpyridinium chloride, on the other hand, underwent rapid scission to pyridine and benzyl sulfide. It appears, therefore, that the linkage between an alkyl group and the nitrogen atom of a quaternary salt is labilized when the nitrogen is attached to or is part of an aromatic system.

It might be predicted that the allyl group would display a mobility similar to that of

(1) For the first paper in this series see Snyder and Speck, THIS JOURNAL, **61**, 668 (1939).

(2) Williams, Waterman, Keresztesy and Buchman, *ibid.*, **57**, 536 (1935).

benzyl. This prediction was confirmed by the rapid cleavage of allyldimethylphenylammonium bromide by aqueous sodium sulfide.

It seemed likely that the less reactive quaternary salts might undergo the cleavage if more vigorous conditions were employed. This was accomplished by the use of the high-boiling solvent, diethylene glycol. Benzyltrimethylammonium bromide, which was unaffected by boiling aqueous sodium sulfide, gave more than 50% of cleavage products when the reaction was carried out at 135–150°. Tetra-*n*-butylammonium iodide, which would be expected to fall among the most stable quaternary salts, underwent cleavage to the extent of at least 70% at 175°.

Since sodium hydrosulfite has been used for the reduction of certain quaternary ammonium compounds,[3] it was desirable to test its action on an easily cleaved salt such as benzyldimethylphenylammonium chloride.[4] Rapid cleavage occurred when an aqueous solution of these reagents was heated. The products were dimethylaniline and a neutral salt which proved to be benzyldimethylphenylammonium-S-benzylthiosulfate (II), identical with the product from the action of sodium thiosulfate on the quaternary salt.[1] Meyer[5] has shown that sodium hydrosulfite undergoes hydrolysis to sodium thiosulfate and sodium bisulfite. This may account for the formation of a thiosulfate derivative in the present case, although the possibility of benzylation prior to conversion to thiosulfate is not excluded.

$$2Na_2S_2O_4 + H_2O \longrightarrow Na_2S_2O_3 + 2NaHSO_3$$

$$2[C_6H_5CH_2N(CH_3)_2C_6H_5]^+Cl^- + Na_2S_2O_3 \longrightarrow$$

I

$$C_6H_5N(CH_3)_2 + 2NaCl +$$

$$[C_6H_5CH_2{-}S{-}SO_3]^-[C_6H_5CH_2N(CH_3)_2C_6H_5]^+$$

II

Experimental

Benzylcyclohexyldiethylammonium chloride was prepared by heating benzyl chloride and N,N-diethylcyclohexylamine in absolute alcohol; m. p. 179° (dec.).

Anal. Calcd. for $C_{17}H_{28}NCl$: Cl, 12.6. Found: Cl, 12.7.

Allyldimethylphenylammonium bromide was prepared from allyl bromide and dimethylaniline in anhydrous ether at room temperature. Because of the extreme hygroscopicity of this salt, its melting point was not determined.

Anal. Calcd. for $C_{11}H_{16}NBr$: Br, 33.0. Found: Br, 32.6.

Cleavage with Aqueous Sodium Sulfide.—The procedure employed was that previously described.[1] No evidence of cleavage was observed with benzyltrimethylammonium bromide, phenyltrimethylammonium iodide or tetra-*n*-butylammonium iodide. Benzylcyclohexyldiethylammonium chloride underwent some cleavage, as shown by the formation of a small amount of a water-insoluble oil. Dibenzyldiethylammonium iodide, heated with aqueous sodium sulfide for three hours, gave about 3% of benzyl sulfide. Benzylpyridinium chloride gave 65% of pyridine and 69% of benzyl sulfide. Allyldimethylphenylammonium bromide gave 41% of dimethylaniline and 44% of allyl sulfide.

Cleavage with Sodium Sulfide in Aqueous Diethylene Glycol.—To a solution of 12.0 g. of sodium sulfide hydrate in 80 cc. of diethylene glycol was added 23.0 g. of phenyltrimethylammonium bromide. The solution was heated to reflux for one hour at 135°, read on a thermometer immersed in the solution. Additional diethylene glycol was added until the boiling point rose to 150°, and refluxing was continued one-half hour. The trimethylamine liberated during the heating was absorbed in standard acid; yield 54%. Benzyl sulfide was extracted from the cold reaction mixture with benzene and crystallized from ether; yield 47%.

Fourteen grams of sodium sulfide hydrate was dissolved in 50 cc. of diethylene glycol and the solution was boiled in an open vessel until the temperature was 175°. To the cooled solution was added 22.0 g. of tetra-*n*-butylammonium iodide. The solution was heated under reflux for fifteen minutes. The cooled solution was extracted with petroleum ether. The tri-*n*-butylamine was separated from the solvent by extraction with dilute acid and treatment with alkali. The yield of tri-*n*-butylamine boiling at 205° was 7.5 g. (70%).

Cleavage with Sodium Hydrosulfite.—To 100 cc. of water was added 24.8 g. of benzyldimethylphenylammonium chloride and 17.4 g. of sodium hydrosulfite. The solution was heated under reflux for fifteen minutes. After cooling it was shaken with ether, which caused crystallization of the heavy oil that had formed during the heating. From the ether extraction of the solid and mother liquor there was obtained 3.5 g. (58%) of dimethylaniline. The dry solid weighed 12.4 g. (60%). A sample crystallized from alcohol and ether melted at 104°; this melting point was not depressed by admixture of authentic benzyldimethylphenylammonium-S-benzylthiosulfate.[1]

Anal. Calcd. for $C_{22}H_{25}O_3NS_2$: C, 63.7; H, 6.03; N, 3.38. Found: C, 63.77; H, 6.26; N, 3.20.

Summary

Quaternary ammonium salts containing both an aromatic group and a benzyl or allyl group attached to the nitrogen atom are readily cleaved by boiling aqueous sodium sulfide, yielding benzyl

(3) Karrer, Ishū, Kahnt and van Bergen, *Helv. Chim. Acta*, **21**, 1174 (1938).

(4) Although this quaternary salt and sodium hydrosulfite have been used as ingredients of mixtures employed in dyeing [German Patents 184,381 and 231,543; *Friedlaender*, **8**, 881; **10**, 439], a search of the literature failed to reveal any statement of their interaction.

(5) Meyer, *Z. anorg. Chem.*, **34**, 43 (1903).

or allyl sulfide and a tertiary amine. Other quaternary salts undergo similar cleavage at higher temperatures in diethylene glycol solution.

Benzyldimethylphenylammonium chloride is rapidly cleaved by sodium hydrosulfite, yielding dimethylaniline and benzyldimethylphenylammonium-S-benzylthiosulfate.

URBANA, ILLINOIS RECEIVED AUGUST 21, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NOTRE DAME]

The Hydrogenation of Substituted Acetylenes with Raney Nickel[1]

BY KENNETH N. CAMPBELL AND MICHAEL J. O'CONNOR

Other workers have shown that the course of the catalytic hydrogenation of substituted acetylenes is profoundly influenced both by the nature of the substituents and by the catalyst employed. With platinum catalysts,[2] in general, there is no change in the velocity of hydrogenation when two atoms of hydrogen have been absorbed, while with the less active palladium catalysts,[2,3] there is frequently a great diminution in velocity, and it is possible to isolate the intermediate olefin in a pure state.

In this connection, it seemed of interest to study the catalytic hydrogenation of substituted acetylenes, using Raney nickel as the catalyst. Dupont[4] has made a similar study, which was, however, limited to 1-heptyne, phenylacetylene, 2-octyne and 1-methoxy-2-nonyne. He reported that the two monosubstituted acetylenes showed little or no change in velocity of reduction when one molar equivalent of hydrogen had been absorbed, but that the disubstituted ones did.

We have extended the investigation to include mono- and dialkylacetylenes, mono- and diphenylacetylenes, and phenylmethylacetylene, in order to determine the effect of substitution on the course of the reaction. We have found that all the acetylenes studied are readily reduced at room temperature, and pressures of three to four atmospheres, and that at the beginning, at least, the reaction is markedly exothermic.

Our results show a relation between the symmetry of the acetylene molecule and the course of the reduction. The reduction curves for the monoalkylacetylenes showed a slight change in slope at half reduction, while the dialkylacetylenes showed a more pronounced change in slope, which was particularly noticeable in the case of the symmetrical dialkylacetylenes. Phenylacetylene and phenylmethylacetylene, which are electronically the least symmetrical of the acetylenes studied, showed no change in slope in the reduction curve at half reduction. Diphenylacetylene, on the other hand, readily absorbed one molar equivalent of hydrogen, and the reaction stopped at this point, yielding isostilbene.

By stopping the reduction when one molar equivalent of hydrogen had been absorbed, it was possible to isolate the corresponding olefin in most cases. Raney nickel seems, therefore, to act catalytically similarly to palladium, and is easier to use. This appears to be a good method for preparing many pure olefins, with the double bond in a definite position, which are not readily obtainable by other methods. When the reduction is carried to completion, pure saturated hydrocarbons are obtained. Analyses made on the crude half-reduction products from the monoalkylacetylenes showed that less than 0.5% of acetylene remained. Since the acetylene used up accounts for practically all of the hydrogen absorbed, it is evident that very little saturated hydrocarbon was present. The physical constants of the 1-hexene and 1-heptene obtained by us compare favorably with those recorded in the literature. The method of analysis was not applicable to the products from the dialkylacetylenes, but since these showed a more pronounced change in slope in the reduction curve than did the monoalkylacetylenes, it is justifiable to assume that the olefins obtained are not appreciably contaminated by acetylenes or paraffins. Dupont[4] showed by means of Raman spectra that the olefins obtained by the half-reduction of 2-octyne and 1-methoxy-2-nonyne contained little or no unreduced acetylene.

(1) Paper No. XXXV on the chemistry of substituted acetylenes; previous paper, THIS JOURNAL, **61**, 1462 (1939).

(2) Zalkind, *Z. physik. Chem.*, **104**, 177 (1923); Zalkind and Mokhnach, *J. Russ. Phys.-Chem. Soc.*, **62**, 1643 (1930); Ott and Schroeter, *Ber.*, **60**, 624 (1927).

(3) Bourguel, *Compt. rend.*, **180**, 1753 (1925); Gredy, *Bull. soc. chim.*, [5] **2**, 1029 (1935); Sherrill, THIS JOURNAL, **60**, 2562 (1938); Stoll and Rouve, *Helv. Chim. Acta*, **21**, 1542 (1938).

(4) Dupont, *Bull. soc. chim.*, [5] **3**, 1030 (1936).

No attempt was made in this work to establish the geometrical configuration of the olefins. Since Raney nickel seems to have a catalytic action similar to that of colloidal palladium, and since *cis* olefins are produced by the reduction of dialkylacetylenes with colloidal palladium,[3] it seems reasonable to assume that the olefins obtained in this study had the *cis* configuration. This is supported by the fact that isostilbene was obtained from the half-reduction of diphenylacetylene.

Following the work of Reasenberg, Lieber and Smith,[5] the promoting effect of small amounts of alkali and/or chloroplatinic acid on the catalytic reduction of amylacetylene and dibutylacetylene was investigated. When chloroplatinic acid and alkali were used together, reduction occurred more rapidly in the case of amylacetylene, but there was no significant change in the velocity of reduction of dibutylacetylene (see Fig. 2).

Experimental

Columns.—Unless otherwise noted, all distillations were made through a Fenske–Whitmore total-condensation, partial take-off column, packed with 3-mm. glass helices. The packed section was 12 mm. × 400 mm.

Monoalkylacetylenes.—These were prepared from the alkyl bromides and sodium acetylide in liquid ammonia by the modified Picon synthesis,[6] and purified by distillation through the column.

Dialkylacetylenes.—These were made from the alkyl bromides, sodamide and sodium acetylide by a modification of the procedure of Bried and Hennion.[7] In the case of the unsymmetrical dialkylacetylenes, the higher alkyl group was introduced first.

Arylacetylenes. (a) **Phenylacetylene.**—This was made by a modification of the method described by Vaughn, Vogt and Nieuwland.[8] Sodamide was prepared from 6 gram atoms of sodium in 2.5 liters of liquid ammonia, by the use of ferric nitrate as catalyst.[8] Three moles of finely powdered, dry, styrene dibromide was added, with vigorous mechanical stirring, to the sodamide solution as rapidly as the reaction permitted. Stirring was then continued for two to three hours, after which the mixture was hydrolyzed with ammonium hydroxide and distilled water, and extracted with ether. The ether solution was washed with 15% hydrochloric acid to remove suspended iron oxides and dissolved ammonia, and then with a dilute solution of sodium carbonate and finally with distilled water. The dried solution was distilled *in vacuo* through the column to give 161 g. (52.5%) of phenylacetylene, b. p. 75° (90 mm.). We found this procedure more convenient than that described in "Organic Syntheses."[9]

(b) **Phenylmethylacetylene.**—Two moles of phenylacetylene was added to a solution of 2.2 moles of sodamide in 2 liters of liquid ammonia. The solution was stirred for ninety minutes, and then 3 moles of dimethyl sulfate was added dropwise, with stirring, from a dropping funnel whose stem extended to the surface of the liquid ammonia. The mixture was stirred for about two hours, and was then worked up as described above. Fractionation of the product through the packed column gave 116 g. (50%) of phenylmethylacetylene, b. p. 113° (84 mm.).

(c) **Diphenylacetylene.**[10]—One mole of unsymmetrical diphenyldichloroethane[11] was added slowly to a solution of 3 moles of sodamide in 3 liters of liquid ammonia. The solvent was allowed to evaporate, and the solid residue was stirred with water to remove inorganic salts. The aqueous mixture was extracted with ether, the ethereal solution was washed with dilute hydrochloric acid, sodium carbonate solution and water. Distillation of the ether solution through a Claisen flask *in vacuo* yielded 142 g. (80%) of diphenylacetylene, b. p. 133° (8 mm.), m. p. 59°. The physical constants of the acetylenes used are recorded in Table I.

TABLE I

PHYSICAL CONSTANTS AND YIELDS OF SUBSTITUTED ACETYLENES

Acetylene	Yield, %[a]	B. p., °C.	Press., mm.	$n^{20}D$	d^{20}_4	MR_D Obsd.	MR_D Calcd.
Butyl	60	71	745	1.3982	0.7140	27.67	27.71
Amyl	65	98	737	1.4087	.7285	32.56	32.42
Dipropyl	61	130	749	1.4249	.7573	37.13	37.04
Dibutyl	57	81	27	1.4330	.7698	46.53	46.32
Ethyl *n*-amyl	35	92	97	1.4295	.7616	42.01	41.70
Ethyl isoamyl[c]	35	87	99	1.4280	.7599	41.98	41.70
n-Pr-iso-Am[c]	35	104.5	97	1.4311	.7681	46.51	46.32
n-Bu-*n*-Am[c]	60	113	61	1.4360	.7760	51.21	50.93
Phenyl	53	75	90	1.5485	.9281	34.89	33.44
Phenyl methyl	50	113	84	1.5650	.9388	40.16	38.06
Diphenyl	80	133	8	M. p. 59°			
2-Me-2-hydroxy-3-octyne	50[b]	102	48	1.4452	.8507	43.82	43.32

[a] Based on the alkyl bromide used. In the case of the dialkylacetylenes, the yield is based on the alkyl halide of higher molecular weight. [b] Prepared from acetone and hexynylmagnesium bromide. [c] These compounds have not been reported previously.

Complete Reduction of Acetylenes.—A mixture of 3 g. of Raney nickel, prepared by the method of Covert and Adkins,[12] 0.2 mole of substituted acetylene and 100 ml. of absolute methyl alcohol was shaken with hydrogen in an apparatus similar to that described by Adams.[13] Calibration of the apparatus with maleic acid showed that 0.1 mole of hydrogen corresponded to a change in pressure of 8.5 lb. (0.6 atm.). The initial hydrogen pressure was about 60 lb. per square inch (4 atm.). In all cases reduction was very rapid at first, and there was considerable liberation of heat. Reduction was usually complete in about thirty minutes. The saturated hydrocarbon was isolated by pouring the filtered solution into water, and distilling the dried organic layer through the packed

(5) Reasenberg, Lieber and Smith, THIS JOURNAL, **61**, 384 (1939).
(6) Hennion, *Proc. Indiana Acad. Sci.*, **47**, 116–121 (1938).
(7) Bried and Hennion, THIS JOURNAL, **59**, 1310 (1937).
(8) Vaughn, Vogt and Nieuwland, *ibid.*, **56**, 2120 (1934).
(9) Hessler, "Organic Syntheses," Coll. Vol. I, p. 428.
(10) This is essentially the method developed in this Laboratory by Dr. John Kroeger, and is a modification of that described by Maxwell, Doctoral Dissertation, Iowa State College, 1933.
(11) Buttenberg, *Ann.*, **279**, 324 (1894).
(12) Covert and Adkins, THIS JOURNAL, **54**, 4116 (1932).
(13) Adams and Voorhees, "Organic Syntheses," Coll. Vol. I, p. 53.

column. The results are recorded in Table II. The products gave negative tests for unsaturation with dilute aqueous alkaline potassium permanganate solution and with bromine in carbon tetrachloride.

TABLE II

PHYSICAL CONSTANTS AND YIELDS OF SATURATED HYDROCARBONS

Hydrocarbon	Yield, %	B. p., °C.	Press., mm.	$n^{20}D$	d^{20}_4	MR_D Obsd.	MR_D Calcd.
n-Hexane	85	68	745	1.3763	0.6591	29.96	29.81
n-Heptane	74	96.5	753	1.3883	.6835	34.55	34.53
n-Octane	70	125	747	1.3987	.7039	38.71	39.14
n-Nonane	57	149.6	745	1.4055	.7173	43.79	43.76
n-Decane	75	173.2	745	1.4122	.7301	48.63	48.38
Ethylbenzene	84	136	745	1.4948	.8663	35.67	35.54

From the data obtained during the reduction (see Table III) curves were plotted showing moles of hydrogen absorbed against time in minutes. Typical curves are shown in Fig. 1. The curves obtained showed that for the symmetrical dialkylacetylenes and the acetylenic carbinol there was a sharp change in velocity at half reduction. The change in velocity was less marked, although still definite, with the unsymmetrical dialkylacetylenes and the monoalkylacetylenes, but in the case of phenylacetylene and phenylmethylacetylene there was no appreciable change in velocity at half reduction. The reduction of diphenylacetylene, which was carried out in benzene solution because the substance is not sufficiently soluble in methyl alcohol, stopped when one molar equivalent of hydrogen had been absorbed, and the product isolated was identified as isostilbene.

TABLE III

REDUCTION DATA FOR SUBSTITUTED ACETYLENES

Time, min.	Moles of hydrogen absorbed by acetylenes[a] Butyl	Et *n*-Am	Dipropyl	Phenyl	Phenyl-methyl	2-Me-2-hydroxy-3-octyne
1	0.047	0.059	0.035	0.035	0.118	0.024
2	.141	.150	.129	.071	.235	.090
3	.188	.212	.188	.130	.282	.165
4	.235	.247	.200	.188	.318	.200
5	.259	.271	.212	.235	.341	.224
10	.318	.341	.260	.337	.365	.318
15	.353	.364	.294	.364	.377	...
20	.377	.377	.320	.370	.377	.353
25	.40	.40	.340	.377	.382	.365
30	.40	.40	.353	.377	.382	.365

[a] In each case 0.2 mole of substituted acetylene was used.

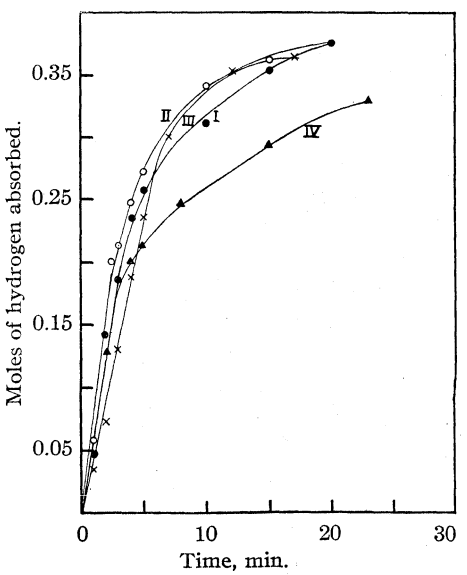


Fig. 1.—●, I, Butylacetylene; ○, II, ethyl-*n*-amyl-acetylene; ×, III, phenylacetylene; ▲, IV, dipropylacetylene.

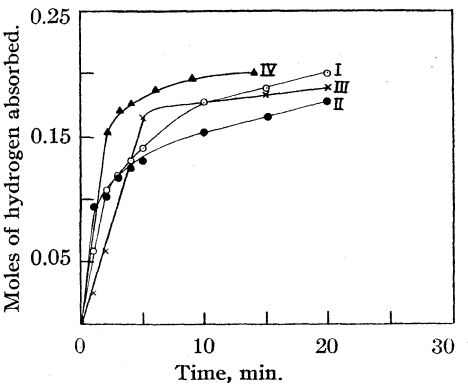


Fig. 2.—○, I, Unpromoted dibutylacetylene; ●, II, dibutylacetylene with alkali and chloroplatinic acid; ×, III, unpromoted amylacetylene; ▲, IV, amylacetylene with alkali and chloroplatinic acid.

Half Reduction of Acetylenes.—The half reductions of the substituted acetylenes were carried out as described above, except that the reaction was stopped when one molar equivalent of hydrogen had been absorbed. This usually required from two to five minutes, whereas in complete reduction the absorption of the second equivalent of hydrogen required fifteen to thirty minutes. Two 0.2-mole runs were combined, and the olefin isolated as described for the saturated hydrocarbons. The properties and yields of the olefins obtained are recorded in Table IV. In the case of styrene, the material tended to polymerize on distillation, and did not give satisfactory physical constants.

In order to determine whether appreciable amounts of substituted acetylene remained when one molar equivalent of hydrogen had been absorbed, analyses were made on the half reduction products of the monoalkylacetylenes. The methyl alcoholic solution from the reduction was filtered to remove the catalyst, diluted to 250 ml. with methyl alcohol and a 10-ml. portion taken for analysis. The sample was treated with 15 ml. of a 2% aqueous solution of silver nitrate, and the nitric acid liberated was titrated to the methyl red end-point with 0.05 *N* sodium hydroxide.[14] The results showed that, in general, at half reduction less than 0.5% of monoalkylacetylene was present before fractionation.

Effect of Promoters.—Following the work of Reasenberg, Lieber and Smith,[5] the promoting effect of alkali

(14) This method has been in common use in this Laboratory for several years.

TABLE IV

PHYSICAL CONSTANTS AND YIELDS OF OLEFINS

Olefin	Yield, %	B.p.,[a] °C.	Press., mm.	$n^{20}D$	d^{20}_4	MR_D Obsd.	MR_D Calcd.
1-Hexene[b]	27	63	742	1.3862	0.6740	29.29	29.44
1-Heptene[b]	77	93	748	1.3990	.7004	33.84	34.06
4-Octene[c]	66	127.0	746	1.4128	.7184	38.86	38.68
3-Nonene[c]	74	147.4	750	1.4173	.7294	43.49	43.30
5-Decene[c]	77	169.6	746	1.4249	.7385	48.47	47.91
7-Me-3-octene[c]	77	140.7	746	1.4168	.7278	43.37	43.30
8-Me-4-nonene[c]	70	163.2	746	1.4229	.7400	48.16	47.91
5-Undecene[c]	86	191.2	750	1.4295	.7516	52.88	52.53
Isostilbene	87	133	8	1.6083	1.0143	60.73	59.18
2-Me-2-hydroxy-3-octene	50	99.4	50	1.4427	0.8387	44.84	45.92
β-Me-styrene	50	166.7	746	1.5420	.9088	40.89	39.69

[a] All boiling points except that for isostilbene were determined by means of the micro-Cottrell apparatus of Willard and Crabtree, *Ind. Eng. Chem., Anal. Ed.*, **8**, 79 (1936). [b] Schmitt and Boord, THIS JOURNAL, **54**, 751 (1932), record the following data: 1-hexene, b. p. 64° (760 mm.), $n^{20}D$ 1.3858, d^{20}_4 0.6732; 1-heptene, b. p. 95° (760 mm.), $n^{20}D$ 1.3999, d^{20}_4 0.6993. [c] These olefins have not been described previously.

and chloroplatinic acid were investigated in the reduction of amylacetylene and dibutylacetylene, as typical examples of mono- and dialkylacetylenes. In the case of amylacetylene, there was no promoting effect when chloroplatinic acid alone was used as promoter, but rather a slight retarding effect was noticed. When alkali and chloroplatinic acid were used together, there was some promotion observed (Fig. 2). In the case of dibutylacetylene, the use of alkali and chloroplatinic acid together resulted in no significant promotion (Fig. 2). The amounts of promoter, catalyst and unsaturated compound used were the same as in the work of Reasenberg, Lieber and Smith,[5] but the pressure was about four atmospheres, rather than one atmosphere.

TABLE V

ANALYTICAL DATA FOR THE NEW OLEFINS AND ACETYLENES

Compound	Calculated % C	Calculated % H	Found % C	Found % H
Et-*i*-Am-acetylene	87.01	12.99	86.95	13.13
Pr-*i*-Am-acetylene	86.87	13.13	86.71	13.31
Bu-*n*-Am-acetylene	86.77	13.23	86.58	13.45
4-Octene	85.62	14.38	85.45	14.61
5-Decene	85.62	14.38	85.80	14.55
3-Nonene	85.62	14.38	85.39	14.47
7-Me-3-octene	85.62	14.38	85.76	14.58
8-Me-4-nonene	85.62	14.38	85.89	14.42
5-Undecene	85.62	14.38	85.73	14.57

Summary

1. The reduction of mono- and disubstituted acetylenes in the presence of Raney nickel has been studied, and a relation shown to exist between the symmetry of the acetylene molecule and the course of the reduction.

2. Several new olefins have been prepared by the half reduction of dialkylacetylenes. The half and complete reduction of acetylenes by means of Raney nickel is a feasible method of preparing certain olefins and saturated hydrocarbons.

NOTRE DAME, INDIANA RECEIVED MAY 22, 1939

[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF HEALTH, UNITED STATES PUBLIC HEALTH SERVICE]

The Conversion of Starch to Crystalline Dextrins by the Action of a New Type of Amylase Separated from Cultures of *Aerobacillus macerans*[1]

BY E. B. TILDEN AND C. S. HUDSON

It was first shown by Schardinger[2] that the cultivation of *Aerobacillus macerans* upon starch solutions produces a mixture of water-soluble dextrins, from which two distinct, non-reducing, crystalline compounds may be readily isolated. Subsequent work by other investigators has not demonstrated with certainty whether these crystalline dextrins represent comparatively simple components of starch itself, or whether they are formed as the result of synthetic activity of the living organism. In the latter case they would seem to be of little importance to the study of the constitution of starch. We now find, however, that when *Aerobacillus macerans* is grown for several weeks upon a potato medium, and the culture fluid is then filtered through a Berkefeld N filter to remove the microörganisms, the filtrate contains an enzyme which will produce the Schardinger dextrins from starch rapidly, and in greater yield than has been previously reported. We infer from this fact that the crystalline dextrins are components of the starch structure, or are closely related to such components.

During the course of the action of the enzyme upon starch there is no significant change in reducing power or optical rotation. In the present study, therefore, the progress of the reaction was followed by measuring the rapid and substantial decrease in viscosity, and also by means of a

(1) Publication authorized by the Surgeon General, U. S. Public Health Service.

(2) F. Schardinger, *Zentr. Bakt. Parasitenk.*, Abt. II, **22**, 98 (1908); **29**, 188 (1911).

simple microscopic test based upon Schardinger's observation that the crystalline alpha and beta dextrins form characteristic crystalline compounds with iodine. By the use of these tests it has been found that the activity of the culture filtrate is usually such that 0.5 ml. will convert 30 mg. of starch in a total volume of 1.5 ml. in thirty minutes at 40°. At 30° the digestion requires twice this period and at 20° four times; at 50°, however, the time taken for digestion is more than half that required at 40°, which indicates that some inactivation has occurred at the higher temperature. The enzyme is active, under the conditions employed, over a *p*H range of 5.6 to 6.4. It is precipitated along with other material by 37.5% acetone in the cold, and can be extracted from this precipitate with one-tenth the original volume of water. Considerable purification is thereby effected, and the activity of the enzyme is unimpaired.

Experimental

Microscopic Iodine Test.—To a drop of 0.1 *N* iodine solution on a spot plate is added 3 drops of the digest. A small quantity of the mixture is transferred with a platinum loop to a microscopic slide. The crystalline iodine compounds may begin to form at once near the edge of the drop, but the progress of the conversion is indicated from the quantity of these crystals that are observed after complete evaporation of the droplet on the slide. Under the microscope the crystals are seen to be a mixture of the green needles and dark blue hexagons characteristic of alpha dextrin, together with the brown prisms formed from beta dextrin. In control tests made upon digests of starch with other amylases, *e. g.*, that of *Aerobacillus polymyxa*, from which the main products are reducing substances, these crystalline iodine compounds were not formed, and the microscopic appearances were entirely different from those observed in the case of the *macerans* digests. This iodine test therefore seems to be specific for the products of the latter enzyme action.

Preparation of the Enzyme.—The potato medium consists of 100 g. of sliced raw potato and 10 g. of calcium carbonate per liter of water. After autoclaving for about an hour at 125° it is cooled and inoculated with a few drops of an active culture of *Aerobacillus macerans*. The new culture is allowed to develop for several weeks at 38°, and the fluid portion is then passed through a Berkefeld N filter. A sample of filtrate which had been kept sterile and cold retained much of its activity for a period of three months.

Details of an Experiment.—A paste containing 57.2 g. of potato starch (equivalent to 50 g. of anhydrous starch) in 2 liters of water was autoclaved at 125° for one hour, cooled to 40°, 100 ml. of a sterile culture filtrate was added under aseptic conditions, and the mixture was diluted with sterile water to give a starch concentration of 2%. The entire experiment was carried out at 40°. Preliminary tests had shown that under the conditions described the digestion should be complete in eight hours. A 250-ml. portion of the mixture was removed aseptically for use in obtaining data on the progress of the reaction, leaving 45 g. of starch in the main body of the solution which was to be used for isolation of the crystalline dextrins.

The change in viscosity was observed at 40° by means of an Ostwald viscosimeter which had an outflow time of ninety seconds for water at this temperature. The initial viscosity of the digest was assumed to be the same as that observed with a separate solution prepared from a culture filtrate which had been previously inactivated by boiling. The outflow time for this solution was 522 seconds, and by expressing viscosity in terms of the ratio t_s/t_w, where t_s is the outflow time for the digest sample, and t_w that for water, the initial viscosity of the digest was 5.80. In one hour the viscosity of the digestion mixture had dropped to 2.62, although the iodine test still showed a blue color, and no crystals were present. In two hours the viscosity was 1.95, the color with iodine was blue-violet, and a few crystals characteristic of Schardinger's iodine compounds had appeared. After four hours the viscosity was 1.11, the color with iodine was brownish-violet, and there was an abundance of the crystalline iodine compounds. By this time the solution had become water-clear, and its rotation in a 2-dm. tube was +8.4°. After six hours the viscosity had become constant at 1.02 and the rotation at +8.1°. The final specific rotation was therefore $[\alpha]_D$ +203°. During the next eight hours there was no change except in the color with iodine, which gradually became nearly a pure brown. Tests for reducing power were made at hourly intervals upon 5-ml. samples of the digest by means of the Shaffer–Hartmann microtechnique[3] and negligible values were obtained at all times. The final reducing power was found to be less than that of a 0.01% solution of glucose. The *p*H, which was initially 6.4, remained constant.

Isolation of the Crystalline Dextrins.—The procedure was that of Schardinger as modified by Lange,[4] who introduced trichloroethylene as a precipitating agent for the crystalline dextrins. The yield of crude product, calculated to the dry basis, was 18 g. or 40%. From this mixture the beta dextrin has been isolated and identified; the remaining material apparently consists largely of the alpha dextrin.

Summary

It is shown that the aqueous fluid from cultures of *Aerobacillus macerans* contains an enzyme which converts gelatinized starch to a high rotating ($[\alpha]_D$+203) mixture of non-reducing dextrins, of which the crystalline alpha and beta dextrins of Schardinger are components, without the production of maltose, glucose or other reducing sugar. We infer, therefore, that these dextrins are not products of the synthetic metabolism of

(3) P. A. Shaffer and A. F. Hartmann, *J. Biol. Chem.*, **45**, 365 (1920–21).

(4) H. Pringsheim, "Chemistry of the Monosaccharides and of the Polysaccharides," McGraw-Hill Book Co., Inc., New York, 1932, p. 280.

the organism but are either the true components of starch or are closely related to such true components. The research is being continued.

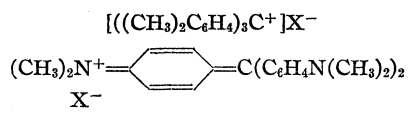
WASHINGTON, D. C. RECEIVED SEPTEMBER 5, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, NO. 201]

Triarylcarbinols. VII.[1] 4′-Dimethylaminobiphenyldiphenylcarbinol and its Relation to the Theory of Color of Dyes

BY AVERY A. MORTON AND WILLIAM H. WOOD

This paper is concerned with the structure of triphenylmethane dyes, particularly with the effect of a dimethylamino group substituted in the 4′-position of a biphenyl nucleus. It will be recalled that Dilthey[2] and Wizinger[3] have abandoned the conventional quinoid formula for dyes in favor of a carbenium, frequently called carbonium, structure in which the central carbon atom is given preference over nitrogen as the seat of basicity. Contrasting models for crystal violet are shown below.



The argument that the positions of nitrogen and carbon in the periodic table should favor a nitrogen base is met by claiming that the basic influence of the dimethylamino group is propagated through the benzene ring to a centrally located and basically enhanced carbon atom so that the latter becomes a superior base. In this scheme the coördinately unsaturated carbon atom is the chromophore which on conversion to the ionized state becomes colored. The dimethylamino group is the auxochrome.

We have applied this view to a system where the two competing, though vinylogously connected, points are separated by an additional phenyl nucleus in order to note, in a quantitative way, whether changes in basicity of the carbonium group are paralleled by changes in the properties of dyes. The sequence of reasoning underlying this work begins with the established fact that replacement of phenyl by a biphenyl nucleus enhances halochromism of triarylcarbinols and therefore by general opinion the basicity of the central carbon atom. This effect is well demonstrated with triphenyl- and trixenylcarbinol. While quantitative comparisons are difficult to make, the latter compound can be estimated qualitatively from colorimetric data of Ziegler and Boye[4] to be over five times stronger than triphenylcarbinol. Moreover, trixenylcarbinol becomes colored in sulfuric acid–acetic acid solution which is about one hundredth the concentration needed to produce color with triphenylcarbinol.[5] There is a definite shift in wave length from 414 to 542 mμ for the larger carbinol. As far as color can be used as the criterion of basicity there is no doubt but that substitution of phenyl by xenyl intensifies this property.

The second link in the chain of arguments is that substituents in the 4′-position of the biphenyl nucleus have their influence propagated through two phenyl nuclei, thus further enhancing the basicity of the central carbon atom. For example, trimethyltrixenyl- and trimethoxytrixenyl-carbinols previously[5] have been observed to show color in acid which is approximately one-tenth and one-hundredth, respectively, the strength needed for trixenylcarbinol. There is also a shift in wave length from 542 for the unsubstituted compound to 575 and 638 mμ for the two substituted compounds, respectively. The evidence is conclusive that there is a definite transfer of influence of substituents over two phenyl bridges and that marked changes in basicity of the central carbon atom can be observed. Indeed, as shown in competitive titrations, the basicity of trimethoxytrixenylcarbinol is not far below that of a dimethylamino group present in a compound of the triarylmethane type.

It then appears reasonable that a dimethylamino substituent in the 4′-position of a carbinol

(1) Previous papers on triarylcarbinols are: Morton and Stevens, THIS JOURNAL, **53**, 2244, 4028 (1931); Morton and Peakes, Jr., *ibid.*, **55**, 2110 (1933); Clapp and Morton, *ibid.*, **59**, 2074 (1937); Morton and Emerson, *ibid.*, **59**, 1947 (1937); **60**, 284 (1938).

(2) Dilthey and Wizinger, *J. prakt. Chem.*, [2] **118**, 321 (1928).

(3) Wizinger, "Organische Farbstoffe," Ferd. Dümmlers Verlag, Bonn, 1933.

(4) Ziegler and Boye, *Ann.*, **458**, 229 (1927).

(5) Morton and Emerson, THIS JOURNAL, **60**, 284 (1938).

which is stronger than triphenylcarbinol might, in the same manner, have an influence transported to the central carbon atom. If Dilthey's view is applicable to this case, the compound should be a dye, possibly more pronounced than the corresponding compound in the triphenylmethane series, but at least with some tendency in that direction. It scarcely would be expected that dye-like properties would be snuffed out entirely. The compound first intended for these tests was *tris*-[4′-dimethylaminobiphenyl]-carbinol, the trixenyl analog of crystal violet. The customary synthesis by sodium condensation applied to preparation of this compound led to an amorphous material which probably contained the desired compound but resisted efforts to purify and crystallize. A pure crystalline compound, however, resulted from the reaction between benzophenone, sodium and 4′-dimethylaminobromodiphenyl. The product, $(CH_3)_2NC_6H_4C_6H_4C(OH)(C_6H_5)_2$, 4′-dimethylaminobiphenyldiphenylcarbinol has one advantage, in that there is only one nitrogen competing against carbon for the anion. Its analog, dimethylaminotriphenylcarbinol, while not strictly a dye has many of the properties of dyes and is correctly considered the prototype of such substances. Unlike the simpler compound, however, the new product gave no color with dilute acids. Not only was it devoid of all properties remotely resembling a dye but the color of the carbinol was not realized until the basicity of the dimethylamino group had been neutralized completely. Moreover, the color of the carbonium salt was yellowish while that of the parent hydrocarbon was red, suggesting that the influence was that caused by a dimethylammonium salt in the 4′-position instead of the expected dimethylamino group. In this connection it is interesting to note that MacLean and Widdows[6] some years ago prepared dimethylaminocinnamyldiphenylcarbinol and found that it gave no color in dilute acids. Furthermore, the *tris*-[4′-dimethylaminobiphenyl]-carbinol, though a crude product, showed in titration experiments that the basicities of the dimethylamino groups were neutralized before any color of a carbonium salt appeared. Apparently no gradual loss of dye-like properties can be observed.

As far as these tests are concerned, there is no tendency toward formation of colors in dilute solution when the distance between the nitrogen atom and a central carbon atom is greater than one benzene ring. The principal seat of basicity in dimethylaminobiphenyldiphenylcarbinol is unquestionably on the nitrogen atom. This location is an eminently reasonable one, too, in all dimethylamino substituted triarylmethane compounds. In an energy transporting system of alternating single and double bonds such as are present in a phenyl nucleus, direction of movement of group influence can be either way. Enhanced basicity of a central carbon atom should accordingly increase the basicity also of the vinylogously connected nitrogen, so that maintenance of the vast natural superiority of nitrogen over carbon as a major sink for basicity of the molecule would thus be favored.

Approximate basicities of a number of amines and trixenylcarbinol have been made (see Table I). The method is not sensitive enough to catch fine differences but does reveal that the behavior of dimethylaminobiphenyldiphenylcarbinol toward perchloric acid is in accord with that expected of dimethylamino substituted compounds in general. The data also show that trixenylcarbinol is definitely stronger than such weak bases as acetamide or benzamide as contrasted with triphenylcarbinol which has been shown[7] to be weaker.

Though the main interest of this research was to test the effect of separating positions of possible basicity, several other interesting observations have been made. Of the three nitroanilines, the meta isomer is by far the strongest base, for it is the only one which can be titrated appreciably with trixenylcarbinol as an indicator. Another interesting point was the five-fold increase in yield of dimethylaminobiphenyl in a sealed tube methylation of the amine as the size of the tube was decreased by half.

Experiments

4′-Dimethylaminobiphenyldiphenylcarbinol.—A solution of 4 g. of 4-bromo-4′-dimethylaminobiphenyl and 2.6 g. of benzophenone in 50 ml. of thiophene-free benzene was refluxed on a steam-bath while 0.7 g. of sodium chips was dropped through a condenser over a three-hour period. The mixture was refluxed for fifteen hours longer and then decomposed with 25 ml. of water. After separation and concentration, the benzene layer was cooled in ice and the yellow amorphous precipitate filtered and dried. Attempts at crystallization were unsuccessful but the material sublimed as a white solid at 200° (0.5 mm.). Recrystal-

(6) MacLean and Widdows, *J. Chem. Soc.*, **105**, 2174 (1914).

(7) Hall and Conant, THIS JOURNAL, **49**, 3047 (1927); Hall, *ibid.*, **52**, 5115 (1930).

lization from alcohol gave fine needles melting at 177–178°; yield 2 g. or 36%; mol. wt. (Rast), 388, 415, 397 (calcd. 379); nitrogen analysis 3.63, 3.55%, calcd. 3.4%. The compound gave a strong red color in concentrated sulfuric acid and a yellow color in dilute solution of perchloric acid in glacial acetic acid. Observation of the light absorption in the Hardy Color Analyzer of the last solution showed the characteristic absorption of tertiary carbinols with a maximum value at 484 mμ.

Titration of the Carbinol.—Mallinckrodt 60% perchloric acid was treated with excess acetic anhydride and diluted with glacial acetic acid until the strength was 0.0421 *N*. The first drop of this solution added to a solution of 0.025 g. (0.000075 mole) of *p*-phenyltriphenylcarbinol[8] caused the appearance of a red color. With 0.028 g. (0.000074 mole) of 4′-dimethylaminobiphenyldiphenylcarbinol 1.9 ml. (0.000080 mole) of the standard acid solution was required before a permanent red color appeared. With 0.014 g. (0.000037 mole) the amount of standard acid required was 0.95 ml. or 0.000040 ml. A mixture of 0.19 g. (0.000057 mole) of *p*-phenyltriphenylcarbinol and 0.0214 g. (0.000057 mole) of 4′-dimethylaminobiphenyldiphenylcarbinol required 1.45 ml. (0.000061 mole) of standard acid. A similar mixture of 0.0182 g. (0.0000373 mole) of trixenylcarbinol and 0.014 g. (0.0000369 mole) of the same dimethylamino compound was neutralized by 0.9 ml. (0.000038 mole) of acid. In all these cases it is apparent that in the presence of 4′-dimethylaminobiphenyldiphenylcarbinol, halochromism is not displayed until enough acid has been added to neutralize the basicity of the dimethylamino group; in absence of this dimethylamino compound it can be observed with the first drop of acid.

TABLE I

In addition to the compounds listed, 2,6-dichloro-4-nitroaniline, diphenyl urea, acetamide, butyramide, benzamide, thiobenzamide, acetanilide, *p*-nitroacetanilide, benzanilide all gave the carbinol color (trixenylcarbinol as an indicator) with the first drop of perchloric acid solution.

Base	Quantity, g.	Moles × 10^5	Acid, ml.	Moles × 10^5
Michler's ketone	0.253	9.44[a]	4.35	18.35
4-Bromo-4′-dimethylaminobiphenyl	.029	11.7	2.75	11.6
Dimethylaniline	.050	41.4	10.4	43.8
m-Nitroaniline	.0566	41.0	9.05	38.1
2,6-Dichloroaniline	.0555	34.2	7.1	30.0
p-Aminobenzoic acid	.0725	52.8	11.8	49.7
p-Aminoacetophenone	.0332	24.6	5.4	22.8
Benzidine	.0410	22.4[a]	10.1	42.6
Anthranilic acid	.0356	26.0	5.6	23.6
Glycine	.0344	45.8	10.2	43.0
o-Nitroaniline	.0543	39.3	No sharp end-point	
p-Nitroaniline	.0619	44.8	No sharp end-point	
sym-Tribromoaniline	.0600	18.2	0.1	...
Diphenylamine	.0565	33.4	3.9	16.4
Urea	.0607	101.1	5.0	21.0
Thiourea	.0525	69.2	12.0	50.1
Diphenylthiourea	.0520	22.8	0.9	3.8

[a] The comparable value is twice this figure.

(8) Clapp and Morton, THIS JOURNAL, **59**, 2074 (1937).

Titration of other Bases Using Trixenylcarbinol as an Indicator.—To ensure that results with the carbinol compound containing the dimethylamino group were not peculiar to this compound a number of bases were titrated in the same manner with 0.0421 perchloric acid in glacial acetic acid. The bases were Eastman Kodak Co. products used without any purification. Results are given in Table I. The series includes enough compounds to show the relative position of trixenylcarbinol as a base.

Titration of Dimethylaminobiphenyldiphenylcarbinol Using Trimethoxytrixenylcarbinol as an Indicator.—The dimethylamino compound 0.0188 g. (0.0000498 mole) in glacial acetic acid with 0.0181 g. (0.0000313 mole) of trimethoxytrixenylcarbinol required only 0.85 ml. (0.0000358 mole) of the standard perchloric acid solution before the blue color of the carbinol appeared. The result indicates that the trimethoxytrixenylcarbinol definitely competes with the dimethylamino compound for the acid and that transfer of group influence through two phenyl nuclei has been appreciable. Similar transfer of basic influence of the dimethylamino groups might therefore be expected.

Attempted Preparation of *tris*-(4′-Dimethylaminobiphenyl)-carbinol.—A solution of 8 g. of 4-bromo-4′-dimethylaminobiphenyl and 3.4 g. of diethyl carbonate in 50 ml. of thiophene-free benzene was refluxed while 2 g. of sodium chips was added over a period of forty-five minutes. After refluxing for sixteen hours longer the excess sodium was decomposed with alcohol and then with water. The mixture was filtered and the benzene layer treated with petroleum ether. A yellow amorphous solid was precipitated. Attempts to isolate a pure carbinol from this mass by crystallization, chromatographic adsorption on alumina, steam distillation to remove impurities, continuous extraction with petroleum ether and with ether, formation of salts with hydrochloric, sulfuric, and perchloric acids, and precipitation of the sodium carbinolate by either sodium or sodium alcoholate were all unsuccessful. The best material was obtained by dissolving the original yellow solid in concentrated sulfuric acid and diluting carefully with water until the sulfate of 4-bromo-4′-dimethylaminobiphenyl was precipitated. The filtrate was then neutralized with ammonia and a solid melting 160–183°, which could not be recrystallized from ether, alcohol or benzene, obtained. No color was observed in dilute acid solution. Titration of 0.0167 g. (equivalent to 0.000027 mole of the expected product) of this material with the standard perchloric acid solution showed that 1.6 ml. (0.000067 mole) could be added before a red carbonium salt color appeared. The product is obviously impure but it is apparent that the reaction produced no product which had any properties of a dye and that the carbinol color was not developed until after considerable neutralization of a stronger base had occurred.

Trixenylcarbinol.—Because so much difficulty was found in attempted syntheses of the above *tris* compound, a number of experiments were made to ensure that the best conditions for preparing the triarylcarbinols by the sodium condensation method were being applied. Best yields were secured when 19 g. of *p*-chlorobiphenyl and 5 g. of diethyl carbonate in 50 ml. of benzene were refluxed on a steam-bath while 5 g. of sodium (cut into chips 0.5 mm.

square and 2 mm. thick while kept under benzene in a beaker) were dropped through the condenser over a period of one-half hour. After twelve hours of refluxing the mixture was decomposed with water, the benzene layer was evaporated to 30 ml. and the carbinol precipitated with petroleum ether. The crude carbinol was then recrystallized either from xylene or alcohol after treatment with decolorizing carbon. Three experiments by this method gave 48, 48 and 47% yields, respectively, and a fourth, for some unexplained reason, gave 55%. Use of sodium sand instead of chips gave only 31%. Pieces of sodium 2–3 mm. in diameter and 2 cm. long produced only 39%. Activation of the chips with a little amyl alcohol before dropping through the condenser lowered the yield to 37%. Freshly distilled and excess diethyl carbonate did not improve the results.

4-Bromo-4′-dimethylbiphenyl.—Methylation of 4-amino-4′-bromobiphenyl (from reduction of the corresponding nitro compound by the method of García-Banús and Medrano[9]) was carried out in sealed tubes using 10 g. of the amino compound, 9 g. of methanol and 3 g. of concentrated hydrochloric acid. The tubes were heated to 140–150° for twelve hours and the products isolated in the conventional manner. The first two runs were made in Carius tubes about 66 cm. in length and gave yields of 0 and 9%. In the next three runs two of the tubes were only 43 cm., while a third was 66 cm. long. The batches were combined and gave an over-all yield of 28%. The final runs were therefore made in tubes only 36 cm. long and gave yields of 42, 44, 45, 42, and 45%. The length of the tube is limited by the volume of the reagent used. Seals of the short tubes must be well annealed in a luminous flame to prevent bursting at reaction temperatures.

(9) García-Banús and Medrano, *Anales soc. españ. fis. quím.*, **20**, 475 (1922); *C. A.*, **17**, 2574 (1923).

Summary

4′-Dimethylaminobiphenyl has been prepared, its failure to have any properties resembling a dye noted, and the absence of any carbonium salt color until neutralization of the basic nitrogen atom observed. These results are not in accord with those predicted from the carbenium theory of triphenylmethane dyes.

Improved conditions for triarylcarbinol formation and for sealed tube methylation of an amine compound have been recorded.

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Triarylcarbinols. VIII. Occurrence of Color with Trixenylcarbonium Salts

BY AVERY A. MORTON AND L. F. MCKENNEY

When trixenylcarbinol is dissolved in nearly dry acetic acid and the solution saturated with dry hydrogen chloride only a slight color is discernible. Upon adding a few drops of water a pronounced red color appears. By adding anhydrous calcium sulfate to the colored solution, the color gradually fades as would be expected if water were removed by the desiccant. It is apparent that water has played a definite part in production of color. Nor is the phenomenon limited to one reagent. Nitromethane, acetonitrile, formamide, urea, methanol, benzamide and many other compounds intensify color in the same way. In all cases intensity of color goes through a maximum as the quantity of agent is increased.

Formation instead of destruction of color with water is remarkable. The action is suggestive of complex formation though efforts to crystallize a complex from the strongly colored solution yielded the carbinol only and the position of the maximum absorption band was not displaced in the case of agents with which the color was intense.

The very weak acid, acetic, will not form a color with the carbinol unless the solution is heated. Nitric acid in acetic acid will produce a color with a few drops of nitromethane but not with water. With still stronger acids, sulfuric and perchloric, colored crystalline salts were obtained. In particular trixenylcarbonium perchlorate, $(C_6H_5C_6H_4)_3CClO_4HClO_4$, was a very stable compound, easily crystallized and purified. Upon electrolyzing a solution of this carbonium salt in nitromethane, nitrobenzene, or glacial acetic acid, the cathode rather than the anode portion became colorless. The same phenomenon was observed with an acetic acid solution of trixenylcarbinol to which a little sulfuric acid had been added, with a nitromethane solution of triphenylcarbonium perchlorate, $(C_6H_5)_3CClO_4$, and with nitromethane solutions of trixenylcarbonium sulfate, nitrate, and chloride. Furthermore, when a very dilute and colorless solution of trixenylcarbonium perchlorate in nitrobenzene was electrolyzed it was about the anode rather than the cathode that color reappeared.

Absence of color at the cathode cannot be due to a chemical reaction such as reduction since pure trixenyl- and triphenylcarbinols were recovered from the cathode compartment after electrolysis of the perchlorate salts in nitromethane. Were reaction at the cathode involved, there would of necessity have been decoloration at the anode due to migration of the supposedly colored cation away from that region. In spite of absence of color at the cathode it was found, in tests with the two perchlorate salts, that the bulk of the triarylcarbinol was isolated from that region. The whole behavior is in agreement with a view that the triarylcarbonium ion, or triarylcarbinol, is not capable of being colored if the perchlorate ion is removed by electrolysis and will appear colored once more when the ion is added.

The above phenomena were differentiated from those of the dye, crystal violet. Electrolysis was carried out in aqueous solution since conductance of this salt in nitromethane proved to be very poor. In this case the cation remained colored. It was deposited and reduced on the platinum anode. The reduced material was recovered and oxidized to reform the dye. Electrolysis of this material was typical of what might be expected. The ammonium ion, carrying the quinoid nucleus, was colored and was conveyed to the cathode compartment where it was reduced. The anode compartment became less colored from migration of the colored cations toward the cathode.

Experiments

Color Formation with Water.—The acetic acid was Mallinckrodt reagent grade which was found to have a melting point of 16.45° corresponding to about 0.1% water by weight. Trixenylcarbinol 0.115 g. (0.00024 mole) was dissolved in 200 ml. of acetic acid and the solution saturated with hydrochloric acid, prepared either from concentrated sulfuric acid and sodium chloride without any drying precautions or from aqueous concentrated hydrochloric acid dropped onto concentrated sulfuric acid, followed by drying over anhydrous aluminum chloride suspended on glass wool. In both cases the resulting acetic acid solution of the carbinol was faintly tinted. Addition of a few drops of water to such a solution caused it to become an intense red color. Samples for color analysis were made up by adding water to 25-ml. portions of the above solution. To maintain a constant volume, enough additional acetic acid was added to each sample to make the total volume equal to 30 ml. The intensity and position of the color band was determined in the Hardy color analyzer using the coördinates which correspond to absorption spectra measurements. The results are given in the table below. The quantity of water is corrected for the amount present in the acetic acid.

TABLE I

Water added, ml.	Acetic acid added, ml.	Total water present, mole	Color intensity[a] D at 542 mμ
0	5.0	0.0014	0.060
0.25	4.75	.0153	.140
0.50	4.50	.0292	.270
1.0	4.0	.0569	.325
2.0	3.0	.1124	.580
3.0	2.0	.1669	.260
4.0	1.0	.2234	.135

[a] D = density, T = transmitted light, $D = \log 1/T$.

The quantity of water plotted against the color intensity is a straight line up to maximum absorption. Beyond that point hydrolysis and precipitation occurred. The maximum absorption was at 542 mμ, a value agreeing well with that, 544, obtained by Burawoy,[1] who used a spectroscope with solutions of trixenylcarbinol and sulfuric acid in acetic acid.

Fading of Color with Calcium Sulfate.—A colored solution formed by dissolving trixenylcarbinol in glacial acetic acid, saturating with hydrogen chloride, and adding a few drops of water, was allowed to remain in contact with anhydrous calcium sulfate (the commercial grade known as Drierite was used). After eighteen hours the color had faded to a very light tint while an identical solution without calcium sulfate remained intensely colored. Addition of two drops of water to the solution which had stood over the drying agent restored the original red color. Tests with magnesium perchlorate and phosphorus pentoxide as desiccants were unsatisfactory because the soluble perchlorate and phosphoric acid themselves developed a color with the carbinol in absence of hydrochloric acid. Sodium sulfate was ineffective as a bleaching agent. The drying action of this last agent is known to be very considerably less than that of calcium sulfate.

Agents Producing Color.—Other compounds besides water have been found to cause a red color in the carbinol–hydrochloric acid–acetic acid solution. In Table II a list of these substances is given. The compounds are arranged in order of descending intensity of color. In the case of agents which imparted approximately equal intensity, the order is based on the moles of reagent required.

Ammonium acetate (ammonia), tetrachloroethane, ethyl iodide, iodobenzene, bromobenzene, phenol, anisole, phenetole, diphenyl ether, acetone, crotonaldehyde, ethyl benzoate, *sym*-trinitrobenzene, and nitrobenzene produced no color under the above conditions. Although small quantities of phenol and tetrachloroethane had no effect, addition of 0.002 g. of the carbinol to phenol or to tetrachloroethane as solvents caused an intense red color to appear.

Crystallization of the Carbinol from the Colored Solution.—The solubility of trixenylcarbinol in glacial acetic acid at room temperature was found to be 2.60 g. per liter. A solution of 0.4888 g. of the carbinol in 200 ml. of nearly dry acetic acid was saturated with dry hydrochloric acid and water added to produce a color. Upon standing crystals of carbinol precipitated from the strongly colored solution. Similar tests were made a number of times with identical results. The crystals were filtered, washed with anhydrous ether, and dried. The melting point varied from

(1) Burawoy, *Ber.*, **64**, 1635 (1931); **66**, 228 (1933).

TABLE II

Compound	Color	Quantity needed to produce maximum color, mole
Nitromethane	Very intense	0.037
Water	Intense	.005
Acetonitrile	Intense	.019
Formamide	Intense	.025
Formanilide	Strong[a]	.0008
Acetanilide	Strong	.0011
Urea	Strong[b]	.0017
Methanol	Strong	.013
Dichlorodiethyl ether	Strong	.035
Propionamide	Medium	.0014
m-Dinitrobenzene	Medium	.0015
Benzamide	Medium	.0041
Acetamide	Medium	.0042
Acetoacetic ester	Medium	.040
Diphenylamine	Light	.003
Ethanol	Light	.017
Benzophenone	Light salmon	.0014
Mesityl oxide	Light salmon[c]	.0022
Acetaldehyde	Light salmon[d]	.018
Iodine (dilute solution in acetic acid)	Light salmon	

[a] Salmon colored instead of red. [b] Color faded in five minutes and a precipitate formed. [c] Color rapidly changed to brown. [d] Color slowly changed to brown.

200 to 201° as compared with the pure carbinol which melts at 206.5–207°.

Solutions of Trixenylchloromethane in Anhydrous Acetic Acid.—Trixenylchloromethane was prepared from the carbinol by reaction with acetyl chloride. The product was recrystallized from dry benzene until it was colorless. Its melting point was 193.0–193.5° with some decomposition. Dry acetic acid was prepared in four different ways to ensure that the color formed with trixenylchloromethane was not due to some impurity. By the first method 400 g. of reagent glacial acetic acid was kept over 50 g. of phosphorus pentoxide for twenty-four hours. It was then distilled through a 20-turn Davis column, all joints being of glass. The portion coming over at 118.4° was again treated with 50 g. more of the pentoxide after which it was distilled through the same column. By the second method, 700 g. of the acid (m. p. 15.65°) was refluxed with 28.3 g. of acetic anhydride and 14 g. of chromic oxide according to the method of Orton and Bradfield.[2] The acid was then distilled through the Davis column mentioned above. The fraction (200 ml.) boiling from 117.6 to 117.7° at 748 mm. was collected. Since both of the above fractions showed a pronounced red color when the chloro compound was dissolved in them, the refluxing with acetic anhydride was repeated in the absence of the chromic acid to ensure that no volatile chromyl compound had been formed. Glacial acetic acid, 700 g., was refluxed for twenty-four hours with 28 g. of acetic anhydride. The fraction which distilled at 118.4 to 118.6° was collected. To ensure further the absence of any inorganic compounds which might produce the color, a physical method of drying was employed. Reagent glacial acetic acid, 200 ml., and 200 ml. of anhydrous thiophene-free benzene were carefully fractionated through the column. A fraction, 100 ml., boiling at 117.8° (750 mm.) was collected and used. With all four samples of acetic acid a light to medium color was obtained when 0.002 g. of trixenylchloromethane was dissolved in 10 ml. of the acid.

Effect of Acetic Acid.—Trixenylcarbinol dissolved in glacial acetic acid was colorless when cold but strongly colored upon heating. The color disappeared when the solution was cooled.

Effect of Nitric Acid.—Trixenylcarbinol, 0.003 g., was dissolved in 15 ml. of glacial acetic acid. To this solution was added 6 drops of red fuming nitric acid (sp. gr. 1.6). No color developed. To 5-ml. portions of this solution were added, respectively, up to 10 drops of water and 1 ml. of nitromethane. The first caused no color while the second produced an intense red solution. Addition of 0.002 g. of the carbinol to concentrated nitric acid produced an intense red color.

Salts of Trixenyl- and Triphenylcarbinols.—Trixenylcarbinol, 1.1 g., was dissolved in 20 ml. of hot acetic anhydride and treated, a drop at a time, with 4 ml. of 60% perchloric acid. Beautiful green plate crystals separated immediately. The solution was cooled in an ice-bath, filtered, and the solid dried for twenty-four hours in an oven at 50–55° or until the analysis for acid content was constant. The yield varied from 80–86%. The analysis was carried out by boiling with standard caustic solution for ten minutes, followed by titration of the excess alkali. The organic matter recovered after this treatment was shown to be pure trixenylcarbinol by its melting point, 206.5–207°. The calculated for $(C_6H_5C_6H_4)_3CClO_4 \cdot HClO_4$ is 29.5% perchloric acid; found 29.6 and 29.7%. The crystals were stable in air and melted sharply at 219.5–220°. They dissolved slightly in benzene, forming colorless solutions which became colored on heating and colorless again on cooling.

Dark red crystals with green iridescence of trixenylcarbonium sulfate could be prepared by a similar reaction. They also could be obtained by cooling a hot solution of trixenylcarbinol in concentrated sulfuric acid. They were spread upon a tile and dried in a vacuum desiccator over solid sodium hydroxide. Because of their hygroscopic nature and the low volatility of sulfuric acid, the analysis was very unsatisfactory: calcd. for $(C_6H_5C_6H_4)_3CHSO_4 \cdot H_2SO_4$ 29.4% sulfuric acid, found 34 and 36%. Pure trixenylcarbinol was recovered as the organic portion from the analysis.

The nitrate was prepared by adding 1 g. of the carbinol to 20 ml. of fuming nitric acid, sp. gr. 1.6. After a half minute it was diluted with an equal volume of water and heated on a steam-bath. The red oil which rose to the top was removed. On cooling, it solidified to a red amorphous mass which reached a constant acid value of 21.3 and 21.4% nitric acid when kept in a vacuum desiccator over caustic. The theoretical for $(C_6H_5C_6H_4)_3NO_3 \cdot HNO_3$ is 21.2%. No nitration of the carbinol had occurred as shown by the melting point of the recovered material. From one preparation a few green (red by transmitted light) needle-shaped crystals of the nitrate salt were obtained which decomposed to a brown oil at 110°. The dark brown triphenylcarbonium perchlorate, prepared in the manner described for the trixenylmethyl compound,

(2) Orton and Bradfield, *J. Chem. Soc.*, 983 (1927).

analyzed within 0.1% of the theoretical for $(C_6H_5)_3CClO_4$ and showed all of the properties already reported by Hofmann[3] and co-workers.

Electrolysis of Trixenylcarbonium Perchlorate and other Salts.—Qualitative observations were made in a V-shaped 11 mm. i. d. tube with platinum electrodes. Solutions of the perchlorate salt were made by addition of a few crystals to anhydrous acetic acid, nitromethane, and nitrobenzene. Upon electrolysis of the resulting colored solutions the cathode compartment became colorless. For analysis of the two compartments a larger cell was made from 23 mm. i. d. tubing with vertical arms 24 cm. apart and 17 cm. high, and provided with a 20-mm. stopcock in the center and smaller cocks for draining the contents from around the platinum electrodes. The perchlorate salt, 150 mg., was dissolved in 130 ml. of Eastman Kodak Company pure nitromethane which had been twice redistilled to yield a fraction boiling at 101°. The current at the start was 14 ma. It rose rapidly to 18 and dropped slowly to 2 within two hundred and twenty minutes. The cathode compartment by that time was entirely colorless. The central stopcock was closed and 15 ml. each drawn off from around the cathode and the anode. The analysis was carried out by adding 5-ml. samples to 0.1 *N* alkali, extracting with ether and reëxtracting the ether layer with water to ensure removal of all of the perchlorate ions. Attempts to titrate the acid portion gave uncertain results because of the presence of traces of nitromethane. The ether layer was evaporated in a weighed beaker and dried to constant weight in an oven at 50–55°. The results are tabulated below.

Trixenylcarbinol	Milligrams per 5 ml. in samples 1 and 2		Average
From cathode compartment	7.3	7.5	7.4
From anode compartment	2.0	2.2	2.1
In original solution	4.0	4.4	4.2

Although the gain, 3.2 mg. around the cathode, was greater than the loss, 2.1 mg. about the anode, the evidence of transference of the carbinol toward the cathode is well beyond experimental error. The triarylcarbinol recovered from either compartment had a melting point of 206.5–207° identical with that of our purest samples. A mixed melting point showed no depression. When examined under the microscope the recovered crystals appeared to be entirely of one kind and identical with trixenylcarbinol.

A solution of 150 mg. of the perchlorate salt in 100 ml. of nitrobenzene had a strong purplish-red color. Upon dilution to one-fifth of this strength the color first appeared red and then turned colorless after a time. Upon electrolysis of this dilute solution a red color reappeared at the anode while the cathode portion remained colorless. Similar disappearances of color, possibly due to hydrolysis, were noted upon dilution of solutions in nitromethane and acetic acid.

Nitromethane solutions of the sulfate (1 mg. per 5 ml.), the chloride (6 mg. per 5 ml.), and the nitrate (12 mg. per 5 ml.) were electrolyzed in the V-shaped cell. In each case the cathode compartment became colorless.

Trixenyl- or triphenylcarbinol was electrolyzed in a solution of commercial glacial acetic acid, Mallinckrodt reagent grade, to which 3–4 drops of concentrated sulfuric acid were added. In both cases the solution became entirely colorless around the cathode.

Electrolysis of Triphenylcarbonium Perchlorate.—When the brown solution of 160 mg. of the perchlorate salt in 140 ml. of nitromethane was electrolyzed the cathode compartment became colorless as in the case of the trixenyl compound. The analysis was carried out in a similar manner and is recorded below.

Triphenylcarbinol	Milligrams per 5 ml. in samples 1 and 2		Average
From cathode compartment	6.9	6.1	6.5
From anode compartment	3.1	3.6	3.4
In original solution	4.0	4.4	4.2

The triphenylcarbinol recovered from the anode and the cathode was shown to be identical with an authentic sample by melting point, mixed melting point, and microscopic examination.

Electrolysis of Crystal Violet.—Solutions of crystal violet—approximately 2.5 mg. per 50 ml. of water—were electrolyzed in the large cell. After ten hours the cathode region was almost colorless and the anode section showed a considerable decrease in color intensity. Some colorless solid material which had been deposited on the platinum cathode was dissolved in hydrochloric acid and treated with lead dioxide. The blue color of crystal violet reappeared.

Summary

Addition of small amounts of water and some other compounds to a solution of trixenylcarbinol in glacial acetic acid saturated with hydrochloric acid causes formation of an intense red color.

Trixenylcarbonium perchlorate and triphenylcarbonium perchlorate have been prepared. Solutions of the former salt when subjected to electrolysis in organic solvents show disappearance of color around the cathode rather than in the anode compartment.

CAMBRIDGE, MASS. RECEIVED JULY 18, 1939

(3) Hofmann, Kirmreuther and Thal, *Ber.*, **43**, 183 (1910).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF SOUTH CAROLINA]

Monoalkyl Phthalates from Normal Aliphatic Alcohols

BY JAMES F. GOGGANS, JR., AND J. E. COPENHAVER

This work was undertaken because of the growing importance of the alkyl phthalates and the possibility of using them as checks for identification of alcohols, as well as to study the type of melting point curve given by these derivatives. Pickard and Kenyon[1] and others have prepared monoesters of the secondary alcohols for use in resolving their racemic mixtures, and some of the metallic salts of the monoesters have been patented for use in synthetic resins, yet very few of the normal monoesters have been described. The melting points and analyses are given in Table I and plotted in Fig. 1.

TABLE I

Ester	M. p. (corr.)	Acid number Calcd.	Found
Methyl[a]	82.4–82.7	311.5	313.1
Ethyl[b]	(47–48)	...	...
Propyl	54.1–54.4	269.6	270.3
Butyl	73.1–73.5	252.6	252.8
Amyl	75.4–75.6	237.6	237.0
Hexyl	24.6–25.4	224.3	222.9
Heptyl	16.5–17.5	212.4	211.8
Octyl	21.5–22.5	201.7	202.2
Nonyl	42.4–42.6	192.0	192.6
Decyl	37.8–38.0	183.2	182.7
Undecyl	43.8–44.1	175.2	175.2
Dodecyl	50.2–50.4	167.9	168.1
Tridecyl	52.4–52.7	161.1	160.2
Tetradecyl	59.8–60.0	154.9	154.6
Pentadecyl	60.3–60.5	149.1	148.9
Hexadecyl[c]	66.7–66.9	143.7	144.0
Heptadecyl	66.6–66.8	138.8	138.4
Octadecyl	72.4–72.6	134.1	133.4
Nonadecyl	70.8–71.0	...	...
Eicosyl	77.1–77.3	...	...

[a] Walker, *J. Chem. Soc.*, **61**, 717 (1892), gave m. p. 82.5°; Cohen, Woodroffe and Anderson, *ibid.*, **109**, 231 (1916); Kitamura, *J. Pharm. Soc. Japan*, **58**, 29–37 (1938), gave m. p. 82–82.5°.

[b] Amann, *Monatsh.*, **36**, 505–8 (1915), gave m. p. 47–48° after keeping at low temperature for a long time for crystallization.

[c] Willstätter, Mayer and Hüni, *Ann.*, **378**, 90 (1911), gave the m. p. as 61–62°.

Experimental

The method of preparation and purification of Pickard and Kenyon was followed with certain modifications. Esters from methyl through butyl were prepared by heating 4 g. of the anhydride with 1 g. of the alcohol at the reflux temperature for thirty minutes. From amyl to octadecyl, 0.5 g. of alcohol was heated with twice the required amount of anhydride at 105–110° for periods varying from thirty minutes to two hours, as the molecular weight of the alcohol increased. With nonadecyl and eicosyl, only 0.25 g. of the alcohol was used.

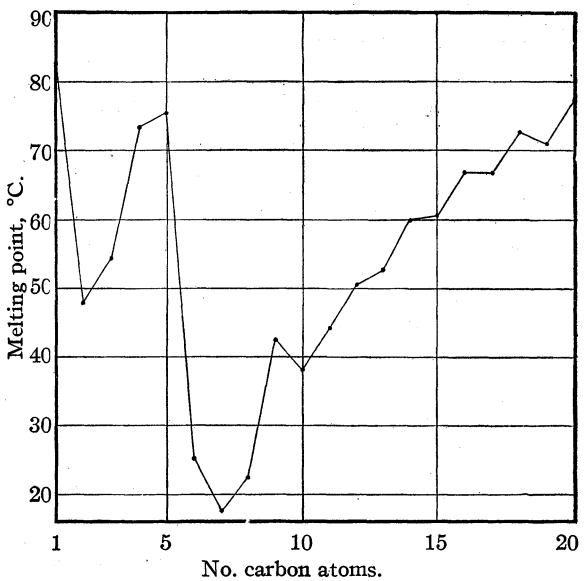


Fig. 1.—Melting points of the monoalkyl phthalates.

For purification, the reaction mass from methyl to hexyl was shaken with 25 cc. of benzene, filtered from excess anhydride and neutralized by dilute sodium carbonate, leaving the mixture slightly acid. The aqueous layer was extracted three times with 50-cc. portions of benzene to remove the unreacted alcohol and possible diesters. The esters were precipitated as colorless liquids or white crystalline solids from the water solution by dilute hydrochloric acid and crystallized three times from a mixture of 90% petroleum ether and 10% benzene.

As the sodium salts of the esters above octyl tend to form emulsions, the following procedure was used. The reaction mass was treated with 25 cc. of ether and filtered to remove the excess anhydride. After evaporating the ether, it was treated for forty-five minutes with 60 cc. of water, warming to 60–65° to hydrolyze any remaining anhydride. The dried residue was dissolved in 10 cc. of chloroform and filtered to remove any phthalic acid. The chloroform was evaporated under vacuum and the esters recrystallized three times from petroleum ether. It was found advantageous to use Dry-ice for cooling the solutions of the esters from hexyl through decyl, the solvent being removed by suction through a small tube tipped with porous alundum.

The melting points were taken, with mechanical stirring, in a 200-cc. bulb, fitted with a side-arm for the thermometer and melting point tube. Standard Anschütz ther-

(1) Pickard and Kenyon, *J. Chem. Soc.*, **91**, 2058–2061 (1907); **99**, 58 (1911); **103**, 1937 (1913).

mometers were used so the melting points may be regarded as corrected. The molecular weights were determined by titrating the esters, dissolved in 50% alcohol, with standard sodium hydroxide. The yields averaged from 35 to 50%.

Discussion

Due to the ease of hydrolysis and the time necessary at low temperature for crystallization, the ethyl ester was not isolated in pure enough form for analysis, hence Amann's value is used in the curve. The esters are white crystalline solids, having very definite melting points and soluble in organic solvents. There is sufficient variation in the melting points through dodecyl so that they could be used very satisfactorily as checks on the identification of the individual alcohols. It will be noted that up to decyl the melting points give a curious pattern and from this ester on, alternation gradually increases, both the odd and even ones forming smooth curves.

This problem was suggested by Dr. E. Emmet Reid, Research Adviser, University of South Carolina, and to him the authors wish to express their appreciation for assistance, and for the higher alcohols, the odd ones from undecyl to heptadecyl being those prepared by Meyer and Reid.[2]

Summary

The monoalkyl phthalates of the normal alcohols from methyl to eicosyl have been prepared and their melting points determined. A melting point curve is shown; it exhibits regular alternation above the decyl ester.

(2) Meyer and Reid, THIS JOURNAL, **55**, 1574 (1933).

COLUMBIA, S. C. RECEIVED AUGUST 15, 1939

[CONTRIBUTION FROM THE KEDZIE CHEMICAL LABORATORY, MICHIGAN STATE COLLEGE OF AGRICULTURE AND APPLIED SCIENCE]

The Sterols of Alfalfa Seed Oil. I

BY L. CARROLL KING AND CHARLES D. BALL, JR.

1. Introduction

The fat constants and fatty acids of alfalfa seed oil have been studied by Jacobson and Holmes,[1] Schuette, Vogel and Wartinbee,[2] and by Schuette and Vogel.[3] As far as can be determined, there has been no previous account of an investigation of the unsaponifiable material from alfalfa seed oil.

About 4% of the oil which can be extracted from alfalfa seed with ethyl ether is unsaponifiable. This unsaponifiable portion consists of a crystalline substance or substances which represent about 35% of the total unsaponifiable, and of a clear, reddish, oily liquid which makes up the remainder.

The crystalline material consists primarily of a sterol very similar to or identical with the sterol isolated by Heyl, Wise and Speer[4] and Clenshaw and Smedley-MacLean[5] from spinach fat and later termed α-spinasterol by Hart and Heyl.[6] Simpson[7] in 1937 isolated α-spinasterol from senega root. The formula first assigned to α-spinasterol by Hart and Heyl[6] was $C_{27}H_{46}O$. Recent work by Larsen[8] on the completely reduced sterol, spinastanol, showed the latter to be identical with fucostanol and stigmastanol, for which the formula $C_{29}H_{52}O$ has been accepted. Since Larsen and Heyl[9] showed α-spinasterol to be doubly unsaturated, the formula for α-spinasterol, therefore, would be $C_{29}H_{48}O$.

The reddish oily fraction gives a positive Liebermann–Burchard reaction, but colors only the sulfuric acid layer in the Salkowski reaction. The Whitby B reaction[10] is positive. Further work on this material is in progress in this Laboratory.

2. Experimental

Extraction of Seed.—Ground alfalfa seed (*Medicago sativa* L.) was extracted continuously with hot diethyl ether. The extract was then filtered and the solvent distilled off in the presence of an atmosphere of carbon dioxide; yield 11.8% of a greenish oil which had an index of refraction of 1.4820 at 15°. The fat constants of this oil were in good agreement with those obtained by Jacobson and Holmes.[1]

Saponification.—To 100 g. of alfalfa seed oil was added 600 ml. of ethyl alcohol and 100 ml. of 50% potassium hydroxide. This mixture was refluxed for one hour,

(1) Jacobson and Holmes, THIS JOURNAL, **38**, 480 (1916).
(2) Schuette, Vogel and Wartinbee, *Oil and Soap*, **15**, 35 (1938).
(3) Schuette and Vogel, *ibid.*, **16**, 16 (1939).
(4) Heyl, Wise and Speer, *J. Biol. Chem.*, **82**, 111 (1929).
(5) Clenshaw and Smedley-MacLean, *Biochem. J.*, **23**, 107 (1929).
(6) Hart and Heyl, *J. Biol. Chem.*, **95**, 311 (1932).
(7) Simpson, *J. Chem. Soc.*, 730 (1937).
(8) Larsen, THIS JOURNAL, **60**, 2431 (1938).
(9) Larsen and Heyl, *ibid.*, **56**, 2663 (1934).
(10) Whitby, *Biochem. J.*, **17**, 5 (1928).

cooled and exhaustively extracted with petroleum ether. The petroleum ether extracts were washed free from potassium hydroxide, using 10% alcohol. The solvent was then evaporated; yield 4 g. of unsaponifiable material.

Separation of Fractions.—The unsaponifiable fraction was taken up in 50 ml. of petroleum ether and allowed to stand. A slow growth of crystalline material took place. After one week this crystalline material was centrifuged, washed twice with petroleum ether, and recrystallized, once from petroleum ether and twice from absolute alcohol. The resulting crystals (Fraction I) were cholesterol-like plates and had a melting point of 164.4–164.8°. The mother liquor from Fraction I was reduced in volume to 25 ml. and allowed to stand. A second crop of crystals identical with Fraction I was obtained.

The mother liquor from the above fraction was placed in the icebox. A slow growth of crystalline material again took place. After two weeks this crystalline substance was separated. It was recrystallized once from petroleum ether and twice from absolute alcohol. The crystals (Fraction II) were elongated hexagonal plate-like structures, and had a melting point of 160–161°.

The mother liquor from the above fractions was evaporated to about 10 ml. and returned to the icebox for three weeks. The crystalline material, which grew slowly, was separated by diluting with cold petroleum ether and centrifuging. The substance was recrystallized once from petroleum ether and three times from absolute alcohol. The crystals (Fraction III) were elongated hexagonal plate-like structures and melted at 155–156°. No further crystalline material could be separated from the mother liquors. The reddish oil remaining weighed 2.6 g. and represented about 65% of the total unsaponifiable fraction.

Characterization of Fraction I.—The Liebermann–Burchard and Whitby B reactions were positive; the Salkowski reaction, negative. A series of esters of Fraction I was prepared. To prepare the acetate the sterol was refluxed in acetyl chloride until solution was effected, and for about ten minutes thereafter. The reaction mixture was cooled and then poured into water. The ester was then filtered off, washed with water and recrystallized twice from alcohol. The benzoyl ester, the *p*-nitrobenzoyl ester and the butyryl ester were prepared according to the procedure given by Hart and Heyl,[6] except that they were recrystallized from absolute alcohol. The phenylurethan was prepared by treating the sterol with phenyl isocyanate in petroleum ether solution. The product was recrystallized twice from absolute alcohol and once from ethyl acetate. Carbon and hydrogen determinations were run on the acetyl, the benzoyl and the *p*-nitrobenzoyl esters by the micro methods of F. Pregl.[11]

A summary of the constants and analyses of these compounds is given in Table I. The melting points of these derivatives checked quite closely with the corresponding derivatives for α-spinasterol cited by Sobotka.[12]

Bromination of Fraction I.—The sterol when dissolved in carbon disulfide and a solution of bromine in carbon disulfide added, gave only a soluble oil. Attempts to brominate in ether gave the same result. An attempt to brominate the acetate in ether solution also resulted in the formation of a soluble oil.

TABLE I

Compound	M. p., °C.	Analysis, % C Calcd.[a]	C Found	H Calcd.[a]	H Found
Sterol	164.4–164.8	84.4	83.0	11.7	11.7
Sterol acetate	180–181	81.93	81.84	11.01	11.21
Sterol benzoate	196–197	83.72	83.52	10.08	10.44
Sterol *p*-nitrobenzoate	211–213	77.00	76.34	9.26	9.49
Sterol phenylurethan	173–174				
Sterol butyrate	123–125				

[a] The required values are calculated from the formula $C_{29}H_{48}O$.

Mixed Melting Point Determinations.—A mixed melting point determination on Fraction I and α-spinasterol[13] gave no depression. The acetyl and *p*-nitrobenzoyl esters of α-spinasterol were prepared according to the same procedure used in preparing the corresponding esters of Fraction I. These compounds had the same melting points as the respective esters of Fraction I, and when corresponding esters from each source were mixed there was no melting point depression.

Preliminary work on Fractions II and III indicated that the crystalline substance in these fractions is also mainly α-spinasterol. However, the melting points of the derivatives corresponding to those for Fraction I were uniformly lower. Mixed melting point data indicated that other material contaminated the sterol. The Liebermann–Burchard, Whitby B, and Salkowski reactions were practically identical with those obtained for Fraction I. Further work on these fractions is in progress.

3. Discussion

A comparison of the melting point data, mixed melting point data, and analysis of the alfalfa seed sterol with that for the sterol reported by Heyl, Wise and Speer,[4] and later termed α-spinasterol by Hart and Heyl,[6] and by Larsen and Heyl[9] indicate that the alfalfa seed sterol is identical or very closely related to α-spinasterol. The observed and calculated values for the percentage of carbon in the free sterol leave something to be desired. However, it is interesting to note that if the data presented by Heyl, Wise and Speer[4] be calculated in the same manner as in the present work and not on the assumption of the presence of 1.0 molecule of water, their values for the percentage of carbon and percentage of hydrogen would be 83.2 and 11.7, respectively, agreeing closely with those reported in this paper. Further, the alfalfa seed sterol failed to give a crystalline bromide. The same observation was made

(11) Roth, translated by Daw, "Quantitative Organic Microanalysis of F. Pregl," P. Blakiston's Son and Co., Inc., Philadelphia, Pa., 1937.

(12) Sobotka, "Chemistry of the Sterids," The Williams and Wilkins Co., Baltimore, Md., 1938.

(13) We are indebted to Dr. Kolloff of the Upjohn Research Laboratories who very kindly supplied us with a specimen of α-spinasterol.

by Larsen and Heyl[9] and by Simpson[7] when they attempted to brominate α-spinasterol.

Summary

1. The unsaponifiable fraction of alfalfa seed oil has been separated into a crystalline substance and an oily mixture.

2. The crystalline substance is believed to be α-spinasterol.

EAST LANSING, MICHIGAN RECEIVED JULY 20, 1939

[CONTRIBUTION FROM THE C. F. KETTERING FOUNDATION FOR THE STUDY OF CHLOROPHYLL AND PHOTOSYNTHESIS]

Porphyrin Studies. III.[1] The Structure of the Porphine[2] Ring System

BY PAUL ROTHEMUND

The importance of the porphine ring system is evident from the fact that it is the fundamental ring system of all the porphyrins. "Chlorins" are dihydroporphines, and the—thus far hypothetical—"Phorbine" ring, which is present in the chlorophylls, differs from chlorin only by the addition of an isocyclic ring in 6,γ-position.

Some time ago the author reported the synthesis of porphine by the interaction of pyrrole and formaldehyde.[3] It was found that many aldehydes can be condensed with pyrrole to yield porphines, in which the four *meso* (*ms*-) positions α, β, γ, and δ, carry the residue from the corresponding aldehyde as substituent. The reaction seems to be a general one of aldehydes, for more than 25 aliphatic, aromatic, and heterocyclic aldehydes gave positive results in this porphyrin formation. In this synthetic work a number of facts relating to the structure of the porphine ring have been observed.

In the second publication quoted above[3] it was mentioned that under certain conditions the reaction mixture from the porphine synthesis contained, in addition to porphine, a porphyrin with a hydrochloric acid number much lower than that of porphine. In comparison with porphine the two main absorption bands of this porphyrin were shifted about 100 Å. toward the red region of the spectrum. The new porphyrin formed only in small quantities, while porphine of hydrochloric acid number 3.3 was the main product. The hydrochloric acid number was 0.5, and the elementary analysis checked with that of porphine within the limits of analytical error. Each of the two porphyrins formed complex metal salts with magnesium ("phyllin"), iron ("hemin"), and copper. The low yields of the porphyrin with hydrochloric acid number 0.5 have prevented the preparation of complex metal salts other than the ones mentioned above so far, but from the component of hydrochloric acid number 3.3 the silver, zinc, cadmium, cobalt and nickel salt were prepared.

The direct determination of the molecular weight of the two porphyrins met with failure so far, but from analytical and spectroscopic data of the free compounds and of their metal complex salts, the author assumes that the new porphyrin isolated in the synthesis of porphine from pyrrole and formaldehyde is the isomer of porphine, and he suggests the term "isoporphine" for it. Two structural formulas may represent the difference in structure of the two compounds: formula I with hydrogen atoms linked to the nitrogen atoms in rings I and II (adjacent rings), and formula II, in which these hydrogen atoms are attached to nitrogen in rings II and IV (opposite rings).

There is, at present, no possibility of assigning one configuration absolutely to either compound, hence the use of the name porphine for structure I, and isoporphine for structure II is still arbitrary.

These structural formulas are drawn to show a double bond between carbon atom γ and the α carbon atom of ring IV (nomenclature of H. Fischer[4]). The presence of a double, not a single, bond between these carbon atoms has been postulated from physicochemical data by Stern.[5]

(1) Paper II, THIS JOURNAL, **58**, 625 (1936).

(2) In preceding papers we spelled "Porphin," because the term was introduced in this form into the chemical literature by H. Fischer for the—at that time hypothetical—fundamental ring system of porphyrins [H. Fischer and P. Halbig, *Ann.*, **448**, 193 (1926)]. Dr. Austin M. Patterson, member for the United States of the Committee on Organic Nomenclature of the International Union of Chemistry, and Chairman of the American Committee, recommended strongly to change the spelling in English to "Porphine," the final *e* signifying the basic character of the compound. He recommended further that the spelling of porphyrin be maintained.

(3) Rothemund, THIS JOURNAL, **57**, 2010 (1935); **58**, 625 (1936).

(4) Fischer, Halbig and Walach, *Ann.*, **452**, 268 (1927); Fischer, Moldenhauer and Süs, *ibid.*, **486**, 107 (1931).

(5) Stern and Wenderlein, *Z. physik. Chem.*, **A175**, 405 (1936).

The structures of porphine and isoporphine given above seem to be the best patterns not only for writing the formulas of nuclear-isomeric porphyrins, but also for the representation of the more complicated, partially hydrogenated compounds with porphine or isoporphine ring, as encountered in the chlorophylls and their derivatives.

Examples of this type of isomerism had been unknown so far. The author and his co-workers were, therefore, greatly interested in checking the synthesis of meso-(= α, β, γ, δ-)-tetrasubstituted porphines[3] with respect to a possible formation of two isomers. These syntheses yielded indeed in many cases two porphyrins with different hydrochloric acid numbers; their separation by fractionation with hydrochloric acid usually worked satisfactorily, and the isolated porphyrins showed characteristic differences in their spectra in ether.

The table gives some of the experimental results in abbreviated form; publication of the details will follow soon.[6]

TABLE I

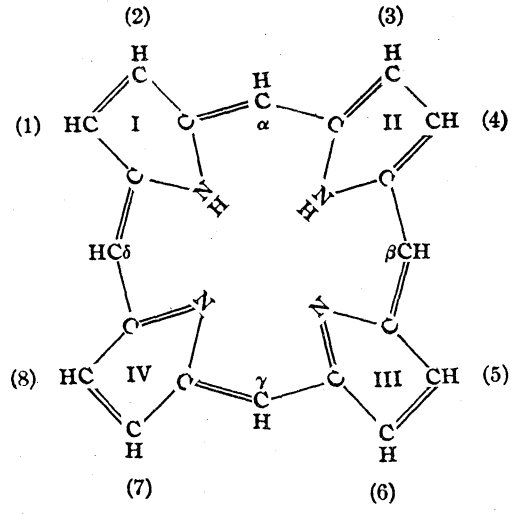
A question mark in a column indicates that the porphyrin has been found in the reaction, but that the purification has not been sufficient to determine its hydrochloric acid number.

Porphyrin	Hydrochloric acid number	
Porphine	3.3	0.5
$\alpha,\beta,\gamma,\delta$-Tetramethylporphine	0.5	0.075
$\alpha,\beta,\gamma,\delta$-Tetrapropylporphine	Near 8	2.3
$\alpha,\beta,\gamma,\delta$-Tetra-*n*-butylporphine	Near 14	7.0
$\alpha,\beta,\gamma,\delta$-Tetraisobutylporphine	?	5.2
$\alpha,\beta,\gamma,\delta$-Tetraphenylporphine	13.5	8.5
$\alpha,\beta,\gamma,\delta$-Tetrakis-3-methoxy-4-hydroxyphenylporphine	1.04	0.45
$\alpha,\beta,\gamma,\delta$-Tetrakis-*o*-hydroxyphenylporphine	15.7	?
$\alpha,\beta,\gamma,\delta$-Tetrakis-*m*-hydroxyphenylporphine	6.0	12.2
$\alpha,\beta,\gamma,\delta$-Tetrakis-*p*-methoxyphenylporphine	4	16.8

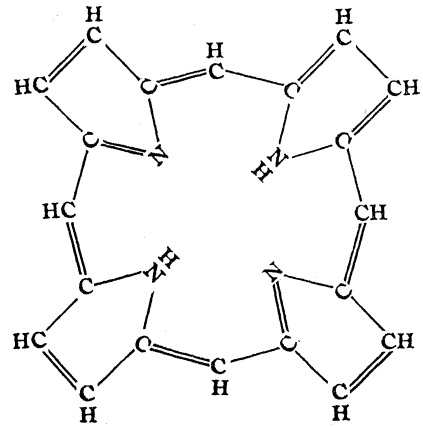
In Fig. 2 the absorption spectra of porphine, isoporphine and of their magnesium complex salts ("phyllins") are given diagrammatically. The characteristic spectroscopic differences are not very large, but they are sufficient to recognize an admixture of about 10 to 20% of one isomer to a solution of the other by visual spectroscopy.

The curve of the molecular absorption coefficient of porphine in ether solution throughout the visible region of the spectrum has been published

(6) Theses in partial fulfilment of the requirements for the degree of Doctor of Philosophy, Graduate School, The Ohio State University (of Th. Londergan, A. Menotti and J. Van Cleve).



Porphine



Isoporphine

Fig. 1.

by Dr. Albers and Dr. Knorr of this Laboratory.[7]

In accordance with the formulas in Fig. 1, we write the structures of the metal complex salts, *e. g.*, the phyllins, in the following manner (Fig. 3).

Haurowitz[8] could not find any connection between ion radius and absorption bands in porphyrins and their metal complex salts, and he concluded that a formula of type I (Figs. 1 and 3) with linkage of the metal to the nitrogen of adjacent rings, is improbable. He formulates the porphine ring as a biradical with ten conjugated double bonds. Stern[5] has set forth several objections to this assumption. It is hoped by the author of this paper that further studies, especially the comparative evaluation of absorption and fluorescence spectra, and the determination of the magnetic susceptibilities, of the porphines and the mesotetrasubstituted porphines will elucidate this matter. The röntgenographic investigation of these porphyrins and their com-

(7) Albers and Knorr, *J. Chem. Phys.*, **4**, 422 (1936).

(8) Haurowitz, *Ber.*, **68**, 1795 (1935); *ibid.*, **71**, 1404 (1938).

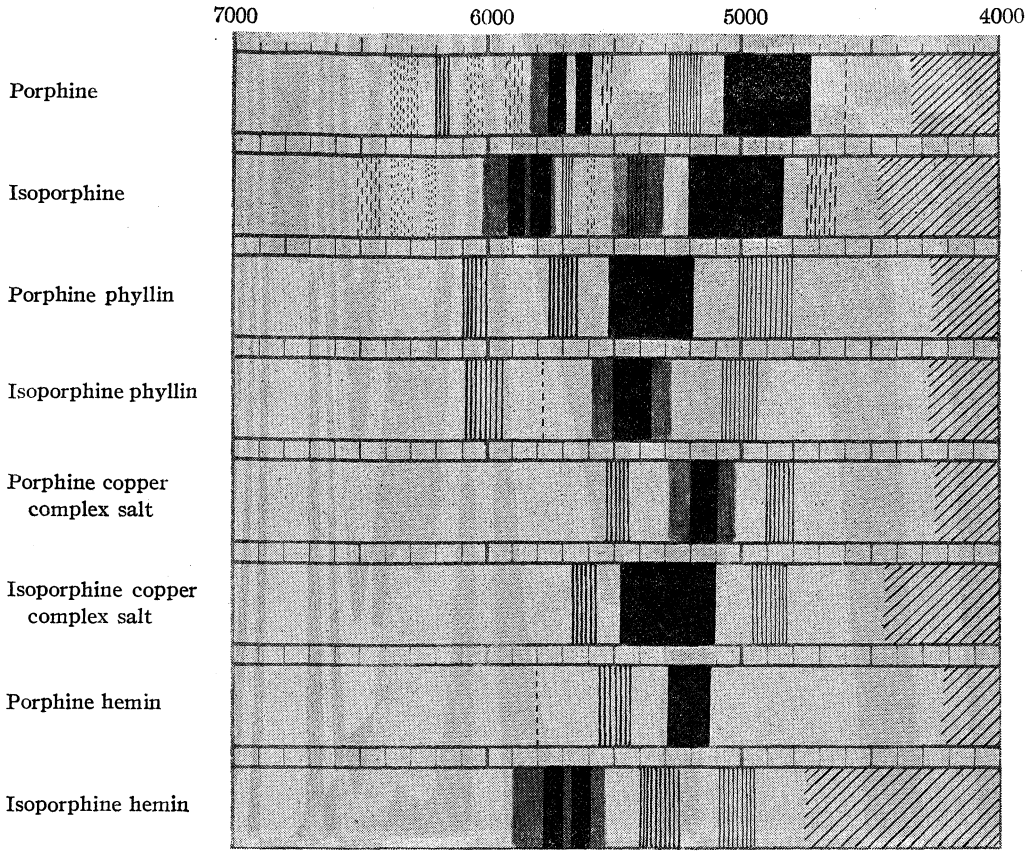


Fig. 2.

plex salts has been started by Professor Blake, Department of Physics, The Ohio State University.

In the issue of *Liebigs Annalen* of June 23, 1939, which has just been received, Helberger[9] described the synthesis of an isomer tetrabenzoporphine, which he named isotetrabenzoporphine. It was obtained from an oxygen-containing "Hydrogenation product 1," which in turn had been prepared by catalytic hydrogenation of *o*-cyanacetophenone. This isomer is especially interesting in connection with our synthesis of $\alpha,\beta,\gamma,\delta$-tetraphenylporphine, and $\alpha,\beta,\gamma,\delta$-tetraphenylisoporphine from benzaldehyde and pyrrole.[10]

(9) Helberger and Von Rebay, *Ann.*, **539**, 187 (1939). In the nomenclature given above (Fig. 1) Helberger's isotetrabenzoporphine would be called tetrabenzoisoporphine; we should like to suggest strongly the adoption of the latter name, *i. e.*, naming the fundamental rings porphine, and isoporphine, respectively, with the necessary prefixes. This method simplifies cataloging, and will avoid difficulties in cases of substances as mentioned in the table: $\alpha,\beta,\gamma,\delta$-tetraisobutylporphine, and its isomer $\alpha,\beta,\gamma,\delta$-tetraisobutylisoporphine.

(10) Reported at the 95th meeting of the American Chemical Society, Dallas-Fort Worth, Texas, April 19, 1938, by Rothemund and Menotti, and at the 49th Annual meeting of the Ohio Academy of Science in Cincinnati, Ohio, April 14, 1939, by A. Menotti. See also footnote 6.

Experimental[11]

For the experimental part reference is made to paper II.[1] The filling of the reaction tubes was the same; the sealed tubes were heated to 140–150° for twenty-four hours, and then worked up as described. Most of the isoporphine formed entered the 1% hydrochloric acid fraction (500 ml.), although a small amount was present in the 3% fraction, which was the main fraction for the isolation of porphine. From the 1% hydrochloric acid fraction isoporphine was transferred into 1 liter of ether by addition of saturated sodium acetate solution. The ether was washed with water to neutral reaction, and fractionated with 0.5% hydrochloric acid; the transfer from hydrochloric acid to ether was repeated for the purpose of further purification. After washing with water, and drying with sodium sulfate the ether was filtered and evaporated. The residue was dissolved in hot pyridine to make a saturated solution, and then ether was added, first drop by drop, and then in larger amount, until about ten times the volume of the original pyridine solution was obtained. Isoporphine crystallized in dark brown needles; its hydrochloric acid number was 0.5. It was soluble in pyridine, chloroform, or acetic acid; the solubility in pure ether was small, but ether containing acetic acid dissolved the substance much better. The substance did not melt, but decomposed upon heating above 250°.

(11) With the coöperation of Mr. B. Patterson.

Anal. Material recrystallized from pyridine–ether (1 vol. + 9–10 vols.) as described above, dried to constant weight over phosphorus pentoxide *in vacuo* at the temperature of boiling chloroform (drying pistol). Calcd. for $C_{20}H_{14}N_4$ (310.3): C, 77.40; H, 4.55; N, 18.05. Found: C, 77.5; H, 4.4; N, 17.7.

Magnesium Complex Salt of Isoporphine (Isoporphine Phyllin).—A solution of 6 mg. of isoporphine in 5 ml. of pyridine, 50 mg. of magnesium oxide, and 25 ml. of 30% methanolic potassium hydroxide were heated in a sealed tube for five hours to 150°. The solution was worked up exactly as described for the porphine phyllin.

Anal. Calcd. for $C_{20}H_{12}N_4Mg$ (332.6): C, 72.22; H, 3.64; N, 16.83; Mg, 7.31. Found: C, 72.0; H, 3.8; Mg, 7.3. (N not determined.)

The phyllin is not stable, when heated on a steam-bath with 5% hydrochloric acid. The complexly linked magnesium is eliminated and the free porphyrin regenerated.

Hemin and Copper Complex Salt of Isoporphine.—These two compounds were prepared analogously to the preparation of the corresponding porphine compounds.[3]

Anal. Calcd. for $C_{20}H_{12}N_4Cu$ (371.9): C, 64.59; H, 3.25; N, 15.06; Cu, 17.10. Found: Cu, 17.0 (digestion of the salt with concentrated sulfuric acid, evaporation of the acid and micro electrolysis of the weakly acid solution—Pregl's method—7 ml. electrolyte, 2.8 v., 35 ma., 50 min. boiling).

Anal. Calcd. for $C_{20}H_{12}N_4FeCl$ (399.6): C, 60.11; H, 3.03; N, 14.01; Fe, 13.96; Cl, 8.89. Found: C, 60.0; H, 3.2; N, 13.6; Cl (micro-Carius), 8.5.

Absorption Spectra

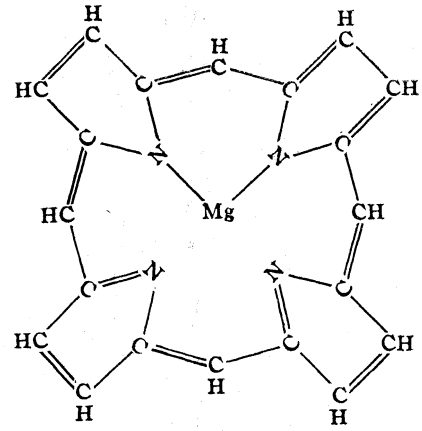
Isoporphine. In Dry Neutral Ether.—I, 650.1–(646.2)–642.4; II, 636.7–(632.6)–628.5; III, 624.3–(622.3)–620.5; IV, 601.5---590.2–(587.0)–583.9---581.3–(577.3)–573.4--; V, 569.6–(567.6)–565.7; VI, 560.2–(558.5)–556.9; VII, 551.7---543.9–(540.4)–537.0---531.0; VIII, 520.4–(502.2)–484.1; IX, 474.9–(469.6)–464.4; shadow 447.0; E. A. 431.5. Intensity: VIII, IV (b, a), VII; V, IX, I; VI = II, III.

Isoporphine Phyllin. (a) **In Dry Neutral Ether.**—I, 609.2–(601.6)–593.9; shadow 578.0; II, 559.3---550.0–(542.7)–535.3---527.0; III, 506.9–(500.4)–493.8; E. A. 428.0. Intensity: II, I, III.

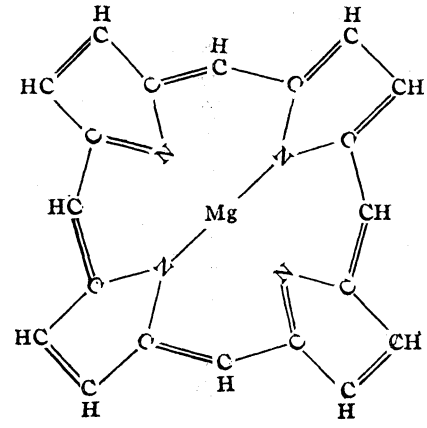
(b) **In the Alkaline Reaction Mixture.**—I, 613.5–(605.0)–596.5; II, 562.5–(547.8)–533.0; III, maximum approximately 501; E. A. 456.0. Intensity: II; I; (III).

Isoporphine Copper Complex Salt (in Pyridine–Ether).—I, 566.6–(562.4)–558.3; II, 547.1–(529.1)–511.1; III, 496.4–(489.8)–483.2; E. A. 445.0. Intensity: II; I, III.

Isoporphine Iron Chloride (Isoporphine Hemin) (in Pyridine–Ether).—I, 589.7---577.3–(574.0)–570.8---566.6–(563.0)–559.4---554.8; II, 540.3–(532.0)–523.8; III, 509.4–(502.2)–495.1; E. A. 475.5. Intensity: I(b, a), II, III.



Porphine phyllin



Isoporphine phyllin

Fig. 3.

Summary

1. The low hydrochloric acid fraction of the porphine synthesis described previously yielded a new porphyrin of hydrochloric acid number 0.5.

2. Elementary analyses of this porphyrin and of some of its salts lead to the conclusion that this porphyrin is an isomer of porphine: "isoporphine."

3. The phyllin, hemin, and copper complex salt of isoporphine have been prepared.

4. The structures of the porphine and isoporphine ring are discussed.

5. A chart comparing the absorption spectra of porphine, porphine phyllin, porphine hemin, and porphine copper complex salt with those of isoporphine and its corresponding salts is presented.

6. The general synthesis for *meso*-tetrasubstituted porphyrins by the author was tested with respect to the possible formation of two porphyrins instead of one; cases in which two porphyrins have been found are given, and the hydrochloric acid numbers of the new porphyrins are listed.

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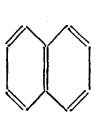
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ALBERTA]

The Structure of Some Naphthalene, Hydrindene and Tetralin Derivatives

BY R. B. SANDIN AND T. H. EVANS[1]

The problem which has to do with the fixation or the non-fixation of the Kekulé ring in such compounds as naphthalene has been attacked from numerous and different viewpoints.[2] There is much chemical evidence in favor of the idea that the double bonds of naphthalene are not free to migrate and that the Erlenmeyer formula (I) is



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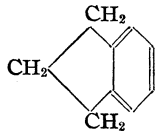

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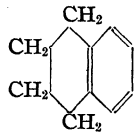


III

to be preferred.[3] The investigations of Fieser and Lothrop,[4] and Baker and Carruthers,[5] provide evidence of this kind. Also recently McLeish and Campbell,[6] working from the standpoint of the reactivity of the halogens in halogenated nitronaphthalene compounds, provide additional evidence in favor of the Erlenmeyer formula. Using Fuson's[7] theory of vinylogy, they have shown that the reactivity of the bromine atom in aromatic bromonitro compounds can be used to detect the presence and position of double bonds in bromonitro derivatives of naphthalene. They have also extended their work to derivatives of hydrindene and tetralin.

The authors of this paper call attention to another reaction which might prove of value in detecting ring stabilization and which, as far as the authors are aware, has never been used specifically for this purpose. The reaction involved is one studied by Nicolet[8] and co-workers. They showed that certain compounds containing bromine or iodine in the benzene ring could undergo hydrolysis in such a way that the halogen was replaced by hydrogen, the solution acquiring oxidizing properties as evidenced by the liberation of free halogen or by the formation of more highly halogenated derivatives. The halogen which reacted in this manner was always ortho or para to an amino or hydroxyl group. In studying the removal of such halogens it was found by Nicolet to be more convenient to perform the hydrolysis in the presence of stannous chloride in order to obviate effects due to resubstitution and oxidation. The important point in connection with the present work is that an arrangement in an aromatic compound of a bromine atom and an amino group in such a way that they are separated by a double bond or a conjugated system of double bonds, gives rise to a so-called "positive" bromine atom. This type of structure might also be added to the list of examples given by Fuson in his theory of vinylogy. A number of aminobromo derivatives of naphthalene have therefore been prepared and their behaviors examined with respect to an acid solution of stannous chloride at the boiling point. This work likewise has been extended to similar derivatives of hydrindene and tetralin. The measurements make no claim to accuracy, but are sufficient to show the relative reactivities of the bromine atom in the compounds examined. The results are found in Table I. The experimental details are given later in this paper.

Franzen and Staüble[9] have done considerable work on the effect of tin and hydrochloric acid and of an acid stannous chloride solution on brominated β-naphthols and β-naphthylamines. Their results are recorded in Table II.

If the Erlenmeyer formula for naphthalene is correct, the first three compounds in Table I should contain reactive bromines, whereas the bromine in 3-bromo-2-naphthylamine should be non-reactive. Also in 1,3-dibromo-2-naphthylamine the 1-bromo atom should be reactive, whereas the 3-bromo atom should be non-reactive. However, if there is no bond fixation, then the bromine in 3-bromo-2-naphthylamine should give rise to oxidizing properties and in the same way both bromines in compound (IV) should be substituted by hy-

(1) Present address: 2063 Stanley Street, Montreal, Quebec.

(2) See excellent discussion of this topic, by Fieser in Gilman, "Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1938, p. 70.

(3) On the other hand, all of the physical evidence points to the existence of valence isomers which contain a double bond at C_{2-3}. Arnold and Sprung, THIS JOURNAL, **60**, 1163 (1938); Pauling and Wheland, *J. Chem. Phys.*, **1**, 362 (1933), etc.

(4) (a) Fieser and Lothrop, THIS JOURNAL, **57**, 1459 (1935); (b) **58**, 2050 (1936).

(5) Baker and Carruthers, *J. Chem. Soc.*, 479 (1937).

(6) McLeish and Campbell, *ibid.*, 1103 (1937).

(7) Fuson, *Chem. Rev.*, **16**, 1 (1935).

(8) (a) Nicolet, THIS JOURNAL, **43**, 2081 (1921); (b) Nicolet and Sampey, *ibid.*, **49**, 1796 (1927); (c) Nicolet and Ray, *ibid.*, **49**, 1801 (1927); (d) Nicolet and Sandin, *ibid.*, **49**, 1806 (1927); (e) Nicolet, *ibid.*, **49**, 1801 (1927).

(9) (a) Franzen and Staüble, *J. prakt. Chem.*, **101**, 58 (1920); (b) **103**, 352 (1922).

TABLE I

REACTION WITH HYDROCHLORIC ACID AND STANNOUS CHLORIDE

	Substance used	Time of hydrolysis, hours	Products recovered and % halogen removed
I	1-Bromo-2-naphthylamine	1.0	90% of β-naphthylamine
			>90% of bromine removed
II	4-Bromo-1-naphthylamine	1.0	90% of α-naphthylamine
			>90% of bromine removed
III	2,4-Dibromo-1-naphthylamine	1.0	90% of α-naphthylamine
			>90% of bromine removed
IV	1,3-Dibromo-2-naphthylamine	1.0	95% of 3-bromo-2-naphthylamine
			>95% of 1-bromo atom removed
V	3-Bromo-2-naphthylamine	10.0	Quantitative recovery of 3-bromo-2-naphthylamine
VI	4,6-Dibromo-5-aminohydrindene	0.5	80% of 4-bromo-5-aminohydrindene, m. p. 54–55°
			80% removal of 6-bromo atom
	4,6-Dibromo-5-aminohydrindene	5.0	25% of 4-bromo-5-aminohydrindene, m. p. 54–55°
VII	4-Bromo-5-aminohydrindene	6.0	30% of unaltered material
VIII	5-Bromo-6-aminotetralin	1.0	60% removal of bromine
IX	5-Bromo-6-acetamidotetralin	2.0	85% of 6-aminotetralin, m. p. 34–5°
X	*o*-Bromoaniline	1.0	56% removal of bromine
	o-Bromoaniline	2.0	75% removal of bromine

TABLE II

Substance used	Conditions of hydrolysis	Result
1,6-Dibromo-2-naphthylamine	Stannous chloride and hydrochloric acid in alcohol; 21 hours	6-Bromo-2-naphthylamine
1,6-Dibromo-2-naphthylamine	Tin and hydrochloric acid	6-Bromo-2-naphthylamine
1,3,6-Tribromo-2-naphthylamine	Tin and hydrochloric acid	3,6-Dibromo-2-naphthylamine
3,6-Dibromo-2-naphthylamine	Tin and hydrochloric acid	Unchanged material
1,6-Dibromo-2-naphthol	Tin and hydrochloric acid	6-Bromo-2-naphthol
1-Nitro-3,6-dibromo-2-naphthol	Stannous chloride and hydrochloric acid	No bromine removed
1,3,6-Tribromo-2-naphthol	Tin and hydrochloric acid	3,6-Dibromo-2-naphthol
1,3,4,6-Tetrabromo-2-naphthol	Tin and hydrochloric acid	3,4,6-Tribromo-2-naphthol
3-Bromo-1-nitro-2-naphthylamine[20]	Tin and hydrochloric acid	3-Bromo-1,2-naphthylenediamine
1,3-Dibromo-2-naphthylamine[20]	Tin and hydrochloric acid; 2 hours	3-Bromo-2-naphthylamine

drogens under the experimental conditions. An examination of Table I definitely points to the Erlenmeyer formula for naphthalene possessing a double bond common to both rings. Attention is called to the high degree of reactivity of the bromine atom in a compound such as 1-bromo-2-naphthylamine and the extraordinary stability of the bromine atom in 3-bromo-2-naphthylamine.

Evidence in favor of the Erlenmeyer formula is also shown from the results presented in Table II. Here again we notice the persistence of the 3-bromo atom such as we have in 1,3,6-tribromo-2-naphthylamine. It might be expected that the 6-bromo atom should have been reactive, as the 6-bromo atom and the amino group are separated by a conjugated system of three double bonds. The fact that this bromine atom shows no reactivity is evidence that the double bond shared by the two rings does not function normally.[6,10]

In connection with the reactivity of the bromine atom in 1-bromo-2-naphthylamine, the proximity of the bromine atom to the adjoining aromatic ring may be of some importance. However, this effect is believed by the authors to be negligible. Franzen and Staüble,[9b] for example, have shown that when 1,3,4,6-tetrabromo-2-naphthol is reduced with tin and hydrochloric acid, the 4-bromo atom remains fixed.

Concerning the stability of the bromine atom in a compound such as 3-bromo-2-naphthylamine it is interesting to note that Nicolet[8e] gives as a possible mechanism for the elimination of a "positive" halogen from *o*-aminobenzene derivatives, first of all the formation of a quinoidal intermediate compound, and second a subsequent 1,3-elimination. On the basis of this conception it might be said that 3-bromo-2-naphthylamine is stable because the quinoidal intermediate is not produced. It is a known fact that 2,3-dihydroxynaphthalene does not yield a quinone on oxidation.[11] Evidently the two hydroxyls function independently and not as though they were connected by a double bond.

(10) Sampey, THIS JOURNAL, **49**, 2849 (1927).

(11) Marckwald, *Ann.*, **274**, 331 (1893); **279**, 1 (1894); Fries and Schimmelschmidt, *Ber.*, **65**, 1502 (1932); Fieser, THIS JOURNAL, **52**, 5219 (1930).

Regarding the structure of hydrindene and tetralin, Mills and Nixon[12] believe that there is bond fixation and give the structure (II) and (III) for these two compounds, respectively. The work of McLeish and Campbell confirms structure (II) for hydrindene derivatives as does also the earlier work of Fieser and Lothrop,[4b] Sidgwick and Springall,[13] and Baker.[14] Although the present work is not conclusive as far as hydrindene is concerned, any inference that might be drawn is in favor of structure (II) being the preferred structure. There is no doubt about the fact that the 6-bromo atom is remarkably reactive. In this respect it is similar to the bromine in 1-bromo-2-naphthylamine. Also the 4-bromo atom has a marked degree of stability although it is not completely unreactive. Similarly, McLeish and Campbell found that the bromine in 4-bromo-5-nitrohydrindene is very slightly reactive. Recently Fieser and Lothrop[2] have found that 5-hydroxy-6-methylhydrindene is capable of forming azo compounds in very weakly alkaline solutions. Also Baker[14] has shown that 5-hydroxy-4-acetylhydrindene is chelated to a certain degree. Finally, it is possible to make 4,6-dibromo-5-aminohydrindene[15] by direct bromination of 5-aminohydrindene. All these facts indicate (as Fieser and Lothrop[2] already have suggested) that the bonds in certain hydrindene derivatives are not fixed so rigidly that the 4–5 and 6–7 bonds cannot, under certain conditions, acquire double bond characteristics. In the authors' work the effect of the alicyclic ring is considered to be negligible, in view of the fact that 2-iodo-4-aminotoluene[3d] shows no evidence of "positive" iodine.

Concerning the structure of tetralin, the present work gives no definite information, since no 7-bromo-6-aminotetralin was available. The present results, however, do show a "positive" bromine in 5-bromo-6-aminotetralin. Contrary to the conclusions that might be drawn from this, McLeish and Campbell[6] found 6-bromo-5-nitrotetralin to be unreactive. Consistent with our results, Schroeter[16] and co-workers have reduced 5-bromo-6-hydroxy-7-nitrotetralin with stannous chloride and obtained a mixture of 5-bromo-6-hydroxy-7-aminotetralin and 6-hydroxy-7-aminotetralin.

For the sake of comparison, a study of the behavior of *o*-bromoaniline has been included. It will be noticed that the bromine reactivity in this case (two isomeric Kekulé or resonating forms) lies between the reactivity shown in the case of the bromine in 1-bromo-2-naphthylamine (the bromine and the amino groups separated by a fixed double bond), and the nonreactivity shown in the case of 3-bromo-2-naphthylamine (bromine and amino groups separated by a fixed single bond). Sampey,[10] working on the polarity of the carbon–halogen bond, has pointed out the remarkable reactivity of the halogens in ortho or para position to the hydroxyl group in halogen naphthols when the latter are treated with an acid stannous chloride solution. Under the same conditions, similar halogen phenols show little reactivity. Again, Hodgson and Leigh[17] call attention to the fact that the chlorine atoms in 2-chloro- and 4-chloronitrobenzenes are displaced much less easily by alkali than those in the corresponding chloronitronaphthalenes. Is it not possible that the difference in reactivity is connected with a stabilized structure for the naphthalene compounds?

Experimental Part

Preparation of Compounds.—1-Bromo-2-naphthylamine,[18] m. p. 63°, 4-bromo-1-naphthylamine,[19] m. p. 103°, and 2,4-dibromo-1-naphthylamine,[20] m. p. 118–119°, were prepared readily.

1,3-Dibromo-2-naphthylamine,[21] m. p. 119°, was prepared by the bromination of *p*-toluenesulfone-2-naphthalide, followed by hydrolysis with concentrated sulfuric acid. By the acid stannous chloride reduction of 1,3-dibromo-2-naphthylamine, there was obtained 3-bromo-2-naphthylamine, m. p. 169° (Consden and Kenyon[20] report 173°).

4,6-Dibromo-5-aminohydrindene,[15] m. p. 70–71°, was prepared by the bromination of 5-aminohydrindene.[14]

An 80% yield of pure 4-bromo-5-aminohydrindene, m. p. 54–55°, was obtained by reduction of 4,6-dibromo-5-aminohydrindene with stannous chloride and hydrochloric acid.

Anal. Calcd. for $C_9H_{10}NBr$: Br, 37.6. Found: Br, 37.3.

The time of reduction was thirty minutes. Longer periods gave a lowered yield. McLeish and Campbell[6] report a melting point of 50–51°. However, their compound was about 6% too high in bromine content and probably contained some unchanged dibromo compound.

5-Bromo-6-acetamidotetralin,[12,22] m. p. 126–127°, was prepared by the bromination of 6-acetamidotetralin in

(12) Mills and Nixon, *J. Chem. Soc.*, 2510 (1930).
(13) Sidgwick and Springall, *ibid.*, 1532 (1936).
(14) Baker, *ibid.*, 476 (1937).
(15) Borsche and Bodenstein, *Ber.*, **59**, 1909 (1926).
(16) Schroeter, *Ann.*, **426**, 83 (1922).
(17) Hodgson and Leigh, *J. Chem. Soc.*, 1031 (1938).
(18) Morgan, *J. Chem. Soc.*, **79**, 814 (1900).
(19) Morgan, Micklethwaite and Winfield, *ibid.*, **85**, 736 (1904).
(20) Consden and Kenyon, *ibid.*, 1591 (1935).
(21) Bell, *ibid.*, 2732 (1932).
(22) Smith, *ibid.*, **85**, 730 (1904).

glacial acetic acid. Acid hydrolysis of the preceding compound gave 5-bromo-6-aminotetralin, m. p. 52.5°.

Determination of Halogen Reactivity.—The method employed was somewhat similar to the one already used by Nicolet.[8] All the compounds were treated under as nearly the same conditions as possible, the only variable factor being the time. It was essential that the acid concentrations should be the same for all runs, since it is known that the rate of halogen removal is directly proportional to the acid concentration but is independent of the stannous chloride concentration.

In this work 0.02 mole of compound was dissolved in a boiling mixture of 25 cc. of glacial acetic acid and 20 cc. of concentrated hydrochloric acid. To this was added enough stannous chloride to give one mole of stannous chloride per gram atom of halogen in the compound being examined. The solution was then boiled in an all-glass apparatus under reflux for a suitable period of time. On boiling, some hydrogen chloride was lost. However, since all the experiments were carried on as nearly as possible under the same conditions, no attempt was made to avoid this loss. The reaction mixture subsequently was transferred to a beaker, treated with concentrated hydrochloric acid and cooled. The precipitated hydrochloric acid salt or stannichloride of the amine was filtered off and treated with sodium hydroxide. The liberated amine was either identified as such or as the acetyl derivative. Its weight was determined and sometimes also its halogen content. The mother liquor from the above amine hydrochloride was treated with sodium hydroxide and any precipitate produced was examined from the standpoint of identity, weight and halogen content.

Summary

Some brominated derivatives of α- and β-naphthylamine, 5-aminohydrindene and 6-aminotetralin have been examined from the standpoint of "positive" bromine content. It is believed that this reaction is useful in detecting double bond fixation. The results indicate that the structures of the naphthalene derivatives are based on the Erlenmeyer formula, and that the preferred structures for the hydrindene derivatives are based on the Mills and Nixon formula. No definite conclusion was reached regarding tetralin.

EDMONTON, ALBERTA, CANADA RECEIVED JULY 3, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ALBERTA]

The Structure of Fluorescein, Sulfonefluorescein and Some of their Halogenated Derivatives

BY R. B. SANDIN, A. GILLIES[1] AND S. C. LYNN

Recently C. G. Le Fèvre and R. J. W. Le Fèvre[2] have determined the dipole moments of xanthone and some of its 2,7-disubstituted derivatives. They conclude that a nearly complete fixation of double and single bonds occurs in the xanthone skeleton (structure (I)). This is in accord with the theoretical prediction of Mills and Nixon:[3] "that fusion of a benzene ring with a 6-membered ring tends toward the stabilization in the former of that Kekulé individual which has a double bond between the points of attachment of the side nucleus."[4]

With the work of Le Fèvre and Le Fèvre in mind, it occurred to the authors of this paper that the xanthene dyes such as fluorescein and sulfonefluorescein and which in the lactoid modifications have a xanthone skeleton, might from a chemical standpoint show ring stabilization.[5]

The regulated dibromination of fluorescein has been examined and has been found to occur in the 4,5-positions.[6] This is contrary to what one would ordinarily expect from a consideration of a steric effect.[7] It is believed by the authors that this type of dibromination is an indication of ring stabilization. If the lactoid structure of fluorescein is assumed, then it is believed that structure (II) is the preferred structure. If, on the other hand, it is the quinoid form which is brominated, then it is assumed that either structure (IV) (two resonating negative ions) or structure (VI) (two

(1) Honors student in chemistry, University of Alberta.

(2) Le Fèvre and Le Fèvre, *J. Chem. Soc.*, 196 (1937).

(3) Mills and Nixon, *ibid.*, 2510 (1930).

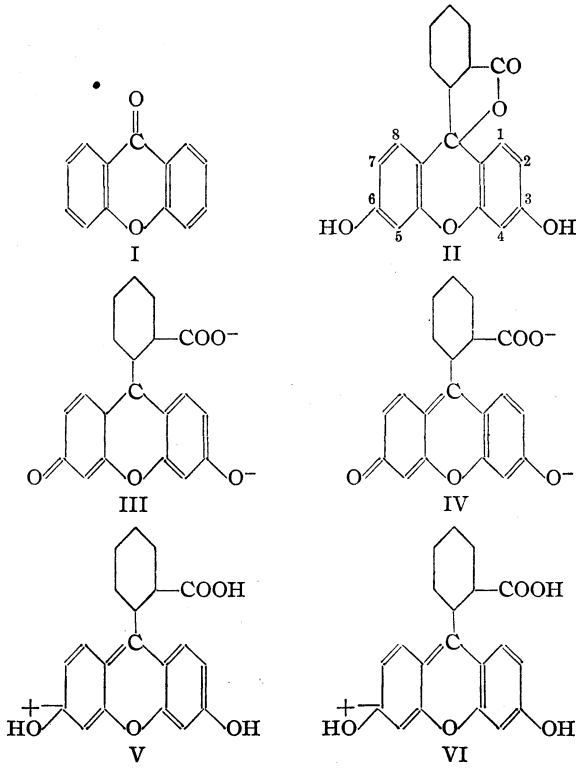
(4) In the case of tetralin, however, it has been found that tetralin, like all ordinary benzene derivatives, can react in both Kekulé forms. Fieser and Lothrop, THIS JOURNAL, **58**, 2050 (1936); Sidgwick and Springall, *J. Chem. Soc.*, 1532 (1936).

(5) For earlier work on the structure of fluorescein and sulfonefluorescein, see (a) Orndorff, Gibbs and Shapiro, THIS JOURNAL, **50**, 819 (1928); (b) Gibbs and Shapiro, *ibid.*, **50**, 1755 (1928); (c) Ramart-Lucas, *Compt. rend.*, **205**, 1409 (1937).

(6) Several text-books on organic chemistry give the structure of mercurochrome to be a mercurated dibromofluorescein in which the bromine atoms occupy the 2,7-positions. Orndorff and Hemmer, THIS JOURNAL, **49**, 1272 (1927), give the structure of dibromofluorescein as a 4,5-dibromo compound. However, Orndorff and Vose, *ibid.*, **46**, 1896 (1924), give a 2,7-structure for the dibromosulfonefluorescein and diiodosulfonefluorescein diacetates.

(7) That the structure of dibromofluorescein is a 4,5-dibromo one has also been shown by Harris, Marriot and Smith, *J. Chem. Soc.*, 1838 (1936). However, they gave no definite proof that the compound they obtained by the alkali fusion of dibromofluorescein was 2-bromoresorcinol which has a melting point of 102–103°. The melting point of 4-bromoresorcinol is almost identical with that of the 2-bromo compound, *viz.*, 103°.

resonating positive carbonium ions) represents the preferred structure. In the case of sulfonefluorescein, only dibromination occurs and again the structure has been shown to be a 4,5-dibromo structure. Since no tetrabromination of sulfonefluorescein takes place no matter how much bromine is used, it is conceivable that ring stabilization is much more pronounced in this case than in the case of fluorescein.



Hewitt and Woodforde[8] have shown that the dinitration of fluorescein occurs at the 4,5-positions, although previous workers had believed that nitration occurred at the 2,7-positions. More recently Ingraffia[9] has shown that fluorescein yields a benzenemonazofluorescein and a benzenebisazofluorescein when allowed to couple with a phenyldiazonium salt. He concludes that fluorescein has a lactoid structure and that the azo derivatives are 2,7-substituted derivatives. However, the authors of this paper believe that the azo derivatives must be 4,5-compounds because on reduction Ingraffia has found that the diaminofluorescein dihydrochloride produced is identical with that prepared from dinitrofluorescein. The authors of this paper also suggest that the structure (IV) (two resonating negative ions), as well as a fixed lactoid structure, will account for the formation of a bisazofluorescein.[10]

Some tetrahalogenated derivatives of fluorescein have also been examined from the standpoint of containing "positive" halogen.[11] Stannous chloride dissolved in hydrochloric acid, it is believed, can be used to detect bond fixation. For example, this reagent has no effect on 3-bromo-β-naphthylamine, whereas with the same reagent the bromine in 1-bromo-β-naphthylamine is very readily replaced by hydrogen. In the present work, tetrabromofluorescein dissolved in dioxane has been refluxed with excess stannous chloride hydrochloric acid reagent for as long as twenty-five hours and the 4,5-dibromo atoms are the only ones which are removed. A similar thing happens with 4,5-dibromo-2,7-dichlorofluorescein, from which only the two bromine atoms are removed. The results indicate that again there is the possibility of bond fixation in such a way that there is a double bond between the phenolic ring and the points of attachment of the side nucleus.

The authors wish to thank Mr. R. McKee for generous help in various phases of this work.

Experimental Part

Preparation of Compounds.—The fluorescein used in this work was prepared and purified according to Orndorff and Hemmer.[6] It was brominated to the dibromofluorescein stage according to Phillips,[12] purified through the diacetate and formed red plates, m. p. 285°. By using acetic anhydride and ethanol as a solvent for the purification of the dibromofluorescein diacetate, the present authors have obtained a melting point of 228–229°. Phillips[12] reports a melting point of 211°. The tetrabromination of fluorescein was carried out according to Orndorff and Hemmer.[6]

The preparation of 2,7-dichlorofluorescein was carried out according to Kolthoff, Lauer and Sunde.[13] It was purified through the diacetate (m. p. 237° from benzene). It was found best to hydrolyze the diacetate by heating it on a water-bath for several hours with 85% sulfuric acid. When alcoholic potassium hydroxide was used as the hydrolyzing agent, the dichlorofluorescein produced invariably had a low chlorine content, probably due to a hydrolytic breakdown of the dichlorofluorescein molecule itself. When dichlorofluorescein was brominated with

(8) Hewitt and Woodforde, *J. Chem. Soc.*, **81**, 893 (1902).
(9) Ingraffia, *Gazz. chim. ital.*, **62**, 781 (1932).
(10) The authors have found that only a diiodofluorescein (presumably 4,5-diiodofluorescein) is produced when an ammoniacal solution of fluorescein is treated with excess iodine dissolved in aqueous potassium iodide. Evidence has also been found that under similar circumstances 2,7-dichlorofluorescein forms a diiodo derivative, whereas 4,5-dibromofluorescein does not. This work is being done now and will be reported on later.
(11) Nicolet and co-workers, THIS JOURNAL, **43**, 2081 (1921); **49**, 1796, 1801, 1806, 1810 (1927).
(12) Phillips, *J. Chem. Soc.*, 724 (1932).
(13) Kolthoff, Lauer and Sunde, THIS JOURNAL, **51**, 3273 (1929).

two moles of bromine, 4,5-dibromo-2,7-dichlorofluorescein was produced.

Anal. Calcd. for $C_{20}H_8Cl_2Br_2O_5$: AgCl + AgI, 41.3. Found: (Carius) 41.4.

Dibromosulfonefluorescein was prepared by the procedure of Orndorff and Vose.[6] No tetrabromination, using excess bromine, was found to occur.

2-Bromoresorcinol was prepared according to Rice[14] and melted at 100°.

4-Bromoresorcinol was made according to the procedure of Sandin and McKee[15] and melted at 100–102°.

3-Bromoresorcinol and 2-bromoresorcinol behave quite differently on sublimation. The latter sublimes much more readily than the former. Also the latter on sublimation tends to produce long needles, whereas the former sublimes to form colonies of small crystals.

Hydrolysis of Dibromofluorescein and Dibromosulfonefluorescein.—The directions of Harris[7] were followed and in both cases 2-bromoresorcinol was isolated and purified by sublimation. There was no depression of the melting point on mixing with synthetic 2-bromoresorcinol. However, when mixed with synthetic 4-bromoresorcinol, the melting point was as low as 75°.

Reduction of Tetrabromofluorescein and Dichlorodibromofluorescein.—To a solution of 50 g. of tetrabromofluorescein in 500 cc. of dioxane, 100 cc. of concentrated hydrochloric acid and 50 cc. of glacial acetic acid was added 150 g. of stannous chloride. The solution was refluxed for fifteen to twenty-five hours. At the end of about six hours, crystals of 2,7-dibromofluorescein began to settle out and the amount increased as the refluxing was continued. It was found that dibromofluorescein is much less soluble in dioxane than the tetrabromo compound. The reaction mixture was cooled, the crystals were filtered off and dissolved in dilute sodium hydroxide. The solution was filtered and the dibromo compound precipitated by the addition of hydrochloric acid. The freshly precipitated material was dark red in color. However, on heating on a water-bath for several hours the material became definitely crystalline and the color changed to a bright yellow. The appearance of the dibromofluorescein at this stage was very much like that of 2,7-dichlorofluorescein which has been digested with hydrochloric acid.

Anal. Calcd. for $C_{20}H_{10}O_5Br_2$: Br, 32.7. Found: Br (Carius), 31.8.

The diacetate was made by refluxing the dibromofluorescein with acetic anhydride. Crystallization of the diacetate from acetic anhydride gave the pure diacetate, m. p. 259° (with preliminary darkening of color).

Anal. Calcd. for $C_{24}H_{14}O_7Br_2$: Br, 27.9. Found: Br (Carius), 27.7.

The diacetate was hydrolyzed with 85% sulfuric acid by heating on the water-bath for several hours. The reaction mixture was diluted with water, the dibromofluorescein filtered off and washed thoroughly with hot water. It formed beautiful yellow crystals, m. p. 300–301°.

Anal. Calcd. for $C_{20}H_{10}O_5Br_2$: Br, 32.7. Found: Br (Carius), 32.6.

The above purified dibromofluorescein was hydrolyzed according to the procedure of Harris.[7] 4-Bromoresorcinol was isolated from the hydrolysis product and its identity established by carrying out mixed melting points with synthetic 2- and 4-bromoresorcinols. Moreover, on sublimation it behaved like the 4-bromoresorcinol. There was also isolated what is believed to be 2-(5′-bromo-2′,4′-dihydroxybenzoyl)-benzoic acid, m. p. 240–241° (with preliminary darkening of color and softening). Harris[7] and co-workers give the melting point of 2-(3′-bromo-2′,4′-dihydroxybenzoyl)-benzoic acid as 200° with softening at 187°.

Anal. Calcd. for $C_{14}H_9O_5Br$: Br, 23.7. Found: Br (Carius), 23.4.

The reduction of dichlorodibromofluorescein was carried out in the same manner. From the reaction mixture there was isolated nearly pure dichlorofluorescein.

Anal. Calcd. for $C_{20}H_{10}O_5Cl_2$: Cl, 17.8. Found: Cl (Carius), 17.5.

Fluorescein dissolved in glacial acetic acid was refluxed with stannous chloride and concentrated hydrochloric acid. At the end of fifteen hours the fluorescein was isolated almost quantitatively as the pure fluorescein diacetate. Evidently stannous chloride has a negligible effect on the conjugated system of double bonds as found in the quinoid modification of fluorescein.

Summary

1. Fluorescein and sulfonefluorescein have been dibrominated and the bromine atoms have been shown to occupy the 4,5-positions. Tetrabromofluorescein and dichlorodibromofluorescein have been reduced with stannous chloride and only the 4,5-dibromo atoms have been removed.

2. To explain these results it is suggested that these compounds have fixed structures according to the Mills and Nixon theory.

EDMONTON, ALBERTA, CANADA RECEIVED JULY 3, 1939

(14) Rice, THIS JOURNAL, **48**, 3125 (1926).

(15) Sandin and McKee, *Org. Syntheses*, **17**, 23 (1937).

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, NO. 722, AND THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

The Molecular Structure of Acetaldehyde

BY D. P. STEVENSON,[1] H. D. BURNHAM AND VERNER SCHOMAKER

Ackermann and Mayer[2] investigated the structure of acetaldehyde by the electron diffraction technique using 6.4 kilovolt electrons. Their photographs showed only two maxima and one minimum; hence it was necessary for them to assign very large uncertainties to their results. Since the distances they reported were considerably shorter than predicted by the covalent radius table,[3] it was decided that the structure of acetaldehyde should be reinvestigated using fast electrons.

Experimental.—Acetaldehyde was obtained by the acid depolymerization of Eastman Kodak Co. paraldehyde and also from a 95% solution of acetaldehyde in water (Eastman). In each case the acetaldehyde was distilled several times *in vacuo*, generous first and last fractions being discarded. From the purified liquid the vapor was allowed to expand into a carefully evacuated bulb which could be attached to the apparatus by means of a ground joint. In order to obtain completely satisfactory photographs, it was found necessary to have the vapor pressure in the sample bulb close to one atmosphere.

The Pasadena apparatus has been described by Brockway.[4a] The Princeton apparatus is similar to the Pasadena apparatus and has been used in other research.[4b] The wave length of the electrons was determined from transmission photographs of gold foil (a = 4.070 Å.), and it was approximately equal to 0.06 Å. for both the Pasadena and the Princeton photographs.

Interpretation.—Since the Pasadena and the Princeton photographs are identical both qualitatively and quantitatively, they will not be discussed separately.

The photographs showed six measurable maxima and minima. Two shelves were also present, the first preceding the first minimum and the second following the fifth maximum. They will be designated by the letters A and B, respectively. The fifth maximum and feature B resemble the maximum and shelf which appear on carbon dioxide photographs at the same value of s.[5] For the visual comparison of the photographs with the theoretical intensity curves, the most important characteristics of the photographs are that (1) the third minimum is deeper than either the second or fourth minimum, and (2) the third maximum is stronger than the fourth maximum. The measured $s\left(s_0 = \frac{4\pi}{\lambda}\sin\frac{\vartheta}{2}\right)$ values of the maxima and minima are given in the fifth column of Table I.

A radial distribution function[6] was calculated using the positions of both the maxima and minima. The coefficients were determined according to the method recommended by Schomaker.[7] These coefficients and the visually estimated intensities are given in columns 3 and 4 of Table I.

$$R(d) = \Sigma_n C_n \frac{\sin d\, s_n}{d\, s_n} \quad C_n = f(I_0, s_n) \qquad (1)$$

A plot of $R(d)$ against d is shown in Fig. 1. The maxima at 1.21, 1.51, and 2.33 Å. correspond to the carbon–oxygen and carbon–carbon bond distances and the non-bonded carbon–oxygen distance, respectively.

TABLE I

Max.	Min.	C_n	I_0	s_0	s^a calcd.	s_c/s_0
A			2	3.59	...	...
	1	− 9	−12	4.35	4.05	(0.931)[b]
1		14	12	6.23	5.88	(0.944)[b]
	2	− 2	− 4	7.45	7.60	(1.020)[b]
2		10	8	8.73	8.42	0.964
	3	− 7	− 6	9.86	9.60	.974
3		4	4	11.26	11.20	.995
	4	− 2	− 2	12.36	12.18	.985
4		2	2	13.73	13.10	(.954)[b]
	5	− 8	− 6	15.12	14.70	.972
5		10	6	16.75	16.40	.979
B				...	...	...
	6	− 2	− 3	20.02	19.52	.975
6		3	3	21.91	21.30	.972
Average of 8 features						.977 ± 0.007

[a] From curve with ρ = 1.25/1.54, α = 121.6°. [b] Omitted from average because of difficulty of measurement

C–C = 1.54 × 0.977 = 1.504 Å.
C–O = 1.25 × .977 = 1.222 Å.
C–O = 2.44 × .977 = 2.384 Å.

The qualitative appearance of the theoretical intensity curves for acetaldehyde is dependent on two parameters, ρ, the ratio of the carbon–oxygen

(1) National Research Fellow.

(2) P. G. Ackermann and J. E. Mayer, *J. Chem. Phys.*, **4**, 377 (1936).

(3) L. Pauling and M. L. Huggins, *Z. Krist.*, **87**, 205 (1934); L. Pauling and L. O. Brockway, THIS JOURNAL, **59**, 1223 (1937).

(4) (a) L. O. Brockway, *Rev. Modern Phys.*, **8**, 231 (1936); (b) J. Y. Beach and D. P. Stevenson, *J. Chem. Phys.*, **6**, 75 (1938).

(5) Verner Schomaker and D. P. Stevenson, THIS JOURNAL, to be published.

(6) L. Pauling and L. O. Brockway, *ibid.*, **57**, 2684 (1935).

(7) Verner Schomaker, American Chemical Society meeting, Baltimore, Md., April, 1939.

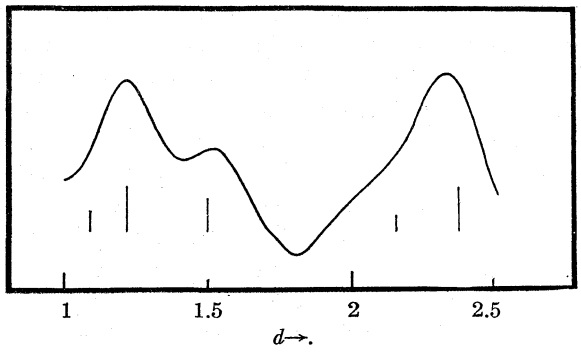


Fig. 1.—Radial distribution function, $R(d)$.

to carbon–carbon distance, and α, the carbon–carbon–oxygen angle. It was assumed that the hydrogen–carbon distance is equal to its value in methane, 1.09 Å., and that the configuration of the methyl group is tetrahedral.

In calculating the theoretical intensity curves it was found necessary to include temperature factors[4a] in the coefficients of the terms involving hydrogen–carbon distances as well as to take into account the effectively larger atomic scattering factor for electrons, $(Z - f)$, of hydrogen,[8] as compared with carbon and oxygen. The modified simple intensity formula thus had the following form

$$I(s) = 6\,\frac{\sin 1.54s}{1.54s} + 3.75\,\frac{\sin 1.09s}{1.09s}\,e^{-a_1s^2} + 3.75\,\frac{\sin 2.16s}{2.16s}\,e^{-a_1s^2} + 8\,\frac{\sin (\text{C–O})s}{(\text{C–O})s} + 8\,\frac{\sin (\text{C–O})s}{(\text{C–O})s}$$

$$a_1 = 0.0022,\ a_2 = 0.0043 \quad (2)$$

The a's are equal to half the mean square of the change in the distance between the hydrogen and the carbon atoms due to the vibrations of the molecule. They were evaluated from the known stretching and bending frequencies of ethane. The method used in their calculation will be discussed in detail by one of us.

It was further found that the terms involving the methyl–hydrogen to oxygen distances and the carbonyl–hydrogen distances could be omitted from the intensity formula without affecting its form or the positions of its maxima or minima.

Nineteen curves were calculated using equation (2). Some of these are shown in Fig. 2. The parameter ρ was varied from 1.30/1.54 to 1.22/1.54 and α from 112 to 127°. All models with ρ greater than 1.26/1.54 could be eliminated because for them the second minimum is deeper than the third and because feature B appears as a small maximum closer to the sixth than to the fifth maximum. For ρ less than 1.24/1.54 and α greater than 123°, the curves are unsatisfactory because the fourth minimum is too shallow and feature B does not have the appearance it has on the photographs. The curves calculated with α less than 119° and all values of ρ may be eliminated because feature B does not appear. Curves for α greater than 123° are unsatisfactory because

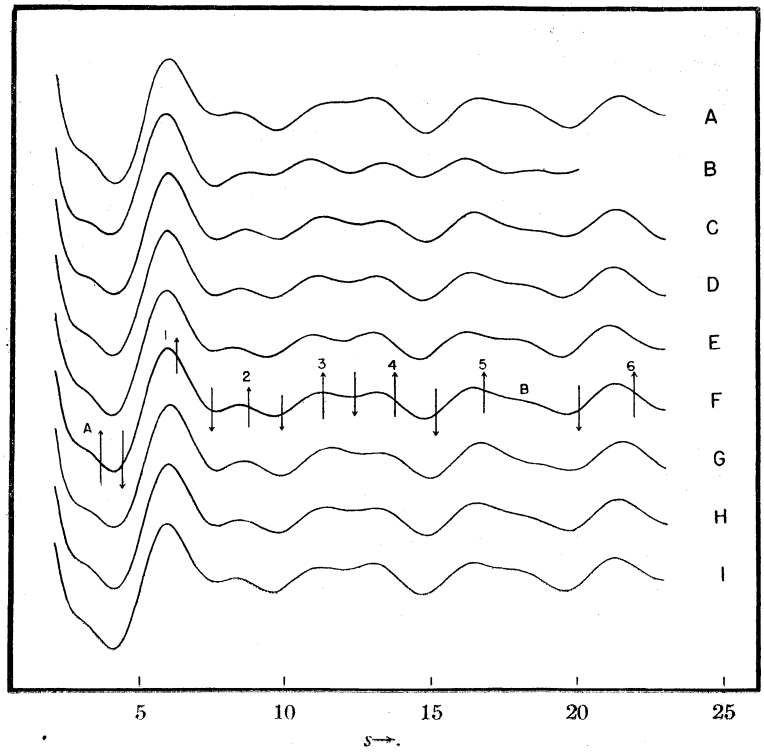


Fig. 2.—Theoretical intensity curves:

Curve A	ρ = 1.22/1.54, α = 121.6°
Curve B	ρ = 1.30/1.54, α = 121.6°
Curve C	ρ = 1.26/1.54, α = 119.3°
Curve D	ρ = 1.26/1.54, α = 121.6°
Curve E	ρ = 1.26/1.54, α = 124.5°
Curve F	ρ = 1.25/1.54, α = 121.6°
Curve G	ρ = 1.24/1.54, α = 119.3°
Curve H	ρ = 1.24/1.54, α = 121.6°
Curve I	ρ = 1.24/1.54, α = 124.5°

(8) L. Pauling and J. Sherman, *Z. Krist.*, **81**, 1 (1932).

B is too pronounced, appearing as a maximum rather than as a shelf following the fifth maximum. The curves calculated for $1.26/1.54 \geq \rho \geq 1.24/1.54$ and $119° \leq \alpha \leq 123°$ are qualitatively satisfactory. Quantitative comparison of the photographs with the curves calculated within the satisfactory ranges of ρ and α all give 1.22 Å. for the carbon–oxygen bond distance, 2.38 Å. for the non-bonded carbon–oxygen distance, and from 1.49 to 1.51 Å. for the carbon–carbon distance. Column 7, Table I gives a typical example of this comparison. Although the model with $\rho = 1.22/1.54$ and $\alpha = 119.3°$ cannot be eliminated, its curve is not so satisfactory as the curves for models with larger values of ρ inasmuch as the fourth minimum is too shallow and the fourth maximum is too weak.

Our final results for the structure are C–C = 1.50 ± 0.02 Å., C–O = 1.22 ± 0.01 Å., C–O = 2.38 ± 0.01 Å., C–H = 1.09 Å. (assumed), and the angle C–C–O = 121 ± 2°.

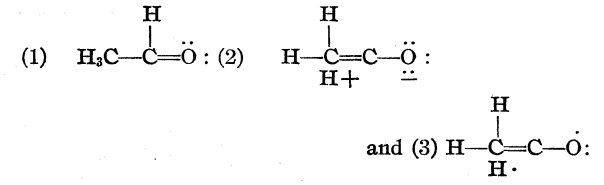
Discussion.—In a recent communication[9] it was reported that the carbon–oxygen distance in formaldehyde is 1.21 ± 0.01 Å. and this distance has been found to be 1.20 ± 0.02 Å.[10] in glyoxal; thus, with our results for acetaldehyde there are three determinations of the length of the carbon–oxygen double bond giving an average of 1.21 ± 0.02 Å.

Infrared and Raman spectra[11] studies of allene and ethylene yield 1.330 Å. for the length of the carbon–carbon double bond. This value has been confirmed recently by a new electron diffraction investigation of ethylene.[12] Thus, taking the carbon–carbon distances as standards, the subtrabend in Pauling's[13] rule for obtaining double bond distances from single bond distances is 1.540[14] − 1.330 = 0.21 Å. The carbon–oxygen single bond distance has been found to be 1.42 ± 0.02 Å. in dimethyl ether,[4a] *t*-butyl alcohol,[15] and *cis*-butene oxide,[4a] 1.43 ± 0.02 Å. in paraldehyde[4a] and *trans*-butene oxide,[4a] 1.44 ± 0.02 Å. in α-methylhydroxylamine,[4a] 1.46 ± 0.04 Å. in 1,4-dioxane,[4a] and 1.41 ± 0.02 Å. in methyl alcohol.[5]

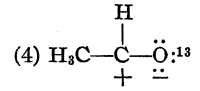
(9) D. P. Stevenson, J. E. LuValle and V. Schomaker, THIS JOURNAL, **61**, 2508 (1939).
(10) J. E. LuValle and V. Schomaker, to be published.
(11) E. H. Eyster, *J. Chem. Phys.*, **6**, 580 (1939).
(12) V. Schomaker, to be published.
(13) L. Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 1939, p. 159.
(14) The carbon–carbon distance in diamond; *cf.* "Strukturbericht."
(15) J. Y. Beach and D. P. Stevenson, THIS JOURNAL, to be published.

Taking 1.42 Å. as the most likely value for the carbon–oxygen single bond distance (small weight may be attached to values found in the cyclic molecules since their complexity makes reliable determination of individual distances exceedingly difficult), the expected carbon–oxygen double bond distance becomes 1.42 − 0.21 = 1.21 Å., in exact agreement with the average found from formaldehyde, glyoxal, and acetaldehyde.

The shortening of the carbon–carbon distance to 1.50 Å. from the covalent value of 1.54 Å. is probably due in part to resonance of the type suggested by Pauling, Springall, and Palmer,[16] for methylacetylene and methyl cyanide, the resonating structures being



and in part to the formal charge effect,[17] resulting from resonance with



However, it is difficult to estimate the relative contributions of the double bond character and of the formal charge.

If the increase of the R–C–O bond angle in going from formaldehyde[9] (120°) to acetaldehyde (121°) is real, it may be interpreted as indicating a greater amount of *p* orbital in the carbon–carbon bond than there is in the corresponding carbon–hydrogen bond.

The agreement with our values of the results of Ackermann and Mayer,[2] C–C = 1.51 ± 0.05 Å., C–O = 1.20 ± 0.05 Å., and the angle C–C–O = 122 ± 5° is remarkable inasmuch as Ackermann and Mayer determined the three parameters from but three measurements.

Summary

From electron diffraction photographs of acetaldehyde the value 1.50 ± 0.02 Å. has been found for the carbon–carbon distance, 1.22 ± 0.02 Å. for the carbon–oxygen distance, and 121 ± 2° for the carbon–carbon–oxygen angle. It is suggested that in general the covalent carbon–

(16) L. Pauling, H. D. Springall and K. J. Palmer, *ibid.*, **61**, 927 (1939).
(17) N. Elliott, *ibid.*, **59**, 1380 (1937).

oxygen double bond distance is about 1.21 Å. instead of 1.24 Å. The structure of acetaldehyde is discussed briefly in terms of resonance among several valence-bond structures.

PASADENA, CALIFORNIA
PRINCETON, NEW JERSEY RECEIVED AUGUST 10, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, OREGON STATE COLLEGE]

The Heat of Combustion of *cis*- and *trans*-Azobenzene[1]

BY R. J. CORRUCCINI AND E. C. GILBERT

In making theoretical calculations of bond energies, Pauling[2] called attention to the unsatisfactory character of the data on the heat of combustion of azobenzene, and a redetermination of this quantity was undertaken in this Laboratory. While the investigation was still in the early stages, Hartley[3a] reported the preparation of the compound in the two isomeric forms, *cis*- and *trans*-, theoretically to be expected but previously never isolated. The two forms exist in equilibrium in solution, transition to the *cis* form being favored by sunlight. In the solid form the *cis* isomer is reported to be stable. In all previous work with azobenzene, therefore, the possibility exists that undetermined percentages of the two forms may have been present.

With this knowledge at hand the standard methods of purification were modified to take advantage of Hartley's findings in order that the two separate isomers might be prepared in the pure state, and the heat of combustion determined for each. In addition these results permit a new approach to the determination of the heat of transition, which has been measured by Hartley[3b] by another method.

The Calorimeter.—The calorimeter system and its calibration have been described previously in detail.[4] The heat of combustion of the *trans* isomer was measured before certain structural changes had been made in the system and hence the energy equivalent was somewhat different from that described in the reference cited. At the time of the work on *trans*-azobenzene the energy equivalent of the calorimeter (without the charge) was found to be 2507.6, 2507.5, 2506.9 (2505.4), 2507.9, 2507.1, with a mean value of 2507.4 ± 0.4 cal. deg.$^{-1}$. For the combustion of *cis*-azobenzene the calorimeter equivalent was that for which details are given,[4] 2550.0 ± 0.2 cal. deg.$^{-1}$.

The results of this paper are given in conventional calories calculated from international joules by dividing by the factor 4.1833[5] and are referred to the standard temperature of 25° in the same manner as previously.[4]

Preparation of Compounds.—Hartley[3] has shown that the formation of the *cis* form is favored by solar radiation, and that, being more polar, this form is consequently more soluble in polar solvents, this preferential solubility being the basis of the separation of the two forms.

Various samples of azobenzene were therefore recrystallized from aqueous ethanol and methanol, and from benzene and chloroform, all in very dim light. All the samples melted at 68.0–68.1° (by the capillary tube method) against a thermometer calibrated by the Bureau of Standards, and were combined for a final recrystallization from aqueous acetone. Any possible small amount of the *cis* form present originally should have been converted due to the temperature effect, or left in solution, it being thirty times as soluble in water as the *trans*-azobenzene. The product was dried in the dark over phosphorus pentoxide and melted at 68.1°. The minimum time for drying of these samples before combustion was eight days.

For the preparation of *cis*-azobenzene the most recent method of Hartley was used.[3b] A saturated solution of azobenzene in glacial acetic acid (500 cc.) was insolated for several hours in bright sunlight, keeping it in an ice-bath to reduce the temperature. This precaution was found to be imperative though not mentioned by Hartley. From this point all operations were carried out in the darkroom. Four hundred fifty cc. of water was added to precipitate the major portion of the *trans*-azobenzene and the solution filtered. The filtrate was diluted further with 500 cc. of water and extracted with chloroform. The extract was washed with water and evaporated immediately with reduced pressure. The products from several exposures were united and recrystallized twice more from petroleum ether (b. p. 40–60°) at temperatures from 20 to −10°, each time being washed with liberal portions of the solvent. The melting point of the compound measured by the "dip" method used by Hartley was 71.6°, slightly above the m. p. (71.4°), previously reported for the substance. The

(1) Taken from a thesis submitted by R. J. Corruccini toward the M. A. degree, Oregon State College, July, 1939. Published with the approval of the Monographs Publication Committee, Oregon State College, as Research Paper No. 26, School of Science, Department of Chemistry.

(2) Pauling, THIS JOURNAL, **54**, 3570 (1932).

(3) (a) Hartley, *Nature*, **140**, 281 (1937); (b) *J. Chem. Soc.*, 633 (1938).

(4) Hughes, Corruccini and Gilbert, THIS JOURNAL, **61**, 2639 (1939).

(5) Rossini, *Chem. Rev.*, **18**, 233 (1936).

compound was kept in the dark over phosphorus pentoxide for four days with no observable change in the m. p., and seven determinations of the heat of combustion were then made. One was discarded because of carbon formation.

The remainder of the compound was then again recrystallized from petroleum ether, no change being observed in the m. p. It also was dried for four days over phosphorus pentoxide in a refrigerator and two more combustions made.

Checking against possible loss due to volatility, a standard sized sample was found to lose only *ca.* 0.02 mg. in weight per hour, which is therefore negligible, since the combustion always followed weighing within less than this interval of time.

Results

The results for the combustion of *trans*-azobenzene are given in Table I, and for *cis*-azobenzene in Table II. The "precision error" of the determinations has been calculated by the method of Rossini.[5] For the *trans* form the accuracy uncertainty assigned to the heat of combustion of the standard benzoic acid (39 e) by the Bureau of Standards is 0.023%. The calibration error "*c*" of the first calorimeter was 0.015% and the reaction error "*b*" for the combustion of *trans*-azobenzene was 0.01%. The resulting accuracy error was 0.03%.

TABLE I

THE ISOTHERMAL HEAT OF COMBUSTION OF *trans*-AZOBENZENE AT 25°

Energy equivalent of the calorimeter 2507.4 ± 0.4 cal. deg.$^{-1}$

True mass of sample, g.	Corr.[a] temp. rise, deg.	Total heat evolved, cal.	Cal. from HNO_3	$-\Delta U_B/m$, cal. g.$^{-1}$	Dev. from mean
0.68454	2.3171	5818.8	11.4	8483.6	+0.3
.73356	2.4840	6238.0	14.0	8484.7	+1.4
.73534	2.4881	6248.5	13.1	(8479.6)	(−3.7)[b]
.73119	2.4750	6215.4	12.9	8482.8	−0.5
.73868	2.5003	6279.0	12.5	8483.4	+ .1
.73187	2.4770	6220.5	13.1	8481.5	−1.8
.72606	2.4578	6172.2	12.5	8483.7	+0.4
			Mean =	8483.3	±0.8

[a] Corrected for heat of stirring, evaporation, etc., and for the energy of ignition of the iron wire. [b] Not used in obtaining the mean.

TABLE II

THE ISOTHERMAL HEAT OF COMBUSTION OF *cis*-AZOBENZENE AT 25°

Energy equivalent of the calorimeter 2550.0 ± 0.2 cal. deg.$^{-1}$

True mass of sample, g.	Corr.[a] temp. rise, deg.	Total heat evolved, cal.	Cal. from HNO_3	$-\Delta U_B/m$, cal. g.$^{-1}$	Dev. from mean
0.70053	2.3460	5991.3	11.9	8535.6	−1.8
.70482	2.3606	6028.7	11.6	8537.2	−0.2
.70636	2.3680	6047.6	13.1	(8543.0)	(+5.6)[b]
.73077	2.4477	6251.2	12.4	8537.3	−0.1
.74352	2.4909	6361.6	12.3	8539.5	+2.1
.72306	2.4222	6186.0	12.0	8538.8	+1.4
.72857[c]	2.4407	6233.4	12.5	8538.4	+1.0
.71989[c]	2.4105	6156.3	11.9	8535.2	−2.2
			Mean =	8537.4	±1.2

[a] Corrected for heat of stirring, evaporation, etc., and for the energy of ignition of the iron wire. [b] Not used in obtaining the mean. [c] These samples were recrystallized once more than the first six samples.

Similarly for the *cis*-azobenzene, the calibration error "*c*" was 0.006% and the reaction error "*b*" 0.014%. Including with these a reasonable allowance of 0.03% for possible lack of purity of the *cis* form, the accuracy uncertainty for this isomer becomes ±0.04%. The question of the purity is obviously an important one. The only criterion available to us was the m. p., which is obviously not of the same order of accuracy as the heat measurements. However, the fact that repeated crystallization failed to change either the m. p. or the heat of combustion gives reasonable confidence in the purity of the compound. Swietoslawski and Bobinska report[7] that their azobenzene was prepared by vacuum distillation and melted at 68.35–68.40°. Samples prepared in our laboratory by this method (three distillations *in vacuo*) melted at 68.1°, the temperature which we obtained for pure *trans*-azobenzene prepared by crystallization. As a further check, all of the *cis* residues which had been through several additional steps of treatment in their preparation were reconverted to the *trans* by heating to 135° for fifteen minutes, at which temperature the *cis–trans* transition is instantaneous.[3b] The *trans*-azobenzene thus formed likewise showed the original melting point of 68.1°.

From $-\Delta U_B$, the heat evolved in the bomb process per gram formula weight, $-\Delta U_R$, the decrease in energy for the combustion reaction at the standard state as defined by Washburn[6] was calculated. In doing this it was assumed that the nitrogen produced in the combustion may be treated as if it were oxygen. $-\Delta H_R$, the heat evolved in the isothermal process in the standard state at constant pressure was also calculated. These results for *trans*-azobenzene are shown in Table III where are also collected the results of other investigators. It seems apparent that in the most recent work, that of Swietoslawski and Bobinska,[7] the azobenzene must have been essentially the pure *trans* form. Since this work

(6) Washburn, *Bur. Standards J. Research*, **10**, 544 (1933).

(7) Swietoslawski and Bobinska, *Roczniki Chem.*, **9**, 723 (1929).

was done before the Washburn corrections were available, and with different conversion units, etc., quantitative comparison is difficult. The value reported by Swietoslawski to the Bureau of Standards is different from that in his published work.

TABLE III

COMPARISON OF DATA ON *trans*-AZOBENZENE

Investigator	$-\Delta U_B$	$-\Delta H_B$[e] kcal. mole^{-1}	$-\Delta H_R$
Petit[a]		1555.2	
Lemoult[b]		1552.6	
S. and B.[c]	1543.7	1544.6	
S.[d]		1545.9	
This paper	1545.7	1546.6	1545.6

[a] Petit, *Ann. chim. phys.*, [6] **18**, 145 (1889). [b] Lemoult, *ibid.*, [8] **13**, 562 (1908). [c] Swietoslawski and Bobinska, ref. 7. [d] Swietoslawski, private communication to U. S. Bur. Stds.; see Kharasch, *Bur. Standards J. Research*, **2**, 425 (1929). [e] Heat evolved at constant pressure without Washburn correction to standard reference state.

The comparative results for the two pure forms from the present work are shown in Table IV. From them may be obtained $-\Delta H$ for the transition *cis* → *trans* at 25°. This amounts to 9.9 kcal. mole^{-1} or 54 ± 4 cal. g.$^{-1}$. Hartley[3b] has found by another method 65 ± 4 cal. as the mean of three determinations. Finally, also, $-\Delta H°_{298.16}$, the heat of formation of the compound, may be calculated using 68,318.1 cal. mole^{-1} as $-\Delta H°_{298.16}$ for water and 94,030 cal. mole^{-1} for carbon dioxide.[8] These results are shown in Table IV.

TABLE IV

SUMMARY OF DERIVED DATA ON *cis*- AND *trans*-AZOBENZENE AT 25°

Substance	*trans*-Azobenzene	*cis*-Azobenzene
Mol. wt.	182.21	182.21
$-\Delta U_B$ kcal. mole^{-1}	1545.7 ± 0.3[a]	1555.6 ± 0.2[a]
$-\Delta U_R$	1544.7 ± .4[b]	1554.6 ± .6[b]
$-\Delta H_R$	1545.6 ± .4[b]	1555.5 ± .6[b]
$-\Delta H°_{298.16}$	−75.65	−85.55

[a] Precision uncertainty. [b] Accuracy uncertainty.

Summary

1. The isothermal heat of combustion of *cis*- and of *trans*-azobenzene has been determined for 25° and constant pressure.

2. The heat of formation for each has been calculated.

3. The heat of the transition *cis* → *trans* has been calculated.

(8) Rossini, *Bur. Standards J. Research*, **22**, 407 (1939).

CORVALLIS, OREGON RECEIVED JULY 31, 1939

[A CONTRIBUTION FROM THE MORLEY CHEMICAL LABORATORY, WESTERN RESERVE UNIVERSITY]

Fluorination of Phosphorus Trichloride[1]

BY HAROLD SIMMONS BOOTH AND ABE ROSCOE BOZARTH[2]

This investigation is a continuation of the studies by this Laboratory on the fluorination of non-polar inorganic halides.[3-8] Booth and Swinehart[3] reported the action of antimony trifluoride in the presence of a catalyst on phosphorus trichloride to give a smooth evolution of gases of unknown composition. The only chlorofluoride of phosphorus reported in the literature is PF_3Cl_2 prepared by Moissan.[9]

The generator used in the preliminary study was similar to that shown in Fig. 1A except that the generator head was attached directly to the flask, without a fractionating column. About 200 g. of reagent grade phosphorus trichloride was placed in the flask, the catalyst was added and powdered sublimed antimony fluoride was fed in, as needed for a smooth reaction, by means of the screw solid feed C, at room temperature. (Approximately two cubic centimeters of the catalyst, $SbCl_5$, per 100 g. of PCl_3 was found to be an optimum amount.) With tap water in the generator head, (H), (+15°) the product was largely PF_3, a small amount of PF_2Cl and very little or no $PFCl_2$.

On the assumption that the fluorination of phosphorus trichloride is stepwise, the application of precise control to the operating variables ought to lead to improvements in the yields of chlorofluorides. In a stepwise reaction probability of excessive fluorination should be a minimum when the reaction zone (generator flask A, Fig. 1A), is maintained at such a temperature that the unfluorinated liquid will be gently boiling and refluxing at the pressure maintained in the system, since then a fluorinated product would immediately distil out of the reaction zone as soon as it was formed, due to its lower boiling point.

The apparatus shown as Fig. 1A was constructed so as to attain this end. The reaction flask A was a two-liter,

(1) Original manuscript received August 24, 1938.

(2) From a thesis presented by A. R. Bozarth, May, 1935, to the Graduate School of Western Reserve University in partial fulfilment of the requirements of the degree of Doctor of Philosophy in Chemistry.

(3) Booth and Swinehart, THIS JOURNAL, **54**, 4750, 4751 (1932).

(4) Booth and Bozarth, *ibid.*, **55**, 3890 (1933).

(5) Booth and Stillwell, *ibid.*, **56**, 1531 (1934).

(6) Booth and Swinehart, *ibid.*, **57**, 1333 (1935).

(7) Booth and Herrmann, *ibid.*, **58**, 63 (1936).

(8) Booth and Morris, *ibid.*, **58**, 90 (1936).

(9) H. M. Moissan, "Le Fluor et Ses Composes," 1900, p. 167.

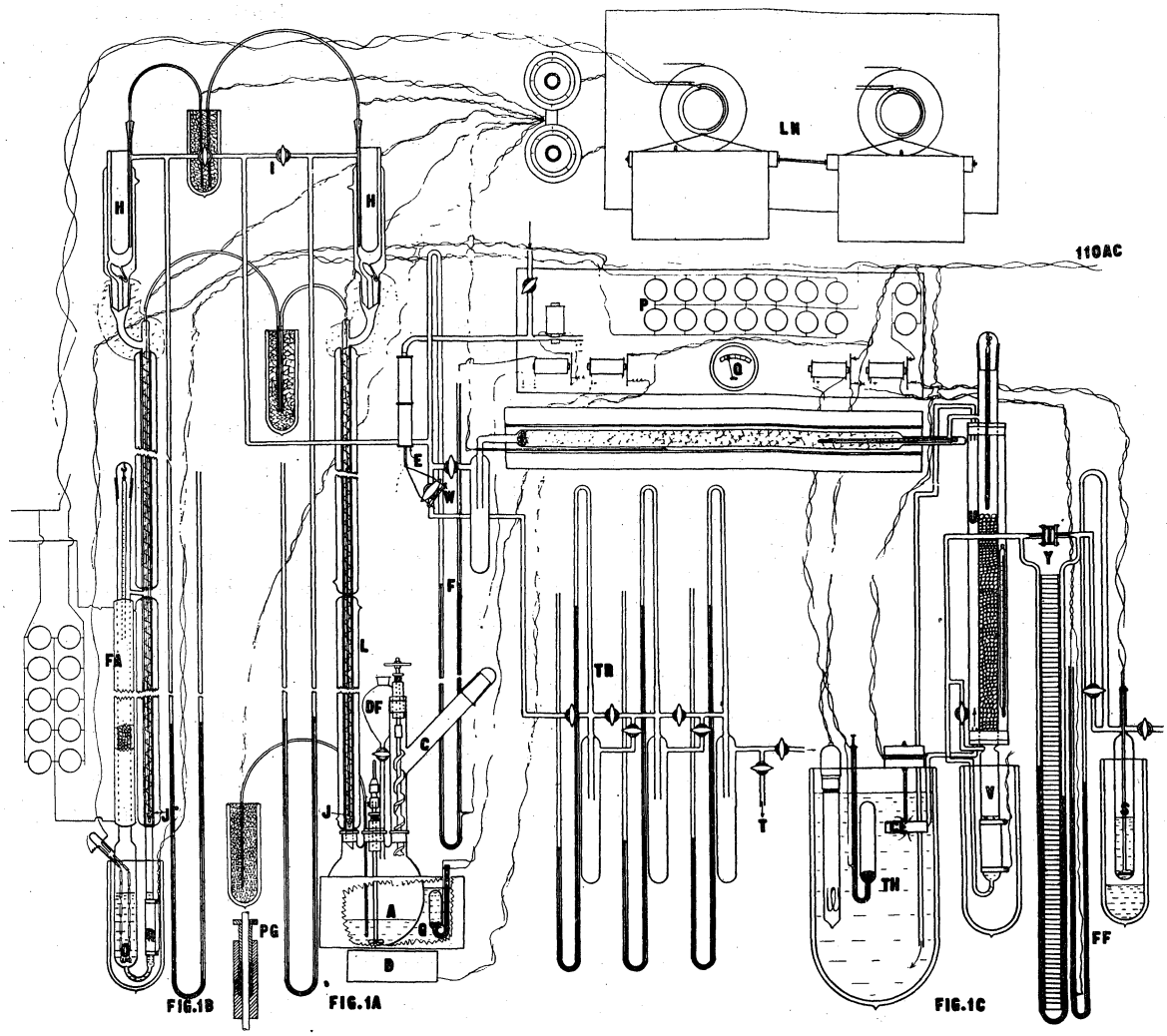


Fig. 1.

Pyrex, three-necked flask. Stirring was accomplished by a brass double-blade propeller which was rendered vacuum-tight at the point of entrance by a gland packed with commercial graphited string packing and lubricated with vacuum pump oil (shown in detail as PG). The temperature of the reaction flask above room temperature was maintained by a thermostatically controlled water-bath heated by an electric heater D, and below room temperature by a thermostatically controlled acetone-bath similar to that used for vapor pressure measurements and controlled either by liquid air or carbon dioxide snow cooling, as described by Booth and Bozarth.[10]

The fractionating column L was identical with that used and already described by the authors[10] except that it was made twice as high to improve the separation. A two-junction thermocouple inserted from the column top through the hollow center tube of the column indicated the temperature of the column bottom at J. A constant temperature was maintained in the still head H either by suitable fixed temperature refrigerants such as tap water, liquid ammonia, carbon dioxide snow wet with acetone, or by automatic thermostatic control with either liquid air or carbon dioxide cooling.[10]

The gaseous product was removed automatically at a constant system pressure by the compressed air operated automatic stopcock W (Fig. 1A) which opened whenever the mercury thread in manometer F completed the relay circuit.

The general method of adjusting the operating variables of the improved generator was as follows.

The bath G (Fig. 1A) was adjusted to the temperature at which fluorination took place. The manometer contact in F (with stopcock I open) was adjusted so as to contact the mercury and thus to open the automatic stopcock to the traps TR, at a pressure equal to the vapor pressure of the unfluorinated halide at the temperature of the reaction flask. A suitable refrigerant was placed in the head (H) or it was thermostatically controlled so as to maintain the head at the temperature at which the desired chlorofluoride had a vapor pressure equal to the op-

(10) Booth and Bozarth, *Ind. Eng. Chem.*, **29**, 470 (1937).

TABLE I

CONTROLLED FLUORINATION—SWARTS REACTION

Run number		II	III	IV[a]	V	VI
Substance fluorinated		PCl_3	PCl_3	$PFCl_2$	$PFCl_2$	PF_2Cl
Substance, cc.		130	130	31	53	15
$SbCl_5$ catalyst, cc.		2–3	2–3	2	2	2
SbF_3, g.		175	175	150	150	.....
Hours to complete		3.5	3.5	...	2.5	3.0
Absolute generator pressure, mm.		234	250	270	247	720
Temp. of reaction zone, °C.		40	39	− 15	− 15	− 50–55
Column temp., °C.	Bottom-J	33	37	− 13	− 15	− 50–55
	Bath-G	40	39	− 13	− 15	− 50–55
	Still head	15	14.2	− 55	− 60–62	−100–150
	Bath in head	Tap water, 12		CO_2 snow–EtOH		Thermostat
Distillation analysis of product	$PFCl_2$, cc. liq.	33	30.5	2.2[a]	14.0	.....
	PF_2Cl, cc. liq.	8.7	10.9	11.8	20.0	4
	PF_3, cc. liq.	11	12.8	7.2	11.5	10
Desired product, %		63	58	62	64	100

[a] The generator flask was not heated at the end of the fluorination to break up the loose addition compound probably formed between SbF_3 and $PFCl_2$, which probably accounts for the loss of some of the $PFCl_2$.

erating pressure. In the first studies upon an unknown gas this latter value must be approximated by means of the Swarts[11] rule and the Clapeyron equation.

The system was evacuated thoroughly and the halide added through the dropping funnel DF without breaking the vacuum. If the halide did not reflux after equilibrium was attained, the temperature of the bath G was increased until it did. The catalyst was then added through DF and allowed to mix well with the halide.

The reaction between phosphorus trichloride and antimony pentachloride is exothermic and the mixture had to be cooled to operating temperature before adding the antimony trifluoride. The contact in manometer F was adjusted until it was about 4 mm. above the mercury. A small amount of antimony trifluoride was fed in. As soon as the fluorination began the lower boiling fluorination product which is fractionated out formed a "gas block" in the still head H and raised the pressure and so caused the automatic stopcock W to open momentarily to remove the accumulated gaseous product. The stopcock I was opened until it allowed the gas to pass each time the automatic stopcock opened with a minimum fluctuation in generator pressure. As soon as the system settled down to equilibrium the temperature of the reaction zone, column bottom and still head, was determined. If the column bottom temperature (at J) was lower than the reaction zone temperature, the temperature of the bath about the flask had to be increased until the column bottom temperature reached a maximum which corresponded closely to the reaction zone temperature at the beginning of the fluorination. Under these conditions only pure unfluorinated halide returned to the reaction zone.

Fluorinations which are comparatively rapid such as fluorination of phosphorus trichloride do not lend themselves to the preparation of the difluoro compound exclusively directly from the unfluorinated halide. Any accumulation of the monofluoro is rapidly fluorinated so that the product is a mixture of the difluoro derivative and the completely fluorinated product. This is due to the fact that the threshold fluorinating temperature lowers with the replacement of each chlorine atom by fluorine in covalently unsaturated non-polar halides.

Table I shows the average data obtained for two runs fluorinating phosphorus trichloride with the conditions controlled to favor $PFCl_2$, two runs fluorinating $PFCl_2$ under conditions favoring PF_2Cl and one run fluorinating PF_2Cl to PF_3. The product condensed in each case was 50 to 75% the product desired, which was the opposite of the yields obtained without precise control, in which the product was 75–90% PF_3 (Table II).

TABLE II

FLUORINATION OF PHOSPHORUS TRICHLORIDE WITHOUT PRECISE CONTROL

Reaction zone at room temp.; press. 760 ± 20 mm.; PCl_3 used, 450 g.

Run	Vol. of catalyst, cc.	Distillation analysis of product, % $PFCl_2$	PF_2Cl	PF_3
VIII	5	16.7	32.0	51.5
IX	10 dropped in	19.8	6.2	74.0
X	20 added at start	0	25.0	75.0
XI	20 at start, total of 60	0	16.7	83.3
XII	1 at start	0	5.88	94.0
XIII	10 at start	8.33	25.0	66.7

Whereas phosphorus trichloride fluorinated smoothly at a temperature of +40° and 250 mm. pressure, $PFCl_2$ can be fluorinated at an equal rate at −13° and 250 mm. pressure; furthermore, it is even possible to fluorinate PF_2Cl to PF_3 at the low temperature of −50 to −55° and 720 mm. pressure. At +40° the rate of fluorination of $PFCl_2$ was quite rapid and that of PF_2Cl was very rapid, while the rate of fluorination of phosphorus trichloride was relatively slow. These facts explain both the difficulty of avoiding fluorination

(11) F. Swarts, *Bull. soc. chim.*, **35**, 1556 (1924).

beyond the first step even under controlled conditions, and the completeness of fluorination under uncontrolled conditions, due to increasing rate with increased fluorination.

Antimony trifluoride does not react with phosphorus trichloride to any appreciable extent in the absence of the catalyst ($SbCl_5$) at the temperatures maintained during this study.

Fluorination of Phosphorus Trichloride in the Vapor Phase by Solid Heated Calcium Fluoride

E. I. du Pont de Nemours and Company[12] have indicated that heated calcium fluoride may act as a fluorinating agent for organic halides in the vapor phase, producing chlorofluoro compounds from aliphatic chlorides.

An apparatus for the vapor phase fluorination of phosphorus trichloride by calcium fluoride was constructed of soda-lime glass as shown in Fig. 1B. The calcium fluoride furnace FA was a glass tube 1.6 cm. in diameter by 60 cm. long, wound with a thin layer of asbestos tape followed by no. 18 nichrome wire, three turns per inch, and then wrapped with heavy asbestos paper. The temperature was controlled by a split lampbank, one-half of which was controlled by the contacts of a recording controlling potentiometer.

C. P. precipitated calcium fluoride was formed into pellets about 0.5 cm. in diameter by a pharmaceutical pellet machine, and then dried at 125–150° before use.

The fluorination of a halide by this reaction was carried out as follows. The temperature of the furnace was indicated by a thermometer, at the exit end of the furnace. The halide was boiled at a constant rate by an internal coil heater O (fed by a constant current). The exit furnace gases passed into the middle of the fractionating column where the fluorinated product was separated from the unfluorinated. The still-head temperature in H was adjusted so as to correspond to the boiling point of the product desired at the pressure maintained in the system. The contact in the manometer F was adjusted so as to make contact and so to open the automatic stopcock W, whenever the pressure rose slightly due to accumulation of fluorinated product in the still head. A thermocouple at J at the column bottom indicated the temperature of the liquid returned to the boiling ampoule O. By controlling the heat input to the auxiliary heating coil, R, the column bottom temperature could be maintained identical with the temperature of the pure halide at the pressure maintained in the system. Under these conditions no fluorinated substance was being returned to the reaction zone and consequently recirculated through the furnace to be further fluorinated.

Although it was not tried, it seems perfectly feasible, by this method, to convert $PFCl_2$ over mainly to PF_2Cl by proper adjustment of operating variables.

(12) French Patent 730,874, May 23, 1932, "Perfectionnements a la Fabrication des Hydrocarbures Acyclique Fluors."

Reaction between Phosphorus Trichloride and Phosphorus Trifluoride at High Temperature

It was thought that perhaps at higher temperatures phosphorus trichloride and phosphorus trifluoride might react to give the equilibrium, $PF_3 + PCl_3 \rightleftarrows PF_2Cl + PFCl_2$. Since we started our experiments, T. Mitobedzki[13] has described a similar reaction for the preparation of the bromochlorides of phosphorus.

The apparatus finally developed is shown as Fig. 1C. The PF_3 was condensed into ampoule S. It was then melted and a Dewar one-third full of liquid air was placed around the ampoule (but not in contact with it). A small heating coil in the liquid phosphorus trifluoride (boiling point −101°) heated it much faster than it cooled, so that the pressure was raised rapidly to 720 mm. When the pressure reached 720 mm. the mercury in manometer FF made contact, closing a relay circuit which interrupted the heating current. The net result was that phosphorus trifluoride was fed at constant pressure (±2 mm.). The rate of flow of the phosphorus trifluoride was indicated by a sharp-edged orifice flow meter Y. The orifice was a thin platinum sheet with a perfect hole 0.013 mm. in diameter drilled in the center. The platinum plate was clamped between two glass flat joints as indicated. A constant flow was obtained by maintaining a constant pressure drop across the orifice. Since the ampoule S was automatically kept at constant pressure and the pressure on the other side of the orifice was kept constant by the contacting manometer F which operated the automatic stopcock W, a constant pressure drop and therefore a constant flow was maintained through the system.

The phosphorus trifluoride was saturated with phosphorus trichloride by being bubbled through the phosphorus trichloride in ampoule V, heated by a coil of nichrome wire fed by a constant current. The temperature of the jacket U was adjusted to that temperature at which phosphorus trichloride has a vapor pressure equal to one-half the total pressure in the system. The mixture leaving the saturator under these conditions contained a one to one molal ratio of phosphorus trifluoride to phosphorus trichloride. A centrifugal pump, CE, pumped water, maintained at constant temperature, from the bath TH through the jacket U. The reaction tube was made of glass, and the furnace temperature was controlled by a recording, controlling potentiometer, LN.

Preliminary runs in a smaller and less refined apparatus showed that at around 230–250° no appreciable reaction occurs; at 500° reaction takes place but phosphorus deposits and probably silicon fluoride is produced by a reaction analogous to that indicated by A. Simon[14,15] between silica and phosphorus trifluoride,

$$4PF_3 + 3SiO_2 \longrightarrow 3SiF_4 + 3O_2 + 4P$$

When the furnace temperature approximated 400° no phosphorus deposited, indicating little or no reaction with the glass tube. Under these con-

(13) T. Mitobedzki, *C. A.*, **27**, 475 (1933).
(14) Mellor, "Treatise on Inorganic Chemistry," Vol. VIII, p. 995.
(15) Simon, German Patent 131,414 (1900).

ditions approximately 30% conversion of phosphorus trifluoride was obtained per pass.

Two runs at 500° in the apparatus just described gave considerable phosphorus and etching. The product, moreover, upon distillation, yielded a constant boiling fraction, probably consisting of SiF_4 and PF_2Cl, as analysis showed a mean value of 14.1% chlorine (calcd. for PF_2Cl, 34%). We were able to purify the $PFCl_2$ fraction and the molecular weight of the product coming from the still gave a mean value of 122, which is in accord with 121.8 found for the calcium fluoride reaction product and the theoretical molecular weight, 121.5. Between 350 and 400° it is possible to get mainly the equilibrium

$$PCl_3 + PF_3 \rightleftharpoons PF_2Cl + PFCl_2$$

At the temperature at which the equilibrium shifts appreciably to the right (400°), other products such as POF_3 and SiF_4 are formed. It was soon found that PF_2Cl readily forms constant boiling point mixtures with POF_3, etc., which are difficult to separate and identify, as their molecular weights are close. Considerable time also is required to attain equilibrium in this reaction. Hence, as a method of preparation this method is of little value.

The possibilities of using a Pyrex or metal tube and a catalyst suggested themselves but they were not tried since the Swarts reaction and the calcium fluoride reaction had been simultaneously modified and improved by precise control so as to produce mainly $PFCl_2$ and PF_2Cl.

Purification

The gases were purified by fractional distillation in an automatic column and their physical properties determined as described by Booth and Bozarth.[10]

Analysis

One hundred-cc. sample bulbs, filled to not over 700 mm. pressure, were weighed against counterpoises. The samples were absorbed at once (to minimize reaction with the stopcock grease) into a sodium hydroxide solution containing 100% excess sodium hydroxide, by placing the lower stopcock tube under the caustic and opening the cock. The gas is absorbed rapidly, the caustic rushing into the bulb with the evolution of heat. The solution was allowed to stand in the bulbs for two to three hours to ensure complete reaction.

The chlorine was determined gravimetrically with the following precautions. The samples were diluted to 200 cc. and acidified with nitric acid and then 30 cc. of concentrated nitric acid was added. It was found that in the presence of this amount of nitric acid the phosphite did not reduce the silver in the cold. If the concentration of nitric acid was too low, boiling immediately threw down metallic silver.

The phosphorus content was determined by oxidation with excess standard iodine solution and back titration of the excess with sodium thiosulfate, according to the method of Rosenheim and Pinsker.[16] The presence of fluorine was established qualitatively. The analytical results are recorded in Table III.

TABLE III

ANALYSIS OF PCl_3

	Chlorine	Phosphorus
Found	77.20	22.70
		22.38
		22.74
Mean	77.20	22.61
Calcd.	77.42	22.55

ANALYSIS OF PF_2Cl

	Chlorine (sample made by Swarts reaction)	Phosphorus (sample made by Swarts reaction)	Fluorine (by difference)
Found	34.04	29.42	
	33.75	29.56	
	33.84		
	33.90		
Mean	33.88	29.49	36.63
Calcd.	33.94	29.69	36.37

ANALYSIS OF $PFCl_2$

	Chlorine (sample made from the calcium fluoride reaction)	Phosphorus (sample made by Swarts reaction)	Fluorine (by difference)
Found	58.59	25.75	
	58.70	25.61	
	58.78		
Mean	58.60	25.68	15.72
Theory	58.63	25.63	15.74

ANALYSIS OF PF_3

	Phosphorus (sample made by Swarts reaction)	Fluorine (by difference)
Found	34.98	
	35.00	
Mean	34.99	65.0
Calcd.	35.24	64.76

Physical Constants and Properties

After preliminary separation of the generation product, each fraction was purified carefully by the distillation technique already described. Finally a middle portion of a fraction coming from the still at constant still-head temperature and constant molecular weight was collected separately. This sample was used for measurement of the physical constants.

$PFCl_2$, Monofluorodichlorophosphine is a colorless gas which can be condensed to a colorless sparkling liquid and frozen to a clear white solid. This substance yields twig-like crystals upon freezing. Table IV gives the physical constants of $PFCl_2$.

$PFCl_2$ hydrolyzes in moist air and is hydrolyzed by water, but does not fume. It is absorbed very rapidly by sodium hydroxide solution with the evolution of heat. The compound appears to be stable: approximately 50 cc. of liquid $PFCl_2$ was stored under pressure in a sealed

(16) Rosenheim and Pinsker, *Z. anorg. allgem. Chem.*, 64, 333 (1909).

glass tube for ten months. At the end of this time the liquid was homogeneous and no excess pressure above that of the vapor pressure of $PFCl_2$ had developed.

PF_2Cl, Difluoromonochlorophosphine is a colorless gas which can be condensed to a colorless sparkling liquid and frozen to a white solid.

TABLE IV

PHYSICAL CONSTANTS OF $PFCl_2$

Vapor pressure $PFCl_2$, $\log p_{mm.} = 7.439 - (1308/T)$

	Pressure, mm. at 0°				
Temp., °C.	Prepared by the Swarts reaction	Prepared by CaF_2 reaction	obsd. mean two methods of prepn.	Pressure Calcd.	Deviation, mm.
−61.22	6.3	6.6	6.5	...	...
−53.92	24.6	27.9	26.2	29.6	+3.4
−44.52	51.3	50.5	50.9	52.1	+1.2
−33.74	92.3	91.2	91.8	94.4	+2.6
−22.96	161.8	161.5	161.7	163.4	+1.7
−12.46	263.2	262.9	263.0	263.8	+0.8
− 8.16	319.7	319.2	319.5	318.1	−1.4
− 3.99	378.8	378.9	378.9	379.4	+0.5
+ 2.28	489.6	490.9	490.3	489.6	−0.7
+ 7.40	596.1	598.7	597.4	597.6	+0.2
+12.85	729.3	734.2	731.8	733.3	+1.5
+14.94	796.0	799.2	797.6	791.6	−6.0
+18.17	881.6	884.9	883.3	888.8	+5.5

Normal boiling point		+13.85 ± 0.05°
Latent heat of evaporation		5950 cal./g. mole
Trouton's constant		20.7
M. p., °C.	Swarts reaction 1934	−144.0 ± 0.2
	Swarts reaction 1933	−144.0 ± .2
	Calcium fluoride reaction	−144.4 ± .2
Mol. weight	Swarts reaction	122.0
	Calcium fluoride reaction	122.0

This gas tends to form difficultly separable mixtures with SiF_4 and POF_3. The molecular weights of SiF_4 (104.06), POF_3 (104.03) and PF_2Cl (104.48) are so near that indication of precise separation by means of the density balance becomes impossible. It was found that the PF_2Cl produced by high-temperature fluorination with calcium fluoride could not be rendered completely pure by repeated distillation, as evidenced by low analytical results and molecular weights.

TABLE V

PHYSICAL CONSTANTS OF PF_2Cl

Vapor pressure PF_2Cl, $\log p_{mm.} = 7.043 - (939.7/T)$

Temp., °C.	Press. obsd., mm.	Press. calcd. from equation	Deviation, mm.
−83.22	125.4	124.4	−1.0
−71.81	236.5	236.0	−0.5
−64.34	346.3	348.3	2.0
−60.73	419.9	423.5	3.6
−55.14	535.8	539.9	4.1
−50.21	668.0	672.3	4.3
−49.23	702.4	701.6	−0.8
−46.20	798.4	800.0	1.6
−42.22	934.4	940.6	6.2

Normal boiling point	−47.3 ± 0.05°
Latent heat of evaporation	4200 cal./g. mole
Trouton's constant	19.1
Melting point, prepared by fluorination of $PFCl_2$ by Swarts reaction	−164.8 ± 0.2°
Molecular weight	105.5

By avoiding leaks and by careful drying, the Swarts reaction yielded samples of PF_2Cl which could be purified to yield a pure fraction for melting point, vapor pressure, and analysis. The physical constants of PF_2Cl are given in Table V.

PF_2Cl hydrolyzes in moist air and water less rapidly than $PFCl_2$ but does not fume. It is absorbed very rapidly by sodium hydroxide solution with the evolution of heat. When stored as a liquid at −78° over long periods it appears to be stable.

PF_3, Trifluorophosphine.—This gas was prepared first by Moissan.[9] It is a colorless gas which can be condensed to a liquid, and frozen to a white solid. It is prepared best by dropping solid antimony fluoride into 200 g. of vigorously stirred phosphorus trichloride and slowly adding the catalyst. Every precaution must be taken to keep the partially fluorinated products in the reaction zone. The product is 80–90% trifluorophosphine (see Table II). A large sample was precisely distilled and the middle portion of the pure fraction used for measurement of the physical constants (Table VI).

TABLE VI

PHYSICAL CONSTANTS OF PF_3

Vapor pressure PF_3 (made by Swarts reaction) $\log p_{mm.} = 7.310 - (761.4/T)$

Temp., °C.	Sample	Press. obsd. mm. at 0°	Press. calcd. from equation	Deviation, mm.
−116.8	A	274.0	275.1	1.1
−113.48	B	345.9	347.4	1.5
−110.02	B	435.0	437.1	2.1
−103.51	A	662.6	662.4	−0.2
−102.61	B	690.9	699.9	8.5
−101.07	A	762.5	767.0	4.5
−100.04	B	800.4	796.4	−4.0
− 99.45	A	844.7	843.5	−1.2
− 97.50	A	945.0	943.4	−1.2

Normal boiling point (Moissan found −95°)	−101.15 ± 0.05°
Latent heat of evaporation	3489 cal./g. mole
Trouton's constant	20.3
Melting point (Moissan, −160°)	−151.5 ± 0.2°
Molecular weight	89.0 (this study); 87.2 (Moissan); 88.0 (theory)

Trifluorophosphine hydrolyzes very slowly in air and when pure it is odorless in toxic concentrations. This property of trifluorophosphine makes it hazardous to handle since any leaks are not detected readily until the operator begins to feel the effects. Its symptoms are a sharp pain in the chest cavity upon inhalation of a deep breath. There is a pronounced rise in body temperature, vomiting is induced in some cases, and the victim feels very weak for several hours. (These are the authors' experiences.) Very small concentrations will cause the sharp chest pain. Trifluorophosphine is absorbed rapidly by sodium hydroxide with the evolution of heat.

Critical Constants

These physical constants were measured by means of the apparatus and improved technique developed in this Laboratory.[17] The critical temperature was taken as that temperature at which the meniscus disappeared from the tube without rising or falling. The temperature above that of the room was maintained by resistance knife heaters; below room temperature by a new method using dry-ice as described by Booth and Bozarth.[10]

Considerable difficulty was encountered while measuring the critical constants of $PFCl_2$. Due to the high critical temperature the sample would liquefy in the upper part of the Cailletet tube exposed to the room. When the pressure was further increased so as to force the sample into the cell the liquid would wet the walls of the capillary and tend to come back past the mercury so that the sample could not be readily forced into the cell without mercury going into the cell also. In contact with mercury at the critical temperature this gas decomposed probably forming halides of mercury and leaving a deposit of yellow phosphorus. By careful manipulation of one sample mercury was kept out of the cell. In this case slight decomposition also was noted; a light brown film, probably elemental phosphorus, was formed. One sample was held at the critical temperature for five and one-half hours; a 2.3° rise in the critical temperature and a 0.94 atm. rise in the critical pressure was noted, simultaneously with the formation of a brown film on the walls of the cell. Table VII lists the critical constants found for this series.

TABLE VII

CRITICAL CONSTANTS OF PCl_3, $PFCl_2$, PF_2Cl AND PF_3

	T_c, °C.	P_c, atm.	
PF_3	−2.05 ± 0.02	42.67	
	−2.05 ± .02	42.70	
Mean	−2.05 ± .02	42.69	
Source: mixture of PF_3 from fluorinating PCl_3 and also $PFCl_2$ by Swarts reaction.			
PF_2Cl	89.17 ± 0.05	44.62	
	89.16 ± .05	44.59	
Mean	89.17 ± .05	44.61	
Source: fluorination of $PFCl_2$ by Swarts reaction			
$PFCl_2$	189.88 ± 0.05	49.60	
	189.80 ± .05	48.99	Best value
Mean	189.84 ± .05	49.3	
Source: Swarts reaction from PCl_3[18]			
PCl_3[18]	285.5[a]	Critical pressure not measurable by the closed tube method.	

[a] t_c measured by the closed tube method.

(17) Booth and Swinehart, THIS JOURNAL, **57**, 1337 (1935).
(18) Br. Pawlewski, *Ber.*, **16**, 2633 (1883).

Reaction of the Fluorination Products with Chlorine.—Chlorine was mixed with one of the chlorofluorides of phosphorus at the entrance of an empty tube 2.0 cm. in diameter and 40 cm. long. The fluoride gas was fed into the reactor tube at constant rate by a gas feed identical with that described in Fig. 1C. It was found that the reaction would not start in a clean glass apparatus but the presence of a single crystal of iodine immediately catalyzed the reaction. The reaction of PF_2Cl and chlorine is evidently exothermic since the chlorination tube warmed to 80–100° whereas the reaction between $PFCl_2$ and chlorine is not as exothermic since the reaction tube temperature remains unchanged. PF_3 and chlorine do not combine readily in the presence of iodine. If, however, the reaction tube is radiated with a carbon arc, rapid reaction takes place to form PF_3Cl_2. Preliminary experiments indicate that Moissan's value for the boiling point of PF_3Cl_2 given as −8.0° is incorrect; the correct value probably lies in the range 0 to 10°.

The products obtained by chlorination of $PFCl_2$ and PF_2Cl, probably $PFCl_4$ and PF_2Cl_3, are unstable liquids having the respective vapor pressures 275 mm. at 75–80° and 387 millimeters at 32°. $PFCl_4$, which decomposes in about thirty hours at 25°, yields as decomposition products a white solid, probably PCl_5, and a colorless gas, probably PF_5. PF_2Cl_3 does not decompose as rapidly; a white solid was apparent after standing for twenty-four hours and decomposition was complete in about six days. Moissan found that PF_3Cl_2 decomposed at 200° to form a white solid, PCl_5, and a gas, PF_5.

Summary

An apparatus and technique applicable to the controlled fluorination of inorganic halides is demonstrated.

The chlorofluorides of phosphorus have been prepared by three methods: (1) The Swarts reaction between PCl_3 and SbF_3 in the presence of $SbCl_5$ as a catalyst. (2) The calcium fluoride reaction, a gas–solid reaction between PCl_3 vapor and hot solid CaF_2. This is the first time to our knowledge that this reaction has been applied to the preparation of chlorofluorides from inorganic halides. (3) The reaction between PCl_3 and PF_3 in a hot tube. This method is unsatisfactory as a method of preparation due to side reactions with the glass to form POF_3 and SiF_4 which are extremely difficult to remove from PF_2Cl by distillation.

Two new gases ($PFCl_2$ and PF_2Cl) were obtained and PF_3 was restudied, using improved technique, with melting and boiling points as follows:

	M. p., °C.	B. p., °C.
$PFCl_2$	−144.0 ± 0.2	13.85 ± 0.05
PF_2Cl	−164.8 ± .2	− 47.3 ± .05
PF_3 (ours)	−151.5 ± .2	−101.15 ± .05
Moissan	−160	− 95

$PFCl_2$, PF_2Cl and PF_3 react with chlorine to produce pentavalent chlorofluorides. $PFCl_2$ and PF_2Cl yield liquid products which are unstable, decomposing at room temperature into PCl_5 and PF_5.

Phosphorus trifluoride when pure is odorless in toxic concentration and therefore care must be exercised in its manipulation.

The critical temperatures and pressures for PF_3, PF_2Cl and $PFCl_2$ have been determined.

CLEVELAND, OHIO RECEIVED AUGUST 9, 1939

[A CONTRIBUTION FROM THE MORLEY CHEMICAL LABORATORY, WESTERN RESERVE UNIVERSITY]

The Fluorination of Phosphorus Tribromide[1]

BY HAROLD SIMMONS BOOTH AND SPENCER G. FRARY

The successful controlled partial fluorination of phosphorus trichloride[2] led us to study the fluorination of phosphorus tribromide by similar methods.

A preliminary generation was made using 36 cc. of C. P. phosphorus tribromide with 3 cc. of bromine as a catalyst. The fluorinator was immersed in a Dewar of water heated to +80°. Sublimed antimony trifluoride[3] was added gradually by a screw feed while the pressure was maintained at 20 mm. of mercury by the pressure regulator. Under these conditions the tribromide refluxed in the column with no refrigerant needed in the stillhead. Fractional distillation[4] of the products obtained by generation at −20° and under 220 mm. pressure yielded PF_3, HCl and HBr in small amounts, PF_2Br, and small amounts of HF. The still residue contained $PFBr_2$ and PBr_3. Since these conditions favored the production of $PFBr_2$, the pressure was raised to about 250 mm. With the same temperature in the fluorinator and ice in the head there was no refluxing of either PBr_3 or $PFBr_2$. The products of this fluorination were 10 cc. of $PFBr_2$, an equal amount of liquid PF_2Br and approximately 30 cc. of liquid PF_3, along with a little HBr and HF due to hydrolysis.

Later, when larger amounts of PF_2Br were needed in order to obtain a good fractional separation and purification, it was found that the yields obtained at 80 and 90° were poorer than those at higher temperatures. With the temperature of the fluorinator at 170°, the yield of partially fluorinated products was doubled.

The Fluorination of Monofluorodibromophosphine by Antimony Trifluoride and Bromine.—Booth and Bozarth[2] have shown that the fluorination of phosphorus trichloride with antimony trifluoride and antimony pentachloride as catalyst is a stepwise reaction and that the intermediate $PFCl_2$ can be fluorinated readily under proper control to PF_2Cl, but that the fluorination threshold temperature lowers with each fluorine atom introduced.

Fluorination of monofluorodibromophosphine was tried first at room temperature and at about 200 mm. absolute pressure. The heat of reaction raised the temperature to such an extent that PF_3 was the only product obtained.

The reaction was slowed by cooling the fluorinator to 0° and by reducing the pressure to 20–30 mm. While the product was chiefly PF_2Br, only about 25% of the material was converted. Warming the fluorinator increased the yield but increased the percentage of the trifluoride at the same time.

Hence the fluorination of phosphorus tribromide by antimony trifluoride and antimony pentachloride is likewise stepwise and closely resembles that of phosphorus trichloride.

Fluorination of Phosphorus Tribromide Using Calcium Fluoride.—On account of the successful fluorination of phosphorus trichloride with calcium fluoride by Booth and Bozarth,[2] it was decided to try fluorinating the tribromide with calcium fluoride pellets. The apparatus was similar to that used in the fluorination of phosphorus chloride except that a vertical condenser cooled with

(1) From a portion of a thesis submitted by Spencer G. Frary in partial fulfilment of the requirements for the Degree of Doctor of Philosophy in Chemistry, to the Graduate School of Western Reserve University, June, 1936. Original manuscript received August 24, 1938.

(2) Booth and Bozarth, THIS JOURNAL, 61, 2927 (1939).

(3) Kindly supplied by the Harshaw Chemical Co., Cleveland, Ohio.

(4) Booth and Bozarth, *Ind. Eng. Chem.*, 29, 470 (1937).

tap water was used to condense the unreacted tribromide. The pressure was kept at about 2 cm. and the ampoule heated to 130–140° by an oil-bath to circulate tribromide vapor rapidly. The tube containing the pellets was heated to about 200°. The reaction proceeded very slowly, twenty-four to thirty-six hours of continuous operation being required to obtain 30 cc. of liquid product. This on distillation yielded 15 cc. of PF_3, 10 cc. of $PFBr_2$ and 5 cc. of PF_2Br, showing that the products were the same as those obtained by the reaction with antimony trifluoride and bromine.

Separation and Identification of the Products of Fluorination of Phosphorus Tribromide.—Since the products of the fluorination ranged in boiling point from −101 to +170°, they easily were roughly separated preliminarily.

The liquid $PFBr_2$ was redistilled several times in a small all-glass column at atmospheric pressure, and a small amount transferred to the isoteniscope for a vapor pressure[5] determination. Samples also were taken for analysis, vapor density, melting point and specific gravity determinations as described previously in publications from this Laboratory.

The fraction containing the PF_2Br was returned to the gas fractionating column and purified by repeated distillation at high reflux ratio at 200 mm. pressure.

Analysis.—Samples for analysis were condensed in weighed bulbs of 2-cc. capacity, attached to the apparatus by conical joints. The bulbs were sealed off at a constriction in the connecting tube and both portions again weighed. The sample, weighing about 2.5 g., was then frozen with liquid air, the tube broken, and dropped into an excess of sodium hydroxide solution in a stoppered 250-cc. Erlenmeyer flask and allowed to stand for twenty-four hours to ensure complete hydrolysis.

Phosphorus was determined by oxidizing the phosphite with an excess of standard iodine solution and back-titrating with sodium thiosulfate according to the method of Rosenheim and Pinsker.[6] Bromine was determined volumetrically by the Volhard method. Fluorides do not interfere with this determination if sufficient ferric nitrate is added to form the colorless complex ferric fluoride with all the fluorine. Since we have no satisfactory method for the determination of fluorine in the presence of phosphites, it was obtained by difference, but its presence was established qualitatively.

TABLE I

ANALYSES

	$PFBr_2$ Found	$PFBr_2$ Calcd.	PF_2Br Found	PF_2Br Calcd.
Phosphorus	14.99		20.5	
	14.95		21.2	
Av.	14.97	14.76	20.85	20.88
Bromine	76.17		53.8	
	76.20		53.2	
Av.	76.19	76.14	53.5	53.66
Fluorine (difference)	8.84	9.10	25.65	25.46

Boiling points were taken from vapor pressure curves drawn from the data in Table II. The latent heat of vaporization was calculated by the Clausius–Clapeyron equation.

TABLE II

VAPOR PRESSURE OF $PFBr_2$

$\log p = 7.866 - (1646.2/T)$

Temp., °C.	Press. obsd.	Press. calcd.	Deviation, mm.
23.5	96	101	5
38.0	186	185	−1
47.0	269	267	−2
54.9	353	351	−2
60.2	426	424	−2
65.3	505	502	−3
77.3	739	738	−1
77.7	746	746	0
78.2	758	757	−1
78.5	762	764	2

VAPOR PRESSURE OF PF_2Br

$\log p = 762.0 - (1217.9/T)$

−51.0	130	134	4
−35.2	315	317	2
−30.9	391	391	0
−23.0	561	564	3
−20.4	630	632	2
−18.2	691	695	4
−16.3	754	753	1
−15.3	779	787	8

The liquid density of $PFBr_2$ was determined in a special pycnometer by the method used by Booth and Herrmann for SO_2ClF.[7]

The vapor density of the PF_2Br was determined by a gas density balance as usual. The $PFBr_2$ was condensed in small bulbs and its vapor density determined in a regular Victor Meyer apparatus, using mercury in a gas buret to measure the volume.

Since these compounds are unstable and react

(5) Booth, Elsey and Burchfield, THIS JOURNAL, **57**, 2064 (1935).
(6) Rosenheim and Pinsker, *Z. anorg. Chem.*, **64**, 333 (1909).
(7) Booth and Herrmann, THIS JOURNAL, **58**, 63 (1936).

with mercury particularly under pressure and at higher temperatures, the critical constants were not determined, but were calculated by the "three-halves" rule.

TABLE III

PHYSICAL CONSTANTS OF THE PHOSPHORUS BROMOFLUORIDES

Subs.	$PFBr_2$	PF_2Br
Mol. wt. Obsd.	218	149
Calcd.	209.8	148.9
M. p., °C.	−115.0	−133.8
B. p., °C.	78.4 ± 0.1	−16.1 ± 0.1
Latent heat of vapn.	7624	5721
Crit. temp. calcd.	254	113
Trouton constant	21.7	22.3
Liquid density	2.1810 at 0°	

The Chemical Properties of the Phosphorus Bromofluorides.—The two bromofluorides condense to clear colorless liquids freezing to white crystalline solids. They fume in air to a greater extent than do either the tribromide or the trifluoride and have a sharp odor. They hydrolyze readily to form phosphorus, hydrobromic and hydrofluoric acids. They react with excess bromine to produce reddish-brown solids which presumably are PBr_4F and PBr_3F_2. These latter are quite unstable and on warming liberate bromine; they were not studied further.

PBr_2F is relatively stable and can be distilled at atmospheric pressure. However, on standing, it very slowly decomposes into PF_3 and PBr_3.

$$3PBr_2F \longrightarrow PF_3 + 2PBr_3$$

It reacts with mercury forming halides of mercury and free phosphorus.

PF_2Br is somewhat less stable than $PFBr_2$ and difficulty was encountered in obtaining it pure. The chemical analysis showed high phosphorus and low bromine, indicating contamination with PF_3. Distillation at low pressure from the column directly into the analysis bulbs and vapor pressure apparatus was necessary in order to obtain samples that gave the results shown in Table III.

If it is allowed to stand at low temperatures as a liquid, part of it decomposes to the fluoride and bromide: $3PF_2Br \longrightarrow 2PF_3 + PBr_3$. When the mixture is transferred from the ampoule the fluoride distils over with the unchanged bromofluoride while the bromide remains behind, causing analyses to be low in bromine and high in phosphorus.

The following experiences suffice to reveal the instability of PF_2Br:

(1) A sample that froze at −133.8° was allowed to stand in the melting point apparatus for several days. It then froze at −144°.

(2) Fifteen cc. of the liquid PF_2Br was held in the column still-pot for ten days at dry-ice temperature (−78°). The pressure rose steadily to almost atmospheric at the end of that time. The sample was then distilled and about 1 cc. of liquid PF_3 and 0.5 cc. of PBr_3 were obtained. This agrees with the equation for the decomposition given above, and indicates a conversion of about 1.5 cc. or 10% in ten days or about 1% per day.

(3) A series of analyses to show how the composition changes is given in Table IV.

TABLE IV

Sample	(1)	(2)	(3)	(4)	(5)	(6)	Calcd.
Phosphorus	30.06	23.0	21.60	21.33	20.5	21.20	20.88
Bromine	29.20	51.33	52.10	53.10	53.8	53.2	53.66
Fluorine	40.74	25.67	26.30	25.57	25.7	25.60	25.46
%PF_2Br from Br content	54.4	95.6	97.1	99.0	100	99.2	

(1) Sample that had stood in the melting point cell for several days before being transferred to the sample bulb. A portion of sample was discarded before transferring to the analysis bulb as well as part of that transferred, to remove some of the PF_3.

(2) Sample that had stood in an ampoule for a short time. Sample taken after about one-third the contents of an ampoule had been removed.

(3) and (4) Samples that were distilled into an ampoule and then immediately transferred to the sample bulbs. About one-sixth of product discarded first.

(5) and (6) Samples distilled directly into analysis bulbs by distillation of middle fraction from column.

Summary

Fluorination of phosphorus tribromide both by the action of antimony trifluoride at 70 and 170° using bromine as a catalyst, and also in the vapor state by reaction with calcium fluoride at 140° yields two new compounds, dibromomonofluorophosphine and monobromodifluorophosphine, as well as phosphorus trifluoride.

Dibromomonofluorophosphine is a clear colorless liquid which boils at +78.4° and freezes at −115.0° to a white solid.

Monobromodifluorophosphine is a gas at ordi-

nary temperatures. It condenses to a colorless liquid boiling at −16.1° and freezes to a white solid at −135.8°.

Both of these compounds hydrolyze on contact with the moisture in the air, react with mercury, liberating phosphorus, combine with bromine to form unstable compounds, probably $PFBr_4$ and PF_2Br_3, and decompose slowly forming PF_3 and PBr_3 at dry-ice temperatures (−78°).

CLEVELAND, OHIO RECEIVED AUGUST 9, 1939

[CONTRIBUTION FROM THE MORLEY CHEMICAL LABORATORY, WESTERN RESERVE UNIVERSITY]

The Fluorination of Phosphoryl Trichloride

BY HAROLD SIMMONS BOOTH AND FREDERIC B. DUTTON[1]

Booth and Swinehart[2] have shown that antimony trifluoride in the presence of a catalyst such as antimony pentachloride causes the progressive fluorination of inorganic non-polar halides. The present investigation is a study of the fluorination of phosphoryl chloride. Phosphoryl trifluoride had been prepared, and its properties first described by Moissan[3] by sparking a mixture of phosphorus trifluoride and oxygen. It has been prepared since by a number of workers using different methods.[4] The intermediate chlorofluorides have not been described previously.

Preparation of Phosphoryl Chlorofluorides.—Phosphoryl trichloride was fluorinated by means of antimony trifluoride using antimony pentachloride as a catalyst, and by means of calcium fluoride pellets at elevated temperatures. The apparatus used in these experiments has been described by Booth and Bozarth.[5]

Fluorination with Calcium Fluoride.—Fluorination by means of calcium fluoride was effected by passing the vapor of boiling phosphoryl trichloride over calcium fluoride pellets contained in an electrically-heated glass tube. The gases on leaving the reactor were so separated in a fractionating column that any unreacted material was returned to the boiling chamber and the fluorinated products were removed continuously. A generation carried out at a pressure of 100 mm. and with the reactor column containing the calcium fluoride pellets held at a temperature of 200° yielded about 90% phosphoryl trifluoride and 10% of higher-boiling substances. A generation carried out at 150° yielded about 35% of the trifluoride, 25% difluoromonochloride, and 40% monofluorodichloride. A generation at 120° gave chiefly the trifluoride but soon stopped and could be continued only by raising the temperature.

Fluorination with Antimony Trifluoride.—Fluorination by means of antimony trifluoride was carried out by slowly adding resublimed, finely crystalline antimony trifluoride[6] to a mixture of 200 g. of phosphoryl trichloride and 50 g. of antimony pentachloride while the liquid mixture was stirred rapidly and maintained at a predetermined temperature. The volatile products of the reaction passed through a condenser which was cooled by running water at about 10°.

A generation carried out with the reaction flask at 75° and a pressure of 190–200 mm. yielded about 55% of phosphoryl trifluoride, 5% of difluoromonochloride and 40% of monofluorodichloride. Higher temperatures (up to the boiling point of phosphoryl trichloride) did not seem to alter the above ratio and lower temperatures increased the yield of the trifluoride at the expense of the other products. The fluorinated products were fractionally distilled in a column, rapidly at first, to effect rough separation of the components. Each component was then carefully refractionated two or more times until further fractionation produced no change in the melting point.

Identification of the Phosphoryl Fluorochlorides

Analysis.—Samples for analysis were condensed in heavy walled bulbs connected to the apparatus by flat-joint connections. After filling, the bulbs were sealed off, weighed, frozen, the necks broken and all dropped into half-normal alkali. The gases dissolved completely on warming. Chlorine was determined either gravimetrically or by the Volhard method, and phosphorus by precipitation as the phosphomolybdate and twice as magnesium ammonium phosphate before ignition to the pyrophosphate.

No particular difficulty was encountered in the analysis of phosphoryl monofluorodichloride or the difluoromonochloride, but phosphoryl trifluoride gave results at first 2–4% low and it was found necessary to evaporate the acidified sample to dryness in a platinum dish to decompose fluophosphates before proceeding with the analysis.

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(1) Submitted by Frederic B. Dutton to the Graduate School, Western Reserve University, in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Chemistry, May, 1937. Reported at the Rochester Convention of the American Chemical Society, September 10, 1937. Original manuscript received August 24, 1938.

(2) H. S. Booth and C. F. Swinehart, THIS JOURNAL, **54**, 4751 (1932).

(3) H. Moissan, *Compt. rend.*, **99**, 655 (1884).

(4) H. Moissan, *ibid.*, **102**, 1245 (1886); H. Moissan, *Bull. soc. chim.*, [3] **4**, 260 (1890); *ibid.*, [3] **5**, 456 (1891); *ibid.*, [3] **5**, 458 (1891); H. Schulze, *J. prakt. Chem.*, [2] **21**, 443 (1880); Thorpe and Hambly, *J. Chem. Soc.*, **55**, 759 (1889); A. Guntz, *Compt. rend.*, **103**, 58 (1886); C. Poulenc and H. Moissan, *ibid.*, **113**, 75 (1891).

(5) H. S. Booth and A. R. Bozarth, *Ind. Eng. Chem.*, **29**, 470 (1937); THIS JOURNAL, **61**, 2927 (1939). Additional illustrations and descriptions of this type of apparatus have been given by H. S. Booth and C. V. Herrmann, *ibid.*, **58**, 63 (1936); H. S. Booth and W. C. Morris, *ibid.*, **58**, 90 (1936).

(6) Kindly furnished by the Harshaw Chemical Company, Cleveland, Ohio.

TABLE I

ANALYSIS OF PRODUCTS OF FLUORINATION OF $POCl_3$

	Phosphorus			Chlorine			Gas density	
	Calcd.	by CaF_2	by SbF_3	Calcd.	by CaF_2	by SbF_3	Calcd.	Found
$POFCl_2$	22.65	22.63	22.31	51.79	51.36	51.97		
		22.67	22.61		51.49	51.97		
POF_2Cl	25.75	25.08	25.39	29.43	29.37	29.54	120.5	119.7
		24.85	25.24		29.65	29.54		
POF_3	29.82	30.07	30.02				104.0	103.4
			29.25					

The gas densities of the phosphoryl trifluoride and difluoromonochloride were determined in a gas density balance as described by Booth and Bozarth.[5]

Physical Properties

Freezing Points.—Freezing points were determined as usual in this Laboratory in a cell containing a magnetic stirrer and a thermocouple, surrounded by two or three concentric glass jackets and finally a Dewar jar containing liquid air. The temperatures were measured by a three-junction thermocouple. The fixed junction was held at the temperature of melting ice and the cooling curves automatically recorded on a Leeds and Northrup Micromax recording potentiometer. Considerable difficulty was encountered in melting and freezing phosphoryl trifluoride. Moissan gave as the boiling point −40°, which is essentially correct, and as the melting point −65°, which is seriously in error. The best determination made in this investigation put the freezing point at −39.4°.[7] The vapor pressure of the solid at the melting point is 771 mm. The liquid has a tendency to superheat with the resulting sudden increase in pressure which either blows a manometer, breaks the apparatus, or both.

On several occasions, when phosphoryl trifluoride had been condensed with liquid air as the refrigerant and this was later changed to dry-ice, the ampoule or cell holding the trifluoride cracked. It was thought that this phenomenon might be the result of a conversion of one solid modification to another. An attempt was made to discover the presence of a transition point by studying the vapor pressure of the solid but it was found that phosphoryl trifluoride condensed with liquid air and then held in dry-ice required two or three days to come to equilibrium, rendering it impractical to make a series of observations of the vapor pressure of the solid at different temperatures.

A second attempt to locate such a transition point was made by the differential method.[8] About 15 cc. of liquid phosphoryl trifluoride was frozen in the bottom of a cell which contained a copper neutral body just above the frozen gas. Two thermocouple wells entered the cell, one terminating in the neutral body and the second at the center of the frozen gas. The entire cell was cooled to liquid air temperature and a warming curve taken. The temperature was observed on the recording potentiometer by means of a 3-junction thermocouple using dry-ice as the fixed junction. At the same time the differential temperature between the neutral body and the frozen gas was observed on a second recording potentiometer by means of a 3-junction thermocouple. The warming curve indicated a change in the rate of warming and the differential curve indicated a maximum at approximately −100°, but neither curve showed a "sharp break"; this indicates a slow transition from one form to another.

TABLE II

VAPOR PRESSURE OF $POFCl_2$

Temp., °C.	P, obsd., mm.	P, calcd., mm.	Deviation, mm.
−30.0	14.6	15.4	0.8
−30.0[a]	14.6	15.4	.8
−20.0	28.1	28.2	.1
−20.0[a]	28.1	28.2	.1
−10.0	48.8	49.4	.6
−10.0[a]	49.4	49.4	.0
0.0	84.8	82.9	−1.9
0.0	83.7	82.9	−0.8
10.0	136.5	134.2	−2.3
20.0	216.1	210.4	−5.7
20.0[a]	217.0	210.4	−6.6
21.2[a]	227.6	221.6	−6.0
25.0	266.9	260.4	−6.5
30.0	326.5	320.0	−6.5
40.0	480.9	473.8	−6.2
49.8	683.1	678.4	−4.7
53.1	764.7	764.2	−0.5
54.9	813.4	813.6	0.2
59.3	942.7	945.6	2.9

[a] Prepared by Swarts reaction; all others by reaction with calcium fluoride. Calculated values were determined by use of the equation $\log p = (-1618.23/T) + 7.8440$.

Vapor Pressure.—The vapor pressure data for phosphoryl monofluorodichloride, which is a liquid at room temperature, were determined in the isoteniscope described by Booth, Elsey and Burchfield.[9] The vapor pressure data for the gases phosphoryl difluoromonochloride and trifluoride were obtained by direct observation of the pressure of the respective liquids held in small glass bulbs, immersed in a thermostat. Temperatures were measured by a resistance thermometer calibrated by the U. S. Bureau of Standards.

(7) Dr. G. Tarbutton, Department of Chemical Engineering, Tennessee Valley Authority, Wilson Dam, Alabama, has found the freezing point of phosphoryl trifluoride to be −39.1°.

(8) G. K. Burgess, *Bull. Bur. Standards*, **5**, 199 (1908).

(9) H. S. Booth, H. M. Elsey and P. E. Burchfield, THIS JOURNAL, **57**, 2064 (1935).

TABLE III

VAPOR PRESSURE OF POF_2Cl

Temp., °C.	P, obsd., mm.	P, calcd., mm.	Deviation, mm.
−62.1[a]	18.9	24.8	6.1
−55.4[a]	30.9	38.8	7.9
−40.2	98.5	97.1	−1.4
−31.1	153.5	159.1	5.6
−20.9	264.4	265.2	0.8
−13.6	376.5	373.1	−3.4
−12.2	397.5	397.4	−0.1
− 9.3[a]	444.4	452.1	7.7
− 5.2	543.2	539.9	−3.3
− 0.1[a]	665.4	668.2	2.8
− 0.1	677.2	668.2	−9.0
1.2[a]	700.0	704.5	4.5
2.2	737.8	733.7	−4.1
6.4[a]	864.6	867.0	2.4
11.3[a]	1047.3	1047.0	0.0
15.1[a]	1206.1	1206.0	0.0

[a] Prepared by Swarts reaction: all others by calcium fluoride. Calculated values were determined by use of the equation $\log p = (-1328.3/T) + 7.6904$.

TABLE IV

VAPOR PRESSURE OF POF_3

Temp., °C.	P, obsd., mm.	P, calcd., mm.	Deviation, mm.
−43.8[a]	637.7	627.9	−9.8
−42.7[a]	670.0	668.2	−1.8
−41.6[a]	701.9	704.0	2.1
−40.2	758.1	751.8	−6.3
−38.9[a]	798.9	798.6	−0.3
−38.4	813.6	817.0	3.4
−37.3	862.3	859.2	−3.1
−35.9	912.5	915.4	2.9
−35.4[a]	942.5	936.1	−6.4
−35.2	954.1	946.3	−7.8

[a] Prepared by Swarts reaction: all others by calcium fluoride. Calculated values were determined by use of the equation $\log p = (-1097.88/T) + 7.5900$.

Critical Constants.—The critical constants and vapor pressure of phosphoryl trifluoride at high pressures were determined in the apparatus of, and as described by, Booth and Swinehart.[10] No difficulty was encountered with the trifluoride, but the difluoromonochloride reacted slowly with the mercury.

TABLE V

CRITICAL DATA

Sample	POF_3 Temp., °C.	POF_3 Pressure, atm.	POF_2Cl Temp., °C.	POF_2Cl Pressure, atm.	
1	24.9	12.5			
2	35.8	17.0			
1	40.3	19.1			
2	48.8	24.3			
1	59.9	30.9			
2	68.1	38.8			
1	73.3	41.7	150.5	43.4	Critical points
2	73.3	41.9	150.8	43.5	Critical points

(10) H. S. Booth and C. F. Swinehart, THIS JOURNAL, **57**, 1337 (1935).

Chemical Properties.—The properties of the phosphoryl fluorochlorides lie between those of the trichlorides and the trifluorides, and are proportional to the fluorine content. They hydrolyze in moist air or water with increasing rapidity, although the hydrolysis of the compounds containing fluorine is complicated by the intermediate formation of fluophosphates.

TABLE VI

PHYSICAL PROPERTIES OF THE FLUORINATION PRODUCTS OF $POCl_3$

	POF_3	POF_2Cl	$POFCl_2$
Boiling point,[a] °C.	−39.8 ± 0.1	3.1 ± 0.1	52.9 ± 0.1
Freezing point, °C.	−39.4	−96.4	−80.1
Liquid density (at 0°)		1.6555	1.5931
Gas density	104.0	120.5	
Critical temperature, °C.	73.3	150.6	
Critical pressure, atm.	41.8	43.4	
Heat of vaporization,[b] cal.	5030	6090	7403
Trouton's constant	21.6	22.03	22.7

[a] From a plot of the vapor pressure data. [b] Calculated by the Clausius–Clapeyron equation.

All four substances are colorless in all states. All three fluorination products have little or no action on nichrome and copper. The trifluoride and the difluoromonochloride have a slight tendency to discolor the surface of mercury after prolonged exposure. When dry, the gases do not attack glass, but no precautions in the way of preliminary drying were sufficient to prevent the formation of a white ring at the surface and a slight cloudiness in the bottom of the container whenever the material was condensed in glass. This is most marked with the trifluoride and the difluoromonochloride and is very slight with the monofluorodichloride.

Phosphoryl difluoromonochloride was passed over sodium amalgam both in the gaseous and liquid states, in an attempt to remove the chlorine and form a condensation product of the formula $(POF_2)_2$. The surface of the amalgam was discolored, but there was no further evidence of reaction in the range of 20–60°.

Summary

The fluorination of phosphoryl trichloride by the Swarts reaction, and in the vapor phase by calcium fluoride pellets, yields two gases, phosphoryl trifluoride boiling at −39.8° first described

by Moissan, phosphoryl difluoromonochloride boiling at 3.1° and a liquid, phosphoryl monofluorodichloride boiling at 52.9°. The freezing points, vapor pressure data, critical constants, gaseous and liquid densities have been determined and recorded along with a few of their chemical properties.

CLEVELAND, OHIO RECEIVED AUGUST 9, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

The Entropy of Cyanogen. Heat Capacity and Vapor Pressure of Solid and Liquid. Heats of Fusion and Vaporization

BY R. A. RUEHRWEIN AND W. F. GIAUQUE

This paper is a report on a low temperature calorimetric investigation on solid and liquid cyanogen, N—C≡C—N. The results have been used to calculate the entropy of the gas by means of the third law of thermodynamics and this value has been compared with one calculated from available molecular data. The two values agree within their respective limits of error.

The measurements were made in a calorimeter with the laboratory designation Gold Calorimeter III and temperatures were obtained by means of Standard Copper–Constantan Thermocouple W-25, both of which have been described previously.[1,2]

Preparation and Purity of Cyanogen.—Cyanogen was prepared by a method similar to one described by Cook and Robinson.[3] Silver cyanide was precipitated from a saturated silver nitrate solution by a slight excess of a 78% solution of potassium cyanide. The silver cyanide was filtered, washed free of excess cyanide and dried in an oven at 130° for twelve hours. The silver cyanide prepared in this way was a pale brown powder. It was then heated in a glass vessel and a temperature of approximately 380° was maintained.

The cyanogen, which was evolved steadily at a pressure of about half an atmosphere, was passed through two tubes containing phosphorus pentoxide and finally condensed in a bulb surrounded by liquid air but protected from it in case of breakage. The phosphorus pentoxide tubes were 3 cm. in diameter and 30 cm. long. The preparation system was evacuated to a pressure of 10^{-5} mm. before the cyanogen was generated; 180 cc. of liquid was prepared. The material was distilled twice, small end-fractions being discarded, and the solid was subjected to a high vacuum to remove any non-condensable gases; 135 cc. of liquid remained after this treatment.

From the effect of premelting on heat capacity measurements below the melting point the liquid-soluble solid-insoluble impurity was estimated to be 5 parts in 100,000 on a molal basis.

The Melting Point of Cyanogen.—A summary of the melting point investigation is given in Table I.

TABLE I

MELTING POINT OF CYANOGEN

0°C. = 273.10°K.

Time	% melted	T, °K. Resistance thermometer	T, °K. Thermocouple
7-27-38			
5:34 P. M.	Heated into melting point		
5:45 P. M.	10	245.281	245.26
8:25 P. M.	10	245.275	245.25
10:00 P. M.	10	245.265	245.27
11:12 P. M.	Supplied heat		
11:30 P. M.	40	245.264	245.30
7-28-38			
11:10 A. M.	40	245.278	245.27
12:08 P. M.	40	245.270	245.27
1:23 P. M.	Supplied heat		
1:45 P. M.	70	245.277	245.28
3:45 P. M.	70	245.269	245.27
5:35 P. M.	70	245.272	245.27
		Accepted value	245.27

The Vapor Pressure of Cyanogen.—The vapor pressure was measured with a Société Génévoise cathetometer with a precision of 0.002 cm. It was used as a comparison instrument for a standard meter suspended between the arms of the manometer, which was protected by a case with uniform temperature. The standard acceleration of gravity was taken as 980.665 cm. sec.$^{-2}$ and the acceleration at this location as 979.973 cm. sec.$^{-2}$. Data given in the "I. C. T."[4]

(1) Giauque and Egan, *J. Chem. Phys.*, **5**, 47 (1937).
(2) Giauque and Ruehrwein, THIS JOURNAL, **61**, 2626 (1939).
(3) Cook and Robinson, *J. Chem. Soc.*, 1001 (1935).
(4) "International Critical Tables," McGraw-Hill Book Co., Inc., New York, N. Y., 1926, Vol. I.

were used to correct the observations to international cm. of Hg, and the meniscus corrections were taken from the work of Cawood and Patterson.[5]

The data have been represented by the equations

Solid cyanogen 202 to 245.27 °K. $\log_{10} P$(inter. cm. Hg) = $(-1795.9/T) - 0.001464T + 9.42442$ (1)

Liquid cyanogen 245.27 to 253 °K. $\log_{10} P$(inter. cm. Hg) = $(-1525.7/T) - 0.0040842T + 8.96542$ (2)

TABLE II

VAPOR PRESSURE OF CYANOGEN

Boiling point 251.95°K. (0°C. = 273.10°K.)

T, °K., resistance thermometer	P inter. cm. Hg	$P_{obsd.} - P_{calcd.}$	$T_{obsd.} - T_{calcd.}$	Remarks
202.422	1.802	−0.001	0.006	Solid
202.660	1.842	− .003	.017	Solid
210.189	3.740	.003	− .009	Solid
215.299	5.861	.002	− .004	Solid
220.090	8.760	.003	− .004	Solid
225.037	13.023	.005	− .005	Solid
229.953	18.960	− .004	+ .003	Solid
235.054	27.533	− .005	+ .003	Solid
240.108	39.191	− .015	+ .006	Solid
245.270	55.360	.000	.000	Triple point
247.350	61.252	.016	− .005	Liquid
250.311	70.452	.001	.000	Liquid
253.068	79.988	.001	.000	Liquid

In Table II the observations have been compared with values calculated from Equations 1 and 2. From Equation 2 the boiling point was found to be 251.95°K.

The vapor pressure of cyanogen has been measured by Terwen,[6] Perry and Bardwell,[7] and Cook and Robinson.[3] Taking pressures as a reference, Terwen's data correspond to temperatures about 0.2° below the present results over the liquid and most of the solid ranges; however, the deviation increases at lower temperatures to 1.3° below when the pressure is about 2 cm.

The results of Perry and Bardwell and the present work agree within a few hundredths of a degree in the liquid and upper solid range but the deviation gradually increases until the observed temperature is 0.8° below the temperature obtained in this research when the pressure was about 2 cm.

Cook and Robinson made only one vapor pressure measurement below the boiling point and the present work is in agreement with this observation within 0.01°.

The melting and boiling points are compared with the values obtained by previous observers in Table III.

TABLE III

MELTING AND BOILING POINT TEMPERATURES OF CYANOGEN

M. p., °K.	B. p., °K.	Observer
....	252.7	Bunsen[8] (1814)
238.7	....	Faraday[9] (1845)
245.18	251.75	Terwen[6] (1916)
245.20	251.94	Perry and Bardwell[7] (1925)
245.27	251.95	This research

The Heat Capacity of Cyanogen.—The amount of cyanogen used for the heat capacity measurements was measured by condensing it in a steel bomb and weighing at room temperature. The bomb was equipped with a gas tight double seated valve and a ground glass joint through which it could be evacuated and filled. The bomb weighed 450 g. and had a capacity of 150 cc., a weight of 119.516 g., which is equivalent to 2.2980 moles of cyanogen, was used for the measurements.

The heat capacity observations are given in Table IV and are shown in Fig. 1. The value marked with an asterisk is high due to premelting. One international joule was taken as 4.1832 cal-

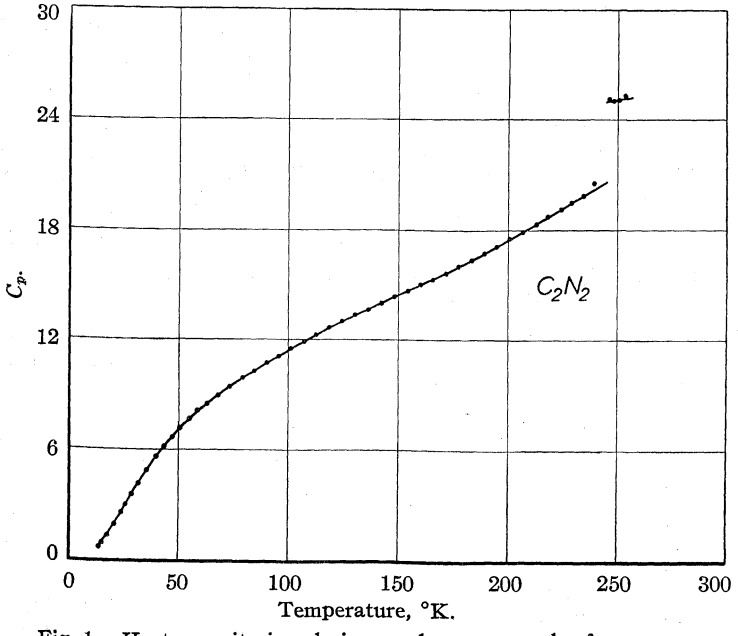

Fig. 1.—Heat capacity in calories per degree per mole of cyanogen.

(5) Cawood and Patterson, *Trans. Faraday Soc.*, **29**, 514 (1933).
(6) Terwen, *Z. physik. Chem.*, **91**, 469 (1916).
(7) Perry and Bardwell, THIS JOURNAL, **47**, 2629 (1925).
(8) Bunsen, *Ann. Physik*, **46**, 101 (1814).
(9) Faraday, *Ann. chim. phys.*, [3] **15**, 277 (1845).

ories in calculating energy. The calorimetric observations were corrected for vaporization into the small unoccupied volume in the calorimeter and the attached line. In making the correction the density of the liquid was taken from the work of Cook and Robinson[3] and the density of the solid was estimated with sufficient approximation for this small correction.

Heat capacity values taken from a smooth curve through the data are given in Table V. The curve should give the heat capacity to within 0.2% above 35°K. At 20°K. the error may be about 1% and at 15°K. as much as 5%.

The Heat of Fusion of Cyanogen.—A summary of the heat of fusion data is given in Table VI. The measurements were started a little below the melting point and ended somewhat above. A correction was applied for the $\int C_p \, d\,T$ and for the small amount of premelting that had occurred at the starting temperature due to the five thousandths of one mole per cent. impurity.

The Heat of Vaporization.—The heat of vaporization was measured by evaporating the cyanogen at constant pressure and absorbing the gas in a bulb containing 10 *M* sodium hydroxide. The absorption bulb had a small mercury trap. The rate of absorption of cyanogen in sodium hydroxide solution of lower concentration than 10 *M* was somewhat slow but the absorption was easily completed when the 10 *M* solution was used. The results are summarized in Table VII.

TABLE IV

MOLAL HEAT CAPACITY OF CYANOGEN

(0°C. = 273.10°K.)

Molecular weight, 52.036, 2.9280 moles in calorimeter.

T, °K.	ΔT	C_p, cal./deg./mole	T, °K.	ΔT	C_p, cal./deg./mole
14.89	1.950	0.840	130.53	5.751	13.39
17.56	2.868	1.268	136.46	6.180	13.67
20.72	3.395	1.883	142.47	5.874	14.04
23.62	2.470	2.534	148.24	5.607	14.39
25.87	2.040	2.993	154.14	5.998	14.71
28.66	3.507	3.501	160.15	5.737	15.05
31.83	2.895	4.135	165.94	5.509	15.34
35.59	4.681	4.846	171.81	5.875	15.68
39.83	3.915	5.544	177.78	5.626	16.06
43.69	3.833	6.133	183.59	5.392	16.44
47.28	3.424	6.625	189.19	5.197	16.77
51.03	4.096	7.142	195.02	5.994	17.15
55.06	4.004	7.675	201.17	5.758	17.54
58.97	4.025	8.115	207.13	5.641	17.90
63.28	4.678	8.506	213.28	5.432	18.34
68.24	5.265	8.965	218.87	5.214	18.74
73.49	5.264	9.435	224.35	5.020	19.14
79.11	5.746	9.929	229.62	4.861	19.49
84.71	5.335	10.27	234.71	4.676	19.88
90.26	5.783	10.73	239.89	4.450	20.59*
95.85	5.410	11.12	245.27	Melting point	
101.49	5.875	11.52	246.32	1.606	25.15
107.20	5.532	11.89	248.46	2.386	25.08
112.96	5.972	12.28	251.07	2.577	25.12
118.77	5.640	12.67	253.82	2.532	25.35
124.64	6.064	13.02	251.95	Boiling point	

TABLE V

MOLAL HEAT CAPACITY OF CYANOGEN

Molecular weight, 52.035. Values taken from a smooth curve through the observations.

T, °K.	C_p, cal. deg.$^{-1}$ mole^{-1}	T, °K.	C_p, cal. deg.$^{-1}$ mole^{-1}
15	0.86	140	13.91
20	1.76	150	14.47
25	2.82	160	15.02
30	3.78	170	15.58
35	4.74	180	16.20
40	5.57	190	16.82
45	6.33	200	17.45
50	7.02	210	18.11
60	8.20	220	18.82
70	9.13	230	19.54
80	9.97	240	20.27
90	10.71	245.27	Melting point
100	11.41	250	25.17
110	12.08	251.95	Boiling point
120	12.73	255	25.27
130	13.35		

TABLE VI

MOLAL HEAT OF FUSION OF CYANOGEN

Melting point 245.27°K. (0°C. = 273.1°K.)

Temperature interval	Heat added per mole	$\int C_p \, d\,T$	Premelting	ΔH, cal. mole^{-1}
242.403–249.404	2142.8	208.0	3.6	1938
242.471–247.672	2084.7	151.7	3.7	1937
242.503–247.575	2082.5	147.7	3.7	1939
			Mean value	1938 ± 1

TABLE VII

MOLAL HEAT OF VAPORIZATION OF CYANOGEN

Boiling point 251.95°K. (0°C. = 273.10°K.). Molecular weight, 52.036.

Moles vaporized	Time of energy input, min.	ΔH, cal. mole^{-1}
0.20791	48	5568
.21620	48	5580
.21630	48	5579
.21737	48	5576
	Mean	5576 ± 5
From vapor pressure equation 2, assuming a Berthelot gas		5624

The value of the heat of vaporization obtained from the vapor pressure observations and given in Table VII includes a gas imperfection correction of −151 cal. mole^{-1}. In obtaining the gas

imperfection, Berthelot's equation was used with $T_c = 401.4°K.$[10] and $P_c = 59.7$ atm.[10]

The value obtained from the vapor pressure measurements is given no weight in comparison with the direct calorimetric result.

The Entropy of Cyanogen.—A summary of the calculation of the entropy from calorimetric data is given in Table VIII. The correction for gas imperfection was calculated from the Berthelot gas expression

$$S_{ideal} - S_{actual} = 27\,RT_c^3P/32T^3P_c$$

The entropy of cyanogen gas has recently been calculated from molecular data by Stevenson,[11] who obtained 57.90 cal. deg.$^{-1}$ mole^{-1} at 298.1°K.

TABLE VIII

THE MOLAL ENTROPY OF CYANOGEN FROM CALORIMETRIC DATA

0–15°K. Debye function, $hc\nu/k = 118$	0.307
15–245.27°K., graphical	24.298
Fusion 1938/245.27	7.901
245.27–251.95°K., graphical	0.678
Vaporization 5576/251.95	22.131
Entropy of actual gas at boiling point	55.32 ± 0.1
Correction for gas imperfection	0.11
Entropy of ideal gas at 1 atm. and 251.95°K.	55.43 cal. deg.$^{-1}$ mole^{-1}

The moment of inertia, $I = 176 \times 10^{-40}$ g. cm.^{2}, is obtained from the electron diffraction measurements of Pauling, Springall and Palmer,[12] who find the C–C distance to be 1.37 Å. and the C–N distance 1.16 Å.

The fundamental frequency assignment was taken from the work and summary of Woo and Badger[13]: $\nu_1 = 860$, $\nu_2 = 2336$, $\nu_3 = 2150$, $\nu_4 = 230$, $\nu_5 = 512$ cm.$^{-1}$. ν_4 and ν_5 refer to deformation vibrations and have an *a priori* weight of 2. ν_5 is estimated from Raman observations on liquid cyanogen and ν_4 has not been observed directly, the 230 cm.$^{-1}$ value having been obtained from differences in ultraviolet bands. Unfortunately, ν_4 and ν_5 are the values of greatest importance in calculating the entropy. An error of 10 cm.$^{-1}$ in the 230 cm.$^{-1}$ value is equivalent to 0.15 cal. deg.$^{-1}$ mole^{-1} in the entropy. The symmetry number is 2.

The values are compared in Table IX.

(10) Pickering, *J. Phys. Chem.*, **28**, 97 (1924).
(11) Stevenson, *J. Chem. Phys.*, **7**, 171 (1939).
(12) Pauling, Springall and Palmer, THIS JOURNAL, **61**, 927 (1939).
(13) Woo and Badger, *Phys. Rev.*, **39**, 932 (1932).

The absolute entropy is obtained by adding R ln 9 = 4.366 cal. deg.$^{-1}$ mole^{-1}, the nuclear spin entropy, to the values given in column 4 of Table IX.

TABLE IX

COMPARISON OF ENTROPY VALUES FROM CALORIMETRIC AND FROM MOLECULAR DATA

Cal. deg.$^{-1}$ mole^{-1}.

	Calorimetric data		Molecular data	
T, °K.	Actual gas	Ideal gas	Less nuclear spin entropy	Absolute entropy
251.95	55.32	55.43	55.67	60.04
298.10	...	57.64	57.88	62.25

The agreement of the two entropy values is within the limit of error of the result based on molecular data. However, the agreement is sufficiently close to show that cyanogen approaches zero entropy as the absolute zero is approached.

Until a more complete investigation and analysis of the cyanogen band spectrum is available, the most reliable value of the entropy is the one based on the third law of thermodynamics, 57.64 cal. deg.$^{-1}$ mole^{-1} at 1 atm. and 298.1°K.

We thank Dr. T. M. Powell for assisting with the measurements.

Summary

The heat capacity of solid and liquid cyanogen has been measured from 15°K. to the boiling point.

The melting and boiling point temperatures were found to be 245.27 and 251.95°K., respectively (0°C. = 273.10°K.).

The heats of fusion and vaporization were determined by calorimetric observation to be 1938 and 5576 cal. mole^{-1}, respectively.

The vapor pressure of solid and liquid was measured and the data have been represented by the equations

Solid cyanogen 202 to 245.27°K. $\log_{10}P$(inter. cm. Hg) = $(-1795.9/T) - 0.001464T + 9.42442$

Liquid cyanogen 245.27 to 253°K. $\log_{10}P$(inter. cm. Hg) = $(-1525.7/T) - 0.0040842T + 8.96542$

The calorimetric data have been used to calculate the entropy of cyanogen gas and this value has been compared with one obtained from molecular data and it is found that the entropy of cyanogen approaches zero near the absolute zero of temperature.

Until more complete information concerning the vibrations of the cyanogen gas molecule is

available the most reliable value of the entropy of cyanogen is the calorimetric one, 57.64 cal. deg.$^{-1}$ mole^{-1} at 298.1°K. and one atmosphere. This value does not include the nuclear spin entropy.

BERKELEY, CALIF. RECEIVED AUGUST 1, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ALBERTA]

The Decomposition of Some Iodonium Salts. Reactions with Mercury, Tellurium and Antimony

BY R. B. SANDIN, F. T. MCCLURE[1] AND F. IRWIN[2]

Recently H. J. Lucas and co-workers[3] have shown that di-*o*-tolyliodonium iodide decomposes at 155° into *o*-iodotoluene, uncontaminated by any isomeric product. They suggest that the mechanism involves a decomposition which proceeds through an intermediate, positively charged *o*-tolyl ion in which the positive charge is carried by a carbon atom. The positive *o*-tolyl ion then combines with the negative iodide ion of the iodonium salt to form a molecule of *o*-iodotoluene.

This plausible mechanism fits in with the fact that it is now known definitely that the I–I bond in diphenyliodonium iodide is an ionic, not a covalent, bond.[4] However, the authors of this paper became interested in the possibility that the decomposition of iodonium salts might, to some extent at least, be a non-ionic one and might proceed through the intermediate formation of free radicals. A non-ionic mechanism might explain the fact that the decomposition temperature of an iodonium salt depends upon the nature of the anion as well as the cation. For example, di-*o*-tolyliodonium bromide decomposes at 178°, the iodide at 155° and the sulfide at room temperature. If the decomposition involved only the positive ion, it is conceivable that the decomposition temperatures would lie closer together. Keeping the positive ion the same, we find roughly that the decomposition temperature of an iodonium salt varies directly with the electronegativity of the negative ion. Again, it is in a reaction such as this where one might look for the formation of free radicals. The latter are likely to be formed from those molecules which readily tend to undergo thermal self-decomposition at comparatively low temperatures (*e. g.*, explosives, endothermic compounds, etc.). Finally, the recent work of Waters[5] and co-workers on the decomposition reactions of the aromatic diazo compounds gave the present workers some hope in the idea that iodonium salts might behave similarly to diazonium salts.[6] Waters has shown that the diazonium chlorides can decompose by a non-ionic mechanism $(PhN_2)^+Cl^- \longrightarrow$ Ph-N=N-Cl $\longrightarrow$ Ph· + N_2 + ·Cl, giving transient free neutral aryl radicals which are identical in chemical behavior with the neutral alkyl radicals[7] which have been studied in the gaseous phase.

The authors of this paper have carried out the decomposition of diphenyliodonium chloride and sulfide and di-*p*-tolyliodonium chloride in the presence of mercury, tellurium and antimony. In all cases, reactions have occurred which suggest the intermediate formation of free aryl radicals. Similarly, Waters[5] has found that benzenediazonium chloride decomposes under acetone kept neutral with chalk, in such a way that mercury, tellurium and antimony are attacked. Waters concludes that in the reaction mixture the free phenyl radical has a transient existence and that the phenyl radical is formed by thermal or photochemical decompositions of organic molecules in the liquid phase as well as in the gaseous phase.[8]

In view of the results obtained, it seems especially tempting to assume that in the decomposition of an iodonium salt, part of it at least can decompose by way of a non-ionic mechanism. The assumption is made that in the iodonium salt the

(1) Present address, 625 Mendota Ct., Madison, Wisconsin.

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(3) H. J. Lucas, E. R. Kennedy and C. A. Wilmot, THIS JOURNAL, **58**, 157 (1936).

(4) Medlin, *ibid.*, **57**, 1026 (1935).

(5) (a) Waters, *J. Chem. Soc.*, 1077 (1938); (b) Makin and Waters, *ibid.*, 843 (1938); (c) Waters, *ibid.*, 113, 2007, 2014 (1937). For a thorough review on free radicals in solution, see Hey and Waters, *Chem. Rev.*, **21**, 169 (1937).

(6) There is a fundamental relationship between diazonium salts and iodonium salts in that the former are quaternary ammonium salts (*i. e.*, fully substituted ammonium salts) and the latter are fully substituted derivatives of the hypothetical $(H_2I)^+X$.

(7) For an excellent treatise see F. O. Rice and K. K. Rice, "The Aliphatic Free Radicals," The Johns Hopkins Press, Baltimore, Md., 1935.

(8) (a) Zartman and Adkins, THIS JOURNAL, **54**, 3398 (1932); (b) Dull and Simons, *ibid.*, **55**, 3898, 4328 (1933); (c) Glazebrook and Pearson, *J. Chem. Soc.*, 589 (1939).

central iodine atom is able, by expanding its valence shell, to act as an acceptor for the chloride or sulfide ion. Subsequent transformations of this complex result from the tendency of the central atom to revert to an octet. The following is suggested as a probable course of the reaction: $(C_6H_5)_2I^+ Cl^- \longrightarrow (C_6H_5)_2I \longleftarrow Cl \longrightarrow C_6H_5I + C_6H_5\cdot + \cdot Cl$. The expanded valence shell has been used to explain the marked difference in the mode of decomposition of the quaternary ammonium bases from the corresponding phosphonium bases. It also has been used in connection with the unusual reactions of, and formation of, the 2- and 3-covalent iodine compounds.[9]

The above conclusions of the authors are based largely upon the analogy between the reactions of iodonium compounds and the reactions of diazonium compounds studied by Waters and coworkers. Dr. H. J. Lucas of the California Institute of Technology has kindly drawn attention to the important role played by the metal in the decomposition reactions. He suggests the possibility of an intermediate, undissociated complex which decomposes at a lower temperature than the salt would otherwise. Such a reaction mechanism would not necessarily involve the formation of free radicals. On this basis also, the decomposition with and without a metal would not necessarily have to proceed via similar mechanisms.

Experimental Part

Preparation of Compounds.—Diphenyliodonium chloride and di-*p*-tolyliodonium chloride were prepared readily by a standard procedure.[3] It seems impossible to isolate an iodonium sulfide compound. Diphenyliodonium hydroxide, for example, when treated with sodium sulfide, produces a bright yellow precipitate (evidently the sulfide) which quickly decomposes into phenyl iodide and phenyl sulfide.[10] For that reason, in any of the decomposition reactions involving an iodonium sulfide salt, a more stable salt such as the chloride was mixed with sodium sulfide, or aqueous hydrogen sulfide, and to this mixture the necessary element such as mercury was added.

Diphenyltellurium dibromide, m. p. 200°, was made according to Krafft and Lyons.[11]

Triphenylstibinic sulfide, m. p. 119–120°, was made from triphenylstibinic chloride according to the procedure of Kaufmann.[12]

Reaction with Mercury.—Diphenyliodonium chloride (3.0 g.) was dissolved in 150 cc. of boiling *n*-propyl alcohol. To this was added about 2.0 cc. of mercury and the mixture was refluxed for about five hours. While the mixture was still hot it was filtered and, on cooling the filtrate, pure phenylmercuric chloride, m. p. 250°, crystallized out. The yield was 1.25 g. The same procedure carried out with the addition of finely divided calcium carbonate gave identical results. In the same manner, di-*p*-tolyliodonium chloride gave *p*-tolylmercuric chloride, m. p. 230°.

Changing the solvent from propyl alcohol to water did not seem to have any appreciable effect on the results. This seems peculiar, since one would expect a solvent such as water to favor an ionic decomposition. Waters[5] has found that the non-ionic decomposition of diazonium salts occurs best in such solvents as acetone and ethyl acetate.

Reaction with Tellurium.—Diphenyliodonium chloride was refluxed in an *n*-propyl alcohol solution with finely divided tellurium. After several hours the unchanged tellurium was filtered off and the filtrate evaporated to a small volume. On the addition of bromine, yellow crystals of diphenyltellurium dibromide, m. p. 199–200°, crystallized out. These crystals, mixed with a sample of synthetic material, produced no depression of the melting point. When water was used as a solvent, only once, out of several attempts, was enough diphenyltellurium dibromide obtained for a melting point determination. These results might indicate that an ionic decomposition occurs in a highly polar solvent such as water. It was also observed that when water was used as the solvent, finely divided tellurium speeded up the decomposition of the iodonium salt.

When a mixture of diphenyliodonium chloride dissolved in water, tellurium, ether and aqueous hydrogen sulfide, was shaken up in a flask for about an hour at room temperature, diphenyltellurium was again formed. The diphenyltellurium dissolved in the ether layer and was isolated as the yellow dibromide.

Similar results to the above were obtained when di-*p*-tolyliodonium chloride was used instead of the phenyl compound. Di-*p*-tolyltellurium was isolated as the yellow dibromide, m. p. 203–204°.

When a mixture of diphenyliodonium chloride and finely divided tellurium was heated in the dry condition in a testtube, diphenyltellurium dichloride, m. p. 158°, was formed. The tellurium had also the effect of lowering the decomposition temperature of the iodonium chloride.

Reaction with Antimony.—A solution of diphenyliodonium chloride in water was shaken up at room temperature with sodium sulfide, finely divided antimony and ether. The ether layer was separated, filtered and, on evaporating to dryness, beautiful crystals of triphenylstibinic sulfide, m. p. 119–120°, were left behind. They had a slight yellowish tinge and when mixed with a synthetic sample produced no depression of the melting point

Summary

1. Diphenyliodonium chloride and di-*p*-tolyliodonium chloride react with mercury in boiling *n*-propyl alcohol to produce phenyl and *p*-tolyl mercuric chloride. With tellurium they give diphenyltellurium and di-*p*-tolyltellurium. Di-

(9) See discussion by Johnson in Gilman, "Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1938, p. 1610.

(10) Hartmann and Meyer, *Ber.*, **27**, 502 (1894).

(11) Krafft and Lyons, *ibid.*, **27**, 1769 (1894).

(12) Kaufmann, *ibid.*, **41**, 2762 (1908); Christiansen, "Organic Derivatives of Antimony," The Chemical Catalog Co., Inc., New York, N. Y., 1925, p. 172.

phenyliodonium sulfide decomposes at room temperature in the presence of tellurium and antimony to give diphenyltellurium and triphenylstibinic sulfide.

2. To account for these reactions, it is suggested that at least a part of the iodonium salt decomposes by way of a non-ionic mechanism.

EDMONTON, ALBERTA, CANADA RECEIVED JULY 3, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

Tyrosinase from the Wild Mushroom, *Lactarius Piperatus*

BY H. R. DALTON AND J. M. NELSON

Kubowitz[1,2] has shown that potato oxidase (tyrosinase) contains copper and that the activity of the oxidase toward catechol as the substrate is proportional to the metal content. After considerable purification a product was obtained which in the presence of acetone, at 0°, occurred in a globular form and contained 0.20% copper. Keilin and Mann[3] have also prepared a highly purified polyphenolase (*i. e.*, tyrosinase) from the common mushroom, *Psalliota campestris*, which had a copper content of 0.30% and an activity toward catechol proportional to the copper content.

The tyrosinase described in the present communication was prepared from the wild mushroom, *Lactarius piperatus*. Highly purified preparations from this source were found to contain 0.23% copper. The activity of these preparations toward catechol was also proportional to the copper content (see Fig. 1). The copper was

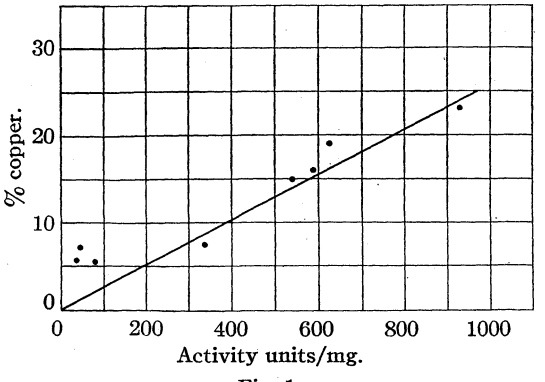

Fig. 1.

easily removed from the enzyme preparation by dilute acids just as Kubowitz noted in the case of the oxidase from potatoes. Contrary to the claims by Yakushiji[4] that the polyphenolase from *Lactarius piperatus* contains a hematin residue; the data in the table clearly show that the iron can be removed completely by one adsorption to kaolin. Only in the case of the two crude preparations, nos. 1 and 2, was iron found to be present and then only in very small amounts. It therefore appears that iron was present only as an impurity in the crude preparations.

Keilin and Mann[3] found no relationship between the activities of their oxidase preparations, from *Psalliota campestris*, toward the two substrates, *p*-cresol and catechol, and were inclined to attribute the activity toward *p*-cresol as involving the presence of some other factor in the reaction mixture. Likewise Adams and Nelson[8] were able to vary, in the case of the oxidase from *Psalliota campestris*, the ratio between the activities toward these two substrates. On the other hand, the last-mentioned investigators were unable by similar procedures, such as the use of various adsorbing materials, to alter the ratio of these two activities in the case of the tyrosinase from *Lactarius piperatus*. Further attempts in the present study to vary this ratio by treating the enzyme solutions with lead acetate and with silver acetate also were unsuccessful. All the preparations examined showed about 10 cresolase units to 1 catecholase unit.

The quantity of copper corresponding to one unit of cresolase is given in the table for several preparations. The rather crude preparations 1, 2 and 3 contain an appreciable quantity of undialyzable copper, which was also noticed by Keilin and Mann[3] in their crude preparations from *Psalliota campestris*, and hence show a high copper value per cresolase unit. Preparations 4 to 8 have lost this extraneous copper and the copper per cresolase unit reaches a constant value of approximately 0.0027 γ. These preparations represent enzyme in which all of the copper seems to be in an active form.

(1) F. Kubowitz, *Biochem. Z.*, **292**, 221 (1937).
(2) F. Kubowitz, *ibid.*, **299**, 443 (1938).
(3) D. Keilin and T. Mann, *Proc. Roy. Soc.* (London), **125B**, 187 (1938).
(4) E. Yakushiji, *Acta Phytochim. Tokyo*, **10**, 63 (1937).

TABLE I

Prepn.	Units/mg. *p*-Cresol	Units/mg. Catechol	Units/cc. *p*-Cresol	Units/cc. Catechol	Dry weight, mg./cc.	Dry weight mg./1000 cresolase units	Cu, mg./cc.	γ Cu per cresolase unit	% Cu (based on dry weight)	Fe, mg./cc.
1	33.8	3.4	65.2	6.5	1.93	28.8	1.1×10^{-3}	0.017	0.057	4×10^{-5}
2	41.8	4.2	46.0	4.6	1.10	23.9	8.0×10^{-4}	.017	.073	2×10^{-5}
3	79.0	7.6	65.5	6.3	0.83	12.7	5.0×10^{-4}	.0077	.062	$>1 \times 10^{-6}$
4	336	33.4	222	22	.66	3.0	5.0×10^{-4}	.0023	.076	[a]
5	540	54	540	54	1.0	1.9	1.5×10^{-3}	.0028	.15	[a]
6	590	65	1000	110	1.7	1.7	2.7×10^{-3}	.0027	.16	[a]
7	625	72	4000	460	6.4	1.6	1.2×10^{-2}	.0030	.19	[a]
8	930	98	4000	420	4.3	1.1	1.0×10^{-2}	.0025	.23	[a]

[a] Indicates that no iron could be detected when as much as 0.5 mg. of enzyme had been used. $\gamma = 0.001$ mg.

PREPARATION OF MATERIALS AND PROCEDURE (TABLE I)

Showing enzyme activity, dry weight per enzyme unit and copper content. All tyrosinase preparations obtained from *Lactarius piperatus*.

Prepn. 1.—Mushrooms dried by being spread out in the laboratory for several days. Broken up and water added—pressed in hydraulic press and the press juice dialyzed for forty-eight hours against water in a rocking dialyzer which kept the liquid in the cellophane sausage casing, continuously in motion.[5] *Prepn. 2.*—Prepn. 1 precipitated with 0.4 satd. ammonium sulfate, precipitate dissolved in water and dialyzed on rocker for forty-eight hours. *Prepn. 3.*—Prepn. 2 adsorbed to kaolin (*p*H 4.5), eluted with disodium phosphate (*p*H 8.4), treated with 0.3 satd. ammonium sulfate and precipitate discarded, made 0.6 satd. with ammonium sulfate and precipitate formed dissolved in water and dialyzed 48 hours on rocker. *Prepn. 4.*—Dried mushrooms treated with water, pressed and liquid made 0.6 satd. with ammonium sulfate, precipitate dissolved in water and enzyme material adsorbed to kaolin (*p*H 4.5), eluted with disodium phosphate (*p*H 8.4), reprecipitated with 0.6 satd. ammonium sulfate, precipitate dissolved in water, dialyzed fourteen hours on rocker followed by dialysis for twenty-four hours in a large bottle of glass distilled water in the icebox. *Prepn. 5.*—Dried mushrooms water pressed, precipitated with 0.6 satd. ammonium sulfate, dissolved in water, reprecipitated with 0.6 satd. ammonium sulfate, dissolved in water, adsorbed to kaolin (*p*H 4.5), eluted with disodium hydrogen phosphate (*p*H 8.4), reprecipitated with 0.6 satd. ammonium sulfate, dissolved in water, reprecipitated with 0.6 satd. ammonium sulfate, dissolved in water, dialyzed for forty-eight hours on rocker. *Prepn. 6.*—Enzyme material in Prepn. 5 adsorbed to kaolin (*p*H 4.8), eluted with disodium hydrogen phosphate (*p*H 8.4), precipitated with 0.4 satd. ammonium sulfate and precipitate formed discarded, solution remaining was made 0.6 satd. with ammonium sulfate and precipitate formed dissolved in water and dialyzed forty-eight hours on rocker. *Prepn. 7.*—Dried mushrooms, water added, pressed, precipitated with 0.6 satd. ammonium sulfate, dissolved precipitate in water, made 0.3 satd. with ammonium sulfate and precipitate discarded, remaining liquid made 0.6 satd. with ammonium sulfate and precipitate formed dissolved in water, adsorption to kaolin (*p*H 4.5), eluted with disodium hydrogen phosphate at *p*H 8.4, reprecipitated with 0.6 satd. ammonium sulfate, precipitate dissolved in water and enzyme material adsorbed to alumina (*p*H 6.5), eluted with disodium hydrogen phosphate (*p*H 8.4), dialyzed fourteen hours on rocker. This solution had only a slight brown color. *Prepn. 8.*—Dried mushrooms, water added, pressed, precipitated with 0.6 satd. ammonium sulfate, dissolved in water, precipitated with 0.2 satd. ammonium sulfate and precipitate discarded, solution made 0.5 satd. with ammonium sulfate, precipitate dissolved in water, adsorbed to bentonite (*p*H 4.5), eluted with disodium hydrogen phosphate (*p*H 8.4), precipitated with 0.6 satd. ammonium sulfate, dissolved in water, treated with alumina (*p*H 6.5) and portion not adsorbed set aside and marked A. Material adsorbed to the alumina was eluted with disodium hydrogen phosphate (*p*H 8.4) and precipitated with 0.6 satd. ammonium sulfate, dissolved in water and treated with alumina (*p*H 6.5) and solution containing portion of enzyme material which failed to adsorb added to A. Process repeated until 90% of the original enzyme material was recovered as material from portions not adsorbed to alumina. The combined solutions were made 0.6 satd. with ammonium sulfate, precipitate dissolved in small volume of water and treated with norite charcoal (*p*H 6.5), filtered, reprecipitated with 0.6 satd. ammonium sulfate, precipitate dissolved in 13 cc. of water (*p*H 6.7), dialyzed four days in large bottle (3 liters) of glass distilled water placed in refrigerator. Water was changed two times each day. The solution thus obtained was nearly colorless.

Enzyme activity was determined by means of the Warburg respirometer,[6] temp. 25°. Graubard and Nelson's[7] method as modified by Adams and Nelson[8] was used for determining units of enzymic activity toward both *p*-cresol and catechol as substrates. In each case one unit represents the amount of enzyme, measured under prescribed conditions, necessary to bring about an oxygen uptake of 10 cu. mm. per minute. Since the oxidations of the two substrates are distinctly different reactions[9] the two kinds of units must not be confused. For this reason the two enzymic actions have been termed for convenience, cresolase and catecholase activities.

Iron was determined by the *o*-phenanthroline method of Saywell and Cunningham.[10] No interference was observed by them from copper, aluminum and magnesium in a solution containing 1×10^{-5} mg. of iron to which had been added 2×10^{-5}, 1×10^{-4} and 1×10^{-4} mg. of copper, aluminum and magnesium, respectively. Copper was determined by the method of Warburg[11] as modified by Warburg and Krebs.[12] Each determination was made with enzyme containing sufficient copper to give a rate of oxygen uptake between 20 and 30 cu. mm. per ten minutes.

The purest enzyme preparation obtained contained 0.23% copper, possessed an activity of 1000 cresolase units per mg. dry weight and 0.0027 γ copper per cresolase unit.

Redfield[13] and Dhéré and Burdel[14] have found a similarity in the visible region of the spectrum

(5) M. Kunitz and H. S. Simms, *J. Gen. Physiol.*, **11**, 641 (1927).

(6) M. Dixon, "Manometric Methods," University Press, Cambridge, 1934.

(7) M. Graubard and J. M. Nelson, *J. Biol. Chem.*, **112**, 135 (1935).

(8) M. H. Adams and J. M. Nelson, THIS JOURNAL, **60**, 2472, 2474 (1938).

(9) C. A. Bordner and J. M. Nelson, *ibid.*, **61**, 1507 (1939).

(10) L. G. Saywell and B. B. Cunningham, *Ind. Eng. Chem., Anal. Ed.*, **9**, 67 (1937).

(11) O. Warburg, *Biochem. Z.*, **187**, 255 (1927).

(12) O. Warburg and H. A. Krebs, *ibid.*, **190**, 143 (1927).

(13) A. C. Redfield, *Biol. Bull.*, **58**, 150 (1930).

(14) C. Dhéré and A. Burdel, *J. physiol. path. gen.*, **18**, 685 (1919).

among a large number of bloods and solutions containing oxyhemocyanin. In general a rather strong band occurs in the region of 570 mμ. Since the hemocyanins are copper proteins like tyrosinase, purified preparations of the latter, from *Lactarius piperatus*, were examined by means of a Zeiss microspectroscopic ocular attached to a microscope, but no similar absorption could be detected in the visible region.

The preparations were also examined in a Hilger quartz spectrophotometer. The quartz cells used for holding the tyrosinase preparations were 1 cm. in depth. Figure 2 represents a curve plotted from data obtained. Dhéré[15] and Kubowitz[2] investigating the ultraviolet absorption spectrum of oxyhemocyanin obtained strong absorption bands in the region of 278 and 350

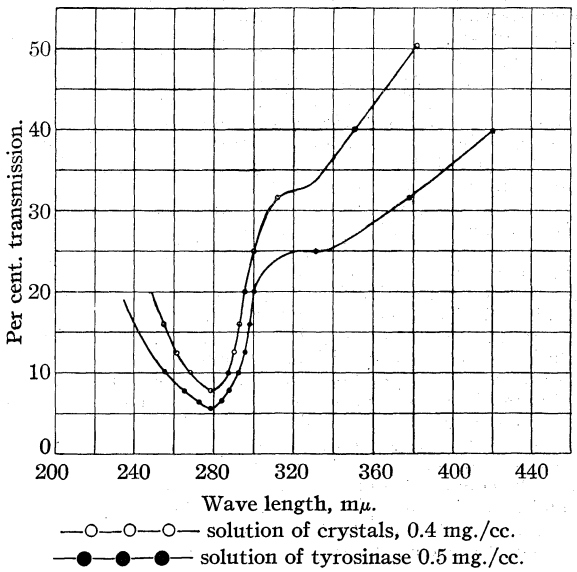

Fig. 2.—Shows the similarity between the absorption curves for a purified tyrosinase preparation and for a solution of the crystals. A weak absorption in the case of the enzyme solution exists in the region from 320 to 340 mμ. The absorption in this region in the case of the solution of the crystals is less pronounced, but when the low concentration of the crystalline material is taken into account, it will be found that the intensity is relatively about the same.

That the similarity of the two curves may be due to the enzyme solution containing uncrystallized material, corresponding to the crystals, can hardly be the case. As already stated in the text, not more than 10% of the dry weight in any purified preparation was obtained in the crystalline form. Assuming that Beer's law holds, it can be shown that these two curves are identical, and that it is unlikely that this would be the case if the crystals and enzyme material were not closely related.

(15) C. Dhéré, *J. physiol. path. gén.*, **19**, 1801 (1920).

mμ which are quite similar to the bands given by the *Lactarius piperatus* tyrosinase. The band at 278 mμ is due to protein.[15]

Ley and Hegge[16] in a study of copper amino acid showed that the band at about 385 mμ is due to copper. The band at about 330 mμ given by the tyrosinase preparations and the band at

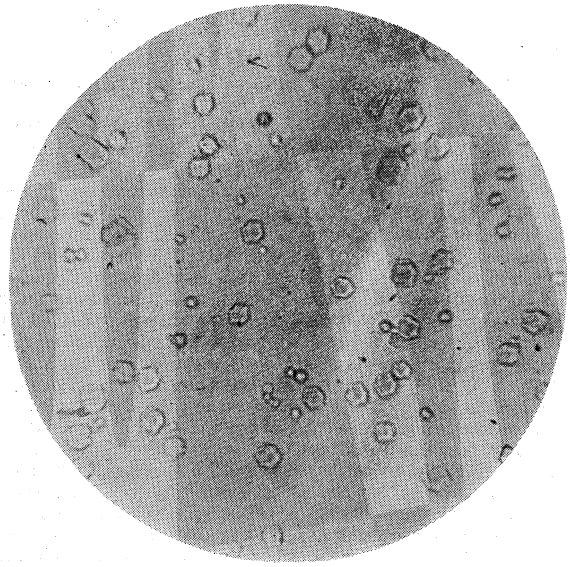

Fig. 3.

about 350 mμ for oxyhemocyanin are probably due to the copper in these complexes, their positions being shifted to some extent as a result of the influence of modifying groups. The failure of Ito[17] to find any indication of an absorption in this region for potato oxidase might be due to this absorption being much weaker than the protein band and likely to be hidden by the general absorption in this region.

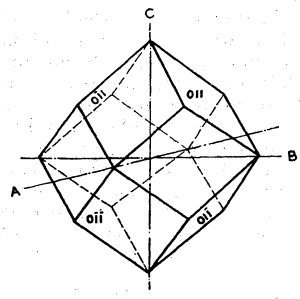

Fig. 4.

As has been stated in a previous communication,[18] a crystalline material was obtained from several preparations of tyrosinase from *Lactarius piperatus*. Rather crude preparations, as well as preparations purified as described in the legend of the table, yielded crystals. In no case, however, was more than 10% of the dry weight of a

(16) H. Ley and H. Hegge, *Ber.*, **48**, 70 (1915).
(17) R. Ito, *J. Biochem. Japan*, **24**, 279 (1936).
(18) H. R. Dalton and J. M. Nelson, THIS JOURNAL, **60**, 3085 (1938).

purified enzyme preparation obtained in a crystalline form. The procedure followed in obtaining the crystals was similar to that usually employed for crystallizing hemocyanin,[19] *i. e.*, by adjusting the *p*H of the enzyme solutions, containing at least 1000 units of cresolase per cc., to about 4.8 by means of sodium acetate buffer and then adding ammonium sulfate until the solution became slightly cloudy. After standing for several hours crystals could be observed. Enzyme preparations which had been treated, in the course of purification, with lead acetate so far have not yielded any crystalline material by the above described procedure.

Since the previous communication it has been possible to obtain perfectly shaped crystals which belong definitely in the isometric system. Their shape is rhombic dodecahedric. They are usually found lying on their 011 faces and when thus viewed through the microscope show hexagonal shapes. Figure 3 is a photomicrograph of these crystals and Fig. 4 is a perspective diagram.

The crystals show thryxotropy, are colorless, stain well with methyl violet, and have an average size of approximately 0.010 mm. Analysis showed 0.25% copper and 13.6% nitrogen. Like solutions of the purified tyrosinase, solutions of the crystals showed no marked absorption in the visible spectrum, but did show an absorption curve similar to that of the enzyme in the ultraviolet (see Fig. 2).

The crystals are insoluble in dilute acids and salt solutions. When freshly prepared they are soluble in dilute alkali (*p*H 8) but become increasingly insoluble on standing. After standing for several weeks they become practically insoluble in 0.1 *M* sodium hydroxide.

The wash water from freshly prepared crystals, after the tenth washing by means of the centrifuge, still showed tyrosinase activity. This activity may possibly be due to enzyme from the concentrated mother liquor still adhering to the crystals. Against this possibility, however, might be mentioned that 3 mg. of crystals dissolved in 20 cc. of secondary sodium phosphate solution and having an activity of 4 cresolase units per cc. showed an increase in activity to 12 units per cc. after standing for three weeks.

Slight increases in activity on standing were also noticed in the case of some solutions of the tyrosinase preparations. The latter observation has been made also by Keilin and Mann[3] and, as they have suggested, may be due to the presence of a proenzyme, which by some unknown process may be activated. Results obtained in this study show that only about 15% of the copper in the crude preparations is in the active form. The remaining copper or at least part of it may be related to this inactive state of the enzyme.

The similarity in composition, spectra and tendency to slight increase in activity on standing, all point to a close relationship between the active enzyme and the crystals. The fact that inactive or only slightly active crystals were obtained from solutions of highly purified preparations in which all the copper appears to be in the active form (γ of copper per cresolase units, see table) suggests the two following possibilities. Either the enzyme becomes, for some unknown reason, inactive when it is crystallized, or an inactive form, such as a proenzyme, accompanies the enzyme as it is purified.

(19) C. Dhéré, *J. physiol. path. gén.*, **18**, 503 (1919).

Summary

1. A method is described for preparing highly purified preparations of tyrosinase from *Lactarius piperatus*.

2. The tyrosinase is shown to be a copper protein.

3. The purest tyrosinase preparation contained 0.23% copper and had a dry weight of one mg. per 1000 cresolase units and 0.0027 γ of copper per cresolase unit.

4. The iron present in the crude preparations of the enzyme can be removed by adsorption methods.

5. Purified enzyme preparations showed no definite absorption bands in the visible region of the spectrum, differing in this respect from the hemocyanins.

6. Two absorption bands were observed in the ultraviolet region: a band due to protein at 273 mμ and a band at about 330 mμ probably due to copper.

7. A crystalline material was obtained, from rather crude as well as from purified preparations of the tyrosinase, having a copper content of 0.25% and 13.6% nitrogen. The crystals were colorless and belonged to the isometric system. The average size was about 0.010 mm.

8. Solutions of the crystals were only slightly active toward *p*-cresol and catechol. This slight

activity showed a tendency to increase when the solutions were permitted to stand for some time. Certain solutions of the freshly prepared tyrosinase also showed this tendency to increase in activity on standing.

9. The ratio of activities of the tyrosinase preparations toward *p*-cresol and catechol could not be altered by various methods of purification, but always remained 10 to 1, respectively. The ratio of the two activities in the case of the solutions of the crystalline material was also 10 to 1.

10. Composition, similarity in absorption spectra, the slight increase in activity when solutions are allowed to stand, all point to a close relationship between the crystals and the highly purified tyrosinase preparations.

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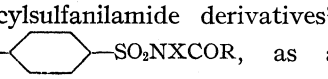
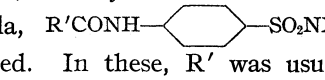
[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE CALCO CHEMICAL COMPANY, INC.]

Sulfanilamide Derivatives. IV. N^1,N^4-Diacylsulfanilamides and N^1-Acylsulfanilamides[1]

BY M. L. CROSSLEY, E. H. NORTHEY AND MARTIN E. HULTQUIST

We have prepared an extended series of N^1-acylsulfanilamide derivatives[2] of the type  , as a continuation of our studies of N^1-substituted sulfanilamides. The scope of the work was extended to include examples where R was alkyl (from one to seventeen carbons in length), alkenyl, aryl, aralkyl, diaralkyl, aralkenyl, cycloalkyl, cycloalkenylalkyl and heterocyclic. Derivatives were also prepared from aliphatic dicarboxylic acids and aryl dicarboxylic acids. A few metanilamide derivatives were prepared, but these appeared to be of little therapeutic interest. X in the above formula was hydrogen, alkyl or a cation.

As intermediates in the preparation of many of the above, N^1,N^4-diacylsulfanilamides of the general formula,  , were synthesized. In these, R′ was usually a methyl group, but several compounds were prepared in which R′ was the same as R. This particular series was not extended since the pharmacological results were not encouraging.

Derivatives in which the N^4-nitrogen of the N^1-acylsulfanilamide was substituted by sulfanilyl- or sodium methylenesulfinate groups were also prepared.

Since inception of this work, the first members of both series have been mentioned. A diacetylsulfanilamide, melting at 240–242°, which from the method of preparation was probably impure N^1,N^4-diacetylsulfanilamide, was described by Scudi.[3] N^1-Acetylsulfanilamide has been described by M. Dohrn and P. Diedrich[4] and is being sold abroad under the name "Albucid" for use against gonorrhea.

Several methods of synthesis were employed, but the one most generally useful involved reaction between N^4-acetylsulfanilamide and an acyl halide in the presence of dry pyridine. This reaction proceeded smoothly, giving good yields of the N^1-acyl-N^4-acetylsulfanilamide. The N^4-acetyl group was then removed by boiling with a slight excess of aqueous sodium hydroxide, to give a solution of the sodium salt of the N^1-acylsulfanilamide, from which the free N^1-acylsulfanilamide was obtained by acidification. Other methods successfully used are given in the experimental part.

Attempts to prepare derivatives by reaction of dry N-acetylsulfanilyl chloride with several carbonamides in pyridine failed. The reason for such failure is not understood and is being investigated further.

N^1-Acyl-N^4-sulfanilylsulfanilamides were prepared by condensing an N^1-acylsulfanilamide with N-acetylsulfanilyl chloride in pyridine, followed by hydrolysis of the acetyl group with aqueous sodium hydroxide.

N^4-Sodium formaldehydesulfoxalate derivatives of N^1-acylsulfanilamides were prepared by warming equimolecular amounts of the starting materials in water until solution was complete, then evaporating to dryness *in vacuo*.

(1) Presented in part before the Division of Medicinal Chemistry, Baltimore meeting, American Chemical Society, April, 1939.

(2) For nomenclature, see Crossley, Northey and Hultquist, THIS JOURNAL, 60, 2217 (1938).

(3) Scudi, *Ind. Eng. Chem., Anal. Ed.*, 10, 346 (1938).

(4) M. Dohrn and P. Diedrich, *Münch. med. Wochschr.*, 85, 2017 (1938).

The compounds usually were obtained as white crystalline materials, although difficulty was met in crystallizing derivatives of unsaturated long chain acids. In many cases the products were first precipitated in sticky, amorphous form and then slowly crystallized. In the series of derivatives of fatty acids, the lower members were moderately water soluble. On ascending the series, the water solubility decreased and solubility in fat solvents increased. Water solubility of derivatives having chains of twelve carbons or more was less than 0.001 g./100 cc. All of the derivatives in which a hydrogen remained on the amide nitrogen formed very soluble

TABLE I

N^1-ACYLSULFANILAMIDES

N^1-Acyl radical	Calcd. mol. wt.	Assay by NaOH	Assay by nitrite	Melting range, °C.	Solubility	Crystalline form
Acetyl[a]	214.3	99.8	99.7	182.0–184.0	S.h.w.	Bipyramidal prisms
Propionyl	228.3	100.1	99.6	134–135	S.h.w.; mod. s.h. alc.	Prisms
Butyryl	242.3	100.2	100.6	125.4–126.6	Recryst. dil. alc.	Long prisms
Isobutyryl	242.3	100.2	100.5	198.5–200	Recryst. dil. alc.	Glistening prisms
2-Ethylbutyryl	270.4	99.5	98.8	189–193.5	Recryst. 60% alc.	Plates
Hexanoyl[a]	270.4	100.0	99.5	129.2–129.9	Recryst. 60% alc.	Long prisms
Heptanoyl	284.4	99.7	99.7	121.8–123.6	Recryst. 60% alc.	Hex. prisms
2-Ethylhexanoyl	298.4	99.2	100.0	165.5–168	Recryst. 70% alc.	Prisms
Octanoyl	298.4	99.5	100.5	101.0–103.0	V.s.hot toluene; ext. s.al.; i.w.; recryst. 60% alc.	Needles from toluene Fine prisms alc.
Decanoyl	326.5	99.4	99.7	119–121	V.s.hot toluene; ext. s.al.; i.w.; recryst. 60% alc.	Fine prisms
Hendecanoyl	340.5	100.4	99.9	112.5–114.5[b]	V.s.hot toluene; ext. s.al.; i.w.; recryst. 60% alc.	Long flat prisms
Dodecanoyl	354.5	100.0	100.0	127–128.5	V.s.hot toluene; ext. s.al.; i.w.; recryst. 80% alc.	Plates and needles
Tetradecanoyl	382.5	98.3	98.5	113.5–117.7	V.s.hot toluene; ext. s.al.; i.w.; recryst. 80% alc.	Fine, irreg. prisms
Octadecanoyl[c]	438.7	102.9	101.8	98–102	Recryst. 70% alc.	Irreg. plates
9-Octadecenoyl	436.7	100.5	...	...	S.toluene, alc.; i.hexane	Non-cryst.
Hexahydrobenzoyl	281.4	99.8	100.4	198.5–200	Recryst. 80% alc.	Needles
Chaulmoogryl	434.6	99.5	99.7	97.9–99.0	Recryst. 60% alc.	Irregular plates
Benzoyl	276.3	99.8	100.6	181.2–182.3	Recryst. 60% alc.	Hex. prisms
p-Nitrobenzoyl	321.3	100.6	100.3	235–240	Recryst. in acetone–alc.	Prisms
p-Aminobenzoyl	291.3	99.5	99.8	197.8–199	Recryst. in acetone–alc.	Needles
Hydrocinnamoyl	304.4	99.8	100.5	160.3–161.5	Recryst. 60% alc.	Glistening leaves
Cinnamoyl	302.4	99.4	99.7	130–133,[d] 174–175	Recryst. 60% alc.	Glistening leaves
4′-Carboxybenzoyl	340.3	100.5	100.8	>225 dec.	Recryst. 80% alc.	Needles
Mandelyl	305.5	100.2	100.6	192.5–194.5 dec.	Recryst. 80% alc.	Needles and prisms
Diphenylacetyl	366.5	99.7	99.3	210.5–212.0	Recryst. 70% acetone; sl.sol.alc.	Rectangular plates
Furoyl	266.3	99.6	99.9	191.5–192.0	Recryst. 60% alc.	Long prisms
2-Phenylcinchoninyl	403.5	99.4	99.2	305–310	Diss. as Na salt and reppted.	White powder
Nicotinyl	277.3	99.8	99.3	256–257.5	Mod. s.h.w.	Silky needles
3-Hydroxy-2-naphthoyl	342.4	100.1	100.5	245–250	Recryst. 70% alc.	Yellow powder

[a] Geneva names are given for acid radicals of six carbons and more because of confusion of their common names with the corresponding alkyl radicals. [b] Also exists in a form which starts melting at 115° and then changes to the higher melting form. [c] Prepared from stearic acid containing palmitic acid. [d] Softens and changes to high melting form at 130°, but melts immediately at 145°, then solidifies.

TABLE II

N^1-ACYLMETANILAMIDES

N^1-Acyl radical	Calcd. mol. wt.	Assay by NaOH	Assay by nitrite	Melting range, °C.	Solubility	Crystalline form
Acetyl	214.3	99.7	97.0	153.5–155.5	S.h.w.	Prisms
Tetradecanoyl	382.5	99.5	100.1	113.5–114.2	Recryst. 80% alc.	Flat prisms

TABLE III

N^1-ALKYL-N^1-ACYLSULFANILAMIDES

N^1-alkyl radical	N^1-acyl radical	Calcd., mol. wt.	Assay by nitrite	Melting range, °C.	Solubility	Crystalline form
Methyl	Dodecanoyl	368.5	100.6	59.3–60.5	V.s.alc., toluene; sl.s. hexane	Fine needles

sodium salts, which were neutral for the lower members of the series, but became increasingly alkaline for the higher members. All of these compounds could be titrated quantitatively to a phenolphthalein end-point, however, while sulfanilamide itself cannot be so titrated, since its sodium salt is highly hydrolyzed at this *p*H.

In general, the derivatives could be hydrolyzed quantitatively to the organic acid and sulfanilamide (or sulfanilic acid) by boiling with alcoholic hydrochloric acid, or more rapidly by heating to 180–200° with 65% sulfuric acid.

The lower members of the series could be titrated quantitatively by diazotization of the N^4-amino group. The higher members were too insoluble in dilute mineral acids to be diazotized directly, but for purposes of analysis were hydrolyzed, by either of the above methods, to sulfanilamide (or sulfanilic acid) and then diazotized. Hydrolysis of the sample before diazotization also permitted nitrite assays of N^1,N^4-diacylsulfanilamides. Analyses by titration with sodium hydroxide and with sodium nitrite were regarded to be of more significance than fundamental analyses by microchemical methods as criteria of purity since presence of isomeric N^4-acylsulfanilamides could not be distinguished by combustion methods.

Alkylation of the N^1-nitrogen gave derivatives which no longer formed salts with cations. These had increased solubility in organic solvents. These derivatives were sensitive to hydrolytic agents and in this resembled the N^1-alkyldisulfanilamides.[5]

A partial rearrangement of certain of these derivatives has been observed. By heating N^1-dodecanoylsulfanilamide for twenty hours at 130–140°, the material darkened, and became semisolid. On dissolving the mixture in hot alcohol, addition of sodium hydroxide to *p*H 9.5, then diluting with water, N^4-dodecanoylsulfanilamide crystallized as fine needles, identified by melting point and inability to titrate with sodium hydroxide.

On boiling an aqueous solution of N^1-acetylsulfanilamide for two hours, small amounts of N^1,-N^4-diacetylsulfanilamide and sulfanilamide were identified. This suggests that two molecules of N^1-acetylsulfanilamide interact with formation of sulfanilamide and N^1,N^4-diacetylsulfanilamide. This interesting reaction will be investigated further.

Pharmacology.—The compounds of the present series have not been investigated in detail pharmacologically. Preliminary results are, however, of considerable interest and center chiefly on derivatives of long-chain fatty acids.

The N^1-acylsulfanilamides were part of our program on disulfanilamides, but the immediate emphasis on long-chain derivatives was due to a suggestion by Dr. D. A. Bryce, our medical director, that some combination of chaulmoogric acid and sulfanilamide might penetrate the tubercle of, and be effective against, tuberculosis. The sodium salt of N^1-chaulmoogrylsulfanilamide seemed to us to be the solution. Lack of chaulmoogric acid led to synthesis from other long-chain fatty acids. It then appeared that the free long-chain derivatives might be of more interest because of their probable fat solubility, and their possible penetration into the bacilli.

While the sodium salts of long-chain N^1-acylsulfanilamides are highly water soluble, they have the characteristics of soaps and are lytic in action. The free long-chain N^1-acylsulfanilamides are almost completely water insoluble, but are soluble in fats and fat solvents. Absorption of these by the oral route appears to be accelerated by administration of fats.

N^1-Dodecanoylsulfanilamide has been investi-

(5) Crossley, Northey and Hultquist, THIS JOURNAL, **60**, 2222 (1938).

TABLE IV

N^1,N^4-DIACYLSULFANILAMIDES

N^1-acyl radical	N^4-acyl radical	Calcd. mol. wt.	Assay by NaOH	Melting range, °C.	Solubility	Crystalline form
Acetyl[8]	Acetyl	256.3	99.5	253.5–255.0	Recryst. alc.	Long prisms
Propionyl	Acetyl	270.3	99.9	242.5–244.3	Sl. s.h.alc.	Prisms
Isobutyryl	Acetyl	284.3	99.5	247–248	Recryst. 80% alc.	Needles
Butyryl	Acetyl	284.3	98.4	238.2–240.0	Recryst. 80% alc.	Needles
Isovaleryl	Acetyl	298.3	100.0	215.0–217.5	Recryst. 80% alc.	Rectangular plates
2-Ethylbutyryl	Acetyl	312.4	99.5	270–272	Recryst. 80% alc.	Rectangular plates
Hexanoyl	Acetyl	312.4	98.9	191–193	Recryst. 60% alc.	Prisms
Heptanoyl	Acetyl	326.4	100.0	205.0–207.5	Recryst. 60% alc.	Prisms
2-Ethylhexanoyl	Acetyl	340.4	99.8	214.0–215.6	Recryst. 60% alc.	Prisms
Octanoyl	Acetyl	340.4	99.3	195.0–197.6	Recryst. 50% alc.	Long prisms
Decanoyl	Acetyl	368.5	99.5	143.2–144.8	Recryst. 70% alc.	Irregular plates
Hendecanoyl	Acetyl	382.5	100.5	153.2–155.0	Recryst. 60% alc.	Glistening plates
Dodecanoyl	Acetyl	396.5	99.1	130–136	Recryst. 95% alc.	Irregular plates
Dodecanoyl	Dodecanoyl	536.5	100.4 (nitrite)	144.0–145.0	Recryst. 95% alc.	Flat prisms
Tetradecanoyl	Acetyl	424.6	99.7	144.2–145.0	Recryst. 80% alc.	Leaflets
9-Octadecanoyl	Acetyl	478.7	99.7	131–135	Recryst.-dil. alc.	Glistening plates
Chaulmoogryl	Acetyl	476.7	99.4			
Benzoyl	Acetyl	318.3	99.3	280–285	V.sl.s.alc., acetone, water; recryst. 80% cellosolve	Needles
Hexahydrobenzoyl	Acetyl	323.4	99.4	210–220–222	Recryst. 80% alc.	Needles
p-Nitrobenzoyl	Acetyl	363.3	99.5	270–272	Dissolved as Na salt in alc. and repptd. with acetic acid	White powder
p-Aminobenzoyl	Acetyl	333.3	99.3	260–263	Recryst. acetone	Needles
Hydrocinnamoyl	Acetyl	346.4	100.0 Nitrite	160–202.8–205.4	Recryst. 60% alc.	Leaflets
Cinnamoyl	Acetyl	344.4	99.8	228–229.5	Recryst. 60% alc.	Needles
Diphenylacetyl	Acetyl	408.5	99.1	248.5–251	Recryst. 60% dioxane	Prisms
Furoyl	Acetyl	308.3	97.3	240.5–241.5	Recryst. 60% alc.	Glistening hexagonal plates
2-Phenylcinchoninyl	Acetyl	445.5	98.9	166–170	Dissolved as Na salt and repptd.	Irregular plates
Nicotinyl	Acetyl	319.3	99.4	295–300	Dissolved as Na salt and repptd.	Fine needles
Dodecanoyl	N-Acetylsulfanilyl	551.71	99.3 (nitrite)	120–150–152	Recryst. AcOEt	Prisms
Dodecanoyl	Sulfanilyl	509.67	98.8 (nitrite)	102–104	Recryst. dil. alc.	Needles

gated more fully than other members of the series. It appears to be equal or slightly superior to sulfanilamide, on an equal weight dosage, in experimental mice infections with various beta hemolytic streptococci. Cavies infected with a human strain of mycobacterium tuberculosis showed only localized lesions when treated with the drug. Animals treated with sulfanilamide showed moderate spread of the infection, while untreated controls developed generalized tuberculosis and died.

The pharmacological study has been made under the direction of D. R. Climenko. Further details are being published elsewhere.[6,7]

Experimental Part

General Methods of Synthesis. 1. Use of Acyl Halide in Pyridine.—This method was the most generally applicable and gave the best yields. It is illustrated by the following synthesis of N^1-dodecanoylsulfanilamide. A 1-

(6) D. R. Climenko, "N^1-Dodecanoylsulfanilamide. I. Absorption, Distribution and Toxicity," *Proc. Soc. Exptl. Biol. Med.*, in press.

(7) D. R. Climenko and Ruth L. Schmidt, "N^1-Dodecanoylsulfanilamide. II. Experimental Infections with Beta Haemolytic Streptococci and Human Tubercle Bacilli," *ibid.*

TABLE V

Abbreviations: AcSA, N^1-acylsulfanilamide; Alc., alcohol; Ext., extremely; i., insoluble; s., soluble; sl., slightly; v., very.

N^1-Acyl radical	Salt	How prepared	Mol. wt.	Nitrite assay	Solubility	Crystalline form
Acetyl	$Na \cdot H_2O$	AcSA + NaOH in H_2O + alc.	254	100.5%	V.s. H_2O sl.s.alc.	Prisms
Acetyl	NH_4	AcSA + NH_4OH in alc.	231.3	100.3	Ext.s.H_2O s.alc.	Thick prisms
Acetyl	$(C_2H_5)_2NH_2$	AcSA + $(C_2H_5)_2NH$ in alc.	287.4	100.1	V.s.H_2O s.alc.	Coarse prisms
Dodecanoyl	Ag	AcSA + Ag_2O in alc.	461.4	99.2	Sl.s.alc. i.H_2O	Light sensitive
Dodecanoyl	Hg^{++}	NaAcSA + $HgCl_2$ in alc.	907.6	99.3	S.alc. s. acetone	Needle clusters
Dodecanoyl	Ca	AcSA + $Ca(OH)_2$ in H_2O	746.6	100.2	V.sl.s.H_2O s.alc.i.toluene	Needles

TABLE VI

SALTS OF N^1,N^4-DIACYLSULFANILAMIDES

N^1-Acyl	N^4-Acyl	Salt	How prepared	Mol. wt.	Nitrite Assay	Solubility	Crystalline form
2-Ethylhexanoyl	Acetyl	Na	Ac_2SA + NaOH in alc.	362.4	100.5%	Ext.s.H_2O Ext.s.alc.	Amorphous
2-Ethylhexanoyl	Acetyl	Mg	Ac_2SA + Mg in H_2O + MeOH	703.1	Calcd. 3.46% Mg Found 3.35% Mg	Ext.s.H_2O Ext.s.alc.	Amorphous

liter, 3-necked flask was equipped with a hook-type agitator and thermometer. Half of 257 g. (1.2 moles) of dry, finely pulverized N^4-acetylsulfanilamide was added with 250 cc. of dry pyridine. The agitator was started and the mixture heated to 90°. One-third of 219 g. (1 mole) of dodecanoyl chloride (boiling range 125–127°(7 mm.)) was added over five minutes, in portions, via a long-stemmed funnel (to prevent the acid chloride from coming into contact with the walls of the flask where it would have reacted with pyridine vapor to give highly colored impurities). The flask was cooled externally to prevent the temperature from exceeding 110°. The balance of the N^4-acetylsulfanilamide was then added, followed by the balance of the dodecanoyl chloride. The temperature was held at 100–110° for fifteen minutes to complete the reaction. The resulting pyridine solution was drowned in 1 liter of water and 250 cc. of concentrated hydrochloric acid. The product, which first separated as an oil, soon crystallized into soft pellets which were filtered and washed well with water. A portion of the crude N^1-dodecanoyl-N^4-acetylsulfanilamide was dissolved at *p*H 9 in water by addition of sodium hydroxide. The solution was treated with decolorizing carbon and the product reprecipitated by acidification. After three recrystallizations, N^1-dodecanoyl-N^4-acetylsulfanilamide was obtained, having the properties listed in Table IV.

The main portion of the crude material was dissolved in 600 cc. of water (to give approximately a 1 molar concentration) with addition of sodium hydroxide to a definite red spot test on phenolphthalein paper. A 1-cc. sample was taken, hydrolyzed by boiling with 5 cc. of concentrated sulfuric acid and 4 cc. of water for fifteen minutes, diluted with ice and water and titrated at 20° with 0.1 *N* sodium nitrite. For each equivalent in the alkaline solution indicated by the nitrite analysis, 1.4 moles of sodium hydroxide was added. The mixture was then boiled for one and one-half hours to hydrolyze the N^4-acetyl group. The hydrolyzed solution was diluted with an equal amount of water, neutralized to about *p*H 9 and treated with activated charcoal. The clarified liquor was acidified and the product obtained as a sticky oil which soon crystallized. It was recrystallized five times from toluene, using activated charcoal. 80% alcohol was used very satisfactorily for purification in other runs on this compound, and was the solvent most generally used for purification of other N^1-acylsulfanilamides. Average yield in these preparations based on the acid chloride was 60%.

2. Preparation from Acid Anhydrides.—This is illustrated by the preparation of N^1,N^4-diacetylsulfanilamide: 214 g. (1 mole) of N^4-acetylsulfanilamide was added gradually with agitation to 350 cc. of acetic anhydride heated at 70–80°. The mixture was then boiled for one hour. A thick slurry of crystals resulted which was drowned and washed well with water. The crystals were dissolved in 800 cc. of hot water by addition of sodium hydroxide to *p*H 8, treated with activated charcoal, cooled and a trace of N^4-acetylsulfanilamide removed by filtration. Crude N^1,N^4-diacetylsulfanilamide was precipitated by acidifying strongly with hydrochloric acid; yield after recrystallization was 60%.

Hydrolysis of the N^4-acetyl group was carried out by boiling one mole of the diacetyl derivative with 2.5 moles of sodium hydroxide in 1-liter water for one hour. The hydrolysate was neutralized to about *p*H 8 with hydrochloric acid and treated with activated charcoal while warm. The clarified solution on cooling and standing deposited a little sulfanilamide which was removed. The solution was acidified to about *p*H 4 and N^1-acetylsulfanilamide containing a little N^1,N^4-diacetylsulfanilamide crystallized. The mixture was warmed at 30–40° with 10% hydrochloric acid. The N^1-acetylsulfanilamide dissolved, while the N^1,N^4-diacetylsulfanilamide was insoluble and was removed by filtration. The filtrate was treated with activated charcoal, neutralized to *p*H 4 and N^1-acetylsulfanilamide crystallized on cooling. It was recrystallized from hot water, in which it was extremely

soluble at the boil, but only 0.9% at room temperature; the yield from N^1,N^4-diacetylsulfanilamide was 32%.

3. Preparation from N^1-Sodium-N^4-acetylsulfanilamide.—Anhydrous N^1-sodium-N^4-acetylsulfanilamide was prepared as follows. Crude N^4-acetylsulfanilamide paste was dissolved by addition of solid powdered sodium hydroxide to form a warm solution of N^1-sodium-N^4-acetylsulfanilamide. This was treated with activated charcoal, then cooled and crystallized. Large crystals formed containing much water of crystallization. These were filtered off and washed with a little ice water. The crystals were melted in a small amount of water and recrystallized to free from excess sodium hydroxide. As much of the adhering mother liquor as possible was removed by filtration, then by washing with very little ice water. The crystals were dried in a vacuum oven at not over 50° until practically anhydrous. Temperature was then raised to 60 to 70° until the product was anhydrous as indicated by hydrolysis of a sample to sulfanilamide and titration with sodium nitrite. The anhydrous material was finely ground and used in preparing various N^1-acylsulfanilamides, of which the following illustrates a method for the preparation of N^1-butyrylsulfanilamide: 236 g. (1 mole) of N^1-sodium-N^4-acetylsulfanilamide was suspended in 400 cc. of anhydrous dioxane; then 108 g. (1 mole) of butyryl chloride was added under agitation. When the reaction moderated, heat was applied to maintain a slow boiling for three hours under reflux condenser. The product was practically insoluble in the dioxane, was removed by filtration, and recrystallized twice from 70% alcohol. The N^4-acetyl group was hydrolyzed by the procedure described above for making N^1-acetylsulfanilamide.

Other solvents used for this method of preparation were xylene, pyridine and higher pyridine bases having a boiling range of 120 to 140°. Pyridine gave the most satisfactory results, since it had the ability to hold both the reactants and the final product in solution. Because the use of pyridine made unnecessary the preparation and drying of N^1-sodium-N^4-acetylsulfanilamide, this method was soon abandoned.

4. Reaction of N^4-Acetylsulfanilamide and an Acyl Halide in the Absence of Base.—Dry fusion of the N^4-acetylsulfanilamide with several acyl halides led in general to colored decomposition products along with the desired N^1-acetyl-N^4-acetylsulfanilamide. By use of inert solvents, fair yields were obtained in certain cases, as illustrated by the following method for preparing N^1-benzoyl-N^4-acetylsulfanilamide: 214 g. (1 mole) of dry N^4-acetylsulfanilamide, 141 g. of benzoyl chloride, and 700 cc. of toluene were agitated and heated under a reflux condenser for twenty hours. There was slow evolution of hydrogen chloride during this period. The toluene was evaporated and the residue dissolved in about 1 liter of water with sodium hydroxide to *p*H 9. The solution was treated with activated charcoal and a little unreacted N^4-acetylsulfanilamide removed. The solution was acidified, the crude product filtered off, and washed well with alcohol to remove benzoic acid. The product was recrystallized from 90% cellosolve giving 40% yield of N^1-benzoyl-N^4-acetylsulfanilamide.

5. Preparation of N^1-Alkyl-N^1-acylsulfanilamides.—Attempts to prepare N^1-alkyl-N^1-acylsulfanilamides by hydrolysis of the corresponding N^4-acetyl derivatives resulted in complete hydrolysis of the N^1-acyl group. Such derivatives were prepared successfully by starting with N-alkyl-nitrobenzenesulfonamides[8] which were acylated by the general procedure, then reduced using iron and acetic acid with addition of toluene. Metanilamide derivatives were made similarly.

Preparation of Acid Chlorides.—Chaulmoogryl chloride for N^1-chaulmoogrylsulfanilamide was prepared from ethyl chaulmoograte obtained through the courtesy of Professor Roger Adams of the University of Illinois. Eastman Kodak Co. technical chaulmoogric acid was found to have an iodine number approximately half of the theoretical value and could not be purified to give satisfactory starting material.

Long-chain acid chlorides from C_8 to C_{14} were prepared by converting technical lauric acid to the mixed acid chlorides with either thionyl chloride or phosphorus trichloride. The mixed acid chlorides were separated by fractionation through a 120-cm. packed column at 5–15 mm. pressure. The resulting acid chlorides had constants in close agreement with literature values.

Heterocyclic acids containing a nitrogen in the ring were converted to the acid chloride–hydrochlorides with thionyl chloride and isolated as solid products by evaporation of excess thionyl chloride. The condensation with N^4-acetylsulfanilamide was carried out in the presence of excess pyridine.

Summary

1. A large series of N^1-acylsulfanilamides was prepared from aliphatic, aromatic, heterocyclic and carbocyclic acids. As intermediates, N^1,N^4-diacylsulfanilamides were prepared in which the N^4-acyl group was usually acetyl. Salts of both series of compounds with various cations also were prepared.

2. Preliminary pharmacological results indicated that N^1-dodecanoylsulfanilamide was effective in mice against infections by beta hemolytic streptococci and arrested the spread of tuberculous infections in cavies.

BOUND BROOK, N. J. RECEIVED JULY 14, 1939

(8) Demény, *Rec. trav. chim.*, **48**, 1145 (1929).

[CONTRIBUTION FROM THE SQUIBB INSTITUTE FOR MEDICAL RESEARCH, DIVISION OF ORGANIC CHEMISTRY]

Stigmasterol 22,23-Dibromide

BY ERHARD FERNHOLZ AND HOMER E. STAVELY

Stigmasterol possesses two double bonds, one in the ring system (5,6), the other in the side-chain (22,23). These differ in reactivity, and it is possible to add preferentially various reagents to one or the other. Bromine,[1] hydrogen bromide,[2] hydrogen chloride,[2] and perbenzoic acid[3] first react with the nuclear double bond, while catalytic hydrogenation leads primarily to the saturation of the side-chain.[4]

We have now succeeded in preparing a dibromide of stigmasterol in which the bromine is situated in the side-chain. Its acetate is obtained by removal of one mole of bromine from the tetrabromide with sodium iodide. Schoenheimer,[5] who first debrominated sterol bromides by this method, stated that the bromine atoms in the side-chain of stigmasterol tetrabromide do not react readily. However, it seems that no efforts were made to investigate the reaction products more thoroughly. The yield in which the new dibromide can be isolated depends to a great extent on the experimental conditions, and a comparatively small yield is obtained when the reaction is carried out in boiling solution as described in the literature.[5] The best yield (60%) is obtained by letting the reactants stand at room temperature for about twenty hours. It was not possible to replace sodium iodide by zinc dust, since even at room temperature in moist ether or in boiling alcohol the debromination did not stop at the dibromide but resulted in the formation of stigmasteryl acetate.

The new dibromide is remarkably stable and has a high melting point (212–213°). It resembles stigmasteryl acetate tetrabromide in this respect and is different from the 4,5-dibromide, which has a low melting point and cannot be recrystallized without decomposition. Although there was little doubt that we were dealing with the 22,23-dibromide and not a 5,6-dibromide isomeric with the one obtained by addition of one mole of bromine to stigmasteryl acetate, we made experiments to prove our supposition.

By saponification with methyl alcoholic potassium hydroxide stigmasterol 22,23-dibromide, m. p. 210°, was obtained without difficulties. The halogen in the side-chain was not noticeably attacked. This compound could be dehydrogenated by Oppenauer's method[6] and a ketone was obtained, m. p. 182–184°, which had an absorption spectrum with a maximum at 240 mμ (log E [molar] 4.08 in absolute alcohol)[7] characteristic for α,β-unsaturated ketones. This proves conclusively the anticipated structure of the new dibromide.

Treatment of the above ketone with zinc dust and acetic acid yielded a ketone of m. p. 125°, stigmastadienone. Under the name stigmastenone Marker and Wittle[8] have described a compound prepared from stigmasterol by catalytic dehydrogenation with copper. This compound correctly should be called stigmastadienone and should be identical with our compound; it melts, however, at 94° which is much lower. The preparation of stigmastadienone from stigmasterol by Oppenauer's method has been described in the patent literature[9] where a melting point of 107° has been recorded. We have prepared stigmastadienone by this method and the substance obtained had a constant melting point of 125°, and was identical with the stigmastadienone prepared from the dibromide.

Experimental

Stigmasteryl Acetate 22,23-Dibromide.—To 5 g. of stigmasteryl acetate tetrabromide in 75 cc. of benzene was added 3 g. of sodium iodide in 25 cc. of ethanol, and the mixture allowed to stand at room temperature for twenty hours. The mixture was then shaken with sodium sulfite to remove free iodine, washed with water, dried over sodium sulfate, concentrated, and filtered. The precipitate was crystallized from benzene–ethanol. The yield of pure acetoxy dibromide was 60%; fine needles, m. p. 212–213°, $[\alpha]^{25}D$ 30 (15.3 mg. in 2.0 cc. chloroform, 1-dm. tube, αD −0.23). Mixed m. p. with stigmasteryl acetate tetrabromide showed a depression of 20°.

Anal.[10] Calcd. for $C_{31}H_{50}O_2Br_2$: C, 60.58; H, 8.21; Br, 26.01. Found: C, 60.73; H, 8.25; Br, 25.91, 26.06.

(1) E. Fernholz, *Ann.*, **507**, 128 (1933).
(2) L. Ruzicka, W. Fischer and J. Meyer, *Helv. Chim. Acta*, **18**, 1486 (1935).
(3) E. Fernholz, *Ann.*, **508**, 215 (1934).
(4) S. Bernstein and E. S. Wallis, *J. Org. Chem.*, **2**, 341 (1937).
(5) *J. Biol. Chem.*, **110**, 461 (1935).
(6) Oppenauer, *Rec. trav. chim.*, **56**, 141 (1937).
(7) This measurement was carried out by Dr. N. H. Coy of the Biological Laboratories of E. R. Squibb and Sons.
(8) Marker and Wittle, THIS JOURNAL, **59**, 2704 (1937).
(9) *C. A.*, **32**, 4174[8] (1938).
(10) The micro-analyses reported in this paper were carried out by Mr. J. F. Alicino, Fordham University.

Two hundred milligrams of the product was debrominated with zinc dust and acetic acid. The bromine-free product had a m. p. of 138–139°; mixed m. p. with stigmasterol acetate gave no depression.

Runs on a larger scale gave poorer yields. A lower melting mixture was isolated from the mother liquor which was reconverted to stigmasterol tetrabromide and used over.

Stigmasterol 22,23-Dibromide.—One gram of stigmasteryl acetate 22,23-dibromide was refluxed with 5% potassium hydroxide in methanol for two hours. After addition of water it was extracted with ether, the ether washed, dried over sodium sulfate, evaporated to dryness and crystallized twice from benzene–ethanol; needles, m. p. 209–210°. Mixed melting point with the starting material gave a depression of 25°.

Anal. Calcd. for $C_{29}H_{48}OBr_2$: Br, 27.95. Found: Br, 27.65.

Stigmastadienone 22,23-Dibromide.—Three and six-tenths grams of stigmasterol 22,23-dibromide, 5 g. of aluminum *t*-butylate, 150 cc. of dry benzene, and 40 cc. of dry acetone were refluxed together overnight. The mixture was washed with dilute sulfuric acid, then with water until neutral, dried over sodium sulfate and evaporated to dryness in a vacuum. The residue was crystallized from acetone, giving 2.6 g. of material, m. p. 173–178°. After recrystallizing many times the m. p. became constant at 182–184°. $[\alpha]^{22}D$ +53° [18.8 mg. in 2.0 cc. chloroform, 1-dm. tube, αD +0.50°].

Anal. Calcd. for $C_{29}H_{46}OBr_2$: C, 61.05; H, 8.13. Found: C, 60.78, 60.87; H, 8.18, 8.11.

Stigmastadienone.—Two hundred milligrams of stigmastadienone 22,23-dibromide was heated on the steam-bath with 250 mg. of zinc dust and 10 cc. of glacial acetic acid for one hour, decanted from the zinc, water added and extracted with ether. The ether was washed with dilute sodium carbonate solution, then with water, dried over sodium sulfate, and evaporated to dryness. The residue was crystallized from ethanol.

The product had a melting range of 80–110° and was probably partially reduced. The semicarbazone was prepared by heating with semicarbazide hydrochloride and potassium acetate in boiling ethanol. It was recrystallized twice from chloroform–ethanol; crystals turned brown at 227°, m. p. 235–237°. The semicarbazone was decomposed by boiling with 3 cc. of 5 *N* sulfuric acid and 6 cc. of ethanol for two hours. Water was added and the precipitate filtered and crystallized from ethanol. The product weighed 45 mg.; narrow leaflets, m. p. 123–124°. After two more crystallizations from ethanol and decolorizing with norit the m. p. was constant at 124–125°.

Anal. Calcd. for $C_{29}H_{46}O$: C, 84.81; H, 11.29. Found: C, 84.80, 84.66; H, 11.24, 11.34.

Stigmastadienone from Stigmasterol.—A mixture of 5 g. of stigmasterol, 6 g. of aluminum isopropylate, 50 cc. of cyclohexanone and 150 cc. of toluene was refluxed for two hours and then poured into cold water. Concentrated hydrochloric acid was added and the aqueous layer discarded. The organic solvents were removed by steam distillation. The crude stigmastadienone was purified by crystallizing from ethanol; narrow leaflets, m. p. 125°, $[\alpha]^{25}D$ +63° (27.7 mg. in 2.0 cc. chloroform, 1-dm. tube, αD +0.87°).

Anal. Calcd. for $C_{29}H_{46}O$: C, 84.81; H, 11.29. Found: C, 84.78; H, 11.08.

A mixed m. p. with stigmastadienone prepared from the dibromide gave no depression.

Summary

Stigmasteryl acetate 22,23-dibromide has been prepared by the removal of one mole of bromine from stigmasteryl acetate tetrabromide.

The position of the bromine atoms has been established by conversion into a α,β-unsaturated ketone, stigmastadienone 22,23-dibromide.

The preparation of stigmastadienone from this dibromide and from stigmasterol has been described.

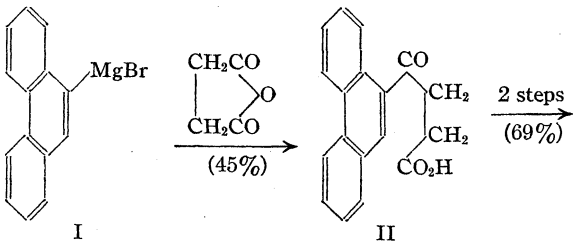
NEW BRUNSWICK, N. J. RECEIVED AUGUST 16, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Methyl Homologs of Triphenylene

BY LOUIS F. FIESER AND LLOYD M. JOSHEL[1]

This work is an extension of investigations undertaken by the junior author in collaboration with Dr. M. S. Newman. Newman and Joshel[2] pointed out that, since the introduction of methyl groups in certain positions into the biologically



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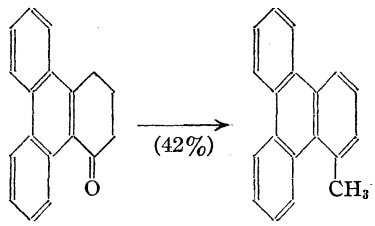
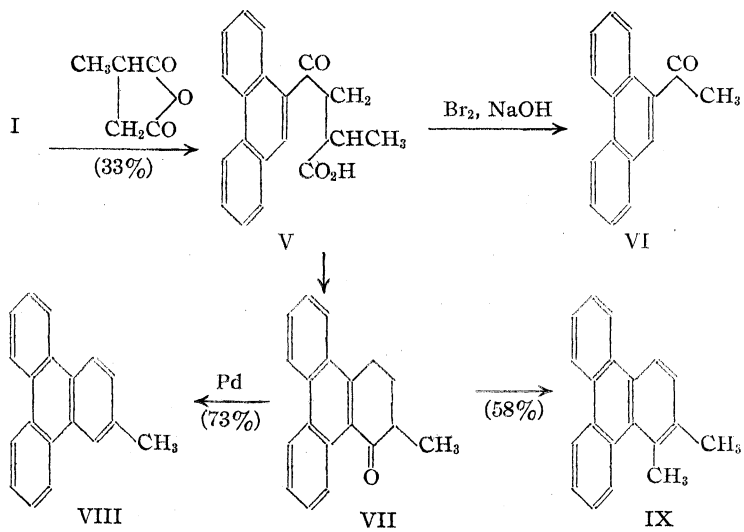


III IV

inactive 1,2-benzanthracene gives rise to powerfully carcinogenic hydrocarbons, it would be of interest to study the methyl homologs of all four of the tetracyclic aromatic hydrocarbons isomeric with 1,2-benzanthracene. The present research is devoted to a synthesis of the two monomethyl triphenylenes and of two of the fourteen possible dimethyl compounds of this series.

Since but little is known concerning the substitution reactions of triphenylene, and since the structures of homologs obtained in this way probably could be established most readily by synthesis, the choice in the present work fell on methods involving the synthetic construction of the tetracyclic system. A convenient approach to 1-methyltriphenylene (IV) already has been worked out by Bergmann and Blum-Bergmann,[3] who synthesized 1-keto-1,2,3,4-tetrahydrotriphenylene (III) by the condensation of 9-phenanthrylmagnesium bromide with succinic anhydride, reduction of the keto acid II and cyclization with phosphorus pentoxide in toluene. By introducing some modifications in these steps, for example by using anhydrous hydrogen fluoride for ring closure (87% yield), the ketone has been obtained in over-all yield of 31%. The ketone reacted readily with methylmagnesium chloride, and the crude carbinol on dehydration followed by dehydrogenation with sulfur was converted into 1-methyltriphenylene, which was purified through the picrate.

The 2-isomer was obtained in an analogous manner starting with methylsuccinic anhydride. The chief acidic product of the Grignard reaction was obtained in 33% yield and identified as having the structure V by a convenient method which was applied recently to an unmethylated product of the general succinoylation reaction.[4] The keto acid was brominated and the crude bromo derivative treated with alcoholic alkali, whereupon it underwent fission to 9-acetophenanthrene (VI). If the methyl group were in the alternate position adjacent to the carbonyl group the cleavage product would be 9-propiophenanthrene. The ketone



I V VI VIII VII IX

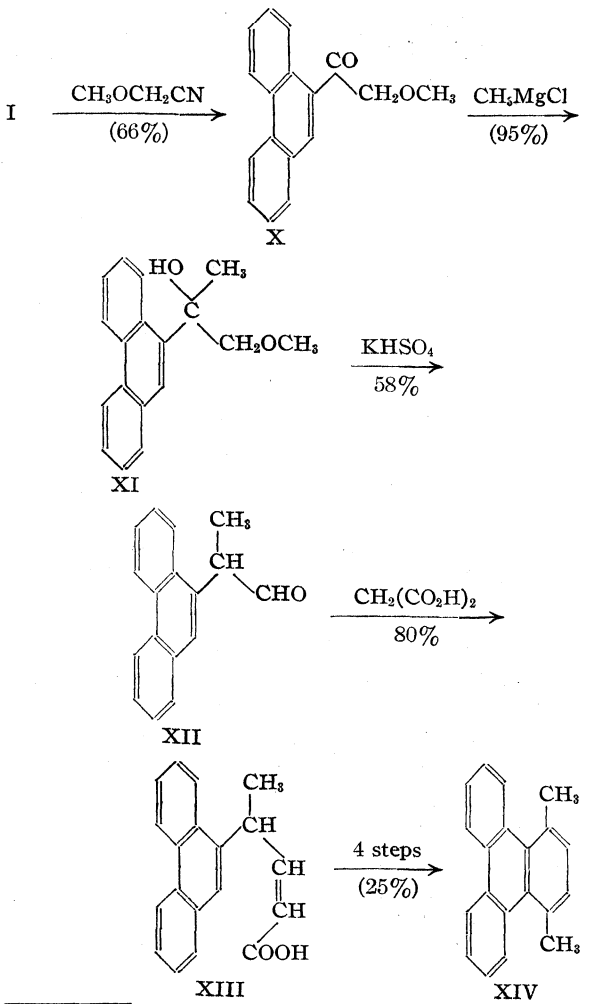
VII, obtained by reduction and cyclization with HF (92% yield), afforded 2-methyltriphenylene (VIII) by Clemmensen reduction followed by dehydrogenation with palladium charcoal. A more

(1) Fellow of the Finney-Howell Research Foundation.
(2) Newman and Joshel, THIS JOURNAL, **60**, 485 (1938).
(3) Bergmann and Blum-Bergmann, *ibid.*, **59**, 1441 (1937).
(4) Fieser and Hershberg, *ibid.*, **61**, 1279 (1939).

novel method of accomplishing this transformation was found in heating the ketone with palladium charcoal at 310°, whereby the aromatic hydrocarbon VIII was produced in excellent yield. By the Grignard process the ketone VII was also converted into 1,2-dimethyltriphenylene (IX), which bears some structural resemblance to 1,2,3,4-dibenzphenanthrene,[5] an active agent for the production of skin tumors.

In the triphenylene series the nearest approach to a structure analogous to that of the carcinogenic 10-methyl-1,2-benzanthracene is met with in the 1-derivative, and the 1,4-dimethyl derivative (XIV) would correspond to the potent 9,10-dimethyl-1,2-benzanthracene. In one attempt to obtain this hydrocarbon we tried to add the methyl Grignard reagent to the carbonyl group of β-(9-phenanthroyl)-propionic acid or its ester, but the experiments were all unsuccessful. Trial was also made of the reaction between 9-phenanthrylmagnesium bromide and the ethyl ester of levulinic acid, in analogy with a condensation reported by Grignard,[6] but the chief product was phenanthrene. A very satisfactory route to the desired hydrocarbon was then found in the utilization of the recently described method of preparing arylacetaldehydes.[7] α-(9-Phenanthryl)-propionaldehyde (XII) was obtained readily by the sequence of Grignard reactions indicated in the chart and dehydration of the resulting carbinol XI. Condensation with malonic acid gave an acid side chain of the required length, and the second methyl group was introduced after reduction and cyclization and the remainder of the process completed by the usual methods.

Tests for carcinogenic properties are being conducted in part by Dr. M. J. Shear and in part by Dr. Shields Warren.



(5) Hewett, *J. Chem. Soc.*, 193, 1286 (1936).

Experimental Part[8]

β-(9-Phenanthroyl)-propionic acid was prepared according to Bergmann and Blum-Bergmann[3] by the action of the Grignard reagent from 81 g. of 9-bromophenanthrene on 25 g. of succinic anhydride. On decomposition with acid part of the product separated in a crystalline condition and was collected by filtration; the rest was extracted from the organic layer with soda. The yield of material of m. p. 179.5–180.5° was 45%.

Treatment of the acid with methylmagnesium chloride in refluxing benzene–ether resulted only in the production of dark oils in the neutral fraction with invariable recovery of starting material.

The **methyl ester** was prepared by adding 21 g. of acid to 500 cc. of methanol containing dissolved hydrogen chloride, refluxing the suspension for four hours, during which time the solid dissolved, distilling about half of the solvent, and adding water. It crystallized from benzene–ligroin in colorless needles, m. p. 88.6–89.4° (21.5 g., 0.6 g. of good material from the mother liquor). Bergmann and Blum-Bergmann[3] report the m. p. 88°, using diazomethane.

Condensation of the ester with methylmagnesium chloride or iodide by the procedure found satisfactory in an analogous case[9] proved unsuccessful; about half of the ester was always recovered unchanged.

γ-(9-Phenanthryl)-butyric Acid.—The keto acid (10.5 g.) was refluxed for twenty-four hours with 30 g. of amalgamated zinc, 100 cc. of toluene, and 100 cc. of concentrated hydrochloric acid, added in portions; fresh zinc and acid were added and boiling continued for another day. On cooling, the product separated in a hard cake and this was collected together with the zinc and the

(6) Grignard, *Ann. chim.*, [7] **27**, 548 (1902); *Compt. rend.*, **135**, 627 (1902).

(7) Fieser, Joshel and Seligman, THIS JOURNAL, **61**, 2134 (1939).

(8) All melting points are corrected. Microanalyses by Lyon Southworth.

(9) Fieser and Johnson, THIS JOURNAL, **61**, 1647 (1939).

reduction product extracted with acetone (very little material was found in the toluene layer), giving 6.85 g. of acid, m. p. 172.8–174°, and 1.05 g. of slightly lower m. p.; yield 79% (compare 53–56% by the Wolff–Kishner method[3]).

1-Keto-1,2,3,4-tetrahydrotriphenylene (III) was prepared by treating 2.6 g. of the above acid with 25 g. of hydrogen fluoride at 0° for forty-five minutes, pouring the mixture onto ice and extracting with ether. Extraction with soda removed a small amount of starting material, and crystallization of the neutral fraction afforded 1.6 g. of ketone, m. p. 97–99°, and 0.5 g., m. p. 95–98° (87%, compare 68% with phosphorus pentoxide[3]). The m. p. of the first crop was not changed appreciably by two recrystallizations from methanol.

1-Methyltriphenylene (IV).—A benzene solution of 5.5 g. of the ketone III was added to the Grignard reagent from 1 g. of magnesium and excess methyl chloride, and after stirring at room temperature for one-half hour, refluxing for a like period, and standing overnight the mixture was worked up as usual. The neutral portion was heated with a crystal of iodine at 200–220° for one-half hour to effect dehydration, 0.75 g. of sulfur was added, and the oil was heated at 230° for one hour and at 230–250° for one-half hour. The distilled product was treated in benzene with 5 g. of picric acid and the once recrystallized picrate dissolved in benzene and passed through a tower of alumina. The hydrocarbon was obtained from benzene–alcohol as almost colorless needles, m. p. 92–93.5°; yield 2.3 g. (42.5%). Recrystallization gave a colorless product, m. p. 93.4–94.2°.

Anal. Calcd. for $C_{19}H_{14}$: C, 94.18; H, 5.82. Found: C, 94.19; H, 5.83.

The **picrate** crystallized from benzene as orange needles, m. p. 177.2–178.2°.

Anal. Calcd. for $C_{25}H_{17}O_7N_3$: N, 8.91. Found: N, 8.80.

α-Methyl-β-(9-phenanthroyl)-propionic Acid (V).—The Grignard reagent from 93.5 g. of 9-bromophenanthrene and 10 g. of magnesium in 250 cc. each of benzene and ether was added in the course of seventy-five minutes to a boiling solution of 37 g. of methylsuccinic anhydride in 250 cc. of ether; refluxing was continued for one-half hour and the mixture worked up the next day. Two crystallizations of the acid fraction from acetone–benzene gave 26 g. of small, colorless needles, m. p. 155–156°, and 4.8 g. of slightly lower melting material; yield 33%. The acidic material in the mother liquor was not investigated.

Anal. Calcd. for $C_{19}H_{16}O_3$: C, 78.06; H, 5.52. Found: C, 77.98; H, 5.75.

For proof of structure, 2.9 g. of V was treated in chloroform solution (50 cc.) with 0.5 cc. of bromine. The reaction seemed slow, but decoloration took place immediately on irradiation for a few seconds with ultraviolet light. The chloroform was evaporated and the remaining viscous oil was dissolved in 30 cc. of alcohol and treated with 5 g. of sodium hydroxide in 15 cc. of water. After twenty-four hours at room temperature the mixture was diluted with water and extracted with ether. The neutral fraction was distilled in vacuum and the 9-acetophenanthrene (0.5 g.) then crystallized from alcohol in long needles, m. p. 73–74°. Mosettig and van de Kamp[10] found the m. p. 74–74.5°; 9-propiophenanthrene[11] melts at 55–57°.

α-Methyl-γ-(9-phenanthryl)-butyric Acid.—The keto acid V (3.0 g.) was reduced by refluxing for twenty-four hours with amalgamated zinc (30 g.), toluene (40 cc.), and concentrated hydrochloric acid (100 cc.), added in portions. Crystallized from toluene–ligroin and then from benzene–ligroin the acid was obtained as colorless needles, m. p. 136.6–137.4°; yield 2.2 g. (77%).

Anal. Calcd. for $C_{19}H_{18}O_2$: C, 81.98; H, 6.52. Found: C, 81.84; H, 6.57.

2-Methyl-1-keto-1,2,3,4-tetrahydrotriphenylene (VII).—The above acid (20.7 g.) was cyclized with hydrogen fluoride (150 g.) and obtained as colorless needles, m. p. 85–86.5° (unchanged on recrystallization) from benzene–ligroin; yield 17.9 g. (92.5%).

Anal. Calcd. for $C_{19}H_{16}O$: C, 87.66; H, 6.20. Found: C, 87.69; H, 6.33.

2-Methyltriphenylene (VIII).—A mixture of 1 g. of the ketone VII and 0.1 g. of palladium charcoal was heated under nitrogen in a sealed tube at 300–310° for seven hours. The product was extracted with benzene and crystallized from benzene–alcohol, giving 0.68 g. (73%) of colorless needles, m. p. 102.6–103.6°.

Anal. Calcd. for $C_{19}H_{14}$: C, 94.18; H, 5.82. Found: C, 94.23; H, 5.88.

The **picrate** formed light orange needles from benzene–alcohol, m. p. 192.4–193°.

Anal. Calcd. for $C_{25}H_{17}O_7N_3$: C, 8.91. Found: N, 9.09.

4′-Keto-1,2,3,4-tetrahydro-3,4-benzpyrene gave no satisfactory reaction product when similarly treated.

2-Methyl-1,2,3,4-tetrahydrotriphenylene was prepared by Clemmensen–Martin reduction of VII (3 g.) as above; it crystallized from benzene–alcohol as colorless needles, m. p. 114–116° (2.2 g., 77.5%). A recrystallized sample melted at 116.2–116.8°.

Anal. Calcd. for $C_{19}H_{18}$: C, 92.63; H, 7.37. Found: C, 92.45; H, 7.42.

A 1.6-g. portion of the tetrahydride was heated with 0.16 g. of palladium charcoal under nitrogen at 215–230° for one-half hour and the temperature was then raised to 310° in the course of one and one-half hours, when nearly the calculated amount of hydrogen had been evolved. The product crystallized from benzene–alcohol as colorless needles, m. p. 104–105°, and gave no depression with the above sample of 2-methyltriphenylene; yield 1.3 g. (83%).

1,2-Dimethyltriphenylene (IX) was prepared from 1.4 g. of the ketone VII and excess methylmagnesium chloride, refluxing for three hours in benzene–ether and using ammonium chloride for decomposition. Following the procedure of Bachmann and Wilds,[12] the crude carbinol was heated under nitrogen with 150 mg. of palladium charcoal at 290–315° for one and one-quarter hours (80% of theoretical hydrogen evolution). The hydrocarbon was extracted with benzene and crystallized from benzene–alcohol, giving 0.8 g. (58%) of colorless needles, m. p. 86.8–87.4°.

(10) Mosettig and van de Kamp, THIS JOURNAL, **55**, 3442 (1933).
(11) Bachmann and Struve, *ibid.*, **58**, 1659 (1936).
(12) Bachmann and Wilds, *ibid.*, **60**, 624 (1938).

Anal. Calcd. for $C_{20}H_{16}$: C, 93.71; H, 6.29. Found: C, 93.58; H, 6.37.

The **picrate** formed orange needles, m. p. 154–155°, from benzene–alcohol.

Anal. Calcd. for $C_{26}H_{19}O_7N_3$: C, 64.33; H, 3.95. Found: C, 64.58; H, 3.97.

Methoxymethyl 9-Phenanthryl Ketone (X).—The Grignard reagent from 15.5 g. of 9-bromophenanthrene and 1.6 g. of magnesium was treated with 3.6 g. of methoxyacetonitrile in benzene and the mixture refluxed for one hour and decomposed with hydrochloric acid the next day. After steam distillation for one hour the product was taken up in ether and distilled, b. p. 220–225° (3 mm.). Two crystallizations from ether afforded 7.9 g. of colorless prisms, m. p. 67.2–68°, and 2.0 g. of material of m. p. 66.5–67.8° (66%).

Anal. Calcd. for $C_{17}H_{14}O_2$: C, 81.57; H, 5.64. Found: C, 81.94; H, 5.75.

Methylmethoxymethyl-9-phenanthrylcarbinol (XI) was prepared from 7.5 g. of X, treated in benzene with a solution of methylmagnesium chloride from 1.2 g. of magnesium. After one hour at room temperature and refluxing for three hours, decomposition was accomplished with ammonium chloride. The product distilled as a yellow glass, b. p. 192–195° (1 mm.), which solidified when rubbed with petroleum ether at −70° but melted below 0°; yield 7.6 g. (95%).

Anal. Calcd. for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.23; H, 7.23.

α-(9-Phenanthryl)-propionaldehyde (XII).—On heating 31.5 g. of the carbinol XI with 3.5 g. of potassium bisulfate at 180° in a Claisen flask a vigorous reaction ensued and was over in about five minutes. The product was then distilled in vacuum and the resulting dark oil dissolved in 100 cc. of benzene and stirred overnight with 100 cc. of saturated sodium bisulfite solution. The crystalline addition compound was collected, washed with benzene, and decomposed by shaking with aqueous sodium carbonate solution and ether. Crystallization of the aldehyde from ether–petroleum ether gave 13.9 g. of colorless needles, m. p. 65.6–67.6°, and a second crop of 2.1 g., m. p. 65–67° (58%). A recrystallized sample melted at 66.2–67.2°.

Anal. Calcd. for $C_{17}H_{14}O$: C, 87.15; H, 6.02. Found: C, 87.23; H, 6.08.

γ-Methyl-γ-(9-phenanthryl)-crotonic Acid (XIII).—A solution of 15.6 g. of the aldehyde in 15 cc. of pyridine was treated with 10.4 g. of malonic acid and 5 drops of piperidine; on heating on the steam-bath the mixture rapidly turned yellow and evolved carbon dioxide, and after ten hours it was poured cautiously into dilute hydrochloric acid. The precipitated reaction product was washed with dilute acid and crystallized from acetone–benzene, giving 11.8 g. of colorless plates, m. p. 172–174°, and 3 g. of slightly less pure material (80.5%). Further purification raised the m. p. to 178.8–179.4° (softening at 173°).

Anal. Calcd. for $C_{19}H_{16}O_2$: C, 82.58; H, 5.84. Found: C, 82.67; H, 5.91.

γ-(9-Phenanthryl)-valeric Acid.—A suspension of 11.8 g. of the unsaturated acid XIII in 150 cc. of glacial acetic acid readily absorbed the calculated amount of hydrogen in the presence of 100 mg. of Adams catalyst. The reduced acid crystallized from benzene–ligroin to give 10.4 g. (87.5%) of colorless prisms, m. p. 83–85° (unchanged by further purification).

Anal. Calcd. for $C_{19}H_{18}O_2$: C, 81.98; H, 6.52. Found: C, 81.92; H, 6.61.

4-Methyl-1-keto-1,2,3,4-tetrahydrotriphenylene was prepared by cyclizing the acid (9.9 g.) with hydrogen fluoride (150 g.) at room temperature. After two hours the solution was poured onto ice and the precipitate coagulated by heating for a few minutes and then collected. Very little acid was removed by digestion with soda, and the neutral product on crystallization from benzene–ligroin gave 6.6 g. of the ketone as colorless prisms, m. p. 99–100.5°, and 1 g., 98.6–101° (82%).

Anal. Calcd. for $C_{19}H_{16}O$: C, 87.66; H, 6.20. Found: C, 87.74; H, 6.26.

1,4-Dimethyltriphenylene (XIV) was prepared from the ketone in 35% yield by the procedure described for the 1-methyl compound. The hydrocarbon crystallized from benzene–alcohol as colorless prisms, m. p. 108.4–109.2°.

Anal.[13] Calcd. for $C_{20}H_{16}$: C, 93.71; H, 6.29. Found: C, 93.62; H, 6.35.

The **picrate** crystallized from benzene in orange-red needles, m. p. 148.4–149.4°.

Anal. Calcd. for $C_{26}H_{19}O_7N_3$: N, 8.66. Found: N, 8.78.

Summary

In order to investigate the possibility that the introduction into triphenylene of suitably located alkyl groups might lead to carcinogenically active hydrocarbons, methods have been developed for the synthesis of the 1- and 2-methyl and the 1,2- and 1,4-dimethyl derivatives of this hydrocarbon. These homologs were obtained from the condensation products of 9-phenanthrylmagnesium bromide with succinic anhydride, methylsuccinic anhydride, or methoxyacetonitrile.

CONVERSE MEMORIAL LABORATORY
CAMBRIDGE, MASSACHUSETTS

RECEIVED AUGUST 16, 1939

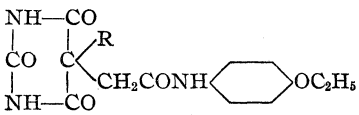
(13) Analysis by Herbert S. Wight.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

Alkylacetanilidobarbituric Acids. III. *p*-Ethoxy Derivatives

BY JOHN A. TIMM

The fact that the administration of mixtures or addition products of hypnotic and antipyretic substances produces an analgesic effect is well known.[1] This series of papers reports the preparation of 5-alkylbarbituric acids in which antipyretic and anesthetic groups replace the second hydrogen atom on the 5-carbon atom. Derivatives of acetanilide[2] and *p*-carbethoxyacetanilide[3] have been reported in the previous papers. The series has been extended in this paper to the preparation of 5-alkyl-5-*p*-ethoxyacetanilidobarbituric acids, *i. e.*, derivatives of the antipyretic, phenacetin



These derivatives, together with those reported in the first two papers of this series, are being tested pharmacologically. The results will be published elsewhere.

Experimental Part

Barbituric Acids Containing the *p*-Ethoxyacetanilido Group.—Equimolecular proportions of the appropriate 5-alkylbarbituric acid and *p*-ethoxychloroacetanilide,[4] a one and one-half molecular proportion of sodium acetate and a one-fourth molecular proportion of potassium iodide were dissolved in 70% alcohol by heating on a water-bath in a flask provided with a mechanical stirrer and a reflux condenser. The heating was continued for twenty-four hours. Crystals of the product separated during the course of the reaction. Approximately one-half of the alcohol was distilled off and the mixture cooled in an ice-bath. The products were recrystallized from absolute alcohol. They are white, crystalline solids which melt with decomposition. The usual difficulty was experienced in crystallizing the isopropyl derivative, which comes out of solution at first as a brown oil.

TABLE I

Barbituric acid, 5-*p*-ethoxyacetanilido-	Melting range, °C., with dec.	Yield, %	N Analyses, % Calcd.	Found	
5-Ethyl-	194–205	60	12.6	12.5	12.6
5-Isopropyl-	210–215	20	12.1	12.1	11.8
5-*n*-Butyl-	231–232	40	11.6	11.6	11.7
5-Isobutyl-	217–219	50	11.6	11.6	11.6
5-Isoamyl-	219–220	80	11.2	11.4	11.5
5-Allyl-	215–218	60	12.2	12.0	12.0

The author wishes to express his appreciation to Mr. Paul M. Hauser and to Mr. DeFrance Clarke, Jr., for their help in the analyses and in the preparation of the intermediates of these compounds.

Summary

The following 5-*p*-ethoxyacetanilidobarbituric acids have been prepared: 5-ethyl-, 5-isopropyl-, 5-*n*-butyl-, 5-isobutyl-, 5-isoamyl-, and 5-allyl-.

NEW HAVEN, CONN. RECEIVED JULY 25, 1939

(1) See Hepner and Frenkenberg, *Ber.*, **65B**, 123 (1932).
(2) Timm, THIS JOURNAL, **57**, 1943 (1935).
(3) Timm and Howard, *ibid.*, **58**, 1805 (1936).
(4) Bistrzycki and Ulffers, *Ber.*, **31**, 2790 (1898).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE PENNSYLVANIA STATE COLLEGE]

Fluorocarbons. The Reaction of Fluorine with Carbon

BY J. H. SIMONS AND L. P. BLOCK[1]

Carbon tetrafluoride has been obtained from the reaction of fluorine with carbon.[2] Ruff and Keim isolated hexafluoroethane from the reaction products and obtained small amounts of higher boiling material, which they assumed to be mixtures of higher molecular weight fluorocarbons, but in insufficient quantity to separate and isolate the compounds. Several difficulties are encountered in the study of this reaction. Frequent and sometimes violent explosions occur; and as the higher molecular weight compounds are produced in relatively small quantities, large amounts of reaction products are necessary in order to isolate them. Ruff, Bretschneider and Ebert[3] studied these explosions in detail and found a

(1) The authors gratefully acknowledge a grant from the American Academy of Arts and Sciences which aided in financing the preparation of these compounds.

(2) Moissan, *Compt. rend.*, **110**, 951 (1890); Lebeau and Damiens, *ibid.*, **191**, 939 (1930); Ruff and Keim, *Z. anorg. allgem. Chem.*, **192**, 249 (1930).

(3) Ruff, Bretschneider and Ebert, *ibid.*, **217**, 1 (1934).

white crystalline compound (CF) which exploded when heated. From the products of these explosions they obtained small quantities of higher boiling material. They suggest the possibility of the reaction proceeding smoothly with proper temperature control. We have attempted to do this without success. There is a short initial period before explosions begin but the amount of products that can be obtained in this time is very small.

Other reactions which might be expected to yield higher molecular weight fluorocarbons so far have produced only hexafluoroethane and tetrafluoroethylene. Fluorine has been caused to react with hydrocarbons[4] either pure or in solution in solvents such as carbon tetrachloride or dichlorodifluoromethane. Fredenhagen and Cadenbach and also Bigelow and Calfee have controlled the explosions frequent in these reactions by the use of a copper gauze catalyst. The reactions of fluorine with compounds of carbon and other halogens also have been studied.[5] The use of other fluorinating agents such as antimony trifluoride on such compounds is also possible but to replace the third halogen atom on a carbon atom is difficult although it may be accomplished in some cases.[6] Hexafluoroethane has been made by the electrolysis of trifluoroacetic acid,[7] and both hexafluoroethane and tetrafluoroethylene have been obtained by the passage of carbon tetrafluoride and dichlorodifluoromethane through an electric arc.[8] Swarts[9] assumed the formation of C_6F_6 and C_6F_{12} from the pressure effect and the proportion of hydrolysis products (CO_2, CO, HF, and CF_4) when hexafluoroethane was passed over a hot platinum wire. These effects could be explained equally well from the recorded leaks in his apparatus and the reaction of hydrogen fluoride with the glass vessel.

Preparation of Fluorocarbon Mixture.—We have been able to overcome the technical difficulties of the reaction of fluorine with carbon and have obtained about 150 cc. of liquid of molecular weight greater than 138. A preliminary report of this work has been published,[10] but we had only a small amount of material then and some of our reported data are in error due to incomplete separation.

A large and constant supply of fluorine was required. Different types of electrolyte cells were tried. The V-shaped cells[11] worked satisfactorily for a short time but the corrosion of the cell wall was excessive in long periods of operation. Cells operating at 70 to 100°[12] with an electrolyte of approximately the composition KF·2HF gave undue corrosion of the positive electrode whether this was nickel or graphite. The most rugged, simple, and generally satisfactory cell for long and constant use was a modification of the cell devised by one of the authors.[13] A description of this cell and the technique of its operation is given in the first volume of "Inorganic Syntheses."[14]

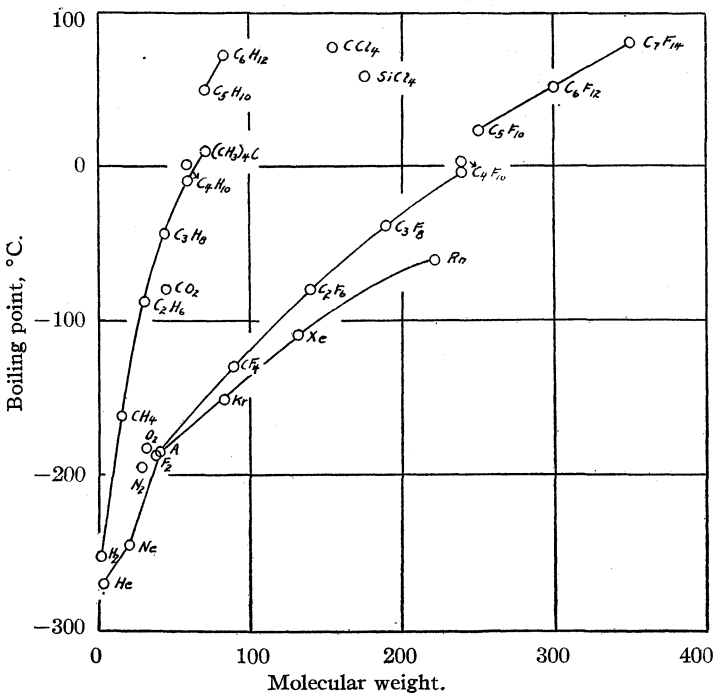


Fig. 1.

Four cells were employed. Two were kept in operation twenty-four hours a day with the operators working in shifts. The other two were either in reserve or in the process of regeneration, cleaning, or repair.

Several different kinds of carbon were used among which

(4) Bancroft and Jones, *Trans. Am. Electrochem. Soc.*, Preprint, 55 (1929); Bigelow, Pearson, Cook and Miller, THIS JOURNAL, **55**, 4614 (1933); Bockemüller, *Ann.*, **506**, 20 (1933); Fredenhagen and Cadenbach, *Ber.*, **67B**, 928 (1934); Bigelow and Calfee, THIS JOURNAL, **59**, 2073 (1937).

(5) Humiston, *J. Phys. Chem.*, **23**, 572 (1919); Bancroft and Whearty, *Proc. Natl. Acad. Sci.*, **17**, 183 (1931); Bigelow and Pearson, THIS JOURNAL, **56**, 2773 (1934).

(6) Henne, *ibid.*, **59**, 1200 (1937); Simons and Lewis, *ibid.*, **60**, 492 (1938).

(7) Swarts, *Bull. sci. acad. roy. Belg.*, **20**, 782 (1934).

(8) Ruff and Bretschneider, *Z. anorg. allgem. Chem.*, **210**, 173 (1933); Thornton, Burg and Schlesinger, THIS JOURNAL, **55**, 3177 (1933).

(9) Swarts, *Bull. soc. chim. Belg.*, **42**, 114 (1933).

(10) Simons and Block, THIS JOURNAL, **59**, 1407 (1937).

(11) Dennis, Veeder and Rochow, *ibid.*, **53**, 3263 (1931); Miller and Bigelow, *ibid.*, **58**, 1583 (1936); Henne, *ibid.*, **60**, 96 (1938).

(12) Lebeau and Damiens, *Compt. rend.*, **181**, 917 (1925); Henne, THIS JOURNAL, **60**, 96 (1938).

(13) Simons, *ibid.*, **46**, 2175 (1924).

(14) Simons, "Inorganic Syntheses," McGraw-Hill Book Co., Inc., New York, **1939**, Vol. I, p. 142.

were Norit and finely divided sugar charcoal. Neither the course of the reaction nor the products obtained appeared to be influenced by the kind of carbon used.

Both an elevated temperature and the addition of a mercury catalyst were employed. The reaction proceeded steadily and without explosions, when the reaction tube was heated to just below a dull red. An amalgamated copper tube was used in some of the earlier work, but it was found that about 1% of a mercury salt such as mercurous or mercuric chloride well mixed with the finely divided carbon was satisfactory. Copper gauze packed in the reaction tube in a manner similar to that found satisfactory for the direct fluorination of hydrocarbons did not prevent explosions. If, however, the gauze was amalgamated or if the carbon was mixed with a mercury catalyst no explosions occurred.

The fluorine, direct from the generator and without the removal of hydrogen fluoride, was passed through the copper tube containing the carbon and catalyst. The gaseous products were bubbled through traps containing sodium hydroxide solution and then collected over water. The gases were purified further by an additional passage through sodium hydroxide solution, then through concentrated sulfuric acid, and finally through phosphorus pentoxide.

The separations were made with the low temperature fractionating column described by one of the authors,[15] and the molecular weights determined in an all glass density balance a design of which has been published recently.[16] The vapor densities were checked by determinations made by the Dumas method. The two methods gave results in close agreement. The perfect gas law was assumed in those determinations. The liquid densities were determined by weighing known volumes in small sealed tubes. The freezing points were determined from warming curves, and the vapor pressures by direct measurement on a mercury manometer, while the material was warming slowly. The bulb, which served as a container, had an internal thermocouple and was surrounded by a heavy copper tube inside a vacuum flask. Three to five hours were required for the warming process. The thermocouples were made from calibrated copper and constantan wire and checked on the apparatus. The precision of the temperature measurements is better than one degree.

Analysis.—The constant boiling fractions of the fluorocarbons were analyzed by the following method. Two to three times the amount of sodium necessary for complete reaction was placed in a nickel boat. This was surrounded with a nickel tube and placed in a quartz tube which was sealed at one end. The open end of the quartz tube was sealed with a vacuum wax to a vacuum system. The air was exhausted and the tube baked out by heating strongly with a burner. An air-free sample of the fluorocarbon (0.5 to 1.0 g.) was weighed in a glass bulb. It was introduced into the vacuum system and condensed into a bulb which connected to the quartz tube. Upon evaporation it produced a pressure in the quartz tube. The quartz tube just below the nickel boat was then heated to a red heat with a gas burner. When the pressure was reduced to nearly zero by the reaction, the heating was stopped. When cold, air was admitted and the quartz tube removed. The excess sodium was removed by reaction with absolute alcohol and the sodium fluoride and carbon washed with alcohol onto a Gooch crucible. It was weighed, the sodium fluoride dissolved by washing with hot water, and it was weighed again. The carbon was burned by ignition and a final weight obtained.

This method was tried with a known sample of carbon tetrafluoride: F, calcd. 86.4%, found 86.1%; C, calcd. 13.6%, found 13.8%. With the higher boiling sample of C_4F_{10} an appreciable amount of sodium carbide apparently was formed. In this case the fluorine was determined by calcium fluoride precipitation. Fluorine also was determined by calcium fluoride precipitation for C_6F_{12}. In all samples the pressure fell to practically zero after reaction, which proved that the compounds did not contain hydrogen atoms in the molecules. The aqueous solution formed by dissolving the salt from the crucible was tested in every case with a silver nitrate solution. Only a trace of precipitate was formed in any sample. This proves that the compounds did not contain halogen other than fluorine, sulfur, etc.

Calcd. for C_3F_8: F, 80.85; C, 19.15. Found: F, 80.5; C, 19.9. Calcd. for C_4F_{10} (low boiling): F, 79.85; C, 20.15. Found: F, 80.5; C, 18.8. Calcd. for C_4F_{10} (high boiling): F, 80.5. Found: F, 78.8. Calcd. for C_5F_{10}: F, 76.0; C, 24.0. Found: F, 76.4; C, 24.2. Calcd. for C_6F_{12}: F, 76.0; C, 24.0. Found: F, 76.1; C, 24.6. Calcd. for C_7F_{14}: F, 76.0; C, 24.0. Found: F, 76.0; C, 23.1.

Results.—The results of our last preparation are given in the table. The first six fractions were obtained as constant boiling cuts. From a boiling temperature at atmospheric pressure of about 25°, there is a continuous rise of the boiling temperature as material is removed during distillation except for two temperatures, 51 and 80°, where constant boiling fractions are obtained. The molecular weights of the constant boiling fractions correspond with the formulas tentatively assigned. Apparently an homologous series of saturated fluorocarbons is formed in the reaction in addition to compounds not belonging to this series. Carbon tetrafluoride and hexafluoroethane are obtained in the largest amounts. Octafluoropropane with its long liquid range can be obtained fairly pure, and two fractions are separated which are apparently the two isomers of decafluorobutane. The determined molecular weight of the lower boiling was less than, and the higher boiling greater than, the theoretical. This is undoubtedly because, with only a small amount of material and a small difference in boiling temperature between the fractions, we crowded both fractions, leaving some lower boiling material in the lower and higher boiling in the upper. The

(15) Simons, *Ind. Eng. Chem., Anal. Ed.*, **10**, 29 (1938).
(16) Simons, *ibid.*, **10**, 587 (1938).

TABLE I

PHYSICAL PROPERTIES OF PRODUCTS OBTAINED IN DISTILLATION OF FLUOROCARBONS

Fraction	Volume of liquid Cc.	%	Assumed formula[e]	M. p., °C.	B. p., °C.	Molecular weight, Found	Calcd.	Liquid density g./cc. at 0.2°	8.8°	20.8°	Vapor pressure $\log_{10} P$ mm. $= -A/T + B$ A	B	ΔH of vaporization, calcd. cal. per mole
1	246	54.5	CF_4[a]	−184	−128	88	88	(1.96 at −184°)					2947
2	57	12.6	C_2F_6[a]	−100.6	− 78.2	138	138	(1.85 at − 78°)					4005
3	37	8.2	C_3F_8	−183	− 38	188	188	1.45			1070	7.43	4920
4	24	5.3	C_4F_{10}	Glass	− 4.7	230	238	1.53	1.49	1.47	1217	7.43	5600
5	6	1.3	C_4F_{10}	Glass	3.0	241	238				1260	7.44	5800
6	25	5.5	C_5F_{10}[b]	*Ca.* −12	23	254–9	250	1.72	1.69	1.67	1350	7.43	6200
7	20	4.4	C_6F_{12}[b]	Glass	51	300–3	300	1.65	1.63	1.60	1500	7.51	6900
8	6	1.3	C_8F_{14}[b]	Glass	80	350–5	350	1.83	1.82	1.78	1610	7.43	7400
9	25	5.5	Mixture[c]		25 to 95								
10	7	1.5	Mixture[d]		95 to 160								

[a] Physical constants from Ruff, *Angew. Chem.*, **46**, 739 (1933). [b] We believe these compounds to be cyclic in structure, fraction number 6 is probably decafluorocyclopentane, number 7 is probably dodecafluorocyclohexane, and number 8 is probably also a derivative of a cyclic compound. [c] This mixture probably contains a variety of fluorocarbons containing from five to eight carbon atoms, inclusive. [d] This mixture probably contains fluorocarbons having from eight to twelve carbon atoms, inclusive. One-third of this mixture boiled between 95 and 105°, one-third between 105 and 120° and the remainder up to 160°. [e] A system of nomenclature for these compounds is desired. They are distinctly not derivatives of hydrocarbons as their properties show. To name them as such requires long names which will become even more cumbersome as more complex compounds with their isomers and substitution derivatives are made and isolated. The authors wish to suggest the following nomenclature: methfluorane, ethfluorane, ethfluorene, profluorane, bufluorane, cyclopentfluorane, methfluorylcyclohexfluorane, etc.

fraction boiling at 23° we have assumed to be decafluorocyclopentane. It has a much higher freezing point than the other fractions and appears to be mostly one compound. However, neither a sharp freezing point nor an entirely reproducible molecular weight could be obtained, and this latter was uniformly higher than the theoretical. As the saturated dodecafluoropentane isomers would boil at about the same temperature, it is assumed that the compound is contaminated with a small amount of them. If this is correct, then the higher fractions having constant boiling temperatures are probably either CF_3 derivatives of decafluorocyclopentane or dodecafluorocyclohexane and its trifluoromethyl derivative. The material from which no constant boiling fractions could be obtained is assumed to be a mixture of higher boiling fluorocarbons probably with many of the isomers present. This would be analogous to petroleum ether.

The substances are colorless and either odorless or very nearly so. They are very stable chemically. Many of the tubes containing these were sealed off while an appreciable pressure of the vapor existed inside. No trace of etching or carbonization could be observed in the Pyrex glass seal, which must have been at least 700°. The different fractions were tested for unsaturation with bromine in carbon tetrachloride solution, and no decolorization could be observed.

Discussion.—The formation of stable compounds of carbon and fluorine containing more than three carbon atoms per molecule indicates the possibility of the synthesis of a large number of similar compounds provided that methods can be discovered. Such compounds should be of considerable interest both theoretically and as useful substances.

To indicate the relatively low attractive force between the molecules of these compounds, a graph is shown in the figure. The molecular weight is plotted against the boiling point. On the same graph are represented the inert gases, the hydrocarbons, and a few other substances. The fluorocarbon curve does not lie greatly above the inert gas curve, whereas the hydrocarbon curve is very much higher. The fluorocarbons approach the inert gases in properties more closely than any other compounds. This curve also shows that we cannot be greatly in error in the formulas of these compounds. The three and four carbon compounds fall on a smooth curve with the previously known one and two carbon compounds. The three higher boiling compounds are slightly above this curve analogous to the positions of cyclopentane and cyclohexane relative to the hydrocarbon curve. The presence in

the molecules of these compounds of one or more hydrogen atoms would both lower the molecular weight and raise the boiling point due to the introduction of an electric moment. This would place the compounds far above the curve.

The authors wish to acknowledge gratefully the assistance in the preparation and separation of these compounds of the following Graduate Students at the Pennsylvania State College: R. L. Bond, J. W. Ford, R. E. McArthur, D. I. Randall, T. K. Sloat, and A. C. Werner.

Summary

A continuous reaction between fluorine and carbon without explosions has been accomplished.

Compounds corresponding in molecular weight to octafluoropropane, two isomers of decafluorobutane, decafluorocyclopentane, a dodecafluorohexane, and a tetradecafluoroheptane have been isolated in addition to carbon tetrafluoride and hexafluoroethane.

The properties of these compounds have been determined. A mixture of fluorocarbons boiling from 25 to 160° has been obtained.

STATE COLLEGE, PENNA. RECEIVED NOVEMBER 2, 1938

[CONTRIBUTION FROM THE PEARSON MEMORIAL LABORATORY OF TUFTS COLLEGE]

The Action of *p*-Tolyl Isothiocyanate on Ethyl Acetonedicarboxylate

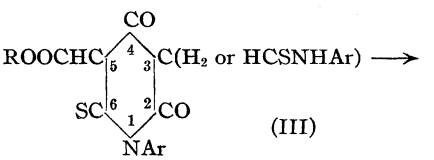
BY DAVID E. WORRALL

In connection with a study of the chemistry of isothiocyanates it seemed desirable to investigate their reactivity toward molecules containing two active methylene groups. Ethyl acetonedicarboxylate (I), a relatively common substance which contains such a system, was selected for this purpose. It quickly became apparent that this ester does not follow the pattern of substances previously studied,[1] but reacts in a highly characteristic manner.

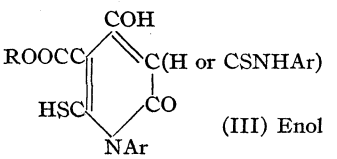
Through the sodium derivative I probably does form the expected thiotoluide, either with one or two equivalents of tolyl isothiocyanate. An additional reaction follows in which the elements of ethyl alcohol are lost. Ring closure suggests itself, particularly as the product contains a nucleus comparatively stable toward acid or alkali which remains intact through certain transformations. Sulfur is labile in the monosulfo derivative; therefore it is concluded that a piperidine ring is formed.

$$ROOCCH_2COCH(COOR)CSNHAr \longrightarrow OCCH_2COCH(COOR)CSNAr\ (II) + ROH$$

The same reaction takes place, using two equivalents of metal and isothiocyanate, although the second methylene group is converted into a thioamide producing III. Sulfur in the side chain is comparatively non-reactive. These pyridones are sufficiently acidic to decompose alkali carbonates forming salts stable toward acetic acid, thus functioning as hydroxypyridines. Because of the presence of tertiary nitrogen, isomerization is restricted to the introduction of two double bonds.



(III)



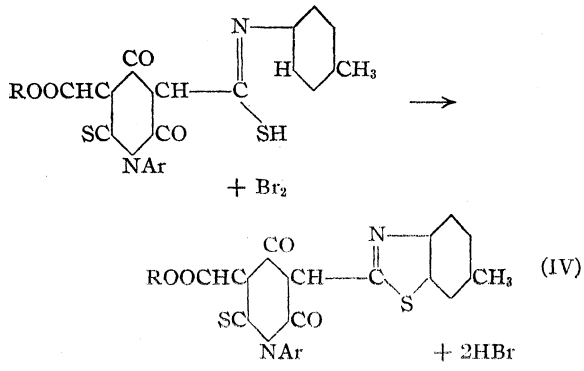
(III) Enol

II and III obviously form thio ethers with methyl iodide in alkaline solution, for the products contain inactive sulfur, whereas the parent substances readily lose this element. Hence one double linkage is located between positions 5 and 6 in the pyridine ring. Further alkylation is possible since the mono methyl ethers still are capable of forming metal derivatives. It is believed that these changes involve the shifting of hydrogen to position 4 rather than 2 which contains oxygen more completely neutralized. With dimethyl sulfate a third hydrogen, that attached to the amide nitrogen is replaced. Ethyltoluidine and a dimethylpyridine dicarboxylate, result from secondary reactions. The carbethoxy group is easily lost both with II and III.

II forms a stable bromine derivative. The methyl ether does likewise, therefore bromine is

(1) Worrall, THIS JOURNAL, **46**, 2834 (1924).

present at position 3. Although III also reacts spontaneously with bromine, liberating hydrogen bromide, the product (IV) contains no bromine and a pair of hydrogen atoms are missing from the molecule. The physical but not the chemical properties have altered considerably. IV is colorless, much less soluble in the usual organic solvents, and much higher melting than III. Sulfur is more mobile, but IV is still soluble in alkali and easily alkylated. The carbethoxy group is more readily hydrolyzed. One of the missing hydrogen atoms must have come from the substituted thioamide group; the other may have originated in either the aniline or the pyridone ring. Despite the fact that a similar reaction apparently takes place with an analogous compound prepared from methyl isothiocyanate,[2] the aniline ring probably is concerned in the reaction. Hugershoff[3] has shown that benzothioazoles result from the action of bromine on arylated thioureas. Moreover, the thioamide obtained by the addition of phenyl isothiocyanate to malonic ester reacts with bromine and definite proof has been found that the product is a thiazole.[2] Therefore, thiazole formation has been assumed here, a reaction in which intermediate bromine derivatives doubtless are formed.



(IV)

Experimental

1-*p*-Tolyl-2,4-dioxo-5-carbethoxy-6-sulfopiperidine.—To 0.25 g. mole of pulverized sodium suspended in ether was added cautiously one equivalent of I. A brisk reaction ensued, following which one equivalent of *p*-tolyl isothiocyanate was dropped into the clear ether solution. The pasty precipitate that formed was dissolved eventually in water containing crushed ice and slowly poured with stirring into cold dilute hydrochloric acid. A bulky solid separated, but on standing it changed into a compact, somewhat pasty mass that was digested with a small volume of cold alcohol; yield 14.3 g. The product was crystallized twice from alcohol, separating finally in bundles of colorless narrow plates, m. p. 174–175° dec.

Anal. Calcd. for $C_{15}H_{15}NO_4S$: C, 59.1; H, 4.9. Found: C, 59.0; H, 5.2.

II is soluble in aqueous sodium carbonate and is precipitated from the alkaline solution by hydrochloric acid, but not by acetic acid. An alkaline solution of II neutralized with acetic acid produces a blue green precipitate with ferric chloride. It is gradually decomposed by long heating with glacial acetic acid, slowly evolving hydrogen sulfide, the formation of which is speeded up by the presence of phenylhydrazine. In both reactions amorphous residues are produced.

1-*p*-Tolyl-2,4-dioxo-6-sulfopiperidine.—One gram of II heated for thirty minutes under a reflux condenser with concd. alcoholic potassium hydroxide was diluted with water, filtered and added dropwise with stirring to cold water containing hydrochloric acid. A bulky amorphous precipitate formed that was filtered with difficulty, thoroughly washed, and dried at room temperature. The resulting grayish powder was used directly for analysis m. p. 158–159°, dec.

Anal. Calcd. for $C_{12}H_{11}NO_2S$: C, 61.8; H, 4.7. Found: C, 61.4; H, 4.8.

1-*p*-Tolyl-2,4-dioxo-5-carbethoxy-6-sulfomethoxypiperidine.—To 2 g. of II dissolved in warm alcohol was added an excess of methyl iodide. A crystalline precipitate almost instantly formed in excellent yield.

Anal. Calcd. for $C_{16}H_{17}NO_4S$: C, 60.2; H, 5.3. Found: C, 59.9; H, 5.5.

It separates from alcohol as slender needles, m. p. indefinite with dec. above 250°. No hydrogen sulfide is liberated on heating with glacial acetic acid either alone or with phenylhydrazine, but the substance retains the property of dissolving in sodium carbonate solution. It forms a sparingly soluble salt with sodium hydroxide which can be recrystallized from a small volume of water. An analysis indicated the presence of one equivalent of sodium.

1-*p*-Tolyl-2,4-dioxo-3-bromo-5-carbethoxy-6-sulfopiperidine.—A small portion of II was brominated in glacial acetic acid, heated for a few minutes on a water-bath and recrystallized from alcohol, separating as tiny pale yellow needles, m. p. 238–239°, dec.

Anal. Calcd. for $C_{15}H_{14}BrNO_4S$: C, 46.9; H, 3.6; Br, 20.8. Found: C, 46.9; H, 3.4; Br, 20.9.

It still is soluble in sodium carbonate solution and reprecipitated unchanged by acid.

1-*p*-Tolyl-2,4-dioxo-3-bromo-5-carbethoxy-6-sulfomethoxypiperidine.—After bromination of the methyl ether of II the product obtained by pouring the mixture into water was recrystallized twice from a small volume of alcohol. Long colorless needles appeared which apparently contained alcohol of crystallization, as on drying at 100° a powder resulted; m. p. 165.5–166.5°.

Anal. Calcd. for $C_{16}H_{16}BrNO_4S$: Br, 20.1. Found: Br, 20.0.

1-*p*-Tolyl-2-oxo-4-methoxy-5-carbethoxy-6-sulfomethoxypiperidine.—A portion of II dissolved in sodium hydroxide solution was shaken with dimethyl sulfate. The

(2) Unpublished results.

(3) Hugershoff, *Ber.*, **36**, 3121 (1903).

product, insoluble in the alkaline solution, was crystallized from dilute alcohol, separating as slender silky needles, m. p. 166°.

Anal. Calcd. for $C_{17}H_{19}NO_4S$: C, 61.3; H, 5.7. Found: C, 61.1; H, 5.9.

This dimethyl derivative is not only insoluble in both aqueous sodium carbonate and sodium hydroxide but does not react with bromine.

1-*p*-Tolyl-2,4-dioxo-5-carbethoxy-6-sulfopiperidine-3-thioformo-*p*-toluide.—Using the customary technique, 0.1 g. mole of I was converted into the metal derivative with two equivalents of sodium. The second equivalent reacted slowly and incompletely even on the application of heat. The clear solution after several hours was poured from unchanged sodium into another flask containing two equivalents of tolyl isothiocyanate. A bulky solid separated after a time from the new mixture. The next morning the entire batch was mixed with ice water, the aqueous layer separated and run carefully with stirring into cold, well-diluted hydrochloric acid. The resulting flocculent precipitate coagulated on standing into a somewhat pasty ball-like mass. It was filtered and thoroughly washed with warm alcohol, yield 18 g.

Anal. Calcd. for $C_{23}H_{22}N_2O_4S_2$: C, 60.8; H, 4.9. Found: C, 61.0; H, 5.0.

III is practically insoluble in alcohol, but dissolves readily in benzene, separating from a mixture of these solvents as shining yellow needles, m. p. 182–184°, dec. It is easily dissolved by alkaline solutions, including concd. ammonia, from which the ammonium salt separates in a few minutes. No reaction takes place with hydroxylamine beyond partial hydrolysis of the ester group. Slow evolution of hydrogen sulfide occurs on long heating with glacial acetic acid. The substance is unchanged on long standing with dilute sodium hydroxide solution. Although unaffected by concd. hydrochloric acid, it is dissolved by cold concd. sulfuric acid, the solution acquiring a blue fluorescence on warming.

1-*p*-Tolyl-2,4-dioxo-6-sulfopiperidine-3-thioformo-*p*-toluide.—A solution containing 2 g. of III dissolved in concd. alcoholic potash was heated for an hour under a reflux condenser, diluted with water and carefully mixed with an excess of acid. The product separated from a large volume of alcohol as lustrous pale yellow irregular plates, m. p. 205–208°, dec.

Anal. Calcd. for $C_{20}H_{18}N_2O_2S_2$: C, 62.8; H, 4.7. Found: C, 62.6; H, 5.0.

It is less soluble than the parent substance in benzene, but more so in alcohol. It is soluble in sodium carbonate solution and reacts with bromine.

1-*p*-Tolyl-2,4-dioxo-5-carbethoxy-6-sulfomethoxypiperidine-3-thioformo-*p*-toluide.—On heating under a reflux condenser 5 g. of III suspended in alcohol containing methyl iodide, the solid rapidly disappeared. An excellent yield of bright yellow needles formed on cooling, m. p. 151–152°.

Anal. Calcd. for $C_{24}H_{24}N_2O_4S_2$: C, 61.5; H, 5.1. Found: C, 61.3; H, 5.1.

The methyl ether slowly dissolved by sodium carbonate solution is precipitated unchanged by acetic as well as by hydrochloric acid. It is readily dissolved by warm alcohol. No hydrogen sulfide is liberated on heating with glacial acetic acid either alone or with phenylhydrazine.

1-*p*-Tolyl-2,4-dioxo-5-carboxy-6-sulfomethoxypiperidine-3-thioformo-*p*-toluide.—A small portion of the monomethyl ether heated for an hour under a reflux condenser with concd. alcoholic potash was isolated in the usual manner. It crystallized from glacial acetic acid in the form of glittering yellow plates, m. p. 232–233° dec.

Anal. Calcd. for $C_{22}H_{20}N_2O_4S_2$: C, 60.0; H, 4.5. Found: C, 60.2; H, 4.6.

Hydrolysis but not decarboxylation took place.

1-*p*-Tolyl-2-oxo-4-methoxy-6-sulfomethoxypiperidine-3-thioformo-*p*-toluide.—The sodium derivative of the monomethyl ether of III was prepared using dilute sodium hydroxide and recrystallizing the colorless needles from a small volume of water. It was then heated to 100° in a sealed tube with alcohol containing methyl iodide for nearly two hours. On pouring the contents after cooling into water, an oil separated. This product dissolved in a small volume of warm alcohol formed tiny snow-white crystals, m. p. 153°.

Anal. Calcd. for $C_{22}H_{22}N_2O_2S_2$: C, 64.4; H, 5.4. Found: C, 64.1; H, 5.3.

It is insoluble in sodium hydroxide solution, and does not react with bromine.

1-*p*-Tolyl-2-oxo-4-methoxy-6-sulfomethoxypiperidine-3,5-dicarboxylate.—A suspension prepared by dissolving 4 g. of III in 150 ml. of warm dilute sodium hydroxide solution and then cooling was shaken with a few ml. of dimethyl sulfate. The sodium salt rapidly disappeared to be replaced by a precipitate that became increasingly pasty. Simultaneously a strong amine-like odor became noticeable. The product, heated on a water-bath for several hours, hardened into a crystalline mass that was repeatedly recrystallized from alcohol. Finally clusters of tiny colorless plates separated, m. p. 177–178°.

Anal. Calcd. for $C_{16}H_{15}NO_6S$: C, 55.0; H, 4.6. Found: C, 55.2; H, 4.7.

A qualitative test revealed the presence of sulfur. While insoluble in aqueous sodium hydroxide the substance is very soluble in alcoholic alkali, remaining in solution on mixing with a large volume of water. It is promptly precipitated from these solutions by acid. The original filtrate contained monomethyl-*p*-toluide, which was isolated by steam distillation from an alkaline mixture. The resulting oil dissolved in acid and formed a nitroso derivative with nitrous acid.

1-(1-*p*-Tolyl-2,4-dioxo-5-carbethoxy-6-sulfopiperidyl)-5-methyl-benzothiazole.—A molar equivalent of bromine was added to 5 g. of III suspended in a small volume of glacial acetic acid. The mixture, which immediately began to yield hydrogen bromide, was heated for an hour on a water-bath. The mustard colored product, practically insoluble in the common organic solvents, was thoroughly washed with warm alcohol; yield 4.3 g. By beating under a reflux condenser with glacial acetic acid, most of the color could be removed.

Anal. Calcd. for $C_{23}H_{20}N_2O_4S_2$: C, 61.1; H, 4.4. Found: C, 61.0; H, 4.3.

IV may be recrystallized in small quantities from nitrobenzene, or better still, aniline, as tiny feathery needles

m. p. above 300°. It is easily dissolved by ammonium hydroxide or concd. sulfuric acid, producing on warming with the latter a bluish fluorescence. Hydrogen sulfide is set free rapidly on heating the substance suspended in glacial acetic acid with phenylhydrazine.

1 - (*p* - Tolyl - 2,4 - dioxo - 5 - carboxy - 6 - sulfopiperidyl)-5-methylbenzothiazole.—IV dissolved quickly in cold ammonium hydroxide, a solution which was slowly run into a large volume of water containing an excess of hydrochloric acid. A bright yellow gelatinous precipitate formed. It was filtered with difficulty, washed thoroughly and dried at room temperature. The color darkened considerably, m. p. 260–261° with dec. and foaming.

Anal. Calcd. for $C_{21}H_{16}N_2O_4S_2$: C, 59.4; H, 3.8. Found: C, 59.4; H, 3.7.

The new substance is soluble in sodium carbonate solution.

1 - (*p* - Tolyl - 2,4 - dioxo - 5 - carbethoxy - 6 - sulfomethoxypiperidyl) - 5 - methylbenzothiazole.—On shaking an ammonia solution of IV with alcohol containing methyl iodide a precipitate quickly formed. The mixture, concentrated to a small volume by distillation, gave a quantitative yield of the product which was recrystallized from a large volume of alcohol. Pale yellow needles separated, m. p. 282–283°, dec.

Anal. Calcd. for $C_{24}H_{22}N_2O_4S_2$: C, 61.8; H, 4.7. Found: C, 61.7; H, 4.8.

The methyl derivative does not react with bromine or phenylhydrazine. On destructive distillation the gases blacken lead acetate paper and have a strong pyridine odor. It still is soluble in ammonia, but this is due to hydrolysis of the carbethoxy group, as an analysis of the product indicated. The product was isolated by precipitation with acid as a semi-gelatinous solid which did not discolor on standing, m. p. 260–261°, dec. The same substance was obtained by the action of concd. nitric acid or warm sulfuric acid.

Summary

It has been shown that ethyl acetonedicarboxylate reacts with one or two equivalents of *p*-tolyl isothiocyanate forming pyridones, which are soluble in alkali and are readily alkylated. An oxypiperidyl benzothiazole apparently results from the action of bromine on the pyridone containing a thioamide group.

MEDFORD, MASS. RECEIVED JULY 11, 1939

[CONTRIBUTION FROM THE PEARSON MEMORIAL LABORATORY OF TUFTS COLLEGE]

Aromatic Amines and 3-Nitro-6-bromonitrostyrene

BY DAVID E. WORRALL AND JACK FINKEL

It has been shown previously[1] that while the additive capacity of nitrostyrene toward the so-called organic bases is comparatively weak and even more so as a rule when substituents are introduced, the nitration of 2-chloronitrostyrene produced an unsaturated compound in which this reactivity is somewhat strengthened. As we wished to determine whether its effect were general, the corresponding bromostyrene has been prepared. The two substances have almost identical chemical properties.

Experimental

α-Nitro-β-(2-bromophenyl)-ethylene (I).—This compound was obtained by the action of triethylamine[2] on bromobenzaldehyde[3] and nitromethane at 25 to 30°; yield, after steam distillation, approx. 60%. It crystallized from ligroin in bundles of yellow needles, m. p. 84°.

Anal. Calcd. for $C_8H_6BrNO_2$: C, 42.1; H, 2.6. Found: C, 42.1; H, 2.8.

α-Nitro-β-(6-bromo-3-nitrophenyl)-ethylene (II).—The product from the nitration of I, using fuming nitric acid, separated from alcohol as small pale yellow needles, m. p. 144–145°.

Anal. Calcd. for $C_8H_5BrN_2O_4$: C, 35.2; H, 1.8. Found: C, 35.1; H, 2.1.

A small portion on oxidation with potassium permanganate produced a substance that crystallized from water as long needles, m. p. 178–179°. It did not depress the melting point of an authentic sample of 6-bromo-3-nitrobenzoic acid prepared from *m*-nitrotoluene, thus indicating that the nitro group is para to the halogen.[4]

α-Bromo - α - nitro - β - (6 - bromo - 3 - nitrophenyl) - ethylene (III).—Five grams of II after bromination was mixed with warm alcoholic potassium acetate. The product crystallized from alcohol in yellow needles, m. p. 146–147°.

Anal. Calcd. for $C_8H_4Br_2N_2O_4$: C, 27.3; H, 1.1. Found: C, 27.6; H, 1.3.

The corresponding chlorine derivative was obtained as yellow needles, m. p. 140–141°.

N,N'-(α,α'-Di-(2-bromophenyl)-β,β'-dinitrodiethyl)-*p*-phenylenediamine.—A small portion of I dissolved in hot alcohol was mixed with one-half the equivalent amount of the base. The yellow crystals were washed with warm alcohol, m. p. 146–147°.

(1) Worrall, THIS JOURNAL, **60**, 2845 (1938).
(2) Worrall, *ibid.*, **56**, 1556 (1934).
(3) Adams and Vollweiler, *ibid.*, **40**, 1737 (1918).

(4) Since the corresponding chlorine derivative must contain a similar arrangement of groups, the name previously assigned to it (ref. 1) is incorrect. The substance should be listed as 3-nitro-6-chloronitrostyrene and corresponding changes made in the names of the addition products.

TABLE I

β-DERIVATIVES OF α-NITRO-β-(6-BROMO-3-NITROPHENYL)-ETHANE

Substance	Formula	M. p., °C.	Analyses, % Calcd. C	Calcd. H	Found C	Found H
o-Toluidino	$C_{15}H_{14}BrN_3O_4$	108–109	47.4	3.7	47.8	3.8
m-Toluidino	$C_{15}H_{14}BrN_3O_4$	103–104	47.4	3.7	47.2	3.6
p-Toluidino	$C_{15}H_{14}BrN_3O_4$	132–133	47.4	3.7	47.4	4.0
o-Anisidino	$C_{15}H_{14}BrN_3O_5$	139–140	45.5	3.5	45.7	3.7
m-Anisidino	$C_{15}H_{14}BrN_3O_5$	159–150	45.5	3.5	45.2	3.5
p-Anisidino	$C_{15}H_{14}BrN_3O_5$	105–106	45.5	3.5	45.7	3.7
p-Phenetidino	$C_{16}H_{16}BrN_3O_5$	134–135	46.9	3.9	47.0	3.9
p-Dimethylaminoanilino	$C_{16}H_{17}BrN_4O_4$	140–141	47.0	4.2	47.2	4.4
Phenylhydrazino	$C_{14}H_{13}BrN_4O_4$	147–148	44.1	3.4	44.3	3.3
DERIVATIVES OF (α,α′-DI-(6-BROMO-3-NITROPHENYL)-β,β′-DINITRO-DIETHYL)						
Ammonia	$C_{16}H_{13}Br_2N_5O_8$	146–147	34.2	2.3	34.7	2.7
p-Phenylenediamine	$C_{22}H_{18}Br_2N_6O_8$	Indefinite	40.5	2.8	40.8	3.1
Benzidine	$C_{28}H_{22}Br_2N_6O_8$	Indefinite	46.0	3.0	45.8	3.5

Anal. Calcd. for $C_{22}H_{20}Br_2N_4O_4$: C, 46.9; H, 3.6. Found: C, 47.0; H, 3.9.

A similar addition product was obtained and analyzed, from III as brown crystals, m. p. indefinite. III, but not II, also formed an addition product with *p*-toluidine, yellow needles, m. p. 103–104°.

The same general procedure previously developed[1] was used in preparing the addition compounds which were obtained usually as yellow needles or narrow plates. The ammonia product was nearly colorless, while the benzidine and phenylenediamine compounds were orange in color.

Summary

3-Nitro-6-bromonitrostyrene has been prepared and also several derivatives. A number of addition products have been obtained with aromatic amines, including *o*- and *m*-anisidine.

MEDFORD, MASS. RECEIVED JULY 11, 1939

NOTES

The Non-interchange of Elementary Radiosulfur with Carbon Disulfide

BY ROBERT A. COOLEY, DON M. YOST AND EDWIN MCMILLAN

Radioactive sulfur (half life eighty to ninety days) finds important application as a tracer in chemical and biochemical investigations,[1] and at some stages in these studies it proves convenient to use carbon disulfide as a solvent for elementary sulfur. In order to be certain that this solvent can be used without danger of loss of the radioactive sulfur, it is necessary to show that there is no interchange between elementary sulfur and carbon disulfide. Judging from the nature and structure of carbon disulfide,[2] any appreciable interchange seems unlikely, but the great solubility of sulfur in carbon disulfide (50.49 g./100 g. carbon disulfide at 25°) suggests the possible rapid reversible formation of complex compounds that might make interchange possible.

The radiosulfur used was formed by bombarding a metal sulfide with 4 Mev. deuterons in the cyclotron at the University of California radiation laboratory. Elementary sulfur was obtained from the metal sulfide by dissolving it in hydrochloric acid and passing the hydrogen sulfide formed into a 1 *N* solution of potassium iodide saturated with iodine. After warming the resulting solution to volatilize the excess iodine, and to coagulate the very fine precipitate, the sulfur was collected as small globules on a sintered glass filter. An appreciable proportion of the sulfur obtained in this manner is in the amorphous (μ) form and is slow to dissolve in carbon disulfide. It has been found by Mr. J. B. Hatcher at this

(1) Borsook, Keighley, Yost and McMillan, *Science*, **86**, 525 (1937).

(2) Pauling, "Nature of the Chemical Bond," Cornell University Press, Ithaca, New York, 1939, p. 182.

Institute that heating the sulfur precipitate in an autoclave is not attended with losses and that it is thereby converted into a readily soluble form.

The exchange experiments were carried out in sealed U-tubes one leg of each containing a solution of about 3 mg. of radiosulfur in 300 mg. of C. P. carbon disulfide. The filled tubes were heated in a thermostat at 100° for forty-two to sixty-eight hours, and after the heating period about one-half of the carbon disulfide was caused to distil into the empty leg of the tube by cooling it with liquid air. The contents of the two legs were subjected to a Carius combustion, and the resulting sulfuric acid was then converted into dry lithium sulfate. Thin layers of the lithium sulfate, all of equal area, about 20 sq. cm., were prepared on metal plates for the measurement of the activity. Lithium rather than the more easily prepared barium sulfate was used in the radioactivity measurements because the barium absorbs the weak (107 Kev. maximum) beta radiation[3] of sulfur more extensively than does lithium. The thickness of the mounted lithium sulfate samples was >0.015 g./sq. cm. and was such that the beta particles from the bottom of a sample could not penetrate to the top and from there reach the electroscope chamber. This arrangement greatly simplifies the quantitative treatment of the results.

In our current experiments with radiosulfur it has been found possible to make the mounted samples of elementary sulfur by reducing barium sulfate to the sulfide with hydrogen at about 900°. Barium sulfide is then treated in the manner described above for the recovery of the sulfur. The reduction procedure was suggested to us by Professor J. E. Bell of this Institute, and the technique for its use was developed by Mr. J. B. Hatcher. Complete reduction of barium sulfate is not attained if the salt melts.

The activity of the lithium sulfate samples was measured with a lead shielded quartz fiber Lauritsen electroscope. A thin aluminum foil, 0.15 mg./sq. cm., served as the window on the ionization chamber. The background was about 0.001 div./min. and varied no more than 30% in a two-week period. By taking background readings immediately before and after readings with the samples, the activities of the latter were determined to ±0.0002 div./sec. The results, corrected for background, are shown in Table I. The same range of the electroscope scale was used throughout in determining the effect due to the background and to the samples, and therefore no correction for linearity of scale was required.

TABLE I

RADIOACTIVITY OF DISTILLATES AND RESIDUES FROM HEATED SOLUTIONS OF RADIOSULFUR IN CARBON DISULFIDE

Expt.		Activity in div./sec.	Time soln. heated at 100°, hours
1	Distillate	0.000014	42
	Residue	.0095	
2	Distillate	− .00017	48
	Residue	.0028	
3	Distillate	.00009	68
	Residue	.0102	

(3) W. F. Libby and D. D. Lee, *Phys. Rev.*, **55**, 245 (1939).

It is evident from the results that there is practically no interchange between sulfur and carbon disulfide even at 100°. The extent of any interchange must be less than 2%, that is, it must be less than the experimental error of the activity measurements. It is also clear that carbon disulfide may be used as a solvent for radiosulfur without fear of loss by interchange.

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RECEIVED AUGUST 4, 1939

Note on the Formation of bis-(β-Diethylaminoethyl) Sulfide

BY ELTON S. COOK AND CORNELIUS W. KREKE

In an attempt to prepare β-diethylaminoethyl mercaptan from 1-bromo-2-diethylaminoethane hydrobromide and sodium hydrosulfide in the presence of sodium ethylate, Lischer and Jordan[1] obtained β,β′-diethylaminodiethyl disulfide. We have tried to prepare the mercaptan using sodium sulfide and hydrogen sulfide by a method based on that employed by Bennett[2] for the preparation of monothioethylene glycol. We did not obtain the desired mercaptan but isolated *bis*-(β-diethylaminoethyl) sulfide.

Experimental Part

1-Bromo-2-diethylaminoethane hydrobromide was prepared by heating redistilled β-diethylaminoethyl alcohol and 66% hydrobromic acid at 135° according to the method of Meyer and Hopff.[3] We found that 40% hydrobromic acid could not be used satisfactorily. The presence of a trace of free bromine greatly facilitated the reaction.

bis-(β-Diethylaminoethyl) Sulfide Dihydrochloride.—One hundred and fifty grams of sodium sulfide (Na_2S $9H_2O$) was heated to 130° for fifteen minutes and saturated with hydrogen sulfide. The solution was cooled to 60–65°, the passage of hydrogen sulfide being continued during the cooling. Then 10.2 g. of 1-bromo-2-diethylaminoethane hydrobromide was added slowly with stirring and the mixture was kept at 55° for fifteen minutes. The mixture was cooled and extracted immediately three times with 100-cc. portions of ether. The ether solution was dried over anhydrous sodium sulfate, the ether removed, and the dried oily residue was taken up in absolute ether. Dry hydrogen chloride was passed in and the dihydrochloride precipitated readily. It was crystallized from absolute alcohol by the addition of absolute ether:

(1) C. F. Lischer and C. N. Jordan, THIS JOURNAL, **59**, 1623 (1937).
(2) G. M. Bennett, *J. Chem. Soc.*, **119**, 418 (1921).
(3) K. H. Meyer and H. Hopff, *Ber.*, **54B**, 2274 (1921).

yield, 2.12 g. (36%) of white crystalline powder, m. p. 245.5–247.5° (corr.).[4] With Grote's reagent[5] a faint orange color developed only after addition of potassium cyanide, as is characteristic of monosulfides.

Anal. Calcd. for $C_{12}H_{30}Cl_2N_2S$: S, 10.53; Cl, 23.23. Found: S, 10.24; Cl, 23.31, 23.35.

bis-(β-Diethylaminoethyl) sulfide dihydrobromide was prepared similarly to the dihydrochloride as a white crystalline powder, m. p. 237.3–237.8° (corr.).

Anal. Calcd. for $C_{12}H_{30}Br_2N_2S$: Br, 40.56. Found: Br, 41.06.

(4) W. E. Lawson and E. E. Reid, THIS JOURNAL, **47**, 2821 (1925), give 247° (corr.) as the melting point of the compound prepared from β,β'-dichlorodiethyl sulfide and diethylamine.

(5) I. W. Grote, *J. Biol. Chem.*, **93**, 25 (1931).

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Relations between Rotatory Power and Structure in the Sugar Group. XXXIV. The Possibility of Different Conformations of the Pyranoid Ring[1]

BY C. S. HUDSON

In a preceding article by Eugene Pacsu[2] he suggests that the exceptional character of the rotations of the α- and β-forms of substances having the pyranoid ring structure in the mannose series may be due to a difference in the conformation of the atoms forming the ring. I thank Dr. Pacsu, with whom I have conferred often during the progress of his research, for this opportunity to publish concurrently the reasons which have led me to take the same viewpoint on this question.

In 1930[3] I expressed the view that the exceptional character of these rotations indicated that the substances had different ring structures, and I assumed that the α-forms were of the furanoid and the β-forms of the pyranoid type. The experiments of Haworth and Hirst[4] and their collaborators, designed to test this view, yielded results which showed that it is not tenable and that the substances in question possess only the pyranoid ring. From then on I have searched for an explanation of these unusual rotations that would be compatible with a pyranoid ring structure. The discovery[5] of a crystalline molecular compound of the α- and β-forms of methyl xyloside suggested the possibility that some of the supposedly pure substances of the mannose series might be compounds of this nature, an hypothesis which easily could account for the exceptional rotations. Many efforts by various ways to separate α-methyl mannopyranoside into components and similar experiments on its tetraacetate and on the tetraacetate of β-methyl mannopyranoside, led to negative results; the hypothesis of the compound nature of any of these substances thus became very improbable but nevertheless the failures did not eliminate it as a possibility. Positive proof that they are true chemical individuals, not molecular compounds, was obtained in the course of experiments[6] on the oxidation of methyl glycosides by periodic acid; their exceptional rotations, as compared with those of their glucose analogs, are not attributable either to ring-size or to any lack of chemical individuality. As was pointed out some years ago,[7] there are several differences of rotation in the mannose pyranoid series that conform closely with analogous differences in the glucose series, provided one compares substances of α-classification only, or of β-classification only. Pacsu now finds similar relationships in the fructose and sorbose pyranoid series. It would seem therefore that the agreement of rotational differences within the α- or the β-series, when coupled with the known disagreement across an α–β pair, probably indicates differences in pyranoid ring conformation.

(1) Publication authorized by the Surgeon General, U. S. Public Health Service. No. XXXIII was published in THIS JOURNAL, **61**, 1658 (1939).

(2) Pacsu, THIS JOURNAL, **61**, 2669 (1939).

(3) Hudson, *ibid.*, **52**, 1680 (1930).

(4) Haworth and Hirst, *J. Chem. Soc.*, 2615 (1930), *et seq.*

(5) Hockett and Hudson, THIS JOURNAL, **53**, 4454 (1931).

(6) Jackson and Hudson, *ibid.*, **61**, 959 (1939).

(7) Hudson, *ibid.*, **48**, 1424 (1926).

CONTRIBUTION FROM THE
NATIONAL INSTITUTE OF HEALTH
U. S. PUBLIC HEALTH SERVICE
WASHINGTON, D. C.

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The Preparation of Seleno Ortho- and Meta-Cresols

BY DUNCAN G. FOSTER

In preparing a series of compounds for the measurement of vapor-phase absorption spectra it developed that the two compounds seleno *o*- and *m*-cresol, $CH_3C_6H_4SeH$, had never been described in the literature. The writer has prepared them by the standard method of treating the tolyl Grignard reagents with elementary selenium,[1] operating in a current of hydrogen. When hydrogen was not used no selenocresols were obtained, but only high-boiling selenides, which perhaps explains why they are not reported.

(1) Taboury, *Ann. chim. phys.*, **15**, 5 (1908).

TABLE I

PREPARATION DETAILS AND ANALYSES

Product	Starting compound	Yield G.	Yield G.	Yield %	M. p. or b. p. °C.	M. p. or b. p. Mm.	Physical form, color	Analysis Calcd.	Analysis Found
o-$CH_3C_6H_4SeH$	*o*-$CH_3C_6H_4Br$	85.5	35	41	99	25	Colorless		
m-$CH_3C_6H_4SeH$	*m*-$CH_3C_6H_4Br$	85.5	40	47	89	16	liquid		
o-$CH_3C_6H_4SeO_2H$	*o*-$CH_3C_6H_4SeH$	4.0	3.3	72	123–125		White needles	C 41.38	C 41.03
									H 3.91
m-$CH_3C_6H_4SeO_2H$	*m*-$CH_3C_6H_4SeH$	7.0	5.7	96	118–119		White needles	H 3.94	C 41.46
							or plates		H 4.07

The compounds are colorless liquids when absolutely pure, but rapidly turn yellow on contact with the air. Direct analyses were found to be impracticable because their acid nature renders the Parr bomb method inapplicable and their instability and toxic properties make handling for carbon and hydrogen determinations difficult. For identification, they were converted to the acids $CH_3C_6H_4SeO_2H$[2] by dissolving in nitric acid and these compounds analyzed for carbon and hydrogen. This does not distinguish them from the ditolyl diselenides, which would behave in the same way, but the boiling points were much too low for them to have been diselenides. The copper salts were also prepared by standard means.[3] They were blue crystalline solids without m. p.

(2) Pyman, *J. Chem. Soc.*, [1] **115**, 166 (1919).

(3) Stoecker and Krafft, *Ber.*, **39**, 2200 (1906).

CHEMICAL LABORATORY
SWARTHMORE COLLEGE
SWARTHMORE, PENNSYLVANIA RECEIVED JUNE 7, 1939

Note on the Preparation of *d*-Galacturonic Acid

BY IRA A. MANVILLE, FRANCIS J. REITHEL AND PAUL M. YAMADA

In a recent article[1] there was described a method for the enzymic preparation of *d*-galacturonic acid from polygalacturonic acid. We have had the pre-publication privilege of using this method for preparing the *d*-galacturonic acid necessary for our work on its nutritional significance. It was found in our laboratory that the method, though far superior to former methods in many respects, gave varying yields. Although this in no way detracted from the excellence of the method, it posed the question as to what factors should be considered in improving the yield.

First of all we tried different pectins. Of these, there seemed to be considerable variation even between "batches." Most satisfactory in our work was General Food's Certo Apple Pectin RX 1 or 2. California Fruit Exchange Citrus Pectin, Sample B-6712, also gave good results. We are not prepared to explain why these are better, but simply state the result of empirical observations and call attention to the importance of this detail.

Secondly, we found that in the preparation of pectic (polygalacturonic) acid, it was quite necessary for the best yield to remove the last trace of the calcium chloride which we used for controlling the swelling of the pectin. This was accomplished as follows. After swelling the pectin in alcohol and calcium chloride, adding sodium hydroxide, acidifying and washing (until no precipitate resulted upon the addition of sodium oxalate or five volumes of alcohol), the resultant pectic acid was suspended again in a volume of water equivalent to that of the alcohol. About half as much sodium hydroxide was added as before. It was then acidified and washed again. The pectic acid obtained has no contamination with pectin or calcium chloride. That the concentration of calcium chloride affects enzymic action is shown by the fact that addition of calcium chloride to the enzyme–pectic acid mixture will inhibit the action of the enzyme.

Thirdly, we found that of those preparations tried, only Röhm and Haas Pectinase 46 AP seemed to yield satisfactory results. This is the enzyme contained in the preparation used by Mottern and Cole.

Several other minor points should be mentioned. After enzyme action is complete, we find it advantageous to add the sulfuric acid before filtration. Further, it is often wise to work up the sludge from the alcohol precipitation by treating it with small amounts of sulfuric acid and carrying it on in the same manner as the original material.

By carefully observing all these points in technique, we have been able to obtain yields as high as 36% of the theoretical and have had no difficulty in obtaining a very pure product which, after recrystallization in the β-form from boiling absolute alcohol, has a melting point of 160°.

The purpose of this note is to aid those using

(1) Mottern and Cole, THIS JOURNAL, **61**, 2701 (1939).

Mottern and Cole's method for the first time in obtaining the best results possible. Full acknowledgment is made to Mottern and Cole for their kindness in letting us use their method and for supplying us with goodly quantities of *d*-galacturonic acid.

NUTRITIONAL RESEARCH LABORATORY
DEPARTMENT OF MEDICINE
UNIVERSITY OF OREGON MEDICAL SCHOOL
PORTLAND, OREGON RECEIVED MAY 26, 1939

Sterols. LXXIV. Acetic Acid Derivatives of Estrone and α-Estradiol

BY RUSSELL E. MARKER AND EWALD ROHRMANN

Estratriene-1,3,5-one-17-oxyacetic acid-3 was first prepared by Ercoli and Mamoli[1] by treatment of estrone in aqueous potassium hydroxide solution with chloroacetic acid. In the present work the 3-oxyacetic acid derivatives of estratriene-1,3,5-one-17-ol-3 and of estratriene-1,3,5-diol-17(α),3 were prepared by the reaction of these substances with ethyl chloroacetate in the presence of an excess of an ethanolic solution of sodium ethylate. Estratriene-1,3,5-one-17-ol-3 was also caused to react in a similar way with α-chloropropionic acid to yield estratriene-1,3,5-one-17-oxymethylacetic acid-3. The acidic substances were characterized further by the formation of the methyl esters.

We wish to thank Parke, Davis and Company for their generous support and assistance rendered during the course of this work.

Experimental Part

Estratriene-1,3,5-one-17-oxyacetic Acid-3.—To a boiling solution of 1 g. of estrone in 40 cc. of absolute ethanol was added 3.5 cc. of ethyl chloroacetate and a solution of 600 mg. of sodium in 20 cc. of ethanol. The mixture was refluxed on the steam-bath for fourteen hours after which 2 g. of potassium hydroxide was added and the refluxing continued for one hour. The mixture was diluted with water and the clear solution acidified with hydrochloric acid. The white solid was taken up in ether and the ethereal solution washed with water and 5% sodium carbonate solution. Evaporation of the ether yielded approximately 150 mg. of unreacted estrone.

The sodium carbonate washing was acidified with hydrochloric acid and the white solid taken up in ether. Evaporation of the ether gave a product which crystallized from aqueous acetone as small white plates, m. p. 209–211°; yield, 750 mg.

Anal. Calcd. for $C_{20}H_{24}O_4$: C, 73.2; H, 7.4. Found: C, 73.5; H, 7.5.

When the reaction was carried out using equivalent amounts of sodium and ethyl chloroacetate, only a poor yield of the acid was obtained.

A solution of 50 mg. of the acid in 10 cc. of 80% ethanol was refluxed for one hour with 75 mg. of hydroxylamine hydrochloride and 100 mg. of sodium acetate. The product was crystallized from 80% ethanol to give white crystals of the **oxime**, m. p. 230–232° dec.

Anal. Calcd. for $C_{20}H_{25}O_4N$: C, 69.9; H, 7.3. Found: C, 70.0; H, 7.4.

The **methyl ester** was prepared by treating 150 mg. of the acid in ether–methanol solution with an excess of an ethereal solution of diazomethane. The product was crystallized from aqueous acetone as white crystals, m. p. 130–132°.

Anal. Calcd. for $C_{21}H_{26}O_4$: C, 73.6; H, 7.7. Found: C, 73.5; H, 7.8.

Estratriene-1,3,5-ol-17(α)-oxyacetic Acid-3.—This was prepared from estratriene-1,3,5-diol-3,17(α) as described for estratriene-1,3,5-one-17-oxyacetic acid-3. The product was crystallized from aqueous acetone to give white crystals, m. p. 182–184°.

Anal. Calcd. for $C_{20}H_{26}O_4$: C, 72.7; H, 7.9. Found: C, 72.6; H, 7.9.

Treatment of the acid in ether–methanol solution with diazomethane yielded the **methyl ester** which crystallized as white crystals from ether–pentane, m. p. 94–96°.

Anal. Calcd. for $C_{21}H_{28}O_4$: C, 73.2; H, 8.2. Found: C, 73.3; H, 8.1.

Estratriene-1,3,5-one-17-oxymethylacetic Acid-3.—This was prepared from estrone and α-chloropropionic acid as described for the preparation of estratriene-1,3,5-one-17-oxyacetic acid-3 except that about three times as much sodium was used. The product was crystallized from aqueous acetone as white crystals, m. p. 195–198°.

Anal. Calcd. for $C_{21}H_{26}O_4$: C, 73.6; H, 7.7. Found: C, 73.3; H, 7.7.

Treatment of the acid in methanol–ether solution with diazomethane yielded the **methyl ester** which crystallized from aqueous acetone as small white crystals, m. p. 137–139°.

Anal. Calcd. for $C_{22}H_{28}O_4$: C, 73.9; H, 7.9. Found: C, 74.1; H, 7.9.

SCHOOL OF CHEMISTRY AND PHYSICS
THE PENNSYLVANIA STATE COLLEGE
STATE COLLEGE, PENNSYLVANIA RECEIVED JULY 24, 1939

(1) Ercoli and Mamoli, *Gazz. chim. ital.*, **68**, 142 (1938).

Identification of Propionic Acid in the Presence of Acetic and Butyric Acids

BY LOUIS MUSICANT AND FRANK J. KASZUBA

Pure propionic acid may be tested for readily in a number of ways, namely, as a derivative of *p*-toluidine,[1] benzylisothiourea[2] and the like; by the formation of 2-ethylbenzimidazole[3]; by its reac-

(1) R. L. Shriner and R. C. Fuson, "Identification of Organic Compounds," John Wiley & Sons, Inc., New York, N. Y., pp. 95, 144.
(2) S. Veibel and H. Lillelund, *Bull. soc. chim.*, [5] **5**, 1153 (1938).
(3) W. O. Pool, H. J. Harwood and A. W. Ralston, THIS JOURNAL, **59**, 178 (1937).

tion with lanthanum nitrate[4]; the behavior of its aqueous iron or copper salt solutions in the presence of amyl alcohol or other immiscible solvents,[5] etc. However, when acetates or butyrates, or both, are also present, some or all of the foregoing tests become inconsistent and unreliable. It is true such mixtures may be analyzed, both qualitatively and quantitatively, with exceptional success by the use of the methods of C. H. Werkman and co-workers.[6] Unfortunately, these procedures require very careful manipulation and are rather time consuming.

A need for a rapid and reliable means of identifying propionates in the presence of the above-mentioned interfering ions was satisfactorily filled by the use of mercurous nitrate.

Mercurous propionate crystallizes in a well-defined form which is quite different from either mercurous acetate or butyrate. Further, it forms readily even when the latter substances are also present. Once one has become familiar with the crystalline characteristics of the pure salts and their mixtures, the possibility of error becomes insignificant. The authors testing numerous unknowns, obtained results which were correct in each and every case.

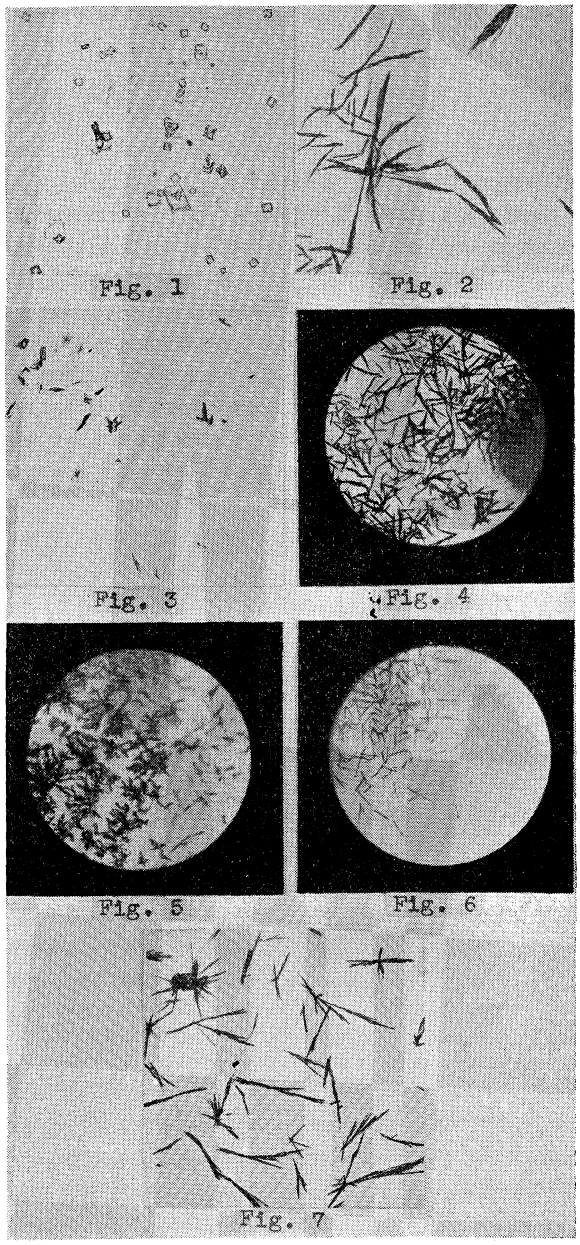
The accompanying photomicrographs illustrate the crystal structures involved. The entire method is brief, simple, and does not require undue care or technique.

In the accompanying photomicrographs the concentrations of the salts were as follows: for Figs. 1, 2 and 3, 2% solutions of the pure sodium salts were used; for the remaining four, equal amounts of 2% solutions of the sodium salts of the ions involved were taken.

Experimental.—A neutral hydrolysate or test solution is vacuum distilled to dryness. The residue is then acidified with concentrated phosphoric acid and the liberated acids are distilled off *in vacuo*. It is advisable to collect the distillate in an 8″ × 1″ (20 × 2.5 cm.) test-tube surrounded by an efficient freezing mixture (salt, 33; pulverized ice, 100; −21°). The test-tube may be connected to the side-arm of the flask by means of a bent piece of ordinary glass tubing. This delivery tube should dip to within 2.5 cm. of the bottom of the receiver.

A capillary introduced into the semi-solid distillate (when acetate is present) will withdraw several drops of acid. This is transferred to a glass slide and a drop of 5% sodium carbonate solution is added (care being taken that the mixture still reacts acid to litmus) and the whole is evaporated to dryness. The residue is dissolved in 2–4 drops of water, and a drop of a saturated solution of mercurous nitrate (acidified with nitric acid to prevent decomposition) is placed alongside, and is allowed to flow into the former. The precipitate is examined immediately with a microscope.

To obtain the photomicrographs, the following procedure was used: one drop of a 2% aqueous solution of sodium propionate (or acetate, or butyrate, or mixtures of any two or all three) was placed on a glass slide and diluted with 2–4



Mercurous salts: 1, acetate; 2, propionate; 3, butyrate; 4, acetate-propionate; 5, acetate-butyrate; 6, propionate-butyrate; 7, acetate-propionate-butyrate.

(4) A. Damour, *Compt. rend. acad. sci. Paris*, **43**, 976 (1857); *Chem. Zentr.*, **28**, 127 (1857).

(5) D. C. Dyer, *J. Biol. Chem.*, **28**, 445 (1917).

(6) O. L. Osburn, H. G. Wood and C. H. Werkman, *Ind. Eng. Chem., Anal. Ed.*, **8**, 270 (1936).

drops of water. A drop of the reagent was then allowed to flow into the test sample (magnification, 100 ×).

Discussion.—The distillation is employed to remove substances which may interfere with the analysis. It also serves to concentrate the acids present. Incidentally, too large an excess of acetic acid is conveniently and simultaneously frozen out.

If only the sodium salts of the acids involved comprise the test substance, the distillation may be dispensed with if one can be sure of at least 0.15 mg. of propionate in the test drop.

The method also may be used to identify either acetates or butyrates when they are present alone. As little as 0.15 mg. present in the test drop permits positive identification.

Formates tend to interfere with the analysis when the concentration is equal to or greater than either of the other anions. When smaller amounts are present, however, propionates may be identified although the crystal structure is slightly altered. Hence, if formates are indicated in a test solution (by the reduction of silver nitrate or mercuric chloride), it is advisable to destroy or otherwise remove them.

Attempts were made to employ other cations for the detection of the ions discussed under similar conditions. Thus, silver, bismuth, antimony, and lead salts of the acids were studied. Also, various cobaltammine complexes were tried. However, none of these were found to be completely suitable.

Acknowledgment.—The authors wish to express their thanks to Dr. W. Schmidt for permission to publish this paper. Thanks are also due to Mr. W. Pera for technical advice on photomicrography and to W. A. Hynes and L. K. Yanowski for supplying samples of the cobaltammine complexes.

AGFA ANSCO CORPORATION
BINGHAMTON, NEW YORK RECEIVED MAY 11, 1939

Saponins and Sapogenins. XIV. The So-called Pyridazine Derivatives of Steroid Diones

BY C. R. NOLLER

The fact that the diketone obtained by the oxidation of chlorogenin[1] has been found to react with hydrazine to give a product the analysis of which checks that of a pyridazine derivative, has led Marker and Rohrmann[2] to postulate that the carbonyl groups of the diketone and hence the hydroxyl groups of chlorogenin occupy the 3,6-positions of the sterol nucleus. Several factors have led us to believe that this is not a likely structure for chlorogenin. Since tigogenin on oxidation gives gitogenic acid, one would expect chlorogenin, if it had the 3,6-formulation, to give digitogenic acid, which is not the case. Moreover, if oxidation opened ring I between C-3 and C-4, a β-keto acid would be formed or if ring I opened between C-2 and C-3 but the nuclear configuration were different, one would expect the ketodibasic acid to be isomerized readily by alkali since digitogenic acid readily is converted to digitoic acid, but the ketodibasic acid was recovered unchanged after alkaline saponification of the dimethyl ester. The opening of ring II between C-6 and C-7 on oxidation would not be expected since in the further oxidation of digitogenic acid ring II is opened between C-5 and C-6 to give a ketotribasic acid, oxydigitogenic acid. Finally the surface film of digitogenin appears to be unlike that of chlorogenin since the former contracts rapidly under pressure giving a solid condensed film which is partially collapsed[3] whereas chlorogenin gives a gaseous film which does not collapse until the pressure reaches 18 dynes per centimeter and which remains mobile even up to 32 dynes per centimeter.[4]

Because of the possibility of polymolecular condensation,[5] we have determined the molecular weight of the condensation product formed from hydrazine and the diketone from chlorogenin and have obtained values of 1410, 1980 and 2770 for three different preparations compared with a calculated value of 425 for a monomolecular pyridazine derivative. It is evident that the formation of condensation products with hydrazine does not prove that the hydroxyl groups of chlorogenin are in the 3,6-positions although the fact that the condensation products are polymolecular does not exclude these positions.

Since molecular weight determinations have not been reported for similar compounds from other steroid diones,[6] it seemed desirable to determine the molecular weight of a typical so-called pyridazine derivative such as that from choles-

(1) Noller, THIS JOURNAL, **59**, 1092 (1937).

(2) Marker and Rohrmann, *ibid.*, **61**, 946 (1939).

(3) Askew, Farmer and Kon, *J. Chem. Soc.*, 1399 (1936).

(4) Noller, THIS JOURNAL, **60**, 1629 (1938).

(5) Zimmerman and Lochte, *ibid.*, **60**, 2456 (1938).

(6) Windaus, *Ber.*, **39**, 2256 (1906); Fernholz, *Ann.*, **508**, 217 (1934); Windaus, Inhoffen and Reichel, *ibid.*, **510**, 259 (1934); Coffey, Heilbron and Spring, *J. Chem. Soc.*, 738 (1936).

tane-3,6-dione. A single preparation gave a value of 3000 compared with 396 for a monomolecular product. It is surprising that the fact has been overlooked that reaction with hydrazine cannot, in the absence of molecular weight determinations, be considered as proof or confirmatory evidence for the 1,4-diketone grouping since Fernholz[6] points out that a pyridazine from a 3,6-dione is possible stereochemically only if one of the double bonds is outside of the heterocycle. Moreover, Marker and Wittle[7] have objected to a deduction of others[8] based on "pyridazine" formation on the grounds that the pyridazine in question was probably a linear polymer.

The reaction with hydrazine of the diketone, m. p. 233–235°, from chlorogenin was carried out in the usual way.[2,6] Methyl alcohol was added to a boiling solution of the product in benzene and on cooling a pale yellow oil separated which solidified on rubbing with more methyl alcohol. Solution in benzene and precipitation with methyl alcohol was repeated three times. The product, which was amorphous, was dried at 130° and 3 mm. pressure. It turned a deep yellow at 240°, light brown at 270° and was a dark brown powder at 300°.

Anal. Calcd. for $C_{27}H_{40}O_2N_2$: N, 6.59. Found: N, 7.05, 6.89. When 0.1661 g. was dissolved in 1.889 g. of benzene, the freezing point was depressed 0.16°. Calcd. mol. wt., 425; found, 2770.

The mother liquors from the above preparation were concentrated, dissolved in benzene and precipitated by methyl alcohol. This product showed the same behavior on heating and was found to contain 6.82% nitrogen. When 0.0534 g. was dissolved in 1.247 g. of benzene, the freezing point was depressed 0.11°, indicating a molecular weight of 1981.

In another preparation a product with different properties was obtained although the conditions were to all outward appearances the same. This product was crystalline but showed the same behavior on heating as the previous products.

Anal. Calcd. for $C_{27}H_{40}O_2N_2$: C, 76.38; H, 9.49; N, 6.59. Found: C, 73.73, 73.80; H, 9.62, 9.22; N, 6.49, 6.84.

This crystalline product had only limited solubility in benzene and the solubility appeared to decrease with repeated crystallizations. This solubility behavior is different from that of all previously recorded products, which appear to be characterized by ready solubility in benzene.

In order to get sufficient material into solution for a molecular weight determination, it was necessary to warm the solution but there was no evidence that the material separated before freezing of the benzene took place. A depression of 0.15° was obtained when 0.0950 g. was dissolved in 2.290 g. of benzene, indicating a molecular weight of 1410. A micro Rast determination in camphor by Mr. L. H. Goodson gave a value of 894 for the molecular weight but decomposition of the compound was evident from the brown color of the solution.

A sample of cholestanedione-3,6, m. p. 169–171°, prepared by the method of Dane and Wang,[9] after reaction with hydrazine and purification from benzene and methyl alcohol, gave an amorphous product which darkened at 190° and melted to a red-brown liquid at 210–220°. Windaus[6] reported obtaining a crystalline product which sintered at 188°.

Anal. Calcd. for $C_{27}H_{44}N_2$: N, 7.06. Found: N, 6.72.

When 0.1235 g. was dissolved in 1.750 g. of benzene the freezing point was depressed 0.12°, indicating a molecular weight of 2999.

When 0.1040 g. of the diketone from chlorogenin was dissolved in 1.845 g. of benzene the freezing point depression was 0.69°, giving a molecular weight of 417 compared with a calculated value of 428.

(7) Marker and Wittle, THIS JOURNAL, **61**, 855 (1939).

(8) Odell and Marrian, *J. Biol. Chem.*, **125**, 333 (1938).

(9) Dane and Wang, *Z. physiol. Chem.*, **245**, 86 (1937).

CONVERSE MEMORIAL LABORATORY
HARVARD UNIVERSITY
CAMBRIDGE, MASSACHUSETTS RECEIVED MAY 10, 1939

Purification of *p*-Acetaminobenzenesulfonyl Chloride

BY L. H. PENCE AND H. C. WINTER

A convenient method for the purification of large quantities of *p*-acetaminobenzenesulfonyl chloride will be of interest to the many investigators engaged in the synthesis of sulfanilamide and related compounds.

The crude acid chloride obtained by the procedure described by Smiles and Stewart[1] in "Organic Syntheses" frequently may be employed in subsequent reactions without further purification; but they state that it must be used immediately after preparation, since it decomposes rapidly on standing. Once the sulfonyl chloride is purified, however, it may be kept indefinitely. According to their procedure recrystallization of the 90 g. of crude product from benzene yielded 70 g. of pure *p*-acetaminobenzenesulfonyl chloride melting at 149°. However, because of the slight solubility of the sulfonyl chloride in this solvent (2% hot and 0.5% cold), recrystallization from benzene has been reported[1] to be impractical for purifying more than a small amount at a time.

The following modification of the above procedure has been used in our laboratory and found to be much better adapted for the purification of large quantities of the compound from the standpoints of both time and convenience.

(1) Smiles and Stewart, *Org. Syntheses*, **5**, 3 (1925).

Dry acetanilide (67.5 g.) is added to freshly distilled chlorosulfonic acid (290 g.) in the usual manner. After the reaction mixture has been poured into crushed ice and water, the precipitated *p*-acetaminobenzene sulfonyl chloride is centrifuged and washed three times with water in the centrifuge. The damp, crude acid chloride is then dissolved easily in ether (1000 cc.), separated from the aqueous layer, and washed with water until the washings no longer give a test for sulfate ion. Four 50-cc. portions of water are usually sufficient. After drying the ethereal solution over anhydrous sodium sulfate for one hour,[2] and filtering, the ether is removed by distillation. When approximately 300 cc. of ether remains, the acid chloride begins to separate, and benzene (1000 cc.) is added. After cooling in the icebox the crystals are transferred to the filter, washed with benzene (200 cc.), and dried *in vacuo* at room temperature. The average yield of several preparations was 70 g. of the colorless crystals of *p*-acetaminobenzenesulfonyl chloride, melting at 149°. An earlier preparation (m. p. 147–148°) had the same melting point after standing for seven months.

(2) Longer drying may cause the acid chloride to crystallize out, as it is less soluble in anhydrous ether.

BIOCHEMICAL RESEARCH FOUNDATION
OF THE FRANKLIN INSTITUTE
PHILADELPHIA, PENNSYLVANIA RECEIVED JUNE 30, 1939

The Action of Titanium Tetrachloride on Benzylglucopyranoside Tetraacetates

BY E. V. PIEL[1] AND C. B. PURVES

Pacsu observed that in absolute chloroform solution titanium tetrachloride and a fully acetylated β-glycoside united to a less soluble, highly colored addition complex. The subsequent decomposition of this complex by water liberated the isomeric α-glycoside acetate in very high yield.[2] While using this reaction to prepare α- from β-benzylglucopyranoside tetraacetate, we noted that a small amount of starting material always could be recovered from the mother liquors of the product. As the yield of the crude, crystalline product was practically quantitative when the heating of the chloroform solution was not unduly prolonged, it was possible to follow the reaction by noting the amounts and the specific rotations of the various fractions (Table I). It was clear that the tetrachloride brought about an equilibrium containing the α- and β-forms of the acetylated glycoside in an approximate ratio of 9:1 and that this equilibrium could be experimentally reached from either side. Although colored addition compounds were formed with tetraacetyl β-methylfructopyranoside,[3] with sucrose acetate or triacetyl β-glucosan,[4] the original materials were recovered unchanged. In these cases the titanium tetrachloride compound initially formed was apparently too stable to rearrange in the experimental conditions.

(1) This article is based on a thesis submitted by Mr. Piel to the Faculty of the Massachusetts Institute of Technology in partial fulfilment of the requirements for the degree of S.B.

(2) Pacsu, *Ber.*, **61**, 1508 (1928); THIS JOURNAL, **52**, 2563, 2568, 2571 (1930).

TABLE I

TITANIUM TETRACHLORIDE (1 MOLE) AND TETRAACETYL GLUCOPYRANOSIDE (1 MOLE) IN BOILING CHLOROFORM SOLUTION

Isomer used, g.	Reflux time, min.	Recryst. fractions	G.	$[\alpha]_D$	α-Isomer,[a] %
β, 20	30[b]	F(1)	14.7	−52.2°	10[b]
		F(2)	4.5	30.0	
β, 20	75	F(1)	15	141.5	86
		F(2)	5	38.3	
β, 50	90	F(1)	42.5	142	93
		F(2)	2.8	2.5	
		F(3)	2.5	32	
β, 20	150[c]	F(1)	14.5	141.6	90
		F(2)	2.7	21	
α, 14	75	F(1)	9.4	141.2	91[d]
		F(2)	2.1	58.5	

[a] As % of the total crystalline product. [b] At 21° instead of at the b. p. Equilibrium was not nearly reached. [c] Too prolonged heating caused slight decomposition and reduced the yield. Fractional recrystallization of F(2) gave 0.5 g. of the pure β-acetate with a rotation of −51.8° in chloroform. [d] The total yield was only 86%. F(2) gave 0.2 g. of pure β-acetate with the correct rotation.

Attention to technical details made the α-benzylglucoside acetate readily available from acetobromoglucose in an over-all yield of 60%, the β-benzyl acetate[5] being an intermediate step. This was greatly superior to the earlier yield (11%) obtained by converting acetobromo to acetoiodoglucose and condensing the latter with benzyl alcohol in quinoline.[6]

Experimental

All rotations were made with sodium light in a 2- or 4-dm. tube at 20 or 21°.

Acetobromoglucose.—A solution made from recrystallized glucose pentaacetate, 50 g., and glacial acetic acid nearly saturated with hydrogen bromide, 75 cc., was kept at room temperature for two hours.[7] Most of the solvent was recovered by evaporation, bath 60° (20 mm.), fortified with hydrogen bromide and used again. Traces were removed from the residual sirup by the addition and evaporation, under diminished pressure, of dry toluene.[8] The recrystallized product was 85–90%.

(3) Pacsu and Cramer, *ibid.*, **59**, 1059 (1937).
(4) Hurd and Cantor, *ibid.*, **60**, 2677 (1938).
(5) Slotta and Heller, *Ber.*, **63**, 1024 (1930).
(6) Helferich and Gootz, *ibid.*, **62**, 2788 (1929).
(7) Fischer, *ibid.*, **44**, 1898 (1911).
(8) *Cf.* Compton, THIS JOURNAL, **60**, 396 (1938).

Tetraacetyl - β - benzylglucopyranoside.—Acetobromoglucose, 110 g., redistilled benzyl alcohol, 265 cc., dry ether, 250 cc., and dry silver oxide, 60 g., were shaken together till the liquid was bromide free.[9] After filtration and evaporation of ether, the excess benzyl alcohol was recovered for the next run by distillation, bath 95–100° (0.1 mm.). A still head lagged with asbestos tape and at least 1 cm. in diameter, together with efficient cooling (ice water) of condenser and receiver, was necessary. The slightly impure product (75%) after complete purification from alcohol had specific rotations of −53.2° in chloroform and −46.7° in dioxane (*c*, 4.0).

Deacetylation gave pure β-benzylglucopyranoside, m. p. 122° (corr.), with rotations of −56.3° in water, −59.5° in dioxane (*c*, 2.0) and −57.6° in methyl alcohol (*c*, 1.5).

Tetraacetyl-α-benzylglucopyranoside.—The β-isomer, 20 g., titanium tetrachloride, 9 g. (1 mole), and pure chloroform, 200 cc., were heated under reflux for seventy-five minutes and the crude product was isolated by Pacsu's methods.[2] Recrystallization from 100 cc. of hot alcohol gave a first fraction of 15 g. and a second fraction, after dilution of the mother liquors with water, of 5 g., the rotations in chloroform being 141.5 and 38.3°, respectively. As those of the pure α- and β-isomers were 144.8 and −53.2°, the α-contents of the two fractions were 99 and 47%, corresponding to an average of 86% for the α-isomer. In a duplicate rearrangement of 153 g. of the β-tetraacetate, the second fraction, 15 g., was twice recrystallized from alcohol and gave 5 g. of the pure starting material with the correct levorotation of −52.8°. Other experiments are summarized in Table I.

Pure tetraacetyl-α-benzylglucopyranoside, m. p. 111°, had rotations of 144.8° in chloroform and 146.0° in dioxane (*c*, 2.5). Deacetylation gave the pure α-benzyl glycoside with rotations of 133.5° in water, 152° in dioxane (*c*, 2.5) and 150.3° in methyl alcohol, m. p. 122° corr.

(9) Such syntheses have been improved by the addition of Drierite [Kreider and Evans, THIS JOURNAL, **58**, 1661 (1936)].

CONTRIBUTION NO. 199 FROM THE
RESEARCH LABORATORY OF ORGANIC CHEMISTRY
MASSACHUSETTS INSTITUTE OF TECHNOLOGY
CAMBRIDGE, MASS. RECEIVED JULY 26, 1939

Benzoylformic Acid from Styrene

BY CHARLES D. HURD, R. W. MCNAMEE AND FRANK O. GREEN

Oxidation of mandelic acid with potassium permanganate is the usual method[1] of synthesizing benzoylformic acid. Yields of 50 to 72% are attained. In place of mandelic acid it has been found that styrene (phenylethylene) may be oxidized in satisfactory yields to benzoylformic acid according to the equation

$$3C_6H_5CH{=}CH_2 + 8KMnO_4 \longrightarrow 3C_6H_5COCOOK + 8MnO_2 + 5KOH + 2H_2O$$

The commercial availability of pure styrene makes this an economical source of benzoylformic acid, whereas mandelic acid is much more expensive. It was established also that crude styrene, which was obtainable from "Drip Oil"[2] by fractional distillation, might be used also in this synthesis.

For some of the work, styrene was prepared by pyrolysis of cinnamic acid.[3] In other experiments, technical styrene[4] was used. This was vacuum distilled before use to remove the inhibitor (*p-t*-butylcatechol) and the polymers. From 3.5 g. of this distilled styrene, 8 g. of styrene dibromide, m. p. 72°, was obtained by reaction with bromine in carbon tetrachloride. The purity of this styrene, therefore, was at least 90%, and probably higher.

Styrene was concentrated from "Drip Oil"[5] for the oxidation experiments by fractionation through an efficient column. The fraction taken, b. p. 141–142°, was about one-half styrene because 2.78 g. of it yielded 3.56 g. of styrene dibromide.

Oxidation of Styrene of 90–100% Purity.—Eighteen grams (0.173 mole) of styrene and 9 g. (0.225 mole) of sodium hydroxide were shaken with 100 cc. of water in a 2-liter flask fitted with an air condenser. To this mixture was added in six portions a hot (70°) solution of 75 g. (0.474 mole) of potassium permanganate in 1500 cc. of water. After each addition the mixture was shaken vigorously for two minutes and cooled under the water tap so that the reaction temperature was kept at about 70°. When all the permanganate had been introduced, the excess was reduced with about 100 cc. of alcohol and the manganese dioxide filtered off and washed with water. The filtrate and washings were combined and evaporated down to 400 cc., then acidified with concentrated hydrochloric acid. The 1.5 g. of benzoic acid which separated was removed by filtration. When the addition of hydrochloric acid failed to precipitate any more benzoic acid the solution was extracted several times with ether. On evaporation of the ether, 20.4 g. of a light yellow liquid remained. This crude benzoylformic acid contained 2 to 3 cc. of water which made it quite insoluble in carbon disulfide. The water was removed by distilling with 7 cc. of toluene. An alternative procedure for removing the water was to dry the ether solution with calcium chloride. The residual acid, 18 g. (0.120 mole) or 69% yield, was dissolved in 30 cc. of carbon disulfide and the solution cooled with ice and salt. About 10 g. of crystals came down in the first crop and 5–6 g. in subsequent crops. Recrystallization gave 14.5 g. (0.096 mole) or 55% yield, of benzoylformic acid which melted at 59–61°.

Oxidation of Styrene of about 50% Purity.—A 26.5-g. fraction, b. p. 141–142°, obtained from drip oil, contained 13.3 g. (0.128 mole) of styrene. The quantities of other reagents were based on the styrene content; hence, 55.5 g. (0.351 mole) of potassium permanganate was used. The experimental details were the same as those outlined previously, but this time no benzoic acid separated after

(1) Acree, *Am. Chem. J.*, **50**, 389 (1913); Hurd and Raterink, THIS JOURNAL, **56**, 1349 (1934); Hurd and McNamee, *Org. Syntheses*, **16**, 89 (1936).

(2) Brown, *Ind. Eng. Chem.*, **20**, 1178 (1928).

(3) *Org. Syntheses*, **8**, 84 (1928).

(4) Grateful acknowledgment is made to the Dow Chemical Company for a generous supply of styrene.

(5) An abundant supply of drip oil was generously furnished by Mr. G. J. Hart, Norshore Gas Co., Waukegan, Ill.

concentration and acidification. The crude benzoylformic acid was a light yellow oil which weighed 12.6 g. It contained about 2 cc. of water which was removed as before. The crystalline benzoylformic acid obtained after purification weighed 7.5 g. (0.05 mole). This is a yield of 39%, based on the styrene content.

When drip oil fractions were taken which contained only 25% of styrene, oxidation to benzoylformic acid was not satisfactory.

CHEMICAL LABORATORY
NORTHWESTERN UNIVERSITY
EVANSTON, ILL.

RECEIVED AUGUST 9, 1939

COMMUNICATIONS TO THE EDITOR

THE ENTROPY AND HEAT CAPACITY OF PROPYLENE

Sir:

Recently[1] Powell and Giauque have published measurements of the heat capacity of solid and liquid propylene which enabled them to determine the entropy change from 0°K. to the boiling point. By comparing this result with an entropy value calculated statistically on the basis of certain assumptions, they concluded that in solid propylene there is random end for end orientation of the molecules. This does not seem very reasonable to us *a priori*, inasmuch as one end is flat (CH_2), the other round (CH_3); one leg is considerably longer than the other and less polarizable; and finally the molecule has an appreciable dipole moment.[2] Furthermore their statistical calculations were based on a set of frequencies

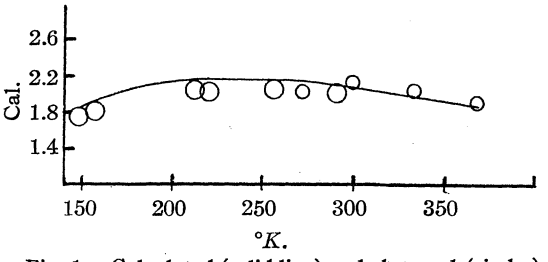


Fig. 1.—Calculated (solid line) and observed (circles) values of torsional heat capacity of propylene gas.

and a potential barrier hindering rotation of the methyl group (700 cal), published by one of us,[3] which are no longer acceptable. These frequencies were estimates obtained by comparison with other molecules, but on carrying the heat capacity measurements to higher temperatures it is found that the original set of frequencies would require a contribution from the internal torsional motion of the methyl group less than the classical value $\frac{1}{2}R$, which is not plausible. Furthermore, an experimental study of the infrared and Raman spectra and a normal coördinate analysis has since been carried out, which, although not yet complete, shows that the estimated frequencies were not satisfactory. The revised frequencies lower somewhat the vibrational entropy at the boiling point, but the main effect is to raise considerably the potential barrier necessary to account for the heat capacity of the gas.

Before the publication of the entropy data we had reached the conclusion that a barrier of about 2000 cal. best fitted the heat capacity measurements when the revised frequencies were used. We have therefore calculated both the entropy at the boiling point and the gaseous heat capacity over a range of temperatures, using a barrier of 2119 cal. and the following frequencies: 432, 580, 921, 940, 1000, 1022, 1100, 1111, 1297, 1399, 1445, 1468(2), 1647, 3000(6) cm.$^{-1}$. Moreover, this calculation was carried out by a method which takes into account the complete dynamics of the molecule, including the coupling of the angular momentum of the top and of the whole molecule. This more complete calculation gave results differing from the values of Pitzer[4] by as much as 19% of the difference between free and hindered rotation. The heat capacities calculated are compared with those observed[5] in Fig. 1. The entropy of the ideal gas at the boiling point (225.35°K.) is calculated to be 59.87 cal., compared with the experimental value of 59.93 cal.

(1) T. M. Powell and W. F. Giauque, THIS JOURNAL, **61**, 2366 (1939).

(2) H. E. Watson, C. G. Rao and K. K. Ramaswamy, *Proc. Roy. Soc.* (London), **143**, 558 (1934).

(3) G. B. Kistakowsky, J. R. Lacher and W. W. Ransom, THIS JOURNAL, **60**, 900 (1938).

(4) K. S. Pitzer, *J. Chem. Phys.*, **5**, 469 (1937).

(5) From ref. 3 and unpublished work.

obtained by assuming *no random orientation* in the solid. The agreement is well within the possible theoretical uncertainties and therefore we do not need, on the basis of the available evidence, to make the assumption that the third law breaks down for this substance.

Further details of the measurements on the heat capacities, on the study of the vibration frequencies, and on the method of calculating thermodynamic properties for molecules containing hindered rotators will be published separately. It should be noted that the vibration frequencies used herein are still provisional so that the value 2120 cal. for the potential barrier is not final; it does, however, correlate all the data now available. It further indicates that 59.93 E. U. is the proper value of the entropy at the boiling point.

(6) National Research Fellow in Chemistry; present address, Sterling Chemistry Laboratory, Yale University, New Haven, Conn.

HARVARD CHEMICAL LABORATORY
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G. B. KISTIAKOWSKY
W. W. RICE
A. J. WELLS
E. B. WILSON, JR.

RECEIVED SEPTEMBER 22, 1939

A PHOTOCHEMICAL PRODUCTION OF REDUCING SUGARS FROM GLYCOSIDES BY ULTRAVIOLET LIGHT

Sir:

Ultraviolet light absorbed by fructosides and glucosides liberates reducing sugars.

A special arrangement of apparatus soon to be published in *Science* made it possible to illuminate aqueous solutions of these glycosides in thermostated quartz tubes where 11 or 12 cc. absorbed about 10^{19} photons of λ 254 mμ per minute. The light flux was measured with the uranyl oxalate actinometer. Portions of the solutions were kept in the dark at the same temperature as the illuminated portions and analyses were made on all portions at the same time and under the same conditions. The ml. of 0.002 *M* sodium thiosulfate entered as hypo in Table I represent the difference between Shaffer–Hartmann–Somogyi (S.–H.–S.) estimations on the dark and illuminated solutions, although the dark reaction was usually negligible. One ml. of hypo was equivalent to 5.6×10^{-5} g. of glucose or 6.1×10^{-5} g. of fructose acid which was reproduced to 0.1 ml. Professor C. B. Purves kindly supplied the glycosides as pure crystals.

Solutions were water white after these photolyses, but the solutions titrated with hypo were sometimes a light amber at the end-point as, for example, in Expts. 3 and 5. Also, strongly photolyzed solutions turned amber after a day or more in the dark at room temperature. The differences in the photochemical efficiencies of the α and β isomers are significant.

The change in the optical activity accompanying the formation of the reducing sugar was measured for solutions of β-benzylfructopyranoside. Rotations of the D lines of sodium were read to 0.02° in a four-decimeter tube at 21.5°.

In a typical experiment, a molar acetate solution at *p*H 3.5 contained 1.8016 g. of β-benzylfructopyranoside in 100 cc. The initial rotation of the solution was −9.45° and the change expected for complete hydrolysis was 5.1° to give a rotation of −4.35°. Three samples illuminated at 10° with light of λ 254 mμ gave observed rotations of −9.00, −8.77 and −8.56°, corresponding to 9, 14 and 18% hydrolysis; and the estimations of reducing sugar gave 9, 13.5 and 18% respectively. The corresponding percentages agree within the limits of error. The calculations based on the S.–H.–S. estimations assumed the

TABLE I

Typical data on glycosides at 0.02 *M* in water; temperature, 23°; volume illuminated, 11 cc.; *p*H of solutions not photolyzed, 6.2; light flux per minute, 8.6×10^{18} photons of λ 254 mμ.

Expt.	Glucopyranosides	*p*H after photolysis	Minutes photolyzed	Hypo, ml.
1	α-Phenyl	3.5	47	6 × 11/5 = 13.2
2	β-Phenyl	3.5	47	8.8 × 11/5 = 19.4
3	α-Benzyl	4.2	64	27.6 × 11/5 = 60.8
4	α-Benzyl	...	30	16.2 × 11/5 = 35.6
5	β-Benzyl	3.7	64	11.2 × 11/2 = 61.5
6	β-Benzyl	...	29	18.2 × 11/5 = 40.0
7	β-(β-Phenylethyl)	4.4	82	7.05 × 11/2 = 38.8
8	β-(β-Phenylethyl) Fructopyranoside	...	32	11.8 × 11/5 = 26.0
9	β-Benzyl	4.5	40	6.4 × 11/2 = 35.0

measured product to be fructose. In the dark reaction α changed to $-9.37°$. These experiments suggest that the main reaction in the photolysis gives the same products as hydrolysis by acids, where the change in α also agreed with the S.-H.-S. estimation of the amount hydrolyzed.

The photochemical efficiency of the measured reaction was independent not only of the light intensity when (5 to 700)10^{16} photons were absorbed per minute by 11 cc. of solution, but also of the *p*H—at least between 3.5 and 6.5. Gross quantum yields were independent of the initial concentration of glycoside but decreased as the liberated alcohol or phenol absorbed a larger fraction of the light incident on the solution.

CONTRIBUTION NO. 431 LAWRENCE J. HEIDT
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CAMBRIDGE, MASSACHUSETTS

RECEIVED SEPTEMBER 11, 1939

THE STRUCTURE OF INSULIN

Sir:

As reported at the Baltimore meeting of the American Chemical Society, I have made an electron density projection of the insulin structure using Crowfoot's $hk \cdot O$ x-ray data [D. Crowfoot, *Proc. Roy. Soc.* (London), **A 164,** 580 (1938)] and assuming (incorrectly) that the true projection has a center of symmetry and that the structure proposed by Wrinch and Langmuir [D. M. Wrinch, THIS JOURNAL, **60,** 2005 (1938); *Science,* **88,** 148 (1938); *Nature,* **143,** 763 (1939); D. M. Wrinch and I. Langmuir, THIS JOURNAL, **60,** 2247 (1938); I. Langmuir and D. Wrinch, *Nature,* **142,** 581 (1938)] is a sufficiently close approximation for the determination of the signs of the structure factors. If the latter assumption is correct, the density at each point of the projection is a sort of average of that at the same point in the true structure and that at another point the same distance on the opposite side of the origin.

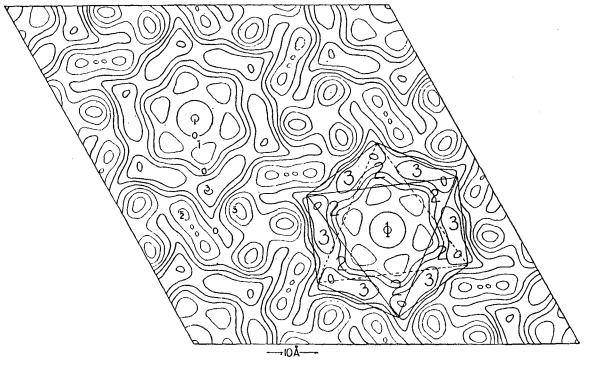

Fig. 1.—Election density projection on (0001), assuming a center of symmetry and that the structure factor signs are as calculated for simplified C_2 octahedron molecules, oriented as indicated.

This projection is here reproduced (Fig. 1), with a projection of Wrinch's "C_2 octahedron," oriented as she has assumed, superimposed. The numbers 1, 2 and 3 designate areas for which one would expect low, medium and high densities, respectively. With a slight change in orientation, the fit is not bad.

It would seem at first that this electron density projection lends support to the hypothesis of a cage or ring molecule or ion of about the size postulated by Wrinch. However, the chief features of the projection depend on the model assumed in deducing the signs of the structure factors. If, for this purpose, one postulates a molecule composed of six point atoms at corners of a regular octahedron, the resultant projection (Fig. 2) shows no indication of a cage structure.

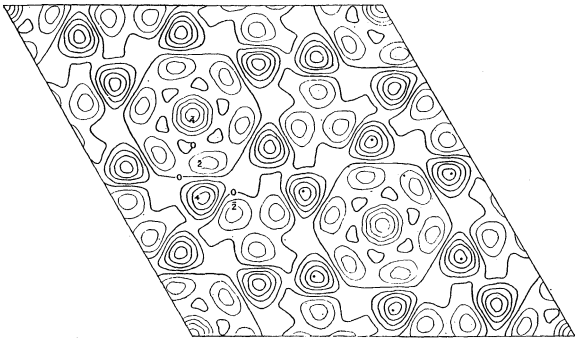

Fig. 2.—Same, except that the structure factor signs are assumed to be as calculated for molecules consisting of six point atoms, distributed as indicated by the dots.

Projections of this sort may prove useful in testing minor features of proposed structures and in suggesting modifications. For example, from Fig. 1 one can deduce that, if the structure contains cage ions even roughly resembling the C_2 cyclol model, the metal ions (Zn) are not at the midpoints of the centerlines joining adjacent cages.

KODAK RESEARCH LABORATORIES MAURICE L. HUGGINS
ROCHESTER, N. Y.

RECEIVED AUGUST 2, 1939

CELLS WITHOUT TRANSFERENCE FOR *p*H DETERMINATION

Sir:

Although methods of routine *p*H-determination have developed rapidly during the last few years, cells with liquid junctions, abandoned in most research work long ago, are still in use. In order to eliminate this source of experimental and theoretical inconvenience Hamer[1] suggested cells of the type

$$H_2, H^+X^- + NaCl, AgCl,Ag$$

The concentration of the sodium chloride added to the solution must, of course, be known and allowed for in calculating the hydrogen ion activity.

For the same purpose we had examined cells of the type

$$H_2, H^+X^- + TlBr(satd.), AgBr, Ag$$

before we had knowledge of Hamer's paper. The solubility of thallous bromide (0.00257 mole per 1000 g. of water at 30°) is high enough to secure a definite potential not influenced by common impurities. On the other hand, the solubility is so low that the activity of the hydrogen ion is practically not altered and the liquid junction potential between a solution containing no thallous bromide and a solution saturated with this salt may be neglected safely. Even this liquid junction might be avoided by saturating with thallous bromide that portion also of the solution which is in contact with the hydrogen electrode.

The applicability of this type of cell is restricted, of course, to solutions which do not form any precipitate when saturated with thallous bromide and do not contain thallous or bromide ions in an amount comparable with the solubility of this salt. In such a case, however, another reference electrode of similar kind may be used, for instance, some organic zinc salt in connection with zinc amalgam or silver sulfate with silver etc.

Applying the usual formula one may obtain from the e. m. f. the quantity $a_{H^+}(\gamma_{Br^-}/\gamma_{Tl^+})^{1/2}$ which is in any case identical with the hydrogen ion activity as far as the principle of ionic strength is valid. In this respect too the method compares not unfavorably with others. This type of cells might prove the most convenient basis of *defining* the term "hydrogen ion activity," which is well known to be arbitrary to some extent.[2]

As we were compelled to interrupt our work on various methods of routine *p*H determination, we wish to offer this suggestion.

(1) W. J. Hamer, *Trans. Electrochem. Soc.*, **72**, 45 (1937).

(2) D. I. Hitchcock [THIS JOURNAL, **58**, 856 (1936)] suggested a different definition of *p*H on the basis of cells without liquid junction and discussed another suggestion made by Scatchard. The general idea of single ionic activities, introduced by Lewis and Randall, has been exhaustively discussed by E. A. Guggenheim (*J. Phys. Chem.*, **34**, 1758 (1930), and previous papers).

BERKELEY, CALIF. OTTO REDLICH
SHANGHAI, CHINA HANS KLINGER

RECEIVED JULY 5, 1939

NEW BOOKS

Methodik der Hormonforschung. (Methods of Hormone Investigation.) By Dr. Phil. Habil. CHRISTIAN BOMSKOV. **Ovar (Follikelhormone, Gelbkörperhormon), Hoden, Hypophysenvorderlappen.** [Ovary (Follicular Hormone, Corpus Luteum Hormone), Testis, Anterior Pituitary.] Georg Thieme Verlag, Rossplatz 12, Leipzig C 1, Germany, 1939. xxix + 1016 pp. 274 figs. 18 × 27 cm. Price, RM. 89; bound, RM. 91.

The work under review forms a second instalment to the volume which bears the same title, noticed in these columns in September 1937 (p. 1771). In the author's view, the subjects here considered constitute the most modern and successful chapters of endocrinology. They are: estrogenic hormones (264 pages), hormones of corpus luteum (72 pages), androgenic hormones (202 pages), hypophyseal hormones (gonadotropic 280 pages, growth-stimulating 41 pages, thyreotropic 61 pages, lactogenic 23 pages, diabetogenic 7 pages, others of doubtful existence 22 pages). Of these, only the sex hormones at present offer extensive possibilities for chemical consideration.

As in the first volume, the author has performed his onerous task with conscientious thoroughness, and has prepared a survey notable for catholicity rather than critical selectivity. The compilation as a whole suffers at times from a certain lack of balance. For example, two whole pages are dedicated to a detailed description of Butenandt's procedure for the isolation of estrone from palm kernel oil, whereas reference to studies on the effects of sex hormones on the metabolism of cholesterol and of carbohydrate is dismissed in a few lines of literature citations, without a hint as to the nature of these effects.

Typographical errors are relatively scarce, but a few

stand out, particularly among the structural formulas of the androgens. In this connection the hope may be expressed that in future editions the systematic nomenclature of the steroids will be critically scrutinized for inconsistencies, and that the admirable stereochemical terminology proposed by Fieser[1] will be adopted.

However, in a work of this character, susceptibility to criticism of detail is inevitable, and investigators in the hormone field can only be grateful to the author for collecting in one place the wealth of detailed anatomical and physiological information otherwise obtainable only by wearisome search through a scattered literature. A smaller supplement is promised, which is to include "hormone-like" substances such as the anti-anemic principle of liver and the physiologically active compounds of the posterior lobe of the pituitary.

(1) Fieser, "A Supplement to The Chemistry of Natural Products Related to Phenanthrene," 1937, p. 398, Reinhold Publishing Corp., New York.

H. T. CLARKE

Ions, Electrons, and Ionizing Radiations. By JAMES ARNOLD CROWTHER, Sc.D., F.Inst.P., Professor of Physics in the University of Reading, Sometime Fellow of St. John's College, Cambridge. Seventh edition. Longmans, Green and Company, Inc., 114 Fifth Avenue, New York, N. Y., 1939. xi + 348 pp. 117 pp. 15 × 22.5 cm. Price, $4.00.

The titles of the different chapters are as follows: I, Introduction; II, The Passage of a Current through an Ionized Gas; III, The Properties of the Gaseous Ions; IV, The Charge on an Ion; V, Ionization by Collision—The Spark Discharge; VI, The Phenomena of the Discharge Tube; VII, Cathode Rays and Positive Rays; VIII, Emission of Electricity by Hot Bodies; IX, Photo-Electricity; X, X-Rays; XI, The α-Rays; XII, The β- and γ-Radiations; XIII, Neutrons, Positrons, Cosmic Radiation; XIV, The Physics of the Nucleus; XV, The Structure of the Atom; XVI, Radioactive Changes; XVII, Radium and its Products.

While the section on cosmic rays and the chapter on the nucleus have been rewritten and very considerably enlarged, it is to be regretted that this procedure has not been used in connection with the other chapters. The result is that many important general references to more recent literature have been omitted, and in some cases statements in one section, copied from previous editions, have not been modified to agree with those made in another section, which are based on the results of more recent investigations. This criticism applies especially to statements about the value of e, the charge on the electron.

The Bohr–Sommerfeld model of the atom is discussed in some detail, but in spite of the fact that the experiments on electron diffraction are mentioned (rather briefly, and not in the same chapter) the author has dismissed the wave mechanical treatment of atomic structure as "beyond the scope of this volume." A discussion of the "electron cloud" model would have added considerably to the value of the book, especially since it can be done without the use of any difficult mathematics. Furthermore, such a discussion would have helped to clarify the remarks on the wave mechanics interpretation of nuclear phenomena given in Chapter XIV.

Since the book is frankly intended to be an elementary introduction to the field of atomic physics, the author is to be commended for his clear and concise description of the methods used in the determination of fundamental physical constants and of the experiments upon which are based our present concepts in atomic physics. However, it would seem to the reviewer that the whole presentation could have been improved considerably by a rearrangement of the material. For instance, the chapter on atomic structure would logically follow that on X-rays. Moreover, certain sections in some chapters could have been inserted, with much better effect, in other chapters.

The binding and printing of the book are fine, and with the exception of inconsistencies in numerical values, mentioned above, there are very few misprints or errors, as far as the reviewer could find.

SAUL DUSHMAN

Pharmacie Galénique. (Galenic Pharmacy.) By A. GORIS and A. LIOT. Volumes I–II. Masson et Cie., Éditeurs, 120 Boulevard Saint-Germain, Paris VI, France, 1939. xvi + 1917 pp. Illustrated. 17 × 25 cm. Price, fr. 390; bound, fr. 450.

The comprehensive scope of this work can best be realized from the chapter headings, which are:

Vol. I. History of Pharmacy
- Medicaments, Aliments, Poisons, Selection and Preservation of Crude Drugs
- Composition of Vegetable Substances
- Assay of Drugs and Pharmaceutical Preparations
- Medicaments Prepared from Substances in their Natural State without any Previous Treatment
- Medicaments Obtained after Previous Treatment of the Crude Drugs
- Medicaments Obtained by Division
- Operations Employing Heat
- Operations Employing a Solvent

Vol. II. Medicaments obtained by Solution and Evaporation
- Soluble Ferments
- Organotherapy (Endocrine Glands)
- Vaccinotherapy
- Serotherapy
- Bacteriotherapy (fermented milk, yeast, etc.)
- Pharmaceutical Preparations Devised to Mask the Taste of the Medicaments Administered in Definite Dosage
- Medicaments to be Applied to the Mucous Membrane
- Medicaments for External Use
- Dressings (for wounds)
- Sterilization
- Disinfection
- Administration and Action of Medicaments, Incompatibilities
- Alteration and Preservation of Medicaments

From the above chapter headings it is readily seen that these volumes include much more than Galenical Pharmacy

which the title indicates. As stated in the preface, the authors have purposefully omitted bibliographies on the various subjects as the treatise is intended for students and pharmacists rather than the research worker.

The authors have drawn upon commercial pharmaceutical companies and hospitals for many of their illustrations of apparatus. Their illustrations (microscopic) of powdered vegetable drugs are excellent. The illustrations of the endocrine glands in color are also very good.

In general, the subject matter does not adhere as closely to the preparations of the Codex as seems to be the practice of most similar American texts in respect to the U. S. P. and N. F.

The presentation of the chemical relationship of various types of compounds is a very desirable feature. Thus the chemical similarity of the sex hormones, the chemical relation of vitamin A to carotene, the chemical formulas for the cardiac glycosides and the ergot alkaloids serve as examples. However, in the case of the last-named group of compounds, the discoverer of ergostetrine is given as John Hopkins instead of Marvin R. Thompson.

The discussion of the vitamins is excellent but may be criticized from the standpoint of not being entirely up-to-date. Thus no mention is made of vitamin B_6, or the identity of the pellagra-preventative factor with nicotinic acid. Under vitamin D, the reader is given the impression that irradiated ergosterol is practically the only source of this vitamin. No mention is made of the various dehydro derivatives of cholesterol which are now definitely known to have marked antirachitic properties.

The reviewer feels that these volumes furnish an excellent text for students of pharmacy and a good reference for practicing pharmacists with the exception of at least one phase of the subject, *viz.*, the vitamins, in which they are not up-to-date.

F. W. HEYL

Gärungschemisches Praktikum. (Experimental Fermentation Chemistry.) Second edition. By Dr. CONRAD BERNHAUER, Professor in the German University in Prague. Verlag von Julius Springer, Linkstrasse 22–24, Berlin W 9, Germany, 1939. xx + 317 pp. 40 figs. 14.5 × 22.5 cm. Price, RM. 15; bound, RM. 16.50.

Introduction of new material and new references has made the second edition 68 pages longer than the first. The main portion of the book consists of fifty-six fermentation experiments on yeasts, bacteria, and molds. Methods for isolation and quantitative determination of fermentation products and intermediary compounds are given. Qualitative and quantitative experiments on the alcoholic, lactic, propionic, butyl, and cellulose fermentations are included. Oxidative fermentations by the acetobacter group and by the molds are well covered. Directions are given for the isolation and culture of many of the organisms used. The probable mechanism of each of the fermentations also is discussed. The literature references are pertinent and fairly complete.

An introduction, a chapter on methods, and an appendix deal with general chemical and bacteriological methods and with industrial aspects of fermentation.

While the book as a whole contains much more practical information than any other work on fermentation of comparable size, it is, of course, not free from errors. Many of these obviously result from describing, as laboratory experiments, procedures which have been taken almost bodily from the literature and have not been tested as laboratory exercises. For example, on page 165 the directions for ether extraction of lactic acid say merely that 100 cc. of culture is to be extracted with ether. Only the well-informed reader will know the *p*H, method, and time of extraction. In the experiment on the ethyl alcohol–acetone fermentation (page 204) the reader is told to determine ethyl alcohol by oxidation to acetic acid, but nowhere in the book is such a method described.

In addition there are many cases where improper procedures are specified. A few examples will be given from the experiment on the acetone–butyl alcohol fermentation (Experiment 29). Fermentation gases for analysis are collected over carbon dioxide-saturated water. Since the fermentation gas contains approximately 40% hydrogen, roughly 40% of this dissolved carbon dioxide will be carried out by the evolved gases. In Experiment 29a, this error would make the apparent volume of carbon dioxide produced about 35% too high.

Acetylmethylcarbinol is determined on a distillate which contains only 80% of the total quantity of this product. The statement is made that under the conditions of the acetone determination, acetylmethylcarbinol reacts with 16 atoms of iodine, whereas the correct value is 6 atoms. In the exercise on isopropyl alcohol formation, grain mash is used as a medium. The reviewer knows of no isopropyl alcohol-forming organism that will grow well on such a medium.

The book is a valuable addition to the literature of fermentation, and presents in convenient form a large number of procedures and numerous references which should be very useful to the fermentation chemist. The experimental procedures given are reliable in outline, but the reader is cautioned against applying them without first consulting the original literature.

M. J. JOHNSON

Micromethods of Quantitative Organic Elementary Analysis. By JOSEPH B. NIEDERL, Ph.D., Associate Professor of Chemistry, and VICTOR NIEDERL, Teaching Fellow, New York University, Washington Square College. John Wiley and Sons, Inc., 440 Fourth Avenue, New York, N. Y., 1938. xvi + 267 pp. 53 figs. 15.5 × 24 cm. Price, $3.00.

The statement taken from the preface that "this book is primarily a laboratory manual for teaching and practicing the methods of quantitative organic microanalysis of pure organic compounds under ordinary laboratory conditions" makes clear the purpose of this book, and the following chapter headings will indicate its scope. The Microchemical Balance; Weighing on a Microchemical Balance; Miscellaneous Weighing Equipment; Miscellaneous Laboratory Utensils; Preparation and Weighing of a Sample for Analysis; Determination of Metals and Residues; Determination of Neutralization Equivalent; Volumetric Determination of Aminoid Nitrogen; Gasometric Determination of Nitrogen; Determination of Carbon and Hy-

drogen; Determination of Halogens; Determination of Sulfur; Determination of Phosphorus; Determination of Arsenic; The Determination of the Molecular Weight by (1) The Ebullioscopic Method (2) The Cryoscopic Method (3) The Vaporimetric Method and (4) The Osmotic Method; Determination of Alkoxy and Alkimide Groups; Determination of Acetyl Groups; Determination of Active Hydrogen; The Teaching of Quantitative Elementary Organic Microanalysis; Installation of a Laboratory for Organic Microanalysis; General Microchemical Literature and Calculations.

Organic microanalysts should be grateful to the authors for their inclusion and extension of the Nitrogen Reduction Table of Küster-Thiel. The measurement of nitrogen is often carried out above the temperature of 24°, the upper limit of the Küster-Thiel tables, consequently the extension of the table to 36° is particularly welcome.

The present book, together with the English translation of the latest edition of Pregl, should do much to spread the use of microanalytical methods in organic chemical laboratories.

W. M. LAUER

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August 15, 1939 to September 15, 1939

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FRANK O. ELLENWOOD AND CHARLES O. MACKEY. "Vapor Charts and Special Tables for Turbine Calculations." John Wiley and Sons, Inc., 440 Fourth Ave., New York, N. Y. 43 pp.

L. ERHARD, Editor. "Blätter für Technikgeschichte." Sechtes Heft. Verlag von Julius Springer, Linkstrasse 22–24, Berlin W 9, Germany. 82 pp. RM. 4.

CHARLOTTE A. FRANCIS AND EDNA C. MORSE. "Fundamentals of Chemistry and Applications." The Macmillan Company, 60 Fifth Avenue, New York, N. Y. 542 pp. $3.00.

GEORGE R. HARRISON, Editor. "Wave Length Tables." The Technology Press (M. I. T.): John Wiley and Sons, Inc., 440 Fourth Avenue, New York, N. Y. 429 pp. $15.00.

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THOMAS P. MCCUTCHEON, HARRY SELTZ AND J. C. WARNER. "General Chemistry. Theoretical and Descriptive." Third edition. D. Van Nostrand Co., Inc., 250 Fourth Ave., New York, N. Y. 685 pp. $3.75.

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ALEXANDER SILVERMAN AND ABRAHAM L. ROBINSON. "Selective Experiments in General Chemistry." D. Van Nostrand Co., Inc., 250 Fourth Ave., New York, N. Y. 310 pp. $2.50.

FOSTER DEE SNELL AND CORNELIA T. SNELL. "Chemicals of Commerce." D. Van Nostrand Co., Inc., 250 Fourth Ave., New York, N. Y. 542 pp. $5.00.

MARY ELVIRA WEEKS. "The Discovery of the Elements." Fourth edition. Journal of Chemical Education, 20th and Northampton Sts., Easton, Pa. 470 pp. $3.00.

HARRY BOYER WEISER. "Colloid Chemistry. A Textbook." John Wiley and Sons, Inc., 440 Fourth Ave., New York, N. Y. 428 pp. $4.00.

G. H. WHITEFORD AND R. G. COFFIN. "Essentials of College Chemistry." Second edition. The C. V. Mosby Co., 3523 Pine Blvd., St. Louis, Mo. 534 pp.

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"Standard Methods for the Sampling and Analyzing of Aluminum and Certain Aluminum Alloys." Aluminum Research Institute, 308 West Washington St., Chicago, Ill. 31 pp.

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[CONTRIBUTION FROM THE DEPARTMENT OF PHYSICS OF THE UNIVERSITY OF FLORIDA]

The Oscillation Frequencies of Nitrites

BY DUDLEY WILLIAMS

In a recent article Penney and Sutherland[1] have surveyed the existing data on the vibrational frequencies of triatomic molecules and triatomic groups occurring in more complex molecules and have determined force constants and angles by the valence-force-field and central-force-field approximations. A comparison of results obtained through these approximations with the results obtained in cases where more detailed analyses were possible, showed that in the majority of cases the valence-force-field is more satisfactory than the older approximation involving central forces. Values for the angles as obtained by the valence-force method agreed with the accepted values to within 10%, while the discrepancies in the values obtained by the central-force method were sometimes larger.

However, in the case of the nitrite ion neither approximation gave satisfactory values for the force constants. It was found that the valence-force-field equation for the angle had no real solution. Although the central-force-field equations gave a reasonable value for the angle, they yielded improbable values for the force constants, the oxygen–oxygen force constant appearing larger than the nitrogen–oxygen force constants. Since the valence-force approximation gave satisfactory results for other triatomic systems with the same number of valence electrons, Penney and Sutherland suggested that further experimental work on the nitrites might be desirable.

(1) W. G. Penney and G. B. B. M. Sutherland, *Proc. Roy. Soc.* (London), **156**, 654 (1936).

It was the object of the present investigation to obtain additional data on the oscillation frequencies of the nitrites through a study of their infrared spectra in the region of the fundamentals. Previous studies of the infrared absorption of nitrites have been made by Maslakowez[2] and by Bailey and Thompson,[3] while Raman studies of nitrites have been reported by Langseth and Welles,[4] by Carrelli, Pringsheim and Rosen,[5] by Bar,[6] and by Dadieu, Jele, and Kohlrausch.[7] The results obtained by these authors are summarized in Table I.

The experimental methods employed in the present study are essentially the same as those reported previously.[8] Solutions of sodium nitrite and potassium nitrite (3 N) were studied and the results obtained are shown in Fig. 1. In this figure the "relative absorption factors" as defined in the previous article[8] are plotted as a function of wave length.

As one may see from the figure, three absorption maxima were observed in the spectrum of each nitrite. In the spectrum of sodium nitrite the positions of the maxima are 7.6, 8.2, and 13.3 μ, while the potassium nitrite bands appear at 7.7, 8.2, and 13.4 μ. The shapes of the absorption

(2) I. Maslakowez, *Z. Physik*, **51**, 696 (1928).

(3) C. R. Bailey and J. W. Thompson, *Nature*, **135**, 915 (1935).

(4) A. Langseth and E. Welles, *Z. physik. Chem.*, **B27**, 209 (1934).

(5) A. Carrelli, P. Pringsheim and B. Rosen, *Z. Physik*, **51**, 511 (1928).

(6) R. Bar, *Nature*, **124**, 692 (1929).

(7) A. Dadieu, F. Jele and K. W. F. Kohlrausch, *Wien. Ber.*, **140**, 293 (1931).

(8) D. Williams and L. Decherd, THIS JOURNAL, **61**, 1382 (1939).

TABLE I

PREVIOUS STUDIES OF THE NITRITE GROUP

Observed frequencies, cm.$^{-1}$	Compounds	Method	Observer
1380 1240	Potassium nitrite crystal	Infrared	Maslakowez
1330 1392 1127 and 1220 707 834	Sodium nitrite crystal	Infrared	Bailey and Thompson
1331 1240 813	Sodium nitrite solution	Raman	Langseth and Welles
2151 1303 785 696	Sodium nitrite solution	Raman	Carrelli, Pringsheim, and Rosen
1333	Powdered sodium nitrite	Raman	Bar
1324 1220 814 715 655 588	Sodium nitrite solution	Raman	Dadieu, Jele, and Kohlrausch

bands of the two solutions are similar except in the case of the low-frequency band. The sodium nitrite band at 13.3 μ has an asymmetry not observed in the corresponding potassium nitrite band; the reason for this difference is not clear. As the three bands shown are the only ones observed between 5 and 16 μ, it is assumed that they arise from fundamental vibrations of the nitrite group. The two sets of fundamentals arising in the crystal reported by Bailey and Thompson[3] apparently are replaced by a single set when the nitrite ion is in solution. The agreement between the present data and the infrared data of Bailey and Thompson seems better than the agreement between independent Raman investigations. Two Raman lines for solutions (814 and 655 cm.$^{-1}$) apparently have no counterparts in the infrared spectrum.

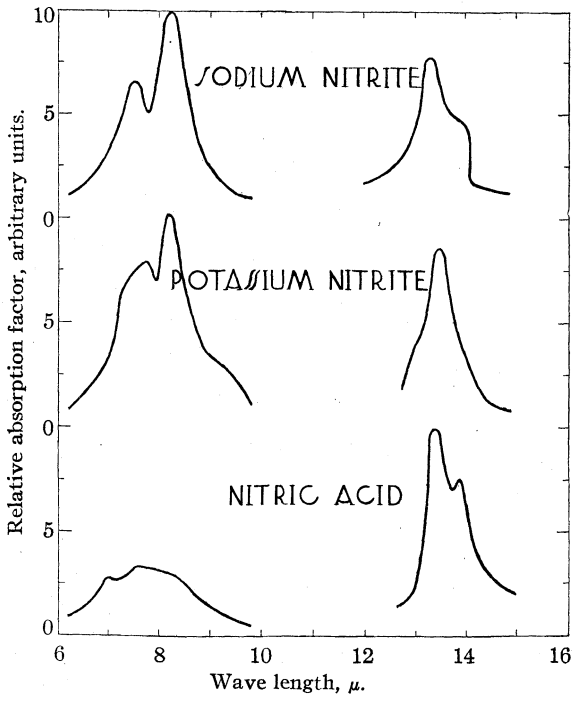


Fig. 1.

In assigning the observed frequencies to the normal vibrations of the nitrite ion there are essentially only two possible choices as it is probable that the lowest frequency arises from the "bending" vibration ν_2. Since the other frequencies are so nearly equal, there is no obvious choice for ν_1, the "central" vibration, and ν_3, the "nonsymmetrical" vibration. Therefore, it was decided to test both the assignments given below in the equations arising from the valence-force and central-force fields.

	ν_1	ν_2	ν_3
Assignment I	1320	750	1220
Assignment II	1220	750	1320

Frequencies are given in cm.$^{-1}$

The valence-force-field relations in the form used in the present work are

$$k_{NO} = mM\nu_3^2/(M + 2m\sin^2\alpha/2) \quad (1)$$

$$k_\alpha = m\nu_1^2\nu_2^2 d_{NO}^2 (M + 2m\sin^2\alpha/2)/\nu_3^2(M + 2m) \quad (2)$$

$$m(\nu_1^2 + \nu_2^2) = [k_{NO}(M + 2m\cos^2\alpha/2)/M] + [K\alpha(M + 2m\sin^2\alpha/2)/M\,d_{NO}^2] \quad (3)$$

where m is the mass of the oxygen atom, M is the mass of the nitrogen atom, α is the angle at the nitrogen, d_{NO} is the nitrogen–oxygen internuclear distance, and the k's are the indicated force constants. From these equations α can be determined by means of a cubic equation in the square of the sine of the half angle. When the observed frequencies are introduced, it is found that neither I nor II gives a real solution for the angle, a result indicating that the valence-force-field is an unsatisfactory approximation for the nitrite group. However, it was decided to assume angles of reasonable magnitude and use these in determining k_{NO} and k_α from (1) and (2). Since other similar groups were found by Penney and Sutherland[1] to have angles between 90 and 130°, these limiting angles were used. The value of 1.13 Å. for d_{NO} is taken from the X-ray data of Zeigler,[9]

(9) G. E. Zeigler, *Phys. Rev.*, **38**, 1040 (1931).

who gives 130° as the value for α in sodium nitrite crystals. The results obtained with the valence-force-field are shown below:

	Assumed angle	k_{NO} dynes/cm.	k_α dyne-cm./radian
Assignment I	90°	6.6×10^5	5.3×10^{-11}
	130°	4.8	7.4
Assignment II	90°	7.9	3.6
	130°	5.8	5.0

The values for k_{NO} are all considerably lower than the corresponding values for other comparable groups, while the values for k_α are all considerably higher. The use of Assignment II and 90° seems to give results more nearly similar to the values obtained for the other groups studied by Penney and Sutherland. However, since the equations yield no real values for α, little emphasis can be placed on this choice.

The central-force-field relations used in the present study are

$$k_{NO} = m\nu_3^2/[1 + (2m/M)\sin^2\alpha/2] \quad (4)$$

$$k_{OO} = mM\nu_1^2\nu_2^2[1 + (2m/M)\sin^2\alpha/2]/2\nu_3^2(M + 2m)\cos^2\alpha/2 \quad (5)$$

$$m(\nu_1^2 + \nu_2^2) = 2k_{OO} + k_{NO}[1 + (2m/M)\cos^2\alpha/2] \quad (6)$$

where the symbols have the same significance as in the first set of equations. When the Assignments I and II are introduced, it is found that I yields two real solutions for α, 86 and 100°, while II leads to no real solutions. Use of Assignment I with the two values for α leads to the following values for the force constants:

	Angle	k_{NO}, dynes/cm.	k_{OO}, dynes/cm.
Assignment I	86°	6.9×10^5	4.3×10^5
	100°	5.9	5.5

Since it is to be expected that k_{NO} is considerably greater than k_{OO}, the α value 86° seems to be the better choice.

Although 86 and 100° are the angles obtained from the central-force-field equations, the angle as determined from X-ray measurements[9] is 130°. Therefore a computation of force constants was made with this angle substituted in (4) and (5). The results are as follows:

	Assumed angle	k_{NO} dynes/cm.	k_{OO} dynes/cm.
Assignment I	130°	4.9×10^5	16.2×10^5
Assignment II[a]	130°	5.8	10.8

[a] When an angle of 90° is assumed, Assignment II gives the force constants: $k_{NO} = 8.0 \times 10^5$, $k_{OO} = 2.8 \times 10^5$ dynes/cm.

Since k_{OO} in each case is much larger than k_{NO}, it is believed that 130° is too large an angle, if the actual force field of the nitrite group at all resembles the central-force approximation. As stated above, Zeigler's X-ray studies were made with sodium nitrite crystals, and it is possible that the angle undergoes a considerable change when the salt is dissolved.

Summarizing the above results, one finds that neither assignment of frequencies is wholly satisfactory on the basis of a valence-force approximation, but that the assumption of an angle of 90° leads to more satisfactory values than the 130° angle obtained from X-ray measurements. With the central-force approximation, Assignment I gives 86° as the value of the angle. Force constants computed for this angle are satisfactory, whereas those based on an angle of 130° are unsatisfactory. Comparison of the force constant k_{NO} with the corresponding force constant of comparable molecules shows that it is relatively smaller, while the constant k_{OO} is relatively greater. Table II gives a comparison of nitrogen dioxide, the nitro group, and the nitrite ion.

TABLE II

CHARACTERISTIC FREQUENCIES, FORCE-CONSTANTS, AND VALENCE ANGLES IN NO_2 GROUPS

Group	ν_1 cm.$^{-1}$	ν_2 cm.$^{-1}$	ν_3 cm.$^{-1}$	α	k_{NO} 10^5 dynes/cm.	k_{OO} 10^5 dynes/cm.
Nitrogen dioxide	1370	640	1620	109°	9.78	3.15
The nitro group	1380	480	1560	106°	9.50	1.56
The nitrite ion	1320	750	1220	86°	6.87	4.31

The last curve in Fig. 1 represents the absorption spectrum of a 65% solution of nitric acid. One might expect the spectrum of this solution to show a marked similarity to the spectra of the nitrates reported previously.[8] Actually, the observed spectrum shows more similarity to the nitrite spectra than to those of other nitrates. Concentrated nitric acid solutions have a region of absorption extending from 6 to 9 μ, and there is evidence of several unresolved bands in this region. It is probable that a part of this absorption may arise from vibrations of the undissociated nitric acid molecule. Raman data which are in agreement with this hypothesis have been reported by Dadieu, Jele, and Kohlrausch,[7] who suggest that the nitric acid molecule has the form HO·NO_2, where the NO_2 group has inner vibrational frequencies of 454, 1300, and 1625 cm.$^{-1}$, the corresponding frequencies of nitro groups in ali-

phatic compounds being 480, 1380, and 1560 cm.$^{-1}$. If this interpretation is correct, the complex absorption bands observed near 13.4 μ may arise from an outer vibration involving OH and NO_2 groups. Although the spectrum of nitric acid has no direct connection with the nitrites, it was included in the present paper, since it can possibly be interpreted in terms of a related NO_2 group.

Summary

The infrared absorption spectra of sodium nitrite and potassium nitrite have been studied between 6 and 16 μ and absorption bands have been observed at 7.6, 8.2, and 13.3 μ. These bands are interpreted as arising from fundamental vibrations of the nitrite group. Force constants and valence angles of the nitrite group are computed by means of the central-force-field approximation. The valence-force-field proves to be an unsatisfactory approximation for the nitrites. The spectrum of nitric acid is discussed.

GAINESVILLE, FLORIDA RECEIVED AUGUST 25, 1939

[CONTRIBUTION FROM THE DIVISION OF INDUSTRIAL AND CELLULOSE CHEMISTRY, MCGILL UNIVERSITY]

Viscosity Relationships of Aqueous Solutions of Sodium Oleate and Various Phenols

BY RALPH G. D. MOORE[1]

Weichherz and Saechtling[2,3] in a viscometric investigation of the system sodium oleate–phenol–water observed the occurrence of viscosity maxima at certain ratios of sodium oleate to phenol, indicating the formation of complexes between these substances. The authors did not consider them to be definite chemical compounds, but rather a loose association of the soap micelle with the phenol. The present paper presents a more extended study of this phenomenon, with the object of ascertaining how far it is characteristic of phenolic substances.

Attempted verification of some of Weichherz and Saechtling's results showed general qualitative agreement but considerable quantitative discrepancy, the present values for viscosities, especially in the region of lower water content, being without exception higher, sometimes of another order altogether. Comparison of the viscosities of solutions of sodium oleate prepared from oleic acid of varying degrees of purity (*cf.* Table II, expts. 1, 2, 3, 4) indicates that the cause of this lack of agreement lies in the relative degree of purity of the two specimens of sodium oleate in question, since Weichherz and Saechtling used Kahlbaum "reinst" (I), while the present author used samples (II) prepared from oleic acid which had been purified rigorously by a method analogous to that later described by Brown and Shinowara.[4] Illustrative of these discrepancies are the following examples.

Solutions of a concentration of 10% or higher in sodium oleate II were found to be metastable at 20°, slowly increasing in viscosity and finally crystallizing, in striking contrast to the reported investigations of Weichherz and Saechtling on solutions containing up to 30% sodium oleate. In a similar manner the viscosities obtained in the present investigation for the ternary system containing phenol were higher than the corresponding values of Weichherz and Saechtling, the former showing, for 90% water content, a maximum of over 1000 cp. at 20°, while in the case of the latter the value was about 17. For the system with 95% water the latter investigators could find no maximum, whereas in the present work the maximum at this concentration was well marked. In addition, the acid soap separation reported by the earlier investigators for this system was not observed, even after keeping the solution for several days. This heterogeneity was only observed (together with the absence of maxima in the viscosity isotherms) when the solutions containing 97% water were examined.

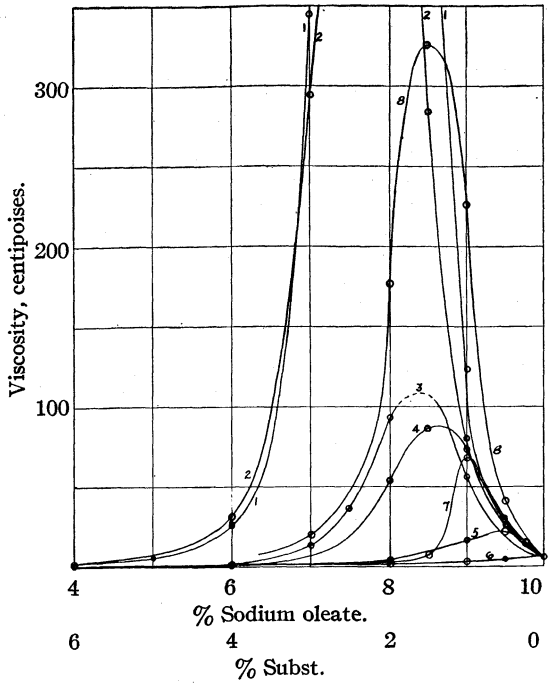
In order to determine whether the ability to cause maxima in the viscosity–concentration isotherms of sodium oleate solutions is a property common to all phenols, the following carefully purified materials have been examined: guaiacol, *p*-cresol, creosol, catechol, resorcinol, *p*-hydroxybenzyl alcohol, vanillyl alcohol, *o*-bromophenol.

(1) Rayonier Pulp and Paper Company Post-Doctorate Research Fellow, 1936–37. Present address: Arthur D. Little, Inc., Cambridge, Mass.

(2) Weichherz and Saechtling, *Kolloid Z.*, **60**, 192 (1932).

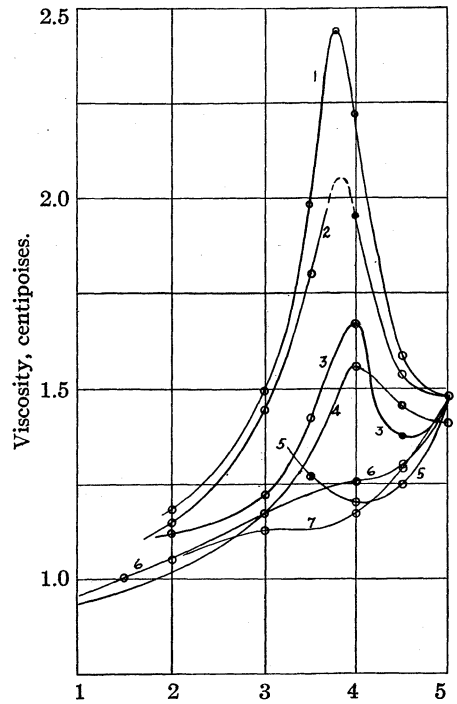
(3) *Ibid.*, pp. 298–306.

(4) Brown and Shinowara, THIS JOURNAL, **59**, 6 (1937).



Percentage by weight of phenolic substance or sodium oleate.

Fig. 1.—Viscosity isotherms at 30° of sodium oleate–phenolic substance–90% water: 1, *p*-cresol; 2, creosol; 3, guaiacol; 4, phenol; 5, resorcinol; 6, vanillyl alcohol; 7, *o*-bromophenol; 8, catechol.



Percentage by weight of phenolic substance or sodium oleate.

Fig. 2.—Viscosity isotherms at 30° of sodium oleate–phenolic substance–95% water: 1, *p*-cresol; 2, creosol; 3, guaiacol; 4, phenol; 5, catechol; 6, vanillyl alcohol; 7, resorcinol.

In addition, a few measurements were made at critical concentrations on vanillin and *p*-hydroxybenzaldehyde. The results of this investigation are to be found in Table II. A comparison of the various substances is given in Figs. 1 and 2, in which the 30° isotherms are selected as being more accurate and eliminating to a large extent the difficulty occasionally encountered in obtaining equilibria at 20° within a reasonable time.

Of all the materials examined, *p*-cresol showed the most marked effect, maximum viscosity at 20° of the system containing 90% water being in the neighborhood of 100–200 poises. As shown by the curves for guaiacol and creosol the effect of introducing a methoxyl group ortho to the hydroxyl was very slight, shifting the position of the maximum slightly to the left of the maximum for the corresponding unmethoxylated phenol, but not affecting the height of the maximum to a very marked extent.

The above four substances produced outstanding effects on the viscosity of sodium oleate solutions containing both 90 and 95% water. In the case of the solutions containing 90% water the effect of catechol was of the same order, but the maximum caused by its isomer resorcinol was much smaller, besides being displaced toward the sodium oleate axis. The same was true for *o*-bromophenol. At 95% water content, on the other hand, none of these compounds caused a maximum in viscosity.

The other phenols investigated, such as vanillyl alcohol, *p*-hydroxybenzyl alcohol, vanillin and *p*-hydroxybenzaldehyde (Table II, expts. 98–102) showed no sign of a maximum even at 90% water content. It is thus clear that the property under investigation is not common to all substances containing a phenolic hydroxyl group.

Regarding the cause of the maxima, little can be added to the speculations of Weichherz and Saechtling.[2] An interesting comparison is obtained by an examination of the electrolytic dissociation constants of some of the phenols used, as given in the "International Critical Tables" (Table I). While complete agreement between the order of the constant and the occurrence and size of the viscosity maxima does not exist, it

appears that the greater the degree of electrolytic dissociation of the phenol, the less is the effect produced on the viscosity–concentration isotherms of sodium oleate–water systems.

TABLE I

ELECTROLYTIC DISSOCIATION CONSTANTS[5]

Substance (Order of decreasing effect on viscosity isotherms)	$K_{25°}$
Phenol	1.06×10^{-10}
p-Cresol	1.1×10^{-8}
Catechol	3.2×10^{-10}
Resorcinol	6×10^{-7}
(*o*-Chlorophenol	3.6×10^{-8})
p-Hydroxybenzaldehyde	1.63×10^{-6}
Vanillin	4.72×10^{-6}

This observation does not support the theory advanced by Weichherz and Saechtling, namely, that the formation of acid soaps, which in the more dilute solutions is preceded by the phenomenon of a maximum viscosity, is a minor cause of the latter. For if the effect produced varies *inversely* as the acidity of the phenols, other things being equal, the formation of acid soaps cannot be a contributory factor to the occurrence of maxima.

Since this work was carried out, an article has appeared by Angelescu and Ciortan[6] which describes the effect of the three isomeric cresols on the viscosity of sodium stearate solutions. The phenomena observed were similar to those which form the basis of the present paper, in that all three isomers caused maxima in viscosity which were affected greatly by the temperature. The authors correlate the observed phenomena with the dielectric constants and electric moments of the three cresols.

Experimental

Apparatus.—Few changes were made in the apparatus of Weichherz and Saechtling.[3] For the thermostat, manual control of electrolytic heating (1% lead acetate solution, lead electrodes) was used and found very satisfactory. Constancy of temperature to within 0.05° was not difficult to maintain during measurements. The thermometers used were graduated in tenths of degrees and calibrated by the Thüringische Landesamt für Mass und Gewicht (1928). The viscometers were of the Ostwald type, of sufficient range of flow time to permit rapid and accurate measurement of viscosities up to 100 cp.; in the following, all values for viscosity are relative to that of water at 20°. Densities were determined by means of a Westphal balance, the tube containing the solutions being jacketed with an electrically heated water-bath.

(5) "International Critical Tables," Vol. VI, 261–302 (1929).

(6) Angelescu and Ciortan, *Kolloid Z.*, **82**, 164 (1938).

Preparation of Materials.—All compounds examined were purified rigorously by redistillation, recrystallization, or other standard procedures. In some cases it was necessary to resort to synthesis to obtain pure materials. A few of the more pertinent details are recorded below.

All oleic acid used was prepared from olive oil by saponification and subsequent partial purification by the lead salt–alcohol method.[7] Final purification was effected by repeated crystallization from a 30–40% solution in 95% ethanol at −30°. Raymond[8] used a similar procedure, and since completion of the present work the suitability of the method has been confirmed by the results of Brown and Shinowara.[4] After three or four recrystallizations the product was an oil with a very pale yellow tinge, m. p. 12–13°, which yielded on vacuum distillation a water-white material of the same m. p. While undoubtedly not 100% oleic acid,[9] this product probably was far purer than that used by Weichherz and Saechtling.[2,3]

The sodium salt, prepared by treating the acid with an equivalent amount of sodium, both first being dissolved in absolute ethanol, was stored in well-stoppered bottles in a desiccator after drying under reduced pressure at 60° over phosphorus pentoxide. Calculated for $C_{17}H_{33}COONa$: Na, 7.56. Found: Na, 7.49.

The *p*-hydroxybenzyl alcohol was obtained without difficulty from *p*-hydroxybenzaldehyde by application of the general method of Adams.[10,11]

Preparation of Solutions and Measurement of Viscosity.—After drying in the Abderhalden pistol under reduced pressure at 60° for at least twelve hours, over phosphorus pentoxide, the sodium oleate was weighed by difference into a stoppered Pyrex flask and dissolved in the calculated amount of air-free, doubly-distilled water at 50°. After the salt had dissolved the calculated amount of a phenol was added and the mixture kept at 50° until equilibrium was attained. Finally the solution, unless perfectly clear, was filtered by air pressure through a prewarmed Jena glass filter, placed in a stoppered flask in the thermostat, and allowed to remain there at 20°.

The usual precautions regarding choice of a viscometer were observed. If accurate filling at 20° was impracticable because of the high viscosity of the solution, it was carried out at 60°, making the necessary correction for difference in density. The mean of five measurements was recorded as the time of flow, except when this was impracticable due to extremely high viscosity. Readings were taken at 20, 30, 40, 60, and 80°, allowing a suitable interval before taking readings for the solution to reach thermal equilibrium. Density measurements were made on the balance of the solution over the same temperature range. To conserve space these values are not recorded with the rest of the data in Table II.

The writer wishes to express his appreciation to Professor H. Hibbert, in whose laboratories this work was carried out, for much helpful advice and criticism, and to acknowledge the assistance

(7) Skellon, *J. Soc. Chem. Ind.*, **50**, 131T (1931).

(8) Raymond, *Chimie & industrie*, Special No. Feb. 1929, p. 523.

(9) Hartsuch, THIS JOURNAL, **61**, 1143 (1939).

(10) Adams and Voorhees, "Organic Syntheses," Coll. Vol. I, 1932.

(11) Adams and Carothers, THIS JOURNAL, **46**, 1675 (1924).

TABLE II

VISCOSITIES OF TERNARY SYSTEMS RELATIVE TO WATER AT 20°

Expt.	Ratio: Sod. oleate	Phenol	Water	20°	30°	40°	60°	80°	Remarks
				(A) System: Sodium Oleate:Phenol:Water					
1[a]	10.00	0.00	90.00	15.85	6.24	3.35	1.54	1.02	Metastable 20°
2[a]	10.00	.00	90.00	17.0	7.64	4.18	1.88	1.21	Metastable 20°
3[b]	10.00	.00	90.00	10.0	4.50	2.70	1.43	0.90	
4[c]	10.00	.00	90.00	5.75	3.23	2.17	1.31		
5	9.00	1.00	90.00	*ca.* 1000	74.5	13.6	2.22	1.06	Homogeneous
6	8.50	1.50	90.00	*ca.* 1500	85.3	14.4	2.22	0.974	Homogeneous
7	8.00	2.00	90.00	730–740	52.3	10.5	1.92	.898	Homogeneous
8	6.00	4.00	90.00	3.23	2.08	1.51	0.981	.665	Homogeneous
9	3.00	7.00	90.00	1.66	1.30	1.05	.705	.557	Homogeneous
10	0.00	10.00	90.00			(0.808)	.570	.446	Clear above 40.15°
11[a]	5.00	0.00	95.00	1.77	1.41	1.14	.808	.608	Homogeneous
12[a]	5.00	.00	95.00	1.84	1.48	1.20	.839	.625	Homogeneous
13	4.50	.50	95.00	2.66	1.45	1.09	.756	.567	Metastable 20°
14	4.00	1.00	95.00	3.37	1.56	1.10	.724	.543	Metastable 20°
15	3.00	2.00	95.00	1.52	1.17	0.945	.658	.504	Homogeneous
16	0.00	5.00	95.00	1.12	0.886	.725	.522	.408	Homogeneous
17	3.00	0.00	97.00	1.42	1.13	.930	.661	.505	Homogeneous
18	2.50	.50	97.00	(1.34)	(1.06)	(.857)	.612	.472	Heterogeneous
19	2.00	1.00	97.00	(1.34)	(1.08)	(.881)	(.600)	.457	below 75°
20	1.00	2.00	97.00	1.17	0.932	.764	.547	.407	Homogeneous
21	0.00	3.00	97.00	1.07	.850	.696	.505	.396	Homogeneous
				(B) System: Sodium Oleate:*p*-Cresol:Water					
22	9.50	0.50	90.00	95.0	25.3	8.82	2.49	1.32	Homogeneous
23	9.00	1.00	90.00	1200	122.8	22.6	3.36	1.44	Homogeneous
24	8.50	1.50	90.00	*ca.* 10,000	480	47.5	4.06	1.47	Homogeneous
25	8.00	2.00	90.00	>10,000	*ca.* 1500	67.1	4.21	1.40	Homogeneous
26	7.00	3.00	90.00	*ca.* 10,000	345	35.7	3.32	1.31	Homogeneous
27	6.00	4.00	90.00	151	26.5	8.09	2.02	1.12	Homogeneous
28	5.00	5.00	90.00	13.8	5.90	3.10	1.35	0.866	Homogeneous
29	4.50	0.50	95.00	1.92	1.59	1.22	0.834	.632	Homogeneous, elastic 20°
30	4.00	1.00	95.00	3.76	2.22	1.32	.811	.609	Sl. turbid, elastic 20°
31	3.80	1.20	95.00		2.44	1.41	.808	.605	Homogeneous
32	3.50	1.50	95.00	4.40	1.98	1.26	.784	.589	Homogeneous, non-elastic
33	3.00	2.00	95.00	2.38	1.49	1.10	.745	.569	Homogeneous
34	2.00	3.00	95.00	1.50	1.18	0.957	.678	.518	Homogeneous
				(C) System: Sodium Oleate:Guaiacol:Water					
35	9.00	1.00	90.00	303	56.9	13.2	2.58	1.27	Homogeneous
36	8.00	2.00	90.00	*ca.* 2000	90.2	15.5	2.53	1.24	Homogeneous
37	7.50	2.50	90.00	360	36.5	8.90	1.99	1.09	Homogeneous
38	7.00	3.00	90.00	59.9	13.3	4.95	1.65	1.05	Homogeneous
39	4.00	6.00	90.00	1.98	1.56	1.26	0.871	0.645	Homogeneous
40	4.50	0.50	95.00	1.68	1.37	1.14	.773	.578	Sl. turbid 20°
41	4.00	1.00	95.00	2.78	1.67	1.17	.777	.598	Sl. turbid 20° elastic
42	3.50	1.50	95.00	2.17	1.42	1.07	.720	.539	Homogeneous
43	3.00	2.00	95.00	1.60	1.22	0.985	.687	.516	Homogeneous
44	2.00	3.00	95.00	1.42	1.12	.913	.650	.493	Homogeneous
				(D) System: Sodium Oleate:Creosol:Water					
45	9.50	0.50	90.00	73	26.4	9.23	2.54	1.32	Metastable at 20°, elastic
46	9.00	1.00	90.00	*ca.* 500	80.0	16.6	2.85	1.30	Clear, metastable
47	8.50	1.50	90.00	*ca.* 3000	284	34.4	3.57	1.49	at 20°

TABLE II (*Continued*)

Expt.	Ratio: Sod. oleate	:	Phenol	:	Water	20°	30°	40°	60°	80°	Remarks
48	8.00	:	2.00	:	90.00	*ca.* 10,000	525	46.7	3.83	1.43	Clear, metastable
49	7.00	:	3.00	:	90.00	*ca.* 10,000	294	32.9	3.33	1.30	at 20°
50	6.00	:	4.00	:	90.00	180	30.9	9.44	2.16	1.03	Clear
51	4.00	:	6.00	:	90.00	5.86	3.56	2.32	1.24	0.820	Clear
52	4.50	:	0.50	:	95.00	1.91	1.54	1.19	0.800	.595	Clear, non-elastic
53	4.00	:	1.00	:	95.00	3.12	1.95	1.26	.795	.598	Turbid, elastic 20°
54	3.50	:	1.50	:	95.00	3.69	1.80	1.21	.776	.587	Clear, non-elastic
55	3.00	:	2.00	:	95.00	2.25	1.44	1.07	.721	.541	Clear, non-elastic
56	2.00	:	3.00	:	95.00	1.47	1.15	0.941	.662	.500	Clear, non-elastic
						(E) System: Sodium Oleate:Catechol:Water					
57	9.50	:	0.50	:	90.00	78	40.5	15.2	4.08	1.87	Opalescent below
58	9.00	:	1.00	:	90.00	800–900	226	39.2	5.55	1.99	60°
59	8.50	:	1.50	:	90.00		326	50			
60	8.00	:	2.00	:	90.00	*ca.* 1200	176	19.2	3.66	1.86	Sl. opalescent
61	7.00	:	3.00	:	90.00	224	19.8	7.81	2.23	1.28	Sl. opalescent
62	4.50	:	0.50	:	95.00	1.55	1.25	1.04	0.767	0.591	Sl. turbid
63	4.00	:	1.00	:	95.00	1.47	1.20	1.02	.794	.622	Sl. turbid
64	3.50	:	1.50	:	95.00	1.59	1.27	1.05	.770	.616	Sl. turbid
						(F) System: Sodium Oleate:Resorcinol:Water					
65	9.75	:	0.25	:	90.00	51.9	14.7	6.03	2.00	1.14	Metastable 20°
66	9.50	:	0.50	:	90.00	70.4	20.2	7.89	2.29	1.16	Clear
67	9.00	:	1.00	:	90.00	41.1	16.3	7.71	2.45	1.24	Clear
68	8.00	:	2.00	:	90.00	5.93	3.82	2.73	1.56	1.01	Heterogeneous over
69	6.00	:	4.00	:	90.00	1.91	1.52	1.24	0.907	0.664	60°
70	3.00	:	7.00	:	90.00	1.46	1.19	1.04	.851	.658	Opalescent 20–80°
71	0.00	:	10.00	:	90.00	1.25	0.992	0.812	.579	.449	Clear
72	4.50	:	0.50	:	95.00	1.59	1.29	1.08	.754	.571	Opalescent 20–80°
73	4.00	:	1.00	:	95.00	1.44	1.17	1.00	.796	.624	Opalescent 20–80°
74	3.00	:	2.00	:	95.00	1.39	1.13	0.967	.720	.538	Opalescent 20–80°
75	2.00	:	3.00	:	95.00	1.32	1.05	.878	.644	.501	Opalescent 20–80°
76	0.00	:	5.00	:	95.00	1.12	0.890	.732	.528	.413	Clear
						(G) System: Sodium Oleate:*p*-Hydroxybenzyl Alcohol:Water					
77	9.50	:	0.50	:	90.00	13.5	6.56	3.76	1.76	1.09	Clear
78	9.00	:	1.00	:	90.00	6.86	4.13	2.76	1.52	1.02	Clear
79	8.50	:	1.50	:	90.00	4.00	2.80	2.12	1.31	0.935	Clear
80	8.00	:	2.00	:	90.00	2.83	2.17	1.73	1.17	0.857	Clear
						(H) System: Sodium Oleate:Vanillyl Alcohol:Water					
81	9.50	:	0.50	:	90.00	8.59	4.97	3.23	1.69	1.12	Clear
82	9.00	:	1.00	:	90.00	4.35	3.10	2.32	1.43	1.04	Clear
83	8.00	:	2.00	:	90.00	2.50	1.98	1.61	1.13	0.847	Clear
84	6.00	:	4.00	:	90.00	(2.02)	1.59	1.29	0.906	.693	Homogeneous above 20°
85	3.00	:	7.00	:	90.00			(1.08)	.745	.571	Homogeneous above 40°
86	4.50	:	0.50	:	95.00	1.66	1.30	1.06	.761	.581	Sl. turbidity below 35°
87	4.00	:	1.00	:	95.00	1.62	1.26	1.01	.700	.540	Turbid below 60°
88	3.00	:	2.00	:	95.00	1.48	1.17	0.949	.659	.501	Turbid below 60°
89	1.50	:	3.50	:	95.00	(1.26)	1.00	.824	.594	.456	Homogeneous above 30°
90	0.00	:	5.00	:	95.00			(.735)	.530	.416	Homogeneous above 40°
						(I) System: Sodium Oleate:*o*-Bromophenol:Water					
91	9.50	:	0.50	:	90.00	58	30.0	12.8	3.34	1.51	Metastable 20°
92	9.00	:	1.00	:	90.00	82	68	25.0	4.99	2.06	Metastable 20°, turbid 20°
93	8.50	:	1.50	:	90.00	7.71	6.28	5.38	2.72	1.56	Sl. turbidity

TABLE II (*Concluded*)

Expt.	Ratio Sod. oleate	Phenol	Water	20°	30°	40°	60°	80°	Remarks
94	8.00	2.00	90.00	4.32	3.68	3.20	2.47	1.50	Sl. turbidity
95	4.50	0.50	95.00	1.51	1.21	1.01	0.749	0.584	Sl. turbidity
96	4.00	1.00	95.00	1.95	1.58	1.33	1.01	.780	Sl. turbidity
97	3.00	2.00	95.00	1.62	1.29	1.06	0.764	.591	Sl. turbidity
	(J) System: Sodium Oleate:Vanillin:Water								
98	9.00	1.00	90.00	4.14	3.49	3.03	2.42	2.29	Sl. turbid, some ppt.
99	8.00	2.00	90.00	3.50	2.98	2.68	2.23	1.98	Sl. turbid, some ppt.
100	4.00	1.00	95.00	1.88	1.53	1.29	0.981	0.846	Sl. turbid, some ppt.
	(K) System: Sodium Oleate:*p*-Hydroxybenzaldehyde:Water								
101	9.00	1.00	90.00	8.16	7.15	6.43	5.42	4.93	Sl. turbid, some
102	8.00	2.00	90.00	2.73	2.31	2.02	1.61	1.41	ppt.

[a] Expts. 1, 11 and 2, 12 were made, respectively, with two different lots of sodium oleate prepared from two lots of oleic acid purified by low temperature recrystallization. The material used in expts. 1 and 11 was used throughout Section A and in Section F, expts. 65–70 inclusive. All other expts. were carried out with the material used in expts. 2 and 12. [b] Sodium oleate was prepared from oleic acid purified by the Skellon barium salt method. [c] Sodium oleate was prepared from a sample of commercial acid.

of Mr. Q. P. Peniston in the preparation of some materials used.

Summary

1. Using a more rigorously purified sodium oleate, earlier observations on the occurrence of maxima in the viscosity of sodium oleate:phenol:water systems have been checked qualitatively but not quantitatively, the present results indicating the maxima to be even more pronounced than previously reported.

2. On extending the investigation to other phenolic substances it was found that not all produced such maxima in the viscosity of sodium oleate solutions. The effectiveness of *p*-cresol, guaiacol and creosol in this regard was of the same order as that of phenol, but in the case of catechol, resorcinol and *o*-bromophenol the maxima were not so marked or even, at lower concentrations of sodium oleate, non-existent. Vanillyl alcohol, *p*-hydroxybenzyl alcohol, vanillin and *p*-hydroxybenzaldehyde did not increase the viscosities of the solutions of sodium oleate examined.

3. Evidence is adduced against Weichherz and Saechtling's[2] theory that the formation of acid soaps is a minor cause of the observed maxima in viscosity.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, CORNELL UNIVERSITY]

The Degradation of Oriented Cellulose Structures by Polarized Ultraviolet Light

BY C. W. MASON AND F. B. ROSEVEAR[1]

Introduction

The photochemical changes produced in cellulose have received attention since Witz[2] in 1883 reported that cotton when exposed to light was changed, in part at least, to "oxycellulose." Although the exact nature of "oxycellulose" can only be inferred at present, and although some reported experiments may have been complicated by effects other than that of light, nevertheless, it appears that a certain portion of the ultraviolet region does produce physico-chemical changes in the cellulose structure.

The structure of cellulose shows very definite differences in properties, depending upon the direction considered. This is indicated macroscopically by its pronounced fibrous nature, microscopically by its strong double refraction, as well as the production of tiny fibrillae by mechanical treatment, and sub-microscopically by the X-ray deduction of its atomic arrangement.

It is reasonable to expect, then, that the anisotropic properties would include the photochemical

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(2) Witz, *Bull. soc. ind. Rouen*, II, 190 (1883).

effect, providing the radiation can be rendered directional in those properties which have to do with its photochemical action.

A directional effect of this sort has been found with potassium nitrate and other nitrates. Narayanswamy and Krishnan[3] noted that in the photochemical breakdown of NO_3^- to NO_2^- in K, Na, NH_4, Sr, Ba, Cd, Pb, and Al nitrates, the rate of decomposition with plane polarized light was greater if the plane of vibration of the light was parallel to the plane of the NO_3^- groups.

The pleochroism of sodium nitrate and potassium nitrate in the ultraviolet, investigated earlier by Krishnan and Dasgupta,[4] supports the observations on decomposition. A selective absorption at about 3000 Å. occurs in solutions of sodium and potassium nitrates. With crystals and plane polarized light, this band is evident if the light is vibrating parallel to the plane of the NO_3 groups, while light vibrating perpendicular to the plane of the NO_3 groups is freely transmitted. A similar effect is noted at about 2600 Å.

Padoa[5] observed that the rate of photochemical decomposition of crystalline *o*-nitrobenzaldehyde, in polarized light, differs with the direction of vibration of the light. Weigert[6] found a similar effect, with tetrachloro-α-cetonaphthalene.

Experimental

I. Selection and Preparation of Cellulose.—Ramie was used, for X-ray evidence indicates that in ramie the molecular chains are not only parallel to each other, but essentially parallel to the fiber axis, rather than spiral as in many fibers.[7-10]

"Degumming" of ramie, following the mechanical "decortication," is accomplished commercially by a wide variety of methods,[11,12] so that even though some available samples of commercial ramie sliver gave a very low copper number, indicating high purity of their cellulose, it was thought best to follow a known procedure, as follows:

Raw, dried, decorticated ramie was: (1) extracted three times with boiling water; (2) refluxed for fifteen-minute periods with three changes of 1% sodium hydroxide; and (3) washed successively with water, 5:95 acetic acid, 1:99 acetic acid, 95% alcohol, absolute alcohol, and ether. The resulting product was free from the yellowish-brown color of the raw ramie. It showed a copper number of 0.10–0.12 as compared to a value of 0.08 for the commercial sliver.

II. Production of Plane Polarized Ultraviolet Light.—Preliminary exposures beneath ordinary glass, Pyrex, and vitreous silica, using Harrison's reagent[13] as a staining test, indicated that only the latter material had sufficient transmission (below 3300–3400 Å.) to permit marked degradation.

A. The Light Source.—The features of the quartz-enclosed mercury vapor arc as well as others are discussed in the First Report of the Committee on Photochemistry, National Research Council.[14] The mercury spectrum, while not continuous, has a rather large number of lines of high intensity distributed throughout the ultraviolet region. As the light source for the experiments, a Hanovia "Advanced Research Model" SC2601-A (110 volts, D.C.) quartz-enclosed mercury arc was used. This lamp gives an arc 6–7 cm. long and about 1 cm. in section.

Decrease in intensity of the arc with age was not found to cause trouble during the exposures. After some 1700 hours, the radiations still had a pronounced photochemical effect on cellulose, and the bulb showed no visible coating, or serious spectral alteration. The fact that the samples for light vibrating perpendicular and parallel to the fibers were run simultaneously renders unimportant any decrease other than a virtual elimination of the active wave lengths, and also any fluctuations in intensity.

B. The Polarizer.—Maximum cross section of the illuminating beam was necessary, to irradiate a quantity of fibers sufficient for analysis. For this and other reasons, polarizing prisms were inadequate; polarizing filters absorb ultraviolet completely.

The polarizer, based on the "pile of plates" principle, was constructed as follows. Two sets of eight polished vitreous silica plates (25 × 50 × 1 mm.) were cleaned carefully, piled face to face and the edges of the piles coated with warm "Piceine." This material when warmed was sufficiently fluid to adhere to the edges of the plates, without creeping between them, and on cooling served to hold the plates together, and to prevent reflection at their edges, because of its blackness and optical contact with the glass. When placed side by side, the two piles composed a reflector 50 × 50 × 8 mm., which was mounted in a duralumin frame so that the incident and reflected beams travelled parallel to the plane separating the two 8-plate halves of the polarizer.

It was found by measurement that the use of more than eight or ten plates added little to the quantity of reflected plane polarized light. A similar conclusion was reached regarding a "pile of plates" polarizer for microscopes.[15]

For the wave length range between 3400 Å. (the approximate upper limit of the spectral region active in degrading cellulose) and 2000 Å. (the approximate transmission limit of vitreous silica) the refractive index of vitreous silica varies from 1.479 to 1.547, corresponding to a variation in polarizing angle of only ±0.5°. By reflection at the polarizing angle of 56°, all wave lengths in the region will be almost completely polarized, over a 1° range.

(3) (a) Narayanswamy, *Trans. Faraday Soc.*, **31**, 1411–1412 (1935); *C. A.*, **30**, 386; (b) Krishnan and Narayanswamy, *Current Sci.*, **3**, 417 (1935).

(4) Krishnan and Dasgupta, *Nature*, **126**, 12 (1930).

(5) Padoa, *Atti Accad. Lincei*, **28**, II, 372 (1919).

(6) Weigert, *Z. Elektrochem.*, **24**, 222 (1918).

(7) Clark, *Ind. Eng. Chem.*, **22**, 474–487 (1930).

(8) Herzog, *J. Phys. Chem.*, **30**, 457 (1926).

(9) Sponsler and Dore, *4th Colloid Symposium Monograph*, 174–202 (1926).

(10) Polanyi, *Naturwissenschaften*, **9**, 337 (1921).

(11) Mathews, "Textile Fibers," John Wiley and Sons, New York, N. Y., 1924, p. 780.

(12) Carter and Norton, *Univ. Louisiana Studies*, No. 26 (1936).

(13) Harrison, *J. Soc. Dyers Colourists*, **28**, 359 (1912).

(14) Forbes, *J. Phys. Chem.*, **32**, 482 (1928).

(15) Johnson, *J. Roy. Microscop. Soc.*, 147 (1921).

Reasonably perfect and economical collimation was obtained by means of a set of narrow, flat, blackened, metal plates lying parallel to the length of the arc and to the direction of the desired light beam (see Fig. 1, p. 10). This produced three parallel channels for the light, 4 mm. wide and 120 mm. long, so that a ray of light from any point on the arc to the polarizing plates deviated not more than 2° from the desired 56° angle of incidence. A collimated beam of light 35 × 75 mm. in cross section was thus obtained.

Due to displacement by the multiple reflection, the polarized beam varies from a maximum intensity on one side, to minimum on the other. This non-uniformity and the difference in intensity between the center and the ends of the beam were taken into account by turning the exposure cell end for end each day, and also in the method of sampling.

III. Method of Exposure.—While the nature of the photochemical degradation of cellulose is by no means clear, it is also true that any observed degradation might be due in part to chemical influences, non-directional in effect.

Cunningham and Doree[16] found that ozone, when passed over cotton fabric, changed it into "oxycellulose." Oguri[17] exposed filter paper to light from a quartz mercury vapor arc, and found that the copper number was definitely lower when ozone was eliminated. Joachim-Henk,[18] and Barr and Hadfield[19] consider the presence of oxygen to be essential, and the action of ultraviolet light one of oxidation. Cunliffe[20] also showed the importance of oxygen and moisture.

Obviously, the *secondary* actions upon cellulose of ozone, hydrogen peroxide, acids, or other products would be wholly independent of the plane of vibration of the incident radiation, and if the primary action of light were to be studied, these complicating factors should be minimized.

An airtight cell, shown in Fig. 1, was used. A duralumin frame formed three chambers, each designed to take a 25 × 50 mm. vitreous silica slide as front window and a glass microscope slide as back window. In each chamber a glass plate carried a thin layer of parallel fibers of purified ramie, half oriented parallel to the vibration direction of the polarized light, and the other half perpendicular to the vibration direction. All the fibers were drawn over the ends or sides of the supporting plates and held in place at the back by a very small amount of glue. Sodium wire in each chamber served to remove oxygen, ozone, water, and carbon dioxide from the air left in the fibers and in the cell after sealing it, and also volatile reaction products of the degradation.

After extruding the sodium wire into each compartment the back windows of the cell were sealed with Apiezon-Q (Shell Oil Co.), a sealing plastic of very low vapor pressure, which can be used like putty. The tightness of these seals was indicated by the fact that during the runs of 500 hours or more, the only change in the sodium was some clouding of the surface; an excess of metallic sodium was present throughout the runs.

Before irradiation, two days' time was allowed for removal of the oxygen, carbon dioxide, and water from the air and fibers in the cell.

With this cell, it was found possible to irradiate a total sample of about 0.1 g., in layers only a few fibers thick.

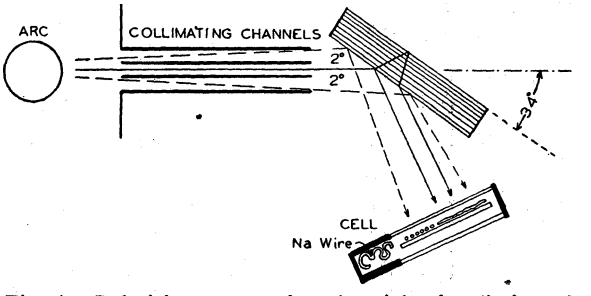

Fig. 1.—Polarizing system for ultraviolet irradiation of fibers.

The fibers present a series of parallel, roughly cylindrical surfaces, on each of which the beam is incident at every angle from perpendicular to grazing incidence. Penetration of light is less efficient than with a plane surface; with polarized light the penetration of light varies, depending upon whether the light vibrates parallel or perpendicular to the axis of the cylinders.

Elimination of reflection factors by immersion in a medium transparent to ultraviolet of appropriate refractive index would introduce prohibitive chemical complications. Consequently the fibers were exposed directly, and a correction computed as follows.

In the method of exposure used, light vibrating lengthwise of the fiber (n_γ) vibrates perpendicular to the "plane of incidence" (the plane containing the incident and refracted rays); light vibrating crosswise of the fiber (n_α) vibrates in the plane of incidence. The first case involves more loss by reflection.

For a plane surface, Fresnel developed mathematical expressions relating the quantity of incident, reflected and transmitted light for each case.[21–23] Vibrations perpendicular to plane of incidence:

$$b = -a\frac{\sin(i - r)}{\sin(i + r)}$$

$$c = 2a\frac{\cos i \sin r}{\sin(i + r)}$$

(16) Cunningham and Doree, *J. Chem. Soc.*, **101**, 497 (1912).

(17) Oguri, *J. Soc Chem. Ind. Japan*, **37**, Suppl. 620–621 (1934).

(18) Joachim-Henk, *Melliand Textil-Ber.*, **18**, 521 (1937); *Am. Dyestuff Reptr.*, **27**, 318 (1938).

(19) Barr and Hadfield, *Dept. Sci. Ind. Res. 2nd Rept. Fabr. Coörd. Res. Comm.*, 95 (1930).

(20) Cunliffe, *J. Text. Inst.*, **19**, T169 (1928).

(21) Preston, "The Theory of Light," Macmillan and Co., London, 1921, pp. 342–354.

(22) Houstoun, "A Treatise on Light," 4th edition, Longmans, Green and Co., New York, 1925. Identical equations are obtained in a more rigorous way by applying the principles of the electromagnetic theory of light, *op. cit.*, pp. 418–421.

(23) Wood, "Physical Optics," 1911, p. 338.

Vibrations in plane of incidence

$$b = -a\frac{\tan(i-r)}{\tan(i+r)}$$

$$c = \frac{2a\cos i \sin r}{\sin(i+r)\cos(i-r)}$$

Since light intensity is proportional to the square of the amplitude

$$I_a:I_b:I_c = a^2:b^2:(c^2 \tan i \cot r)$$

where a, b, and c are the amplitudes of the incident, reflected, and refracted beams, I_a, I_b, I_c the corresponding intensities, and i and r the angles of incidence and refraction, respectively. The term, tan i cot r, is applied to the refracted beam, to take into account the refractive index of the medium[21] (p. 93) which the light is entering.

For a *cylindrical* surface, i varies from 0 to 90° on either side of perpendicular incidence. Hence, by evaluating the term c^2 tan i cot r in terms of a^2 and summing over the angular range 0 to 90°, values for the intensity of refracted (penetrating) light, in terms of the incident intensity, are obtained.

For light vibrating perpendicular to the plane of incidence (n_γ)

$$I_c \text{ is proportional to } \int_0^{\frac{\pi}{2}} a^2 \frac{\sin 2i \sin 2r}{\sin^2(i+r)}\,di$$

For light vibrating in the plane of incidence (n_α)

$$I_c \text{ is proportional to } \int_0^{\frac{\pi}{2}} a^2 \frac{\sin 2i \sin 2r}{\sin^2(i+r)\sin^2(i-r)}\,di$$

These summations were evaluated graphically. The intensity terms were calculated for several angles of incidence, the values being recorded in Table I and plotted in Fig. 2.

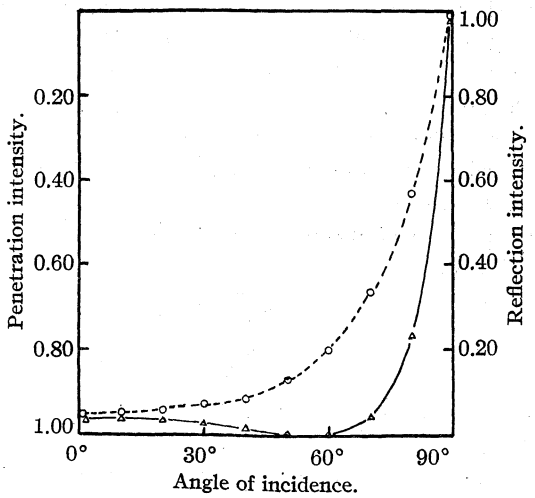

Fig. 2.—Intensity of penetration and of reflection of light, as a function of angle of incidence.

TABLE I

CALCULATED VARIATION IN INTENSITY OF REFRACTED BEAM WITH ANGLE OF INCIDENCE

i	I_c for light vibrating lengthwise (n)	I_c for light vibrating crosswise (n)
0°	0.952	0.956
10°	.948	.957
20°	.942	.963
30°	.930	.973
40°	.908	.984
50°	.870	.995
60°	.800	1.000
70°	.663	0.959
80°	.436	.765
90°	.000	.000

In calculating values for the first column, the refractive index used was $n_\gamma = 1.568$, for the second column, $n_\alpha = 1.530$, both values for 5893 Å. The corresponding refractive indices in the ultraviolet are not known, but the absorption spectrum of cellulose does not exhibit any marked bands that might indicate anomalous dispersion, and comparison of Fig. 2 with a similar published diagram for crown glass ($n = 1.523$)[24] will show that refractive index variations of the magnitude involved make practically no difference in the shape and position of the curves.

Since the value of (c^2 tan i cot r) for $i = 0°$ is indeterminate, it must be obtained from the relationship $a^2 = b^2 + c^2$ tan i cot r and Young's equation[21] (p. 352). No data on possible ultraviolet pleochroism of cellulose fibers have been determined, but even if this exists it is unlikely that the differences in the absorption coefficient for the two orientations would have sufficient influence on the reflection factor to render these curves inapplicable, especially since the absorption of cellulose is relatively low in the spectral region used.

If the total area of the graph represents one intensity unit of incident light, the curve divides this area into the relative amounts penetrating (above) and reflected (below). By planimetry the areas above the curves are: 0.77 for light vibrating parallel to n_γ, 0.91 for light vibrating parallel to n_α.

Thus, the fibers oriented parallel to the vibration direction of the incident light were penetrated by only 0.77/0.91 or 0.85 as much light as those lying perpendicular. The degradation values for fibers in the latter orientation were therefore reduced by the factor, 0.85.

(24) Hardy and Perrin, "Principles of Optics," McGraw-Hill Book Co., New York, N. Y., 1932, p. 28.

Actually, the effective penetration, for vibrations either crosswise or lengthwise of the fibers, is probably greater, because of imperfections in their assumed cylindrical surfaces, and because adjacent fibers may absorb some light that would otherwise be lost by the first reflection. The difference in penetration may therefore be somewhat less than the factor 0.85 indicates.

V. Determination of Amount of Degradation.—Of the common criteria for evaluating the degradation of cellulose, copper number was selected, as the most adaptable to the very small samples available.

A critical survey of methods up to 1931 is given by Burton and Rasch.[25] Doree[26] summarizes several methods which are in favor in the textile industry. Probably the most important variation from the original method is the elimination of strongly alkaline Cu^{++} solution containing tartrate, in favor of a solution made alkaline with Na_2CO_3–$NaHCO_3$ as proposed by Braidy[27] and Koehler and Marqueyrol.[28]

Amick[29] concludes that the copper number method for evaluating glucose is too much subject to variations in conditions to have any significance in expressing structural changes in glucose, but if conditions are fixed rigidly, analytical results can be duplicated.

Results on cellulose likewise can be duplicated if conditions are maintained comparable, but where variations in the history and condition of sample as well as differences in conditions of the experiments are introduced, absolute interpretations are not justified. The chief value of the copper number determination is in making comparisons of an empirical nature.

Heyes[30] gives a micro-method for copper number, which requires 0.25 g. By modifying the Heyes method, sufficiently accurate checks could be obtained on 0.01 g. of exposed ramie, permitting several determinations on the 0.1-g. samples.

The method finally adopted follows.

Solutions used were:

A. Carbonate-bicarbonate: 150 g. anhydrous sodium carbonate, 50 g. anhydrous sodium bicarbonate in 1 liter of solution.

B. Copper sulfate: 100 g. $CuSO_4 \cdot 5H_2O$, in 1 liter of solution.

C. Ferric sulfate: 4 g. $Fe_2(SO_4)_3$ and 100 cc. concd. sulfuric acid per liter of solution.

D. Sulfuric acid for washing: H_2SO_4:H_2O = 1090. (Solutions C and D as well as all distilled water used, were boiled free of air to minimize the possibility of oxidation of cuprous oxide.)

E. Standard potassium permanganate solution: approximately 0.004 *N*.

Such a low normality was chosen by experiment since it gave, for the sample weight used, the best compromise between a high buret reading and a sharp end-point. The solution was standardized against sodium oxalate, according to the method of Fowler and Bright.[31]

0.009–0.011 g. of the fibers in cuttings about 1 mm. long, were weighed into a dry 15 × 15 cm. test-tube; moisture "regain" was slight enough to be negligible. To this was added 10 ml. of digestion mixture (9.5 ml. solution A and 0.5 ml. of solution B) which had been preheated in a boiling water-bath for ten minutes previously. A stirring rod with a bent lower end, and short enough not to protrude, was inserted into each test-tube. A small glass crucible in the mouth of the tube served as a reflux condenser. The tube was supported in the boiling water-bath so that the digestion mixture was completely below the level of the liquid, and with the aid of forceps to grasp the rod, its contents were stirred gently (in order to avoid beating in air) every ten minutes for three hours.

Ten minutes before the close of the digestion period, the stirring rod was removed, and the carbonate adhering to it was washed into a sintered glass filtering funnel.

When the three-hour digestion was complete, the tube was cooled in cold tap water for five minutes, and the supernatant liquid poured into the filter funnel. The fibers were washed once with 3 cc. of distilled water, by decantation, and the washings added to the digestion liquor. To the washed fibers 1 ml. of ferric sulfate solution C was added, rinsing down the sides, and the tube of fibers was replaced in the water-bath for five minutes. During this time almost all of the digestion liquor was filtered with suction, leaving just enough in the funnel to cover the few fibers present. To the funnel, arranged over a filtering bell jar, and covered with a watch glass, was added 2 ml. of 10:90 sulfuric acid from a pipet. (It is important that all the residual alkali be destroyed by this step, as it was found that local neutralization of the next solution containing Fe^{++} ions precipitated ferrous hydroxide, which is very susceptible to oxidation.)

The Fe^{++}–Fe^{+++} solution was transferred to the funnel, and filtered into a 25-ml. Erlenmeyer flask under the bell jar; the fibers in the test-tube and funnel were washed with 1 ml. of ferric sulfate solution, then with three 2-ml. portions of 10:90 sulfuric acid, and finally with water.

Titrating was done promptly with the 0.004 *N* potassium permanganate, using a micro-buret with a drawn-out tip, which delivered a drop of 0.014 ml. volume.

The end-point is a colorless solution produced by neu-

(25) Burton and Rasch, *Bur. Standards J. Research*, **6**, No. 4, 603–19 (1931).

(26) Doree, "Methods of Cellulose Chemistry," Chapman and Hall, London, 1933.

(27) Braidy, *Rev. gén. mat. color.*, **25**, 35 (1921).

(28) Koehler and Marqueyrol, *Mém. poudres*, **18**, 73 (1921).

(29) Amick, *J. Phys. Chem.*, **31**, 1441 (1927).

(30) Heyes, *J. Soc. Chem. Ind.*, **47**, 90T (1928).

(31) Fowler and Bright, *Bur. Standards J. Research*, **15**, 493 (1935).

tralization of the faint blue color of the solution with the excess potassium permanganate. Further potassium permanganate produces a pink tint. Since all of these colors are very faint, the titration was carried out by artificial light with a Daylite glass filter, in a screened compartment. Comparison was made with distilled water containing one drop of potassium permanganate solution, and with an untitrated copper number solution. With such control, the end-point could be duplicated to plus or minus one drop (±0.014 ml.).

The ferric sulfate solution proposed by Heyes was too concentrated for this titration, masking the faint end-point with a yellow-green color. The solution used contained one-tenth as much ferric sulfate.

A micro-buret which did away with the troubles of lubricating a stopcock of small bore, and which delivered a drop of 0.014 ml. volume was improvised as follows. A 1-ml. graduated pipet was drawn out in a flame to a finer tip. This buret was then clamped vertically, a thin-walled rubber tube fixed to the upper end, and passed down to the desk top and under a weighted roller, by the movement of which liquid could be drawn up or expelled.

The blank for the determination was obtained on 10 cc. of digestion mixture without fibers, going through the actual procedure from the first filtration on. Three drops of potassium permanganate were required to produce the colorless end-point, this being equivalent to 0.04 ml., a value which was deducted from all final buret readings. On the basis of a 10-mg. sample, the blank was equivalent to a copper number of 0.11–0.12.

$$\text{Cu no.} = \frac{\text{ml. of } KMnO_4 \times \text{Normality} \times 0.0635}{\text{Weight of sample in grams}}$$

The accuracy obtainable is indicated by the following values on ramie sliver after exposure through vitreous silica, without the polarizer

15 hours: (at 15 cm. distance) 0.658, 0.637, 0.647, 0.555, 0.643.
10 hours: (at 15 cm. distance) 0.513, 0.580, 0.582.
7 hours: (at 5 cm. distance) 3.68, 3.58, 3.68.

Results

The first run of five hundred and thirty-five hours of irradiation, gave rather erratic results for the determination of copper numbers:

Vibrations lengthwise (n_γ)
0.316, 0.317, 0.254, 0.265, av. 0.29
Vibrations crosswise (n_α)
0.373, 0.269, 0.487, 0.257, 0.572, av. 0.39
Average, corrected by reflection factor 0.85 = 0.33

The inconsistency of these results is ascribed to poor samplings of the fibers, and to partial reoxidation of hydroxide as mentioned in the analytical procedure. In a second run, care was taken to avoid this by acidifying before adding Fe^{+++} solution to the cuprous oxide-stained fibers, and better mixing of the sample was obtained by agitating the cuttings of fibers by an air jet.

The second run, lasting eight hundred and forty hours, yielded more consistent copper numbers.

Vibrations lengthwise (n_γ)
0.37, 0.41, 0.33, 0.32, av. 0.36
Vibrations crosswise (n_α)
0.56, 0.67, 0.60, 0.49, 0.43, av. 0.55
Average corrected by reflection factor 0.85 = 0.47

Longer exposures, giving large copper numbers, would have emphasized the difference in degradation with orientation. (Measured by the amount of degradation, eight hundred and forty hours of exposure to the rather weak polarized light used was roughly equivalent to less than fifteen hours exposure to unpolarized light at 15 cm. distance.)

The exposed material might have been divided into fewer and larger samples for analysis, minimizing the error in the determination, but it was thought that, in view of the lack of high precision of the method, a larger number would be more significant, if they showed a consistent trend. This is certainly the case in the second run, for although the values show a considerable spread, none of the results for one orientation overlap those for the other, and the increase in copper number is roughly proportional to the longer time of irradiation.

The evidence presented for the greater photochemical degradation by light vibrating crosswise of the fibers, although definite, is only qualitative. The optical complexity of the specimen, so different from the transparent plane parallel surfaced ones ordinarily used in photochemical experiments, the non-uniform distribution of illumination and penetration, the probable presence of cellulosic material not oriented parallel in the fiber—all these factors would tend to minimize the difference of degradation for the two orientations, so that the observed difference of approximately 25% is far from insignificant.

Discussion

Photochemical action is initiated by absorption of light energy. For any substance, inorganic or organic, where absorption arises from the arrangement of atoms in a fixed structure such as a molecule or crystal lattice, the absorbed activating energy is very probably applied to deformation of this structure. If the light energy is polarized, the direction of maximum deformability should be that of strongest absorption, and of most pronounced photochemical action, as was found in the photolysis of inorganic nitrates.[2-4]

Cellulose is believed to be built up of "glucose residues," chained end to end by a hemiacetal

linkage, as in cellobiose. The molecules are arranged parallel to the fiber length; lateral spacings between chains are relatively great. In agreement with Wooster's[32] and Bragg's[33] generalizations, the highest refractive index is found for vibrations lengthwise of the chain structure. Greatest deformability, and the consequent maximum photochemical degradation, should take place crosswise of the chains, since their length and parallelism would prevent lengthwise deformation.

It is generally accepted that photochemical degradation of cellulose fibers results in shortened chain length with an increase in reducing and acidic properties due to the breaking of oxygen linkages, and a consequent increase in copper number. Comparisons of chain length by viscosity, etc., were not feasible on the small samples irradiated, but the chemical changes observed correspond to those to be expected from the above process, if the light energy by virtue of its transverse vibrations breaks some of the oxygen links in the cellulose chain.

The present work illustrates qualitatively the generalization that the properties of crystalline matter differ with direction, a factor that should never be ignored in dealing with ordered structures. With the recent development of methods for producing oriented aggregates of other long chain compounds such as oils, the study of the anisotropic photochemical properties of their molecules becomes possible.

(32) Wooster, *Z. Krist.*, **80**, 495 (1931); "Crystal Physics," Cambridge Univ. Press, Cambridge, 1938, pp. 175–187.

(33) Bragg, "The Crystalline State," Vol. I, G. Bell and Sons, London, 1933, p. 186; "Atomic Structure of Minerals," Cornell Univ. Press, Ithaca, 1937, p. 120.

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Summary

Using a silica "pile of plates" polarizer, to give polarized ultraviolet light, parallel ramie fibers were irradiated, in a cell containing metallic sodium, to eliminate air or moisture that might cause secondary non-directional reactions. With light vibrating crosswise of the fibers, degradation was greater than with vibrations lengthwise, by about 25%, as measured by copper number determined on 10-mg. samples. From analogy with simpler compounds, it is concluded that photochemical degradation of cellulose chains is greatest if they are oriented so that the light energy vibrates in the direction in which they are most deformable.

ITHACA, N. Y. RECEIVED SEPTEMBER 2, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF OREGON STATE COLLEGE]

A Simple Wet Combustion Method for the Determination of Carbon, Oxygen Equivalence and Empirical Formula by Iodic Acid Oxidation*

BY BERT E. CHRISTENSEN AND J. FRED FACER

More work pertaining to organic combustions has been described in the literature than perhaps any other single analytical procedure. The fact that so much attention has been devoted to this determination testifies to its importance. The problem of determining carbon and hydrogen has been approached in several ways.[1–6] In spite of all these developments there is still need for simpler techniques, less expensive equipment and methods by which the occasional determination can be made with some degree of ease.

A study of the means by which the above problem may be answered leads to one possibility, the wet combustion process. This would entail the measurement of "oxygen consumed" as an alternative for the determination of moisture. Dichromate and iodate have been cited as excellent reagents for this purpose. Of these iodate is outstanding[7] since little, if any, decomposition (unless carried out above 200°) or carbon monoxide formation accompanies its reduction.

A survey of the literature reveals that Strebinger[8]

(*) Published with the approval of the Monographs Publication Committee, Oregon State College, Research paper No. 24, School of Science, Department of Chemistry.

(1) Glockler and Roberts, THIS JOURNAL, **50**, 828 (1928).

(2) W. R. Kirner, *Ind. Eng. Chem., Anal. Ed.*, **6**, 358 (1934).

(3) H. Lieb and H. G. Krainick, *Mikrochemie*, **9**, 367 (1931).

(4) J. Lindner, *Ber.*, **59**, 2561, 2806 (1926).

(5) M. Nicloux and A. Boivin, *Compt. rend.*, **184**, 890 (1927).

(6) E. Sucharda and B. Bobranski, *Z. anal. Chem.*, **77**, 462 (1929).

(7) Christensen, Williams and King, THIS JOURNAL, **59**, 293 (1937).

(8) Strebinger, *Z. anal. Chem.*, **58**, 97 (1919).

was among the first to use iodate in this connection. He determined the oxygen requirement of an organic compound and from this and the known carbon and hydrogen content he calculated the percentage of oxygen in the compound. Later Stanek and Nemes[9] used this same reagent to determine not only the "oxygen consumed," but in addition the carbon dioxide evolved. The hydrogen content was calculated from the "oxygen consumed" plus other values by means of rather complicated equations.

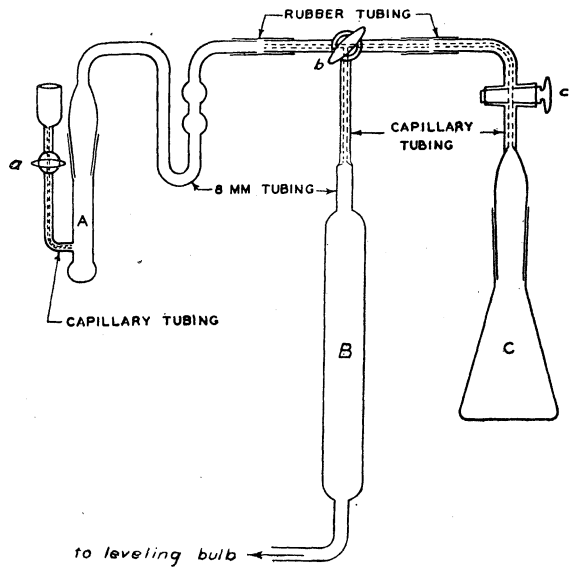


Fig. 1.

Williams[10] also has pointed out the importance of being able to determine the amount of oxygen required for complete combustion of organic material. He has developed this idea and in his paper on "Oxidation Equivalent Analysis"[11] describes a simple method for the determination of molecular structure based only on "oxygen consumed" and molecular weight data. The success of this method, however, hinges upon a fairly accurate means of obtaining the molecular or equivalent weight of the compound in question.

It was the opinion of the authors that the ideas presented by Williams could be much further utilized as a tool for the determination of molecular structure. Such an objective would only require the development of a simple procedure for the determination of carbon dioxide evolved from the reaction mixture. Due to the nature of the evolved gases (CO_2, I_2, Cl_2) it is apparent that a gravimetric method, such as described by Stanek and Nemes[9] for the determination of carbon dioxide, would not be as desirable as a volumetric procedure. For this reason a modified Pettenkofer method[12] using a volumetric principle was devised.

Apparatus.—This apparatus is illustrated diagrammatically in Fig. 1. The reaction vessel A (total volume 20 ml.) was constructed from no. 15 standard taper joint and a capillary stopcock. The gas reservoir B consisted of a three-way stopcock, a 100 ml. buret and a leveling bulb. Mercury was used as the confining fluid. The reaction flask for the analysis of carbon dioxide was designed from a 250-ml. Erlenmeyer flask, a no. 20 standard taper joint and capillary stopcock.

Procedure.—The conditions for iodate oxidation are described adequately in the literature.[8,9,11] The analysis as modified for measurement of carbon dioxide is very simple.

The reaction vessel is charged with 10–20 mg. of organic material[13] and sufficient potassium iodate to constitute approximately 100% excess[14] and the system flushed with carbon dioxide free air.

Closing capillary stopcock a, the three-way stopcock b is then opened so as to permit the flow of emitted gases into the gas reservoir which is maintained at a slight vacuum by means of the leveling bulb.

The carbon dioxide flask is then charged with 10 ml. of approximately 0.25 *N* barium hydroxide, partially evacuated, and then connected to the other arm of the three-way stopcock.

Three ml. of pure concentrated sulfuric acid (carbon free) are now introduced into the reaction vessel by means of the stopcock a. The charge is now ready for combustion.

By means of a phosphoric acid bath[15] the temperature of the reaction chamber is kept at approximately 190 ± 5° for twenty to forty minutes. The gases which are generated during this time pass through the U-tube containing approximately 1 ml. of concentrated potassium iodide solution, to the gas holder B. By operating stopcocks b and c the carbon dioxide is readily transferred to the reaction flask C.

At the end of the heating operation stopcock a is opened and 5 ml. of 50% sulfuric acid (to decrease the free air space) is introduced. The gas which has accumulated in gas reservoir B is then transferred to reaction flask C.

An Ascarite tower is now connected to the apparatus

(9) Stanek and Nemes, *Z. Anal. Chem.*, **95**, 244 (1933).
(10) R. J. Williams, THIS JOURNAL, **59**, 288 (1937).
(11) Williams, Rohrmann and Christensen, *ibid.*, **59**, 291 (1937).
(12) Lunge and Ambler, "Technical Gas Analysis," Gurney and Jackson, London, 1934, p. 221.
(13) Samples such as hydroquinone which are rapidly oxidized in the cold by iodic acid can be treated successfully by first wetting the sample with a drop or two of 50% sulfuric acid before introducing the concentrated acid. The presence of a platinum boat in the reaction mixture should be avoided since it apparently catalyzes the decomposition of iodate.
(14) One milli-equivalent of oxygen will completely oxidize 2 mg. of paraffin, 7.5 mg. of glucose, or 4 mg. of benzoic acid. From the nature of an unknown compound one can approximate in most cases the iodate requirement with sufficient accuracy as to make a preliminary oxidation unnecessary.
(15) Christensen and King, *Ind. Eng. Chem., Anal. Ed.*, **9**, 194 (1936).

through stopcock a, and sufficient air (carbon dioxide free) is flushed through the system to sweep all the carbon dioxide into the evacuated flask C, bringing it to atmospheric pressure.

Determination of Carbon Dioxide.[16]—The flask C is now removed and allowed to stand for twenty minutes. Ten ml. of water and 5 ml. of acetone (to improve end-point) are then added and the excess barium hydroxide is *neutralized* to the thymol blue end-point. In order to give as sharp a change as possible 0.8 *N* hydrochloric acid is added at the rate of approximately one-half drop per second. When within about 0.3 to 0.4 ml. of neutrality, 0.05 *N* acid is used to establish the end-point. In case of oxidation of an unknown compound the 0.8 *N* hydrochloric acid required can be approximated sufficiently for this purpose so as not to introduce any complications.

To prevent the diffusion of air into the flask during titration, a rubber sheet (such as is used for dental dam) was fitted loosely over the mouth of the flask. The tip of the buret was inserted through a small hole in the rubber. This arrangement kept out the air without complicating the procedure whatsoever.

Having *neutralized* the excess barium hydroxide, the solution containing the barium carbonate precipitate is then made slightly acid to methyl red with a known amount of 0.05 *N* hydrochloric acid. In order to ensure removal of the last traces of carbon dioxide, the solution is boiled for five minutes. The amount of standard acid required to neutralize the barium carbonate can now be determined accurately by back titration with 0.05 *N* sodium hydroxide to the methyl red end-point. From these data the amount of carbon dioxide evolved can be computed.

Preliminary experiments using either carbon dioxide evolved from sodium carbonate or direct titration of solutions of sodium carbonate consistently gave high values for recovered carbon dioxide. This constant deviation was found to depend on quantity of precipitate and was thought to be due primarily to the apparent adsorption of barium hydroxide by the barium carbonate. In order to avoid using a blank, the hydrochloric acid was standardized with the carbon dioxide (evolved from either sodium carbonate or from the combustion of succinic acid) by means of the above procedure.

Determination of Oxygen Consumed.—The reaction vessel A is removed and the mixture transferred to a 1-liter Erlenmeyer flask, then diluted to approximately 100 ml. and steamed until disappearance of the iodine color. Sufficient sodium carbonate to neutralize about all but 1 ml. of the concentrated sulfuric acid is now added. Two grams of potassium iodide are introduced and the solution is then titrated with 0.1 *N* sodium thiosulfate. This measures the excess iodate.

The amount of iodate used was found to be consistently greater than the theoretical due to traces of organic matter in the sulfuric acid and to thermal decomposition. This necessitated the use of a blank which amounted to 0.90 mg.

(16) This procedure was later modified as follows: 10 ml. of standard barium hydroxide was measured by automatic pipet and introduced into vessel C. The amount of carbon dioxide absorbed was determined by titrating the excess barium hydroxide with 0.05 *N* hydrochloric acid to thymol blue end-point. The same precautions such as use of rubber sheet, acetone, etc., were taken here as in the case of the titration of barium carbonate.

Discussion and Results

The results of a number of typical runs are tabulated in Table I.

Calculation of Hydrogen.—Having determined both the percentage of carbon and the oxygen requirement of the compound, the percentage of hydrogen can be calculated readily from the equations of Strebinger

$$\% \text{ H} = \frac{(\%O_R + 100 - 11/3\% \text{ C})}{8.93}$$

where O_R is the oxygen requirement in grams per hundred grams of sample. With compounds containing other elements in addition to carbon, hydrogen and oxygen, these calculations can be applied to the residue after correcting for such elements.

Determination of the Empirical Formula.—From the above data it is possible to make some very interesting calculations. By way of illustration one may take a specific case in which the following designations can be used

$C_xH_yO_z$ = formula of unknown
M = molecular weight
N = number of atoms of oxygen required to oxidize one molecule of compound
E = grams oxidized by 1 gram atom of oxygen

then

$$M = \frac{12\,x}{\%\text{ C}} \qquad M = NE$$

$$NE = \frac{12\,x}{\%\text{ C}} \qquad \frac{N}{x} = \frac{12}{\%\text{ CE}} = R$$

$$N = Rx$$

Since N and x are integers, there must be one integer which multiplied by R will give the other integer. The possible integers (which fit this equation) can be ascertained rapidly with a slide rule.

Suppose that from the analysis of an unknown compound (benzoic acid) one obtains the following data: E = 8.12 (8.14 calcd.), % C = 69.3 (68.8 calcd.). Calculating the value of R we obtain 2.13. This would give x and N the possible integral values listed below.

x	N	M[17]
7	14.92	122
8	15.05	138
15	32.00	260

Which value of x, N and M is the correct one can be established readily by means of the Diophantine equations derived by Milne[10] in which

(a) $y = (6N - M + 22z)/2$
(b) $z = (M - 6N + 2y)/22$
(c) $x = (M - 2N - 18z)/8$

(17) M is always an even integer except in the case of odd molecules.

TABLE I

Mg sample	Taken	Mg. KIO_3 Used	Corr.	Ml. HCl used (Neutralize $BaCO_3$)	Milli-eq. CO_2 found	Carbon, % Found	Carbon, % Calcd.	Hydrogen, % Found	Hydrogen, % Calcd.	E Found	E Calcd.
Succinic acid											
16.34	255.3	83.4	82.5	22.12	1.107	40.66	40.68	5.16	5.12	16.96	16.88
16.38	251.5	83.7	82.8	22.21	1.111	40.71		5.12		16.93	
18.44	253.2	94.8	93.9	25.02	1.250	40.67		5.18		16.81	
15.15	256.7	78.0	77.1	20.68	1.033	40.91		5.08		16.82	
Hydroquinone											
14.19	254.3	144.3	143.4	30.91	1.545	65.34	65.44	5.55	5.49	8.47	8.48
11.76	252.7	119.5	118.6	25.69	1.283	65.46		5.49		8.49	
15.60	251.4	158.6	157.7	34.00	1.699	65.33		5.55		8.47	
Benzoic acid											
10.04	258.7	107.0	106.1	23.13	1.156	68.84	68.84	4.88	4.95	8.13	8.14
12.94	252.0	137.2	136.3	29.78	1.488	69.05		5.08		8.10	
12.05	251.1	128.3	127.4	27.68	1.383	69.02		4.97		8.10	
Cinnamic acid											
10.12	256.1	117.4	116.5	24.55	1.227	72.73	72.96	5.44	5.44	7.44	7.41
15.07	251.6	175.1	174.2	36.70	1.833	72.96		5.43		7.41	
10.38	254.8	120.2	119.3	25.22	1.261	72.88		5.48		7.42	
Vanillin											
16.47	252.3	158.7	157.8	34.70	1.735	63.22	63.15	5.35	5.30	8.93	8.95
12.13	250.5	116.4	115.5	25.55	1.277	63.18		5.23		8.99	
Sucrose											
15.69	252.6	96.1	95.2	21.94	1.097	41.94	42.10	6.67	6.48	14.11	14.25
13.09	257.9	79.3	78.4	18.36	0.9181	42.08		6.43		14.29	
12.24	253.4	74.5	73.6	17.22	.8613	42.22		6.46		14.25	
Acetylsalicylic acid											
9.94	249.8	85.8	84.9	19.90	.9952	60.07	60.00	4.43	4.47	10.02	10.00
15.17	253.7	131.5	130.6	30.45	1.522	60.21		4.58		9.94	
14.15	250.4	122.8	121.9	28.52	1.425	60.44		4.48		9.94	
Phenyl salicylate											
10.41	250.8	117.0	116.1	25.28	1.263	72.82	72.89	4.66	4.71	7.68	7.66
12.82	251.4	144.7	143.8	31.21	1.560	73.08		4.71		7.63	
12.37	248.7	139.4	138.5	30.00	1.500	72.94		4.72		7.65	
13.69	249.8	155.0	154.1	33.34	1.667	73.04		4.80		7.60	

x, y, z, N and M are integral values. Below are listed the values of y and z derived from equations (a), (b), and (c).

Value of x	Corresponding value of z	Corresponding value of y
7	2	6
8	2.22	4
15	4.23	10

It is evident that the formula can be none other than $C_7H_6O_2$.

In certain cases where molecular weight is large or where considerable error is made in the determination of either E or percentage carbon, several *possible* solutions may be obtained. Even under these rather adverse conditions it is still possible to determine the correct formula. In such cases differences in chemical behavior, the determination of molecular or equivalent weights are a direct aid in determining the correct solution.

With the percentage carbon and "oxygen consumed" data it is also possible to ascertain the nature of the errors made during a determination (such as incorrect weights, wet or partially dehydrated samples, incomplete combustion) merely from the nature of carbon to oxygen ratios which are obtained.

Other Applications.—On many occasions it is only necessary to determine the percentage carbon to serve as a check on the purity of a preparation. For such purposes this method is especially adaptable, particularly on the micro scale. Furthermore, certain compounds which are not completely oxidized at 200° can be treated successfully at a higher temperature. In such cases

oxygen equivalent data may be obtained by the dichromate method.

Limitations.—The one limitation to this method is the use of iodic acid as an oxidizing agent. Not all compounds are completely oxidized by this reagent at 200°. The literature, however, reveals that a great many compounds can be oxidized successfully by iodic acid under conditions here specified.

In the case of compounds with high molecular weights, the determination of the molecular formula has the same limitations in accuracy as do the traditional combustion methods.

The question of compounds containing nitrogen, sulfur and halogens has not yet been investigated in this Laboratory. However, both Strebinger, and Stanek and Nemes have oxidized successfully a number of such compounds with iodic acid. It is the opinion of the authors that the presence of nitrogen, halogen, or sulfur in an organic compound which can be completely oxidized should offer no complications to the method here described.

When one considers (1) the simple apparatus, (2) adaptability of the procedure to intermittent operation, (3) the amount of information derived from a single analysis, and (4) rapidity of analysis (less than two hours), it is evident that this method offers at least a partial solution to an important organic technique.

Summary

A simple apparatus for the determination of oxygen equivalence and percentage carbon by means of iodic acid oxidation has been described.

A modification of the Pettenkofer method for the determination of carbon dioxide has been devised.

Equations have been derived by means of which the empirical formula of an organic compound can be established readily from the data supplied by the above method.

CORVALLIS, OREGON RECEIVED MAY 10, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE SCHOOL OF PHARMACY, UNIVERSITY OF MARYLAND]

Fluorinated Aromatic Mercurials

BY MELVIN F. W. DUNKER AND EDGAR B. STARKEY

The preparation and properties of some fluorinated aromatic mercurials are described. These compounds have been tested for antiseptic activity and the results are reported in detail elsewhere.[1]

The direct mercuration of fluorobenzene by refluxing in glacial acetic acid with mercuric acetate yielded about 10% of *o*-fluorophenylmercuric chloride. The mercuration of *p*-fluorophenol with mercuric acetate in water at room temperature yielded a monomercurial assumed to have the mercury ortho to the hydroxyl since *p*-chlorophenol is reported to mercurate in that position.[2] The fluorophenylmercuric chlorides were prepared as shown by the equations below

$$O_2N{-}C_6H_4{-}NH_2 \xrightarrow[HNO_2]{HBF_4} O_2N{-}C_6H_4{-}N_2BF_4 \xrightarrow{\Delta}$$

$$O_2N{-}C_6H_4{-}F \xrightarrow[H_2 + Pd]{Sn + HCl\ or} F{-}C_6H_4{-}NH_2 \xrightarrow[HNO_2]{HBF_4}$$

$$F{-}C_6H_4{-}N_2BF_4 \xrightarrow[HgCl_2]{SnCl_2} F{-}C_6H_4{-}HgCl$$

While the replacement of the diazonium group with mercury does not always give yields which are entirely satisfactory, yet the compounds so prepared are generally obtained more pure, or in a form more easily purified, than when other methods are employed. This has been noted before.[3]

Experimental

Fluoronitrobenzenes.—The diazotization of *p*-nitroaniline as previously described[4] yielded the theoretical quantity of *p*-nitrobenzenediazonium fluoborate (ortho, 92%; meta, 92%). The decomposition of the diazonium fluoborate was carried out as described by Schiemann,[5] the same sand being used for repeated decompositions of the same diazonium compound. The decomposition of 1 mole of *p*-nitrobenzenediazonium fluoborate in 20-g. portions gave 82 g. of *p*-nitrofluorobenzene or 58% of the theoretical (ortho, 13%; meta, 43%).

Fluoroanilines.—The reduction of 100 g. (0.7 mole) of *p*-nitrofluorobenzene with tin and hydrochloric acid yielded 58 g. (75%) of *p*-fluoroaniline (ortho, 70%; meta, 89%).

(1) Accepted for publication in the *Journal of Bacteriology*.

(2) German Patent 234,851.

(3) Nesmejanow, *et al.*, *Ber.*, **62**, 1010 (1929); *ibid.*, **67**, 130 (1934).

(4) Dunker, Starkey and Jenkins, THIS JOURNAL, **58**, 2308 (1936).

(5) Schiemann and Pillarsky, *Ber.*, **62**, 3035 (1929).

The theoretical yield of *p*-fluoroaniline was obtained by the reduction of *p*-nitrofluorobenzene in 95% alcohol with hydrogen and palladium catalyst on charcoal.

Fluorophenylmercuric Chlorides.—The diazotization of the fluoroanilines gave the following yields of dry diazonium compounds: para, 86%; ortho, 70%; meta, 98%. The replacement of the diazonium group with mercury was carried out as described in an earlier paper.[4] *p*-Fluorophenylmercuric chloride was obtained in small glistening plates soluble in alcohol, acetone, glacial acetic acid, slightly soluble in benzene and insoluble in water. It was crystallized from hot glacial acetic acid and melted at 293–294°, decomposing slowly at the melting point (24% yield). *o*-Fluorophenylmercuric chloride was prepared similarly in 24% yield from *o*-fluorobenzenediazonium fluoborate. It was very soluble in alcohol and acetone and was recrystallized from ether, the crystals melting at 159–160°. *m*-Fluorophenylmercuric chloride was prepared in 28% yield from *m*-fluorobenzenediazonium fluoborate by the same procedure. Its solubility behavior was similar to that of the para isomer and its melting point 250–251° (all m. p. corrected).[6]

Anal.[7] Calcd. for C_6H_4ClFHg: Hg, 60.6. Found: Hg for ortho 60.5, 61.2; for meta 60.4, 60.9; for para 60.7, 60.8.

Mercuration of Fluorobenzene.—A mixture of 20 g. (0.21 mole) of fluorobenzene, prepared according to Balz and Schiemann,[8] 65 g. of mercuric acetate and 100 cc. of glacial acetic acid was refluxed for twelve hours. The cold reaction mixture was treated with dilute hydrochloric acid and then diluted with water to 700 cc. The white amorphous solid was filtered off and partially dried. The mixture was extracted with hot glacial acetic acid and the extractive, after crystallization from alcohol, gave 7 g. (about 11%) of needles melting at 156° and giving no depression of m. p. when mixed with a sample of pure *o*-fluorophenylmercuric chloride. The remainder of the white solid was amorphous, could not be separated into fractions by further crystallizations and melted over a wide range of temperature.

***p*-Fluorophenol.**—*p*-Fluorophenol was prepared from *p*-fluoroaniline in 40% yield as described by Rinkes[9] and also from *p*-phenetidine by introducing the fluorine according to the method of Schiemann and then deëthylating with aluminum chloride.[10]

Mercuration of *p*-Fluorophenol.—A solution of 13 g. (0.116 mole) of *p*-fluorophenol in 180 cc. of water was treated with a solution of 36 g. (0.113 mole) of mercuric acetate in 100 cc. of water acidulated with acetic acid. The mixture was allowed to stand for four days at room temperature and yielded 34 g. of crystals which were slightly soluble in benzene and water, soluble in acetone, alcohol and glacial acetic acid. When the compound was crystallized from glacial acetic acid, it melted at 193–194° with decomposition. A small amount (about 1 g.) of a dimercurial was formed which was not isolated in pure condition.

Anal. Calcd. for $C_8H_7O_3FHg$: Hg, 54.1. Found: Hg, 52.9, 53.1.

***p*-Fluorobenzoic Acid.**—*p*-Fluorotoluene was prepared from *p*-toluidine by the Schiemann method[5] in 70% yield. A yield of 58% of *p*-fluorobenzoic acid melting at 183–184° was obtained on oxidation with potassium permanganate. *p*-Fluorobenzoic acid was also prepared as described by Schiemann and Winkelmüller in 50% yield.[11]

Mercuration of *p*-Fluorobenzoic Acid.—The direct mercuration of *p*-fluorobenzoic acid as described under fluorobenzene gave a poor yield of a monomercurial. The mercurichloride was a white powder which could not be crystallized from alcohol, acetone or benzene. On heating, the mercurial slowly turned yellow above 230° and melted with decomposition at 239°.

Anal. Calcd. for $C_7H_4O_2ClFHg$: Hg, 53.5. Found: Hg, 53.4.

3-Nitro-4-fluorobenzoic Acid.—The nitration of *p*-fluorobenzoic acid by the method of Rouche[12] gave 3-nitro-4-fluorobenzoic acid, melting at 121–122° in 50% yield.

3-Amino-4-fluorobenzoic Acid.—The reduction of the above compound using hydrogen and palladium catalyst gave 11 g. (98%) of 3-amino-4-fluorobenzoic acid. Several crystallizations from boiling water (with charcoal) yielded tan needles. The free acid melted with decomposition at 182–183°. The hydrochloride crystallized from water in small white plates which began to darken at 215° and melted with decomposition at 240–243°. The acetylamino derivative also was prepared and obtained as white needles from water, melting with decomposition at 245–246° if heated rapidly to 240°. The acetylamino compound decomposed from 200° up if heated slowly.

Anal. Calcd. for $C_9H_8O_3FN$; N, 7.11. Found: N, 7.16, 7.23, 7.03; av., 7.14.

2-Fluoro-5-carboxybenzenediazonium Fluoborate.—The diazotization of 8 g. of 4-fluoro-3-aminobenzoic acid yielded 10 g. (77%) of cream-colored diazonium compound, decomposition point 185°.

4-Fluoro-3-chloromercuribenzoic Acid.—The replacement of the diazonium group with mercury as described[4] gave a poor yield of highly colored mercurial. However, by repeated solution of the compound in acetone and precipitation with petroleum ether, there was obtained a small amount of cream-colored amorphous powder melting at 240–241° with decomposition. The mixed melting point of this compound with the mercurial prepared by direct mercuration was 239° with decomposition.

As additional evidence that, in the mercuration of *p*-fluorobenzoic acid, the mercury entered the ring adjacent to the fluorine, the following is offered. The compound decomposed with effervescence at its melting point and a deposit of white needles which were identified as *o*-fluorophenylmercuric chloride (mixed m. p.) sublimed on the upper portion of the tube.

Summary

1. The three isomeric fluorophenylmercuric

(6) Kharasch, Pines and Levine, *J. Org. Chem.*, **3**, 347 (1938), reported 291° for the para compound and 243° for the meta.

(7) Mercury analyses throughout according to Tabern and Shelberg, *Ind. Eng. Chem., Anal. Ed.*, **4**, 401 (1932).

(8) Balz and Schiemann, *Ber.*, **60**, 1186 (1927).

(9) Rinkes, *Chem. Weekblad*, **9**, 778 (1912).

(10) Swarts, *Bull. acad. roy. méd. Belg.*, 265 (1913).

(11) Schiemann and Winkelmüller, *Org. Syntheses*, **13**, 52 (1933).

(12) Rouche, *Bull. acad. roy. méd. Belg.*, 534 (1921).

chlorides have been prepared and characterized, the ortho derivative being reported for the first time.

2. The preparation and properties of the new mercurials 4-fluoro-3-chloro-mercuribenzoic acid and 4-fluoro-2-acetoxymercuriphenol are reported.

3. The preparation and melting points are given for 4-fluoro-3-aminobenzoic acid, its hydrochloride and acetyl derivative and the decomposition point for 2-fluoro-5-carboxybenzenediazonium fluoborate, all of which are new.

BALTIMORE, MARYLAND RECEIVED JUNE 26, 1939

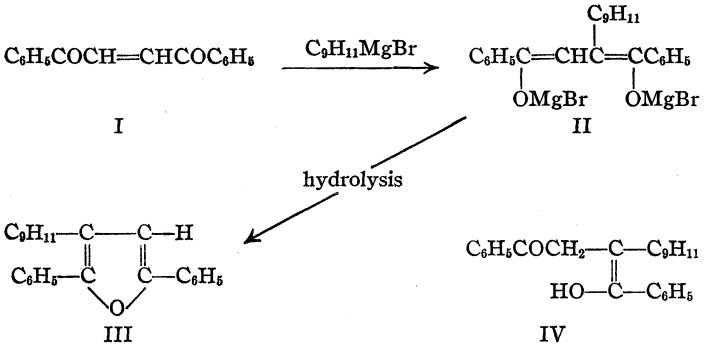
[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY, UNIVERSITY OF VIRGINIA]

The 1,4-Diphenyl-2-mesityl 1,4-Diketones

BY ROBERT E. LUTZ AND CHARLES J. KIBLER

The preparation of this series of compounds was undertaken in order to study the effect of reactions of a mesityl group substituted directly at the ethylene linkage of the unsaturated 1,4-diketone system, and to determine the effect of this mesityl group on the tautomerism of the corresponding triketone enol and hydroxyfuranone.

The starting point in the synthesis was dibenzoylethylene, I. Mesitylmagnesium bromide adds to the unsaturated diketone readily, presumably through 1,4-addition followed by enolization at the remaining carbonyl, to give the dienolate II.[1] On hydrolysis 2,5-diphenyl-3-mesitylfuran, III, was formed exclusively and in good yield, with no indication of the formation of the expected and hoped for saturated diketone, $C_6H_5COCH_2CH(C_9H_{11})COC_6H_5$, which remains as yet unknown. This result is not particularly surprising, however, since it is known that phenylmagnesium bromide adds to dibenzoylstyrene with the formation of large amounts of the corresponding tetraphenylfuran along with the expected saturated diketone, tetraphenyl-1,4-butanedione.[1b,2] The mesityl group not only offers no hindrance to furanization but actually facilitates the reaction considerably. It seems very likely that the dienolic intermediate II on hydrolysis undergoes prompt ketonization at the unhindered enolic group to produce the monoenol, IV, with a normally reactive carbonyl now available for furan ring closure, and with the remaining and hindered enolic group, in the favorable configuration indicated, persisting long enough for reaction to be complete even under these mild conditions.



The unsaturated 1,4-diketone of this series, VI, is easily obtained by the nitric–acetic acid oxidation of the furan, III, and is assigned the *cis* configuration on the basis of this mode of preparation.[3] It is reduced easily by zinc and acetic acid, sodium hydrosulfite, and catalytic hydrogen; but the furan III was the only crystalline product obtained. In the catalytic hydrogenation an attempt was made to follow the course of the reaction. Piperidine was added in the hope that ketonization would be catalyzed with the production of the saturated diketone instead of the furan. A non-crystalline product was obtained which spontaneously on standing for eight days, or immediately when treated with acetic anhydride and sulfuric acid, gave the furan, and which very evidently contained the monoenol IV. Undoubtedly, then, the reduction was 1,6.

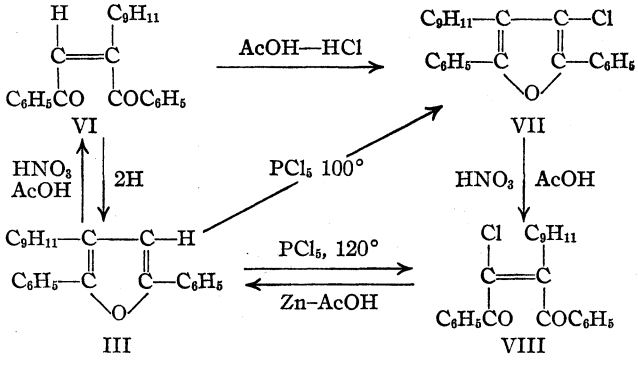
The unsaturated diketone VI reacts with dry hydrogen chloride in acetic acid to give the chlorofuran VII which is obtained also by direct chlorination of the furan III with phosphorus pentachloride at 100° (at a higher temperature, however, some of the unsaturated chloro diketone VIII is

(1) *Cf.* (a) Lutz and Tyson, THIS JOURNAL, **56**, 1341 (1934); (b) Lutz and Reveley, *ibid.*, **61**, 1854 (1939).

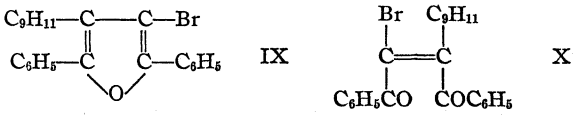
(2) Hahn and Murray, *ibid.*, **36**, 1484 (1914).

(3) *Cf.* (a) Lutz and Wilder, *ibid.*, **56**, 979 (1934); (b) Lutz, Tyson, Sanders and Fink, *ibid.*, **56**, 2679 (1934); (c) Lutz and Wilder, *ibid.*, **56**, 2145 (1934); (d) Lutz and Eisner, *ibid.*, **56**, 2698 (1934).

formed through the oxidizing action of the reagent[3c]). The nitric–acetic acid oxidation of the chlorofuran gives the unsaturated chloro diketone in good yield. This compound as would be expected is reduced by zinc and acetic acid to the furan III. The structures of these halogen derivatives are evident from their modes of formation and from their reactions as outlined in the diagram.

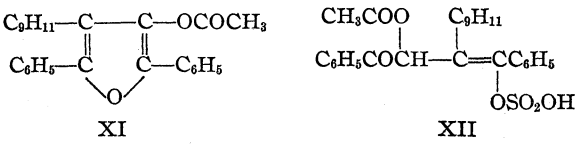


The bromofuran IX was obtained by reactions similar to those described above, from the furan III and phosphorus pentabromide, and from the unsaturated diketone VI and hydrogen bromide in acetic acid or phosphorus pentabromide. Oxidation of the bromofuran gives the unsaturated bromo diketone X which is reduced directly to the furan III by zinc and acetic acid.



In the reactions of diphenylmesitylfuran described above, it is noteworthy that halogenation occurs readily and only in the vacant β-position in the furan nucleus. Evidently the mesityl group does not hinder substitution or oxidative ring fission.

The unsaturated diketone VI reacts with acetic anhydride and sulfuric acid to give the acetoxyfuran XI, a reaction not easily carried out on types with mesityl groups in the terminal positions and directly attached to the carbonyl groups.[4] The mechanism of the reaction very probably involves 1,4-addition of acetic anhydride or its equivalent (such as a mixed anhydride, to give XII as intermediate) followed by furanization between the enolized group and the remaining and reactive carbonyl group.



In conclusion it may be stated that the substitution of mesityl in the 2-position on the chain of dibenzoylethylene and in the β-position of the furan nucleus has introduced no unexpected hindrance to typical reactions.

The synthesis and study of the triketone enolhydroxyfuranone tautomerism in this series is in progress.

Experimental Part

2,5-Diphenyl-3-mesitylfuran, III.—Seven grams of powdered dibenzoylethylene in 1-g. portions was added with efficient stirring to a solution of three equivalents of mesitylmagnesium bromide in 60 cc. of absolute ether. The reaction was immediate and vigorous. The resulting clear brownish solution was refluxed for fifteen minutes and decomposed in ice water acidified with hydrochloric acid. The product, isolated by extraction with ether, was digested with ethanol, the furan crystallizing in nearly pure condition in 65% yield. It crystallized from acetone as flat colorless needles melting at 157.5–158°.[5]

Anal. Calcd. for $C_{25}H_{22}O$: C, 88.7; H, 6.55. Found: C, 88.6, 88.8; H, 6.6, 6.7.

An attempt was made to show that the furan was not actually formed until after hydrolysis or partial hydrolysis by carrying out the reaction in the presence of an excess of iodine for the purpose of oxidizing the dienol as fast as it was liberated. Only the furan was obtained. This is without significance, however, since the rate of furanization is evidently unusually high and since one case is now known where a dienol, oxidizable by air, is rearranged instead into the saturated diketone when treated with iodine under conditions similar to those employed here (namely, the dienol formed in the catalytic reduction of the dimolecular alkaline condensation product of di-(trimethylbenzoyl)-ethylene[6]).

The furan reacted with three parts of phosphorus pentachloride when the two solids were fused together and heated at 100° for one hour. Largely unchanged material was obtained on hydrolysis of the reaction mixture, but a small amount of the chlorofuran VII was isolated upon fractional crystallization. In a similar experiment with heating for five minutes at 120°, followed by hydrolysis and fractional crystallization, again unchanged material was recovered together with a small amount of the chloro unsaturated diketone VIII. The furan reacted at room temperature with five parts of phosphorus pentabromide with the formation of a red oil which was allowed to stand

(4) *Cf.* Lutz and Wood, THIS JOURNAL, **60**, 229 (1938). 1,2,4-Trimesityl-2-butenedione-1,4 and 1,4-dimesityl-2-phenyl-2-butenedione-1,4 do not give acetoxyfurans under the usual conditions (Lutz and Kibler, papers to appear shortly).

(5) The melting points of all analytical samples are corrected.

(6) Lutz and Disque, unpublished results.

for twenty-five minutes. On hydrolysis and crystallization of the resulting solid product from ethanol, the bromofuran X was obtained in 64% yield.

cis-**1,4-Diphenyl-2-methyl-2-butenedione-1,4 (Dibenzoylmesitylethylene), VI.**—A suspension of 5 g. of diphenylmesitylfuran III in 25 cc. of concd. acetic acid, cooled to 10°, was treated with 20 cc. of a 1–3 mixture of concd. nitric and acetic acids, also cooled to 10°. The furan dissolved immediately with evolution of oxides of nitrogen. The solution was allowed to stand at 10° for one hour and was then decomposed in water. After several hours the coagulated product was filtered off and crystallized from ethanol, giving 4.3 g. (90%) of nearly pure material. It crystallized from ethanol or methanol as rectangular plates or rosets melting at 98.5–99.5°.

Anal. Calcd. for $C_{25}H_{22}O_2$: C, 84.7; H, 6.3. Found: C, 84.5; H, 6.3.

Sunlight was without action on the unsaturated diketone in ethanol solution or in chloroform containing iodine.

Reduction. (a) A mixture of 0.5 g. of the unsaturated diketone, an excess of zinc dust, and 50 cc. of concd. acetic acid was allowed to react in the cold and was then heated slowly to boiling. The furan III was the sole product isolated; yield 65%. Similar results were obtained when the zinc dust was added to a boiling solution of the unsaturated diketone in concd. acetic acid.

(b) A mixture of 0.5 g. of sodium hydrosulfite, 0.5 g. of the unsaturated diketone and 70% ethanol was refluxed for thirty minutes and diluted with water. Fractional crystallization from ethanol gave 0.2 g. of the furan and 0.15 g. of unchanged material.

(c) A solution of 0.5 g. of the unsaturated diketone in 70% ethanol with 0.1 g. of platinum oxide catalyst absorbed one molecule of hydrogen in fifteen minutes. Filtering and diluting with water and extracting with ether gave an oil which could not be induced to crystallize. A sample of the oil was treated with acetic anhydride containing a trace of sulfuric acid; on subsequent hydrolysis the product crystallized without difficulty and proved to be the furan. The oily product on standing for eight days deposited crystals of the furan which was identified.

4-Chloro-2,5-diphenyl-3-mesitylfuran, VII.—A solution of 0.7 g. of the unsaturated diketone VI in 20 cc. of concd. acetic acid was saturated at room temperature with dry hydrogen chloride. In a short time 0.42 g. of analytically pure chlorofuran VII crystallized as truncated prisms melting at 102.5–103.5°. On diluting the filtrate with water 0.15 g. of nearly pure furan was obtained; total yield 77%. Further crystallization of the main product did not change the melting point.

Anal. Calcd. for $C_{25}H_{21}OCl$: Cl, 9.5. Found: Cl, 9.6.

cis-**3-Chloro-1,4-diphenyl-2-mesityl-2-butenedione-1,4, VIII.**—A suspension of 0.15 g. of the chlorofuran VII in 2 cc. of concd. acetic acid was treated with 0.2 cc. of a mixture of 0.2 cc. of concd. nitric acid and 0.5 cc. of concd. acetic acid, at room temperature. After standing for ten minutes the furan dissolved and 0.1 g. of the unsaturated chloro diketone VII crystallized as thick hexagonal plates melting at 127.5–128°. Recrystallization from methanol and from ethanol did not change the melting point.

Anal. Calcd. for $C_{25}H_{21}O_2Cl$: C, 77.2; H, 5.46. Found: C, 77.2; H, 5.3.

Reduction to the furan III was effected quickly in the usual way by the action of zinc dust in boiling concd. acetic acid (one minute).

4-Bromo-2,5-diphenyl-3-mesitylfuran, IX.—To a solution of 0.5 g. of VI in 5 cc. of concd. acetic acid at room temperature was added slowly 2 cc. of a 30% solution of hydrogen bromide in concd. acetic acid. The product crystallized and after standing for five minutes the solution was partly diluted with water and the product crystallized from ethanol, giving 0.37 g. (65%) of nearly pure bromofuran IX. It was purified by further crystallizations from isopropanol; truncated prisms of melting point 126–127°.

Anal. Calcd. for $C_{25}H_{21}OBr$: C, 71.9; H, 5.1. Found: C, 72.1; H, 5.4.

In an alternative procedure 0.1 g. of VI was mixed thoroughly with 0.5 g. of phosphorus pentabromide and allowed to react for an hour, the temperature being maintained at 0°. Hydrolysis and crystallization from ethanol gave 0.07 g. of pure bromofuran.

cis-**3-Bromo-1,4-diphenyl-2-mesityl-2-butenedione-1,4, X.**—A solution of 0.3 g. of the bromofuran IX in 3 cc. of concd. acetic acid was treated with 1 cc. of a 1–3 mixture of concd. nitric and acetic acids at room temperature. After standing for fifteen minutes the product was precipitated with water and crystallized from ethanol; yield 95%. It crystallized from methanol as hexagonal plates melting at 103–104.5°. It was stable in the solid state in the dark but turned deep pink when exposed to light. Ethanol solutions appeared not to be affected by exposure to sunlight.

Anal. Calcd. for $C_{25}H_{21}O_2Br$: C, 69.3; H, 4.9. Found: C, 68.8, 69.5; H, 5.0, 5.2.

Reduction to the furan III was effected quickly by zinc dust and concd. acetic acid (one minute) in the usual way.

4-Acetoxy-2,5-diphenyl-3-mesitylfuran, XI.—A solution of 0.5 g. of VI in 10 cc. of acetic anhydride was treated with 10 drops of concd. sulfuric acid. Reaction was indicated by coloration and warming. After standing for five minutes and hydrolysis in ice water, the product was isolated by extraction with ether. It crystallized (cubic) from ethanol; yield, 0.44 g. (78%); m. p. 124.5–126.5°. It was not very stable and further crystallization by the ordinary methods lowered the melting point.

Anal. Calcd. for $C_{27}H_{24}O_3$: C, 81.8; H, 6.1. Found: C, 82.2, 82.1; H, 6.4, 6.5.

Summary

Mesitylmagnesium bromide adds 1,4 to dibenzoylethylene but gives diphenylmesitylfuran instead of the expected saturated diketone.

The unsaturated diketone was made by the nitric–acetic acid oxidation of the furan. Reduction of this gives the furan, even with catalytic hydrogen in 70% ethanol. It was converted into an acetoxyfuran.

The chloro and bromo derivatives of the furan and the unsaturated diketone are described.

The presence of the mesityl group does not hinder typical reactions.

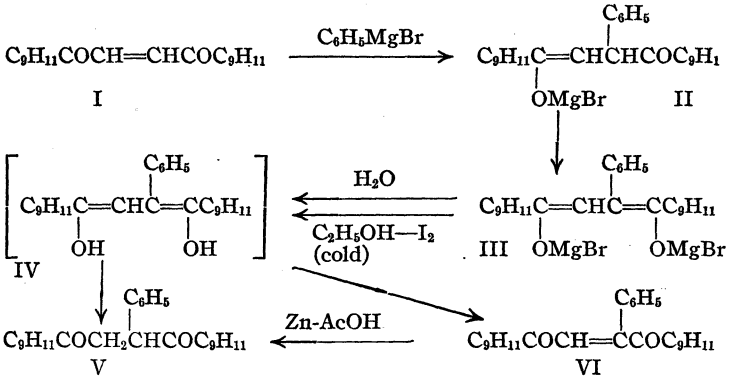
CHARLOTTESVILLE, VIRGINIA
RECEIVED AUGUST 30, 1939

[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY, UNIVERSITY OF VIRGINIA]

The 1,4-Dimesityl-2-phenyl 1,4-Diketones

BY ROBERT E. LUTZ AND CHARLES J. KIBLER

This series of compounds has been made in order to study the effect of terminal mesityl groups on the reactions of the saturated and unsaturated 1,4-diketone systems and on the ease of furan ring closure and ring fission. Interest centers in a comparison of the reactions of this series with, first, those of di-(trimethylbenzoyl)-ethylene, I, and, second, those of dibenzoylphenylethylene, $C_6H_5COCH{=}C(C_6H_5)COC_6H_5$. In the case of di-(trimethylbenzoyl)-ethylene the reactions of the conjugated systems are relatively unimpaired and like those of dibenzoylethylene itself, but of course the individual carbonyl group reactivities are lowered. In the case of dibenzoylphenylethylene, as compared with dibenzoylethylene, the full conjugated system is nearly as easily reduced, one α,β-unsaturated ketone system appears to react normally with the other definitely hindered, the ethylene linkage is unreactive as also is one of the carbonyls, but furan ring closure is if anything facilitated as also is the reverse reaction, oxidative fission of the furan ring.



1,4-Dimesityl-2-phenyl-1,4-butanedione, V, has been made from di-(trimethylbenzoyl)-ethylene, I, by 1,4-addition of phenylmagnesium bromide,[1] the reaction proceeding as indicated in the diagram through the monoenolate II to the dienolate III. The proof that the excess of phenylmagnesium bromide causes the enolization of II to III rests on the hydrolysis of the product under oxidizing conditions with the formation of the unsaturated 1,4-diketone, VI, which could only have been produced by oxidation of the dienol IV.[2] The reaction between the Grignard reagent and di-(trimethylbenzoyl)-ethylene, then, can be manipulated to give good yields of the unsaturated diketone, VI. Since the nitric–acetic acid oxidation method has proved to be useless in the case of 2,5-dimesitylfurans, this oxidation of the dienol becomes the logical preparative method.

Dibenzoylphenylethylene and dibenzoylmesitylethylene, whatever the method of synthesis, appear to have the *cis* configuration with respect to the aroyl groups, and are obtainable by the oxidation both of the corresponding furans and the dienols.[2,3] It is probable, therefore, that the unsaturated diketone under discussion, VI, is also *cis*.

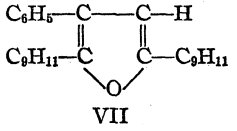
Reduction of the unsaturated diketone proceeds easily with zinc and acetic acid to give the saturated diketone exclusively.

Furan ring closure from the saturated diketone, V, could not be brought about by the usual procedure using acetic anhydride and sulfuric acid. Since di-(trimethylbenzoyl)-ethane itself cannot be dehydrated under these conditions,[4] it might appear that ring closure by this method is to some extent hindered by the mesityl groups; however, di - (trimethylbenzoyl) - dimethylethane, $C_9H_{11}COCH(CH_3)CH(CH_3)COC_9H_{11}$, is furanized with extraordinary ease under comparable conditions.[5] It can only be said that the 1,4-dimesityl com-

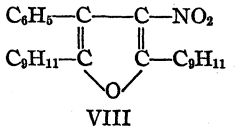
(1) Lutz and Tyson, THIS JOURNAL, **56**, 1341 (1934).
(2) Lutz and Reveley, *ibid.*, **61**, 1854 (1939).
(3) (a) Lutz and Wilder, *ibid.*, **56**, 979 (1934); (b) Lutz, Tyson, Sanders and Fink, *ibid.*, **56**, 2679 (1934); (c) Lutz and Kibler, *ibid.*, **61**, 3007 (1939).
(4) Lutz, Johnson and Wood, *ibid.*, **60**, 716 (1938).
(5) Lutz and Taylor, *ibid.*, **55**, 1593 (1933).

pounds are less consistent in their behavior toward dehydrating agents than the 1,4-diketones with aryl groups which have no ortho substituents.

Furanization of the saturated diketone to VII was accomplished smoothly by the action of hydriodic acid at 150°, and also by the prolonged action of boiling acetic acid saturated continually with dry hydrogen chloride. The second of these procedures, which was only partially successful in the case of di-(trimethylbenzoyl)-ethane, proved to be very satisfactory here. It is worthy of note that the 2-phenyl group in V definitely has facilitated furan ring closure as do the 2-phenyl and 2-mesityl groups when substituted in dibenzoylethane.



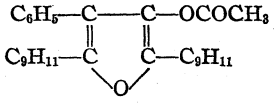
VII



VIII

Attempts to oxidize dimesitylphenylfuran, VII, using concentrations of the nitric–acetic acid reagent which are effective in the oxidation of various 2,5-diphenylfurans to the corresponding *cis* unsaturated 1,4-diketones, failed to open the furan ring; instead, substitution of one nitro group was the result. In view of the ease of nitration at the β-positions in dimesitylfurans and the relative unreactivity of the aryl nuclei,[6] the structure VIII has been assigned.

Attempts to convert the unsaturated diketone VI into the acetoxyfuran IX by the action of acetic anhydride or acetyl chloride and sulfuric acid failed, thus closing the door to one possible path for the preparation of the corresponding triketone enol, the synthesis of which is now being undertaken by other methods.



IX

Experimental Part

2,5-Dimesityl-3-phenylfuran, VII.—Attempts to dehydrate dimesitylphenylbutanedione V with acetic anhydride and sulfuric acid under a variety of conditions from 0° to the boiling point failed. Two methods were found, the best being presented under (a).

(a) A solution of 1.0 g. of V in 25 cc. of concd. acetic acid and 1 cc. of water was refluxed gently, dry hydrogen chloride being passed through the boiling solution for thirty hours. On cooling 0.53 g. of nearly pure furan crystallized and 0.34 g. was obtained by diluting the filtrate with water and recrystallizing. It was crystallized from concd. acetic acid; rectangular plates, m. p. 104–105.5° (corr.).

Anal. Calcd. for $C_{28}H_{28}O$: C, 88.4; H, 7.4. Found: C, 88.2; H, 7.7.

(b) A mixture of 0.2 g. of V and 1 cc. of hydriodic acid (sp. gr. 1.7, protected with hypophosphorous acid) was heated in a sealed tube at 145–150° for one hour. The resinous product crystallized from ethanol giving a 74% yield of the furan.

2,5-Dimesityl-4(?)-nitro-3-phenylfuran, VIII.—A suspension of 0.1 g. of dimesitylphenylfuran, VII, in 1 cc. of concd. acetic acid, supercooled to 10°, was treated with 0.4 cc. of a 1–3 mixture of concd. nitric and acetic acids. The temperature was maintained at 10° for one hour. The product began to separate within a few minutes. Filtration gave 0.07 g. of nearly pure nitro derivative. After two crystallizations from isopropanol it separated as cubic prisms melting at 164–165° (corr.).

Anal. Calcd. for $C_{28}H_{27}O_3N$: C, 79.0; H, 6.4; N, 3.3. Found: C, 78.9; H, 6.3; N, 3.36.

1,4-Dimesityl-2-phenyl-2-butenedione-1,4, VI.—Five grams of powdered di-(trimethylbenzoyl)-ethylene, I, was added in half-gram portions to 3 equivalents of phenylmagnesium bromide in 60 cc. of absolute ether with thorough and continued mechanical stirring. The reaction was immediate and vigorous, producing a clear brown solution. This was then refluxed for a few minutes, cooled to 0°, and added slowly over ten minutes to a vigorously stirred solution of 6 g. of iodine in 200 cc. of ethanol cooled in an ice-bath. The temperature of the mixture varied between 0 and 10°. Stirring was continued for ten minutes and water containing sodium bisulfite and acidified was added to destroy the excess of iodine. Extraction with ether and subsequent concentration to small volume produced 2.9 g. of pale yellow crystals; yield 46%. Repeated crystallization from ethanol gave truncated prisms melting at 109–110° (corr.).

Anal. Calcd. for $C_{28}H_{28}O_2$: C, 84.8; H, 7.1. Found: C, 84.7; H, 7.1.

Substitution of quinone for iodine in the above oxidation produced similar results.

Reduction by means of zinc dust and boiling concd. acetic acid in the usual way produced the saturated diketone in good yield.

Attempts to convert the unsaturated diketone into the acetoxyfuran under varied conditions failed. Using acetic anhydride and concd. sulfuric acid at temperatures up to 50°, no reaction occurred, and at higher temperatures up to 100° intractable resins were obtained. Using acetyl chloride instead gave similar results but at lower temperatures from 0 to 25°.

Summary

1,4-Dimesityl-2-phenyl-2-butenedione-1,4 is made by the reaction between phenylmagnesium bromide and di-(trimethylbenzoyl)-ethylene, followed by oxidative hydrolysis of the resulting dienolate.

(6) Lutz and Kibler, work on the nitration of the 2,5-dimesitylfurans, to be published shortly.

Dimesitylphenylfuran is made by dehydration of the saturated diketone. It is not oxidized by the nitric–acetic acid reagent.

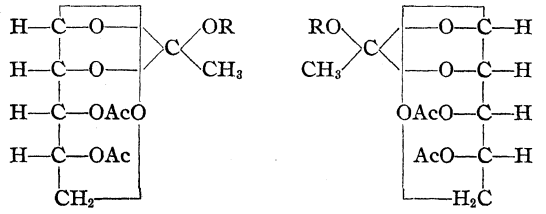
CHARLOTTESVILLE, VIRGINIA RECEIVED AUGUST 30, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

The Preparation of *d*- and *l*-Ribosidodihydroxyacetone Tetraacetates with an Orthoester Structure

BY CLARENCE W. KLINGENSMITH AND WILLIAM LLOYD EVANS

In a previous communication[1] the synthesis of the first pairs of disaccharide antipodes, β-*d*- and β-*l*-arabinosidodihydroxyacetone tetraacetates and β-*d*- and β-*l*-xylosidodihydroxyacetone tetraacetates, and the synthesis of the first disaccharide racemate, β-*d*,β-*l*-arabinosidodihydroxyacetone tetraacetate were reported. In this communication another pair of antipodes containing *d*- and *l*-ribose and dihydroxyacetone is reported. The behavior of this pair of ribose derivatives as well as the synthesis of methyl-*d*-riboside triacetate (II) with an orthoester structure by Levene and Tipson[2] indicates that the orthoester structures, (I) and (III), should be assigned to them.



I. R = $AcOCH_2COCH_2$-. III. R = $AcOCH_2COCH_2$-.
II. R = CH_3-.

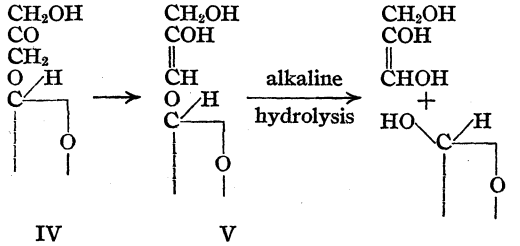
In conformity to the nomenclature proposed by Haworth, Hirst and Stacy[3] for methylglycoside acetates with an orthoester structure, our compounds are named diacetyl *d*-ribose-1,2-ortho-3′-acetoxyacetonyl acetate (I) and diacetyl *l*-ribose-1,2-ortho-3′-acetoxyacetonyl acetate (III).

Methylglycoside acetates with an orthoester structure were first obtained by Fischer, Bergmann and Rabe,[4] and the nature of their structures was first explained by Bott, Haworth and Hirst[5] and independently by Freudenberg and Scholz.[6] This type of methylglycoside acetate has been obtained with rhamnose,[4,7] mannose,[5,8,9] lyxose,[10] maltose,[6,11] 4-[β-*d*-glucosido]-*d*-mannose,[12] ribose,[2] *d*-α-glucoheptose,[3] turanose,[13] fructose,[14] and talose,[15] and is characterized by (a) one acetyl group that is stable to alkaline hydrolysis and (b) extreme sensitivity to acids.

The orthoester structures of diacetyl *d*-ribose-1,2-ortho-3′-acetoxyacetonyl acetate and diacetyl *l*-ribose-1,2-ortho-3′-acetoxyacetonyl acetate differ from the orthoester structure of the methylglycoside acetates in that the acetoxyacetonyl group, $AcOCH_2COCH_2$-, of the former is substituted for the methyl group of the latter. The presence of the acetoxyacetonyl group made it impossible for us to demonstrate the stability of one acetyl group to alkaline hydrolysis in contrast to the removal of the other three normal acetyl groups. In an acetyl determination by the method of Kunz and Hudson,[16] diacetyl *d*-ribose-1,2-ortho-3′-acetoxyacetonyl acetate gave a value that was 9.4% higher than the theoretical value for four groups or 46% higher than the theoretical value for three groups. Kreider and Evans[17] previously reported that the acetyl values of oligosaccharide acetates that contained dihydroxyacetone were about 10% high by the method of Kunz and Hudson. Bernier[18] also obtained high acetyl values with dihydroxyacetone monoacetate. These high values are in accord with

(1) L. C. Kreider and W. L. Evans, THIS JOURNAL, **58**, 797 (1936).
(2) P. A. Levene and R. S. Tipson, *J. Biol. Chem.*, **92**, 109 (1931).
(3) W. N. Haworth, E. L. Hirst and M. Stacy, *J. Chem. Soc.*, 2864 (1931).
(4) E. Fischer, M. Bergmann and A. Rabe, *Ber.*, **53**, 2362 (1920).
(5) H. G. Bott, W. N. Haworth and E. L. Hirst, *J. Chem. Soc.*, 1395 (1930).
(6) K. Freudenberg and H. Scholz, *Ber.*, **63**, 1969 (1930).
(7) W. N. Haworth, E. L. Hirst and E. J. Miller, *J. Chem. Soc.*, 2469 (1929).
(8) J. K. Dale, THIS JOURNAL, **46**, 1046 (1924).
(9) P. A. Levene and H. Sobotka, *J. Biol. Chem.*, **67**, 771 (1926).
(10) P. A. Levene and M. L. Wolfrom, *ibid.*, **78**, 525; **79**, 471 (1928).
(11) K. Freudenberg, H. Hochstetter and H. Engels, *Ber.*, **58**, 666 (1925).
(12) H. S. Isbell, *Bur. Standards J. Research*, **7**, 1115 (1931).
(13) E. Pacsu, THIS JOURNAL, **55**, 2451 (1933).
(14) E. Pacsu, *ibid.*, **57**, 745 (1935).
(15) W. W. Pigman and H. S. Isbell, *Bur. Standards J. Research*, **9**, 189 (1937).
(16) A. Kunz and C. S. Hudson, THIS JOURNAL, **48**, 1978 (1926).
(17) L. C. Kreider and W. L. Evans, *ibid.*, **58**, 1661 (1936).
(18) C. L. Bernier, Master's Thesis, The Ohio State University, 1932.

the work of Evans and Cornthwaite,[19] who found that dihydroxyacetone in alkaline solution was converted into lactic, acetic, and formic acids as well as other substances. The fact that our acetyl value by the Kunz and Hudson method was abnormally high for three groups can be accounted for on the basis of the findings of Gehman, Kreider, and Evans.[20] They presented evidence to show that the dihydroxyacetone portion of oligosaccharides (IV) containing dihydroxyacetone was susceptible to alkaline hydrolysis by virtue of their possible rearrangement to the enediol structure (V).

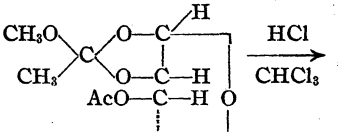


IV V

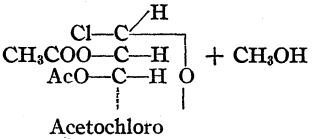
In an analogous manner, the *d*-ribose-1,2-ortho-3′-hydroxyacetonyl acetate (VI), formed by the removal of the three normal acetyl groups in the alkaline hydrolysis (Kunz and Hudson acetyl determination) of diacetyl *d*-ribose-1,2-ortho-3′-acetoxyacetonyl acetate (I), may rearrange to the enediol structure (VII). This may then undergo alkaline hydrolysis to the trioseenediol (VIII), the precursor of lactic acid and *d*-ribose-1,2-orthoacetic acid (IX), which may suffer further hydrolysis to *d*-ribose (XI) by first rearranging to 2-monoacetyl-*d*-ribose (X).

The rearrangement of *d*-ribose-1,2-orthoacetic acid (IX) to 2-monoacetyl-*d*-ribose (X) is in harmony with the evidence presented by Pigman and Isbell[15] to show that orthoacid derivatives are unstable to alkali.

The behavior of diacetyl *d*-ribose-1,2-ortho-3′-acetoxyacetonyl acetate and diacetyl *l*-ribose-1,2-ortho-3′-acetoxyacetonyl acetate in dry alcohol-free chloroform containing dry hydrogen chloride was analogous to the behavior of the methylglycoside acetates with an orthoester structure. Isbell[12,15] observed that the rotations of 4-[β-*d*-glucosido]-methyl-*d*-mannoside heptaacetate and of methyl-*d*-taloside tetraacetate with orthoester structures changed rapidly in chloroform solution containing dry hydrogen chloride and that acetochloro-4-[β-*d*-glucosido]-*d*-mannose and acetochloro-*d*-talose were formed.

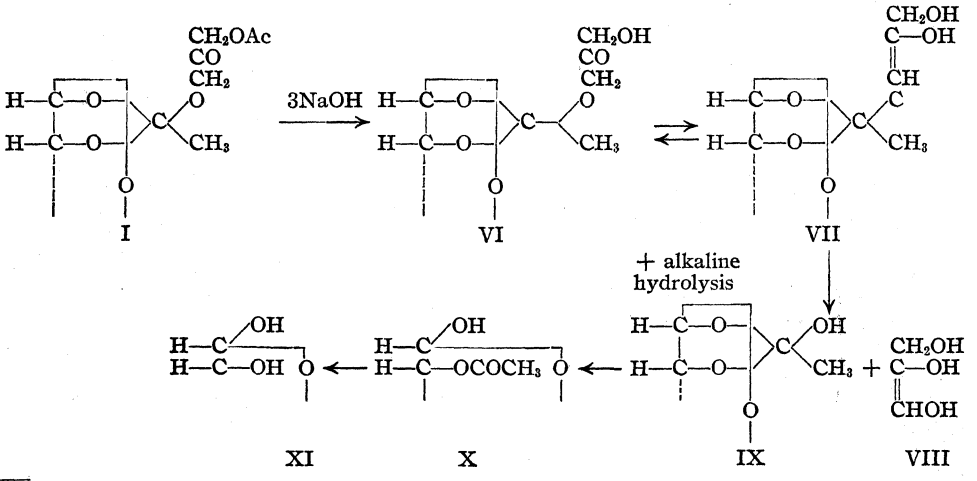


Methylglycoside acetate with an orthoester structure



Acetochloro derivative

A similar rotation change occurred with our ribose derivatives, (I) and (III), and evidence that the acetochlororiboses were formed was observed. Furthermore, the isomeric compound, the β-*d*-arabinosidodihydroxyacetone tetraacetate of Kreider and Evans,[1] which does not possess an orthoester structure, showed no reaction with hydro-



I VI VII IX VIII X XI

(19) W. L. Evans and W. R. Cornthwaite, THIS JOURNAL, **50**, 486 (1928).

(20) H. Gehman, L. C. Kreider and W. L. Evans, *ibid.*, **58**, 2388 (1936).

gen chloride in chloroform solution. Hence, it is concluded that the behavior of the ribose derivatives, (I) and (III), is to be attributed to an orthoester structure.

The possibility that diacetyl *d*-ribose-1,2-ortho-3′-acetoxyacetonyl acetate and diacetyl *l*-ribose-1,2-ortho-3′-acetoxyacetonyl acetate contain β-biosidic links was also eliminated by the fact that the calculated specific rotations of β-*d*-ribosidodihydroxyacetone tetraacetate (unknown compound) and β-*l*-ribosidodihydroxyacetone tetraacetate (unknown compound) are −112.3 and +112.3°, respectively, which are in complete disagreement with the observed specific rotations of −11.6 and +11.8°. These rotations were calculated from the value of A as given by Kreider and Evans[1] and from the value of B which was calculated from the rotatory values of the individual asymmetric carbon atoms of a pentose tetraacetate which were obtained by a method analogous to that of Isbell.[21]

A racemate, diacetyl *d,l*-ribose-1,2-ortho-3′-acetoxyacetonyl acetate, also is described. Other compounds which are reported in the literature for the first time are *l*-ribose tetraacetate, *d,l*-ribose tetraacetate and acetobromo-*l*-ribose.

Experimental Part

Preparation of Known Starting Materials.—*d*- and *l*-ribose were prepared from *d*- and *l*-arabinose, respectively, according to the directions of Karrer, *et al.*[22] The *d*-ribose, which was recrystallized once from absolute ethanol, was acetylated by the procedure of Levene and Tipson[2] to *d*-ribose tetraacetate, m. p. 109.5–110.0° (corr.), $[\alpha]^{28}D$ −56.0° (*c*,[23] 3.0; pure chloroform). A product with these same constants was obtained by the acetylation of a sample of *d*-ribose that had been purified by conversion to *d*-ribose *p*-bromophenylhydrazone, m. p. 165.0–165.5° (corr.), and subsequent hydrolysis with benzaldehyde according to the procedure given by Karrer.[22] The values of *d*-ribose tetraacetate as reported by Levene and Tipson[2] are given here for comparison: m. p. 110°, $[\alpha]^{25}D$ −52.0° (chloroform). Acetobromo-*d*-ribose, m. p. 94.5–95.5° (corr.), $[\alpha]^{25}D$ −223.9° (*c*, 3.0; pure chloroform), was obtained from the tetraacetate according to the directions of Levene and Tipson.[2] The values of acetobromo-*d*-ribose as given in the literature[2] are presented here for comparison: m. p. 96°, $[\alpha]^{25}D$ −209.3° (*c*, 2; chloroform). Dihydroxyacetone monoacetate was prepared by the method of Fischer, Baer and Feldmann.[24] The silver carbonate was prepared as in the previous communication.[1] The Drierite used as the internal desiccant was finely powdered and preheated at 235° for two hours. The benzene used as the reaction medium and the solvent for the acetobromo riboses was thiophene-free, dried and distilled over sodium and preserved over Drierite.

***l*-Ribose Tetraacetate.**—This compound was prepared from *l*-ribose (once recrystallized from absolute ethanol), according to the procedure used by Levene and Tipson[2] in the preparation of *d*-ribose tetraacetate. After two recrystallizations from ethanol (95%), the melting point, m. p. 109.5–110.0° (corr.), and specific rotation, $[\alpha]^{30}D$ +56.0° (*c*, 3.5; pure chloroform), were constant. The yield of the pure crystalline product was 58% of the theoretical. The acetylation of a sample of *l*-ribose that was purified by conversion to *l*-ribose *p*-bromophenylhydrazone, m. p. 165.0–165.5° (corr.), and subsequent hydrolysis with benzaldehyde by the procedure of Karrer[22] gave a product with the same constants.

Anal. Calcd. for $C_5H_6O_5(COCH_3)_4$: acetyl, 12.58 ml. of 0.1 *N* NaOH per 100 mg. Found: acetyl, 12.60 ml.

***d,l*-Ribose Tetraacetate.**—Equal portions (200 mg.) of *d*-ribose tetraacetate and *l*-ribose tetraacetate were dissolved in warm ethanol (95%). Upon cooling the solution, crystallization took place. The product melted at 90.5° (corr.). The observed rotation in a 2-dm. micro polarimeter tube was ±0.0° (*c*, 2.4; pure chloroform). The melting point of each constituent taken separately was 109.5–110.0°, a mixed melting point of the two active isomers was 84.5–86.5° (corr.), and a mixed melting point of the racemic modification and a small amount of either active isomer was 88.0–90.0° (corr.). These facts seem to indicate that the racemic modification is a molecular compound.

Acetobromo-*l*-ribose.—This compound was prepared essentially according to the procedure of Levene and Tipson[2] for the preparation of acetobromo-*d*-ribose except that *l*-ribose tetraacetate was substituted for *d*-ribose tetraacetate. The yield was 69–75% of the theoretical based on the *l*-ribose tetraacetate as compared with the 60% yield reported by Levene and Tipson. This higher yield was attributed to the fact that the solution of the *l*-ribose tetraacetate in the acetic acid–hydrogen bromide reagent was allowed to stand at room temperature (20–25°) for two hours rather than for one hour. The product was recrystallized once from ether and petroleum ether: m. p. 94.5–95.5° (corr.), $[\alpha]^{23}D$ +224.8° (*c*, 3.1; pure chloroform).

Anal. Calcd. for $C_{11}H_{15}O_7Br$: Br, 23.58. Found: Br, 23.68.

Diacetyl *d*-Ribose-1,2-ortho-3′-acetoxyacetonyl Acetate.—This compound was prepared from acetobromo-*d*-ribose and dihydroxyacetone monoacetate essentially according to the directions of Kreider and Evans[1] for the preparation of β-*d*-arabinosidodihydroxyacetone tetraacetate. After the manner of Reynolds and Evans[25] the acetobromo-*d*-ribose was dissolved in benzene and dropped into the reaction flask over a period of forty-five minutes rather than adding the solid substance portion-wise. Iodine (1 mole) was used as a catalyst after the manner of Helferich, Bohm and Winkler.[26] The yield was 18–20%

(21) H. S. Isbell, *Bur. Standards J. Research*, **3**, 1041 (1929).

(22) P. Karrer, *et al.*, *Helv. Chim. Acta*, **18**, 1435 (1935).

(23) In this paper, *c* represents the concentration in grams per 100 ml. of solution.

(24) H. O. L. Fischer, E. Baer and L. Feldmann, *Ber.*, **63**, 1732 (1930).

(25) D. D. Reynolds and W. L. Evans, THIS JOURNAL, **60**, 2559 (1938).

(26) B. Helferich, E. Bohm and S. Winkler, *Ber.*, **63**, 990 (1930).

of the theoretical based on the acetobromo-*d*-ribose. The crude product was recrystallized to constant melting point and rotation by dissolving in pure chloroform or benzene, decolorizing with Carboraffin, evaporating to a thin sirup and adding 10–15 volumes of dry alcohol-free ether. It crystallized in needle-like clusters; m. p. 97.0–98.0° (corr.), $[\alpha]^{24}D$ −11.6° (*c*, 1.8; pure chloroform).

Anal. Calcd. for $C_8H_{10}O_7(COCH_3)_4$: acetyl, 10.26 ml. of 0.1 *N* NaOH per 100 mg. Found: acetyl (Freudenberg[27]), 10.25 ml.

This substance was soluble in chloroform, acetone, and benzene; moderately soluble in alcohol; and slightly soluble in ether and water. It was very sensitive to hydrogen chloride in chloroform solution. When 0.2075 g. was dissolved in 15.08 ml. of dry alcohol-free chloroform containing 0.011 g. of dry hydrogen chloride, the first rotation observed in a 2-dm. tube six minutes after dissolution was −3.03°. On the basis of a specific rotation of −11.6°, the initial rotation in chloroform alone was calculated to be −0.32°, indicating that a very rapid rotation change had taken place. No further change in rotation was observed even after standing for fifteen minutes. The hydrogen chloride was then removed from the solution by shaking with silver carbonate, after first adding a few grams of powdered Drierite to remove the water formed by the neutralization reaction. The solid materials were removed by filtration. Upon evaporating the solvent from the filtrate a sirup was obtained which could not be brought to crystallization. The sirup gave a positive test for halogen and evolved acid fumes after standing several weeks at room temperature which indicated the presence of acetochloro-*d*-ribose.

Diacetyl *l*-Ribose-1,2-ortho-3′-acetoxyacetonyl Acetate.—This compound was prepared and purified in exactly the same manner as the *d*-isomer except that acetobromo-*l*-ribose was substituted for acetobromo-*d*-ribose: yield, 18–20% of the theoretical, m. p. 97.0–98.0° (corr.), $[\alpha]^{25}D$ +11.8° (*c*, 3.2; pure chloroform). It crystallized in needle-like clusters.

Anal. Calcd. for $C_8H_{10}O_7(COCH_3)_4$: acetyl, 10.26 ml. of 0.1 *N* NaOH per 100 mg. Found: acetyl (Freudenberg[27]), 10.10 ml.

This substance was soluble in chloroform, acetone, and benzene, moderately soluble in alcohol, and slightly soluble in ether and water. The behavior of this compound in chloroform solution containing hydrogen chloride was analogous to the *d*-isomer. When 0.5211 g. was dissolved in 25.72 ml. of dry alcohol-free chloroform containing 0.162 g. of dry hydrogen chloride, the first rotation observed in a 4-dm. tube five minutes after dissolution was +9.45°. On the basis of a specific rotation of +11.8°, the initial rotation in chloroform alone was calculated to be +0.95°, indicating that a rapid rotation change had occurred. After removing the hydrogen chloride and the solvent as described in the case of the *d*-isomer, a sirup was obtained which could not be brought to crystallization. The sirup gave a positive test for halogen and evolved acid fumes after standing for a few weeks. The behavior of this sirup was indicative of the presence of acetochloro-*l*-ribose.

Diacetyl *d,l*-Ribose-1,2-ortho-3′-acetoxyacetonyl Acetate.—Equal portions (52 mg.) of the two isomers were dissolved in benzene and evaporated to a thin sirup. Upon adding a large volume of anhydrous ether, crystallization took place. The product melted at 124.5–125.0° (corr.). The melting point of the constituents taken separately was 97.0–98.0°. The observed rotation in a 2-dm. micro polarimeter tube was ±0.0° (*c*, 1.7; pure chloroform). These facts indicate that a true racemate was formed.

Acknowledgment.—The authors wish to thank H. J. Dauben, who prepared a large part of the *l*-ribose that was used in this work.

Summary

1. The preparation of the following pair of disaccharide antipodes in crystalline condition is described: diacetyl *d*-ribose-1,2-ortho-3′-acetoxyacetonyl acetate and diacetyl *l*-ribose-1,2-ortho-3′-acetoxyacetonyl acetate. The racemate, diacetyl *d,l*-ribose-1,2-ortho-3′-acetoxyacetonyl acetate is also described.

2. These are the first examples of orthoester derivatives which contain a group other than the methyl and ethyl groups as a part of the ortho structure.

3. A possible explanation for the high acetyl values of diacetyl *d*-ribose-1,2-ortho-3′-acetoxyacetonyl acetate by the Kunz and Hudson method is presented.

4. *l*-Ribose tetraacetate and acetobromo-*l*-ribose are reported for the first time. The racemate, *d,l*-ribose tetraacetate, is described.

COLUMBUS, OHIO RECEIVED AUGUST 21, 1939

(27) K. Freudenberg and M. Harder, *Ann.*, **433**, 230 (1923).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

Monoalkyldioxanes

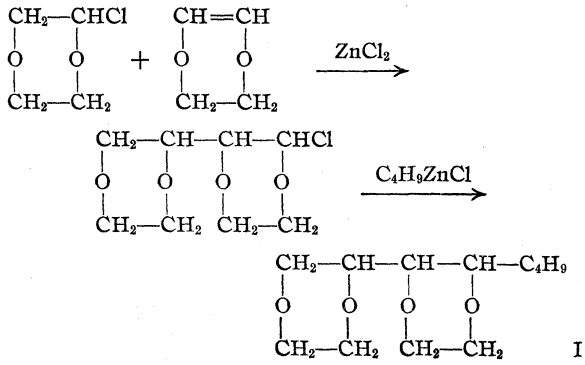
BY R. K. SUMMERBELL AND R. R. UMHOEFER

Methods of synthesizing dialkyl-, diaryl-, and monoaryldioxanes have been reported previously.[1,2] The analogous method is applied here to the problem of the monoalkyldioxanes. Variations in the procedure indicate the best yields to be obtained by adding pure monochlorodioxane to the Grignard solution.

In the previous work on dialkyldioxanes,[2] it was found advantageous to treat the Grignard reagent with zinc or cadmium chlorides before carrying out the reaction with the 2,3-dichlorodioxane. As there is little possibility of a dehalogenating side reaction, no advantage was anticipated in the present case, and none was found.

Because of the tendency of monochlorodioxane to decompose on standing, it was always freshly prepared before each reaction. Monochlorodioxane is best made by adding dry hydrogen chloride to dioxene at 0° and distilling the resulting mixture. The yields of monochlorodioxane are lowered by using benzene or ethyl ether as solvents. The conversion of dioxene to monochlorodioxane seems to be incomplete, even with the use of excess hydrogen chloride, since slight amounts of dioxene are recovered on distillation of the reaction product.

A mixture of dioxene and monochlorodioxane, in the presence of polymerizing catalysts, when treated with a Grignard reagent yields, besides the expected alkyldioxane, a small amount of a solid product. No solid by-product was obtained in cases where the monochlorodioxane was distilled before the reaction with the Grignard reagent or when the polymerizing catalysts were omitted. The compound obtained by the use of the butyl Grignard reagent in the presence of zinc chloride had the empirical formula $C_{12}H_{22}O_4$. As the compound is without any very reactive functional groups, the four oxygen atoms are probably constituents in two dioxane rings. From these data formula I, 2-butyl-3-dioxanyldioxane, can be advanced as the possible structure of the compound. As acyl halides[3] and α-chloroethers[4,5] in the presence of catalysts may be added to ethylenic hydrocarbons, the probable mechanism by which the 2-butyl-3-dioxanyldioxane is formed is shown by the equation.



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Additional evidence for the structure of the solid has been secured by similarly preparing the corresponding by-product 2-ethyl-3-dioxanyldioxane with the use of the ethyl Grignard reagent.

A New Synthesis of Substituted Dioxanes.—Another synthesis of substituted dioxanes was suggested by the fact that β-chloroethyl ether is converted to dioxane when heated with 5% sodium hydroxide at 200°,[6] or by other reagents.[7]

This method has been applied in synthesizing ethyldioxane from β-chloroethyl β-bromo-α-ethylethyl ether. A mixture of equivalent amounts of acetaldehyde and ethylene chlorohydrin was treated with dry hydrogen chloride at 0° to form β-chloroethyl α-chloroethyl ether.[8] This ether when brominated according to the method of Boord[9] yielded β-chloroethyl α,β-dibromoethyl ether. The reaction of this substance with ethylmagnesium bromide resulted in the desired β-chloroethyl β-bromo-α-ethylethyl ether. When this ether was treated with 10% potassium hydroxide at 200° for three and one-half hours, a 17% yield of ethyldioxane was obtained. By varying the starting materials and Grignard reagents used, this appears to be a general method for the synthesis of many other substituted dioxanes.

Properties of the Monoalkyldioxanes.—The homologous series of the monoalkyldioxanes

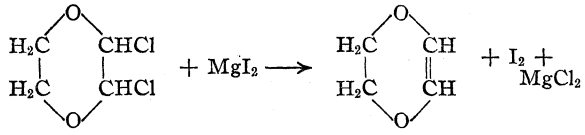
(1) Summerbell and Christ, THIS JOURNAL, **55**, 4547 (1933).
(2) Summerbell and Bauer, *ibid.*, **57**, 2364 (1935); **58**, 759 (1936).
(3) Norris and Couch, *ibid.*, **42**, 2329 (1920).
(4) Straus and Thiel, *Ann.*, **525**, 151 (1936).
(5) Nenitzescu and Przemetzki, *Ber.*, **69**, 2706 (1936).
(6) French Patent 711,595; *C. A.*, **26**, 1947 (1932).
(7) British Patent 435,110; *C. A.*, **30**, 1387 (1936).
(8) Grignard and Purdy, *Bull. soc. chim.*, **31**, 982 (1921); *Compt. rend.*, **175**, 200 (1922).
(9) Boord, THIS JOURNAL, **52**, 653 (1930).

exhibits a uniform variation in physical properties. However, the relationship of refractive index and density appears to be uncommon,[10] in that the slope of the plot of refractive indices of the monoalkyldioxanes, against density, is negative. Methyldioxane, as is dioxane itself, is infinitely soluble in water. Ethyldioxane dissolves to a considerable extent and propyl and butyldioxanes are not appreciably soluble. The lower members of the series have a characteristic, slightly displeasing, ethereal odor. The unpleasantness of the odor increases with higher members of the series.

Dioxane forms addition products with picric acid[11] and hydroquinone[12] which can serve as derivatives. The action of these reagents was tried on the monoalkyldioxanes, but in no case was it possible to isolate an addition compound.

A New Preparation of Dioxene.—Previously dioxene has been prepared only by the action of aliphatic Grignard reagents on 2,3-dichlorodioxane.[2] The reaction of light metals with 2,3-dichlorodioxane was found by Böeseken[13] to result only in tar. He also noted in the reaction of 2,3-dichlorodioxane with sodium iodide in boiling acetone that free iodine was liberated and a precipitate of sodium chloride formed, but he was not able to isolate dioxene.

As the reaction of inorganic iodides on α,β-dihalogen compounds is a method of obtaining double bonds under mild conditions,[14] it seemed desirable to apply this procedure to the synthesis of dioxene. It has been found that a mixture of magnesium and magnesium iodide in dry ether dehalogenates 2,3-dichlorodioxane to yield dioxene. This combination is useful because magnesium iodide is appreciably soluble in ether.



$$Mg + I_2 \longrightarrow MgI_2$$

Furthermore magnesium reacts with the liberated iodine to reform magnesium iodide. The formation of dioxene probably occurs through the intermediate formation of 2,3-diiododioxane.[15]

The use of the combination of magnesium and magnesium iodide in anhydrous solvents as a dehalogenating agent for α,β-dihalogen compounds holds many possibilities of being applicable to those compounds which may be decomposed under more vigorous conditions.

Experimental

Monoalkyldioxanes.—The properties and analyses of the monoalkyldioxanes are given in the tables.

TABLE I

PROPERTIES OF MONOALKYLDIOXANES

Alkyl group	B. p., °C.	Mm.	d^{20}_4	$n^{20}D$	MR_D[b] Calcd.	Found
Methyl-	109–110	746.5	0.977	1.4188	26.38	26.39
Ethyl-	132.5–133	750	.955	1.4263	30.99	31.17
n-Propyl-	155.6–157.1	746[a]	.943	1.4298	35.61	35.64
n-Butyl-	178–179	735[a]	.932	1.4336	40.23	40.26
Allyl-	156–158	747.6[a]	.937	1.4442	35.14	36.35

[a] Corrected temperatures. [b] The calculated values were obtained by using the atomic values from Gilman, "Organic Chemistry," p. 1738. The found values are calculated from the formula of Lorenz and Lorentz.

TABLE II

ANALYSES OF MONOALKYLDIOXANES

Alkyl group	Formula	Percentage composition Calcd. C	Calcd. H	Found C	Found H
Methyl-	$C_5H_{10}O_2$	58.82	9.80	58.53	9.77
Ethyl-	$C_6H_{12}O_2$	62.07	10.34	62.31	10.24
n-Propyl-	$C_7H_{14}O_2$	64.57	10.76	64.31	10.74
n-Butyl-	$C_8H_{16}O_2$	66.62	11.62	66.22	11.19
Allyl-	$C_7H_{12}O_2$	65.57	9.37	65.39	9.58

Allyldioxane.—The procedure that has given the most satisfactory yields of the monoalkyldioxanes was that used in synthesizing allyldioxane. This method will be given in detail.

The allyl Grignard reagent was prepared from 181.5 g. (1.5 moles) of allyl bromide, 36.4 g. (1.5 moles) of magnesium and 600 cc. of dry ether.[16]

The monochlorodioxane was prepared by conducting, with stirring, 2.4 moles of dry hydrogen chloride into 51.6 g. (0.6 mole) of dioxene at 0°. The resulting mixture, on fractional distillation, yielded 50 g. (68.5%) of monochlorodioxane, b. p. 57–65° (25 mm.).

The monochlorodioxane was then added dropwise to the allylmagnesium bromide solution. The reaction mixture was stirred for one-half hour after all the monochlorodioxane had been added. Then excess Grignard reagent was hydrolyzed by slowly adding iced, dilute hydrochloric acid and the ether layer was separated, dried over sodium sulfate, decanted and then fractionally distilled. The fraction which distilled at 148–157° was collected as allyldioxane; yield, 37.8 g. (72.5%). The material was refluxed over sodium for several hours and fractionally distilled twice, b. p. 156–158° (corr.) at 747.6 mm.; d^{20}_4 0.937; $n^{20}D$ 1.4442.

The monoalkyldioxanes were purified by distillation from metallic sodium through a 40-cm. Podbielniak type column. In most cases the refractive indices of the first

(10) Kurtz and Ward, *J. Franklin Inst.*, **222**, 563 (1936).
(11) A. Faworsky, *J. Russ. Phys.-Chem. Soc.*, **38**, 741 (1906).
(12) Evans and Dehn, THIS JOURNAL, **52**, 3204 (1930).
(13) Böeseken, Tellegen and Henriquez, *ibid.*, **55**, 1284 (1933).
(14) Finkelstein, *Ber.*, **43**, 1528 (1910).
(15) C. F. Van Duin, *Rec. trav. chim.*, **43**, 341 (1924).
(16) Gilman and McGlumphy, *Bull. soc. chim.*, **43**, 1322 (1928).

and last portions of the distillate were the same. The allyldioxane, in contrast to the other alkyldioxanes, decomposed considerably when refluxed with sodium. The solid decomposition products were shaken with dilute sodium hydroxide and benzoyl chloride, extracted with ether, and, after drying over sodium sulfate, the ether was allowed to evaporate. A small amount of crystals formed on the side of the beaker and a viscous oil remained on the bottom. The crystals were collected and recrystallized three times from dilute alcohol, m. p. 70°. A mixed melting point with authentic ethylene dibenzoate was at 70–71°. This indicates ethylene glycol to be a reaction product of allyldioxane and sodium.

Reaction of Monochlorodioxane with Butyl Grignard Reagent Using Zinc Chloride.—The Grignard reagent was prepared from 205 g. (1.5 moles) of butyl bromide, 36.4 g. (1.5 moles) of magnesium and 700 cc. of dry ether. To this Grignard reagent was added 204 g. (1.5 moles) of anhydrous zinc chloride dissolved in 300 cc. of dry ether. The mixture was then refluxed for one hour on a water-bath kept at 40°.

The monochlorodioxane was prepared by dissolving 51.6 g. (0.6 mole) of dioxene in 100 cc. of dry benzene and passing into the solution at 0° 1.5 moles of dry hydrogen chloride. The solution was allowed to stand for three hours at room temperature, the color changing from colorless to yellow. Then excess hydrogen chloride was removed under the reduced pressure of the water pump.

The solution of monochlorodioxane was added dropwise to the organometallic mixture at 0°. The reaction mixture was allowed to stand at room temperature for ten hours, and was then refluxed on a water-bath for six hours. The flask was cooled in an ice-bath, and cold water slowly added to the reaction mixture. The precipitate that formed was dissolved by adding dilute sulfuric acid and the ether layer was then separated, dried over sodium sulfate, decanted and fractionally distilled. A fraction which distilled at 40–65° at 18 mm. was collected. The liquid residue which remained solidified on cooling. The fraction of butyldioxane was distilled twice from sodium: yield, 9.5 g. (11%); b. p. 178.2–179.2° (corr.) at 735 mm.; d^{20}_4 0.932; $n^{20}D$ 1.4336.

2-Butyl-3-dioxanyldioxane.—The solid residue from the first distillation of butyldioxane was extracted with petroleum ether, treated with norite and the solvent evaporated. The crystalline residue (1 g.) was recrystallized from dilute alcohol, needles, m. p. 101–102°. The solid was insoluble in water and was not affected by dilute hydrochloric acid or dilute sodium hydroxide. It dissolved in concentrated sulfuric acid without darkening. The material was recovered unchanged after being dissolved in acetyl chloride for one-half hour. The molecular weight, determined by the cryoscopic method using benzene, was found to be 242.

Anal. Calcd. for 2-butyl-3-dioxanyldioxane ($C_{12}H_{22}O_4$): C, 62.61; H, 9.56; mol. wt., 230. Found: C, 62.38, 62.29; H, 9.47, 9.39.

A number of experiments were tried in attempts to increase the yield of the solid compound. Aluminum chloride and zinc chloride were used as catalysts with mixtures of monochlorodioxane and dioxene before the reaction with butylmagnesium bromide. Benzene and carbon disulfide were employed as solvents in the preparation of monochlorodioxane. In most cases a small amount of the solid was obtained. However, the polymerizing agents tended to lead to the formation of tars. A later experiment using magnesium bromide as the catalyst in the synthesis of 2-ethyl-3-dioxanyldioxane appeared to be more satisfactory.

2-Ethyl-5-dioxanyldioxane.—Approximately 0.28 mole of dry hydrogen chloride was bubbled into a solution of 12 g. (0.14 mole) of dioxene and 200 cc. of dry benzene. The resulting mixture was allowed to stand at room temperature for four and one-half hours after adding 7.4 g. of dioxene and a solution of magnesium bromide prepared from one-half gram of bromine in 5 cc. of ether and excess magnesium. Excess hydrogen chloride was then removed from the colorless, turbid solution under the reduced pressure of the water pump.

To this solution was added a filtered Grignard reagent prepared from 64.8 g. of ethyl bromide, 14.4 g. of magnesium and 300 cc. of ether. After standing overnight, excess Grignard reagent was hydrolyzed by slowly adding dilute hydrochloric acid. The ether layer was separated, dried over sodium sulfate and fractionally distilled. A 3.6-g. fraction of ethyldioxane which distilled at 100–138° was collected. The residue (9.5 g.) did not crystallize on standing for several days in the refrigerator. It formed a glass on cooling with dry ice. The material was then heated in a bath at 150° under 20 mm. pressure. About 1 g. of distillate (ethyldioxane) was obtained. The residue contained a few crystals after standing for several days in the refrigerator. The mixture was dissolved in petroleum ether and decanted from some insoluble, colored tar. The petroleum ether was then evaporated and the residue warmed under reduced pressure to remove all the petroleum ether. The material did not crystallize on standing two weeks in the refrigerator. It was then vacuum distilled (1 mm.). The distillate formed an oily mass of crystals after several days. The crystals were filtered, and crystallized twice from dilute methanol: yield 0.5 g., m. p. 97.5°.

A mixed melting point with the solid from the butyldioxane synthesis (m. p. 102°) showed a large depression. The material is slightly soluble in water and easily soluble in organic solvents.

Anal. Calcd. for 2-ethyl-3-dioxanyldioxane ($C_{10}H_{18}O_4$): C, 59.40; H, 8.97. Found: C, 59.41; H, 9.02.

Ethyldioxane from β-Chloroethyl β-Bromo-α-ethylethyl Ether

α-Chloroethyl β-Chloroethyl Ether.—This ether was prepared according to the procedure of Grignard and Purdy[8] by conducting approximately 4 moles of dry hydrogen chloride into a mixture of 88 g. (0.67 mole) of paraldehyde and 161 g. (2 moles) of ethylene chlorohydrin at 0°. The yield of crude, dry α-chloroethyl β-chloroethyl ether was 227 g. (79%).

β-Chloroethyl α,β-Dibromoethyl Ether.—The crude α-chloroethyl β-chloroethyl ether (227 g. or 1.58 moles) was cooled to 0° in an ice-bath and 254 g. (1.58 moles) of bromine added in small portions over a period of two and one-half hours. The reaction product was then placed under reduced pressure to remove hydrogen chloride.

The material, yellow in color, separated into two layers on standing. The small top layer appeared to be water; yield, 420 g. (99%).

One-half, 210 g., of the β-chloroethyl α,β-dibromoethyl ether on distillation yielded a 154 g. (73%) fraction which distilled at 110–113° (12 mm.). This material was without color but turned light yellow on standing a short time. It fumed in air. A portion of the material was redistilled, b. p. 108° (12 mm.).

Anal. Calcd. for $C_4H_7OClBr_2$: total halogen, 73.33. Found: total halogen, 73.55.

β-Chloroethyl β-Bromo-α-ethylethyl Ether.—The unpurified β-chloroethyl α,β-dibromoethyl ether (210 g., 0.79 mole) was added during one hour to a solution at 0° of ethylmagnesium bromide prepared from 108.9 g. (1 mole) of ethyl bromide, 24 g. of magnesium and 450 cc. ether. The reaction mixture was stirred for one-half hour at room temperature. Then excess Grignard reagent was destroyed by slow addition of dilute hydrochloric acid and the ether layer was removed and dried over calcium chloride. After standing for two days the solution had a deep green color. The ether was then removed on a water-bath and the liquid residue vacuum distilled. A 42.5 g. (25%) fraction was obtained which distilled at 92° (12 mm.). The distillate was at first colorless but soon turned pink in color. After standing for two days it became dark amber in color.

A portion of the material was redistilled. A fraction which distilled at 92–93° (12 mm.) was colorless and remained so on standing; d^{20}_4 1.388; $n^{20}D$ 1.4770.

Anal. Calcd. for $C_6H_{12}OClBr$: total halogen, 53.55. Found: total halogen, 54.10.

Ethyldioxane.—Thirty grams of β-chloroethyl β-bromo-α-ethylethyl ether was refluxed for twenty-six hours with 30 g. of potassium hydroxide and 270 cc. of water. At the end of that time a test for halogen was obtained from the aqueous portion; however, a considerable amount of insoluble material remained. The mixture was divided into two equal portions. One portion was heated at 200–205° (bath temp.) in a monel metal bomb for one and one-half hours. The dark turbid solution was then extracted four times with a total of 150 cc. of ether. The combined ether extracts were dried over sodium sulfate and fractionally distilled. Eight-tenths gram (10%) of ethyl dioxane was obtained, b. p. 132–136°.

The other portion of the dihalogen ether and potassium hydroxide mixture was heated at 200–205° (bath temp.) for three and one-half hours. After working up the product as before, 1.4 g. (17%) of ethyldioxane was obtained, b. p. 132–136°.

Dioxene.—The reaction was carried out in a three-necked, five-liter flask equipped with a dropping funnel, bulbed condenser fitted with a calcium chloride tube and a mercury-sealed Hershberg stirrer.[17] In the flask were placed 82.6 g. (3.4 moles) of magnesium turnings and 1200 cc. of dry ether. Then 91.5 g. (0.4 mole) of iodine was added in small portions. The formation of the magnesium iodide occurred readily with the liberation of considerable amounts of heat. When the mixture became colorless, 314 g. (2 moles) of 2,3-dichlorodioxane mixed with 200 cc. of ether was added dropwise, with vigorous stirring, at such a rate that the color of the mixture due to the liberated iodine was never darker than light brown (nine hours). One-half hour after the addition of the last of the 2,3-dichlorodioxane, the mixture became colorless. It was then poured onto cracked ice and the ether layer separated, dried over sodium sulfate, decanted and fractionally distilled. A fraction which distilled at 93–95° was collected as dioxene: yield 84.3 g. (49%).

The synthesis of dioxene by this method has been carried out using varying proportions of magnesium iodide and 2,3-dichlorodioxane. Greater yields of dioxene were obtained with the use of larger amounts of magnesium iodide, and the reaction, particularly after a considerable amount of the 2,3-dichlorodioxane had been added, appeared to proceed more smoothly. In all cases the reaction proceeded at a decreasing rate. This is possibly due to coprecipitation of the iodide ion with the insoluble magnesium chloride. The effect of varying the ratio of magnesium iodide to 2,3-dichlorodioxane on the yield of dioxene is shown in the following table.

Ratio, moles iodine/ moles 2,3-dichlorodioxane	Yield, %
1:20	31
1:10	44
1:5	49

(17) Hershberg, *Ind. Eng. Chem., Anal. Ed.*, **8**, 313 (1936).

Summary

A series of monoalkyldioxanes has been prepared for the first time. The densities, refractive indices and boiling points vary in a uniform manner with increasing size of alkyl group. An uncommon relationship of refractive index and density exists for the series.

A solid by-product from the synthesis of the monoalkyldioxanes has been indicated to be the 2-alkyl-3-dioxanyldioxane. The mechanism for the formation and a method for the synthesis of the compounds are given.

A general method for the synthesis of substituted dioxanes by means of substituted β-halogenethyl ethers has been discussed. The procedure has been applied in the synthesis of ethyldioxane from β-chloroethyl β-bromo-α-ethylethyl ether.

A mixture of magnesium and magnesium iodide in dry ether has been found to be a new and excellent reagent for dehalogenating α,β-dihalogen compounds. It was used in the synthesis of dioxene from 2,3-dichlorodioxane.

EVANSTON, ILLINOIS RECEIVED JUNE 14, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

Dioxadiene

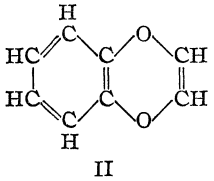
BY R. K. SUMMERBELL AND R. R. UMHOEFER

I. Introduction

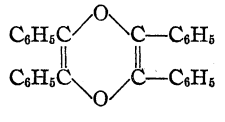
The synthesis of dioxene[1] and the subsequent investigation of its properties has shown this compound to differ in many respects from dioxane. Thus while dioxane is soluble in all proportions with water, dioxene is insoluble. The boiling point of dioxene is seven degrees below that of dioxane. Also the ability to form the unique addition products characteristic of dioxane is no longer evident. Consideration of the contrast in properties of these compounds has led us to synthesize dioxadiene (I), a compound with two double bonds.

Dioxadiene, although hitherto unknown, has long been listed in chemical abstracts under the name of Dioxin. It is used as the fundamental or parent nucleus for the cataloging of dioxane, dioxene, and their derivatives. The term dioxadiene has been proposed previously to designate the compound discussed here.[2,3]

Condensed forms of the dioxadiene nucleus such as benzodioxadiene (II)[4] and dibenzodioxadiene have long been known. Tetraphenyldioxadiene (III) is the only non-condensed derivative of dioxadiene that has been prepared and studied thus far.[3] The presence of so many phenyl groups, raising the molecular weight and modifying the properties of the double bonds, limits the usefulness of such compounds as material for the study of the dioxadiene nucleus.



II



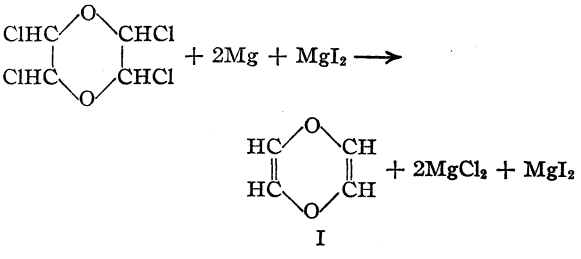
III

II. Synthesis of Dioxadiene

A new synthesis of dioxene from 2,3-dichlorodioxane using a mixture of magnesium and magnesium iodide in ethyl ether as a dehalogenating reagent has been reported.[6] An obvious extension of the method to the synthesis of dioxadiene would be the application of the same dehalogenating reagent to 2,3,5,6-tetrachlorodioxane.

Although dioxene is readily prepared from 2,3-dichlorodioxane, there is a considerable difference in reactivity of 2,3-dichlorodioxane and 2,3,5,6-tetrachlorodioxane. The dichlorodioxane is easily hydrolyzed in ten to fifteen minutes by heating with water, while the tetrachloro compound requires three or four hours for hydrolysis. No reaction could be observed when the symmetrical tetrachlorodioxane was treated with magnesium iodide dissolved in ethyl ether.

The reaction was modified by using the higher boiling *n*-butyl ether as a solvent. Because of the possibility that the dioxadiene would be polymerized at the high temperature required for the reaction, the apparatus was so arranged that the dioxadiene would distil from the reaction mixture as it was formed. The method produced yields of dioxadiene as high as 64% of the theoretical.



I

III. Physical Properties

An interesting physical property of dioxadiene is the boiling point, 75°, which is 26° less than that of dioxane. This large difference is found also in the furan series, where the boiling point of furan is 33° less than that of tetrahydrofuran. Vinyl ether shows a much smaller decrease in boiling point compared with ethyl ether. Correspondingly, a large difference exists between the calculated and observed values of the molar refractivity of both dioxadiene and furan. On the basis of these comparisons the unsaturation of dioxadiene is nearer to that of furan than that of vinyl ether.

Dioxadiene is insoluble in water. This may be explained by assuming that resonance involves the electron pairs of the oxygen so that they are

(1) Summerbell and Bauer, THIS JOURNAL, **57**, 2364 (1935).

(2) Footnote by Hurd, Suter and Summerbell, THIS JOURNAL, **57**, 2364 (1935).

(3) Madelung and Oberwegner, *Ann.*, **490**, 201 (1931); *ibid.*, **526**, 195 (1936).

(4) Moureu, *Compt. rend.*, **128**, 559 (1889).

(5) Ullmann and Stein, *Ber.*, **39**, 622 (1906).

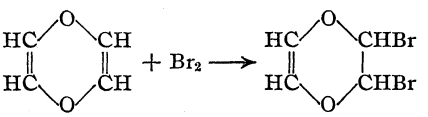
(6) Summerbell and Umhoefer, THIS JOURNAL, **61**, 3016 (1939).

not available for hydrogen bond formation with the solvent.

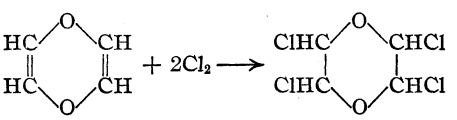
IV. Chemical Properties

The chemical properties of dioxadiene in general are those of an unsaturated ether. However, it shows a greater stability toward dilute acid solutions than other unsaturated ethers such as dioxene and vinyl ether.

Dioxadiene polymerizes in two to three weeks to a hard colorless solid which does not melt below 250°. The polymer is insoluble in water, benzene, dioxane and camphor and hence its molecular weight has not been determined. The polymerized material gave a slight reaction with bromine water. Dioxadiene reacts vigorously with bromine. When brominated in carbon tetrachloride solution, a solid crystalline product, containing two atoms of bromine, was obtained with practically no evolution of hydrogen bromide. The reaction is probably one of addition of bromine to only one of the double bonds. Dioxadiene



reacts with chlorine to form the symmetrical tetrachlorodioxane. This reaction is of importance, as it is an excellent proof of the structure of dioxadiene, since the derivative obtained by this reaction was one of the known isomers.



Hydrogen chloride adds to dioxadiene to form the 2,5-dichlorodioxane. Dioxadiene reacts readily with a solution of mercuric chloride to yield an amorphous solid of unknown structure. Analysis indicates the product to be a dimercury derivative. Slight color changes of doubtful significance were observed when dioxadiene was treated with maleic anhydride and with picric acid; however, no compounds could be isolated.

In all of the above reactions, dioxadiene has behaved in a manner to be expected of an unsaturated aliphatic compound where the unsaturation is conjugated to a limited extent. The name dioxadiene seems more appropriate than dioxin.

Attempts to prepare dioxadiene from more available intermediates were unsuccessful. These included the treatment of diglycolic acid anhydride and glycolide with zinc dust and the pyrolysis of the acetate of dimeric glycol aldehyde.

Experimental

Dioxadiene.—To 23 g. of magnesium turnings in 500 cc. of dry *n*-butyl ether in a one-liter, three-necked flask equipped with an efficient mercury-sealed stirrer connected with a condenser by a bent tube of large diameter, 80 g. of iodine was added in small portions. After all the iodine had reacted, the flask was immersed in an oil-bath and the latter heated to 140°. With good stirring, 35.5 g. of 2,3,5,6-tetrachlorodioxane (m. p. 141–142°) was added in 1–2 g. lots. The reaction was accompanied by vigorous ebullition of the mixture, resulting in the distillation of the dioxadiene along with a considerable amount of *n*-butyl ether. After about 100 cc. of distillate had been collected, 100 cc. of *n*-butyl ether was added to the reaction flask. When all the tetrachlorodioxane had reacted, the bath temperature was raised to 155° and an additional 25 cc. of distillate collected; time, one and one-half hours. The distillate (300 cc.), slightly colored with iodine, was distilled from an ordinary distilling flask and the low boiling fraction (up to 115°) was fractionated through a 40-cm. Podbielniak type column. An 8.4 g. (64%) fraction was obtained, b. p. 73–78°. In another preparation of dioxadiene under the same conditions, a 48% yield was obtained. However, all the material distilled at a constant boiling point of 75° at 746 mm.; d^{20}_4 1.115; $n^{20}D$ 1.4350; *MR*, calcd. 20.84; found, 19.66.

Anal. Calcd. for $C_4H_4O_2$: C, 57.12; H, 4.76. Found: C, 57.18; H, 4.94.

Reaction of Dioxadiene with Bromine.—To a solution of 1.18 g. (0.0142 mole) of dioxadiene in 15 cc. of dry carbon tetrachloride at 0° was added slowly 2.28 g. (0.0142 mole) of bromine dissolved in 10 cc. of carbon tetrachloride. The dioxadiene readily reacted with the bromine. No further reaction of the dioxadiene with bromine occurred when an additional small quantity of the bromine solution was added. This was indicated by the persistence of the bromine color. The carbon tetrachloride was removed in a vacuum desiccator, and the crystalline residue was recrystallized from petroleum ether as needles, m. p. 55–57°; yield 2.98 g. (87%). After another recrystallization from petroleum ether, the material melted at 58°. The compound decomposed over a period of several weeks when exposed to the atmosphere.

Anal. Calcd. for $C_4H_4O_2Br_2$: Br, 65.55. Found: Br, 65.97.

Symmetrical Tetrachlorodioxane.—A solution of 1.3 g. of dioxadiene in 40 cc. of dry carbon tetrachloride was saturated with chlorine at room temperature. After evaporation of the carbon tetrachloride from a water-bath, the residue (0.5 g.) was crystallized three times from methyl alcohol: needles, m. p. 139–140°. A mixed melting point with 2,3,5,6-tetrachlorodioxane (m. p. 142–143°) melted at 139–140.5°.

Anal. Calcd. for $C_4H_4O_2Cl_4$: Cl, 62.81. Found: Cl, 62.35.

2,5-Dichlorodioxane.—Approximately 0.35 mole of dry hydrogen chloride was passed into a solution of 4.9

g. of dioxadiene and 5 cc. of dry carbon tetrachloride. Some solid separated during the reaction. After the carbon tetrachloride was removed in a vacuum desiccator, the residue was warmed with petroleum ether and the solution decanted from some insoluble material. The petroleum ether solution on cooling deposited needle-like crystals of 2,5-dichlorodioxane, m. p. 117–118°.[7] The material decomposed on standing. It was readily hydrolyzed by water and the solution yielded the *p*-nitrophenylosazone of glycol aldehyde when treated with *p*-nitrophenylhydrazine; m. p. 300° (uncorr.).

Mercuration of Dioxadiene.—A solution of 1 g. of dioxadiene in 5 cc. of alcohol was added to 71.5 cc. of a cold solution which contained 3.22 g. of mercuric chloride and 6.23 g. of sodium acetate–$3H_2O$. A white precipitate formed immediately. After standing overnight in a refrigerator, the solid was filtered and washed with water several times. The material after air drying weighed 3.28 g. The theoretical yield for a disubstituted compound is 3.30 g. The product showed no definite melting point, and was insoluble in alcohol, dioxane, benzene or a mixture of alcohol and acetic acid. The material was washed several times more with water and dried in a desiccator.

Anal. Calcd. for $C_4H_2O_2Hg_2Cl_2$: Hg, 72.39. Found: Hg, 71.56, 70.11.

(7) 2,5-Dichlorodioxane, needles, m. p. 118–119°, has been isolated as a product of the chlorination of dioxane by L. Rochen of this Laboratory. It is an unstable solid easily hydrolyzed by water.

Summary

1. Dioxadiene has been prepared for the first time.

2. The physical and chemical properties have been studied. These indicate that the unsaturation is modified to a marked extent by conjugation with the ether oxygens.

EVANSTON, ILLINOIS RECEIVED JUNE 17, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. LXXV. Cholesterol Derivatives

BY RUSSELL E. MARKER AND EWALD ROHRMANN

The present work is a continuation of a previously reported investigation[1] on 7-keto-cholesterol derivatives. In the previous work it was observed that 7-ketocholesteryl chloride upon catalytic hydrogenation in acetic acid solution gave a mixture of products from which cholestyl chloride was isolated. Indications of the presence of 7-hydroxycholestyl chloride were also obtained.

We have now observed that when the hydrogenation of $\Delta^{5,6}$-unsaturated 7-keto compounds is conducted in a neutral medium with Adams catalyst the essential product is a saturated 7-keto compound. This selective reduction of the ethylenic linkage most probably is due to the slightly hindered nature of the carbonyl group at C-7.

The catalytic hydrogenation of 7-ketocholesteryl chloride in neutral solution with Adams catalyst yielded 7-ketocholestyl chloride identical with that prepared previously by the oxidation of crude 7-hydroxycholestyl chloride.[1] A similar reduction of 7-ketocholesteryl acetate gave 7-ketocholestyl acetate evidently identical with the product which Windaus and Kirchner[2] obtained by the hydrogenation of 7-ketocholesteryl acetate with palladium catalyst in an acidic medium. When the hydrogenation of 7-ketocholesteryl acetate was carried out in acetic acid solution with Adams catalyst followed by alkaline hydrolysis of the reduction products, 7-hydroxycholestanol was obtained. This was identical with the product obtained by the reduction of 7-ketocholestanol with aluminum isopropylate. Mild oxidation of this diol with chromic anhydride yielded 7-ketocholestanone first reported by Windaus and Kirchner.[2]

Dimroth and Trautmann[3] reported the preparation of $\Delta^{5,6}$-cholestenol-7 by the reduction of $\Delta^{5,6}$-cholestenone-7 with aluminum isopropylate. No analytical data were given on their product which melted at 93–94°. The substance was reported to yield a benzoate, m. p. 108–109°. We have prepared $\Delta^{5,6}$-cholestenol-7 by the reduction of 7-hydroxycholesteryl chloride with sodium and amyl alcohol. The product, m. p. 106°, gave a benzoate, m. p. 147°. Bromination of the substance followed by mild oxidation with chromic anhydride and subsequent debromination gave $\Delta^{5,6}$-cholestenone-7 of m. p. 126°, while catalytic hydrogenation in neutral medium gave cholestanol-7.

It is improbable that our $\Delta^{5,6}$-cholestenol-7 differs from that of Dimroth and Trautmann in the configuration of the hydroxyl group as in both

(1) Marker, *et al.*, THIS JOURNAL, **59**, 619 (1937).

(2) Windaus and Kirchner, *Ber.*, **53**, 614 (1920).

(3) Dimroth and Trautmann, *ibid.*, **69**, 669 (1936).

cases the hydroxyl group was formed by reduction of a carbonyl group with aluminum isopropylate, a reaction which appears to give largely one isomer at C-7. It is possible that the two benzoates may be polymorphic forms.

In the present paper we are also reporting the incidental preparation of 3-acetyl-4-hydroxycholesterol which was prepared by the oxidation of cholesteryl acetate with selenium dioxide.[4-7] The substance was obtained in two polymorphic forms.

We wish to thank Parke, Davis and Company for their generous help and assistance in the various phases of this work.

Experimental Part

7-Ketocholestyl Chloride.—A mixture of 1.6 g. of 7-ketocholesteryl chloride, 400 mg. of Adams catalyst and 120 cc. of ether was shaken with hydrogen at 3 atmospheres pressure for four hours at 25°. The product was crystallized from acetone as thick white prisms, m. p. 136–138°. This gave no depression with an authentic sample of 7-ketocholestyl chloride.

Anal. Calcd. for $C_{27}H_{45}OCl$: C, 77.1; H, 10.7. Found: C, 77.1; H, 10.5.

The substance gave an **oxime** which crystallized from aqueous ethanol, m. p. 152–154°.

Anal. Calcd. for $C_{27}H_{46}OClN$: C, 74.35; H, 10.6. Found: C, 74.35; H, 10.7.

Hydrogenation of the Acetate of $\Delta^{5,6}$-Cholestenol-3(β)-one-7.—A mixture of 5 g. of the acetate, 500 mg. of Adams catalyst and 150 cc. of ether was shaken with hydrogen at 3 atmospheres pressure for seven hours at 25°. The mixture was filtered, the filtrate evaporated and the residue crystallized from acetone–methanol to give white plates, m. p. 147–148°.

Anal. Calcd. for $C_{29}H_{48}O_3$: C, 78.3; H, 10.9. Found: C, 78.4; H, 10.6.

Hydrolysis of the resulting acetate of cholestanol-3(β)-one-7 by refluxing with an excess of ethanolic potassium hydroxide gave a product which crystallized from acetone–methanol as white plates, m. p. 128–130°, solidifying almost at once and remelting at 157–159°.

Anal. Calcd. for $C_{27}H_{46}O_2$: C, 80.5; H, 11.5. Found: C, 80.8; H, 11.7.

The hydrolysis product gave an **oxime** which crystallized from aqueous ethanol as fine white needles, m. p. 232–233°.

Anal. Calcd. for $C_{27}H_{47}O_2N$: C, 77.6; H, 11.3. Found: C, 77.2; H, 11.5.

Cholestanediol-3(β)-7(α). (a) By Hydrogenation of 7-Ketocholesteryl Acetate.—A mixture of 5 g. of 7-ketocholesteryl acetate, 500 mg. of Adams catalyst and 150 cc. of glacial acetic acid was shaken with hydrogen at 3 atmospheres pressure at room temperature for fourteen hours. The mixture was filtered and the filtrate evaporated *in vacuo*. The residue which would not crystallize was hydrolyzed with ethanolic potassium hydroxide and the product crystallized from acetone to give white plates, m. p. 164–166°.

Anal. Calcd. for $C_{27}H_{48}O_2$: C, 80.1; H, 11.95. Found: C, 80.2; H, 11.9.

The filtrate containing crude 7-hydroxycholestanol was evaporated to dryness and the crystalline residue dissolved in 125 cc. of glacial acetic acid. To this solution was added 2 g. of chromic anhydride in 20 cc. of 80% acetic acid. After standing at room temperature for two hours the solution was diluted with water and the precipitated solid taken up in ether. The ethereal extract was washed with sodium carbonate solution and the ether evaporated. The residue was crystallized from acetone as white needles, m. p. 186–187°.

Anal. Calcd. for $C_{27}H_{44}O_2$: C, 80.9; H, 11.1. Found: C, 81.2; H, 11.2.

(b) By Aluminum Isopropylate Reduction of the Acetate of Cholestanol-3(β)-one-7.—A mixture of 1.2 g. of cholestanol-3(β)-one-7 acetate, 1.5 g. of aluminum isopropylate and 40 cc. of dry isopropyl alcohol was refluxed on the steam-bath for fourteen hours. Most of the solvent was distilled off over a period of three hours. The residue was diluted with water and the precipitate extracted with ether. The product crystallized from acetone as white plates, m. p. 163–165°. It gave no depression with the product of the catalytic hydrogenation of 7-ketocholesteryl acetate.

$\Delta^{5,6}$-Cholestenol-7.—To a boiling solution of 3 g. of 7-hydroxycholesteryl chloride was added 6 g. of sodium over a period of four hours. The mixture was then cooled, diluted with ether and washed well with water. The ether and amyl alcohol was evaporated on the steam-bath. The residual oil which would not crystallize was sublimed in high vacuum. The material distilling at 130–160° was crystallized from acetone to give 800 mg. of thick white prisms, m. p. 105–106°.

Anal. Calcd. for $C_{27}H_{46}O$: C, 83.9; H, 12.0. Found: C, 83.9; H, 12.0.

When treated with benzoyl chloride in pyridine at room temperature for two days the product yielded a benzoate which crystallized from methanol as white needles, m. p. 145–147°.

Anal. Calcd. for $C_{34}H_{50}O_2$: C, 83.2; H, 10.3. Found: C, 83.1; H, 10.1.

Hydrogenation of $\Delta^{5,6}$-Cholestenol-7.—A mixture of 400 mg. of $\Delta^{5,6}$-cholestenol-7, 500 mg. of Adams catalyst, 50 cc. of ether and 25 cc. of absolute ethanol was shaken with hydrogen at 45 pounds (3 atm.) pressure for ninety minutes. The mixture was filtered, the filtrate diluted with water and the ether layer separated. The ether was evaporated and the residue crystallized from ethanol to give white needles, m. p. 115–117°. This gave no depression with an authentic sample of cholestanol-7, m. p. 116–117°.

$\Delta^{5,6}$-Cholestenone-7.—To a solution of 500 mg. of $\Delta^{5,6}$-cholestenol-7 in 5 cc. of ether was added a slight excess of bromine in 2 cc. of glacial acetic acid. No crystalline bromide was obtained. The solution was diluted with

(4) Rosenheim and Starling, *J. Chem. Soc.*, 377 (1937).
(5) Butenandt and Hausmann, *Ber.*, **70**, 1154 (1937).
(6) Marker, Kamm and Wittle, THIS JOURNAL, **60**, 1071 (1938).
(7) Marker and Rohrmann, *ibid.*, **60**, 1073 (1938).

water, extracted with ether and the ether evaporated at room temperature. The residue was dissolved in 10 cc. of benzene. To this solution was added a solution of 500 mg. of chromic anhydride in 15 cc. of 80% acetic acid, and the mixture stirred for five hours at room temperature. The benzene layer was washed with water and the solvent evaporated. The residue was dissolved in 20 cc. of glacial acetic acid and the solution heated on the steam-bath for thirty minutes with 2 g. of zinc dust. The solution was decanted into water and the precipitated solid extracted with ether. After washing with dilute sodium carbonate solution the ether was evaporated and the residue crystallized from acetone to give white needles, m. p. 125–126°.

Anal. Calcd. for $C_{27}H_{44}O$: C, 84.3; H, 11.5. Found: C, 84.3; H, 11.7.

3-Acetyl-4-hydroxy-cholesterol.—A mixture of 50 g. of cholesteryl acetate in 250 cc. of benzene was oxidized with a solution of 20 g. of selenium dioxide in 500 cc. of 98% acetic acid as described in a previous paper for sitosteryl acetate. The product was crystallized from acetic acid and after treatment with Norite it was crystallized from methanol to give white needles, m. p. 163–165°.

Anal. Calcd. for $C_{29}H_{48}O_3$: C, 78.3; H, 11.1. Found: C, 78.2; H, 10.9.

The acetic acid filtrate from the above initial crystallization upon standing deposited pale tan plates. After treatment with Norite and crystallization from methanol–ether the product formed white plates, m. p. 189–191°. The mixture with the product of m. p. 163–165° melted over an intermediate range of 163 to 184°.

Anal. Calcd. for $C_{29}H_{48}O_3$: C, 78.3; H, 11.1. Found: C, 78.3; H, 11.0.

Both polymorphic forms yielded the diacetate of 4-hydroxycholesterol, m. p. 162–163°, on refluxing with acetic anhydride. Hydrolysis of both forms with ethanolic potassium hydroxide yielded 4-hydroxycholesterol, m. p. 174–175°.

Summary

Reduction of 7-ketocholesterol derivatives with hydrogen and Adams catalyst in neutral medium tends to reduce the ethylenic linkage, yielding a saturated 7-keto compound.

$\Delta^{5,6}$-Cholestenol-7 has been prepared by the reduction of 7-hydroxycholesteryl chloride with sodium and amyl alcohol.

The preparation of 4-hydroxycholesteryl acetate by the oxidation of cholesteryl acetate with selenium dioxide is reported.

STATE COLLEGE, PENNA. RECEIVED JULY 7, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

The Photolysis of Azomethane and of Azomethane–Acetaldehyde Mixtures

BY FRANCIS E. BLACET AND ALVIN TAUROG

Several investigators are in agreement that at elevated temperatures the thermal[1,2] and photochemical[3,4] decomposition of acetaldehyde involves the reactions

$$CH_3 + CH_3CHO \longrightarrow CH_4 + CH_3CO \quad (1)$$
$$CH_3CO + M \longrightarrow CH_3 + CO + M \quad (2)$$

However, the evidence for these reactions in room temperature photolysis is indirect,[5] being based upon analyses of decomposition products, and is opposed by the experimental proof that CH_3CO is fairly stable[6] below 60°, as well as by a rather high calculated minimum value of 17 kcal. for the energy of activation of reaction 2.[7] By mixing azomethane and acetaldehyde vapors at room temperature, and irradiating the mixture with λ 3660 Å., which is not absorbed by the aldehyde but which dissociates azomethane to give free methyl radicals,[8] the present authors have obtained additional information which pertains to this mechanism. A brief study has been made also of the gaseous decomposition products and the quantum yield of azomethane photolysis.

Experimental Method

Azomethane was obtained by preparing dimethylhydrazine dihydrochloride after the manner of Hatt[9] and oxidizing this with cupric chloride by the method suggested by Jahn.[10] This oxidation process was found to be definitely superior to the potassium chromate method of Thiele.[11] Ramsperger's procedure[12] was followed in purifying the azomethane.

Radiant energy was obtained from a high pressure mercury arc and a quartz monochromator. The gas train was similar to that which has been described[13] except that a second storage reservoir and mercury trap was added to accommodate the azomethane. This reservoir was pro-

(1) Rice and Herzfeld, THIS JOURNAL, **56**, 284 (1934).
(2) Allen and Sickman, *ibid.*, **56**, 1251 (1934).
(3) Leermakers, *ibid.*, **56**, 1537 (1934).
(4) P. A. Leighton, *J. Phys. Chem.*, **42**, 749 (1938).
(5) Blacet and Volman, THIS JOURNAL, **60**, 1243 (1938).
(6) Spence and Wild, *J. Chem. Soc.*, 352 (1937).
(7) E. Gorin, *J. Chem. Phys.*, **7**, 256 (1939).
(8) Burton, Davis and Taylor, THIS JOURNAL, **59**, 1038 (1937).
(9) Hatt, "Organic Syntheses," John Wiley and Sons, Inc., New York, N. Y., Vol. XVI, 1936, p. 18.
(10) Jahn, THIS JOURNAL, **59**, 1761 (1937).
(11) Thiele, *Ber.*, **42**, 2575 (1909).
(12) Ramsperger, THIS JOURNAL, **49**, 912 (1927).
(13) Leighton and Blacet, *ibid.*, **54**, 3165 (1932).

tected from the light of the room, and was kept at −80° to diminish photodecomposition of the vapor by stray light and to reduce the vapor pressure enough to allow mercury traps of moderate length to be used.

The gaseous decomposition products were determined by the Blacet–Leighton method of microanalysis. Residual azomethane vapor in the gas was removed with a sintered glass bead containing 12 *N* hydrochloric acid, followed by solid potassium hydroxide. The alkali also removed residual acetaldehyde. Fuming sulfuric acid was used to test for unsaturated hydrocarbons, silver oxide for carbon monoxide, copper oxide and potassium hydroxide at approximately 300° for hydrogen, and saturated hydrocarbons were removed by combustion with a hot platinum coil.[14] The percentage nitrogen was calculated from the difference in volume of a sample taken for analysis and the sum of the volumes of the other gases found present.

Quantum yields for pure azomethane decomposition were determined in essentially the same manner as previously described for aldehyde photolysis[13] except that calculations were made in two different ways, one based on the pressure change in the system and the other based on the free nitrogen produced in the reaction. Special care was taken to exclude atmospheric nitrogen from the reaction system and the storage reservoirs by flushing them with carbon dioxide several times and evacuating by means of a Toepler pump. Possible residual carbon dioxide was removed from the gaseous decomposition products in the same operations which took out the excess azomethane. All photochemical experiments were performed at 30° and with the wave length 3660 Å.

The absorption spectrum of azomethane vapor was taken using a model E-316 Hilger spectrograph and a hydrogen discharge as the radiation source.

Experimental Results

The azomethane made by the cupric chloride method was water white in the liquid state. A column of the vapor 40 cm. in length, having a pressure of 300 mm. at 22.5°, gave continuous absorption between λ 3020 and 3850, with a maximum at 3380 Å. A second region of continuous absorption began at λ 2570 and extended to shorter wave lengths. In agreement with Ramsperger,[15] no discontinuous absorption was observed at lower pressures.

In a Paneth type experiment azomethane was found to remove tellurium mirrors readily when irradiated with λ 3660.[16]

Azomethane.—The apparatus used in this work was equipped with thermopile and galvanometer for energy measurements and although the primary object of the investigation was to study azomethane–acetaldehyde mixtures, a few quantum yield determinations of pure azomethane photolysis were made. This seemed especially worth while since the two previous quantum yield studies are in disagreement: Ramsperger[15] having reported a value of approximately 2 while Forbes, Heidt and Sickman[17] have given yields approaching unity as a maximum. In both of these cases quantum yields were based upon the experimental fact that the pressure after the complete thermal decomposition of azomethane was 2.04 times the original pressure.

In Table I are the results of analyses of the non-condensable gas produced in several runs on azomethane which differed from one another only in initial pressure. The percentages given represent the average of 2 or 3 separate analyses which differed in most cases by 5–10% from the mean value. Tests for unsaturated hydrocarbons with fuming sulfuric acid gave an average reduction in volume of less than 0.3%. No evidence for propane was found.

TABLE I

ANALYSES OF NON-CONDENSABLE PRODUCTS FROM AZOMETHANE

Pressure, mm.	% hydrogen	% methane	% ethane	% nitrogen
13	1.5	9	40	49
31	2.5	4	39	54
32	0.5	3	40	56
49	2.0	7	33	57
57	2.0	7	38	53
80	3.0	9	32	56
Average %	1.9	6.5	37	54

Quantum yields, Φ, were determined in the four cases listed in Table II. The run at 13 mm. should be discounted with respect to the others since at very low pressures experimental errors may be very large. The third column in this table gives the yield calculated from the pressure change in the reaction system assuming the overall reaction

$$(CH_3)_2N_2 + h\nu \longrightarrow C_2H_6 + N_2 \qquad (3)$$

The yield in the fourth column was calculated from the nitrogen produced, the assumption be-

TABLE II

QUANTUM YIELDS OF AZOMETHANE PHOTOLYSIS

Pressure, mm.	ΔP, mm.	Φ calcd. from ΔP	Φ calcd. from N_2
13	0.67	0.37	0.59
49	1.01	.70	0.97
57	1.01	.71	1.1
80	0.93	.85	1.1

(14) Blacet and Volman, *Ind. Eng. Chem., Anal. Ed.*, **9**, 44 (1937).

(15) Ramsperger, THIS JOURNAL, **50**, 123 (1928).

(16) The authors are indebted to Professor P. A. Leighton and the Chemistry Department of Stanford University for the Paneth apparatus and to Mr. D. H. Volman for performing the experiments with it.

(17) Forbes, Heidt and Sickman, THIS JOURNAL, **57**, 1935 (1935).

ing that one molecule of nitrogen was formed per decomposition process irrespective of secondary reactions.

Azomethane-Acetaldehyde Mixtures.—The first few runs in which the azomethane pressure was about one-half to one-third the acetaldehyde pressure gave no carbon monoxide in the photolysis products. However, by going to lower ratios appreciable amounts of carbon monoxide were found as shown in Table III. The percentages given are of the non-condensable gas in each case. Complete analyses of the gas were not made in these experiments.

TABLE III

CARBON MONOXIDE AND HYDROGEN FROM PHOTOLYSIS OF AZOMETHANE–ACETALDEHYDE MIXTURES

Azomethane pressure, mm.	Acetaldehyde pressure, mm.	% CO	% H_2
139	501	0.7	4.6
98	500	.9	4.7
66	505	.2	8.1
48	501	2.5	3.6
25	427	4.0	2.5
14	501	6.8	1.0
7.5	487	11.6	3.0
3.0	503	14.3	2.2

Discussion of Results

Azomethane Photolysis.—The removal of tellurium mirrors in the Paneth experiment indicates that some free radicals are produced at room temperature when azomethane is irradiated with λ3660; however, the experiments were qualitative and do not exclude the possibility of partial dissociation directly into stable molecules. The formation of radicals in the thermal dissociation had previously been demonstrated.[18,19]

The average of 54% nitrogen in the non-condensable gases formed in the photolysis of azomethane is in excellent agreement with 54.7% reported by Burton, Davis and Taylor.[8] These authors have explained this high percentage by assuming that methyl radicals produced thus

$$(CH_3)_2N_2 + h\nu \longrightarrow 2CH_3 + N_2 \qquad (4)$$

may react with additional azomethane to give condensable products in some such manner as the following

$$CH_3 + (CH_3)_2N_2 \longrightarrow (CH_3)_2N_2CH_3 \qquad (5)$$
$$CH_3 + (CH_3)_2N_2CH_3 \longrightarrow (CH_3)_2N_2(CH_3)_2 \qquad (6)$$

The methane percentage is also in qualitative agreement with that reported by these authors. Although no completely satisfactory mechanism has been given for the formation of this hydrocarbon, the over-all reaction

$$2CH_3 + 2(CH_3)_2N_2 \longrightarrow 2CH_4 + (CH_3N_2CH_2)_2 \qquad (7)$$

should be mentioned as a type of process which might occur in competition with reactions 5 and 6. Davis, Jahn and Burton[20] have found that nitric oxide greatly diminishes the amount of hydrocarbons produced in azomethane photolysis. They interpret this to mean that reaction 3 does not occur to an appreciable extent and have suggested that the large amount of ethane production in the absence of nitric oxide is the result of some process which follows reaction 5. If such a mechanism were to occur, one would expect the free methyl to attack the azomethane itself giving C_2H_6 and CH_3N_2. Since CH_3N_2 is unstable[8] and dissociates immediately after formation to give CH_3 and N_2 the net result would be a chain process for which there is no photochemical evidence at room temperature.

The possibility that reaction 3 would occur in the absence of, but not in the presence of, nitric oxide should not be ignored. If azomethane remains activated for an appreciable length of time before dissociating, as indicated by the work of Forbes, Heidt and Sickman,[17] it is conceivable that it would react directly with nitric oxide, thus partially suppressing both reactions 3 and 4. The initial nitric oxide pressures in the above-mentioned experiments varied from 9.9 to 20.5 mm. The small but definite percentage of hydrogen found is difficult to account for without postulating the formation of an equivalent amount of unsaturated hydrocarbons. It is possible that these were formed but escaped detection by dissolving in the 12 *N* hydrochloric acid used to remove the excess azomethane.

The evidence indicates that the quantum yield of azomethane decomposition calculated from the free nitrogen formed in the process is more reliable than the one calculated from a pressure increase in the system. If the low value obtained at 13 mm. pressure may be discounted, the yield is unity within experimental error over the pressure range 49 to 80 mm. at 30°. This is in accord with the conclusions reached by Forbes and his collaborators,[17] in spite of the fact that the two methods of arriving at the value of unity are not entirely consistent with each other.

It is interesting to note that if one assumes both

(18) Leermakers, THIS JOURNAL, **55**, 3499 (1933).
(19) Rice and Evering, *ibid.*, **55**, 3898 (1933).
(20) Davis, Jahn and Burton, *ibid.*, **60**, 10 (1938).

primary processes given above and reactions 5, 6 and 7 as the only secondary reactions which occur, he can show from the percentages of methane, ethane and nitrogen given in Table I that the quantum yield given from pressure increase should be approximately 74% of that calculated from the nitrogen. Experimentally, the last three values of Table II give an average for the pressure method which is 71% of the nitrogen method. The small amount of hydrogen was ignored in this calculation.

The Photolysis of Azomethane–Acetaldehyde Mixtures.—Table III shows that under the proper experimental conditions azomethane will photosensitize the decomposition of acetaldehyde. It is probable that this process is initiated by free methyl radicals as indicated in reaction (1). The fact that the percentage of carbon monoxide is not appreciable until the ratio of acetaldehyde to azomethane is of the order of 10 to 1, is an additional indication that free methyls react with azomethane and that the energy of activation of this process is less than that for the aldehyde reaction. Such a conclusion is in accord with the low hydrocarbon to nitrogen ratio discussed above and also explains the failure of Burton, *et al.*,[8] to detect carbon monoxide in a similar experiment with a mixture of azomethane and acetaldehyde since the molecular ratio used by them was approximately 1 to 1. The hydrogen percentages found are somewhat erratic; nevertheless, they lead to the conclusion that this gas comes from the azomethane and not from the acetaldehyde. All of these results are consistent with reactions (1) and (2). At the same time it must be recognized that others have presented strong objections to reaction (2) as a room temperature process and it is possible that carbon monoxide was produced by reactions not considered in this discussion.

Summary

1. The quantum yield of azomethane decomposition by λ 3660 Å. at room temperature and in the pressure range 49 to 80 mm., has been found to be unity when calculated on the basis of the number of molecules of free nitrogen formed per quantum absorbed. Quantum yields calculated on the basis of pressure increase in the reaction system averaged 0.75. The nitrogen method is considered more reliable.

2. Analyses of the gaseous photodecomposition products of azomethane gave an average of 1.9% hydrogen, 6.5% methane, 37% ethane and 54% nitrogen. A mechanism is suggested which would account for all gases except the hydrogen.

3. It has been shown by the detection of carbon monoxide that azomethane will photosensitize the decomposition of acetaldehyde when the ratio of acetaldehyde to azomethane is greater than 10 to 1. This is interpreted as meaning that free methyl radicals produced in the photolysis of azomethane will react with either azomethane or acetaldehyde, preferably with the former.

LOS ANGELES, CALIF. RECEIVED AUGUST 18, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

The Contact Potential of an Iodine Film on Tungsten

BY M. J. COPLEY AND R. W. SPENCE[1]

Monomolecular films of oxygen and of hydrogen on metals have been widely investigated, but little information is available about the properties of halogen films. Van Pragh[2] exposed a platinum surface to iodine vapor, noted its effect on the accommodation coefficient of argon on platinum, and concluded that, at a pressure of 0.027 mm., an iodine film is formed below 1565°K. Glockler and Calvin[3] in their determination of the electron affinity of iodine from thermionic data taken in the presence of iodine vapor, found no evidence of adsorption of iodine on tungsten at temperatures above 2000°K. with pressures as high as 10^{-4} mm. Hendricks, Phipps and Copley[4] measured the degree of surface ionization taking place when molecular rays of the potassium halides impinged upon a hot tungsten filament. The course of the ionization curves showed that, at temperatures below 1600°K., for the specific rate of arrival (4.3×10^{13} molecules

(1) Present address: University of Illinois College of Pharmacy, Chicago, Illinois.

(2) Van Pragh, *J. Chem. Soc.*, 798 (1933).

(3) Glockler and Calvin, *J. Chem. Phys.*, **3**, 20 (1935).

(4) Hendricks, Phipps and Copley, *ibid.*, **5**, 868 (1937).

cm.$^{-2}$ sec.$^{-1}$) used in their experiments, surfaces were formed having work functions considerably higher than the work function of clean tungsten. They suggested that these high work function surfaces were due to adsorbed films comprised of halogen atoms. In the case of potassium iodide the work function of the WI surface was determined as 5.27 volts.

In order to learn more about the properties of an iodine film on tungsten, its contact potential relative to clean tungsten has been determined. The contact potential method[5-9] of studying adsorbed films on metallic surfaces makes use of the infra-saturation current from a hot filament to the clean and to the coated metal. If A and B are two filaments, A at a constant elevated temperature and B cold, the current between the two filaments is determined by their potential difference. At small positive potentials, within the infra-saturation region, the current varies as the $^3/_2$ power of the potential and hence is very sensitive to voltage changes. If the current-volts characteristic of the system is measured with filament B clean, then measured again with filament B coated, and the current in each case plotted against the voltage, the second curve, while parallel to the first, is displaced along the voltage axis. The magnitude of this displacement represents the contact potential difference between the clean and the coated surface.

Experimental

The apparatus used in making the contact potential measurements is shown in Fig. 1. A and B were aged

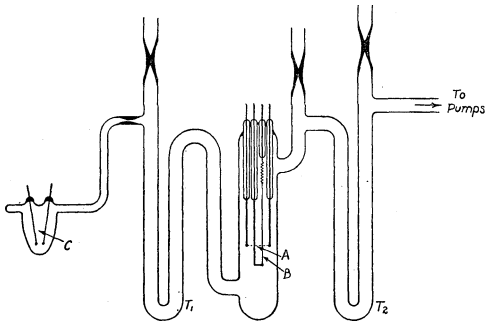


Fig. 1.—Diagram of contact potential cell.

tungsten filaments, 3.4 and 5.6 cm. in length, respectively, and both 0.00767 cm. in diameter, mounted at right angles to one another in a Pyrex glass tube. The vertical filament was kept taut by a tungsten spring attached to its upper end. No spring was used with the horizontal filament, but when the filament was spot-welded onto the leads, the leads were pinched together slightly to keep it under tension. This arrangement of the filaments[8] ensured that practically all the current measured flowed from a short section at the center of the hot filament to the cold filament; thus the electron source was homogeneous and nearly equipotential.[8] T_1 and T_2 were liquid air traps to freeze out iodine and mercury. The system was evacuated by means of two mercury vapor pumps (not shown in figure) in tandem and was pumped continuously during a run. Carefully purified thallous iodide was used as a source of iodine. It was placed in the electrolytic cell C and after fusion electrolyzed by means of two platinum-tipped tungsten electrodes sealed through the glass wall.

In order to obtain a vacuum sufficiently good to ensure clean surfaces, it was found necessary to give the system a thorough bake-out. This was accomplished by surrounding the entire system, with the exception of the pumps and the electrolytic cell C, by a furnace maintained at 500° for a period of twenty-four to forty-eight hours. Meanwhile the electrolytic cell containing the thallous iodide was hand torched. During this torching the thallous iodide was distilled repeatedly from the cell into the side tube where it was fused and allowed to run back. After such a bake-out, when the filaments had been flashed, the electron emission from the hot filament to the cold filament would usually remain constant for an hour, even without liquid air around the contact potential cell. It was extremely important to have such a high vacuum, since surrounding the contact potential cell with liquid air invariably introduced fluctuations in the galvanometer circuit.

The emission current was measured by the electrical circuit shown in Fig. 2. The currents for heating and flashing

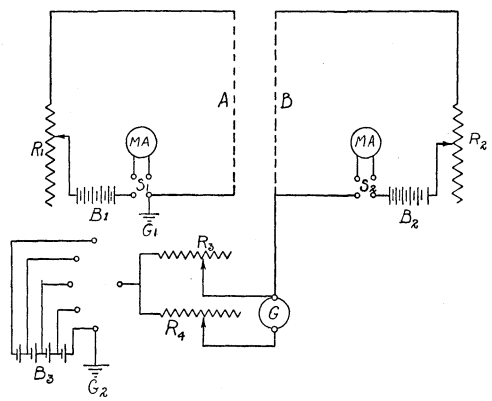


Fig. 2.—Electrical circuit for contact potential measurements.

the filaments were supplied by storage batteries B_1 and B_2, and were adjusted by the rheostats R_1 and R_2. The resistance boxes R_3 and R_4 constituted a shunt arrangement for the galvanometer G. Potentials between the two filaments were obtained from the bank of 2-volt storage cells B_3. The contact potential cell was surrounded by a shield of copper gauze to eliminate anomalous effects.

The apparatus was checked by measuring the contact potential of a WO film relative to clean tungsten. In

(5) Richardson and Robertson, *Phil. Mag.*, **43**, 162 (1922).
(6) Langmuir and Kingdon, *Phys. Rev.*, **34**, 129 (1939).
(7) Reimann, *Phil. Mag.*, **20**, 594 (1935).
(8) Bosworth and Rideal, *Proc. Roy. Soc.* (London), **A162**, 1 (1937).
(9) Bosworth, *Trans. Faraday Soc.*, **35**, 397 (1939).

making this measurement the filaments were flashed at 2700°K. and readings were taken of the infra-saturation current at voltages ranging from 0 to 8 volts. The emitter filament was kept at 2350°K. and the collector filament at room temperature. After the current-volts characteristic had been measured for the clean collector, air was admitted into the system through a capillary while the collector filament was kept at 1200°K. After the excess air had been removed, the emitter filament was flashed at 2700°K. and then adjusted at 2350°K. and the current-volts characteristic again was measured. The two sets of data when plotted gave curves which were closely parallel; however, the one for the WO surface was shifted along the voltage axis in the positive direction. Several determinations gave values for the contact potential ranging from −1.70 to −1.73 volts, in excellent agreement with the values reported by Reimann[7] and by Bosworth and Rideal.[8]

The procedure for obtaining the W–WI contact potential was identical with that outlined above for determining the W–WO contact potential. To form an iodine film, the thallous iodide was electrolyzed and the iodine caught in liquid air trap T_1; then it was allowed to vaporize from this trap and come in contact with the filaments. It was found necessary, in order to obtain a film showing a maximum contact potential, to hold the collector filament at an elevated temperature; 1000°K. was finally adopted.

Results

Figure 3 shows a plot of current versus volts for a typical run. The base curve for the clean tungsten could be duplicated in different runs, even when the vacuum had been broken in the intervening time, if a satisfactory baking-out process was again given to the system. The two curves in every case were very nearly parallel, particularly in the range 4 to 8 volts. The values obtained for the contact potential in twelve separate determinations were, respectively: −0.94, −0.90, −0.88, −0.90, −0.95, −0.93, −0.93, −0.88, −0.95, −0.87, −0.91, and −0.91 with an average value of −0.91 volt.

As stated in a previous paragraph it was necessary to keep the collector filament at 1000 to 1200°K. during the exposure to the iodine vapor. When the collector filament was kept at room temperature during the coating process and the contact potential determined, a value of −0.42 volt was obtained. This difference is presumably due to the formation of a molecular rather than atomic film. Attempts to activate such a molecular film by flashing to 1000°K. or above always gave a value of the contact potential lower than −0.91 volt, indicating some evaporation of the iodine. This behavior of iodine is different from that observed by Reimann[7] for oxygen with tungsten. He found that the value of the W–WO contact potential was the same whether the temperature of the filament during the exposure to oxygen was room temperature or any other temperature for which the film was stable. An attempt was made to obtain more information on this point by admitting air with the collector filament cold; in every case a value in the neighborhood of −0.85 volt instead of −1.70 volts was obtained. It should be pointed out, however, that Reimann formed his WO surfaces with pure oxygen evolved from heated barium peroxide which was present in the contact potential cell.

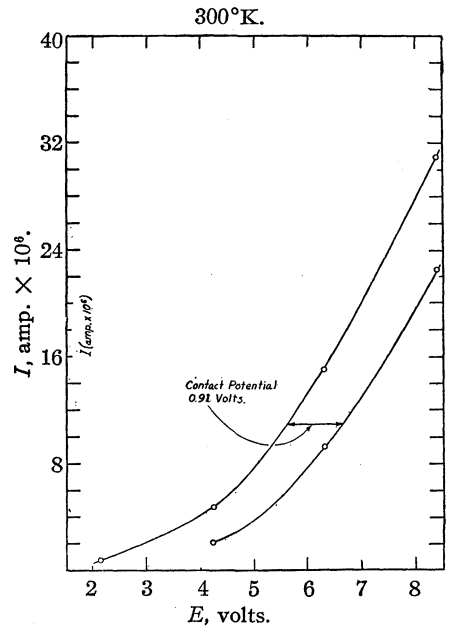


Fig. 3.—Current–volts characteristics of W and of WI surfaces.

If an iodine film was heated to 1250°K. for several minutes between contact potential measurements, the second determination was always low. This indicates that at 1250°K. the rate of evaporation of an iodine film is noticeable. At 1500°K. the rate of evaporation is rapid; however, to remove the last trace of iodine and duplicate the current-volt characteristic of clean tungsten it was necessary to flash to 2000°K.

Eckart[10] has shown that the contact potential difference between two surfaces is

$$V_{12} = \varphi_1 - \varphi_2 \qquad (1)$$

where φ_1 and φ_2 are, respectively, the work function of the clean and coated surfaces. Hence using 4.52 volts for the work function of clean tungsten and 0.91 volt, the average value for

(10) Eckart, *Z. Physik*, **47**, 38 (1928).

V_{12}, we obtain for φ_2 a value of 5.43 volts. This value for the work function of a WI surface is in satisfactory agreement with the value 5.27 volts calculated from surface ionization measurements by Hendricks, Phipps and Copley,[4] since their result was obtained by extrapolating data taken over a short temperature range.

The large negative value of the W–WI contact potential suggests that the adsorbed iodine atoms on the surface are highly polarized. Thus on the surface of the coated filament there is an electrical double layer with the negative ends of the dipoles facing out. The dipole moment μ of the adsorbed atoms may be estimated by the formula

$$\mu = V_{12}/2\pi\ \sigma \qquad (2)$$

where V_{12} is the contact potential and σ is the concentration of atoms per cm.^{2}. Assuming that the measurements have been made on a complete monolayer and that the lattice structure is the same as for a cesium film,[11] σ may be taken as 4.8×10^{14} atoms cm.$^{-2}$. Substituting in equation (2) gives a value of 1.0 Debye units for μ.

Summary

Evidence is presented that iodine forms a stable film on tungsten. Above 1250°K. the film evaporates at a noticeable rate, but flashing to 2000°K. is required for its complete and rapid removal.

The contact potential difference at room temperature between a clean tungsten surface and an iodine-coated tungsten surface was found to be −0.91 volt. The magnitude of the dipole moment of the adsorbed atoms in the complete film is estimated as 1.0 Debye unit.

(11) Taylor and Langmuir, *Phys. Rev.*, **44**, 423 (1933).

URBANA, ILLINOIS RECEIVED AUGUST 19, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, STANFORD UNIVERSITY]

Activity Coefficients in Concentrated Aqueous Solutions of Strong Electrolytes Described by a Formula Containing the Mean Ionic Diameter as Single Parameter. I. Theory and Application to the Alkali Chlorides, Bromides and Iodides[1]

BY PIERRE VAN RYSSELBERGHE AND SYLVAN EISENBERG

I. Introduction

If one wishes to represent the activity coefficient of a strong electrolyte by means of a formula valid at all concentrations, from infinite dilution to saturation, it is usually assumed necessary to introduce two parameters: the mean ionic diameter or distance of closest approach between a positive and a negative ion, a, and a coefficient B which, multiplied by the first power of the concentration C, gives a term representing, in a purely empirical manner, the effect of repulsive forces. The corresponding formula is associated with the names of Hückel[2a] and Harned,[2b] and can be written as follows, in the case of one single electrolyte being present

$$\log f_{\pm} = -\frac{z_+z_-\epsilon^2\kappa}{2DkT(1+\kappa a)} + BC \qquad (1)$$

in which $f_{\pm}$ is the mean rational activity coefficient of the ions, z_+ and z_- are the absolute values of the valences of the positive and of the negative ions, ϵ is the elementary charge of positive electricity, D is the dielectric constant of the solvent, k is Boltzmann's constant, T is the absolute temperature, κ is defined by the formula

$$\kappa = \sqrt{\frac{4\pi n\epsilon^2(\nu_+{z_+}^2 + \nu_-{z_-}^2)}{DkT}} \qquad (2)$$

in which n is the number of molecules of salt per cc., ν_+ and ν_- the numbers of positive and negative ions corresponding to one molecule of salt. The reciprocal of κ is often designated as the *radius of the ionic atmosphere.* The number n and the concentration C are connected by the formula

$$C = n \times 1000/N \qquad (3)$$

in which N is Avogadro's number.

For aqueous solutions of uni-univalent electrolytes at 25°, formula (1) can be transformed into the following

$$\log_{10} f_{\pm} = -0.5059\,\frac{\sqrt{C}}{1+\frac{a}{3.042}\sqrt{C}} + BC \qquad (4)$$

in which a is expressed in Ångströms.[3]

(1) Paper presented at the Meeting of the Pacific Division, American Association for the Advancement of Science, Stanford University, June, 1939.

(2) (a) E. Hückel, *Physik. Z.*, **26**, 93 (1925); (b) H. S. Harned, Chap. XII of Taylor's "Treatise on Physical Chemistry," 2d ed., pp. 797, *et seq.*, D. Van Nostrand and Co., New York, 1931, where earlier references will be found.

(3) The numerical values of the constants used are: $\epsilon = 4.770 \times 10^{-10}$, $\pi = 3.1416$, $N = 6.064 \times 10^{23}$, $D = 78.54$, $k = 1.371 \times 10^{-16}$, $T = 298.1$, $\log 10 = 2.3026$.

The first term on the right of formula (1) or (4) represents the decrease in thermodynamic activity due to the electrostatic interactions between ions, while the second term, in which the empirical constant B is positive, represents the combined effect of short-range repulsive forces between ions, interaction between ions and solvent, possible departure from complete dissociation at high concentrations, variation of dielectric constant with concentration, deviations from spherical symmetry for the ions, etc. The first term results from the Debye–Hückel theory; the second one corresponds, at least in some respects, to the van der Waals forces between molecules of gases or liquids. Therefore, we shall designate these terms as Debye–Hückel (D. H.) and van der Waals (W.) terms, respectively. When the W. term becomes larger than the D. H. term as concentration rises, the repulsive forces outweigh the electrostatic attractions between ions and their atmospheres, and the activity coefficient becomes larger than unity. In an interesting discussion of the properties of concentrated electrolytes, Onsager[4] suggests expressing the W. term as an ordinary covolume correction of van der Waals, which amounts to considering the repulsive forces as having a potential equal to zero at all distances r larger than a from the center of each ion and rising suddenly to infinity at $r = a$. Onsager states that the values of a to be introduced in the W. term "need not agree exactly with those that are used in computing the coulomb energy, because the picture of 'hard billiard balls' is certainly too simple." He states, however, that "there seems to be a fairly close correspondence. A more complete study of this question might be worth while; it would show to what extent the thermodynamic functions of different electrolytes form a one-parameter family in regard to their dependence on the concentration, and give us more detailed information about the short-range forces." The present work is an answer to this query. The first step is to establish as correct an expression as possible for the W. term, taking into account excluded spheres, overlapping of such spheres, etc. Both the D. H. and the new W. terms are then expressed in terms of the same a and the activity coefficient is represented by a *one-parameter* formula. The theory leading to the new expression for the W. term is given in the next section. The resulting formula is then applied to a systematic interpretation of the activity data of the alkali chlorides, bromides and iodides. Other salts will be studied in subsequent communications.

(4) L. Onsager, *Chem. Rev.*, **13**, 73 (1933).

We should note here that a remarkable attempt at setting up a one-parameter formula is Guggenheim's[5] modification of Brönsted's specific interaction theory, in which the D. H. term contains the same a (3.08 Å. at 0°) for all electrolytes, and the W. term is linear in the concentration, the coefficient being the parameter and representing the specific interaction between positive and negative ions. This formulation is satisfactory at ionic strengths lower than 0.1 and the parameter has the interesting property of conserving its value in all mixtures where the corresponding pair of ions is present.

II. The van der Waals or Covolume Terms in the Activity Coefficient of a Strong Electrolyte

The problem before us is to compute the partition function representing the mutual exclusion from certain portions of space of a mixture of N_α molecules of one kind and N_β molecules of another kind. The diameters of these ions are, respectively, D_α and D_β. The problem is extremely complicated and, as noted by Fowler,[6] several solutions to be found in the literature are entirely fallacious. In the second edition of his "Statistical Mechanics," Fowler gives a solution due to Ursell,[7] which supersedes all previous ones. Ursell's theory is quite general and can be applied to a mixture of any number of kinds of molecules. He treats completely the case of two kinds and finds for the partition function [$B(T)$ in Ursell's notation]

$$Z = V^{N\alpha+N\beta}Y \qquad (5)$$

with

$$\log Y = -\frac{1}{V}\left\{N_\alpha^2\left(\frac{2}{3}\pi D_\alpha^3\right) + N_\alpha N_\beta\left(\frac{4}{3}\pi D_{\alpha\beta}^3\right) + N_\beta^2\left(\frac{2}{3}\pi D_\beta^3\right)\right\} - \frac{1}{V^2}\left[\frac{5}{16}N_\alpha^3\left(\frac{2}{3}\pi D_\alpha^3\right)^2 + 4\pi^2 N_\alpha^2 N_\beta D_\alpha^3\left\{\frac{2}{9}D_{\alpha\beta}^3 - \frac{1}{8}D_{\alpha\beta}^2 D_\alpha + \frac{1}{144}D_\alpha^3\right\} + \frac{5}{16}N_\beta^3\left(\frac{2}{3}\pi D_\beta^3\right)^2 + 4\pi^2 N_\alpha N_\beta^2 D_\beta^3\left\{\frac{2}{9}D_{\alpha\beta}^3 - \frac{1}{8}D_{\alpha\beta}^2 D_\beta + \frac{1}{144}D_\beta^3\right\}\right] \qquad (6)$$

In this formula $D_{\alpha\beta}$ is the sum of the radii of the two kinds of molecules. We thus have

$$D_{\alpha\beta} = (D_\alpha + D_\beta)/2 \qquad (7)$$

(5) E. A. Guggenheim, *Phil. Mag.*, [7] **19**, 588 (1935).

(6) R. H. Fowler, "Statistical Mechanics," 2nd edition, Cambridge University Press, 1936, pp. 241 *et seq.*

(7) H. D. Ursell, *Proc. Camb. Phil. Soc.*, **23**, 685 (1927).

In applying this result to electrolytes we shall assume that

$$D_\alpha = D_\beta = D_{\alpha\beta} = a \qquad (8)$$

a being the distance of closest approach which also appears in the D. H. term. If N is the number of molecules of salt in the volume V we have

$$N_\alpha = \nu_+ N \qquad N_\beta = \nu_- N \qquad (9)$$

Taking (8) and (9) into account, formula (6) becomes

$$\log Y = -\frac{N^2}{V}(\nu_+ + \nu_-)^2\left(\frac{2}{3}\pi a^3\right) - \frac{5}{16}\frac{N^3}{V^2}(\nu_+ + \nu_-)^3\left(\frac{2}{3}\pi a^3\right)^2 \qquad (10)$$

Let

$$v = \frac{4}{3}\pi a^3 \qquad (11)$$

represent the volume of the sphere of protection of an ion. Formula (10) becomes, making $\nu_+ + \nu_- = \nu$

$$\log Y = -\frac{\nu^2 N^2}{2V}v - \frac{5\nu^3 N^3}{64V^2}v^2 \qquad (12)$$

or, expressing it in terms of the total number of ions present, $N_i = N_\alpha + N_\beta = \nu N$

$$\log Y = -\frac{1}{2}\frac{N_i^2}{V}v - \frac{5}{64}\frac{N_i^3}{V^2}v^2 \qquad (13)$$

The corresponding contribution to the Helmholtz free energy of the ions in the solution is

$$F_{iw} = -kT\log Y = N_i kT\left[\frac{1}{2}\frac{N_i}{V}v + \frac{5}{64}\left(\frac{N_i}{V}\right)^2 v^2\right] \qquad (14)$$

On account of the practical incompressibility of solutions, F_{iw} can be assumed equal to the corresponding Gibbs free energy G_{iw} which is such that

$$G_{iw} = N_i \Delta\mu_{iw} = N_i kT\log f_{\pm w} \qquad (15)$$

in which $\log f_{\pm w}$ corresponds to the van der Waals term in $\log f_\pm$. From (14) and (15) we deduce

$$\log f_\pm = \frac{1}{2}\frac{N_i}{V}v + \frac{5}{64}\left(\frac{N_i}{V}\right)^2 v^2 \qquad (16)$$

or, in terms of the molar concentration C and Avogadro's number N

$$\log f_\pm = \frac{1}{2}\nu v N C \times 10^{-3} + \frac{5}{64}v^2\nu^2 N^2 C^2 \times 10^{-6} \qquad (17)$$

Expressing a in Ångström units we have, when $\nu = 2$

$$\log_{10} f_\pm = 1.10313 \times 10^{-3} a^3 C + 8.7564 \times 10^{-7} a^6 C^2 \qquad (18)$$

The complete formula for the activity coefficient of a uni-univalent strong electrolyte in aqueous solution at 25° is thus

$$\log_{10} f_\pm = -0.5059\frac{\sqrt{C}}{1 + \frac{a}{3.042}\sqrt{C}} + 1.10313 \times 10^{-3} a^3 C + 8.7564 \times 10^{-7} a^6 C^2 \qquad (19)$$

Such a formula may be expected to hold for values of a large enough to make the approximations involved in the derivation of the D. H. term acceptable. For uni-univalent electrolytes a should be larger than 2.

It is interesting to note that if formula (14) is applied to imperfect gases one finds that the correction to be added to the pressure $P = NkT/V$ is given by

$$P_w = -\frac{\partial F_w}{\partial V} = \frac{NkT}{V}\left[\frac{1}{2}\frac{N}{V}v + \frac{5}{32}\frac{N^2}{V^2}v^2\right] \qquad (20)$$

Introducing the van der Waals covolume b

$$b = 4N \times \frac{4}{3}\pi\left(\frac{a}{2}\right)^3 = \frac{1}{2}Nv \qquad (21)$$

we find

$$P_w = \frac{NkT}{V}\left[\frac{b}{V} + \frac{5}{8}\left(\frac{b}{V}\right)^2\right] \qquad (22)$$

This formula gives precisely the first two terms derived by Boltzmann[8] by taking account of the possibility of more than two of the spheres of force surrounding the molecules intersecting one another.

III. Remarks Concerning the Dependence of Activity Coefficients on the Mean Ionic Diameter

We have drawn a set of standard curves corresponding to our formula (19) for round values of a ranging from 2 to 6 Å. in steps of 0.5 Å. These curves have been used in one of our methods of determining a empirically for various salts, as is explained in another section of this paper. It is interesting, at this place, to report the theoretical values of the concentration C for which $f_\pm$ is a minimum and those for which it has reached again the value *one*. These concentrations have been read from our standard curves and are reported in Table I.

TABLE I

CONCENTRATIONS AT WHICH $f_\pm$ IS A MINIMUM AND CONCENTRATIONS AT WHICH $f_\pm$ IS EQUAL TO UNITY, FOR VARIOUS VALUES OF THE IONIC DIAMETER a. (1–1 ELECTROLYTES)

a, Å.	C, moles/liter for $f_\pm$ minimum	C, moles/liter for $f_\pm = 1$
2.0	7.9	21.3
2.5	4.0	16.2
3.0	1.4	10.3
3.5	1.0	5.8
4.0	0.64	3.2
4.5	.36	2.0
5.0	.30	1.2
5.5	.20	0.81
6.0	.14	0.56

(8) L. Boltzmann, "Vorlesungen über Gastheorie," 1896, Vol. II, § 51; see J. H. Jeans, "The Dynamical Theory of Gases," Cambridge University Press, 3rd ed., 1921, p. 133.

In view of the often expressed opinion that constants or parameters in the various equations for activity coefficients should be determined from data corresponding to rather low concentrations, we wish to indicate that the activity coefficient is a rather insensitive function of the parameter a at low concentrations, particularly for small values of a, but that at high concentrations it becomes a very sensitive function of a.

We have of course

$$\frac{\mathrm{d}\log f_{\pm}}{\mathrm{d}\log a} = \frac{\mathrm{d}f_{\pm}}{f_{\pm}} \Big/ \frac{\mathrm{d}a}{a} \cong \frac{\Delta f_{\pm}}{f_{\pm}} \Big/ \frac{\Delta a}{a} \qquad (23)$$

Let us consider $\Delta a = 0.5$ Å. with $a = 2$ Å. We have then $\Delta \log f_{\pm} = \log f_{\pm}(2.5) - \log f_{\pm}(2.0)$. The percentage variation of a is 0.5/2.25 or 22%. The corresponding variations of $\log f_{\pm}$, calculated according to our formula (19), are reported in Table II. In the same manner we have calculated the variations of $\log f_{\pm}$ corresponding to $\Delta a = 0.5$ Å. with $a = 4$ Å. In this case the percentage variation of a is 12%. The variations of $\log f_{\pm}$ are reported in the second half of Table II. These figures are very illuminating and show that, if one uses a formula with a as single parameter, the choice of the best empirical value for this parameter should be based, to a large extent, on data at high concentrations. We have devised, for this purpose, a method derived from the theory of least squares. Another striking proof of the lack of sensitivity of $f_{\pm}$ toward a change in a in the dilute range is that afforded by the curves of Fig. 1 which represent the variation of $\log f_{\pm}$ with a for various round concentrations. It will also be shown in another section of this paper that, when a has been determined from data in the concentrated range, very accurate values of $f_{\pm}$ can be calculated for the dilute range, while the opposite procedure in which a values are derived from data in the dilute range gives sometimes very erratic results.

TABLE II

VARIATIONS OF LOG $f_{\pm}$ CORRESPONDING TO VARIATIONS OF 0.5 Å. IN a, FOR $a = 2$ AND $a = 4$ Å.

C, moles per liter	Log $f_{\pm}$ (2)	Log $f_{\pm}$ (2.5)	$\Delta f_{\pm}/f_{\pm}$, %
0.001	−0.01566	−0.01559	0.007
.01	− .04738	− .04658	.080
.1	− .13156	− .12525	.631
1	− .29636	− .26025	3.611
2	− .35285	− .29555	5.730
5	− .41237	− .30708	10.529
10	− .42575	− .25084	17.491
	Log $f_{\pm}$ (4)	Log $f_{\pm}$ (4.5)	
0.001	−0.01529	−0.01507	0.022
.01	− .04400	− .04207	0.193
.1	− .10589	− .09143	1.446
1	− .14436	− .03980	10.456
2	− .09464	+ .11530	20.994
5	+ .15555	+ .78954	63.399
10	+ .75450	+2.48895	173.445

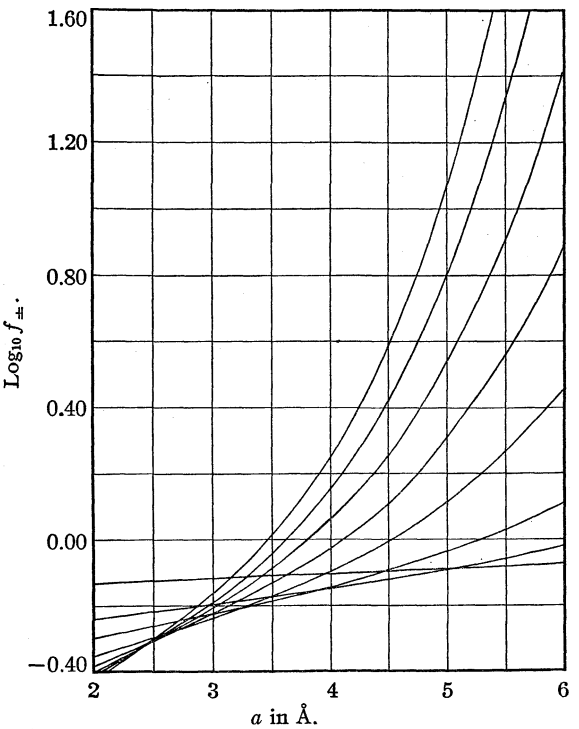


Fig. 1.—Logarithms of activity coefficients plotted against the mean ionic diameter for various round concentrations (6, 5, 4, 3, 2, 1, 0.5 and 0.1 molar from right-hand top to right-hand bottom).

IV. Determination of the Mean Ionic Diameter by the Method of Least Squares

The first step in the determination of the parameter a of a given salt consists of solving the seventh-degree equation in a corresponding to our formula (19) for some particular concentration. Only one of the solutions of this equation has physical significance and is considered as a first approximation to the exact value of a. We then calculate, for a series of round concentrations from 0.1 molar up to 4 or 5 molar, the residuals v_i defined by

$$v_i = \log \bar{f}_i - \log f_i + (\partial \log f_i/\partial \bar{a})\,\Delta\bar{a} \qquad (24)$$

in which f_i is the activity coefficient calculated by our formula (19) for the approximate value $\bar{a}$ of a, $\bar{f}_i$ is the experimental activity coefficient and $\Delta\bar{a}$ the correction to be applied to $\bar{a}$. We then calculate the sum

$$S = \sum_{i=1}^{i=r} v_i^2 \qquad (25)$$

r being the number of experimental points considered, and we minimize it by the condition

$$\partial S/\partial \Delta\bar{a} = 0 \qquad (26)$$

from which we deduce

$$\Delta\bar{a} = \frac{\sum_{i=1}^{i=z} (\log f_i - \log \bar{f}_i) x_i}{1.539 \sum_{i=1}^{i=r} x_i^2} \qquad (27)$$

where x_i is given by

$$x_i = C_i \left[\frac{1}{(3.042 + \bar{a}\sqrt{C_i})^2} + 2.150 \times 10^{-3}\bar{a}^2 + 0.3413 \times 10^{-5}\bar{a}^{-5} C_i \right] \qquad (28)$$

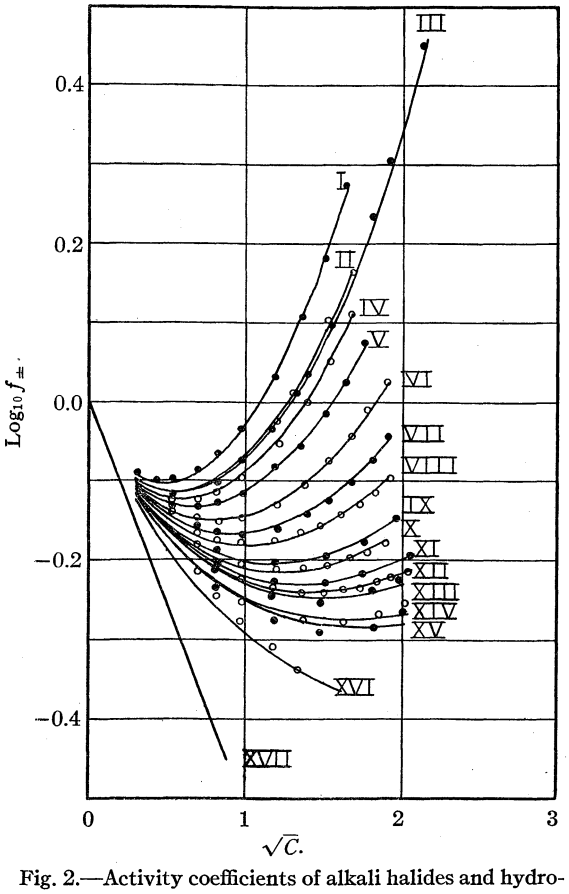


Fig. 2.—Activity coefficients of alkali halides and hydrochloric acid. The solid lines represent predicted values. The open circles represent experimental points for the even numbered salts. The solid circles represent experimental points for the odd numbered salts: I, LiI; II, LiBr; III, HCl; IV, LiCl; V, NaI; VI, NaBr; VII, NaCl; VIII, KI; IX, KBr; X, KCl; XI, RbCl; XII, RbBr; XIII, RbI; XIV, CsCl; XV, CsBr; XVI, CsI; XVII, Debye–Hückel limiting slope.

V. Application of the Theory to the Alkali Chlorides, Bromides and Iodides

The activity data used for our calculations are those of Robinson.[9] The activity coefficients γ corresponding to molalities m are converted into the rational ones $f_\pm$ by the well-known formula

$$\log f_\pm = \log \nu + \log (1 + 0.018\, \nu m) \qquad (29)$$

and the molalities are transformed into volume concentrations by means of the density data. The weighted a's obtained by the method described above for the chlorides, bromides and iodides of lithium, sodium, potassium, rubidium and cesium in aqueous solution at 25° are given in the second column of Table III. On Fig. 2 we give the $\log f_\pm$ curves corresponding to these weighted a's, and the experimental $\log f_\pm$'s, indicated by circles, are seen to be in close agreement with these curves except in the case of cesium bromide and cesium iodide, for which appreciable departures occur.[10] It is to be noted that, particularly in the case of cesium iodide, with $a = 2.067$ Å., we are in a range of a values to which the Debye–Hückel theory is not strictly applicable. Improvements would probably be noticed if the Debye–Hückel term in our formula (19) were corrected according to the methods suggested by Bjerrum[11a] and by Gronwall, La Mer and Sandved.[11b]

Besides the a's calculated by the method of least squares, we have also determined, for a number of round concentrations ranging from 0.1 to 4–5 molar, the a's which give exact agreement with the theory. For this purpose we have used the curves of Fig. 1 from which the a's are directly read. They are reported in the third column of Table III (average values and average deviations). The results are indeed remarkable, with the sole exception of those for cesium iodide. In the last column of Table III we give the sums of the standard ionic radii for the crystals on the basis of Pauling's[12] data. We notice that, for the salts of lithium and sodium,

(9) R. A. Robinson and D. A. Sinclair, THIS JOURNAL, **56**, 1830 (1934); R. A. Robinson, *ibid.*, **57**, 1161 (1935); see also O. Redlich and P. Rosenfeld, activity data in Landolt–Börnstein-Roth Tables, Dritter Ergänzungsband, Verlag von Julius Springer, Berlin, 1936, pp. 2138–2171.

(10) We also give on Fig. 2 the curve for hydrochloric acid, which almost coincides with that for lithium bromide. This case will be analyzed further in another communication.

(11) (a) N. Bjerrum, *Det. Kgl. Danske Vidensk. Selsk. Math.-fysik. Medd.*, VII, No. 6 (1926); (b) T. H. Gronwall, V. K. La Mer and K. Sandved, *Physik. Z.*, **29**, 358 (1928).

(12) L. Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 1939, p. 338.

the a's in solution are larger than the sums of the standard crystalline radii, undoubtedly on account of hydration, which is relatively more important for the lithium than for the sodium salts. With the potassium salts, a in solution is practically equal to the sum of radii in the crystal, while for the rubidium and cesium halides, the a's in solution are smaller than the sums of the standard crystalline radii.

TABLE III

MEAN IONIC DIAMETERS OF THE ALKALI CHLORIDES, BROMIDES AND IODIDES IN AQUEOUS SOLUTION AND SUMS OF THE STANDARD CRYSTALLINE RADII

Salts	a least squares, Å.	a for exact agreement, Å.	Sums of ionic radii in crystal, Å.
LiCl	4.544	4.48 ± 0.05	2.413
LiBr	4.738	4.63 ± 0.10	2.558
LiI	5.064	5.08 ± 0.02	2.775
NaCl	3.727	3.79 ± 0.09	2.764
NaBr	3.989	4.01 ± 0.04	2.909
NaI	4.308	4.29 ± 0.02	3.126
KCl	3.218	3.29 ± 0.07	3.137
KBr	3.300	3.39 ± 0.09	3.282
KI	3.551	3.67 ± 0.13	3.499
RbCl	3.061	3.07 ± 0.03	3.290
RbBr	2.980	3.00 ± 0.03	3.435
RbI	2.914	2.92 ± 0.03	3.652
CsCl	2.719	2.65 ± 0.07	3.462
CsBr	2.653	2.58 ± 0.07	3.607
CsI	2.067	2.26 ± 0.23	3.824

It seems reasonable to assume that the ions of the three potassium salts are unhydrated, or practically so, and that they can come into exact contact without deformation, since the differences $a - b$, in which b designates the sum of the standard ionic radii, are 0.081, 0.018 and 0.052 Å. for the chloride, bromide and iodide, respectively. It is then also logical to assume, at least as a working hypothesis, that the three halide ions are unhydrated in all these alkali halide solutions. Subtracting from the a's the standard crystalline radius of the negative ion we get the figures of the second column of Table IV.

We see that the resulting radii for Li^+ in the three halides are practically the same, showing that the amount of hydration, which can be characterized by the quantity

$$h_+ = a - (r_+ + r_-) \qquad (30)$$

given in the third column of Table IV, is constant for the three salts. We have a similar situation for the Na^+ ion. The h_+'s values for K^+ can probably be neglected, as assumed above. For the three rubidium salts we get negative values of h_+, but the differences $a - r_-$ are all positive.

TABLE IV

IONIC RADII OF THE POSITIVE IONS IN SOLUTIONS OF THE ALKALI CHLORIDES, BROMIDES AND IODIDES

Salts	$a - r_-$, Å.	$a - (r_- + r_+)$, Å
LiCl	2.738	2.131
LiBr	2.787	2.180
LiI	2.896	2.289
NaCl	1.921	0.963
NaBr	2.038	1.080
NaI	2.140	1.182
KCl	1.412	0.081
KBr	1.349	.018
KI	1.383	.052
RbCl	1.255	− .229
RbBr	1.029	− .455
RbI	0.746	− .738
CsCl	.913	− .743
CsBr	.702	− .954
CsI	− .101	−1.757

This could be explained by assuming that, at closest approach, the positive and negative ions penetrate each other, the center of the positive ion being outside the negative one. The difference represents the distance between the center of the positive ion and the surface of the negative one. We have the same situation with cesium chloride and cesium bromide, but with cesium iodide $a - r_-$ is negative, showing that, on the basis of the above suggestion, the center of the positive ion is now inside the negative ion, at 0.101 Å. from the surface of the latter. We have represented on Fig. 3 the variation of a with the

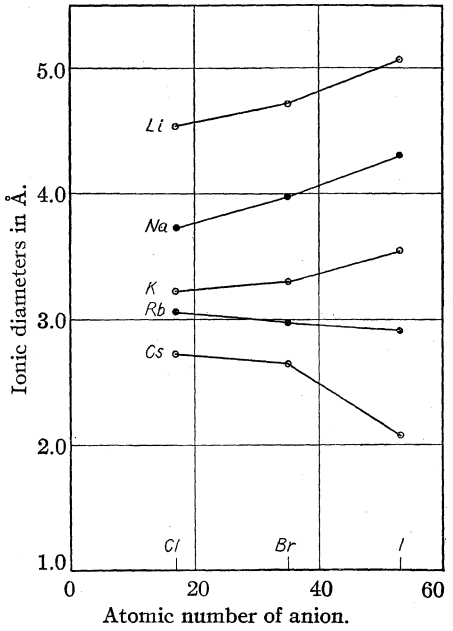


Fig. 3.—Ionic diameters of alkali salts in aqueous solutions plotted against the atomic number of the anion.

atomic number of the negative ion for each alkali metal and on Fig. 4 the variation of a with the atomic number of the positive ion for each halogen.

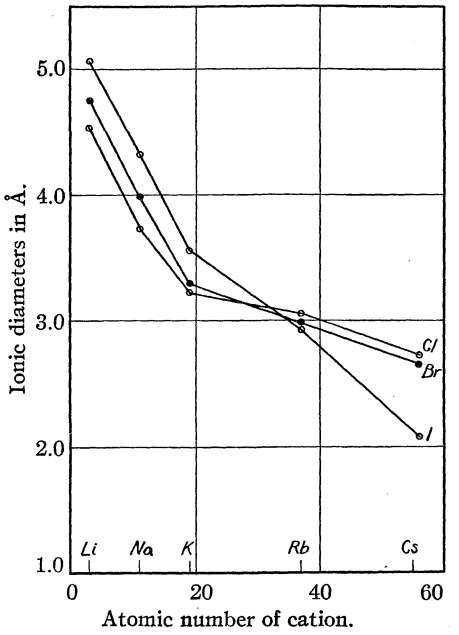


Fig. 4.—Ionic diameters of alkali salts in aqueous solutions plotted against the atomic number of the cation.

VI. Activity Coefficients in the Dilute Range. Concluding Remarks

We have calculated the activity coefficients of 0.001 and 0.01 molar solutions of the fifteen halides using the weighted a's of Table III, which were all determined from data at concentrations larger than 0.1 molar. For eight of the salts experimental values are available and the agreement is surprisingly good, as shown in Table V. As noted above already, the reverse procedure, by which a would be calculated from these data in the dilute range, gives erratic results (a becoming sometimes as large as 7 Å.). Inspection of Fig. 1 and our remarks of section III should make this point perfectly clear.

TABLE V

ACTIVITY COEFFICIENTS OF DILUTE ALKALI CHLORIDES, BROMIDES AND IODIDES

Salts	C = 0.001 $f_\pm$ exptl.	$f_\pm$ calcd.	C = 0.01 $f_\pm$ exptl.	$f_\pm$ calcd.	Ref.
LiCl	0.9631	0.9656	0.8954	0.9057	13
LiBr	.9663	.9658	.9096	.9066	13
LiI		.9658		.9078	
NaCl	.9659	.9652	.9063	.9026	13
NaBr	.966	.9654	.9141	.9037	13
NaI	.966	.9656	.917	.9049	14
KCl	.9652	.9652	.9026	.9007	13
KBr	.9651	.9652	.9037	.9012	13
KI	.965	.9652	.905	.9020	15
RbCl		.9649		.8997	
RbBr		.9649		.8999	
RbI		.9649		.8997	
CsCl		.9649		.8991	
CsBr		.9649		.8989	
CsI		.9645		.8968	

We wish to point out that our one-parameter formulation leads to better agreement with the data than the interesting but more complicated treatment proposed by Scatchard.[16] We believe that the effect of the ionic charges on the dielectric constant of the solution and the other interactions analyzed by Scatchard are implicitly contained in our equation and that they all affect the value of a. Scatchard uses the ionic radii corresponding to the crystal lattices reported by Pauling in 1928,[17] and it should be pointed out that these values are somewhat smaller than the corrected ones recently published by Pauling.[12] It also should be noted that our treatment constitutes, at least for the salts discussed in the present paper, a definite improvement on the only other one-parameter treatment so far proposed, namely, that of Guggenheim,[5] whose range of applicability is limited by an ionic strength of 0.1.

We already have obtained a number of promising results with other 1–1 electrolytes and with some 2–1, 2–2 and 3–1 electrolytes, as well as with some non-electrolytes, which appear to follow our equation (19) when the electrostatic term is left out. These results and other work at present in progress will be reported in subsequent papers.

Summary

1. The problem of expressing the activity coefficients of strong electrolytes as functions of a single parameter, the distance of closest approach between positive and negative ions or mean ionic diameter, is stated.

2. The van der Waals or covolume terms in the activity coefficient formula are derived on the basis of a theory due to Ursell. A term proportional to the volume concentration and to the cube of the distance of closest approach, and another one proportional to the square of the vol-

(13) G. Scatchard and S. S. Prentiss, THIS JOURNAL, **55**, 4355 (1933).

(14) G. Karagunis, A. Hawkinson and G. Damköhler, *Z. physik. Chem.*, **A151**, 433 (1930).

(15) Landolt–Börnstein–Roth Tables, ref. 9.

(16) G. Scatchard, *Chem. Rev.*, **19**, 309 (1936).

(17) L. Pauling, THIS JOURNAL, **50**, 1036 (1928); *Z. Krist.*, **67**, 377 (1928).

ume concentration and to the sixth power of the distance of closest approach, are added to the Debye–Hückel expression for the logarithm of the activity coefficient.

3. It is shown that only at high concentrations do the activity coefficients become sufficiently sensitive functions of the distance of closest approach to make the determination of this parameter really precise.

4. The determination of this parameter by the method of least squares is described.

5. The theory is applied to the alkali chlorides, bromides and iodides with remarkable success. A set of mean ionic diameters is obtained, and various remarks as to the extent of hydration, penetration of ions at contact, etc., are derived from a comparison of these diameters with the sums of the standard crystalline radii.

6. Activity coefficients in 0.001 and 0.01 molar solutions are calculated with the weighted mean ionic diameters obtained at high concentrations. In eight cases out of fifteen comparison with experimental values is possible and shows more than satisfactory agreement.

STANFORD UNIVERSITY, CALIF.

RECEIVED AUGUST 11, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE STATE COLLEGE OF WASHINGTON]

The Bromination of 4-Phenylphenyl Acetate

BY STEWART E. HAZLET AND HARRY A. KORNBERG

In previous reports it was shown that although the bromination of 4-phenylphenol results in substitution at a position ortho to the hydroxyl group, when the benzenesulfonate[1] or the benzoate[2] of the phenol is brominated, the substitution occurs at the position in the molecule most remote from the ester linkage (*viz.*, *p'*). The study of the introduction of bromine into the esters of 4-phenylphenol has been extended now to 4-phenylphenyl acetate, which is analogous to the benzenesulfonate and the benzoate previously considered.

It was suggested in an earlier report[2] that perhaps steric hindrance is responsible for the change in directive influence when hydroxyl is modified to benzenesulfonyloxy or benzoyloxy. In the work here reported (see Chart I for the outline) the hydroxyl of 4-phenylphenol (I) was replaced by the acetyloxy group. On the basis of the calculations of Latimer and Porter[3] the acetyloxy group of compound II should possess the same residual charge as the benzoyloxy group in one of the compounds previously studied. The acetyloxy group is, however, much smaller than the benzoyloxy group and should be expected to exert less steric effect. Therefore it was considered possible that the bromination of 4-phenylphenyl acetate (II) might result in substitution in a position ortho with respect to the acetyloxy group. This was realized; it was found that the first bromine atom to enter 4-phenylphenyl acetate (II) gave rise to 2-bromo-4-phenylphenyl acetate (IV). Furthermore, under conditions only slightly different from those used in the preparation of compound IV and in the earlier studies,[1,2] a second atom of bromine entered the ester molecule (II) in the same relative position as in the case of the phenol (I), *viz.*, the second ortho position; thus 2,6-dibromo-4-phenylphenyl acetate (VI) was formed.

A bromine substitution product of compound II, 4-(4-bromophenyl)-phenyl acetate (IX), isomeric with compound IV obtained by direct bromination of the acetate (II) was prepared by the acetylation of a phenol (VIII) of known structure. The two isomers had distinctly different physical properties.

The experimental steps and the proofs of structure of the compounds are outlined in Chart I, and the details of procedures are given in the Experimental Part.

Experimental Part

4-Phenylphenyl Acetate (II).[4]—This compound was prepared in almost quantitative yield by gently refluxing for three hours one mole of 4-phenylphenol (I) and 0.25 mole of anhydrous sodium acetate in an excess of acetic anhydride. The reaction mixture was allowed to cool, poured into ten volumes of water, and permitted to stand overnight. The ester was collected by filtration and recrystallized from methanol. The colorless, irregular crystals melted between 87 and 88°.

2-Bromo-4-phenylphenyl Acetate (IV).—Fifteen grams of 4-phenylphenyl acetate (II) was dissolved in 30 ml. of

(1) Hazlet, THIS JOURNAL, **59**, 1087 (1937).
(2) Hazlet, Alliger and Tiede, *ibid.*, **61**, 1447 (1939).
(3) Latimer and Porter, *ibid.*, **52**, 206 (1930).
(4) Kaiser, *Ann.*, **257**, 95 (1890).

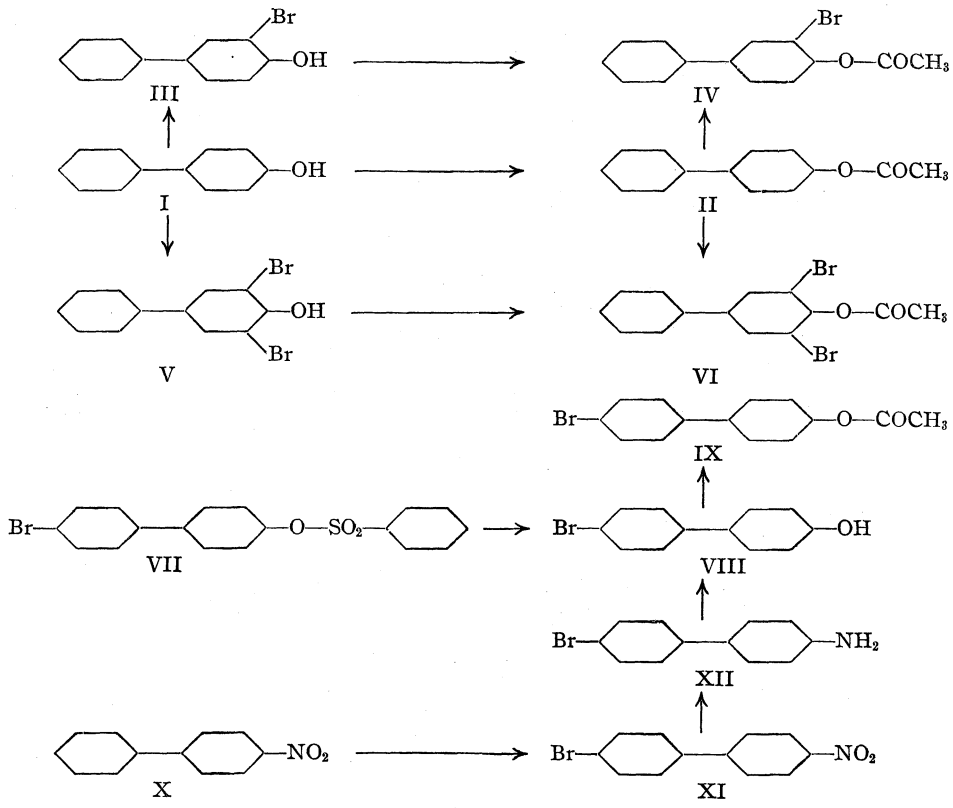


CHART I

glacial acetic acid. The mixture was stirred vigorously and was heated to 100 ± 2° in an oil-bath. A trace of iron powder was added, and then 6 ml. of bromine (approximately 1.5 moles) was added dropwise over a period of thirty minutes. The heating and stirring were continued for ten hours. Upon pouring the cooled mixture into 400 ml. of water, a dark brown viscous mass separated. After adding an excess of sodium carbonate solution, the mixture was extracted with ether. The viscous liquid (23.1 g.), which was obtained from the ether solution, was dissolved in boiling methanol. Upon cooling, a brown solid separated. Ligroin[5] was used for recrystallizations. The product (11.7 g., 57% yield) was obtained as elongated hexagonal plates; m. p. 74–75°.

This compound (IV) was also prepared from 5 g. of 2-bromo-4-phenylphenol (III)[2] in 20 ml. of acetic anhydride; 0.25 mole of anhydrous sodium acetate was added. The mixture was heated for five hours on a steam-bath, cooled, and poured into 300 ml. of cold water. The crude product (4.7 g.) represented a 90% yield. After treatment with Norite and two recrystallizations from methanol, the product was obtained as colorless hexagonal plates; m. p. 74–75°.

Anal. Calcd. for $C_{14}H_{11}O_2Br$: Br, 27.5. Found: Br, 27.6.

When equal amounts of the two samples prepared by the different methods were mixed, there was no depression of the melting point.

(5) The boiling range of the ligroin used in all of the experimental work was from 90 to 120°.

2,6-Dibromo-4-phenylphenyl Acetate (VI).—Fifteen grams of 4-phenylphenyl acetate (II) was treated as in the bromination described above except that 8 ml. of bromine (approximately 2 moles) was used, the temperature of the oil-bath was 110 ± 2°, and the time of the reaction was eight hours. The product was recovered as indicated in the case of the monobromo compound (IV). The yield of the crude material was only 40% (14.8 g.), and after several treatments with Norite and recrystallizations from ligroin, the colorless irregular crystals obtained (4.2 g.) represented only a 16% yield; m. p. 81–83°.

Anal. Calcd. for $C_{14}H_{10}O_2Br_2$: Br, 43.3. Found: Br, 43.4.

A second method was also used for the preparation of this compound (VI). To 0.8 g. of 2,6-dibromo-4-phenylphenol (V)[2] in 20 ml. of acetic anhydride, 0.5 g. of sodium acetate was added. The mixture was gently refluxed for two hours, cooled, poured into 200 ml. of water, and allowed to stand overnight. After filtration, treatment with Norite, and recrystallization from ligroin, the product was obtained in almost quantitative yield as irregular crystals which melted between 81.5 and 83°.

Anal. Calcd. for $C_{14}H_{10}O_2Br_2$: Br, 43.3. Found: Br, 43.7.

A mixture of equal amounts of this compound prepared by the two different methods melted from 81 to 83°.

4-(4-Bromophenyl)-phenyl Acetate (IX).—4-Phenylnitrobenzene (X) was converted to 4-(4-bromophenyl)-nitrobenzene (XI),[6] the nitro compound was reduced to 4-

(6) Le Fèvre and Turner, *J. Chem. Soc.*, 2041 (1926).

(4-bromophenyl)-aniline (XII),[7] and the amine converted to 4-(4-bromophenyl)-phenol (VIII).[7] The crude product so obtained was refluxed with an excess of acetic anhydride and 0.25 mole of anhydrous sodium acetate for two hours, and the product (IX) was recovered in the usual manner. A mixture of ligroin and benzene was used for recrystallizations. The product was obtained as colorless irregular plates; m. p. 128–129°. On the basis of the amount of compound X used, the yield was low.

Anal. Calcd. for $C_{14}H_{11}O_2Br$: Br, 27.5. Found: Br, 27.2.

A sample of 4-(4-bromophenyl)-phenol (VIII) obtained by the hydrolysis of 4-(4-bromophenyl)-phenyl benzenesulfonate (VII)[1] was also used for the preparation of this compound (IX). The yield of the crude acetate (IX) corresponded to 92% on the basis of the benzenesulfonate used. The m. p. 128–129° was the same as for the product described above, the crystals were similar, and a mixture of samples of the two preparations melted between 128 and 129°.

(7) Bell and Robinson, *J. Chem. Soc.*, 1127 (1927).

Summary

1. Although the bromination of 4-phenylphenyl benzenesulfonate or 4-phenylphenyl benzoate yields the 4-(4-bromophenyl)-phenyl ester, the introduction of bromine into 4-phenylphenyl acetate results in substitution in the ortho position (or positions) with respect to the acetyloxy group. The behavior of the acetate, therefore, is analogous to that of 4-phenylphenol.

2. These results are in keeping with a previous suggestion that steric effects may determine the positions taken by substituents entering an ester molecule.

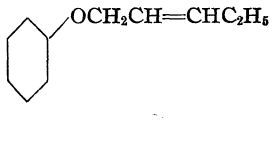
PULLMAN, WASHINGTON RECEIVED AUGUST 21, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

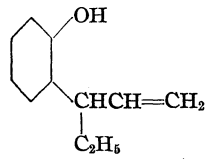
The Rearrangement of Phenyl Allyl Ethers. III. The Synthesis of α-(ortho-Methoxyphenyl)-propionic Acid

BY WALTER M. LAUER AND LOUIS I. HANSEN[1]

The rearrangement of γ-ethylallyl phenyl ether (I) yields both o-(α-ethylallyl)-phenol (II), and o-(α,γ-dimethylallyl)-phenol (III).[2]



I



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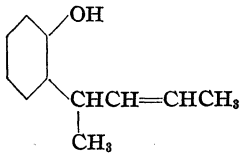
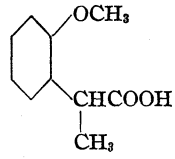


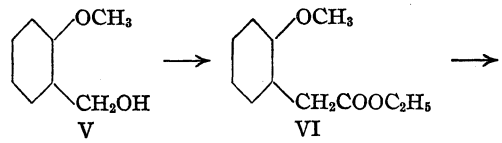
III



IV

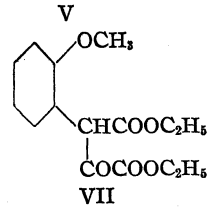
The structure of the abnormal rearrangement product (III) is based upon several lines of evidence which need not be considered here. However, one method of approach which was used involves the conversion of this abnormal rearrangement product into α-(o-methoxyphenyl)-propionic acid (IV). This acid has not been described previously. Therefore, it was the purpose of the present study to synthesize this acid and to compare it with the product obtained by the degradation of the abnormal rearrangement product (III).

A number of promising syntheses were studied and the desired acid was prepared in two independent ways. The synthetic product proved to be identical with that obtained from the abnormal rearrangement product. An outline of the most satisfactory synthesis follows

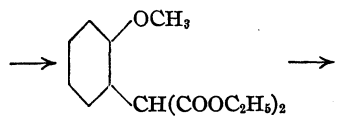


V

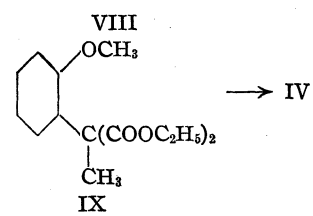
VI



VII



VIII



IX

IV

The corresponding compounds in the para series were also prepared.

(1) Abstract of Ph.D. thesis, submitted to the University of Minnesota, March, 1938. Paper III, THIS JOURNAL, **58**, 1392 (1936).

(2) Lauer and Filbert, THIS JOURNAL, **58**, 1388 (1936); Hurd and Puterbaugh, *J. Org. Chem.*, **2**, 381 (1938).

In addition, α-(*o*-methoxyphenyl)-butyric acid was synthesized, since this acid is related to the normal rearrangement product (II), in the same way that α-(*o*-methoxyphenyl)-propionic acid is related to the abnormal rearrangement product (III).

Experimental

***o*-Methoxybenzyl alcohol** (V) (b. p. 130–131° at 15 mm.) was prepared from *o*-methoxybenzaldehyde according to the excellent procedure of Davidson and Bogert[3] using a crossed Cannizzaro reaction.

The α-naphthylurethan (m. p. 135–136°) was prepared.[4]

***o*-Methoxybenzyl chloride** was prepared by saturating a solution of 112 g. of *o*-methoxybenzyl alcohol in 500 ml. of benzene with dry gaseous hydrogen chloride according to the directions of Pschorr[5]: yield, 112 g. (88%); b. p. 104–105° at 10 mm.

***o*-Methoxybenzyl cyanide** was obtained by refluxing the chloride (85 g.) in acetone (900 ml.) with a concentrated aqueous solution containing potassium cyanide (80 g.).

Ethyl *o*-methoxyphenylacetate (VI), (b. p. 137–138° at 13 mm.).—A mixture of *o*-methoxybenzyl cyanide (104 g.), alcohol (104 ml.) and a solution of potassium hydroxide (46 g.) in water (50 ml.) was refluxed for ten hours. The reaction mixture was then poured into water, cooled and filtered, and extracted with ether. The aqueous alkaline solution was warmed on the steam-bath to remove the ether and some of the alcohol. Acidification with 10% sulfuric acid produced an oil (100 g.) which solidified on standing. Crystallization from a petroleum ether–ether mixture yielded the pure acid, m. p. 123–124°. The *o*-methoxyphenylacetic acid was esterified.

Diethyl *o*-Methoxyphenylmalonate (VIII).—Absolute alcohol (172 ml.), in a three-necked flask fitted with a mercury-sealed stirrer, reflux condenser and dropping funnel, was treated with sodium (5.64 g.). After the reaction mixture had cooled to 60°, freshly distilled ethyl oxalate (35.8 g.) was added rapidly with vigorous stirring. The addition of the ethyl ester of *o*-methoxyphenylacetic acid (47.5 g.) followed. Stirring was discontinued and the reaction mixture was then poured into a beaker. The sodium salt crystallized out after standing at room temperature for several hours. The thick paste was stirred thoroughly with dry ether (200 ml.) and then filtered. The *o*-methoxyphenyl oxalacetic ester was liberated from its sodium salt with dilute sulfuric acid and then extracted from the aqueous solution with ether. The combined ether extracts were dried over sodium sulfate. After the ether had been removed by distillation, the residual oil was heated by means of a metal or oil-bath. The pressure was reduced to approx. 15 mm. and the temperature was raised gradually to 125°, at which temperature the evolution of carbon monoxide began. The temperature was then increased slowly to 175° and maintained approximately four hours until the evolution of carbon monoxide was complete. The distillate combined with the residue in the distilling flask yielded diethyl *o*-methoxyphenyl malonate (36 g., b. p. 162–164° at 4.5 mm.) upon distillation under reduced pressure.

Anal. Calcd. for $C_{14}H_{18}O_5$: C, 63.2; H, 6.8. Found: C, 63.8; H, 7.2.

Diethyl Ester of *o*-Methoxyphenylmethylmalonic Acid (IX).—Sodium (1.3 g.) was dissolved in absolute alcohol (15.5 g.) contained in a three-necked flask fitted with a mercury-sealed stirrer, reflux condenser and dropping funnel. Diethyl *o*-methoxyphenylmalonate (15 g.) was then added slowly with cooling. The reaction mixture was allowed to remain in an ice-bath for two hours after the addition of the ester. At the end of this period the reaction mixture was heated in a steam-bath and methyl iodide (8.4 g.) was added dropwise. The reaction mixture was heated under reflux until it became neutral to litmus, and then poured into water. The oily layer was separated and the aqueous layer extracted with ether. The combined ether extracts were then dried over sodium sulfate. Distillation yielded a product (12.5 g.) boiling at 152–153° under a pressure of 2.8 mm.

The unmethylated malonic ester was separated from the methylated ester by means of fractional hydrolysis at room temperature with a dilute solution (4.5%) of potassium hydroxide. After the ether solution of the mixture of esters had been shaken with the alkali for a period of six hours, the aqueous layer was acidified with dilute hydrochloric acid. Extraction with ether yielded a solid which, upon crystallization from a mixture of ether and petroleum ether, melted at 137.5–138° with decomposition. Decarboxylation gave *o*-methoxyphenylacetic acid (m. p. 123–124°).

A second treatment of the ether solution with dilute potassium hydroxide at room temperature for a four-hour period did not yield any isolable acid. The ether solution upon distillation gave an oil (b. p. 150–151° at 2.6 mm.) which solidified (m. p. 42–43°).

Anal. Calcd. for $C_{15}H_{20}O_5$: C, 64.29; H, 7.14. Found: C, 64.14; H, 7.15.

Hydrolysis and Decarboxylation of the Diethyl Ester of *o*-Methoxyphenylmethylmalonic Acid.—A solution of the pure ester (2 g.) in alcohol (15 ml.) was refluxed for one hour with a slight excess of potassium hydroxide solution (10%). The reaction mixture was then poured into water and acidified with dilute hydrochloric acid. Extraction with ether gave a solid which, upon crystallization from a mixture of ether and petroleum ether, melted at 148.5–149° with decomposition.

Anal. Calcd. for $C_{11}H_{12}O_5$: C, 58.9; H, 5.4. Found: C, 58.6; H, 5.8.

Decarboxylation was accomplished by refluxing the dibasic acid in xylene for two hours. After the xylene was removed by distillation under reduced pressure, an oil which solidified remained. Crystallization from a mixture of ether and petroleum ether yielded the desired monobasic acid of m. p. 101–102°.

A mixed melting point taken with the acid prepared by the degradation of the abnormal rearrangement product (III) showed no depression.

α-(*o*-Methoxyphenyl)-butyric acid was prepared by the ethylation of diethyl *o*-methoxyphenylmalonate using ethyl iodide. The procedure was similar to that used for

(3) Davidson and Bogert, THIS JOURNAL, **57**, 905 (1935).
(4) Bickel and French, *ibid.*, **48**, 747–751 (1926).
(5) Pschorr, *Ann.*, **373**, 76 (1910).

methylation. Diethyl *o*-methoxyphenylethylmalonate is a solid of m. p. 66–67°.

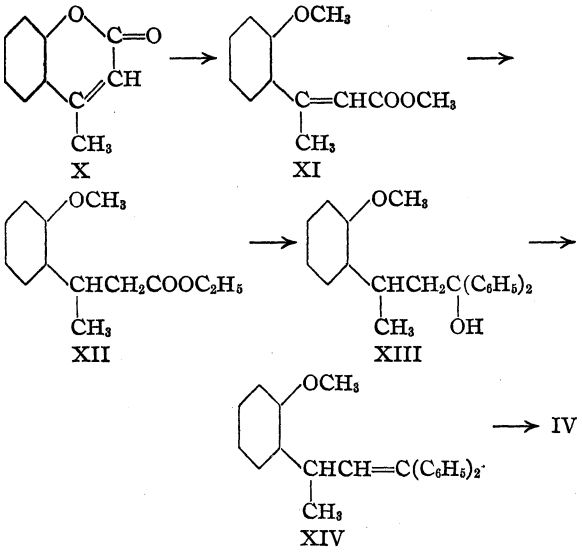
Anal. Calcd. for $C_{16}H_{22}O_5$: C, 65.3; H, 7.5. Found: C, 65.0; H, 7.5.

Hydrolysis and decarboxylation yielded the solid α-(*o*-methoxyphenyl)-butyric acid (m. p. 56–57°; b. p. 165–166° at 10 mm.).

Anal. Calcd. for $C_{11}H_{14}O_3$: C, 68.0; H, 7.2. Found: C, 67.5; H, 6.9.

The physical properties of a few of the para compounds are: (a) ethyl *p*-methoxyphenylacetate, b. p. 148–150° at 14.5 mm.; (b) diethyl *p*-methoxyphenylmalonate, b. p. 161–162° at 3 mm., $n^{20}D$ 1.4988; (c) diethyl *p*-methoxyphenylmethylmalonate, b. p. 160–161° at 3.5 mm., $n^{20}D$ 1.4990. (*Anal.* Calcd. for $C_{15}H_{20}O_5$: C, 64.3; H, 7.1. Found: C, 63.9; H, 7.0); (d) *p*-methoxyphenylmethylmalonic acid, m. p. 149.5–150°. (*Anal.* Calcd. for $C_{11}H_{12}O_5$: C, 59.0; H, 5.4. Found: C, 59.1; H, 5.4); (e) α-(*p*-methoxyphenyl)-propionic acid, m. p. 56–57°.

A second but less satisfactory synthesis of α-(*o*-methoxyphenyl)-propionic acid made use of the following series of reactions



4-Methylcoumarin (X), prepared according to the directions of Stoermer and Sandow,[6] was converted to the **methyl ester of *o*-methoxy-β-methylcinnamic acid (XI)** using the procedure of these same investigators. Difficulty was experienced in the catalytic reduction of XI, consequently the ester was hydrolyzed to the acid by means of alcoholic potassium hydroxide.

Reduction of *o*-methoxy-β-methylcinnamic acid to the corresponding saturated acid was accomplished by the use of sodium amalgam. The unsaturated acid (18 g., 0.09 mole) was dissolved in 100 cc. of water containing sodium hydroxide (3.68 g., 0.09 mole). To this solution 4% sodium amalgam (150 g.) was added over a period of six hours, maintaining a temperature of 50° throughout. After twelve hours, reduction was complete. The filtered aqueous solution was then acidified with 10% sulfuric acid and extracted with ether. The combined ether extracts, after drying with sodium sulfate, yielded an oil which was distilled under reduced pressure (b. p. 172° at 9 mm.). After standing at room temperature for approximately one month, the product finally solidified (m. p. 49–50°).

Anal. Calcd. for $C_{11}H_{14}O_3$: C, 68.14; H, 7.23. Found: C, 68.26; H, 7.25.

Ethyl *o*-methoxy-β-methylhydrocinnamate (XII) (b. p. 153–154° at 9 mm.) was prepared by refluxing the saturated acid with absolute ethyl alcohol in the presence of a small amount of concd. sulfuric acid.

The conversion of the ester to the **carbinol XIII** was brought about in the following manner. To a solution of the Grignard reagent prepared from phenyl bromide (54.2 g.) and magnesium (8.3 g.) and ether (1500 cc.) was added an ether solution of the hydrocinnamate (29 g.). The rate of addition of the ester was regulated so that the reaction mixture refluxed slowly. After the addition of the ester, the mixture was refluxed for an additional two hours. The ether was then removed by distillation and the residue was heated on the steam-bath for one hour. The reaction mixture was decomposed with ice and sulfuric acid, and then extracted with ether. The combined ether extracts were washed with water and after the ether was removed, the residue was steam distilled to remove the diphenyl. The residual oil in the distilling flask was then taken up in ether and dried. The product (35 g.), which was obtained after the removal of the ether, did not crystallize.

The carbinol XIII was dehydrated in accordance with the procedure of Schlenk and Bergmann[7] by refluxing with acetic anhydride. The yellow oil which resulted from this dehydration could not be crystallized but was oxidized directly.

Oxidation of XIV.—A solution of XIV (2 g.) in acetic acid (15 ml.) was placed in a bath at 50–60°. To this solution was added dropwise chromic acid (1.5 g.) dissolved in water (3 ml.) and acetic acid (6 ml.). After oxidation was complete, the reaction mixture was steam distilled. Benzophenone was isolated from the steam distillate. The contents of the distilling flask were then subjected to extraction with ether, and the ether extract was shaken with a 5% solution of sodium carbonate. The alkaline aqueous extract, after acidification with sulfuric acid (10%), produced an oil, which upon distillation at reduced pressure yielded a crystalline solid (m. p. 101–102°). This solid proved to be the desired acid IV.

Summary

α-(*o*-Methoxyphenyl)-propionic acid has been synthesized in two different ways. It is identical with the product previously obtained by the degradation of the abnormal rearrangement product of γ-ethylallyl phenyl ether. This synthesis therefore supplies evidence of the correctness of the structures which have already been assigned to the abnormal rearrangement product of γ-ethylallyl phenyl ether and to its degradation product.

MINNEAPOLIS, MINN. RECEIVED MAY 29, 1939

(6) Stoermer and Sandow, *Ber.*, **53**, 1285 (1920).

(7) Schlenk and Bergmann, *Ann.*, **463** 50 (1928).

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

The Rearrangement of Phenyl Allyl Ethers. IV. An Examination of the Pyrolysis Product of Phenyl Allyl Ether for Evidence of Para Rearrangement

BY WALTER M. LAUER AND ROBERT M. LEEKLEY

The para rearrangement of phenyl allyl ethers, while not as common as ortho rearrangement, has nevertheless been observed. For example, Claisen and Eisleb[1] obtained methyl 2-hydroxy-3-methyl-5-allylbenzoate by heating methyl 2-allyloxy-3-methylbenzoate and recently Mumm and his co-workers[2] have studied the para rearrangement of substituted allyl ethers of this same methyl *o*-cresotinate. That para rearrangement is not confined to cases in which both ortho positions are blocked becomes apparent from a study by Staudinger of the rearrangement of γ,γ-dimethylallyl *o*-anisyl ether. The rearrangement product upon methylation and subsequent degradation yielded veratric acid.

In view of these facts it was considered advisable to reëxamine the pyrolysis of phenyl allyl ether for evidence of para rearrangement. The results of this study show that no appreciable amount of *p*-allylphenol is formed.

Although Claisen has shown conclusively that the product obtained by the pyrolysis of allyl phenyl ether is *o*-allylphenol, the methods which were used were such that a small amount of *p*-allylphenol in the rearrangement product might have escaped detection. In the present investigation a method sufficiently sensitive for the detection of even a small amount of *p*-allylphenol was used. *o*-Allylphenol and *p*-allylphenol are not easy to separate, but the corresponding hydroxybenzaldehydes are easily separated, since salicylaldehyde forms a copper derivative but *p*-hydroxybenzaldehyde does not. If a mixture of the two aldehydes is treated with a solution of copper acetate, the salicylaldehyde is precipitated as the copper derivative and the *p*-hydroxybenzaldehyde may be removed by extraction with ether. This method was tested with known mixtures of the two aldehydes, and in one of these tests seventy milligrams of *p*-hydroxybenzaldehyde was recovered from a mixture that contained 10 g. of salicylaldehyde and 100 mg. of *p*-hydroxybenzaldehyde. The rearrangement product obtained by the pyrolysis of allyl phenyl ether was converted to the corresponding hydroxybenzaldehyde by isomerization with potassium hydroxide followed by ozonolysis.

No trace of *p*-hydroxybenzaldehyde could be found in the salicylaldehyde produced from the rearrangement product. It was therefore concluded that if any *p*-allylphenol was formed by the rearrangement of allyl phenyl ether, it must be in very small amount.

This conclusion was confirmed in other ways. A sample of *o*-allylphenol which had been prepared by the decarboxylation of 3-allyl-4-hydroxybenzoic acid was compared with one prepared by the rearrangement of allyl phenyl ether. There were no significant differences in refractive indices or in melting points of the crude phenylurethans between the two samples.

Experimental

***o*-Allylphenol** (b. p. 110–113° at 23 mm.; $n^{20}D$ 1.5453) prepared by the rearrangement of allyl phenyl ether, was isomerized to *o*-propenylphenol by means of methyl alcoholic potassium hydroxide according to the procedure of Claisen.[3] Completeness of isomerization was established by means of a quantitative determination of the —CH=CHCH$_3$ group using mercuric acetate.

The ozonide, prepared in ethyl acetate from 14 g. of propenylphenol was decomposed by reductive cleavage according to the method of Hahn and Wassmuth.[4] Acetaldehyde was identified as one of the cleavage products by means of its dimethone (m. p. 138.5–140°).

The residue, after removal of the ethyl acetate and the acetaldehyde, was shaken with a saturated solution of sodium bisulfite. The bisulfite addition product, washed with ether, was decomposed with dilute sulfuric acid. Extraction with ether, followed by removal of the ether, yielded a residue which was treated with copper acetate. The copper derivative of salicylaldehyde weighed 7.86 g. and the residue of ether-soluble material weighed 301 mg. The ether solutions of the several components indifferent to the copper acetate treatment were combined. Salicylic acid was identified, but no phenylhydrazone precipitated after treatment with phenylhydrazine hydrochloride and sodium acetate, even though the addition of a small amount of *p*-hydroxybenzaldehyde produced an immediate precipitate.

Separation of Salicylaldehyde and *p*-Hydroxybenzaldehyde.—A mixture containing salicylaldehyde (10 g.) and *p*-hydroxybenzaldehyde (0.1 g.) was shaken for three

(1) Claisen and Eisleb, *Ann.*, **401**, 21 (1913).
(2) Mumm and Möller, *Ber.*, **70**, 2214 (1937).
(3) Claisen *Ann.*, **418**, 69 (1919).
(4) Hahn and Wassmuth, *Ber.*, **67**, 696 (1934).

hours with ether (50 ml.) and a saturated aqueous copper acetate solution (150 ml.). After the mixture had been allowed to stand overnight, it was filtered. The precipitate, washed with ether, weighed 9.65 g. The filtrate was extracted, first with the ether that had been used to wash the precipitate, and then twice with fresh ether. The combined ether extracts were concentrated to 50 ml. and then shaken with more of the saturated copper acetate solution (100 ml.). The precipitate after washing with ether weighed 2.1 g. The filtrate was again extracted with ether and the extract treated with copper acetate as before. This time 0.7 g. of copper derivative was obtained, making a total of 12.45 g. (99.5%). The filtrate from the last crop of copper derivative was extracted with ether. The ether extract yielded 71 mg. (71%) of pure *p*-hydroxybenzaldehyde (m. p. 115–116.5°) after suitable treatment.

Pyrolysis of Ethyl *p*-Allyloxybenzoate.—One-half hour at 230–250° converted the ethyl *p*-allyloxybenzoate to ethyl 3-allyl-4-hydroxybenzoate (m. p. 77–78° after crystallization from benzene), in 89% yield.

Hydrolysis and Decarboxylation of Ethyl 3-Allyl-4-hydroxybenzoate.—Hydrolysis was accomplished by boiling for three hours with 2 *N* sodium hydroxide. Crystallization from a mixture of ether and petroleum ether yielded the acid of m. p. 127–128°; yield 85%. Decarboxylation of the acid (8 g.) by heating with quinoline (10 g.) yielded *o*-allylphenol (b. p. 93–94° at 8 mm.; $n^{20}D$ 1.5450).

Pyrolysis of *p*-Allyloxybenzoic Acid.—*p*-Allyloxybenzoic acid (m. p. 162–163°, Claisen reported 162°) was obtained by the hydrolysis of its ethyl ester. This acid (10 g.) was heated with quinoline (10 g.) and a trace of copper powder for eight hours at 200–210°. The pyrolysis product was dissolved in a mixture of ether and petroleum ether (1:2), extracted three times with dilute sulfuric acid, once with water, and five times with aqueous sodium hydroxide (10%). The alkaline extract was acidified and then extracted with ether. The ether extract yielded on distillation a 60% yield of *o*-allylphenol (b. p. 97–98° at 11 mm., $n^{20}D$ 1.5452).

Phenylurethan of *o*-Allylphenol.—This derivative was prepared from each of the three samples of *o*-allylphenol in exactly the same way. A mixture of the phenol (340 mg.), phenyl isocyanate (240 mg.) and a trace of dry pyridine was heated for one hour at 100°. The phenylurethan was extracted from diphenylurea with boiling petroleum ether (b. p. 90–100°). The phenylurethan obtained from the petroleum ether was then placed in a vacuum desiccator. The melting point of the derivative was taken without further purification.

The melting points of the phenylurethans were as follows: (1) from *o*-allylphenol prepared by decarboxylation of 3-allyl-4-hydroxybenzoic acid, m. p. 103.5–104.5°; (2) from *o*-allylphenol obtained by the pyrolysis of allylphenyl ether, m. p. 103.5–104.5°; (3) from *o*-allylphenol obtained by the pyrolysis of *p*-allyloxybenzoic acid, m. p. 104–105°. One crystallization of the phenylurethans was sufficient to raise the melting point to 106–107° (Claisen reported 106.5° as the m. p. of the pure compound) in each case.

Summary

The pyrolysis product of allyl phenyl ether was examined for evidence of para rearrangement. The rearrangement of this ether proceeds without the formation of any appreciable amount of *p*-allylphenol, however.

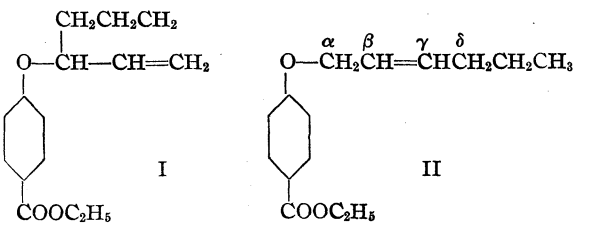
MINNEAPOLIS, MINN. RECEIVED MAY 29, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

The Rearrangement of Phenyl Allyl Ethers. V. The Isomeric Ethyl *p*-(α- and γ-Propylallyloxy)-benzoates

BY WALTER M. LAUER AND ROBERT M. LEEKLEY[1,2]

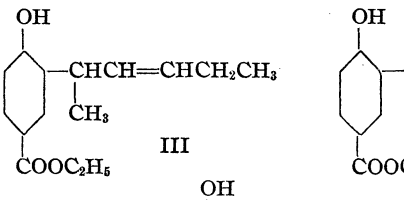
The substituted allyl ethers of ethyl *p*-hydroxybenzoate lend themselves admirably to rearrangement studies since both the ethers and their rearrangement products are converted to solid acids by hydrolysis. This circumstance makes possible a more precise study of the nature of the rearrangement products. Furthermore, since the para position is blocked by the carbethoxyl group the possibility of para rearrangement is eliminated. In view of these facts, the isomeric ethers, ethyl *p*-(α-propylallyloxy)-benzoate (I) and ethyl *p*-(γ-propylallyloxy)-benzoate (II) were chosen for investigation.



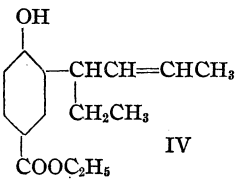
Several years ago, it was reported[3] that rearrangement of γ-ethylallyl phenyl ether leads to *o*-(α,γ-dimethylallyl)-phenol. That *o*-(α-ethylallyl)-phenol was also formed during this rearrangement was demonstrated by Hurd and Pollack.[4] The formation of *o*-(α-ethylallyl)-

(1) Abstract of Ph.D. thesis submitted July, 1938.
(2) Shevlin Fellow, 1937–1938.
(3) Lauer and Filbert, THIS JOURNAL, **58**, 1389 (1936).
(4) Hurd and Pollack, *J. Org. Chem.*, **3**, 550 (1939).

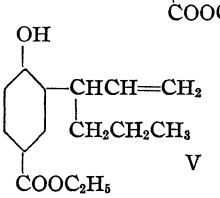
phenol involves the usual transposition from the α- to γ-carbon atom of the unsaturated chain, whereas the formation of the abnormal rearrangement product, *o*-(α,γ-dimethylallyl)-phenol, requires a migration of the aromatic residue to either the β- or δ-carbon atom. A choice between these two possibilities should be feasible in the case of II, for if a shift to the β-carbon occurs, the abnormal rearrangement product should be III, while a shift to the δ-carbon should lead to structure IV for the abnormal rearrangement product.



III



IV

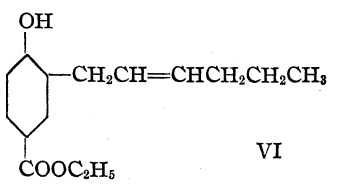


V

The present work demonstrates that ethyl 3-(α-methyl-γ-ethylallyl)-4-hydroxybenzoate (III) results along with the normal rearrangement product, ethyl 3-(α-propylallyl)-4-hydroxybenzoate (V). Therefore, at least in this case, it must be concluded that a β (or ϵ) and not a δ shift is involved in the formation of the abnormal rearrangement product.

Ethyl *p*-(α-propylallyloxy)-benzoate (I) was obtained, along with its isomer, ethyl *p*-(γ-propylallyloxy)-benzoate (II), by the action of 3-chloro-1-hexene on ethyl *p*-hydroxybenzoate. This mixture of esters, which consisted of approximately 75% of the α-substituted allyloxy isomer, upon hydrolysis yielded the corresponding acids, which were separated by fractional crystallization. The lower melting acid, upon ozonolysis gave formaldehyde, and on esterification yielded the desired ethyl *p*-(α-propylallyloxy)-benzoate.

Rearrangement of the ester (I) produced the normal rearrangement product, ethyl 3-(γ-propylallyl)-4-hydroxybenzoate (VI).



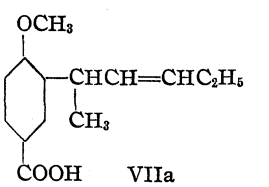
VI

The structure of the rearrangement product (VI) was established in the following way. Methylation followed by hydrolysis yielded a 3-hexenylanisic acid, which upon ozonolysis gave butyraldehyde. Furthermore, the rearrangement product did not reduce a hot mercuric acetate solution, but did so after isomerization with a strong potassium hydroxide solution which is known to convert allylbenzenes into propenylbenzenes.

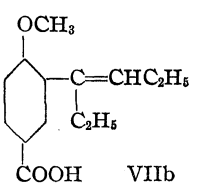
Ethyl *p*-(γ-propylallyloxy)-benzoate (II) was prepared from 1-chloro-2-hexene and ethyl *p*-hydroxybenzoate. This reaction occurred without an α-γ-transposition since a freezing point curve indicated that the product did not consist of a mixture of esters. Hydrolysis of the ester yielded *p*-(γ-propylallyloxy)-benzoic acid, which was in turn reduced to *p*-(*n*-hexyloxy)-benzoic acid. The saturated acid, which was obtained in the above manner, was found to be identical with a sample prepared from *n*-hexyl bromide and ethyl *p*-hydroxybenzoate.

A mixture of rearrangement products was obtained by the pyrolysis of ethyl *p*-(γ-propylallyloxy)-benzoate. This mixture was methylated and then hydrolyzed to produce two 3-hexenylanisic acids, which were separated by fractional crystallization.

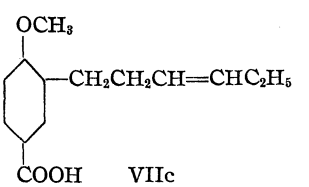
The lower melting acid was shown to be 3-(α-methyl-γ-ethylallyl)-4-methoxybenzoic acid, VIIa. The structure was proved in the following way. Ozonolysis produced propionaldehyde. There are only three possible 3-hexenylanisic acids which contain a continuous six-carbon chain from which propionaldehyde could be formed. These three compounds possess the structures, VIIa, VIIb and VIIc.



VIIa



VIIb



VIIc

Of these three structures VIIb was eliminated since the acid did not reduce mercuric acetate. If structure VIIc were the correct one, 3-(*n*-hexyl)-anisic acid would be formed by catalytic reduc-

tion. Actually, the hexylanisic acid which was formed by reduction was not identical with the sample prepared by the reduction of 3-(γ-propylallyl)-anisic acid. Therefore the lower melting of the two 3-hexenylanisic acids which were derived from the rearrangement products was 3-(α-methyl-γ-ethylallyl)-4-methoxybenzoic acid, VIIa.

The higher melting isomeric 3-hexenylanisic acid was 3-(α-propylallyl)-4-methoxybenzoic acid, since ozonolysis produced formaldehyde.

The rearrangement of ethyl p-(γ-propylallyloxy)-benzoate (II), therefore, leads to two rearrangement products. In order to estimate the relative amounts of these two products, the original mixture of pyrolysis products was ozonized. The dimethones of the volatile aldehydes were separated by fractional crystallization. On the basis of this rather inaccurate method it was estimated that the ratio of abnormal to normal rearrangement product was approximately two to one.

Experimental

p-(α-Propylallyloxy)-benzoic Acid.—A solution of ethyl p-hydroxybenzoate (55 g.) in acetone (200 ml.) was placed in a flask fitted with a reflux condenser, a dropping funnel and a mercury-sealed stirrer. Anhydrous potassium carbonate (50 g.) was then added and the reaction mixture was refluxed gently on the steam-bath while 3-chloro-1-hexene (39.5 g.; b. p. 63–64° at 110 mm.; $n^{20}D$ 1.4310) was added. The reaction mixture was heated under reflux with stirring for twelve hours. After this period most of the acetone was removed by distillation. Enough water to dissolve the salt was added and the product was extracted with ether (150 ml. total). Petroleum ether (100 ml.) was then added to the ether extract and the acidic components were removed by extraction with four portions of aqueous sodium hydroxide (5%). After most of the solvent had been removed by distillation, the product was heated on the steam-bath under diminished pressure for several hours. During this time 3-chloro-1-hexene (13 g.) distilled. The residue which did not distil at 12 mm. at the temperature of the steam-bath was distilled in a Hickman still. Three fractions were collected (b. p. 105–106° at approx. 0.05 mm.) and their refractive indices determined: (1) $n^{20}D$ 1.5150; (2) $n^{20}D$ 1.5162; (3) $n^{20}D$ 1.5173. The drift in the refractive index was considered to be an indication that the product was not a single compound.

Fraction 1 was hydrolyzed with methyl alcoholic potassium hydroxide (25%). The substituted benzoic acid, crystallized twice from a mixture of benzene and petroleum ether, melted at 138–139°. It was shown to be p-(γ-propylallyloxy)-benzoic acid.

The mother liquor from the first crystallization was evaporated to dryness and the residue crystallized from petroleum ether alone. Recrystallization from dilute methyl alcohol yielded a solid of m. p. 76–77°, which proved to be p-(α-propylallyloxy)-benzoic acid. This compound showed unusual behavior when melted. If the melted sample was chilled, it immediately solidified to an allotropic form, melting at 35–38°, which could again be transformed to the higher melting variety.

Anal. Calcd. for $C_{13}H_{16}O_3$: C, 70.91; H, 7.27. Found: C, 71.14; H, 7.80.

Ozonolysis of p-(α-Propylallyloxy)-benzoic Acid.—The ozonide, prepared in ethyl bromide solution from the acid (230 mg.), was decomposed according to the method of Whitmore.[5] Formaldimethone (150 mg.; m. p. 187–188.5°) was obtained.

Ethyl p-(α-Propylallyloxy)-benzoate.—The dried (at 60°) silver salt, was converted to the ethyl ester by means of ethyl iodide in dry ether. The ester (b. p. 95–97° at 0.5 mm., $n^{20}D$ 1.5130) was distilled in a Hickman still.

Anal. Calcd. for $C_{15}H_{20}O_3$: C, 72.53; H, 8.12. Found: C, 72.76; H, 8.21.

Pyrolysis of Ethyl p-(α-Propylallyloxy)-benzoate.—The ester (9.1 g.) began to boil at 220° under 40 mm. pressure, but as the rearrangement proceeded the temperature of the liquid rose gradually to 246°. Further heating was not accompanied by any boiling point increase.

The rearrangement product was dissolved in petroleum ether (40 ml.) and extracted with aqueous sodium hydroxide (5%). The alkaline extract was acidified with dilute sulfuric acid and the phenolic product was extracted with ether. Evaporation of the ether extract produced a solid which upon crystallization from petroleum ether melted at 75–76.5°.

Anal. Calcd. for $C_{15}H_{20}O_3$: C, 72.53; H, 8.12. Found: C, 72.49; H, 8.08.

This rearrangement product, ethyl 3-(γ-propylallyl)-4-hydroxybenzoate did not reduce mercuric acetate in glacial acetic acid.

3-(γ-Propylallyl)-4-methoxybenzoic Acid.—Ethyl 3-(γ-propylallyl)-4-hydroxybenzoate (920 mg.) was added to a solution of sodium methoxide (25 ml. of methyl alcohol containing 200 mg. of metallic sodium). Dimethyl sulfate (2 ml.) was then added and the reaction mixture was refluxed for forty-five minutes. The reaction mixture was again refluxed after the addition of aqueous sodium hydroxide (20 ml., 20%). Dilution of the reaction mixture with water (100 ml.) followed by acidification with dilute sulfuric acid yielded the solid acid (650 mg.); m. p. 107–108°, after crystallization from dilute methyl alcohol. This compound did not reduce a hot solution of mercuric acetate in glacial acetic acid.

Anal. Calcd. for $C_{14}H_{18}O_3$: C, 71.75; H, 7.75. Found: C, 71.73; H, 7.89.

Ozonolysis of 3-(γ-propylallyl)-4-methoxybenzoic acid produced butyraldehyde which was identified as the dimethone (m. p. 131.5–133.5°).

3-Hexyl-4-methoxybenzoic Acid.—The saturated acid (m. p. 113.5–114°) was prepared from 3-(γ-propylallyl)-4-methoxybenzoic acid by catalytic reduction using a palladium (on calcium carbonate) catalyst.

Anal. Calcd. for $C_{14}H_{20}O_3$: C, 71.14; H, 8.54. Found: C, 70.95; H, 8.68.

(5) Whitmore, THIS JOURNAL, **54**, 3711 (1932); **56**, 180 (1934).

3-(1-Hexenyl)-4-hydroxybenzoic Acid.—Ethyl 3-(γ-propylallyl)-4-hydroxybenzoate (1.75 g.) was heated for one hour at 155–160° with potassium hydroxide (4 g.) and water (2 ml.). The reaction mixture was then dissolved in water and acidified. Ether extraction yielded the crude product (1.2 g.) which after several crystallizations from benzene melted at 134–135°.

Anal. Calcd. for $C_{13}H_{16}O_3$: C, 70.91; H, 7.27. Found: C, 70.57; H, 7.65.

A precipitate was formed when a few drops of a solution of mercuric acetate in glacial acetic acid were heated with several crystals of 3-(1-hexenyl)-4-hydroxybenzoic acid.

Ethyl *p*-(γ-Propylallyloxy)-benzoate.—Ethyl *p*-hydroxybenzoate (55 g.) dissolved in acetone (200 ml.), was placed in a flask fitted with a dropping funnel, a reflux condenser, and a stirrer. Anhydrous potassium carbonate (50 g.) was added and the reaction mixture was refluxed gently while 1-chloro-2-hexene (39.5 g.) was added slowly through the dropping funnel. After the reaction mixture was stirred under reflux for twelve hours, most of the acetone was distilled off. Enough water to dissolve the salt was added and the resultant solution was extracted with ether. Petroleum ether was added to the ether extract and acidic impurities were removed from the non-aqueous extract with sodium hydroxide (5%). Distillation using a Hickman still yielded a pure product (45 g., b. p. 115–116° at 0.2 mm., $n^{20}D$ 1.5197, m. p. 14.1°).

Anal. Calcd. for $C_{15}H_{20}O_3$: C, 72.53; H, 8.12. Found: C, 72.78; H, 8.13.

***p*-(γ-Propylallyloxy)-benzoic Acid.**—Hydrolysis of the ester (twenty-five minutes with 5 ml. of 25% methyl alcoholic potassium hydroxide) yielded the salt, which was dissolved in water and converted to the free acid with dilute sulfuric acid. Crystallization from benzene and petroleum ether gave a product which melted at 139.5–140.5°. It was identical with the *p*-(γ-propylallyloxy)-benzoic acid which was obtained as a side-product in the preparation of *p*-(α-propylallyloxy)-benzoic acid.

Anal. Calcd. for $C_{13}H_{16}O_3$: C, 70.91; H, 7.27. Found: C, 70.64; H, 7.17.

The reduction product, ***p*-hexyloxybenzoic acid** melted at 104.5–106.5°.

p-Hexyloxybenzoic acid was also prepared by the action of *n*-hexyl bromide on a solution of ethyl *p*-hydroxybenzoate in alcoholic sodium ethoxide. After hydrolysis with methyl alcoholic potassium hydroxide and acidification with dilute sulfuric acid, the acid was obtained. Purification yielded a product (m. p. 105.5–107°) which was identical with that obtained by the reduction of the *p*-(γ-propylallyloxy)-benzoic acid.

Anal. Calcd. for $C_{13}H_{18}O_3$: C, 70.23; H, 8.17. Found: C, 70.28; H, 8.16.

Pyrolysis of Ethyl *p*-(γ-Propylallyloxy)-benzoate.—The ester (56 g.) was heated to boiling (213–241°) at 40 mm. pressure for a period of one and one-half hours. A petroleum ether (b. p. 60–68°) solution of the rearrangement products was extracted with sodium hydroxide (5%). The alkaline solution was then acidified with dilute sulfuric acid and extracted with ether. Distillation of the ether extract yielded a colorless, viscous oil (53 g., $n^{20}D$ 1.5367, b. p. 183–188° at 5 mm.). This oil did not reduce a hot solution of mercuric acetate in acetic acid. On standing for about one month, a sample of the pyrolysis product partially solidified. The mixture of isomeric phenols was analyzed.

Anal. Calcd. for $C_{15}H_{20}O_3$: C, 72.53; H, 8.12. Found: C, 72.61; H, 8.11.

Ozonolysis of the pyrolysis product yielded formaldehyde and propionaldehyde, identified as formaldimethone and propionaldimethone, respectively.

3-(α-Propylallyl)-4-methoxybenzoic Acid and 3-(α-Methyl-γ-ethylallyl)-4-methoxybenzoic Acid.—The rearrangement product (26 g.) of ethyl *p*-(γ-propylallyloxy)-benzoate was dissolved in a solution of sodium ethoxide, and methylated with dimethyl sulfate. A mixture of hexenylanisic acids (m. p. 104–114°) was obtained in almost quantitative yield.

The two hexenylanisic acids were separated by fractional crystallization. Dilute methyl alcohol, dilute acetic acid and petroleum ether were used as solvents, but petroleum ether was found to be the most suitable for purification of the higher melting isomer. The higher melting (m. p. 142.5–143.5°) component, **3-(α-propylallyl)-4-methoxybenzoic acid,** was obtained in pure form after twenty-one crystallizations. This product did not reduce a hot mercuric acetate solution.

Pure **3-(α-methyl-γ-ethylallyl)-4-methoxybenzoic acid** was isolated from the petroleum ether mother liquors. The mother liquors richest in the more soluble fraction were evaporated to dryness and the residues combined and recrystallized from dilute acetic acid until there was no further change in melting point (m. p. 113–114°). 3-(α-Methyl-γ-ethylallyl)-4-methoxybenzoic acid did not reduce mercuric acetate.

Anal. Calcd. for $C_{14}H_{18}O_3$: C, 71.75; H, 7.75. Found: C, 71.45; H, 8.00.

Ozonolysis of 3-(α-methyl-γ-ethylallyl)-4-methoxybenzoic acid, yielded propionaldehyde, which was identified as the dimethone (m. p. 153.5–154.5°; m. p. reported 155°)[6] and its anhydride (m. p. 142–143°; m. p. (Vorländer) 142–143°; m. p. (Klein and Linser) 148°).[7]

Ozonolysis of 3-(α-propylallyl)-4-methoxybenzoic acid yielded formaldehyde which was identified as formaldimethone (m. p. 188–189°).

3-(1-Methylamyl)-4-methoxybenzoic acid (m. p. 125–126°) was prepared by the catalytic reduction of 3-(α-methyl-γ-ethylallyl)-4-methoxybenzoic acid using a palladium catalyst (on calcium carbonate).

Anal. Calcd. for $C_{14}H_{20}O_3$: C, 71.14; H, 8.54. Found: C, 70.85; H, 8.86.

3-(1-Ethylbutyl)-4-methoxybenzoic acid (m. p. 145–146°) was obtained by the catalytic reduction of 3-(α-propylallyl)-4-methoxybenzoic acid.

Anal. Calcd. for $C_{14}H_{20}O_3$: C, 71.14; H, 8.54. Found: C, 70.94; H, 8.70.

Hydrolysis of Rearrangement Product of Ethyl *p*-(γ-propylallyloxy)-benzoate.—A solution of sodium hydroxide (5.3 g.) and the rearrangement product (13.1 g.)

(6) (a) Klein and Linser, *Mikrochemie*, Pregl Festschrift, 204, 1929; (b) Kao and Yen, *Science Repts. Natl. Tsing Hua Univ.*, Series A, **1**, 185 (1932).

(7) Vorländer, *Z. anal. Chem.*, **77**, 251 (1929); ref. 6b.

in water (100 ml.) was refluxed for one hour. Acidification produced an oil which finally solidified. The higher melting isomer, 3-(α-propylallyl)-4-hydroxybenzoic acid (m. p. 133–134°), was obtained in pure form by a series of crystallizations from benzene and petroleum ether.

Anal. Calcd. for $C_{13}H_{16}O_3$: C, 70.91; H, 7.27. Found: C, 71.01; H, 7.15.

All attempts to isolate the more soluble isomer in pure form were unsuccessful.

Methylation of 3-(α-propylallyl)-4-hydroxybenzoic acid with dimethyl sulfate gave a 97% yield of 3-(α-propylallyl)-4-methoxybenzoic acid (m. p. 142–143°).

Anal. Calcd. for $C_{14}H_{18}O_3$: C, 71.75; H, 7.75. Found: C, 71.45; H, 7.55.

Summary

The rearrangement of the isomeric ethyl p-(α- and γ-propylallyloxy)-benzoates has been investigated, with the following results.

Ethyl α-propylallyloxybenzoate undergoes rearrangement to form ethyl 3-(γ-propylallyl)-4-hydroxybenzoate, whereas ethyl γ-propylallyloxybenzoate gives two rearrangement products, namely, ethyl 3-(α-propylallyl)-4-hydroxybenzoate and ethyl 3-(α-methyl-γ-ethylallyl)-4-hydroxybenzoate.

The formation of this latter rearrangement product constitutes an additional example of an abnormal phenyl allyl ether rearrangement and supplies evidence for the view that in the case of an abnormal rearrangement, the aromatic residue becomes attached to the β-carbon atom, while the normal rearrangement leads to a transposition of the aromatic residue to the γ-carbon atom.

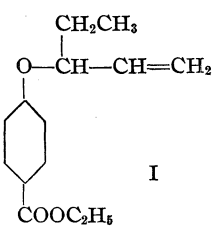
MINNEAPOLIS, MINN. RECEIVED MAY 29, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

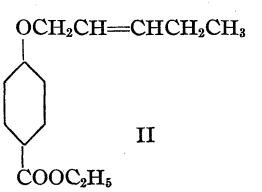
The Rearrangement of Phenyl Allyl Ethers. VI. The Isomeric Ethyl p-(α- and γ-Ethylallyloxy)-benzoates

BY W. M. LAUER AND H. E. UNGNADE[1]

Certain phenyl allyl ethers upon rearrangement lead to products which one would not expect on the basis of the rearrangement pattern outlined by Claisen. Such so-called abnormal rearrangement was first observed several years ago in the case of γ-ethylallyl phenyl ether.[2] The preceding paper in this series[3] furnishes an additional example, namely, ethyl p-(γ-propylallyloxy)-benzoate. Since in this latter case it was possible to effect a separation of derivatives of the normal and abnormal rearrangement products, a similar study of the behavior of the lower homolog, ethyl p-(γ-ethylallyloxy)-benzoate, II, was undertaken. The isomeric compounds, ethyl p-(α-ethylallyloxy)-benzoate, I, and ethyl p-(α,γ-dimethylallyloxy)-benzoate, III, were also prepared and investigated.

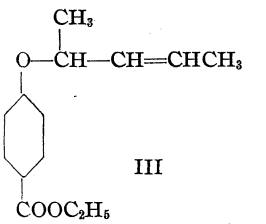


I

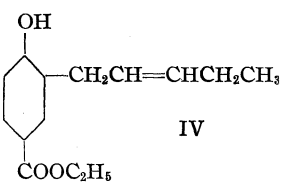


II

Ethyl p-(α-ethylallyloxy)-benzoate, I, on pyrolysis yielded the normal rearrangement product, IV, together with a small amount of 1,3-pentadiene and ethyl p-hydroxybenzoate. That the rearrangement product is the normal one is indicated by the fact that the corresponding substituted anisic acid yielded propionaldimethone on ozonolysis.

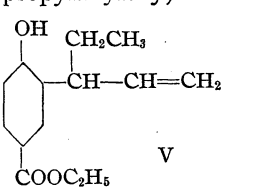


III

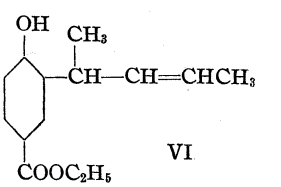


IV

Ethyl p-(γ-ethylallyloxy)-benzoate, II, gave both normal and abnormal rearrangement products, V and VI, thus paralleling the behavior of the previously reported case of ethyl p-(γ-propylallyloxy)-benzoate.



V



VI

3-(α-Ethylallyl)-4-methoxybenzoic acid, derived from the normal rearrangement product, V, was

(1) Abstract of Ph.D. thesis submitted November, 1938.
(2) Lauer and Filbert, THIS JOURNAL, **58**, 1388 (1936).
(3) Lauer and Leekley, *ibid.*, **61**, 3043 (1939).

obtained in pure form by fractional crystallization. Repeated attempts to isolate the corresponding derivative of the abnormal rearrangement product, VI, were unsuccessful. However, there can be little doubt of its presence since ozonolysis of the pyrolysis product always yielded formaldimethone and acetaldimethone.

Ethyl *p*-(α,γ-dimethylallyloxy)-benzoate, III, on pyrolysis yielded 1,3-pentadiene and ethyl *p*-hydroxybenzoate, in amounts which corresponded to slightly more than 50% cleavage of the phenyl ether. Methylation of the rearrangement product, followed by hydrolysis, yielded a product which upon crystallization showed the properties of a mixture. Ozonolysis of this mixture gave acetaldimethone and a small amount of formaldimethone. If ozonolysis can be relied upon, then it must be concluded that ethyl *p*-(α,γ-dimethylallyloxy)-benzoate, III, also yields an abnormal as well as a normal rearrangement product.

Experimental

Ethyl *p*-(α-Ethylallyloxy)-benzoate (I) was prepared from 3-chloro-1-pentene (31 g., b. p. 48–48.5° at 150 mm., $n^{20}D$ 1.4258) and ethyl *p*-hydroxybenzoate (49.2 g.) in the presence of acetone (150 g.) and potassium carbonate (41 g.). The combined ether–petroleum ether extracts were shaken three times with aqueous sodium hydroxide (10%), dried over potassium carbonate, and distilled in a Hickman still; fraction 1, b. p. 89–90° at 0.1 mm. (11.5 g.); fraction 2, b. p. 90–95° at 0.1 mm. (2 g.); residue 2.5 g.

Hydrolysis of fraction 1 with potassium hydroxide (30 g.) in methanol (90 g.) for a period of twenty minutes gave a mixture of acids upon acidification with sulfuric acid. Fractional crystallization from benzene, petroleum ether, aqueous methanol, and aqueous ethanol finally yielded the pure ***p*-(α-ethylallyloxy)-benzoic acid,** m. p. 108–109°, since ozonolysis yielded formaldimethone.

Hydrolysis of fraction 2 and the residue gave only *p*-(γ-ethylallyloxy)-benzoic acid (m. p. 156.5–157.5°).

Pure *p*-(α-ethylallyloxy)-benzoic acid (1.36 g.) was converted to the ethyl ester (1.40 g.), through the silver salt. The ethyl ester gave a negative phenol test.[4]

Pyrolysis of Ethyl *p*-(α-Ethylallyloxy)-benzoate.—The ethyl *p*-(α-ethylallyloxy)-benzoate (1.40 g.) began to boil at 200° at 40 mm. After one hour of heating the boiling point remained constant at 236°.

The small amount of material which collected in the trap was treated with bromine at the temperature of liquid air. The reaction mixture was then allowed to come to room temperature and the excess bromine removed under diminished pressure. The crystalline product weighed 200 mg. and was identified as 1,2,3,4-tetrabromopentane (m. p. 113–114°, yield 8.6%). A petroleum ether (b. p. 60–68°) solution of the main rearrangement product was shaken with aqueous sodium hydroxide (5%). The alkaline solution after acidification with dilute sulfuric acid was extracted with ether. Evaporation of the ether yielded a residue which was heated with a sodium hydroxide solution (5%) for one hour. Acidification gave 0.86 g. of rearrangement product, melting at 101–102° after crystallization from petroleum ether.

The rearrangement product, dissolved in alcoholic sodium ethoxide, was *methylated* with dimethyl sulfate (1.1 g.), and then converted to the methoxy acid (0.65 g.). Two crystallizations from dilute methyl alcohol and one from petroleum ether yielded a pure product (m. p. 117–117.5°, 200 mg.). The **3-(γ-ethylallyl)-4-methoxybenzoic acid** obtained in this manner did not reduce mercuric acetate nor did it give a positive phenol test.

Anal. Calcd. for $C_{13}H_{16}O_3$: C, 70.90; H, 7.27. Found: C, 70.73; H, 7.62.

Ozonolysis of 3-(γ-Ethylallyl)-4-methoxybenzoic acid.—One hundred and ten milligrams in ethyl bromide (60 ml.) at 0°, followed by reductive cleavage, gave a dimethone (110 mg.) which proved to be propionaldimethone (m. p. and mixed m. p. 151–151.5°). The dimethone was converted to its anhydride by heating with glacial acetic acid containing a small amount of sulfuric acid. After one crystallization from petroleum ether, the anhydride melted at 139–140°. Mixed with the anhydride obtained from an authentic specimen of propionaldimethone, the melting point showed no change.

Ethyl *p*-(γ-ethylallyloxy)-benzoate (II) was obtained by refluxing a mixture consisting of *p*-hydroxybenzoic ester (61.6 g.), potassium carbonate (64 g.), acetone (200 ml.) and 1-chloro-2-pentene (40 g.). The major portion of the acetone was removed under diminished pressure and water in sufficient quantity to dissolve the solids was then added. Extraction with an ether–petroleum ether mixture gave an extract, which in turn was extracted three times with aqueous sodium hydroxide, and dried. Distillation in a Hickman still yielded pure ethyl *p*-(γ-ethyallyloxy)-benzoate (b. p. 108–109° at 0.1 mm.; freezing point 34.1°; 41 g.).

Anal. Calcd. for $C_{14}H_{18}O_3$: C, 71.75; H, 7.75. Found: C, 71.64; H, 7.61.

Hydrolysis of the phenyl ether (20 g.) gave a practically quantitative yield of *p*-(γ-ethylallyloxy)-benzoic acid (m. p. 157–158°).

Anal. Calcd. for $C_{12}H_{14}O_3$: C, 69.87; H, 6.84. Found: C, 69.53; H, 6.79.

Reduction of *p*-(γ-ethylallyloxy)-benzoic acid with hydrogen and platinum oxide in methanol yielded *p*-(*n*-amyloxy)-benzoic acid (m. p. 123–124°). Admixing with an authentic specimen of this saturated acid produced no change in the melting point.

Ozonolysis of *p*-(γ-ethylallyloxy)-benzoic acid at 0° in ethyl bromide and ethyl acetate, followed by decomposition of the ozonide, yielded propionaldimethone (m. p. and mixed m. p. 149–150°). Conversion of the dimethone to its anhydride by heating in glacial acetic acid containing sulfuric acid gave a product which after crystallization from petroleum ether melted at 140–141°. An authentic specimen of propionaldimethone produced an anhydride melting at the same temperature.

Pyrolysis of ethyl *p*-(γ-ethylallyloxy)-benzoate (40.5 g.) was carried out at a pressure of 40 mm. The temperature

(4) Folin and Ciocalteu, *J. Biol. Chem.*, **73**, 627 (1929).

rose from 195 to 233° and then remained constant. The liquid air trap collected pentadiene (0.13 g., 13.3% yield), which on bromination yielded 1,2,3,4-tetrabromopentane (m. p. 113.5–114.5°).

The main product was shaken with aqueous sodium hydroxide and low-boiling petroleum ether. The alkaline solution on acidification gave a solid product (39.88 g.), which showed a negative test with mercuric acetate. All attempts to separate this mixture of phenols failed. Similarly, attempts to separate the products of hydrolysis were unsuccessful.

Methylation of the Pyrolysis Product.—The mixture of phenols (38 g.), dissolved in sodium methoxide, was treated with dimethyl sulfate (48 g.). After most of the methanol was distilled off the residue was refluxed with aqueous potassium hydroxide (10%). Acidification produced the methoxy acids.

Repeated crystallization yielded only one *pure* fraction, which proved to be 3-(α-ethylallyl)-4-methoxybenzoic acid (m. p. 164.5–165.5°).

Anal. Calcd. for $C_{13}H_{16}O_3$: C, 70.91; H, 7.27. Found: C, 70.84; H, 7.52.

Many impure fractions possessing a crystal form differing from that of 3-(α-ethylallyl)-4-methoxybenzoic acid were obtained, but, unfortunately, only 3-(α-ethylallyl)-4-methoxybenzoic acid was obtained in pure form.

Ozonolysis of a sample (500 mg.) of 3-(α-ethylallyl)-4-methoxybenzoic acid gave formaldimethone (m. p. 186–188°, 200 mg.), but ozonolysis studies on the mixture of pyrolysis products always yielded formaldimethone and acetaldimethone, which were separated and identified. Pyrolysis therefore yielded both 3-(α-ethylallyl)-4-methoxybenzoic and 3-(α,γ-dimethyallyl)-4-methoxybenzoic acid.

Ethyl p-(α,γ-Dimethylallyloxy)-benzoate, III.—4-Chloro-2-pentene (23.5 g.) was added slowly to a mixture of potassium carbonate (35 g.), ethyl p-hydroxybenzoate (37.5 g.) and acetone (150 g.) and then refluxed for nine hours. Ether extraction of the aqueous solution yielded the ethyl ester of p-(α,γ-dimethylallyloxy)-benzoic acid (b. p. 108–114° at 0.1 mm.; 16.5 g.).

Anal. Calcd. for $C_{14}H_{18}O_3$: C, 71.75; H, 7.75. Found: C, 71.77; H, 7.75.

Hydrolysis of the ester III (3 g.) gave p-(α,γ-dimethylallyloxy)-benzoic acid (melting point 131–132°; 2 g.).

Anal. Calcd. for $C_{12}H_{14}O_3$: C, 69.87; H, 6.84. Found: C, 69.97; H, 7.04.

Ozonolysis of ethyl p-(α,γ-dimethylallyloxy)-benzoate (400 mg.) followed by reductive cleavage yielded acetaldimethone (300 mg.).

Pyrolysis of the ether, III (10 g.), at 40 mm. pressure was carried out between the temperatures of 208 and 223° for a period of one hour. Penta-1,3-diene (b. p. 41–42°, 1.4 g., 58.5% yield) collected in the liquid air trap. Bromination of this diene yielded 1,2,3,4-tetrabromopentane (m. p. 113–114°).

Anal. Calcd. for $C_5H_8Br_4$: C, 15.47; H, 2.08. Found: C, 15.49; H, 2.14.

The maleic anhydride addition product (m. p. 61–62°) was also prepared.

The liquid pyrolysis product was treated with aqueous sodium hydroxide (5%) and petroleum ether. The petroleum ether solution yielded only a small amount of a pale yellow oil which was not investigated. The aqueous alkaline layer was acidified and extracted with ethyl ether. The ether extract yielded p-hydroxybenzoic acid (2.7 g.) identified as the ethyl ester (m. p. 115°), and an oil (4.4 g.) which did not crystallize. The oil was saponified. **Methylation** with dimethyl sulfate followed by saponification with aqueous sodium hydroxide (10%) yielded an acid upon acidification with dilute sulfuric acid. After four crystallizations the melting range was 128–132°, and it was concluded that the product was a mixture. The mixture was analyzed.

Anal. Calcd. for $C_{13}H_{16}O_3$: C, 70.90; H, 7.27. Found: C, 70.73; H, 7.62.

The mixture (100 mg., m. p. 128–132°) obtained by methylation was ozonized at 0° in ethyl bromide. Reductive cleavage yielded volatile aldehydes which were converted to their dimethones (150 mg.). After five crystallizations two pure dimethones were obtained, namely, formaldimethone and acetaldimethone, although the amount of formaldimethone was very small (7 mg.).

Summary

The rearrangement of the isomeric ethyl p-(α- and γ-ethylallyloxy)-benzoates has been investigated, with the following results.

Ethyl α-ethylallyloxy-benzoate yields ethyl 3-(γ-ethylallyl)-4-hydroxybenzoate upon rearrangement, whereas ethyl γ-ethylallyloxybenzoate gives two rearrangement products, namely, ethyl 3-(α-ethylallyl)-4-hydroxybenzoate and ethyl 3-(α,γ-dimethylallyl)-4-hydroxybenzoate.

A study of the rearrangement of ethyl α,γ-dimethylallyloxybenzoate has furnished some evidence that the normal rearrangement product may be accompanied by an abnormal one.

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Ethers of *p*-Hydroxybenzoic Acid as Derivatives for the Identification of Alkyl Halides

BY W. M. LAUER, P. A. SANDERS, R. M. LEEKLEY AND H. E. UNGNADE

The authors have had occasion to prepare a number of ethers of *p*-hydroxybenzoic acid during the last few years. These derivatives have much to recommend them for identification purposes, even though there are already several different types of derivatives which are useful for the identification of alkyl halides.[1]

A procedure which is suitable for the preparation of small amounts of the ethers follows. A solution of metallic sodium (0.2 g.) in absolute alcohol (5 ml.) is prepared in a 25-cc. Erlenmeyer flask fitted with a reflux condenser. Ethyl *p*-hydrobenzoate (1 g.) is dissolved in the alcoholic solution of sodium ethoxide and then the alkyl halide (1 ml.) is added. After refluxing for one-half to one hour, a considerable portion of the alcohol is removed by distillation and the residue is treated with water to dissolve the precipitated sodium halide. The aqueous solution is then extracted with ether and the ether extract is shaken with three portions (5 ml. each) of aqueous sodium hydroxide (10%). The ether solution is concentrated and a saturated solution (5 m.) of potassium hydroxide in methyl alcohol is added. The reaction mixture is heated for approximately ten minutes. The precipitated potassium salt is then dissolved in water and the solution acidified (congo red) with dilute sulfuric acid. Extraction with ether yields the *p*-alkoxybenzoic acid, which is crystallized from a suitable solvent. In a number of cases benzene or mixtures of benzene and petroleum ether were used.

Several substituted *p*-allyloxybenzoic acids are included in the following table. It is a well-known fact that certain substituted allyl halides undergo the α,γ-transposition upon ether formation, yielding mixtures of isomeric products. Several mixtures of this kind were separated, but usually such separations are quite difficult. This, of course, is not true in the case of allyl chloride and α,γ-dimethylallyl chloride, which give *p*-allyloxybenzoic acid and *p*-(α,γ-dimethylallyloxy)-benzoic acid, respectively.

Unfortunately several of the *p*-alkoxybenzoic acids possess melting points which show only a slight difference. The same situation exists in the case of some of the other types of derivatives in common use for characterization purposes. A mixed melting point determination renders identification certain, however. It should be noted that *p*-(*n*-alkoxy)-benzoic acids exhibit mesomorphism.[2] Thus *p*-(*n*-butoxy)-benzoic acid, upon melting at 147–148° changes to a cloudy viscous liquid which exists over a definite temperature range. The cloudy liquid clears sharply at 160° and this temperature appears to be as characteristic of the substance as the transition at 147–148°.

TABLE I

MELTING POINTS OF ETHERS OF *p*-HYDROXYBENZOIC ACID

Ether	M. p., °C.
Methyl	180–182[a]; 184[b]
Ethyl	195[b]
n-Propyl	145.5–147[a]; 145[b] (154[b])
Isopropyl	160–163[a]
n-Butyl	147–148[a]; 147[b] (160[b])
Isobutyl	140–141[c,d]
s-Butyl	121–123[c]
n-Amyl	123–124[c]; 124[b] (151[b])
Isoamyl	141–142[a]
n-Hexyl	105.5–107[c]; 106[b] (153[b])
n-Heptyl	92[b], (95[b], 148[b])
n-Octyl	100[b] (104[b], 148[b])
n-Nonyl	92[b] (99[b], 141[b])
n-Decyl	92[b] (120[b], 149[b])
n-Dodecyl	95[b] (129[b], 137[b])
Cetyl	100[b] (131[b], 133[b])
Benzyl	188–190[a]
Allyl	160–162[a]; 162–163[c]
α-Methylallyl	155–156[c]
γ-Methylallyl	176.5–178[c]
α-Ethylallyl	108–109[c]
γ-Ethylallyl	156.5–158[c]
α,γ-Dimethylallyl	131–132[c]
α-Propylallyl	74.5–75.5[c]
γ-Propylallyl	139.5–140[c]

[a] Cohen and Dudley, *J. Chem. Soc.*, **97**, 1737 (1910). Uncorrected values. [b] Bennett and Jones, *ibid.*, 424 (1939). Values in parentheses refer to liquid–liquid transition temperatures. All values are corrected. [c] Present work. Uncorrected values. [d] *Anal.* Calcd. for $C_{11}H_{14}O_3$: C, 68.04; H, 7.27. Found: C, 67.94; H, 7.32.

Summary

The use of ethers of *p*-hydroxybenzoic acid as derivatives for the identification of alkyl halides is suggested. A number of such ethers have been prepared and a convenient procedure is described.

MINNEAPOLIS, MINNESOTA RECEIVED AUGUST 23, 1939

(1) Shriner and Fuson, "Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1935; Kamm, "Qualitative Organic Analysis," John Wiley and Sons, Inc., New York, N. Y., 1932; see also Merritt, Levey and Cutter, THIS JOURNAL, **61**, 15 (1939).

(2) Jones, *J. Chem. Soc.*, 2660 (1929); 1874 (1935); Bennett and Jones, *ibid.*, 420 (1939).

[CONTRIBUTION FROM THE RESEARCH LABORATORIES, SWIFT & COMPANY]

Synthetic Glycerides of Unsaturated Fatty Acids. I. Mono- and Trilinolein

BY HOWARD C. BLACK AND CHARLES A. OVERLEY

Glycerides of known constitution of the saturated fatty acids have been prepared by Fischer[1] and King[2] in high degrees of purity. However, the synthesis of pure glycerides of unsaturated acids has been complicated by the difficulty encountered in preparing the acid chlorides of such acids.

In the present paper a new method for the synthesis of unsaturated glycerides is proposed. It consists of the preparation of glycerides from the acid chlorides of bromine addition products of unsaturated fatty acids and subsequent removal of the bromine to yield the unsaturated glycerides. Linoleic acid has been selected for the initial work because of the ease of preparation and purification of its crystalline tetrabromide. Also recent work has shown quite definitely that the debromination of the tetrabromide yields only the natural linoleic acid.[3,4] In addition, linoleic esters are of interest because of their biological importance.[5] The acid chloride of the tetrabromo derivative of linoleic acid was prepared in crystalline form. From it the mono- and triglycerides were prepared according to the methods of Fischer as described by King and debrominated to yield mono- and trilinolein, respectively.

Experimental

Tetrabromostearic acid was prepared by bromination of the acetone-soluble fraction[4] of cottonseed oil fatty acids. The method of Rollet[6] as modified by McCutcheon[3] was employed, m. p. 115.5°.

9,10,12,13-Tetrabromostearoyl Chloride.—Eighty grams of tetrabromostearic acid in a round-bottomed flask under reflux condenser was placed in an oil-bath at 120°. When the acid had melted 15 g. (1.2 mole) of thionyl chloride was added in small portions through the condenser over the period of an hour. Only slight darkening occurred. It was allowed to cool to room temperature and stand overnight. The oil was taken up in 250 ml. of anhydrous petroleum ether and placed at −26° for several hours. The shiny, white plates which separated were filtered in the freezer and washed with cold petroleum ether until most of the excess thionyl chloride was removed. The product was carefully dried *in vacuo:* yield 78.0 g.; m. p. 59.5–60.0°; total halogen as Br, 59.92; calcd., 60.28. The m. p. was not changed by subsequent recrystallizations from anhydrous ether or petroleum ether. In comparison to other aliphatic acid chlorides this product is quite stable.

Mono-(9,10,12,13-tetrabromo)-stearin.—To a cold mixture of 10.0 g. (0.075 mole) of acetoneglycerol and 9.6 g. (0.075 mole) of quinoline in a glass-stoppered Erlenmeyer flask was added in small portions with cooling and shaking 45 g. (0.073 mole) of 9,10,12,13-tetrabromostearoyl chloride dissolved in 20 ml. of dry chloroform. The mushy mixture was allowed to stand for forty-eight hours at room temperature. The material was then taken up in 150 ml. of cold ether and washed successively several times with cold 0.5 *N* sulfuric acid, saturated sodium bicarbonate solution and water. After being dried over anhydrous sodium sulfate the ether solution was allowed to stand at −26°. The gummy precipitate was filtered and recrystallized from 1:1 ether–petroleum ether at −26°: yield 35.5 g.; m. p. 51.5–52.0°. The monoglyceride was liberated from the acetone condensation product by dissolving 35 g. of the latter in 300 ml. of ether, cooling in an ice-bath and adding 300 ml. of cold concentrated hydrochloric acid in portions with vigorous shaking. The mixture was let stand overnight at −26° and the semicrystalline solid filtered and washed free of chlorides with cold water. It was dried *in vacuo* and recrystallized from 500 ml. of ether at 0°. The product appeared as plates when examined under the high power microscope: yield 26 g.; m. p. 101.5–102.0°; Br, 47.60, calcd., 47.45.

Tri-(9,10,12,13-tetrabromo)-stearin.—To a cold mixture of 2.2 g. (0.024 mole) of glycerol and 9.6 g. (0.075 mole) of quinoline in a glass-stoppered Erlenmeyer flask was added with shaking and cooling 45 g. (0.073 mole) of 9,10,12,13-tetrabromostearoyl chloride in 30 ml. of dry chloroform. The semisolid mass was let stand at room temperature for two days and taken up in 600 ml. of ether and washed successively with 0.5 *N* sulfuric acid, saturated sodium bicarbonate solution and water. The ether solution was dried over anhydrous sodium sulfate and placed at 0°. The crystals which separated appeared to be needles under low power and long thin plates under high. They were recrystallized from ether: yield 30.5 g.; m. p. 81.0–81.5°; Br, 51.97, calcd., 52.18.

Debromination of Mono-(9,10,12,13-tetrabromo)-stearin.—This was carried out by treating 20-g. lots of the tetrabromo derivative with 20 g. of 30-mesh zinc and 50 ml. of anhydrous alcohol. The zinc had been washed with dilute hydrochloric acid, then with water and carefully dried. The flask was gently warmed in a water-bath until the beginning of the vigorous exothermic reaction, which was controlled by cooling the flask with ice. Finally the alcohol was refluxed for half an hour and the zinc removed by filtration. The flask and zinc were washed with 150 ml. of anhydrous petroleum ether. The filtrate and washings were washed several times with water and finally dried over anhydrous sodium sulfate and evaporated *in vacuo*. The nearly colorless oil was taken up in 30 ml. of a 1:1 ether–petroleum ether mixture and let stand at −26° overnight. Shiny crystals separated.

(1) Fischer, *Ber.*, **53**, 1621 (1920).
(2) Averill, Roche and King, THIS JOURNAL, **51**, 866 (1929).
(3) McCutcheon, *Can. J. Research*, **B16**, 158 (1938).
(4) Riemenschneider, Wheeler and Sando, *J. Biol. Chem.*, **127**, 391 (1939).
(5) Burr and Burr, *ibid.*, **86**, 587 (1930).
(6) Rollet, *Z. physiol. Chem.*, **62**, 410 (1909).

After being filtered and dried they melted to a colorless viscous oil at room temperature: yield 8.9 g.; iod. value 142.1; calcd. for monolinolein 143.3; sap. value 158.5, calcd. 158.3; $n^{20}D$ 1.4758; m. p. determined by placing a drop in an ordinary m. p. tube and letting stand in a beaker of alcohol at −26° for several hours and then warming slowly, 14.0–15.0°. When the debromination was carried out with 0.4 *N* alcoholic hydrochloric acid, 0.5 g. of an oil was isolated from the filtrate; iod. value 158.3; sap. value 178.0; $n^{20}D$ 1.4636.

Debromination of Tri-(9,10,12,13-tetrabromo)-stearin.—This was carried out as described for the monoglyceride. The product did not crystallize at −26°. It had the following constants: iod. value 171.2; calcd. for trilinolein 173.3; sap. value 191.2, calcd. 191.5; $n^{20}D$ 1.4709; m. p. determined as above, −5.0–4.0°. Nothing distilled when the oil was heated to 250° in a vacuum of 0.5 mm.

Rebromination of the Linoleins.—Three grams of trilinolein dissolved in 50 ml. of petroleum ether took up bromine at 20° to yield 4.5 g. of gummy material which could not be crystallized. Three grams of monolinolein was dissolved in 50 ml. of petroleum ether and bromine dissolved in petroleum ether added at 20° with stirring; 2.5 g. of gummy material separated, m. p. 92–95°. Recrystallization from ether yielded crystals melting at 101.5–102.0°, mixed m. p. with mono-(9,10,12,13-tetrabromo)-stearin, 101.5–102.0°. An oil which could not be crystallized was isolated from the filtrate.

Saponification of the Linoleins and Rebromination of the Acid.—Six grams of each of the glycerides was let stand overnight with 75 ml. of 5% alcoholic sodium hydroxide and the fatty acids isolated by acidification and extraction with petroleum ether. Five grams of acid from each of the glycerides was brominated in 80 ml. of petroleum ether at 20°, yielding 4.5 g. of crystals melting at 115.5°. Likewise 5 g. of linoleic acid obtained by debromination of tetrabromostearic acid was brominated to yield 4.5 g. of crystals melting at 115.5°; mixed m. p. with the tetrabromide of the acid isolated from the linoleins 115.5°.

Discussion

The advantage of the present method for preparation of unsaturated glycerides is that the double bonds are protected from polymerization and oxidation until the final step, thus yielding the glycerides with a minimum amount of impurities. The method is limited to the glycerides of the unsaturated fatty acids, the bromine derivatives of which yield the natural acids on debromination. That the unsaturated glycerides synthesized in this case very probably contain the natural linoleic acid is indicated by the identity of the tetrabromides of the acid isolated from the glycerides with the tetrabromide of natural linoleic acid. The yields of solid tetrabromide obtained on bromination of the acids isolated from the glycerides agree with those reported for the bromination of natural linoleic acid.[3,4] At least the position of the double bonds has not been shifted and it is unlikely that *cis–trans* isomerization has occurred since several investigators have shown that the acid regenerated by debromination of the solid tetrabromo derivative is identical with natural linoleic acid.[3,4,6,7,8] There is no reason to assume that debromination of the acid radical in the glycerides should produce a different configuration than debromination of the free acid.

When the debromination was carried out in neutral solution there was no evidence of interesterification, but when alcoholic hydrochloric acid was used with the monoglyceride a small amount of material with constants corresponding roughly to those of ethyl linoleate was isolated. Attempts to carry out the debromination in certain other solvents were unsuccessful.

Rebromination of the unsaturated glycerides produced the anticipated results. When linoleic acid is brominated, approximately a 50–50 yield of solid and liquid tetrabromide is obtained.[3,4] There is no reason to assume that the bromination of linoleic glycerides should proceed differently. Indeed, bromination of monolinolein yielded a 40–45% yield of the solid bromo monoglyceride, as well as some oily material. Since no homogeneous product could be isolated from the bromination of trilinolein, it is reasonable to assume that both the liquid and solid derivatives of the fatty acid radicals were formed. Suzuki[9] has reported the isolation of the bromine addition products of several triglycerides from fish oils. He did not report a derivative of trilinolein and only a few addition products of mixed glycerides of linoleic acid.

Summary

A new method for the synthesis of unsaturated glycerides has been proposed. It consists of the preparation of glycerides from acid chlorides of bromine addition products of unsaturated fatty acids and subsequent removal of the halogen to yield the unsaturated glycerides. The method has been applied to mono- and trilinolein.

In addition to mono- and trilinolein, 9,10,12,13-tetrabromostearoyl chloride and mono- and tri-(9,10,12,13-tetrabromo)-stearin have been synthesized.

CHICAGO, ILLINOIS RECEIVED AUGUST 5, 1939

(7) Birosel, *Nat. and Appl. Bull. Univ. Philippines*, **2**, 103 (1932).
(8) Brown and Frankel, THIS JOURNAL, **60**, 54 (1938).
(9) Suzuki and Yokoyana, *Proc. Imp. Acad. (Japan)*, **3**, 526 (1927); also later papers.

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF MERCK & CO., INC.]

Erythrina Alkaloids. VI. Studies on the Constitution of Erythramine

BY KARL FOLKERS AND FRANK KONIUSZY

The isolation and characterization of a new alkaloid, erythramine, from the seeds of *Erythrina sandwicensis* Deg. and *Erythrina subumbrans* (Hassk.) Merrill has been described.[1] The microanalyses on the crystalline erythramine base, hydriodide, hydrobromide, and the hydrochloride showed that erythramine has the empirical composition $C_{18}H_{21}NO_3$. The present paper reports the results of our studies of its constitution.

A Friedrich determination showed that one methoxy group is present, and that there is no group attached to the nitrogen atom. A Kuhn–Roth carbon-methyl determination gave a negative result. The presence of a methylenedioxy group was shown by hydrolysis with sulfuric acid and reaction of the formaldehyde with the added phloroglucinol. It follows that all three oxygen atoms of erythramine exist in ether linkage. This conclusion was confirmed by a lack of reaction between erythramine and acetic anhydride or with benzoyl chloride.

Methyl iodide reacted with the base to yield a crystalline erythramine methiodide; therefore, erythramine is a tertiary base. The negative methylimide group determination limits the probable alkaloidal formulations of the tertiary nitrogen to either a $-\overset{|}{C}=N-$ linkage of a ring or a ring system with the nitrogen atom common to two nuclei.

The presence of a methylenedioxy group presupposes the presence of one benzenoid nucleus.[2] Catalytic hydrogenation with Adams platinum catalyst under two atmospheres pressure resulted in the formation of a dihydroerythramine. This absorption of only two atoms of hydrogen was all that could be brought about, and considering the usual stability of alkaloidal oxygenated benzenoid nuclei to hydrogenation under such conditions, it seemed evident that the unsaturation of erythramine consisted of one benzenoid nucleus and one ethylenic double bond.

If the tertiary nitrogen atom were in the form of a $-\overset{|}{C}=N-$ linkage of a ring, then the hydrogenation would have produced a secondary nitrogen atom and dihydroerythramine would be a secondary base. However, a dihydroerythramine methiodide was readily formed, and this substance eliminates the formulation of the tertiary nitrogen atom of erythramine as a part of a $-\overset{|}{C}=N-$ linkage. These data lead to the formulation of the tertiary nitrogen atom of erythramine as being common to two nuclei. In this connection it is to be noted that three stages of Hofmann degradation proved that two other *Erythrina* alkaloids, α- and β-erythroidine, possessed tertiary nitrogen atoms common to two nuclei of the ring system.[3]

From this information concerning the nature of the three oxygen atoms, the nitrogen atom, and the unsaturation of erythramine, it has been deduced that this alkaloid possesses four nuclei, exclusive of the methylenedioxy bridge, which in all probability are six-membered rings.

It is now of interest to consider the relationship of alkaloids of known structure which have been isolated from species of genera belonging to the same subfamily, *Papilionaceae*, of the family *Leguminosae* to which the genus *Erythrina* belongs. From plants of this subfamily, the only alkaloids of known structure are represented by the "lupin" alkaloids, sparteine, and the related lupanine, anagyrine, cytisine, lupinine, matrine, and by the indole alkaloid, physostigmine. Although the "lupin" alkaloids possess a nitrogen atom common to two nuclei, they also possess a second nitrogen atom (except lupinine) so that there is this fundamental difference from erythramine and erythroidine ($C_{16}H_{19}NO_3$).[3,4] The subfamily, *Papilionaceae*, is quite large, and of the above alkaloids of known structure, only physostigmine is obtained from species of the genus *Physostigma* which is in the same tribe, *Phaseoleae*, with the genus *Erythrina*. The magnitude of even the tribe *Phaseoleae* is evident since forty-eight genera have been assigned to it by Bentham. Again, physostigmine possesses two nuclear nitrogen atoms and differs in other respects

(1) Folkers and Koniuszy, THIS JOURNAL, 61, 1232 (1939).

(2) The ultraviolet absorption spectrum will be described at a future time in connection with other studies.

(3) Folkers and Koniuszy, Abstracts of Papers, 97th Meeting of the American Chemical Society, Baltimore, Md., April, 1939, Division of Organic Chemistry, page 17.

(4) Folkers and Major, THIS JOURNAL, 59, 1580 (1937).

from erythramine. Thus, erythramine or α- and β-erythroidine cannot be compared readily with any of the alkaloids of known structure derived from plants of the same tribe or of a related tribe as the genus *Erythrina*. Furthermore, the indole character of hypaphorine, which has been found to occur[1] in many species of *Erythrina*, is not necessarily translatable into the properties of the accompanying erythramine.

One of the oldest known relationships between physiological action and chemical constitution is that of the curare action of quaternary ammonium compounds, as discovered by Crum-Brown and Fraser. Although erythramine is a tertiary base, it causes a selective and strong curare-like action at the threshold dose of 7 mg. of the hydrobromide per kilogram of frog. Dr. Klaus Unna, of the Merck Institute of Therapeutic Research, found that the synthetic quaternary erythramine methiodide was one-fifth as active as the tertiary base. Hydrogenation of erythramine to its dihydro derivative decreased the curare-like activity to about one-thirtieth of that for the natural alkaloid.

Further insight on the constitution of erythramine will be described by experiments made on another new *Erythrina* alkaloid, erythraline, which is very closely related to erythramine.

Experimental Part

Functional Groups of Erythramine.—A sample of erythramine hydriodide (m. p. 249°; $(\alpha)_D$ + 220°) from *Erythrina sandwicensis* Deg. was used.

Anal. Calcd. for $C_{18}H_{21}NO_3 \cdot HI$: C, 50.60; H, 5.15. Found: C, 50.66; H, 5.13. The micro Friedrich determination showed: OCH_3, 7.17%; N-CH_3, negative. Calcd. for one OCH_3, 7.26%.

In three separate test-tubes were placed 20-mg. samples, respectively, of erythramine base, hydrastine base, and hydrocotarnine base; the fourth tube was a blank. In each of the four tubes were added 5 ml. of 40% sulfuric acid and 60 mg. of phloroglucinol. When all had dissolved, the tubes were heated in a beaker of boiling water for twenty minutes. Erythramine, hydrastine, and hydrocotarnine each gave a heavy red precipitate of a phloroglucide while the blank remained colorless. Thus, erythramine contains a methylenedioxy group.[5] The methoxy and methylenedioxy groups account for the three oxygen atoms in the molecule and are in agreement with the failure of erythramine to react with acetic anhydride or benzoyl chloride.

Stability of Erythramine.—The free base cannot be stored satisfactorily under ordinary conditions because of progressive decomposition. Small samples were kept in evacuated vials at dry-ice temperature. When the free base was required, it generally was obtained from the hydriodide just before the experiment.

Erythramine hydrohalide salts were stable either dry or in solution.

The stability of erythramine in alkaline solution was tested as follows. A quantity of 106 mg. of pure erythramine hydriodide was dissolved in 30 ml. of water, heated to 100° on the steam-bath, and when 1 ml. of 5% sodium hydroxide was added, white globules of insoluble erythramine base formed. After the addition of 1.5 ml. of ethanol to cause homogeneity, the solution was refluxed for two hours. The cooled solution was diluted to 50 ml. and extracted with chloroform. The yield of base (gum) after solvent removal was 74 mg. (99.9%). It was converted to the hydrobromide, which had the established properties.

Purity of Erythramine.—It was found essential that erythramine hydriodide show a melting point of 245° (slow bath) or 249° (normal bath) and an optical rotation of +220–221° before use. In one instance, a sample of hydriodide showing m. p. 241–242° (slow bath) and $(\alpha)_D$ +219° would not yield crystalline dihydroerythramine hydriodide after hydrogenation. The same sample yielded a hydrobromide which melted at 204–205° instead of the established 228°.

Erythramine Methiodide.—A quantity of 200 mg. of erythramine base was dissolved in 1.5 ml. of absolute methanol and treated with 1 ml. of redistilled methyl iodide. The solution was warmed on the steam-bath and then concentrated until the volume was 1.5 ml. After standing overnight at 10°, a crystalline methiodide derivative separated as yellowish-white gleaming platelets; m. p. 96–98°, $(\alpha)^{28}_D$ +176°, C = 0.355, H_2O.

Anal. Calcd. for $C_{18}H_{21}NO_3 \cdot CH_3I$: C, 51.69; H, 5.48. Found: C, 51.61; H, 5.22.

Dihydroerythramine Hydriodide.—In the first experiment, erythramine hydriodide (322.5 mg.) in 50 ml. of water could not be hydrogenated with Adams platinum catalyst (25 mg.) at atmospheric pressure.

When 814 mg. of erythramine base was dissolved in 50 ml. of water containing 2 ml. of concentrated hydrochloric acid, and hydrogenated over 100 mg. of Adams platinum catalyst at two atmospheres pressure, the absorption of hydrogen stopped (one mole) after one hour. After filtration, the solution was made alkaline with sodium bicarbonate and extracted ten times with chloroform. Distillation of the solvent yielded 820 mg. of gum. This was treated with 348 mg. of sodium iodide in 5 ml. of absolute ethanol, and acidified with acetic acid. A first crop of 622.4 mg. of dihydroerythramine hydriodide was obtained. After crystallizations from absolute ethanol, the melting point was constant at 214–215° with decomposition. Analyses made on this material after drying at 25° *in vacuo* indicated non-stoichiometric solvation. Therefore, the salt was dried at 140° and 2 mm. for two hours: $(\alpha)_D$ 0°; C = 0.500, H_2O.

Anal. Calcd. for $C_{18}H_{23}NO_3 \cdot HI$: C, 50.35; H, 5.63. Found: C, 50.28; H, 5.48.

Dihydroerythramine Base.—When 100 mg. of dihydroerythramine hydriodide was dissolved in water, treated with sodium bicarbonate, extracted with chloroform, etc., 53.5 mg. of a colorless gummy base was obtained.

(5) Gadamer and Winterfeld, *Arch. pharm.*, **262**, 601 (1924).

This was dissolved in 5 ml. of dry ethyl ether and then treated with 10 ml. of petroleum ether. After filtration to remove flocculent material, the filtrate was concentrated by gentle warming to a volume of *ca.* 2 ml. The concentrate was cooled in an ice-bath and the sides of the flask were scratched. Tiny white crystals separated, which melted at 89–90°.

Anal. Calcd. for $C_{18}H_{23}NO_3$: C, 71.75; H, 7.69. Found: C, 71.82; H, 7.60.

Dihydroerythramine Hydrobromide Monohydrate.—A quantity of 99 mg. of pure dihydroerythramine hydriodide yielded 64 mg. of gummy base by the usual procedure. It was dissolved in 1 ml. of absolute ethanol, treated with 0.3 ml. of 40% hydrobromic acid, and a little dry ether was added. After filtration of flocculent precipitate, the solution was allowed to stand overnight at 10°. The hydrobromide (34 mg. yield) melted constantly at 240° after recrystallization from ethanol. For analysis, the salt was dried at 25° *in vacuo*.

Anal. Calcd. for $C_{18}H_{23}NO_3 \cdot HBr \cdot H_2O$: C, 54.00; H, 6.54. Found: C, 54.26; H, 6.04.

Drying of 5 mg. of this monohydrate at 140° and 2 mm. for two hours caused a decrease in weight of only 0.04 mg. (0.8%). The anhydrous hydrobromide could not be obtained. Longer drying periods initiated thermal decomposition.

Dihydroerythramine Methiodide Hemihydrate.—A quantity of 52 mg. of dihydroerythramine base was dissolved in 1 ml. of methanol and 1 ml. of redistilled methyl iodide. Ethyl ether was added to the point of turbidity. Crystals of the methiodide separated after refrigeration overnight; m. p. 160–161°. The substance was dried at 78° and 2 mm. for two hours before analysis.

Anal. Calcd. for $C_{18}H_{23}NO_3 \cdot CH_3I \cdot {}^1/_2H_2O$: C, 50.45; H, 6.01. Found: C, 50.61; H, 6.13.

This substance could not be dehydrated at 140° *in vacuo* without decomposition.

Acknowledgment.—We wish to express our appreciation to Mr. B. A. Krukoff for his advice on botanical matters and to Mr. Douglass Hayman and Mr. Wilhelm Reiss for their coöperation in performing the microanalyses.

Summary

Erythramine, which has the empirical composition $C_{18}H_{21}NO_3$, contains one methoxy group and one methylenedioxy group. The nitrogen atom is tertiary and in all probability is common to two nuclei of the molecule. The unsaturation consists of one benzenoid nucleus and one ethylenic double bond. The molecule appears to contain four six-membered nuclei exclusive of the methylenedioxy bridge.

Erythramine methiodide was about one-fifth as active and dihydroerythramine was about one-thirtieth as active as the natural erythramine for curare-like action in frogs.

RAHWAY, N. J. RECEIVED JULY 28, 1939

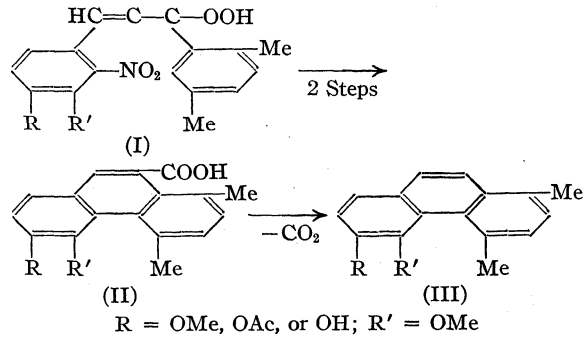
[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF COLUMBIA UNIVERSITY]

The Synthesis of Some New 1,4-Dimethylphenanthrenes Structurally Related to Morphol

BY JACK TARKINGTON CASSADAY[1] AND MARSTON TAYLOR BOGERT

In a recent communication,[2] we described the preparation of 1,4-dimethyl-6,7-dihydroxyphenanthrene from *p*-xylylacetic acid and 6-nitroveratraldehyde by the Pschorr reaction. The work recorded in the present paper consists of the extension of that investigation by substituting 2-nitroveratraldehyde and 2-nitroacetovanillin for the 6-nitroveratraldehyde, resulting in the production of the 5,6-dimethoxy and 5-methoxy-6-hydroxy derivatives of 1,4-dimethylphenanthrene, and their 10-carboxylic acids.

In the case of the 1,4-dimethyl-5,6-dimethoxyphenanthrene, or 1,4-dimethyl-5-methoxy-6-hydroxyphenanthrene, the methoxyl groups could not be hydrolyzed by the process which proved effective with the 6,7-dimethoxy isomer,[2] or by any of the other methods used. This is in agreement with the experience of other investigators. Pschorr and Sumuleanu[3] found it impossible to demethylate 3,4-dimethoxyphenanthrene. Mo-



R = OMe, OAc, or OH; R′ = OMe

(1) Ferguson Fellow at Columbia University, 1938–1939.

(2) Cassaday and Bogert, THIS JOURNAL, **61**, 2461 (1939).

(3) Pschorr and Sumuleanu, *Ber.*, **33**, 1810 (1900).

settig and Burger[4] were unsuccessful in their attempts to demethylate either a 3-methoxyacetylphenanthrene or the corresponding carboxylic acid.

The 5-methoxy-6-hydroxy derivative was prepared primarily because it carried its hydroxyl group in the position which Eddy's investigations[5] have shown to be most favorable for the development of analgesic properties. Unfortunately, however, it was not appreciably soluble in water.

Both of the above compounds (III) are closely related structurally to morphol (3,4-dihydroxyphenanthrene), and to methylmorphol (3-methoxy-4-hydroxyphenanthrene), a degradation product of the alkaloid codeine.

It may be recalled that morphol has a stronger analgesic action than 3-hydroxyphenanthrene.

Acknowledgments.—We are indebted to the Ella Sachs Plotz Foundation and to the National Academy of Sciences for financial assistance in the purchase of the chemicals and apparatus required for this investigation. Our thanks are due also to Mr. Saul Gottlieb, of these Laboratories, who carried out the necessary microanalyses.

Experimental

2-Nitroveratraldehyde was prepared by the method of Slotta and Lauersen,[6] but the introduction of nitrogen during the methylation of the acetovanillin was found unnecessary, and a simple 3-necked flask was employed instead of their more elaborate apparatus. The process of Pschorr and Sumuleanu[7] proved much less satisfactory, because of the formation of a mixture of isomers in the nitration of the acetovanillin.[8]

α-(*p*-Xylyl)-2-nitro-dimethylcaffeic Acid (I).—A mixture of 32.4 g. of potassium *p*-xylylacetate, 33.5 g. of 2-nitroveratraldehyde, and 285 g. of freshly distilled acetic anhydride, in a 3-necked flask equipped with a mechanical stirrer and mercury seal, a reflux condenser carrying a calcium chloride guard tube, and a thermometer, was stirred for eight hours at 105–110°. Excess of acetic anhydride was hydrolyzed by the addition of hot water, maintaining the temperature of the mixture below 120°. It was then poured into very dilute hydrochloric acid containing cracked ice. After standing for a few minutes, the supernatant solution was decanted from the tarry precipitate and fresh water added, under which the tar became crystalline more quickly. One crystallization from dilute acetic acid gave a 67% yield of the product sought, sufficiently pure for reduction to the amino acid. Five additional crystallizations from the same solvent resulted in white crystals, m. p. 205.5–206.5° (corr.).

Anal. Calcd. for $C_{19}H_{19}O_6N$: C, 63.9; H, 5.3; N, 3.9. Found: C, 64.3; H, 5.6; N, 4.0.

α-(*p*-Xylyl)-2-nitro-3-methoxy-4-acetoxycinnamic Acid (I).—Application of the above process to a mixture of 35 g. of potassium *p*-xylylacetate, 33 g. of 2-nitroacetovanillin prepared as described by Slotta and Lauersen,[6] and 250 g. of acetic anhydride, gave a 50% yield of pale tan acid, m. p. 202.5–203.5° (corr.), pure enough for reduction to the amino acid. After two recrystallizations from glacial acetic acid, in one of which Norite was used, the acid was obtained in crystals of a pale greenish tint, m. p. 211–214° (corr.).

Anal. Calcd. for $C_{20}H_{19}O_7N$: C, 62.3; H, 4.9; N, 3.6. Found: C, 62.3; H, 5.1; N, 3.7.

α-(*p*-Xylyl)-2-amino-dimethylcaffeic acid was prepared by reduction of the nitro acid with ferrous sulfate and ammonium hydroxide essentially as described for the 6-amino isomer in our previous paper[2]; yield, 61–67% of a light gray crude acid, m. p. 110–113° (corr.). No appreciable amount of acetic acid could be left in the amino acid, or it turned black on drying. Attempts to purify further this gray crude failed, and an analytically pure amino acid was not secured.

Hydrochloride.—This was prepared easily by dissolving the amino acid in dilute alcohol containing a little hydrochloric acid, recrystallizing the product from the same solvent, and drying the crystals in an evacuated desiccator. When left in an oven at 110°, the compound decomposed partially.

Anal. Calcd. for $C_{19}H_{21}O_4N\cdot HCl$: C, 62.7; H, 6.1. Found: C, 62.4; H, 6.2.

α-(*p*-Xylyl)-2-amino-3-methoxy-*p*-coumaric acid was prepared similarly from the nitromethoxyacetoxy acid. There was obtained an 80% yield of the crude acid, as a pale yellow solid, m. p. 198.5–200° (corr.), pure enough for cyclization. Six recrystallizations from 95% alcohol gave lemon colored needles, m. p. 203–204° (corr.).

Anal. Calcd. for $C_{18}H_{19}O_4N$: C, 69.0; H, 6.1. Found: C, 68.8; H, 6.2.

It will be observed that in this reduction the acetyl group of the initial nitro acid was hydrolyzed off. Pschorr[9] had a similar experience in the reduction of the α-phenyl-2-nitro-3-methoxy-4-acetoxycinnamic acid.

1,4-Dimethyl-5,6-dimethoxyphenanthrene-10-carboxylic Acid (II).—This was secured from the corresponding aminodimethylcaffeic acid by following the directions for the preparation of the 6,7-dimethoxy isomer,[2] except that potassium hydroxide was found preferable to ammonium hydroxide for solution of the 10-carboxylic acid prior to its precipitation by dilute hydrochloric acid. The yield of crude acid, pure enough for decarboxylation, was 50%. By redissolving in dilute potassium hydroxide, reprecipitating in dilute hydrochloric acid containing ice, recrystallizing twice from dilute alcohol, decolorizing with Norite, and three recrystallizations from 95% ethanol, it was obtained in white crystals, m. p. 180.5–181.5° (corr.).

Anal. Calcd. for $C_{19}H_{18}O_4$: C, 73.5; H, 5.8. Found: C, 73.7; H, 6.0.

(4) Mosettig and Burger, THIS JOURNAL, **55**, 2981 (1933).
(5) Eddy, *J. Pharmacol.*, **48**, 183 (1933); **51**, 75 (1934).
(6) Slotta and Lauersen, *J. prakt. Chem.*, [2] **139**, 220 (1934).
(7) Pschorr and Sumuleanu, *Ber.*, **32**, 3405 (1899).
(8) Raiford and Stoesser, THIS JOURNAL, **50**, 2556 (1928).
(9) Pschorr, *Ber.*, **33**, 1822 (1900).

Attempts to hydrolyze the methoxyl groups of this compound by the action of hydrobromic or hydriodic acid proved futile. Only black tars resulted, which gave no color reactions with ferric chloride. Nor could any pure acetyl derivatives be secured from them.

1,4 - Dimethyl - 5 - methoxy - 6 - hydroxyphenanthrene-10-carboxylic Acid (II).—Following the same procedure, 17.5 g. of the crude α-(*p*-xylyl)-2-amino-3-methoxy-*p*-coumaric acid gave a 47% yield of the crude phenanthrenecarboxylic acid, sufficiently pure for decarboxylation. No satisfactory solvent was found for further purification of this crude acid. Recourse was had therefore to acetylation.

Acetate.—A mixture of 1.765 g. of the crude acid, 0.882 g. of fused sodium acetate, and 15 cc. of acetic anhydride, was refluxed for two hours, the excess of acetic anhydride then hydrolyzed by the addition of hot water, and the mixture poured into 100 cc. of water and ice. The gummy solid which separated was removed, dissolved in acetic acid, and the solution placed in a refrigerator. After 2–3 hours, crystals separated, which were recrystallized thrice, once using Norite. White blades were thus obtained, m. p. 170.5–171.5° (corr.).

Anal. Calcd. for $C_{20}H_{18}O_5$: C, 71.0; H, 5.3. Found: C, 71.2; H, 5.4.

From 120 g. of 2-nitroacetovanillin and 80 g. of potassium phenylacetate, Pschorr[9] obtained only 3 g. of 5-methoxy-6-hydroxyphenanthrene-10-carboxylic acid.

1,4-Dimethyl-5,6-dimethoxyphenanthrene (III).—When a mixture of 5 g. of the 10-carboxylic acid with 1 g. of dry copper powder was distilled at a pressure of 25 mm., a thick red oil was obtained, which was easily crystallized from 95% ethanol; yield, 47%; m. p. 71.5–72.5° (corr.). After four recrystallizations from the same solvent, the product formed white crystals, m. p. 73.5–74° (corr.), insoluble in alkali.

Anal. Calcd. for $C_{18}H_{18}O_2$: C, 81.2; H, 6.8. Found: C, 81.2; H, 7.0.

The carboxylic acid could not be decarboxylated by refluxing with quinaldine and basic copper carbonate.

This compound is a homolog of dimethylmorphol. Attempts to hydrolyze the methoxy groups by hydrochloric, hydrobromic, or hydriodic acid, resulted in tars, which gave an intense green-red fluorescence in most organic solvents tried. Neither an acetate nor a picrate could be isolated in crystalline form. One sample of the dimethoxy compound was heated in a sealed tube for sixteen hours at 200° with alcoholic potassium hydroxide, following the technique of Campbell, Dodds and Lawson,[10] but the product gave no ferric chloride color reaction, and no pure compound could be isolated.

1,4-Dimethyl-5-methoxy-6-hydroxyphenanthrene (III) was prepared by distilling a mixture of 7 g. of the 10-carboxylic acid (II) with 1.4 g. of dry copper powder at 25 mm. pressure and crystallizing the resultant viscous yellow oil from alcohol; yield 42%; m. p. 133–134° (corr.). After two recrystallizations from alcohol, the compound appeared as white crystals, m. p. 136.5–137° (corr.).

Anal. Calcd. for $C_{17}H_{16}O_2$: C, 81.0; H, 6.4; MeO, 12.3. Found: C, 81.2; H, 6.6; MeO, 11.0.

These crystals were soluble in cold olive oil, acetone or alkali, as well as in warm glycol.

In another run, 8 g. of the crude carboxy acid yielded 2.9 g. of the crystalline 1,4-dimethyl-5-methoxy-6-hydroxyphenanthrene.

In Pschorr's experiments[9] on the decarboxylation of 2 g. of 5-methoxy-6-hydroxyphenanthrene-10-carboxylic acid, he obtained only an oil, from which he prepared 0.3 g. of the 5-methoxy-6-acetoxyphenanthrene.

Efforts to hydrolyze the methoxyl group of the above (III) with either hydrobromic or hydriodic acid gave much the same results as with the 1,4-dimethyl-5,6-dimethoxyphenanthrene, and proved equally futile.

Summary

1. 1,4 - Dimethyl - 5,6 - dimethoxyphenanthrene and 1,4-dimethyl-5-methoxy-6-hydroxyphenanthrene have been synthesized from *p*-xylylacetic acid and 2-nitroveratraldehyde or 2-nitroacetovanillin. It is planned to investigate their analgesic properties.

2. The successful cyclization of 2-amino-3-methoxy-*p*-coumaric acid by the Pschorr reaction was accomplished without blocking the free hydroxyl group.

3. The methoxyl groups in 1,4-dimethyl-5,6-dimethoxyphenanthrene, or 1,4-dimethyl-5-methoxy-6-hydroxyphenanthrene, could not be hydrolyzed by any of the methods tried.

NEW YORK, N. Y. RECEIVED AUGUST 23, 1939

(10) Campbell, Dodds and Lawson, *Nature*, **141**, 78 (1938).

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF COLUMBIA UNIVERSITY]

The Application of the Pschorr Reaction to alpha-(para-Xylylene)-2,5-di-(6′-amino-dimethylcaffeic Acid). The Synthesis of 9,10-Dimethyl-2′,3′,6′,7′-tetramethoxy-1,2,5,6-dibenzanthracene

BY JACK TARKINGTON CASSADAY[1] AND MARSTON TAYLOR BOGERT

Akin and Bogert[2] were unsuccessful in their attempts to hydrolyze the methylenedioxy groups of 9,10-dimethyl-2′,3′,6′,7′-di-(methylenedioxy)-1,2,5,6-dibenzanthracene to the corresponding tetrahydroxy compound.

We have therefore carried out the synthesis of the analogous tetramethoxy derivative (VI), and endeavored to hydrolyze its methoxy groups but, although evidence was secured of its probable presence, we were unable to isolate the tetrahydroxy derivative (VII) in purity.

We were led to undertake this synthesis because it has been shown in a recent paper[3] that, while the methylenedioxy groups of 1,4-dimethyl-6,7-methylenedioxyphenanthrene could not be hydrolyzed by any of the methods employed,[2] the analogous 6,7-dimethoxy derivative gave a 35% yield of the pure dihydroxy compound when refluxed with a mixture of glacial acetic and hydrobromic acids. Since this 6,7-dihydroxy derivative possessed appreciable solubility in water, it was hoped that the solubilities of the analogous tetrahydroxydibenzanthracene (VII) would also prove favorable for pharmacological testing. 9,10-Dimethyl-1,2,5,6-dibenzanthracene[2] is cancerigenic. It is therefore a matter of some importance to discover what activity, if any, its tetramethoxy and tetrahydroxy derivatives possess.

In applying the Pschorr reaction to the amino-caffeic acid (II), the amino groups were replaced by hydroxyls (III) when sodium nitrite, sulfuric acid and copper powder were used. Similar results have been reported by Cook,[4] and by Mayer and English.[5]

Dropping sulfuric acid (23%) into a solution of the amino acid, potassium hydroxide, and sodium nitrite,[6] or using isoamyl nitrite and 10% alcoholic hydrogen chloride,[7] failed to accomplish the desired cyclization. Mixtures of unidentifiable products resulted in all cases. Only when dioxane was employed as the solvent, with isoamyl nitrite, sodium hypophosphite, and copper powder, was the cyclization achieved satisfactorily. Pyridine could not be substituted for the dioxane. The dihydroxy acid (III) was decarboxylated by dry distillation at 2–3 mm. pressure, and the tetramethoxy acid (V) by digestion in quinaldine with basic copper carbonate.

The hydrolysis of the tetramethoxy derivative (VI), and of its dicarboxylic acid (V), was sought by various methods, but none proved satisfactory. The most promising seemed to be the use of hydrobromic and hydriodic acids. No pure tetrahydroxy derivative was isolated, although some alcoholic extracts of the products gave green color reactions with ferric chloride, and a tetraacetate was obtained, but not in sufficient amount to saponify successfully.

Great difficulty was experienced in securing satisfactory analytical figures for several of these polycyclic compounds, especially the nitro derivatives, but whether this was due to inadequate purification, or to combustion troubles, was not clear. Similar difficulties have been reported by Gulland and Virden,[8] Kondo and Ochiai,[9] Cook,[4,10] Akin and Bogert,[2] Hewett,[11] and others.

Acknowledgments.—Our grateful thanks are due to the Ella Sachs Plotz Foundation and to the National Academy of Sciences for the financial aid which made this investigation possible. We are under obligations also to Mr. Saul Gottlieb, of these Laboratories, who conducted the microanalyses of our difficultly combustible products.

Experimental

α-(*p*-Xylylene)-2,5-di-(6′-nitro-dimethylcaffeic Acid) (I).—By digestion of a mixture of 59 g. of potassium *p*-xylylene-2,5-*bis*-acetate[2] and 86.4 g. of 6-nitroveratraldehyde[3] in 400 g. of acetic anhydride, and pouring the mixture into an excess of very dilute hydrochloric acid, a crystalline mass was secured, which was washed with acetone or methanol, to remove unaltered initial materials and tar.

(1) Ferguson Fellow at Columbia University, 1938–1939.
(2) Akin and Bogert, THIS JOURNAL, **59**, 1564 (1937).
(3) Cassaday and Bogert, *ibid.*, **61**, 2461 (1939).
(4) Cook, *J. Chem. Soc.*, 1472 (1932).
(5) Mayer and English, *Ann.*, **417**, 65 (1918).
(6) Stamatoff and Bogert, *Rec. trav. chim.*, **52**, 584 (1933).
(7) Akin, Stamatoff and Bogert, THIS JOURNAL, **59**, 1268 (1937).
(8) Gulland and Virden, *J. Chem. Soc.*, 931 (1928).
(9) Kondo and Ochiai, *Ann.*, **470**, 224 (1929).
(10) Cook, *J. Chem. Soc.*, 1597 (1933).
(11) Hewett, *ibid.*, 193 (1938).

Two washings with 300-cc. portions of acetone left the crude product as a pale tan solid, which decomposed between 295 and 310°, and was practically insoluble in methanol, ethanol, ether, dioxane, chloroform, acetic acid, acetone, benzene, or other solvents tried. The yield was 85%. Boiling the product for five hours with methanol and sulfuric acid had little esterifying effect, and most of the initial nitro acid was recovered unchanged. The compound therefore was dissolved repeatedly in alkali, precipitated by dilute hydrochloric acid, then washed thrice with hot acetone and dried. Pale yellow crystals were thus obtained, which darkened and decomposed above 300°.

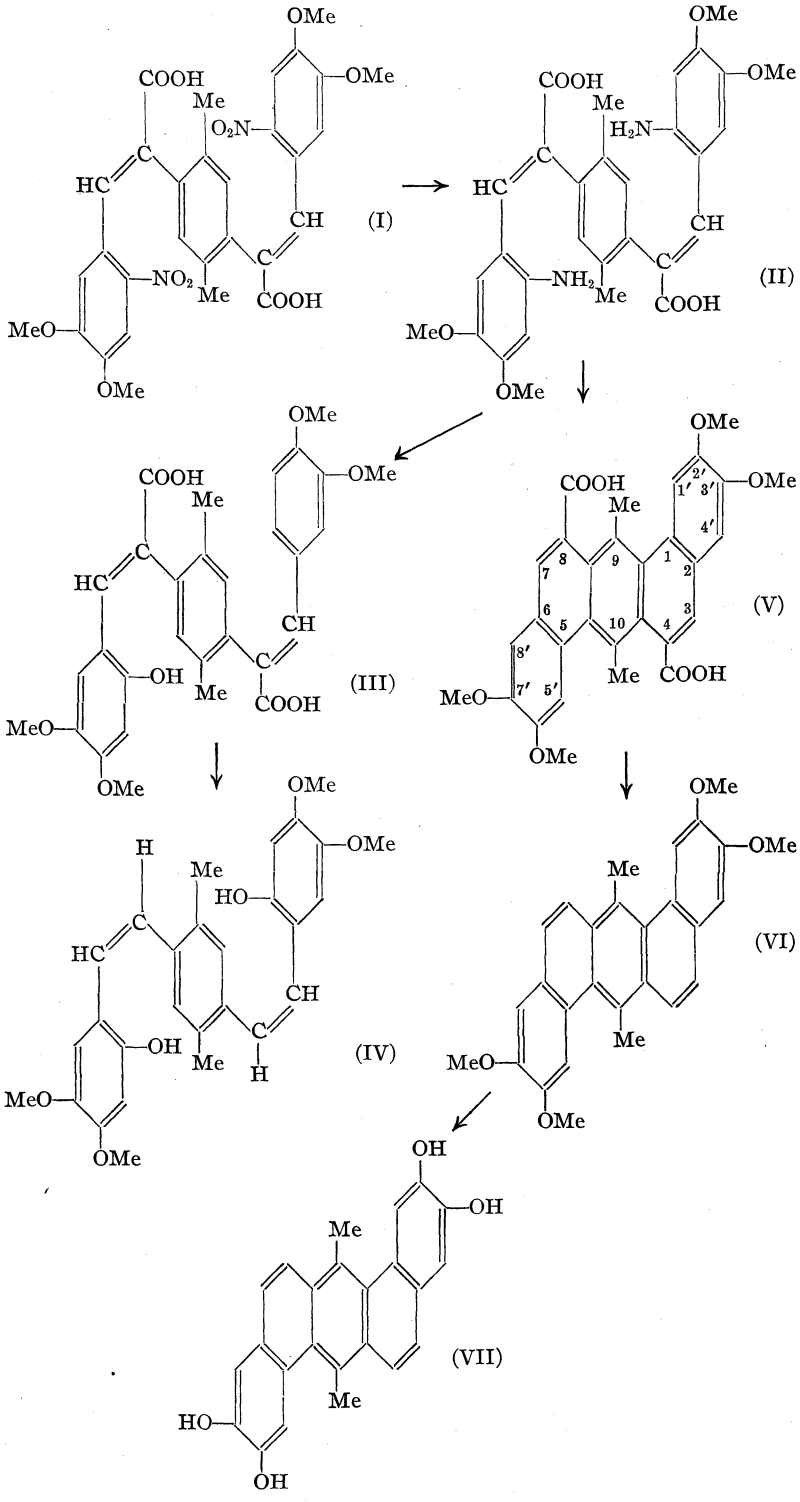
Anal. Calcd. for $C_{30}H_{28}O_{12}N_2$: C, 59.2; H, 4.6. Found: C, 58.5; H, 4.8.

α - (*p* - Xylylene) - 2,5 - di - (6′ - amino-dimethylcaffeic Acid) (II).—A hot solution of 30 g. of the crude nitro acid (I) in 85 cc. of ammonium hydroxide and 340 cc.. of water was added to a boiling solution of 173 g. of ferrous sulfate heptahydrate in 30 cc. of ammonium hydroxide and 715 cc. of water. During the next hour, 300 cc. of ammonium hydroxide was added. The solution was then precipitated by acetic acid, the mixture heated to boiling, cooled and filtered. The yield of crude amino acid so obtained varied from 50 to 60%. As in the case of the antecedent nitro acid (I), no suitable solvent could be found by which to purify the crude acid. Purification through the hydrochloride or acetyl derivative was also unsatisfactory. It was treated, therefore, as the crude nitro acid, *viz.*, by repeated solution in alkali and precipitation with acetic acid, followed by washing with alcohol and drying. The pale yellow crystals thus secured decomposed above 300°.

Anal. Calcd. for $C_{30}H_{32}O_8N_2$: C, 65.7; H, 5.8. Found: C, 65.4, 65.2; H, 6.2, 5.9.

Diazotized and coupled with "H" acid, the amino acid gave a deep purple solution.

FLOW SHEET



α - (*p* - Xylylene) - 2,5 - di - (6′ - hydroxy - dimethylcaffeic Acid) (III).—To an aqueous solution containing 1.42 g. of sodium nitrite and 2.5 g. of potassium carbonate, there was added 6.8 g. of the amino acid (II), and the resulting solution was run slowly into 100 cc. of ice-cold sulfuric acid (5 *N*), some drops of octyl alcohol being used to check foaming. After stirring for a few minutes, copper powder was added and the stirring continued for four hours, keeping the temperature at 0–5°. The mixture was transferred to a glass-stoppered bottle and shaken for fifteen

hours at laboratory temperature. The solid was removed, dissolved in sodium carbonate solution, and reprecipitated with dilute hydrochloric acid; yield, 6.2 g. This material was dried, extracted in a Soxhlet with 150 cc. of methanol for eight hours, the extract concentrated to 25 cc., and the solute precipitated by gradual addition of water; yield, 66%. After two recrystallizations from dilute methanol, a pale brown solid was obtained, which decomposed at 245–255°.

Anal. Calcd. for $C_{30}H_{30}O_{10}$: C, 65.5; H, 5.5. Found: C, 65.4; H, 5.6.

The compound contained no nitrogen, and gave no coupling reaction with "H" acid. The hydroxyl groups could not be methylated with methyl sulfate. Cook[4] has reported a similar failure to esterify the phenolic hydroxyls of an analogous compound by use of this same methylating agent.

2,5 - Di - (2' - hydroxy - 4',5' - dimethoxystyryl) - *p*-xylene (IV).—The dihydroxy acid (III) was distilled at 3 mm. pressure from a flask immersed in a metal bath the temperature of which was above 360°. The first receiver was surrounded by ice water, and this was followed by two traps in acetone–"Dry-ice" baths. A pale yellow sublimate collected in these traps, which were removed from the cooling baths and allowed to warm up to laboratory temperature before admitting air to restore the atmospheric pressure. The sublimate could then be shaken out of the traps without the use of any solvent. It decomposed between 55 and 60°, and became gummy in the presence of moisture. Three runs were made, the result being the same in all three.

Anal. Calcd. for $C_{28}H_{30}O_6$: C, 72.7; H, 6.5. Found: C, 73.1; H, 6.8.

9,10 - Dimethyl - 2',3',6',7' - tetramethoxy - 1,2,5,6-dibenzanthracene-4,8-dicarboxylic Acid (V).—To a solution of 20 g. of the amino acid (II) in 335 cc. of dioxane, there was added 11.1 cc. of sulfuric acid followed by 22 cc. of carefully purified isoamyl nitrite. After two hours of stirring at room temperature, the diazo solution was stirred into a solution of 138 g. of sodium hypophosphite in 138 cc. of water and containing some copper powder, keeping the temperature at 45–55°. After all the diazo solution had been run in, the temperature of the mixture was raised to 80°. The yield of crude product was 90%. This was washed with boiling acetic acid (8 cc. per g.). There remained a 59% yield of pale tan dicarboxylic acid (V), which decomposed at about 296° (±4°), and was pure enough for conversion into the tetramethoxydibenzanthracene (VI). Crystallized thrice from acetic acid, it formed white crystals, which decomposed at 315–317° (corr.). A second lot was crystallized six times from acetic acid and dried at 110° for eight hours. In the following analyses, the first figures were obtained with the first lot, the second ones with the second lot.

Anal. Calcd. for $C_{30}H_{26}O_8$: C, 70.0; H, 5.1. Found: C, 69.5, 69.6; H, 5.9, 6.1.

When the compound was boiled with methanol and sulfuric acid for five hours, it was recovered unchanged.

9,10 - Dimethyl - 2',3',6',7' - tetramethoxy - 1,2,5,6-dibenzanthracene (VI).—A mixture of 11 g. of the crude dicarboxylic acid (V), 2.2 g. of basic copper carbonate, and 66 cc. of freshly distilled quinaldine, was refluxed for six hours at 250°, cooled, and extracted with 700 cc. of ether. The ether extract was washed twice with dilute hydrochloric acid, once with dilute potassium hydroxide, and finally with water. Ethanol was added and the ether distilled off. The solid which separated, when crystallized from alcohol, formed pale yellow crystals, insoluble in alkali; yield 25–30%. Its solutions exhibited a pale blue fluorescence. After two more crystallizations from alcohol, the crystals melted at 137–138° (corr.).

Anal. Calcd. for $C_{28}H_{26}O_4$: C, 78.9; H, 6.1; mol. wt., 426. Found: C, 78.1, 78.5; H, 6.9, 7.3; mol. wt. (Rast, average), 441.

Dry distillation of the dicarboxy acid (V) with copper powder alone failed to yield any appreciable quantity of the decarboxylated compound (VI).

Attempts to Obtain the 9,10-Dimethyl-2',3',6',7'-tetrahydroxy-1,2,5,6-dibenzanthracene (VII).—Many experiments were carried out with both the tetramethoxydibenzanthracene (VI) and its dicarboxylic acid (V), to hydrolyze their methoxyl groups, but they were uniformly unsuccessful and no analytically pure tetrahydroxy derivative (VII) could be isolated from the black tars which were formed in most cases. Hydrochloric, hydrobromic, and hydriodic acids were the attacking reagents, as well as potassium hydroxide, and the evidence for the presence of the tetrahydroxy derivative seemed strongest when hydriodic acid was used upon either (V) or (VI). Alcohol extracts of some of these tarry products, especially those obtained with hydriodic acid, gave green color reactions, like catechol, with ferric chloride. Two typical experiments follow.

A mixture of 1 g. of (V) or (VI) with 15 cc. of hydrobromic acid (48%) and 30 cc. of glacial acetic acid was refluxed for one to two hours. Poured into water, the black liquid gave a gray flocculent precipitate, which was removed, washed and dried, giving 0.8 g. of a black powder.

A mixture of 2 g. of (V) or (VI) with 10 cc. of hydriodic acid (sp. gr., 1.7) and 20 cc. of acetic acid was refluxed for three hours and the solution poured into water. The precipitate which separated was exceedingly difficult to filter and was therefore washed with water by decantation and siphoning, until the washings were no longer colored and the solid was pale gray. By centrifugation, a gray jelly was obtained, which dried to a dark gray powder, which always gave a characteristic green ferric chloride test in alcoholic solution.

Tetraacetate.—The black powder (0.8 g.), obtained above by the action of hydrobromic acid upon (V) or (VI), was refluxed for two hours with acetic anhydride (5 cc.) and fused sodium acetate, and the crude product crystallized thrice from a mixture of ethanol and ethyl acetate. A pale tan powder resulted, which decomposed at 300–350° without melting, and could not be distilled under reduced pressure.

A similar compound was obtained by the action of acetic anhydride upon the dark gray product of the action of hydriodic acid upon (V) or (VI). Attempts to saponify this to the tetrahydroxy compound proved fruitless with the minute amount of material at our command.

In the following analyses, the first figures are for the hydrobromic acid product, the second for the hydriodic acid product.

Anal. Calcd. for $C_{32}H_{26}O_8$: C, 71.4; H, 4.8. Found: C, 71.2, 71.1; H, 5.7, 5.8.

Summary

1. 9,10 - Dimethyl - 2′,3′,6′,7′ - tetramethoxy-1,2,5,6-dibenzanthracene, and its 4,8-dicarboxylic acid, have been prepared by the Pschorr reaction from *p*-xylylene-*bis*-(acetic acid) and 6-nitroveratraldehyde.

2. In the diazotization of the intermediate aminodimethylcaffeic acid, cyclization results only when dioxane is used as the solvent. In aqueous solutions, the amino groups are replaced by hydroxyls.

3. Attempts to prepare the corresponding tetrahydroxydibenzanthracenes by hydrolysis of the methoxyl groups proved unsatisfactory.

4. The dibenzanthracene and its dicarboxylic acid were synthesized for testing as possible carcinogens.

NEW YORK, N. Y. RECEIVED AUGUST 30, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ALBERTA]

The Nitration of Diphenyliodonium Nitrate

BY R. B. SANDIN, F. T. MCCLURE[1] AND F. IRWIN[2]

The nitration of diphenyliodonium nitrate has been the subject of considerable research.[3] It is an interesting problem, from the standpoint of the influence of groups present in the benzene ring, on the course of further substitutions. According to Vorländer, Robinson, Ingold and others,[4] the most strongly meta-directing groups are the positive poles directly attached to the benzene ring. For example, phenyltrimethylammonium nitrate is nitrated exclusively in the meta position.[5] In this case the orienting group is $-N(CH_3)_3^+$. Again, a group may be meta-directing because the group as a whole carries a permanent dipole as in NO_2. On the other hand, ortho–para orientation is associated with those radicals which lose electrons to the ring as in the case of the methyl group, or which carry unshared pairs of electrons so that conjugation with the double bonds of the ring is possible as in NH_2.[6]

The nitration of a compound such as diphenyliodonium nitrate might be expected to be similar to the nitration of phenyltrimethylammonium nitrate, since the orienting group is $-IC_6H_5^+$. Vorländer[3a] in his work showed that meta-nitration did take place. By repeated crystallization of the reaction product he isolated pure di-*m*-nitrophenyliodonium nitrate. This gave *m*-iodonitrobenzene and *m*-nitrophenol (free from *o*-derivative) with sodium hydroxide. Any *p*- or *o*-compound may thus have been separated. On reading Vorländer's experimental work, the reader might draw the conclusion that nitration occurs almost exclusively in the meta position. Regarding the nitration, Vorländer has this to say: "*p*-Nitro-phenol ist vielleicht in spuren, *o*-Nitrophenol überhaupt nicht vorhanden, ... *o*-Nitro-phenol war nicht einmal durch seinen Geruch nachzuweisen." The experimental work which Vorländer reports gives no indication of ortho–para nitration.

However, the iodine atom in $-I(C_6H_5)_2^+$ has unshared electrons and is at the same time the positive end of a dipole. On the basis of unshared electrons one might expect the formation of some ortho and para derivatives along with the meta compound. Meta-directing groups usually do not contain unshared electrons in the shell of the atom which is directly joined to ring carbon.[7]

There is also another difference between phenyltrimethylammonium nitrate and diphenyliodonium nitrate to be considered. Since the positive electricity resides at the nucleus of the charged atom, the amount of damping action arising through the passage of the effect, through the

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(2) Honors student in Chemistry, University of Alberta.

(3) (a) Vorländer and Büchner, *Ber.*, **58**, 1893 (1925); (b) Challenger and Rothstein, *J. Chem. Soc.*, 1258 (1934).

(4) (a) Vorländer, *Ber.*, **52**, 262 (1919); (b) Allan, Oxford, Robinson and Smith, *J. Chem. Soc.*, 401 (1926); (c) Goss, Ingold and Wilson, *ibid.*, 2440 (1926); (d) Flürscheim and Holmes, *ibid.*, 1562 (1926); (e) Ingold, *Ann. Repts. Chem. Soc.*, **23**, 130 (1926).

(5) Vorländer and Siebert, *Ber.*, **52**, 283 (1919).

(6) For discussions on the directive influence of substituent groups, see also Gilman, "Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1938, pp. 140 and 1881; Lucas, "Organic Chemistry," American Book Co., New York, N. Y., 1935, p. 360; Waters and Lowry, "Physical Aspects of Organic Chemistry," D. Van Nostrand Co., New York, N. Y., 1936, p. 439; Watson, "Modern Theories of Organic Chemistry," Oxford University Press, London, 1937, p. 57.

(7) Vorländer, *Ber.*, **58B**, 1893 (1925), has shown that $-IO_2$ in which the iodine atom has unshared electrons is meta-directing. Recently, Masson, Race and Pounder, *J. Chem. Soc.*, 1669 (1935), have nitrated iodoxybenzene and have obtained about 99.5% meta-nitration.

successive shells of electrons belonging to the charged atom itself, would be smaller for the former than for the latter compound. On this basis it might be expected that the iodonium compound would show weaker *m*-reactivity.

It was in connection with a study of phenyl derivatives of several elements occupying consecutive or adjacent positions in the periodic table that Challenger and Rothstein[3b] carried out the nitration of diphenyliodonium nitrate. They carried out the nitration under the conditions followed by Vorländer. The composition of the resulting iodonitrobenzenes was determined by thermal analysis and the nitrophenols simultaneously produced were not examined. Their results showed a para-nitration which varied from 14 to 20.2% (average 17.5%). They also definitely isolated *p*-iodonitrobenzene. However, they say that "a method whereby both the nitrated phenyl groups were obtained as halogenonitrobenzenes would have been preferable."

It was with the object of trying to confirm the results of Challenger, especially from the standpoint of the more desirable procedure which he mentions, that the authors of this paper have reëxamined the nitration of diphenyliodonium nitrate. In the authors' procedure the nitrated material was isolated as the nitrated iodonium iodide, which was then caused to rearrange into a mixture of iodonitrobenzenes. Both phenyl groups were therefore isolated as halogenonitrobenzenes. The mixture was examined from the standpoint of thermal analysis and also any *p*-iodonitro-benzene was very readily isolated from the mixture because of its limited solubility in ethanol.

The work of the present authors confirms the work of Challenger. Thermal analysis indicates a minimum of 18.5% of para nitration. At least 10% of the reaction mixture can be isolated as pure *p*-iodonitrobenzene and by taking into consideration the solvent effect of the ethanol, the amount of para-nitration can be shown to be at least 14%.

In the rearrangement of the nitrated iodonium iodide, it is believed that it is quite safe in assuming that the meta nitrated material will yield a *m*-iodonitrobenzene, the para nitrated material a *p*-iodonitrobenzene, and so on. In support of this there is the work of Lucas and co-workers[8] which shows that the decomposition of di-*o*-tolyliodonium iodide produces only *o*-iodotoluene and not a mixture of iodotoluenes. Moreover, the authors have not been able to detect the formation of any *p*-iodonitrobenzene as a result of the decomposition of pure di-*m*-nitrophenyliodonium iodide.

(8) Lucas, Kennedy and Wilmot, THIS JOURNAL, **58**, 157 (1936).

Experimental Part

Preparation of Materials.—A method similar to that of Lucas[8] and co-workers was followed for the preparation of the iodonium salts. The reaction between iodosobenzene and iodoxybenzene in the presence of a small amount of silver oxide was found to take place very readily and in a relatively short period of time. Diphenyliodonium nitrate was prepared by adding potassium nitrate to the aqueous extract produced in the above reaction. Care was taken to keep the volumes of solution as small as possible because of the solubility of the iodonium nitrate. The latter compound finally was crystallized several times from water, from which it separated in a pure condition.

Di-*m*-nitrophenyliodonium iodide was made similarly from *m*-nitroiodoxybenzene and *m*-nitroiodosobenzene. In this case, however, the yields were relatively small and the reaction required a longer period of time. The iodide was produced by adding potassium iodide to the aqueous extract of iodonium base. The salt was purified by crystallizing from water, in which it is difficultly soluble. It was shown to be pure by analysis. Vorländer[3a] reports that di-*m*-nitrophenyliodonium iodide melts at 142–144°. The authors have found that the melting point is 158–159°. It should be mentioned here that, usually, by the melting point of an iodonium salt is meant the decomposition temperature, and at this temperature very often the products are in a liquid condition.

Nitration of Diphenyliodonium Nitrate and Decomposition of the Nitrated Iodonium Iodides.—Ten grams of diphenyliodonium nitrate was added during five minutes to 50 cc. of nitrating mixture (130 cc. of concentrated nitric acid, 327 cc. of concentrated sulfuric acid), kept cool in an ice–water mixture. The reaction mixture was allowed to stand for about thirty minutes at room temperature, after which it was poured into 1 liter of a mixture of crushed ice and water. The mixture was heated until all of the precipitate had dissolved. Potassium iodide was then added to the clear solution and the very insoluble iodonium iodide was formed. After cooling to room temperature the iodide was filtered off by suction and washed with small quantities of cold water. After air drying, the yield of nitrated iodonium iodide was found to vary from 13.4 to 14.2 g.

The decomposition of the compound was effected by immersing a 250-cc. flask, containing the compound, in a glycerol-bath heated to the required temperature. The rearrangement also could be brought about by holding the flask directly in the low flame of a Bunsen burner. The rearrangement was practically instantaneous and was accompanied by the liberation of some iodine. The main reaction proceeds as follows: $(m\text{-}O_2NC_6H_4)_2I_2 \longrightarrow 2m\text{-}O_2NC_6H_4I$.

The rearranged product in some cases was treated directly in the flask with enough boiling ethanol to bring about complete solution. It was filtered immediately and on cooling the filtrate, almost pure *p*-iodonitrobenzene

separated out. A second crystallization from ethanol usually gave crystals melting at 171–172°. The yield of pure *p*-iodonitrobenzene was determined and an estimation of the amount remaining in the solvent was made. For this purpose the solubility in 95% ethanol at 25° was taken as 0.76 g. in 100 cc. of solution. There was also taken into consideration a loss due to a side reaction which liberates iodine. This sometimes was as high as 9%. On this basis, then, the amount of para nitration was calculated to be about 14%.

When the rearranged product was examined from the standpoint of thermal analysis it was first of all shaken up with a dilute solution of sodium thiosulfate. The iodine-free mixture was then extracted with chloroform, the chloroform solution was separated, washed with water, dried and evaporated to dryness. The melting point of the residue was determined and from the tables given by Challenger and Rothstein[3b] the amount of para nitration was calculated to be 19%. In this work it was assumed that no ortho compound was present,[3b] and no attempt was made to fractionate the material prior to a melting point determination.

Pure di-*m*-nitrophenyliodonium iodide was treated according to a procedure similar to the above, and no *p*-iodonitrobenzene could be detected.

Some typical experiments are recorded in Tables I and II.

TABLE I

Experiment	I	II
Yield of nitrated iodonium iodide, g.	13.4	14.2
Yield of *p*-iodonitrobenzene, g.	1.20	1.34
p-Iodonitrobenzene remaining in solvent, g.	0.60	0.45
Loss due to iodine liberation, g.	0.16	0.16
p-Nitration, %	14.6	13.9

TABLE II

Experiment	III	IV
Yield of nitrated iodonium iodide, g.	13.4	13.7
M. p. of rearranged material	88°	89°
p-Nitration, %	18.5	19.0

Summary

Diphenyliodonium nitrate has been nitrated and the work of Challenger and Rothstein, which shows that a considerable amount of para nitration occurs along with meta nitration, has been confirmed.

EDMONTON, ALBERTA, CANADA
RECEIVED AUGUST 25, 1939

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

The Dipole Moments and Structures of Ozone, Silicobromoform and Dichlorogermane

BY GEORGE L. LEWIS AND CHARLES P. SMYTH

The structures of the molecules of the three inorganic substances, ozone, silicobromoform and dichlorogermane contain contributions from several forms among which resonance exists. It has seemed desirable to investigate the relation of each of these structures to its dipole moment.

The dipole moments were obtained in the usual manner from the dielectric constants ϵ and the densities d of solutions of the substances in non-polar solvents by means of the equations

$$P_{12} = \frac{\epsilon - 1}{\epsilon + 2}\frac{c_1M_1 + c_2M_2}{d}$$

and

$$P_2 = \frac{P_{12} - P_1}{c_2} + P_1$$

in which P_{12} is the polarization of the mixture, and c_1 and c_2, M_1 and M_2, and P_1 and P_2 are, respectively, the mole fractions, molecular weights and polarizations of the individual components, the subscript 2 referring to the polar substance. The values of P_∞ obtained by extrapolating the $P_2 - c_2$ curves to infinite dilution are used to calculate the dipole moment μ by means of the equation

$$\mu = 0.0127 \times 10^{-18}\sqrt{(P_\infty - MR_D)T}$$

in which MR_D is the molar refraction for the D sodium line and T is the absolute temperature.

Preparation of Materials

Heptane.—Material from the American Petroleum Corporation was used without purification, d^{25}_4 0.67958, $n^{25}D$ 1.38428.

Carbon Tetrachloride.—Purification of this solvent was carried out by standard methods:[1] d^{25}_4 1.58431, $n^{25}D$ 1.45717, ϵ^{25} 2.223.

Oxygen.—Tank electrolytic oxygen was passed through concentrated sulfuric acid and over phosphorus pentoxide and condensed by means of liquid air: $d^{-192.5}_4$ 1.1937, $\epsilon^{-192.2}$ 1.505.

Ozone.—A solution of ozone in liquid oxygen was prepared by passing a stream of purified oxygen through an ozonizer and condensing the product directly in the dielectric cell or the pycnometer surrounded by liquid air. The concentration of the solution was determined by allowing the liquid to evaporate through neutral potassium iodide solution in three gas washing bottles in series into a large aspirator bottle. The volume, measured within 0.1%, was then used to determine the total number of moles of oxygen plus ozone; the mole fraction of ozone was determined iodimetrically with sodium thiosulfate.

Silicobromoform.—A pure specimen of silicobromoform was given us by Professor W. C. Schumb of the Massachusetts Institute of Technology.

(1) Williams and Krchma, THIS JOURNAL, **48**, 1888 (1926).

Dichlorogermane.—About 1 cc. of dichloromonogermane was prepared by Messrs. S. R. Ginsburg and A. J. Grossman by a method outlined elsewhere.[2] Because of its instability, the material was not of a high degree of purity. It was kept in a sealed tube under its own pressure immersed in liquid air until the solutions in carbon tetrachloride were made up.

Experimental Methods

The dielectric constants were measured at a frequency of 520 kilocycles with a crystal-controlled heterodyne beat apparatus described elsewhere,[3] an accuracy of 0.05% being attained. The densities at 25° were measured with an Ostwald–Sprengel pycnometer. After being suspended in the constant temperature kerosene bath for twenty minutes, the pycnometer was set to the mark in the customary manner, removed from the bath, rinsed with distilled ether, wiped with a clean handkerchief, and weighed. Densities were reproducible to ±0.00001. For measurements of the density of liquid oxygen and oxygen solutions of ozone, the pycnometer used was a glass bulb with a very fine capillary opening. The volume of the bulb was determined by weighing full of mercury and was corrected for change with temperature. The weight of the liquid was determined from the volume of gas formed on evaporation just as in the determinations of the concentrations of the solutions. The density of the liquid oxygen could be reproduced to 0.001.

The solutions of silicobromoform and dichlorogermane were made up in an atmosphere of carbon dioxide by the simple device of placing dry-ice on the bottom of a large can, placing a glass-stoppered weighing flask containing a weighed amount of solvent upon a platform just above the dry-ice, holding the tube containing the active substance near the bottom of the can when opening it and immediately adding the active solute to the weighed solvent without removal from the can. Decomposition in the dilute solutions thus prepared was too slow to affect the accuracy of the measurements.

TABLE I

DIELECTRIC CONSTANTS, DENSITIES AND POLARIZATIONS

c_2	ϵ	d	P_2
Oxygen–Ozone (t = −192.4°)			
0.00000	1.505	1.1937	(3.86 = P_1)
.00855	1.534	1.1983	26.1
.00950	1.537	1.1989	25.9
.00970	1.537	1.1990	25.4
Heptane–Silicobromoform (t = 25°)			
0.00000	1.917	0.67958	(34.49 = P_1)
.05473	1.960	.75500	45.6
.08327	1.982	.79433	45.8
.12972	2.019	.84834	46.3
.16718	2.048	.90996	46.5
Carbon Tetrachloride–Dichlorogermane (t = 25°)			
0.00000	2.2282	1.58436	(28.20 = P_1)
.01175	2.3010	1.58651	122.5
.01762	2.3375	1.58747	121.8
.02616	2.3963	1.58895	123.9

(2) Ginsburg, Grossman and Smyth, to be published.

(3) Lewis and Smyth, *J. Chem. Phys.*, **7**, Nov. (1939).

TABLE II

MOLAR REFRACTIONS, POLARIZATIONS AND DIPOLE MOMENTS

Substance	MR_D	$P_\infty(t°)$	$\mu \times 10^{18}$
O_3	7.6	26 (−192.4°)	0.49
$SiHBr_3$	33	46 (25°)	.79
GeH_2Cl_2	21.8	123 (25°)	2.21

Experimental Results

The dielectric constants, densities and polarizations are given in Table I. Table II lists in the second column molar refractions, calculated from the refractive index of gaseous ozone given by "International Critical Tables," and calculated for silicobromoform from the atomic refractions given by Eisenlohr[4] and for dichlorogermane from the atomic refractions obtained from Landolt–Börnstein and from the data of Miller.[5] The succeeding columns give the polarization at infinite dilution P_∞ with the corresponding temperatures in parentheses and the dipole moments.

Discussion of Results

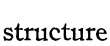
The three solutions of ozone in liquid oxygen were the most concentrated directly obtainable with the ozonizer employed. Extrapolation of their values of P_2 gives $P_\infty = 31$, but they are so close together that, in view of the small moment of the molecule, their differences from one another and from the true value of P_∞ are probably within the experimental error. The value 26 is, therefore, taken as being within two units of the correct value. If 31 is used instead of 26, the moment comes out higher by only 0.07. The temperature at which these measurements were made was so low as to raise a question of the necessity of applying the usually negligible quantum theory correction to the polarization. However, the probable moments of inertia of the molecule proved to be so large as to render the correction negligible. The molar refraction 7.6 calculated for gaseous ozone at 0° and 760 mm. seems a little high as compared to the value 4.05 calculated for gaseous oxygen under similar conditions from the refractive index in Landolt–Börnstein, but, even if the value were as low as 6.0 instead of 7.6, the moment would be raised only to 0.51. It is interesting to note that the polarization 3.86 found for liquid oxygen, which agrees closely with the values found by Kanda,[6] is lower than the value 4.01 calculated for MR_D from the refractive in-

(4) Eisenlohr, "Spektrochemie organischer Verbindungen," F. Enke, Stuttgart, 1912.

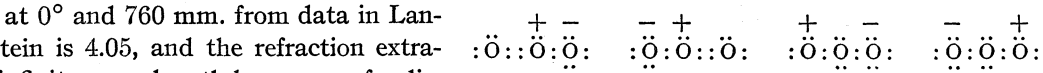
(5) Miller, THIS JOURNAL, **56**, 2360 (1934).

(6) Kanda, *J. Chem. Soc. Japan*, **12**, 473 (1937).

dex and density of liquid oxygen given by Landolt–Börnstein. The value of MR_D calculated for the gas at 0° and 760 mm. from data in Landolt–Börnstein is 4.05, and the refraction extrapolated to infinite wave length by means of a dispersion formula is 3.96. The same dispersion in the liquid would give $MR_\infty = 3.92$, which differs from the polarization 3.86 by no more than the uncertainty arising from the experimental errors in both figures. It is evident that not only is the dipole moment of the oxygen molecule zero but also the atomic polarization $P_A = P - MR_\infty$ is so small as to differ from zero by less than the experimental error. A very small atomic polarization is characteristic of small molecules.

The small but finite moment found for the ozone molecule shows that the symmetrical triangular structure  , in which each oxygen is linked by a single bond to the two other atoms in the molecule, is impossible as this structure would have zero moment. It also shows the impossibility of a linear molecule in which a central oxygen is joined by identical bonds to one on each side of it. The infrared spectrum[7] has been interpreted as indicating a triangular molecule, the angles of the triangle varying somewhat with the interpretation. The best results seem, however, to point to a molecule in which two atoms are bound to a central atom with an obtuse angle between the two bonds. Benedict[8] even went so far as to calculate the angle as 122° and the bond distance as 1.29 Å. This bond distance value is close to that for the single oxygen–oxygen bond[9] 1.32 Å., while the distance should probably be close to and slightly less than the double bond distance 1.14 Å. This cannot, therefore, be regarded as a satisfactory determination of the bond angle.

The natural expectation that the structure of ozone should be more or less analogous to that of sulfur dioxide is strengthened by the spectroscopic investigations. Electron diffraction[10] shows the sulfur dioxide molecule to be a triangle with the O–S–O angle 124 ± 15° and the sulfur–oxygen separation 0.05 Å. less than the sum of the covalent radii for a double bond. A larger O–O–O angle might be expected in the ozone molecule because of the smaller size of the central atom. The electronic structures which seem likely to contribute to the ground state of the molecule are the following



The first two structures, in which each atom has its complete octet of electrons, should make the largest contribution. All these structures are bent, the O–O–O angle being not less than 120°. The dipole moment should arise wholly from the first two structures and should be in the line bisecting the O–O–O angle, as the components of all the moments perpendicular to this line should cancel out. The moment of the molecule is the resultant of two equal moments in the two O–O bonds, that is, $2m\cos(\Theta/2) = 0.49$, where Θ is the O–O–O angle. If $\Theta = 120°$, $m = 0.49$, and, if $\Theta = 170°$, $m = 3$, which is about the size of the ordinary semi-polar bond between atoms of different elements[11] and identical with that between sulfur and oxygen.

The nitrogen–oxygen bond in the nitro group, which consists of equal contributions from a double bond form and from a single semi-polar bond form has a moment 3.3. On the other hand the molecule of nitrogen dioxide has been found to have a small moment like that of ozone, Williams, Schwingel and Winning[12] reporting a value 0.51 at 23.4°, which decreased with rising temperature, and Schultz[13] finding a constant value 0.29. The nitrogen dioxide molecule, although it possesses one less electron, presumably has a triangular structure somewhat similar to that of ozone and, like ozone, the resultant of contributions from different forms. The resultant of the moment of these bonds would be in the line bisecting the O–N–O angle. The small difference in electronegativity between nitrogen and oxygen seems to have little effect upon the moment. The identity of the two bonded atoms might be expected to reduce the polarity of a semi-polar bond between them as compared to that of a bond between two atoms of different electronegativities, but the effect of electronegativity difference between the elements upon the moment of a semi-polar bond between them has thus far been obscured by the uncertainties of the bond moments. The dipole moment does not prove that the O–O–O angle is wider than 120°, but places the probable limits at 120 and

(7) Stuart, "Molekülstruktur," Verlag von Julius Springer, Berlin, 1934, p. 314.
(8) Benedict, *Phys. Rev.*, **43**, 580 (1933).
(9) Pauling, *Proc. Natl. Acad. Sci.*, **18**, 293 (1932).
(10) Cross and Brockway, *J. Chem. Phys.*, **3**, 821 (1935).
(11) Smyth, THIS JOURNAL, **60**, 183 (1938).
(12) Williams, Schwingel and Winning, *ibid.*, **58**, 197 (1936).
(13) Schultz, *Z. Physik*, **109**, 517 (1938).

160°. It thus may be concluded that the ozone molecule is a triangular structure consisting of contributions from different forms. The two oxygens linked to the central atom form an angle of, perhaps, 140°. The two oxygen–oxygen bonds would then be expected to have lengths of about 1.13 Å. and moments not far from 0.7.

The low moment found for silicobromoform, $SiHBr_3$, is consistent with the low values for the chlorosilanes found by Brockway and Coop in the vapor state[14] and published after our measurements had been carried out. The value of $SiHBr_3$, 0.79, is lower than the moment of $SiHCl_3$, 0.85, just as that of $CHBr_3$,[15] 0.99, is lower than that of $CHCl_3$, 1.05, but the exact differences are uncertain because of solvent effect. Brockway and Coop have pointed out that the reduction of moment in the di- and trichlorosilane molecules because of mutual induction between the dipoles is less than in the corresponding carbon compounds because the larger size of the silicon separates the dipoles more. Although the moment of silicobromoform is smaller than that of bromoform, the difference is relatively smaller than that between methyl chloride and monochlorosilane. This same dependence of induction upon the size of the central atom has been observed[2] recently in the cases of mono and dichloro compounds of carbon, silicon, germanium and tin in extension of relations previously noted.[11]

The moment of dichlorogermane, 2.20, is larger than that of methylene dichloride, 1.56, and much larger than that of dichlorosilane, 1.17, but much smaller than the moment of $(C_2H_5)_2SnCl_2$, 3.85, which should be close to the tin analog of these other compounds. If Müller's empirical equation for solvent effect[16] applies to GeH_2Cl_2 as it does to CH_2Cl_2, a gas value 2.34 may be calculated for GeH_2Cl_2, which, for our present considerations, is not a material alteration from the solution value. The increase in moment with increase in the size and positive character of the central atom when the individual dipoles have their positive ends toward the latter has been observed before.[11,17] The sharp decrease from the carbon to the silicon compound in the cases of CH_2Cl_2 and SiH_2Cl_2 and $CHBr_3$ and $SiHBr_3$ as well as in the other chlorosilanes must arise in part, at least, from a resonance which involves contributions from forms containing positive halogen linked by a double bond to the central atom. This involves a shortening of the silicon–halogen bond below the sum of the single covalent bond radii of the two atoms, which amounts to 7.0% in $SiHCl_3$ and 7.4% in $SiCl_4$, as compared to 0% in CCl_4, 5.9% in $GeCl_4$, and 3.8% in $SnCl_4$. The percentage lowerings are calculated from the bond radii given by Pauling[9] and the interatomic distances summarized by Brockway.[14,18] They indicate clearly that the contribution of the doubly-bonded form, which, through having a positive charge on the halogen, lowers the total dipole moment of the molecule, is greatest in the silicon compounds. This would tend to make the moments of the silicon compounds have minimum values, but the difference between the bond shortenings in the two tetrachlorides appears too small to account wholly for the large difference in moment between the silicon and the germanium compounds. Undoubtedly, the more electropositive character of the germanium contributes largely to the difference.

Summary

The dipole moment of ozone has been measured in solution in liquid oxygen. It indicates that the molecule is a bent structure with a very obtuse angle between the bonds of two oxygens attached to a central atom. These two identical bonds have some polar character as a result of resonance among forms containing semi-polar bonds.

The moments of silicobromoform and dichlorogermane, measured in heptane and carbon tetrachloride solutions, respectively, show that silicon compounds tend to have minimum moments in the group of carbon, silicon, germanium and tin compounds, which, otherwise, increase in the order named.

PRINCETON, NEW JERSEY RECEIVED JULY 15, 1939

(14) Brockway and Coop, *Trans. Faraday Soc.*, **34**, 1429 (1938).
(15) Smyth and Rogers, THIS JOURNAL, **52**, 2227 (1930).
(16) Müller, *Physik. Z.*, **34**, 689 (1933).
(17) Smyth, *J. Phys. Chem.*, **41**, 209 (1937).
(18) Brockway, *Rev. Modern Phys.*, **8**, 231 (1936).

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

The Dipole Moments and Structures of Certain Nitro Compounds and Amines

BY GEORGE L. LEWIS AND CHARLES P. SMYTH

The dipole moments of trinitromethane or nitroform, tetranitromethane and nitrogen pentoxide have been determined with the object of studying the molecular structures and the interactions of immediately adjacent nitro groups. A brief account is included in this paper of the determination and interpretation of the moments of cyclohexylamine and morpholine. The moments were obtained with the apparatus and methods previously described.[1,2]

Preparation of Materials

Benzene.—Benzene was purified as in the work previously described.[1]

Carbon Tetrachloride.—Carbon tetrachloride was purified as in the work previously described.[2]

Tetranitromethane.—Tetranitromethane, prepared according to the method of Chattaway[3] by the action of virtually dry nitric acid on acetic anhydride, was dried over anhydrous sodium sulfate and distilled in an all-glass apparatus under reduced pressure at 35°; $n^{25}D$ 1.43822; d^{25}_4 1.62294.

Nitroform.—This compound was prepared according to the method of Hantzsch and Rickenberger[4] by the acidification with concentrated sulfuric acid of $KC(NO_2)_3$, which was formed by the action of alcoholic potash upon tetranitromethane; m. p. 19°.

Nitrogen Pentoxide.—The method of preparation was essentially that of Russ and Pokorny.[5] Fuming nitric acid was mixed with an equal volume of concentrated sulfuric acid and distilled from it into phosphorus pentoxide, which was kept at about −20° and stirred until the mixture had the consistency of a paste. The resulting nitrogen pentoxide was sublimed in a stream of ozonized oxygen and collected along with oxygen and ozone in a tube immersed in liquid air. Upon warming after removal from the liquid air, the oxygen and ozone evaporated, leaving the white solid.

Cyclohexylamine.—Material from Merck and Company was distilled, dried over calcium chloride and then sodium, distilled onto fresh sodium in an atmosphere of nitrogen, and redistilled: b. p. 133.8°; d^{25}_4 0.86253.

Morpholine.—Material very kindly given us by the Carbide and Carbon Chemical Corporation was dried over calcium chloride and then over sodium, distilled onto fresh sodium in an atmosphere of nitrogen, and redistilled. The middle fraction was retained and measured without further purification; b. p. 128.7°; $n^{25}D$ 1.45227; d^{25}_4 0.99619.

Experimental Results

The dielectric constants ϵ and densities d of the solutions containing mole fraction c_2 of the polar solute and the polarizations P_2 of the polar solute are given in Table I, while the molar refractions MR_D, the polarizations P_∞ obtained by extrapolating the P_2–c_2 curves to infinite dilution, and the dipole moments μ are listed in Table II.

TABLE I

DIELECTRIC CONSTANTS, DENSITIES AND POLARIZATIONS AT 25°

c_2	ϵ	d	P_2
Carbon Tetrachloride–Tetranitromethane			
0.00000	2.227	1.58431	(P_1 = 28.18)
.04039	2.240	1.58241	42.0
.08421	2.251	1.58160	41.2
.14291	2.264	1.58268	40.5
.18437	2.275	1.58364	40.4
.26079	2.295	1.58527	40.3
.30898	2.317	1.58639	40.7
1.00000	2.521	1.62294	40.62
Carbon Tetrachloride–Nitroform			
0.00969	2.308	1.57998	169.8
.01350	2.339	1.57888	167.0
.02944	2.466	1.57345	160.3
.03994	2.546	1.56703	157.7
Carbon Tetrachloride–Nitrogen Pentoxide			
0.00000	2.223	1.5844	(P_1 = 28.11)
.05934	2.368	1.5813	58.6
.08624	2.435	1.5800	57.9
.09361	2.452	1.5793	57.6
.10243	2.473	1.5790	57.3
Benzene–Cyclohexylamine			
0.00000	2.276	0.87344	(P_1 = 26.67)
.12935	2.559	.87084	65.7
.20884	2.743	.86946	65.8
.27445	2.892	.86815	65.6
Benzene–Morpholine			
0.08588	2.574	0.88422	73.4
.18193	2.934	.89684	71.6
.22967	3.128	.90295	70.7
.27621	3.316	.90875	69.9
.35608	3.665	.91851	68.7
1.00000	7.33	.99619	59.3

TABLE II

MOLAR REFRACTIONS, POLARIZATIONS AND DIPOLE MOMENTS

Substance	MR_D	P_∞	$\mu \times 10^{18}$
$C(NO_2)_4$	31.72	41.7	(0.71)
$CH(NO_2)_3$	25.01	177	2.71
N_2O_5	20	60	1.39
$C_6H_{11}NH_2$	30.5	65.7	1.32
OC_4H_8NH	23.59	75.3	1.58

(1) Lewis and Smyth, *J. Chem. Phys.*, **7**, Nov. (1939).
(2) Lewis and Smyth, THIS JOURNAL, **61**, 3063 (1939).
(3) Chattaway, *J. Chem. Soc.*, **97**, 2099 (1910).
(4) Hantzsch and Rickenberger, *Ber.*, **32**, 628 (1899).
(5) Russ and Pokorny, *Monatsh.*, **34**, 1027 (1913).

The molar refractions were calculated for tetranitromethane and morpholine from the refractive indices and densities herein reported and that for nitrogen pentoxide as the refraction of N_2O_4 plus half that of O_2 obtained from data in Landolt–Börnstein. The molar refraction of cyclohexylamine was calculated from similar data in Landolt–Börnstein and that of nitroform was the value of von Auwers and Harres.[6]

Discussion of Results

Tetranitromethane was measured because, although two previous investigators had found moments for it in solution so small as to be indistinguishable from zero, absorption measurements[7] and X-ray analysis of the crystal[8] had been interpreted as indicating that it was not a symmetrical molecule but actually trinitromethyl nitrite. Mark and Noethling assumed a linear nitrite structure, which now seems highly improbable. After the measurements in the present paper had been carried out, a determination in the vapor state was published indicating a moment indistinguishable from zero. The results of these measurements are summarized in Table III.

TABLE III

DATA ON TETRANITROMETHANE

Investigators	Temp., °C.	MR_D	P_∞	$(\mu \times 10^{18})$	Solvent
Williams[9]	25	31	32.5	0.2	C_6H_6
Weissberger and Sängewald[10]	25	35.3	36.2	.19	CCl_4
Coop and Sutton[11]	81.8	36.0	38.6	.39	Gas
Lewis and Smyth	25	31.72	41.7	.71	CCl_4

As Coop and Sutton say that the polarization may be "somewhat greater than the above value, but not by more than 3 cc.," and, as our value may be as much as 1 cc. high, the agreement is satisfactory. The value of Weissberger and Sängewald is also low by probably no more than the experimental error. Coop and Sutton's value of the molar refraction was taken as the average of the value of Weissberger and Sängewald, which may have a considerable error because of being determined in dilute solution, and of a value privately communicated to them by M. W. Lister. The value 31.72 determined in the present work agrees closely with that of von Auwers and Ottens[12] 31.44 and is higher than the sum 29.4 of the refractions of four alkyl nitro groups and one carbon atom taken from Landolt–Börnstein. The value 31.7 is, therefore, to be regarded as the molar refraction. This leaves a difference between the polarization and the refraction of about 10 cc., which would give a moment 0.7.

The moment of the symmetrical tetranitromethane molecule should, of course, be zero, while that of trinitromethyl nitrite would depend upon rotation around the single O–N bond of the nitrite group and would vary from 3.4 to 0 with variation in the position around this bond. Complete freedom of rotation would give a moment 2.4, but repulsion within the molecule should make the general region of the zero moment position more probable, which would mean an average moment possibly less than 1.0. The possibility that the tetranitromethane is really trinitromethyl nitrite is not wholly excluded if the moment is as large as 0.7. However, measurements on nitrobenzene in the vapor state[13] gave an atomic polarization 6 for nitrobenzene as compared to 1.0 for fluorobenzene and 1.8 for chlorobenzene, and similar measurements on nitromethane[14] gave an atomic polarization 6.1 as compared to 1.2 for phosgene and 0 for hydrogen cyanide obtained at the same time and small values for the alkyl halides obtained at other times. The large errors which commonly accumulate in atomic polarization values make any discussion of it necessarily approximate, but it would appear that a large atomic polarization may be associated with the nitro group. If the atomic polarization of two mononitro compounds is 6, it would not be surprising for a molecule containing four nitro groups to have an atomic polarization of 10. It seems reasonable, therefore, to attribute the difference between the polarization and the refraction to atomic polarization and report the moment as zero and the molecule, therefore, as the symmetrical tetranitromethane and not trinitromethyl nitrite. A determination of structure by the electron diffraction method just published[15] obtains the interatomic distances to be expected on the assumption of a symmetrical tetranitromethane. Before leaving the subject of tetranitromethane, attention should be directed to the somewhat unusual

(6) Von Auwers and Harres, *Ber.*, **62B**, 2287 (1929).
(7) Harper and Macbeth, *J. Chem. Soc.*, **107**, 87 (1915).
(8) Mark and Noethling, *Z. Krist.*, **65**, 435 (1927).
(9) Williams, *Physik. Z.*, **29**, 27 (1928).
(10) Weissberger and Sängewald, *Ber.*, **65**, 701 (1932).
(11) Coop and Sutton, *J. Chem. Soc.*, 1269 (1938).
(12) Von Auwers and Ottens, *Ber.*, **57B**, 446 (1924).
(13) McAlpine and Smyth, *J. Chem. Phys.*, **3**, 55 (1935).
(14) Smyth and McAlpine, THIS JOURNAL, **56**, 1697 (1934).
(15) Stosick, THIS JOURNAL, **61**, 1127 (1939).

occurrence of a minimum in the density–concentration curves in the very dilute region of its solutions in carbon tetrachloride.

No account of atomic polarization has been taken in the calculation of the moment of nitroform in Table II. The addition of 8 cc. to the refraction, a maximum value for atomic polarization, would lower the moment by only 0.07. The solvent effect has presumably already lowered it by more than this from its true gas value. The ratio of the value 2.71 to the solution value of nitromethane is 0.85, while the ratio of the chloroform moment to that of methyl chloride is 0.56. If there were no inductive action between neighboring dipoles, the moments of the mono- and the tri-substituted molecules should be equal as required by their tetrahedral structures. The lowering of the moment by induction is much less in nitroform than in chloroform, for not only is the ratio of the tri- to the mono-substituted compound 0.85 as compared to 0.56, but the absolute lowering is only 0.5 as compared to 0.8. The total polarizability of the nitro group is slightly greater than that of chlorine as shown by its refraction of 6.7 as compared to 5.97, but its polarizability per atom and per displaceable electron is only a little more than a third of that of chlorine and that for the chlorine electrons. In some positions of the nitro groups as they rotate around the C–N bonds, an oxygen of one nitro group may come very close to that of another with a considerable resultant lowering of the N–O dipole moments, but if, as it was found necessary to assume in the electron diffraction investigation of tetranitromethane[15] and as should be equally probable here, the nitro groups are undergoing rotatory oscillation about the C–N bonds in such a way as to keep the oxygen–oxygen repulsions minimized as far as possible, the oxygens are somewhat removed from neighboring dipoles and the inductive effects should be smaller than those in chloroform. The smaller reduction in dipole moment is thus accounted for.

The nitrogen pentoxide molecule should consist of two nitro groups attached to a central oxygen. A rather early electron diffraction investigation[16] indicated a symmetrical molecule with a 180° valence angle for the central oxygen. As this structure would have zero moment, the considerable moment 1.39 given in Table II shows it to be impossible. Evidently, the molecule is bent and a very rough value of the oxygen valence angle may be calculated from the group and bond moments involved. If from the solution value of nitromethane 3.2, the approximate moment of the H–C bond 0.3 is subtracted, a moment 2.9 is obtained for the nitro group. If induction reduces this by 10% as compared to the 15% reduction in nitroform, the group moment is 2.6. This moment in each half of the molecule is opposed by the N–O bond moment, which is about 0.3.[17] The moment of each half of the molecule is, therefore, 2.3, acting approximately in the direction of the oxygen valence bonds. The moment of the molecule as a whole should, therefore, be $2 \times 2.3 \cos(\theta/2) = 1.39$, where θ is the oxygen valence angle. This gives $\theta = 145°$, which seems rather large. However, electron diffraction[18] gives an oxygen valence angle 100° in OF_2 and 115° in OCl_2, in which latter molecule the repulsion between the two attached atoms should be larger. Calculation of the dimensions of the OCl_2 and $O(NO_2)_2$ molecules shows that, for a given oxygen valence angle, steric repulsion between the two nitro groups must be much greater for certain positions in the rotation of the groups about their bonds to the central oxygen than the repulsion between the two chlorine atoms. Thermal oscillation around these bonds should, therefore, tend to widen the oxygen valence angle and may be sufficient to account for the large value 145° estimated approximately. It should be remarked that the bond moment calculated from the moment and valence angle of the OCl_2 molecule was consistent with other indications of its size.[19] Neglect of atomic polarization in calculating the moment of nitrogen pentoxide presumably raises its value somewhat, but the presence of impurity due to decomposition of the unstable substance tends to compensate for this. It is thus clearly established that the molecule is bent, but the angle of bending is only very approximately estimated.

The moment of cyclohexylamine 1.32 is 0.2–0.3 higher than those of secondary alkyl amines, about the same size as those of the primary alkyl amines, and smaller than those of the aryl primary amines as would be expected. Its behavior is thus normal.

The moment of morpholine 1.58 in Table II is slightly higher than the value 1.48 recently pub-

(16) Maxwell, Mosley and Deming, *J. Chem. Phys.*, **2**, 331 (1934).

(17) Smyth, THIS JOURNAL, **60**, 183 (1938).

(18) Brockway, *Rev. Modern Phys.*, **8**, 231 (1936).

(19) Smyth, *J. Phys. Chem.*, **41**, 209 (1937).

lished by Partington and Coomber,[20] which does not affect its interpretation. The dioxane molecule, which has two possible forms, a Z-shape and a U-shape, has been shown by its moment[21,22] to exist almost wholly in the Z-form. Similarly, the moment found for morpholine, which has two possible Z-forms and four possible U-forms, agrees well with the identical values calculated for the two Z-forms. Our reasoning has agreed with that of Partington and Coomber in leading to the conclusion that the morpholine molecule exists primarily in its Z-forms, although the presence of U-forms is not entirely excluded.

Summary

The dipole moments of tetranitromethane, nitroform and nitrogen pentoxide have been determined in carbon tetrachloride solution and those of cyclohexylamine and morpholine have been measured in benzene solution. Tetranitromethane is concluded to have a large atomic polarization but zero dipole moment, which means that it is not trinitromethyl nitrite as sometimes suggested. The moment of nitroform is consistent with its tetrahedral structure, inductive effects in the molecule being smaller than those in chloroform, probably because of the lower polarizability of the atoms and of a staggering of the nitro groups in their rotation around their bonds to the central carbon atom. The moment of cyclohexylamine is of the same size as those of the primary alkyl amines, as it should be. The moment of morpholine shows that it exists primarily in the Z- or chair-shaped forms of the molecule.

(20) Partington and Coomber, *Nature*, **141**, 918 (1938).
(21) Hunter and Partington, *J. Chem. Soc.*, 87 (1933).
(22) Smyth and Walls, THIS JOURNAL, **53**, 2115 (1931).

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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

Allylic Rearrangements. IX. The Isolation and Rearrangement of Primary and Secondary Pentenyl, Hexenyl and Heptenyl Bromides[1,2]

BY WILLIAM G. YOUNG, LAWRENCE RICHARDS AND JULIAN AZORLOSA

In the first paper[3] of this series it was recognized for the first time that the so-called crotyl bromide was actually a mixture of primary and secondary butenyl bromides which were far more mobile than previously suspected. Although they could be separated by low-temperature fractional distillation, they rearranged even at room temperature to an equilibrium mixture. Later papers[4] have pointed out that studies involving the formation or reaction of these butenyl bromides must take into consideration the possibility of an allylic rearrangement during the reaction, and also a thermal rearrangement after the products are formed. Since other alkenyl bromides have been prepared and used in the synthesis of many types of compounds without recognition by investigators of the need for carefully controlled conditions, there exists, therefore, a need for a careful and extended study of the alkenyl bromides, their equilibria and reactions.

It is the purpose of this paper to discuss the separation and thermal rearrangement of the primary and secondary pentenyl, hexenyl and heptenyl bromides. A separation of the hexenyl bromides[5a] and the synthesis of several pure primary alkenyl bromides[5b] have been reported, but it will be shown that sufficient precautions were not used in the isolation of the pure compounds.

Experimental Part

Preparation of Materials

Alkylvinylcarbinols.—The ethyl, propyl and butylvinylcarbinols used as a source of the desired vinyl bromides were prepared in 60% yields by the action of the appropriate Grignard reagent on acrolein according to the method of Delaby[6] as modified by Prévost.[7]

(1) This work was accomplished with the aid of a grant from the Board of Research of the University of California.

(2) The terms primary alkenyl and secondary alkenyl bromides are used to designate the two allylic isomers, R—CH=CHCH$_2$Br and R—CHBrCH=CH$_2$ respectively. Accordingly, the terms primary pentenyl, hexenyl and heptenyl bromides refer to 1-bromo-2-pentene, 1-bromo-2-hexene, and 1-bromo-2-heptene, respectively. Similarly, secondary pentenyl, hexenyl and heptenyl bromides refer to 3-bromo-1-pentene, 3-bromo-1-hexene, and 3-bromo-1-heptene, respectively.

(3) Winstein and Young, THIS JOURNAL, **58**, 104 (1936).

(4) (a) Young, Winstein and Prater, *ibid.*, **58**, 289 (1936); (b) Young and Winstein, *ibid.*, **58**, 441 (1936); (c) Young and Lane, *ibid.*, **59**, 2051 (1937); (d) **60**, 847 (1938); (e) Young, Lane, Loshokoff and Winstein, *ibid.*, **59**, 2441 (1937); (f) Young, Kaufman, Loshokoff and Pressman, *ibid.*, **60**, 900 (1938).

(5) (a) Van Risseghem and Gredy, *Compt. rend.*, **202**, 489 (1936); (b) Delaby and Lecomte, *Bull. soc. chim.*, [5] **4**, 749 (1937).

(6) Delaby, *Compt. rend.*, **175**, 967 (1922).

(7) Prévost, *Ann. chim.*, [10] **10**, 113, 147 (1928).

Alkenyl Bromide Mixtures.—The pentenyl, hexenyl and heptenyl bromide mixtures used in this work were prepared by the action of a mixture of 240 ml. of 48% hydrobromic acid and 24 ml. of 95% sulfuric acid on one mole of the appropriate alkylvinyl carbinol for two days at room temperature. The bromides were all washed with dilute bicarbonate solution, then with water and dried over calcium chloride before distillation. The yields varied from 75–90% for different runs.

Fractional Distillations of the Bromide Mixtures.—All distillations were conducted at pressures of 1–5 mm. The 80-cm. fractionating columns were packed with glass helices and were surrounded with an appropriate thermostated liquid, when the distillation temperature was appreciably below room temperature. All materials were stored in a refrigerator at −15 to −20° between distillations, and the various fractions were collected in receivers maintained at −78° during the distillations to avoid the thermal rearrangements which were known to occur even at room temperatures with the butenyl bromides.[3] Since the bromide mixtures, as prepared, contained 80–90% of the primary alkenyl bromides, these isomers were readily isolated by low temperature fractionations. The criteria of purity of the isolated compounds were the constancy of the refractive indices upon repeated distillation and the agreement of the Carius analyses with the theoretical values.

The isolations of the secondary alkenyl bromides involved what may be described as a three-stage process. In the first stage, the secondary forms, present as 10–20% of the original bromide mixtures, were removed by fractionation and stored until sufficient amounts had been collected for the third stage. In the second stage, the mixtures almost completely freed of their secondary bromides were heated until equilibrium had been established. These rearranged mixtures were then treated as in the first stage. In the case of the pentenyl bromides, the first and second stages were combined by slowly fractionating at a distillation head temperature of 70–80°. The process in this case was continuous since the secondary isomer was re-formed by rearrangement in the boiler as rapidly as it was removed at the top of the column. In the third stage, the accumulated mixtures rich in the secondary forms were fractionated as practised in the isolation of the primary alkenyl bromides. The physical properties of the bromides prepared by the method described above are listed in Table I. See the discussion of results for explanation of difficulty encountered during the isolation of the secondary heptenyl bromide.

Determination of Physical Properties.—Refractive indices were determined with the aid of a Zeiss–Abbe refractometer with water-jacketed prisms and the D sodium line as a light source. The alkenyl bromides have been found to attack optical glass and slowly deposit a hard white film upon the surface of the prism of the refractometer. Consequently, small glass cells containing the alkenyl bromides were fastened to the prism face with α-bromonaphthalene while the measurements were taken.

Densities were determined with a 10-ml. cone-shaped pycnometer having a thermometer ground in the neck. All density measurements were made at 25.00°, and the values were corrected to vacuum. As a precautionary measure the samples were checked with a refractometer before and after the densities were taken.

Boiling points were determined by rapidly distilling small amounts of the pure bromides at reduced pressures through a small Vigreux type column. The refractive indices were determined before and after the distillations in order to show that no rearrangements had occurred during the distillations.

The pure compounds were analyzed for bromine by the method of Carius.

Composition of the Equilibrium Mixtures at 100°.—Small samples of each pure bromide were sealed in dry test-tubes and heated at 100° in a steam-bath until no changes were observed in the refractive indices. The primary and secondary alkenyl bromides rearranged to the same refractive indices, showing that equilibria were established. This required from one to eight hours depending on the alkenyl bromide and the particular sample being rearranged. Except in the case of the heptenyl bromides (see below) the composition of each equilibrium mixture (Table III) was determined from the refractive index of the mixture and the refractive index of each pure isomer. The assumption was made that the refractive indices are additive for each of the isomeric pairs and the validity of this assumption which had been tested in the case of the butenyl bromides[3] was also demonstrated for mixtures of the two pentenyl bromides (see Table II).

Estimation of the Composition of the Heptenyl Bromide Equilibrium Mixture.—Although only the primary heptenyl bromide has been isolated in a pure state and hence data are not available to

TABLE I

THE PHYSICAL PROPERTIES OF THE PRIMARY AND SECONDARY ALKENYL BROMIDES[2]

Alkenyl bromide		B. p., °C	Press., mm.	$n^{25}D$	d^{25}_4	% bromine Obsd.	% bromine Calcd.
Butenyl	Primary[3]	49	93	1.4795	1.3335	59.13	59.2
	Secondary[3]	31	93	1.4602	1.2998	59.25	59.2
Pentenyl	Primary	43.5	30	1.4777	1.2606	53.56	53.63
	Secondary	30.5	30	1.4626	1.2417	54.06	53.63
Hexenyl	Primary	28	9	1.4761	1.2049	49.18	49.01
	Secondary	22	9	1.4627	1.1849	48.97	49.01
Heptenyl	Primary	32	3	1.4745	....[a]	45.35	45.14
	Secondary	23–25	3	1.4560–1.4590	....	38.46[b]	45.14

[a] Due to an oversight this material was used before density measurements were taken. [b] This fraction was shown to contain heptadiene by bromine absorption.

TABLE II

EVIDENCE FOR THE VALIDITY OF THE ADDITIVE RELATIONSHIP OF REFRACTIVE INDICES IN ANALYZING ALKENYL BROMIDE MIXTURES

Mixture	% primary pentenyl bromide	$n^{25}D$ obsd.	$n^{25}D$ calcd.
(1)	51.7	1.4704	1.4704
(2)	36.4	1.4681	1.4682

TABLE III

COMPOSITION OF THE ALKENYL BROMIDE EQUILIBRIUM MIXTURES AT 100°

Alkenyl bromides	$n^{25}D$ at equilibrium	% primary bromide
Butenyl[2]	1.4767	85.5
Pentenyl	1.4747	80.1
Hexenyl	1.4742	85.8
Heptenyl	1.4737	Estimated 89.0

calculate the composition of the heptenyl bromide equilibrium mixture, nevertheless it has been possible to *estimate* the composition by two independent methods. It had been noticed that the conversion of methyl,[4c] ethyl[8] and propyl[8] vinylcarbinols into bromide mixtures using standard method VI[4c] (phosphorus tribromide + pyridine at −75°) gave approximately 47% primary bromide. Hence, the assumption could be made that 47% primary heptenyl bromide would be produced using the same standard method on butylvinylcarbinol. The bromide mixture, thus prepared, possessed refractive indices $n^{25}D$ 1.4691 and 1.4690 for two different preparations. After rearrangement at 100° these preparations came to equilibrium at $n^{25}D$ 1.4736 and 1.4738, respectively. Consequently we know that these preparations which contained 47% primary bromide increased on an average of 0.00465 refractive index unit in rearranging to equilibrium. The change in composition which will cause a change of 0.00465 refractive index unit was determined by recording the observed difference between the refractive indices of the primary and secondary butenyl, pentenyl and hexenyl bromides shown in Table I, and extrapolating to get the difference for the heptenyl system. Knowing that this difference of 0.0110 unit equals 100% change in composition, we find that the change of 0.00465 unit during rearrangement of the bromide mixture represented an increase of 42% in primary bromide content. Since the mixture started with 47% primary bromide, the equilibrium mixture must have approximately 89% primary bromide. In view of the fact that a similar calculation based on data obtained upon conversion of the primary heptenol into bromide mixtures by standard method VI gave the same value for the composition of the heptenyl bromide equilibrium mixture, we feel justified in using this estimate until it has been possible to isolate the pure secondary heptenyl bromide and thus get a more direct evaluation of the composition of the equilibrium mixture.

Mobility of the Alkenyl Bromides.—The absolute mobilities or rates of rearrangement of the alkenyl bromides have not been determined. The rearrangements are very sensitive to minute traces of catalytic substances and it has been impossible to obtain reproducible results. Qualitative observations have indicated that at 100° the order of decreasing mobility is: butenyl, hexenyl, pentenyl, and heptenyl, respectively.

Discussion of Results

Separation of the Alkenyl Bromides.—Careful and repeated fractional distillation at low temperatures has resulted in the isolation of the pure primary and secondary forms of the pentenyl bromides (1-bromo-2-pentene and 3-bromo-1-pentene), and the hexenyl bromides (1-bromo-2-hexene and 3-bromo-1-hexene). In the case of the heptenyl bromides, the pure primary form (1-bromo-2-heptene) was obtained, but the pure secondary form (3-bromo-1-heptene) has not yet been isolated. This is due to the fact that the primary heptenyl bromide could readily be isolated in quantity by low temperature fractional distillation of a bromide mixture. However, in an attempt to produce the secondary isomer continuously by high temperature fractionation (above 100°) of a mixture rich in the primary form as had been done with the butenyl and pentenyl bromides, the mixture lost hydrogen bromide, forming some heptadiene, although this fact was not apparent at the time. Consequently, the fraction which was thought to be mainly secondary bromide was later found to be low in bromine content and to contain some heptadiene (see Table I). Likewise the refractive index of this fraction was lower than anticipated for the secondary isomer, $n^{25}D$ 1.4560 to 1.4600. From our knowledge of the other secondary alkenyl bromides the 3-bromo-1-heptene would be expected to have a value of $n^{25}D$ 1.4637. A new supply of material must be synthesized before another attempt can be made to purify this bromide.

Previous Preparations of the Alkenyl Bromides.—The pentenyl, hexenyl and heptenyl

(8) Young, Richards and Azorlosa, unpublished work.

TABLE IV

CALCULATION OF COMPOSITION OF ALKENYL BROMIDES PREVIOUSLY DESCRIBED BY OTHER INVESTIGATORS

Bromide	Investigator	Refractive index, n_D	Calcd. composition % prim.	% sec.	Notes
Butenyl	Delaby and Lecomte[5b]	1.4815 (16°)	87.0	13.0	Although reported as pure primary bromide, this is the equilibrium mixture
Pentenyl	Hurd and McNamee[10b]	1.4757 (21°)	73.5	26.5	
Pentenyl	Hurd and Pollock[10c]	1.4654 (20°)	2.0	98.0	Frac. 1
		1.4769 (20°)	78.2	21.8	Frac. 2. Ozonization gave 18.5% secondary and 81.5% primary
	Delaby and Lecomte[5b]	1.4731 (20°)	53.0	47.0	Reported as the pure primary isomer
Hexenyl	Van Risseghem and Gredy[5a]	1.4657 (20°)	3.7	96.3	Reported to be pure secondary bromide
		1.4777 (20°)	93.3	6.7	Reported to be pure primary bromide
		1.4744 (21°)	72.4	27.6	Reported to be equil. mxt. from 30 dist. of *s*-bromide (see Table III)
		1.4750 (21°)	76.8	23.2	Reported to be equil. mxt. from 22 dist. of prim. bromide (see Table III)
	Hurd and Parrish[10a]	1.4715 (26°)	69.4	30.6	
	Delaby and Lecomte[5b]	1.4778 (16°)	79.0	20.9	Reported as the pure primary isomer
Heptenyl	Hurd and Parrish[10a]	1.4693 (24°)	51.0	49.0	
	Delaby and Lecomte[5b]	1.4760 (17°)	59.0	41.0	Reported as the pure primary isomer

bromides have been synthesized many times for one purpose or another but in most cases the investigator was unaware of their mobility and hence thought that only one product, the primary isomer, $R-\underset{H}{\overset{H}{C}}=\underset{H}{\overset{H}{C}}-CBr$ reported by Bouis,[9] was present. Fortunately, in a few cases sufficient data have been given so that we can use our refractive index data and calculate the composition of the materials reported. Table IV contains this information. Van Risseghem and Gredy[5a] have reported the separation of the primary and secondary hexenyl bromides (1-bromo-2-hexene and 3-bromo-1-hexene). If they had not underestimated the mobility of the bromides and as a result used too high a distillation temperature (50–60°) they would have made a successful separation. Actually their primary bromide contained 6.7% of the secondary isomer and the secondary bromide contained 3.7% of the primary form. Their attempt to attain equilibrium by repeated distillation at 100° in a sealed tube could not possibly give an equilibrium mixture. Judging from our experience the bromides are mobile enough so that the secondary form would be continually formed in the boiling liquid to replace the secondary form which is removed in excess in the vapor. Hence the final distillate would of necessity contain more secondary bromide than that present at equilibrium, regardless of the number of distillations performed. Moreover, the composition probably would depend upon the conditions maintained during the last distillation rather than on the previous distillations. Their secondary hexenyl bromide after thirty distillations ($n^{21}D$ 1.4744) was actually 72.4% primary bromide instead of the 85.8% called for by our equilibrium measurements and the 90–95% which they report. Likewise, their primary bromide after twenty-two distillations ($n^{21}D$ 1.4750) contained 76.8% primary bromide in place of the 90–95% which they reported. It should be noted that these two products contained far more secondary bromide than these authors report by Raman measurements and that they differ in composition by 5%, although they were reported to be identical in composition.

The results by Hurd and co-workers[10] are of particular interest because they offer a comparison of refractometry and ozonolysis methods of analysis. The approximate agreement observed in the case of the pentenyl bromides is gratifying, especially since there seems to be complete disagreement between our results and those obtained from Raman and infrared absorption measurements. For example, Delaby and Lecomte[5b] have synthesized bromides from the alkylvinylcarbinols and claim to obtain only pure primary bromides. However, analysis of their results using refractive index data shows that in every case their product was a mixture of both the primary and secondary bromides. In order to justify our confidence in the refractive index method of analysis,

(9) Bouis, *Bull. soc. chim.*, [4] **41**, 1160 (1927).

(10) (a) Hurd and Parrish, THIS JOURNAL, **57**, 1732 (1935); (b) Hurd and McNamee, *ibid.*, **59**, 104 (1937); (c) Hurd and Pollock, *J. Org. Chem.*, **3**, 565 (1939).

it should be recalled that a mixture of butenyl bromides comparable to that reported by Delaby and Lecomte was actually fractionated[3] at low temperatures into fractions comparable in size to those expected from refractive index analysis.

Further confirmation of the above conclusions has been obtained in this Laboratory[8] from experiments on the *controlled* conversion of alkylvinylcarbinols into bromides with phosphorus tribromide. In each case approximately 47% secondary bromides was present.

Summary

Several pure primary and secondary alkenyl bromides of the type R—C(H)=C(H)—CBr(H)(H) and R—C(H)(Br)—C(H)=CH(H) (R = Et to Bu) have been isolated for the first time.

The isomeric bromides have been rearranged at 100° to equilibrium mixtures the compositions of which have been determined.

The refractive index method of analysis of alkenyl bromide mixtures has been tested further with pentenyl bromide mixtures.

Conflicting reports in the literature concerning the composition of bromides made from alkylvinylcarbinols have been discussed and corrected values calculated.

LOS ANGELES, CALIF. RECEIVED JULY 17, 1939

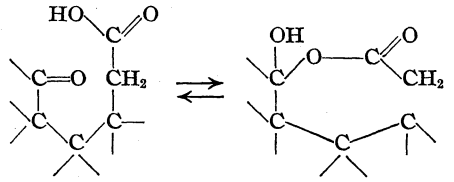
[CONTRIBUTION FROM THE UNIVERSITY OF MARYLAND]

Cerin and Firedelin. V. A Study of Friedonic Acid[1]

BY NATHAN L. DRAKE AND JOHN K. WOLFE[2]

Friedonic acid, a monobasic keto acid, is produced from friedelin by vigorous oxidation.[3] The acid is esterified readily, but neither free acid nor ester yields the ordinary derivatives of a carbonyl compound. However, the fact that the acid can be reduced both by sodium and alcohol and by hydrogen in the presence of a catalyst to an hydroxy acid which spontaneously undergoes inner esterification to yield a lactone, make it clear that friedonic acid is a keto acid and not an hydroxy acid. It is the purpose of this paper to present additional evidence of the presence of a carbonyl group in friedonic acid, and to show the relation of carbonyl to carboxyl.

From the reaction products of one of many routine oxidations of friedelin was isolated a substance, isomeric with friedonic acid, which melted at 126–127°. The same compound had been isolated earlier by Campbell,[4] but never in quantity sufficient to warrant further investigation. We have found that this product, which is unaffected by dilute sodium hydroxide in the cold, can be converted into a methyl ester identical with the methyl ester of friedonic acid, and that friedonic acid, when allowed to stand at room temperature for some time in alcoholic solution containing sodium ethoxide, is converted in part into this same compound (m. p. 126–127°). We shall call this substance "isomer A." The possibility that this substance is an hydroxylactone formed by interaction of the carboxyl and carbonyl of friedonic acid has been considered



Such a formulation would account for the fact that both isomer A and friedonic acid yield the same methyl ester, and that isomer A cannot be titrated with alkali in the cold, but does give normal values of saponification equivalent. The failure of "isomer A" to take up alkali in the cold makes it very unlikely that stereoisomerism only is involved in the difference between friedonic acid and this isomer. However, our ignorance of a suitable method of preparing the substance has rendered further work upon it impossible. Our supply of this material has been limited to several grams obtained for some unknown reason during a routine preparation of friedonic acid, and a very small amount formed by the action of sodium alkoxide on friedonic acid as mentioned above.

(1) Presented before the Division of Organic Chemistry at the Baltimore meeting of the Amercian Chemical Society, April, 1939.
(2) From the Ph.D. dissertation of John K. Wolfe.
(3) Drake and Campbell, THIS JOURNAL, **58**, 1681 (1936).
(4) Campbell, Thesis, U. of Md., 1936.

We have attempted again and again to produce isomer A, but all experiments, except the one mentioned above from which only a very small quantity of product was isolated, have failed. When isomer A was treated with methylmagnesium iodide[5] in the "Grignard machine," 0.58 mole of methane was evolved, and 3.0 moles of reagent consumed. A similar experiment with friedonic acid resulted in the liberation of 1.57 moles of methane and the consumption of 4.15 moles of reagent. The methyl ester of friedonic acid liberated 0.52 mole of methane and consumed 3.0 moles of reagent. Apparently enolization of a carbonyl group of methyl friedonate is responsible for the evolution of methane when this substance is treated with methylmagnesium iodide, and the results obtained with isomer A would lead one to conclude that the same carbonyl group is present in this substance. This situation would not be possible in the "hydroxylactone" formula.

The possibility that isomer A is the lactone of an hydroxy keto acid also has been considered, but the practically quantitative formation of methyl friedonate from it definitely eliminates this possibility.

When friedonic acid is treated with acetic anhydride a mixed anhydride results. It was hoped that this reaction might yield the acetyl derivative of the "hydroxylactone" from which gentle hydrolysis or alcoholysis might form isomer A. However, treatment of the mixed anhydride with 70% ethanol regenerates friedonic acid. An attempt was made to prepare a similar mixed anhydride from isomer A, but the substance was recovered unchanged from the reaction mixture.

In order to obtain additional evidence supporting the presence of a carbonyl function in friedonic acid, its absorption spectrum in the near ultraviolet was determined.[6] A decided maximum of absorption (log ϵ = 1.55) was found at 2900 Å. Many alicyclic ketones show absorption in this range.[7] Conjugation of a double bond with the unsaturation of the carbonyl group causes a shift of the characteristic carbonyl absorption into the neighborhood of 2500 Å. (log ϵ = 4.1). The observed absorption spectrum of friedonic acid confirms our earlier belief that the acid is not an α,β-unsaturated ketone.

(5) Philip Wingate, Thesis, U. of Md., 1939.

(6) We are indebted to Mr. P. A. Cole of the Washington Biophysical Institute for the absorption spectrum data.

(7) Waters and Lowry, "Physical Aspects of Organic Chemistry," D. Van Nostrand Co., Inc., New York, N. Y., 1937, pp. 398-399.

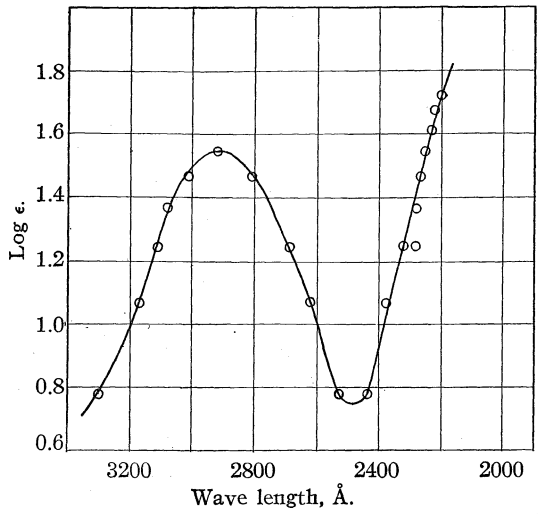


Fig. 1.—Absorption spectrum of friedonic acid, 1% in cyclohexane.

When friedonic acid was heated to a temperature about 40° above its melting point in an atmosphere of nitrogen, a new product was formed by elimination of water and loss of carbon dioxide. Quantitative determination of the water and carbon dioxide formed showed that approximately one mole of each was produced per mole of acid. The product, norfriedelene, gave a strong test for unsaturation using tetranitromethane, and absorbed one mole of hydrogen to yield norfriedelane which gave no color with tetranitromethane. In keeping with its unsaturated character, norfriedelene reacted with one mole of perbenzoic acid in chloroform and was transformed into an epoxide. These transformations are quite comparable to the behavior of 12-ketocholanic acid, which when heated to 300° loses water and carbon dioxide to yield dehydronorcholene.[8] Apparently the condensation involves the α-methylene group of friedonic acid; the subsequent decarboxylation, characteristic of α,β-unsaturated acids,[9] produces norfriedelene.

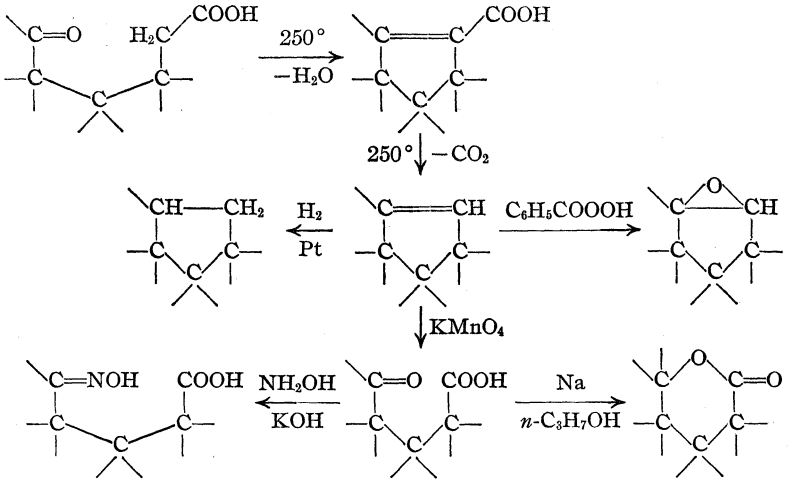
Oxidation of norfriedelene by means of potassium permanganate in glacial acetic acid according to Wieland[10] produced a new acid ($C_{29}H_{48}O_3$), norfriedonic acid, a keto acid differing from friedonic acid by methylene group and by its ability to form the usual derivatives of the carbonyl group. The lactone of the related hydroxy acid was obtained earlier directly from friedelin.[3] The

(8) Wieland and Schlichting, *Z. physiol. Chem.*, **150**, 273 (1925).

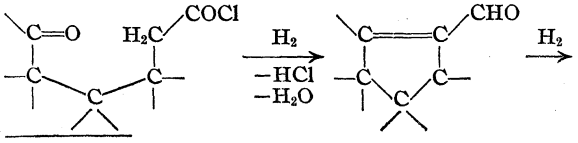
(9) Hurd, "The Pyrolysis of Carbon Compounds," The Chemical Catalog Co., New York, N. Y., 1929, pp. 349-354.

(10) Wieland and Wiedensheim, *Z. physiol. Chem.*, **186**, 229 (1930).

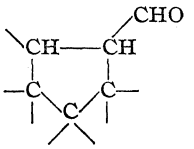
fact that carbonyl derivatives are readily obtained both from norfriedonic acid and its methyl ester indicates very clearly that some interaction of carbonyl and carboxyl groups is responsible for the failure of friedonic acid (and methyl friedonate) to yield such derivatives. The pyrolysis of friedonic acid and the other reactions given above can be represented



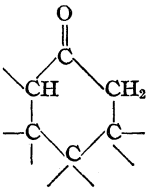
Friedonic acid yields a non-crystalline acid chloride when treated with thionyl chloride. Reduction of the acid chloride in xylene by hydrogen in the presence of a palladium–barium sulfate catalyst[11] produced a substance $C_{30}H_{50}O$, isomeric with friedelin. This new substance differs markedly from friedelin in regard to the reactivity of its carbonyl group. A 2,4-dinitrophenylhydrazone formed readily and the compound gave no test for unsaturation with tetranitromethane. This new substance also differed from friedelin by being easily oxidized to an acid containing the same number of carbon atoms and only two oxygen atoms. The isomer of friedelin must, therefore, be a saturated aldehyde, formed by a process quite analogous to the one involved in the production of norfriedelene from friedonic acid. Reduction of the double bond first formed may take place before production of the aldehyde, but more likely involves 1,4-addition to the α,β-unsaturated system in the aldehyde first produced. The formation of this aldehyde, norfriedelanylformaldehyde, can be represented



(11) Rosenmund, *Ber.*, **54**, 437 (1921).



From the data presented above and in earlier papers, it seems reasonable to conclude that friedonic acid is an epsilon-keto acid whose carbonyl group is highly sterically hindered, and that friedelin must contain the unit of structure



Experimental

Preparation of Friedonic Acid.—The procedure employed in oxidizing friedelin to friedonic acid was much the same as that used in earlier work.[3] The oxidation mixture was heated under reflux for ten hours, and at the end of that time concentrated to about one-fifth of its original volume. Five volumes of water was then added to the boiling solution, and the resulting precipitate was filtered hot, washed thoroughly with water, and dried in a desiccator over potassium hydroxide to constant weight; yield, 24.5 g. of light green solid from 24 g. of friedelin. The crude acid was pulverized and shaken well with 800 ml. of cold ethyl ether. The residual friedelin was filtered off, washed with ether, and used again without purification in a subsequent oxidation; yield, 8.0 g. of friedelin. The ethereal solution was extracted repeatedly with 10% sodium hydroxide until no more sodium salt precipitated in the aqueous layer. The precipitated sodium salt was returned to the separatory funnel and washed twice with ether. When the resultant emulsion was centrifuged three layers were produced; the upper ethereal layer was decanted, and the lower green aqueous layer poured off through holes punched in the compact intermediate layer of sodium salt. A suspension of the sodium salt was then acidified with concentrated hydrochloric acid in a separatory funnel and separated from the aqueous layer by extraction. The ethereal solution was then evaporated to dryness, the gummy residue taken up in 25 ml. of 95% ethanol, seeded with a few crystals of friedonic acid and cooled in the icebox overnight; yield of crude friedonic acid, 7.3 g. (m. p. 196–198°). Recrystallization of the crude acid from ethanol yielded 6.0 g. of pure acid which crystallized as colorless needles having parallel extinction and melted at 205–207°. The ethereal solution from which the acid was originally extracted was combined with that obtained during centrifugation, washed free from sodium hydroxide and evaporated to dryness. The solid residue was diluted with alcohol and filtered; the product was nearly pure friedelin (3.5 g.). Of the 24 g. of friedelin sub-

jected to oxidation, 11.5 g. was recovered, 12.5 g. oxidized, and 6.0 g. of friedonic acid obtained (48% yield).

Isomer A.—Friedonic acid (0.2 g.) was dissolved in 25 ml. of ethyl alcohol, containing 1 g. of dissolved sodium, and was allowed to stand at room temperature for forty-eight hours. The mixture was acidified, diluted with water, and filtered. On recrystallization of the solid from ethyl alcohol, 0.1 g. of friedonic acid was obtained. The filtrate from the crystallization was evaporated to dryness and triturated with a little ethyl alcohol in the cold. The undissolved crystals were filtered and recrystallized from ethyl alcohol; a small quantity of a nicely crystalline substance melting at 126–127° was obtained. When treated with 0.02 *N* sodium hydroxide this product showed no acidic properties. A mixed melting point with the substance obtained from friedelin by oxidation showed no depression.

Anal. Calcd. for $C_{30}H_{50}O_3$: C, 78.54; H, 11.00. Found: C, 78.49, 78.65; H, 11.09, 11.08.

Methyl Friedonate.—One gram of friedonic acid (m. p. 205–207°) was dissolved in 50 ml. of methyl alcohol containing 0.1 g. of dissolved sodium. Five ml. of methyl sulfate was added and the mixture refluxed for one and one-half hours. Half of the solvent was evaporated, the mixture diluted with 100 ml. of water, and extracted twice with ether. The solid obtained by the removal of the ether was recrystallized from methyl alcohol, from which it formed silky needles, which after several recrystallizations melted at 157–158°.

Anal. Calcd. for $C_{31}H_{52}O_3$: C, 78.75; H, 11.09; methoxyl, 6.56. Found: C, 78.58, 78.87; H, 11.08, 11.22; methoxyl, 6.58, 6.52.

Methyl friedonate also was prepared from sodium friedonate by the action of methyl iodide, and from friedonic acid by use of diazomethane. Melting points and mixed melting points of all samples were the same.

Reduction of Friedonic Acid. Friedololactone.—Friedonic acid (0.5 g.) was hydrogenated in glacial acetic acid in the presence of Adams platinum catalyst. Twelve hours were required to complete the reduction. The catalyst was filtered off and the resulting solution was diluted with water (100 ml.). The jelly-like precipitate was filtered, dried, and recrystallized from ethyl acetate to a melting point of 308–312°. This product showed no depression in melting point when mixed with friedololactone previously obtained.[3]

Methyl Friedonate from "Isomer A."—One gram of "isomer A" (m. p. 126–127°) when treated with sodium methoxide and dimethyl sulfate in the same manner as friedonic acid above, yielded a product which after several recrystallizations from methyl alcohol melted at 157–158°. A mixed melting point with methyl friedonate prepared from pure friedonic acid showed no depression.

Norfriedelene.—Friedonic acid (2.93 g.) was heated in an atmosphere of nitrogen for two and one-half hours at 250°. The water and carbon dioxide evolved were collected and weighed in absorption tubes. The melt was cooled and the solid material obtained recrystallized three times from an ethyl acetate–benzene mixture to a constant melting point of 228.5–230°. The product, of which 1.82 g. was obtained, gave a yellow color with tetranitromethane, showing the presence of unsaturation.

Anal. Calcd. for $C_{29}H_{48}$: C, 87.79; H, 12.21. Found: C, 87.75, 87.94; H, 12.28, 12.26.

Norfriedelane.—One-half gram of norfriedelene was hydrogenated in ethyl ether–ethyl acetate solution in the presence of 0.1 g. of Adams platinum catalyst. After five hours the hydrogenation was complete; the solvent was removed and the product recrystallized from benzene to constant melting point. Norfriedelane gave no color with tetranitromethane and melted at 220–221°; it crystallized as colorless needles having a slight oblique extinction (about 3.2°).

Anal. Calcd. for $C_{29}H_{50}$: C, 87.36; H, 12.65. Found: C, 87.41, 87.44; H, 12.79, 12.82.

Norfriedonic Acid.—Two grams of powdered norfriedelene, 3 g. of powdered potassium permanganate, and 120 ml. of glacial acetic acid, previously distilled from chromic anhydride, were stirred vigorously for eight hours at room temperature. Five grams of sodium bisulfite was added and the mixture diluted with 400 ml. of water. The acid was extracted with ether and converted into sodium salt by addition of 10% sodium hydroxide. The mixture was centrifuged, separated, and the sodium salt acidified with hydrochloric acid. After several crystallizations from ethyl alcohol, 0.75 g. of acid melting at 215–217° was obtained. The residues from crystallizations contained 0.95 g. of amorphous material which could not be induced to crystallize.

Anal. Calcd. for $C_{29}H_{48}O_3$: C, 78.31; H, 10.89. Found: C, 78.20, 78.27; H, 11.02, 11.03.

Norfriedonic acid crystallizes in the form of colorless needles having parallel extinction.

Methyl Norfriedonate.—Esterification of norfriedonic acid by dimethyl sulfate and alkali and by diazomethane yielded a product which melted at 166–167°.

Anal. Calcd. for $C_{30}H_{50}O_3$: C, 78.54; H, 11.00; mol. wt., 458. Found: C, 78.52, 78.63; H, 10.87, 10.94; $-OCH_3$, 6.87, 6.78; mol. wt. (from $-OCH_3$), 452, 458.

Norfriedololactone.—Norfriedonic acid (0.1 g.) was dissolved in 10 ml. of *n*-propanol; the mixture was refluxed and 0.05 g. of sodium added. After cooling, the mixture was diluted with 30 ml. of water and made acid to Congo red with concd. hydrochloric acid. The white precipitate was filtered and recrystallized from ethyl acetate; 10 mg. of a product melting at 288–290° was obtained. This product showed no depression in melting point when mixed with norfriedololactone obtained in earlier work.[3]

The Oxime of Norfriedonic Acid.—Norfriedonic acid (0.25 g.) and 0.15 g. of hydroxylamine hydrochloride were dissolved in 10 ml. of ethyl alcohol. A solution of 0.15 g. of potassium hydroxide in 5 ml. of ethyl alcohol was added and the mixture was refluxed for thirty minutes. The resulting mixture was diluted with water (25 ml.) and acidified with 10% sulfuric acid. The solution was extracted twice with benzene and ethyl alcohol mixture (90–10). The solvent was removed and the solid residue recrystallized from a benzene–ethyl alcohol mixture (50–50). The oxime (0.22 g.) melted at 270.5–273°, and crystallized as colorless needles having parallel extinction.

Anal. Calcd. for $C_{29}H_{49}O_3N$: C, 75.75; H, 10.73. Found: C, 75.94, 75.93; H, 10.83, 10.90.

The Oxime of Methyl Norfriedonate.—Methyl norfriedonate (0.2 g.) and 0.15 g. of hydroxylamine hydrochloride were dissolved in 5 ml. of pyridine and allowed to stand at room temperature for twenty-four hours. The mixture was then diluted with water, filtered, and washed well with water. The product (0.17 g.) was recrystallized from methyl alcohol. The oxime melted at 193–195°, and crystallized in the form of colorless prisms having parallel extinction.

Anal. Calcd. for $C_{30}H_{51}O_3N$: C, 76.04; H, 10.86. Found: C, 75.93, 75.85; H, 11.01, 10.72.

The 2,4-Dinitrophenylhydrazone of Methyl Norfriedonate.—Methyl friedonate (0.2 g.) was dissolved in 5 ml. of ethyl cellosolve and 0.12 g. of 2,4-dinitrophenylhydrazine dissolved in 5 ml. of cellosolve was added to this solution; two drops of concd. hydrochloric acid was then added and the mixture refluxed for five minutes. The solution was allowed to stand overnight to complete crystallization, and the product formed was recrystallized from ethyl alcohol–benzene mixtures; it (0.15 g.) melted at 233–234°, and formed bright yellow prisms having oblique extinction.

Anal. Calcd. for $C_{36}H_{53}N_4O_6$: C, 67.62; H, 8.38. Found: C, 67.36; H, 8.40.

Norfriedelanylformaldehyde (I).—One gram of friedonic acid and 5 ml. of thionyl chloride were heated to reflux on a steam-bath for about thirty minutes. Excess thionyl chloride was removed *in vacuo* and the residue was placed in a desiccator over potassium hydroxide for forty-eight hours; the acid chloride could not be induced to crystallize. Xylene (15 ml.), previously dried over sodium, was added along with 2 g. of palladium–barium sulfate catalyst[11] and hydrogen was passed through the mixture at 150° for seven hours during which time 1 g. of fresh catalyst was added; the hydrogen chloride evolved was collected and titrated with 0.05 *N* sodium hydroxide. The quantity of hydrogen chloride produced was approximately 85% of that calculated for one mole per mole of substance. The solvent was removed under reduced pressure, and the partially crystalline mass was treated with ethyl acetate. After several recrystallizations from ethyl acetate, 0.20 g. of a substance which melted at 222–225° and crystallized in the form of colorless prisms having a slight oblique extinction (extinction $\angle$ *ca.* 19.4°) was obtained. From the mother liquors 0.3 g. of friedonic acid was recovered via its sodium salt.

Anal. Calcd. for $C_{30}H_{50}O$: C, 84.43; H, 11.82. Found: C, 84.51, 84.66; H, 11.80, 12.10.

The Oxime of I.—Prepared in the usual way, this oxime was purified by several recrystallizations from ethyl acetate. It separates from ethyl acetate in the form of very small colorless crystals which melt at 255–259°.

Anal. Calcd. for $C_{30}H_{51}NO$: C, 81.57; H, 11.65. Found: C, 81.50, 81.64; H, 11.62, 11.54.

The 2,4-Dinitrophenylhydrazone of I.—Fifty mg. of I was dissolved in 5 ml. of ethyl cellosolve and mixed with a solution of 25 mg. of 2,4-dinitrophenylhydrazine in 5 ml. of ethyl cellosolve. One drop of concd. hydrochloric acid was added and the mixture refluxed for fifteen minutes during which time yellow needles separated from the mixture. After several recrystallizations from benzene 36 mg. of substance melting with decomposition at 312–314° was obtained. This material crystallized as bright yellow needles having parallel extinction.

Anal. Calcd. for $C_{36}H_{54}N_4O_4$: C, 71.26; H, 8.97. Found: C, 71.13, 71.21; H, 8.84, 8.85.

Norfriedelanylformic Acid.—To 0.3 g. of I dissolved in 50 ml. of glacial acetic acid at 100° was added a solution of 60 mg. of chromic anhydride dissolved in 30 ml. of acetic acid. The mixture was then evaporated to 20 ml. total volume and diluted with 50 ml. of water. The crystals formed were filtered, dried, dissolved in ether, and the ethereal solution extracted twice with 10% sodium hydroxide solution. The aqueous layer was centrifuged and acidified with hydrochloric acid. The solid formed was filtered and recrystallized from glacial acetic acid. The product was an acid (0.22 g.), which crystallized in the form of long colorless needles having parallel extinction and melted at 307–308°.

Anal. Calcd. for $C_{30}H_{50}O_2$: C, 81.37; H, 11.39. Found: C, 80.90, 81.10; H, 11.40, 11.46.

Methyl Norfriedelanylformate.—Norfriedelanylformic acid (0.04 g.) was dissolved in 10 ml. of methyl alcohol containing 0.05 g. of dissolved sodium. One ml. of dimethyl sulfate was added. The mixture was refluxed for one-half hour and crystals formed from the boiling mixture. The cooled mixture was filtered, and the crystals dried and recrystallized from a mixture of pyridine and methyl alcohol. Twenty-five mg. of methyl ester melting at 230–231.5° was obtained. This substance crystallizes in the form of very thin plates having parallel extinction.

Anal. Calcd. for $C_{31}H_{52}O_2$: C, 81.51; H, 11.49. Found: C, 81.15; H, 11.47.

Summary

1. An isomer of friedonic acid, called for the present "isomer A," has been isolated and its conversion to methyl friedonate described.

2. Pyrolysis of friedonic acid has been shown to result in the production of an unsaturated hydrocarbon, norfriedelene, which has been hydrogenated to norfriedelane.

3. Oxidation of norfriedelene was found to yield norfriedonic acid, a monobasic keto acid of which carbonyl and carboxyl derivatives have been made.

4. Reduction of friedonyl chloride has been shown to result in the formation of an aldehyde isomeric with friedelin. The aldehyde has been oxidized to the corresponding acid.

5. Friedonic acid is apparently an epsilon-keto acid containing a highly blocked carbonyl group.

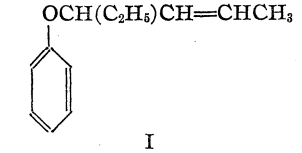
COLLEGE PARK, MD. RECEIVED AUGUST 25, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

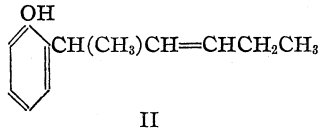
The Chemistry of Vitamin E. XIX. Alkenylation of Phenol with 4-Chloro- and 4-Bromo-2-hexene; Rearrangement of the Phenyl Ether[1]

BY LEE IRVIN SMITH, HERBERT E. UNGNADE, WALTER M. LAUER AND ROBERT M. LEEKLEY

α-Ethylcrotyl phenyl ether (I) was obtained by Hurd and Cohen[2] by action of 4-chlorohexene-2 upon an acetone solution of phenol in the presence of potassium carbonate.



I

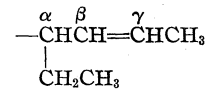


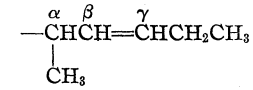
II

When distilled under reduced pressure, the ether partially rearranged into a phenol which was regarded as *o*-(α,δ-dimethylcrotyl)-phenol, II.

Incidental to the synthesis and examination of substances related in structure to the tocopherols, we have repeated the synthesis of the ether I and have determined the structures of two of the by-products formed along with the ether I. The ether was prepared both from 4-chloro- and 4-bromohexene-2 and phenol under varied conditions. The product was always a mixture, which consisted of the ether I along with mono- and dialkenylphenols. The disubstitution product was formed in fairly large amounts when equimolecular proportions of the phenol and halide were used, but the amount of this could be diminished by using an excess of phenol. The mixture was separated readily by extracting the monoalkenylphenol with aqueous alkali, followed by extraction of the dialkenylphenol with Claisen's alkali.[3] The phenyl ether which was not extracted by the alkali was purified by high vacuum distillation, for only under these conditions could it be obtained free from phenolic impurities. The ether was found to undergo rearrangement even at 100° at a measurable rate: at this temperature, 0.88% of the ether rearranged in twenty-four hours, while at 120°, rearrangement proceeded to the extent of 9.6% in twenty-four hours. These results support the observation of Hurd and Cohen[2] that the ether rearranges during distillation.

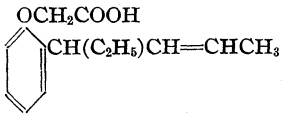
In order to ascertain whether or not the various products were homogeneous, the phenyl ether, monoalkenylphenol and dialkenylphenol were ozonized. Reductive cleavage of the ozonides gave mixtures of aldehydes in each case and it therefore appears that the compounds are not pure. All of them are probably mixtures of α,γ-allylic isomers containing the following groupings



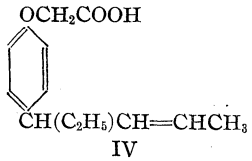


Oxidation of the ether likewise led to a mixture of phenoxy acids; a mixture also resulted on reduction to the saturated ether, the constants of which differed somewhat from those given for 3-phenoxyhexane by Hurd and McNamee.[4] Cyclization of the mixture of monoalkenylphenols with pyridinium chloride gave an alkali-insoluble product which was a mixture, probably of isomeric chromans.

The monoalkenylphenol portion was converted to aryloxyacetic acids by reaction of their sodium salts with ethyl bromoacetate. From the mixture of aryloxyacetic acids so obtained, there was isolated, after many crystallizations, small amounts of two pure isomeric acids, $C_{14}H_{18}O_3$, one melting at 95.2–96° and the other at 110–110.5°. These acids both gave acetaldehyde and small amounts of formaldehyde upon ozonolysis; it appeared therefore that both contained the α-ethylcrotyl group and hence the isomerism did not lie in the nature, but rather in the position, of the side chain. If so, one acid must be the ortho compound III, and the other the para compound IV.



III



IV

Acting upon this assumption, the unsaturated

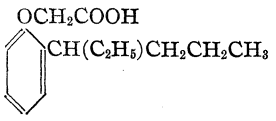
(1) Paper XVIII, THIS JOURNAL, **61**, 2424 (1939).

(2) (a) Hurd and Cohen, THIS JOURNAL, **53**, 1917 (1931); (b) see also Hurd and Puterbaugh, *J. Org. Chem.*, **2**, 384 (1938).

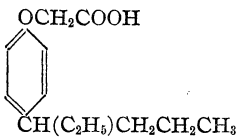
(3) Claisen, *Ann.*, **418**, 96 (1919).

(4) Hurd and McNamee, THIS JOURNAL, **54**, 1648 (1932).

acids III and IV were reduced to the saturated acids, and these two saturated acids, V and VI, were synthesized.



V



VI

The synthetic acids were identical with the acids obtained from the monoalkenylphenols; it follows therefore, that among the monoalkenylphenols obtained by action of a 4-halo-2-hexene and potassium carbonate upon phenol in acetone there are two which contain the α-ethylcrotyl group in the *o*- and *p*-positions, respectively, to the hydroxyl group. These results, however, are not sufficient to map the course of the reaction beyond the data given, for the acids III and IV were obtained only in small amounts and it is certain that other substances were present in the monoalkenylphenol portion of the reaction product.

The dialkenylphenol portion of the product was also a mixture. In view of the complexity of the monoalkenylphenol mixture, the dialkenylphenol portion must be very complicated indeed. No pure compounds were isolated from this mixture but because of its complex nature and because our interest lay more in the monoalkenylphenols and the cyclic compounds derived from them, not a great deal of work was done upon it. The components of the mixture were, however, all 2,6-dihexenylphenols, because the mixture was insoluble in aqueous alkali, soluble only in Claisen's alkali, was phenolic, and could not be rearranged by heating. The insolubility in aqueous alkali eliminates a 2,4-dialkenylphenol, for these are completely soluble. The constituents of the mixture, therefore, must be related as stereoisomers, or allylic isomers, or both.

All of the products obtained from the reaction between phenol and the unsaturated halides were tested by Dr. H. M. Evans for vitamin E activity.[5] The phenyl ether I, as well as the monoalkenylphenols and the isomeric cyclic compounds derived from them, were inactive in 50-mg. doses. The dialkenylphenol, however, was active when fed at this level.

Experimental Part[6]

Hexene-2-ol-4.—The procedure given by Hurd and Cohen[2] was followed, 3 moles of ethylmagnesium bromide being added to 2 moles of crotonaldehyde. This resulted in a decrease of secondary products. The yield was 128–133 g., b. p. 60–60.5° under 21 mm., 64–65° under 25 mm.; $n^{20}D$ 1.4345–1.4346.

4-Chloro-2-hexene.—The alcohol (132 g.) containing anhydrous sodium sulfate (50 g.) was cooled in ice and salt and dry hydrogen chloride was passed into it. When saturated, the mixture was allowed to stand for several hours at 0°, when it was again saturated with the gas, increasing the weight a total of 53.5 g. The mixture was allowed to stand overnight at 0°. Water was added, the oily layer was separated, washed with water, then with dilute bicarbonate and dried over potassium carbonate. Fractionation of this oil gave 111 g. of product boiling at 66–67° under 110 mm.; $n^{20}D$ 1.4385; $n^{20}D$ 1.4382 for a specimen prepared from the alcohol and phosphorus pentachloride.

4-Bromo-2-hexene.—The alcohol (42 g.) and aqueous hydrobromic acid (250 g., 40%) were allowed to stand, with frequent shaking, for twenty-four hours. Water was added and the oil worked up as described for the chloro compound above. Fractionation under 20 mm. pressure gave 7 g. of the monobromo compound, b. p. 35–39°, and 30 g. of the dibromo compound, b. p. 90–110°. Although the yield was poor, the product, contrary to the statement of Hurd and Puterbaugh,[2b] could be obtained this way. The procedure used for the chloride was not tried for preparation of the bromide, but in view of our success with this method generally for converting allylic alcohols to halides[7] we believe that a good yield of the bromide could be obtained using gaseous hydrogen bromide at 0°. However, it remains to be established whether or not this bromide (and also the chloride) is a pure substance or a mixture of allylic isomers.

Phenyl α-Ethylcrotyl Ether I (and Allylic Isomer).—Phenol and potassium carbonate were placed in a flask equipped with an efficient reflux condenser. The halide was added to the cooled (0°) mixture, which was then refluxed until a negative Beilstein test was obtained. Water and petroleum ether were added, and the aqueous layer was removed and extracted with petroleum ether. The combined organic layers were extracted several times with aqueous sodium hydroxide (10%) and then with Claisen's alkali. The residual petroleum ether solution was washed with water and dried over potassium carbonate. After removal of the solvent, the ether I was distilled under high vacuum. The phenols in the aqueous alkaline extraction were precipitated by passing carbon dioxide into the solution. These were removed by ether extraction. The extracts were dried over potassium carbonate, the solvent was removed and the residue was distilled. The Claisen's alkali extracts were diluted with water, acidified with sulfuric acid and extracted with ether. After drying over sodium sulfate the ether was removed and the residue was distilled. The results of several experiments are given in Table I, and the properties of the compounds are given in Table II.

Cyclization of the Monoalkenylphenols.—The monoalkenylphenol fraction (6 g.) was refluxed with pyridinium chloride (1 g.).[8] The initial b. p. was 222°; after sixty

(5) Paper XIII in this series, *J. Org. Chem.*, **4**, 376 (1939).

(6) Microanalyses by J. W. Opie and H. H. Hoehn.

(7) Paper IX in this series, *J. Org. Chem.*, **4**, 334 (1939).

(8) (a) Claisen, *Ann.*, **401**, 26 (1913); (b) Bartz, Miller and Adams, THIS JOURNAL, **57**, 371 (1937).

TABLE I

RESULTS OF ALKENYLATION EXPERIMENTS

Phenol, g.	Halide, g.	K_2CO_3, g.	Acetone, cc.	Time, hrs.	Phenyl ether	Products, g. Mono alkenyl-phenol	Di-alkenyl-phenol
8.0	(Cl) 10	11.7	20	4	5.0[a]	..	..
5.0	(Br) 7	7.3	16	8	6.0[a]	..	..
183.0	(Cl) 229	268.0	200	8	60.0[a]	45	48
94.0	(Cl) 111	140.0	150	24	47.0	22	5

[a] Part of the ether was lost in these experiments by rearrangement during distillation. Thus, the 60 g. of ether in run 3 (distilled under 18 mm. pressure), was accompanied by 45 g. of high boiling material (b. p. 128–168° under 18 mm.) which contained 13 g. of alkali soluble phenol, b. p. 129–132° under 15 mm., $n^{20}D$ 1.5292. The alkali insoluble remainder of the 45 g. was redistilled; this gave 15 g. of the ether and 13 g. of the higher boiling, alkali insoluble, rearrangement product.

TABLE II

PROPERTIES OF ALKENYLATION PRODUCTS

Compound	B. p., °C.	p, mm.	$n^{20}D$
Phenyl ether I[a]	103 –106	13	1.5059
	116 –120	18	1.5054
	34.5– 35.5	10^{-5}	1.5053
Monoalkenylphenols	135 –137	10	1.5296
	141 –144	12	1.5299
Dialkenylphenols[b]	169 –170	9	1.5220
	175 –179	11	1.5224
	60	10^{-6}	1.5225

[a] The pure phenyl ether shows 0.9 mole of active hydrogen in the Grignard machine. This is probably due to cleavage by the Grignard reagent: see Lüttringhaus, *et al.*, *Ber.*, **71**, 1673 (1938). The authors are indebted to W. W. Prichard for this analysis.

[b] d^{20}_{20} 0.9394; *MR* calcd., 82.31; found, 83.83. *Anal.* Calcd. for $C_{28}H_{26}O$: C, 83.72; H, 10.08. Found: C, 83.62; H, 9.93. The density and refractive index values of this dihexenylphenol as functions of the temperature lie closely on straight lines.

minutes the b. p. dropped to 216° and remained constant. The product boiled at 106–108° under 10 mm.; $n^{20}D$ 1.5225. It was insoluble in alkali.

Conversion of the Monoalkenylphenols to Aryloxyacetic Acids.—The monoalkenylphenol fraction (3.391 g.) and ethyl bromoacetate (5 cc.) were added to a solution of sodium ethoxide (0.45 g. of sodium in 20 cc. of ethanol). The mixture was refluxed for six hours. Aqueous sodium hydroxide (10 cc., 25%) was added and the mixture was refluxed for four hours longer. The alcohol was distilled out under reduced pressure and the solid residue removed and dissolved in water. Addition of acid precipitated the aryloxyacetic acids (4.340 g.). These did not reduce mercuric acetate in hot acetic acid, hence the double bond had not shifted toward the ring.

The mixture of acids was fractionally crystallized alternatively from petroleum ether and from aqueous acetic acid. After many crystallizations (approximately 30) small amounts (80–100 mg.) of two pure acids were obtained. These were III and IV, melting at 110–110.5° and 95.2–96°, respectively.

Anal. Calcd. for $C_{14}H_{18}O_3$: C, 71.80; H, 7.69. Found (III, m. p. 110–110.5°): C, 71.93; H, 7.99. Found (IV, m. p. 95.2–96°): C, 71.84; H, 7.99.

Ozonolysis.—The acid III (20 mg.) in chloroform (60 cc.) was ozonized at 0°. The ozonide was reductively cleaved using essentially Whitmore's method[9] and the volatile aldehyde was distilled into aqueous dimethone solutions (1%). The crude precipitate (35 mg.) was crystallized first from aqueous ethanol and then from petroleum ether. The bulk of the product was acetaldehydedimethone, m. p. 138–139°; mixed m. p. with an authentic specimen (m. p. 140–141°), 139–140°. A small amount (about 1 mg.) of formaldehydedimethone, m. p. 168–170°, also was obtained. Acid IV (20 mg.) was similarly treated; the crude dimethone weighed 35 mg. and it consisted almost entirely of acetaldehydedimethone, m. p. 138.5–139.5°; mixed m. p., 139.5–140.5°. A trace of formaldehydedimethone, m. p. 178–180°, was also obtained.

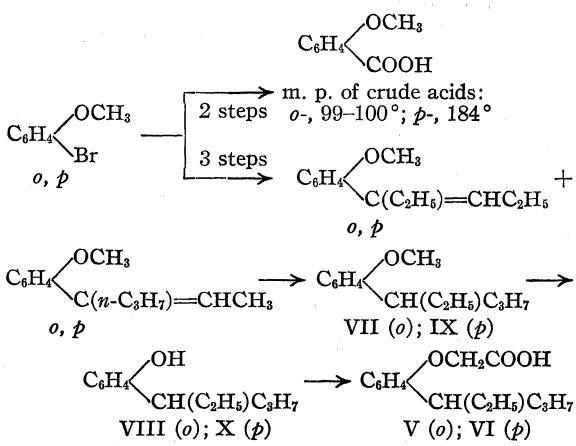
Reduction.—The pure acid III, m. p. 110–110.5°, (85 mg.) was reduced in absolute ether using a platinum oxide catalyst. After removal of the catalyst, the solvent was evaporated. The crystalline residue was taken up in ether and extracted with aqueous sodium bicarbonate (10%). Acidification of the aqueous layer precipitated ***o*-(3-hexyl)-phenoxyacetic acid** (V). After several crystallizations from petroleum ether, the acid melted at 65–66° although not sharply. Unfortunately there was insufficient material for further purification. The synthetic acid (see below) when first obtained melted at 65°; when completely purified, it melted sharply at 75–76°. The isomeric acid IV, m. p. 95.2–96° (120 mg.) was catalytically reduced in methanol using a platinum oxide catalyst. The product, an oil, was the methyl ester of the reduced acid. This was hydrolyzed by warming it for thirty minutes with aqueous sodium hydroxide (5 cc., 10%) and ethanol (5 cc.). Acidification of the mixture produced an oil which was removed by ether extraction. The ether solution was extracted with sodium bicarbonate; acidification of the bicarbonate solution precipitated ***p*-(3-hexyl)-phenoxyacetic acid** (VI) which was recrystallized from petroleum ether. It melted at 81–82°; when mixed with the synthetic acid (m. p. 82–83° see below) it melted at 81–83°.

Synthesis of *o*- and *p*-(3-Hexyl)-phenoxyacetic Acids. (V and VI.)—Since these acids were *o,p*-isomers, it was very important that the two bromoanisoles, *o*- and *p*-, be absolutely pure and not contaminated with each other. *o*-Bromophenol, prepared according to "Organic Syntheses"[10] from phenol, was converted into *o*-bromoanisole,

(9) Whitmore, THIS JOURNAL, **54**, 3711 (1932); **56**, 180 (1934).
(10) *Org. Syntheses*, **14**, 15 (1934).

but this product gave, via carbonation of the Grignard reagent, an *o*-anisic acid most of which melted at 92°, but which did not melt completely even at 105°. Recrystallization from petroleum ether did not give a product with a better m. p. Accordingly, it was decided to synthesize *o*-bromoanisole by a method involving intermediates the purity of which could be checked at each step. The routes from the bromoanisoles to the acids V and VI involved the same steps; these are shown in the chart.

SYNTHESIS OF *o*- AND *p*-(3-HEXYL)-PHENOXYACETIC ACIDS V AND VI



Ortho Series (experimental by H. E. UNGNADE)

***o*-Nitroanisole** (150 g.) in ethanol (100 cc.) was reduced with hydrogen (1200 lb. (80 atm.) pressure) at 100° in the presence of Raney nickel. The yield of ***o*-anisidine,** b. p. 100–101° under 9 mm., was 102 g. This anisidine gave an acetyl derivative which, without purification, melted at 85–86°.[11] The anisidine was converted to *o*-bromoanisole through the Sandmeyer reaction, according to the procedure of "Organic Syntheses"[12]; the yield of *o*-bromoanisole, b. p. 214–215°, was 100 g. One gram of this material was converted to the Grignard reagent, which was then carbonated. The crude *o*-anisic acid so produced melted at 99–100°.[13]

Hexanol-3.—To a Grignard solution prepared from ethyl bromide (93.8 g.) and magnesium (20.6 g.) was added purified butyraldehyde (62 g.). The product, isolated and purified in the usual way, boiled at 132–135° and weighed 40 g.

Hexanone-3.—The hexanol (40 g.) was oxidixed by dropping it, with stirring, into sodium dichromate (81.6 g.) in sulfuric acid (68 g.) and water (400 cc.) at such a rate that the temperature was maintained at 50–55°. The upper layer was separated, the aqueous layer was extracted with ether and the ether extract was combined with the organic layer. The solution was washed with sodium hydroxide solution (10%), then once with water and finally with calcium chloride solution. After drying over calcium chloride, the ether was removed and the residue fractionated. The main fraction (34 g.) was hexanone-3, b. p. 121–123.5°.

3-(*o*-Methoxyphenyl)-3-hexanol and *o*-Hexenylanisoles.—*o*-Bromoanisole (56 g.) was converted into the Grignard reagent, and to this was added hexanone-3 (30 g.) in ether. The product was isolated in the usual way, but the carbinol was not purified. Instead, it was distilled at atmospheric pressure with sulfuric acid (2 drops). The distillate was washed with sodium carbonate, then with water, and dried over calcium chloride. Fractionation gave 40 g. of a mixture of ***o*-hexenylanisoles** boiling at 120–125° under 14 mm.

***o*-(3-Hexyl)-anisole, (VII).**—The unsaturated anisole mixture (40 g.) was reduced in methanol (100 cc.) by hydrogen (42 lb. (3 atm.) pressure) in the presence of a platinum oxide catalyst. The product (37 g.) boiled at 104–105° under 9 mm.

Anal. Calcd. for $C_{13}H_{20}O$: C, 81.42; H, 10.41; *MR* calcd., 60.3. Found: C, 81.38; H, 10.77. $n^{20}D$ 1.4975–1.4976; d^{20}_{20} 0.9242; *MR* found, 60.8.

***o*-(3-Hexyl)-phenol, (VIII).**—The methoxy compound VII (10 g.), hydriodic acid (32 g., d. 1.50), acetic acid (70 cc.) and acetic anhydride (5 cc.) were refluxed for two hours. The mixture became homogeneous after an hour and a half. The cooled mixture was made alkaline with aqueous sodium hydroxide, and the phenol was liberated by passing a stream of carbon dioxide into the alkaline solution. The mixture was extracted with ether, the extract was thoroughly washed with water and dried over magnesium sulfate. After removal of the ether, the residue was distilled. The phenol VIII (5 g.) boiled at 109–111° under 10 mm. It was colorless, possessed a faint aromatic odor and was fairly soluble in 5% aqueous alkali.

Anal. Calcd. for $C_{12}H_{18}O$: C, 80.89; H, 10.18; *MR* calcd., 55.8. Found: C, 80.27, 80.10; H, 9.55, 10.22; $n^{20}D$ 1.5099; d^{20}_4 0.9531; *MR* found, 55.8.

***o*-(3-Hexyl)-phenoxyacetic Acid (V).**—Ethyl bromoacetate (5 cc.) was added to a solution of the phenol VIII (3.56 g.) in sodium ethoxide (0.46 g. of sodium in 20 cc. of absolute ethanol). Following the procedure described above for the phenol mixture, the acid V (m. p. 65° after one crystallization) was isolated. Crystallized several times from petroleum ether, it melted at 75–76°.

Anal. Calcd. for $C_{14}H_{20}O_3$: C, 71.19; H, 8.48; neut. equiv., 236. Found: C, 70.81; H, 8.69; neut. equiv., 239.

Para Series (experimental by R. M. LEEKLEY)

***p*-Bromophenol** was prepared according to "Organic Syntheses"[12] (p. 123) and was converted to *p*-bromoanisole by a procedure also given in "Organic Syntheses"[12] (p. 50). A small amount of the ***p*-bromoanisole** was converted to the Grignard reagent and the latter was carbonated. The crude *p*-anisic acid so obtained melted at 184°.[14]

3-(*p*-Methoxyphenyl)-3-hexanol and *p*-Hexenylanisoles.—*p*-Bromoanisole (40 g.) (0.25 mole) in ether (150 cc.) was converted into the Grignard reagent, and to this was added hexanone-3 (20 g., 0.20 mole) in ether (50 cc.). The product was isolated in the usual way and, after re-

(11) Kaufmann, *Ber.*, **42**, 3482 (1909), gives the m. p. as 87–88° after purification.

(12) "Organic Syntheses," Coll. Vol. I, John Wiley & Sons, Inc., New York, N. Y., 1932, p. 131.

(13) Claisen, *Ann.*, **418**, 87 (1919), gives the m. p. as 100–101° after purification.

(14) Oppenheim and Pfaff, *Ber.*, **8**, 893 (1875).

moval of the solvent, a drop of sulfuric acid was added and the residue distilled under atmospheric pressure. The distillate was again distilled from a drop of sulfuric acid, the second distillate was dried over calcium chloride and redistilled under 15 mm. pressure. The portion boiling at 125–130° (23 g.) was a colorless, mobile liquid, $n^{20}D$ 1.5223, consisting of the *p*-hexenylanisoles.

Anal. Calcd. for $C_{13}H_{18}O$: C, 82.04; H, 9.54. Found: C, 82.04; H. 9.52.

***p*-(3-Hexyl)-anisole (IX).**—The above hexene (9.9 g.) in methanol (100 cc.) was reduced with hydrogen (45 lb. (3 atm.) pressure) in the presence of 0.2 g. of palladized calcium carbonate (5% palladium). The catalyst was removed, most of the methanol was evaporated and the residue was washed with water. The oil was separated with a little ether, dried over calcium chloride, and distilled. The hexane (5.4 g.) boiled at 125–125.5° under 15 mm., $n^{20}D$ 1.4988.

Anal. Calcd. for $C_{13}H_{20}O$: C, 81.18; H, 10.49. Found: C, 81.51; H, 10.12.

***p*-(3-Hexyl)-phenol (X).**—The *p*-methoxy compound IX (16.5 g.), acetic acid (40 cc.) and constant boiling hydriodic acid (60 cc.) were refluxed for three and one-half hours. The mixture was made alkaline with aqueous sodium hydroxide (25%) and the alkaline solution was saturated with carbon dioxide to liberate the phenolic product. The mixture was extracted with ether and the ethereal solution was dried over magnesium sulfate. After removal of the ether, the residue was distilled under reduced pressure (14 mm.) from a flask with a short neck. The distillate then was redistilled. The fraction boiling at 134–145° under 14 mm. solidified to a mushy solid which melted slightly above room temperature. It was almost colorless and weighed 5 g.

Anal. Calcd. for $C_{12}H_{18}O$: C, 80.83; H, 10.18. Found: C, 80.51; H, 9.87.

***p*-(3-Hexyl)-phenoxyacetic Acid (VI).**—Ethyl bromoacetate (5 g.) was added to a solution of the phenol X (3.56 g.) in sodium ethoxide (0.46 g. of sodium in 20 cc. of absolute ethanol). Using the procedure described above for handling the phenol mixture, the ethereal solution of acid VI was extracted with saturated sodium bicarbonate. Acidification of the bicarbonate solution produced an oil which solidified when rubbed with a glass rod. The solid was removed and crystallized from petroleum ether, then from dilute acetic acid, and again from petroleum ether. At this point the product weighed 280 mg., but it was not analytically pure. Three more crystallizations from petroleum ether (b. p. 90–100°) gave a product which melted at 82–83°. When mixed with the acid VI (m. p. 81–82°) obtained from the monoalkenylphenol mixture the substance melted at 81–83°.

Anal. Calcd. for $C_{14}H_{20}O_3$: C, 71.19; H, 8.48. Found: C, 71.10; H, 8.63.

Summary

1. Phenol in the presence of potassium carbonate and acetone reacts with 4-chloro- and 4-bromohexene-2 to give mono- and diallylation products as well as a phenyl ether.

2. All of these products are mixtures.

3. The monoalkenylphenol portion of the reaction product contains ortho and para α-ethylcrotylphenol. These phenols were isolated as the corresponding aryloxyacetic acids, which were reduced to the 3-(*o*- and *p*-carboxymethyl)-hexanes, and the structures of these were proved by synthesis.

4. The diallylation product consisting of 2,6-diallylated phenols showed vitamin E activity in 50-mg. doses. The phenyl hexenyl ether, the mono allylated phenols, and the cyclized products derived from them, showed no vitamin E activity.

MINNEAPOLIS, MINNESOTA RECEIVED JULY 17, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE STATE COLLEGE OF WASHINGTON]

The Odor of Alkoxy Diphenyls

BY C. M. BREWSTER AND IVAN J. PUTMAN, JR.

In a study of the osmophoric properties of ethers it seemed of interest to examine alkyl ethers of the hydroxy-diphenyls, as few compounds of this class have been prepared or studied, and the substitution of a phenyl radical for a nuclear hydrogen atom might be expected to weaken the strong odor of the mononuclear phenolic ethers.

Durrans[1] in his extensive survey of the odors of organic compounds stated that while etherification nearly always produces compounds of pleasant aromatic odor, the replacement of the hydroxyl hydrogen by an alkyl group may or may not strengthen the odor. In methyl *p*-tolyl ether, for example, the odor is strengthened, but in eugenol methyl ether the introduction of the same alkyl group markedly weakens the odor. We have found little difference in intensity of odor between the alkyl ethers and the unsubstituted phenols in the present series of compounds.

(1) Durrans, *Perf. Ess. Oils Rec.*, **10**, 104–136 (1919).

The most unusual fact in connection with the odor of these ethers is that in each case the ortho compound is stronger in odor than the para, although even with the ortho ethers the odor is faint, whether examined at room temperature or heated to 100°. This is contrary to the results summarized by Durrans, who found that in most instances the para ether has the stronger odor.

Unsaturation in the substituted alkyl group does not seem to be of great importance; a slight strengthening of odor was noted in the allyl ethers, without appreciable change in character.

There is no marked difference in procedure in making the ethers described in this paper, except that the reactions take place more slowly and with greater difficulty than in forming the mononuclear ethers,[2] which is to be expected from the greater molecular weight. When a third phenyl group is introduced, as in the benzyl ether of *p*-hydroxydiphenyl, the reactivity is increased since the radical has the effect of an alkyl group.

Experimental

2-Diphenyl-propyl Ether.—A mixture of 15 g. of *o*-hydroxydiphenyl and 3.8 g. of sodium hydroxide was refluxed on a water-bath with 85 cc. of acetone[3] for one hour. Fifteen grams of propyl bromide was added in small portions, and the mixture gently refluxed for six hours. Soon after addition of the propyl bromide a granular precipitate of sodium bromide began to separate. At the end of the reaction the solvent was removed by distillation, and the yellow liquid dissolved in ether, washed twice with water, and the ether solution dried with sodium sulfate. The ether solution was refluxed with activated carbon for one hour, filtered, the ether distilled off and the residual oil fractionated *in vacuo*. The water-white liquid has a faint aromatic odor, b. p. 303°; yield from 15 g. of the phenol, 17 g.

Anal. Calcd. for $C_{15}H_{16}O$: C, 84.85; H, 7.60. Found: C, 84.48, 84.52; H, 7.65, 7.67.

The methyl ether of *o*-hydroxydiphenyl was prepared by the same method, using methyl iodide as the halide. The colorless oil has a faint, slightly pungent fruity-aromatic odor; b. p. 288°. Borsche and Scholten[4] used methyl sulfate; they give the b. p. as 274°; yield from 10 g. of the phenol, 9 g.

The ethyl ether of *o*-hydroxydiphenyl was prepared easily by the method which we used for the propyl ether; the halide used was ethyl bromide. Hönigschmid[5] used a somewhat different procedure; our simpler method gives an equally pure product, m. p. 34°. The odor of the crystals is faint and aromatic, resembling that of the methyl ether, but somewhat sweeter and more flower-like; yield from 10 g. of the phenol, 9 g.

2-Diphenyl-isopropyl Ether.—Ten grams of *o*-hydroxydiphenyl and 2.5 g. of sodium hydroxide were refluxed in 75 cc. of acetone for one hour, then 15 g. of isopropyl bromide was added in small portions, and the reaction mixture gently boiled for six hours. To determine the progress of the reaction, a few drops were removed, the solvent evaporated, the residue shaken with dilute sodium hydroxide and ligroin, and the alkaline layer acidified. The product when refined and fractionated *in vacuo* was a water-white liquid of faint aromatic odor, b. p. 315–317°, with slight decomposition at this temperature; yield from 10 g. of the phenol, 10 g.

Anal. Calcd. for $C_{15}H_{16}O$: C, 84.86; H, 7.60. Found: C, 84.72; H, 8.13.

2-Diphenyl-allyl Ether.—Following the procedure for the propyl ether, allyl bromide was used and almost immediately after the addition of the first portion the solution became cloudy and sodium bromide began to separate. After three hours of refluxing the reaction was complete. The product when purified and fractionated *in vacuo* gave a colorless liquid which has the same pleasant odor as the propyl ether; slightly stronger, but weaker than the ethyl ether. The boiling point is 312°, with slight darkening which begins about 280°. There is no marked change or further decomposition even when the ether is held for one hour at a temperature above 280°. Auwers and Wittig[6] obtained a less stable ether from *o*-hydroxydiphenyl, sodium ethylate and allyl bromide, for when heated to 250° they obtained a green colored oil with bluish fluorescence, and proved that their ether had undergone the Claisen shift. From 12 g. of the phenol we obtained a yield of 13 g. of the ether.

Anal. Calcd. for $C_{15}H_{14}O$: C, 85.67; H, 6.72. Found: C, 85.39; H, 6.79.

2-Diphenyl-benzyl Ether.—When benzyl chloride was condensed similarly, the yield was about 25%, even after refluxing the mixture for six hours. The unchanged benzyl chloride was distilled off, and the residue washed repeatedly with 25% aqueous sodium hydroxide to remove unchanged *o*-hydroxydiphenyl. The pale yellow liquid was dissolved in ether and refluxed with activated carbon; the filtrate was deep orange but on evaporation of the ether and continued drying at 55°, it became light yellow again. It is a nearly colorless, viscous liquid which boils with slight decomposition at 324°; yield, from 12 g. of the phenol, 4 g. At room temperature the compound is practically odorless, but when heated to 100° it has a pleasant nut-like odor.

Anal. Calcd. for $C_{19}H_{16}O$: C, 87.65; H, 6.20. Found: C, 87.46; H, 6.26.

4-Diphenyl-ethyl Ether.—The reaction mixture was prepared and refluxed as for the ortho compound; changes in appearance during the reaction were the same. Acidification of the filtrate gave no precipitate of *p*-hydroxydiphenyl; the yield was nearly quantitative; minute white

(2) We obtained only small yields when alcohol was used as solvent, although with mononuclear phenolic ethers this solvent is quite satisfactory.

(3) Claisen and Eisleb [*Ann.*, **401**, 29 (1913)] recommended the use of acetone as solvent in the preparation of ethers. If a higher boiling point solvent is necessary, methyl ethyl ketone is to be preferred.

(4) Borsche and Scholten, *Ber.*, **50**, 601 (1917).

(5) Hönigschmid, *Monatsh.*, **22**, 569 (1901).

(6) Auwers and Wittig, *J. prakt. Chem.*, **108**, 99–112 (1924).

leaflets from alcohol, m. p. 76°. The compound is odorless; yield from 12 g. of the phenol, 11 g.

Anal. Calcd. for $C_{14}H_{14}O$: C, 84.58; H, 7.36. Found: C, 84.26; H, 7.16.

The methyl ether of *p*-hydroxydiphenyl, first prepared by Werner,[7] was obtained in nearly quantitative yield, using methyl iodide as the halide, m. p. 90°. The very minute water-white granular crystals have no odor.

4-Diphenyl-propyl Ether.—Propyl bromide was condensed with *p*-hydroxydiphenyl as in the preparation of the ortho ether. The product when purified and crystallized from alcohol gave white leaflets, m. p. 76–77°. It is difficultly soluble in petroleum ether; yield from 10 g. of the phenol, 9 g., odorless.

Anal. Calcd. for $C_{15}H_{16}O$: C, 84.85; H, 7.60. Found: C, 84.62, 84.71; H, 7.55, 7.60.

4-Diphenyl-isopropyl Ether.—Isopropyl bromide was used as the halide. The reaction in acetone took place more slowly than in the case of the ortho ether. Dull white needles were obtained from slow evaporation of an alcoholic solution, and hexagonal leaflets from more concentrated solutions; m. p. 73°, odorless; yield from 10 g. of the phenol, 4 g.

Anal. Calcd. for $C_{15}H_{16}O$: C, 84.85; H, 7.60. Found: C, 84.51; H, 7.66.

4-Diphenyl-allyl Ether.—Large transparent leaflets from alcohol; m. p. 86–87°, odorless; yield from 12 g. of the phenol, 14 g. The melted crystals show a slight darkening when heated to 290°, but there is no further decomposition when maintained at or above this temperature for one hour.

Anal. Calcd. for $C_{15}H_{14}O$: C, 85.67; H, 6.72. Found: C, 85.43; H, 6.79.

4-Diphenyl-*n*-butyl Ether.—Butyl bromide was used as the halide. The filtrate on acidification gave negligible quantities of unchanged *p*-hydroxydiphenyl; large white leaflets from alcohol; m. p. 74–75°, odorless; yield from 10 g. of the phenol, 13 g.

Anal. Calcd. for $C_{16}H_{18}O$: C, 85.67; H, 6.72. Found: C, 85.43; H, 6.79.

4-Diphenyl-benzyl Ether.—Using benzyl chloride as halide, the odorless ether was obtained in nearly quantitative yield; from 12 g. of the phenol, 18 g. of the ether was prepared; heavy white plates from alcohol, m. p. 136°.

Anal Calcd. for $C_{19}H_{16}O$: C, 87.45; H, 6.20. Found: C, 87.35, 87.65; H, 6.25; 6.20.

We were not successful in preparing the *s*-butyl, *t*-butyl or *n*-amyl ether by this method using acetone as solvent, nor by trials with copper as catalyst, nor with benzene as solvent. However, preliminary trials with reagents heated in sealed tubes have been attended with some success and will be reported on later.

Summary

Several new alkyl ethers of *o*- and *p*-hydroxydiphenyls have been prepared by a simplified method. The ortho ethers possess a fragrant odor, but the para ethers are odorless.

PULLMAN, WASHINGTON RECEIVED AUGUST 30, 1939

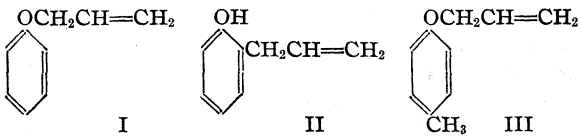
(7) Werner, *Ann.*, **322**, 167 (1902).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ROCHESTER]

The Claisen Rearrangement. I. A Kinetic Study of the Rearrangement of Allyl *p*-Tolyl Ether in Diphenyl Ether Solution

BY JOHN F. KINCAID AND D. S. TARBELL

The rearrangement of allyl aryl ethers, illustrated by the conversion of allyl phenyl ether (I) to *o*-allylphenol (II), has been investigated extensively since its discovery by Claisen,[1] and numerous features of the reaction mechanism have been established. The object of our work is to make a kinetic study of the rearrangement of allyl ethers of various types to obtain further information about the Claisen rearrangement. We wish to report a study of the kinetics of the rearrangement of allyl *p*-tolyl ether (III) in diphenyl ether solution at 214.7, 200.6, and 185.8°. At the second temperature the effect of acids, bases, and oxygen on the rate was studied, and the rate of the rearrangement of the pure liquid allyl *p*-tolyl ether was measured at the two lower temperatures.



I II III

Experimental

Preparation of Materials

Allyl *p*-tolyl ether was prepared by the method of Hurd and Yarnall,[2] using Eastman redistilled *p*-cresol, allyl bromide, and sodium hydroxide in aqueous acetone solution. The reaction mixture was worked up by the procedure referred to, and in addition the ether was washed several times with sodium hydroxide solution to remove unreacted cresol. The product was distilled through a modified Widmer vacuum-jacketed column at 4 mm. and

(1) Claisen, *Ber.*, **45**, 3157 (1912).

(2) Hurd and Yarnall, THIS JOURNAL, **59**, 1686 (1937).

bath temperature of 110–115°, b. p. 65 ± 1°, due to pressure fluctuations, d^{35}_4 0.9494. A blank determination showed that this sample contained 0.5% of its rearrangement product or an equivalent amount of acetylatable material. Some of the rate runs were made with a sample of ether prepared in a similar manner containing 1.8% of rearrangement product, but proper corrections were applied in both cases.

Diphenyl ether (Dow technical grade) was stirred overnight with sodium wire while being heated on the steam-bath and the precipitate filtered off; treatment with another batch of sodium gave no appreciable reaction. The material was then stirred with mercury to remove sulfur compounds, but this appeared to be unnecessary, as no darkening of the metal occurred. After removing the mercury by filtration, the diphenyl ether was washed with dilute hydrochloric acid, sodium hydroxide solution, water, dried with calcium chloride, followed by solid potassium hydroxide, and distilled in a nitrogen atmosphere, some samples being distilled at atmospheric pressure, and some in vacuum. A blank determination on this ether showed no acetylatable material present within the experimental error.

The fact that different samples of allyl *p*-tolyl ether and diphenyl ether gave identical values for the rate constant was shown by values of k of 8.03×10^{-5} for a new solution, compared to 8.13×10^{-5} for the stock solution with which most of the runs at 200° were made.

Dimethylaniline was distilled with acetic anhydride, washed free of acid with sodium carbonate solution and water, dried over potassium hydroxide and distilled, b. p. 192–192.5°. A blank determination showed no acetylatable material present.

Method of Analysis.—The reaction was followed by a modification of the Verley and Bölsing[3] method for determining phenols, which consists in the quantitative acetylation of the phenol by a mixture of acetic anhydride and pyridine, followed by the determination by titration of the unused acetic anhydride. An amount of the reaction mixture containing from 0.2 to 0.4 g. of the rearrangement product was weighed into a 50-cc. iodine flask, 2 cc. of an approximately 2 molar solution of acetic anhydride in pyridine was pipetted in, and the mixture heated for an hour on the steam-bath. In order to obtain consistent results, it was found necessary to put a liquid seal of mercury around the stopper, and the stopper was held in place by rubber bands. After cooling, the contents of the flask were transferred to a beaker containing 100 cc. of water, using carbon tetrachloride to rinse the flask, and the acetic acid titrated with 0.2 *N* alkali with vigorous stirring. Since it was impossible to use indicators in the presence of the organic liquids, the titrations were carried out with a Beckmann *p*H meter to a *p*H of 8.6. Analyses of known mixtures showed the average deviation to be about 1%, and the error in analysis was very rarely as great as 2.5%. Runs in which the mixture was heated longer than an hour showed that no appreciable percentage of the ether rearranged on heating for an hour at 100°.

Experimental Procedure.—Preliminary experiments showed that considerable material was lost by evaporation when the rearrangement reaction was carried out in glass-stoppered flasks at 200°, so that the rate constants for longer runs were as much as 25% low. Consequently, the data given below were obtained by a procedure in which each sample was placed in a glass tube, the tube cooled in an ice-bath, and sealed off after being evacuated by an oil pump. In a trial experiment in which a tube containing a one molar solution was pumped out with an oil pump for thirty minutes at room temperature, the constant was only 4% lower than that obtained by the usual technique. Therefore the loss by evaporation during the evacuation of the tubes under the conditions used was negligible. Runs were carried out by completely immersing the sample in a well-stirred oil thermostat, kept constant to 0.1° by a mercury thermoregulator and relay. Constancy of the thermostat temperature was checked by a thermometer reading to 0.1°, and the temperature at each setting of the thermostat was determined by a one-junction copper–constantan thermocouple which was calibrated against the melting point of tin. The temperatures are estimated to have an absolute accuracy of ±0.3°, and to have a relative accuracy of ±0.1°.

The time necessary for the sample to come to the bath temperature after its immersion, estimated from blank experiments, was found to be about two hundred seconds,[4] and this was subtracted from all the observed times of reaction. This figure, although not known very accurately, is important only for the shorter runs.

Isolation of the Product of the Rearrangement.—Forty grams of allyl *p*-tolyl ether was heated in sealed tubes without solvent for thirteen hours at 200°, and analysis in the usual way showed that 97.7% (average of two analyses) of the theoretical amount of the rearrangement product was present. The product (40.3 g.) was distilled in a nitrogen atmosphere through the modified Widmer column at a pressure of two to three mm. and distillation temperature ranging from 68.7 to 73.7°. Each fraction was analyzed in duplicate for phenolic hydroxyl and the molecular weights calculated are given in the table.

RESULTS OF FRACTIONATION

Fraction	Wt., g.	Mol. wt.[a]
1	1.3	151.3
2	16.5	149.2
3	13.1	150.8
4	3.4	148.1
5 (Residue)	2.4	

[a] Molecular weight of 2-allyl-4-methylphenol, 148.2.

Fraction 5 was transferred to a 5-cc. Claisen flask and redistilled, getting 0.8 g., b. p. 76–87° at 2 mm., molecular weight 162.6, and 1.55 g. of undistillable material. The 3.6 g. of material not accounted for was held up in the Widmer column, and evidently was mainly the normal rearrangement product, since fraction 4 had the correct molecular weight. The possibility that the undistillable part of fraction 5 was formed during the distillation rather than during the rearrangement was eliminated by redistilling fractions 1, 2, 3, and 4 under the same conditions, when no non-volatile residue was found.

Effect of Oxygen on the Rearrangement.—Four tubes were prepared to contain varying amounts of air and oxy-

(3) Verley and Bölsing, *Ber.*, **34**, 3354 (1901).

(4) MacDougall, Lauer and Spielman [THIS JOURNAL, **55**, 4089 (1933)] used a correction of three minutes in a similar case.

gen, and the rate measured at 200.2°. Tube 1 contained 1 atm. of pure oxygen, tube 2 was evacuated and sealed by the usual method, tube 3 was alternately frozen and melted two times under vacuum to remove all dissolved gases, and tube 4 had air bubbled through it for thirty hours before being evacuated and sealed as usual. The rate constants after being corrected to 200.6° for the four samples were 7.87, 7.48, 7.41, and 7.89, each multiplied by 10^{-5}. The allyl *p*-tolyl ether employed in these experiments had been freshly distilled to remove any traces of peroxide. While these results indicate that the rate of the rearrangement is not appreciably affected by the presence of oxygen, the occurrence of some side reaction under these conditions is indicated by the yellow color of the reaction mixture. Runs carried out with the usual technique were colorless even after the heating had been continued until the rearrangement was virtually complete.

Experimental Results

TABLE I

FIRST ORDER RATE CONSTANTS AT 200.6°

Time, sec.	$k \times 10^5$, sec.$^{-1}$	% reaction
4.77% Allyl *p*-tolyl ether and 95.23% diphenyl ether		
2260	7.65	15.88
4600	7.34	28.66
8320	7.30	45.52
12460	7.43	60.21
21580	7.89	81.77
	Mean 7.52	
13.30% Allyl *p*-tolyl ether and 86.70% diphenyl ether		
1960	7.96	14.45
3580	8.03[a]	24.93
5260	8.29	35.36
12040	8.54	64.22
14980	8.89	73.61
22240	8.55	85.08
	Mean 8.38	

[a] Solution of new materials, 14.22%.

22.81% Allyl *p*-tolyl ether and 77.19% diphenyl ether		
1180	9.04	10.11
3340	8.66	25.14
6940	8.67	45.20
11980	9.51	68.00
19300	9.76	84.80
	Mean 9.13	
100% Allyl *p*-tolyl ether		
1315	9.82	12.12
1570	9.65	13.81
2950	10.49	26.61
3280	10.60	29.37
7120	14.81	65.16
8380	16.61	75.13
8680	17.10	77.34
12.00% Allyl *p*-tolyl ether, 9.81% dimethylaniline and 78.19% diphenyl ether		
2140	8.87	17.29
4900	8.58	34.31
11860	8.34	62.81
19180	8.81	81.54
	Mean 8.65	
13.43% Allyl *p*-tolyl ether, 0.81% acetic acid and 85.76% diphenyl ether		
1600	10.0	14.79
2320	9.41	19.62
5200	9.28	38.28
10600	9.62	63.93
19780	9.88	85.82
	Mean 9.64	

TABLE II

FIRST ORDER RATE CONSTANTS AT 185.8°

Time, sec.	$k \times 10^5$, sec.$^{-1}$	% reaction
14.22% Allyl *p*-tolyl ether and 85.78% diphenyl ether		
5200	2.68	13.02
11080	2.56	24.64
18280	2.56	37.32
31540	2.72	57.56
43000	2.87	70.88
	Mean 2.69	
100% Allyl *p*-tolyl ether		
4600	3.06	13.11
8080	3.28	23.24
10720	3.62	32.13
17800	4.74	57.01
26860	6.30	81.62

TABLE III

FIRST ORDER RATE CONSTANTS AT 214.7°

Time, sec.	$k \times 10^5$, sec.$^{-1}$	% reaction
14.22% Allyl *p*-tolyl ether and 85.18% diphenyl ether		
580	24.9	13.46
1360	22.9	26.55
2260	22.6	39.97
4060	22.5	59.92
6940	22.7	79.34
	Mean 23.1	

The results of runs performed at the three temperatures are tabulated in Tables I to III. The first order rate constants k were calculated from the usual equation

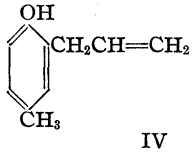
$$k = (1/t)\ 2.303 \log x_0/x \qquad (1)$$

in which x_0 is the initial percentage of reactant and x is the percentage of reactant remaining at time t (in seconds). The results show that the reaction is strictly unimolecular over the range of temperature and concentration studied; at 200.6° the concentrations measured cover a nearly five-fold range, from 4.77 to 22.81% (approximately 0.3 to 1.5 molar), in addition to the measurements on the pure liquid. The first order "constants" for the pure liquid (Tables I and II) show a marked increase as the reaction proceeds, but the initial rate in the pure liquid extrapolates to the same value as in solution. It should be emphasized that the use of equation (1) in this case leads to rate constants for the longer runs which

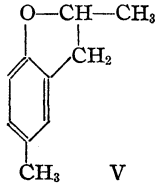
are much too low since a constant value for k is assumed in the integration leading to equation (1). Actually the rate of the rearrangement of the ether in the presence of 80% of 2-allyl 4-methylphenol is more than four times as great as it is at the beginning of the reaction, although the rate constants for 80% reaction given in Tables I and II are only about double the initial values.

The effect of dimethylaniline on the rate is of interest because Claisen[5] stated that better yields were obtained in some cases of the rearrangement when a basic solvent was used, and dimethylaniline is frequently employed as solvent when the reaction is carried out on a preparative scale. As the data in Table I show, 10% of dimethylaniline has no appreciable effect on the rate of the rearrangement.

It seemed likely that the upward drift of the rate constants in the pure liquid was due to the catalytic effect of the phenol formed acting as an acid. To test the possibility that the reaction was acid catalyzed, a run was made using as solvent a 0.81% solution of acetic acid in diphenyl ether, but the rate was not affected appreciably (Table I). The possibility of error due to isomerization[6] of the 2-allyl 4-methylphenol (IV) formed by rearrangement to a coumarane derivative V by the acid present was eliminated by trial runs



IV

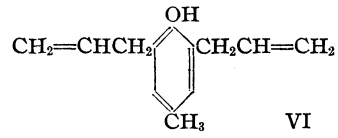


V

with known amounts of the phenol. An attempt to measure the effect of a stronger acid, chloroacetic, failed, because runs with known samples showed the analytical method was not reliable in the presence of chloroacetic acid; the results indicated qualitatively that there was no striking increase in the rate, however.

The rate of rearrangement is not affected by the presence of air or oxygen, as is clear from runs described in the experimental part.

To find whether side reactions take place during the rearrangement, the isolation of the products of the reaction described in the experimental part was carried out. The results show that less than 1% of 2,6-diallyl-4-methylphenol (VI) was



VI

formed, which Hurd and Yarnall[2] isolated in a few per cent. yield from the rearrangement of allyl p-tolyl ether carried out at higher temperature. We obtained 4% of non-volatile rearrangement product, possibly analogous to the dimer[7] isolated from the rearrangement of allyl phenyl ether. The rest of the material isolated, amounting to 87%, was pure rearrangement product, and the material not accounted for which was held up in the still was probably mainly the same thing. Since polymerization should be less important during rearrangement in solution than in the pure liquid, it seems safe to conclude that in solution the reaction is at least 95% quantitative.

Discussion

The energy of activation, ΔE, for the reaction was computed from the mean values of the rate constants for the 14% (1 molar) solutions at the three temperatures. The constants of the Arrhenius equation, $k = A \exp(-\Delta E/RT)$, were found to be 1.60×10^{11} sec.$^{-1}$ and 33.1 kcal./mole for A and ΔE, respectively. These quantities may be interpreted with the aid of the equation due to Eyring[8] for the absolute rate of any reaction

$$k = (kT/h)\,\kappa \exp(\Delta S^{\ddagger}/R) \exp(-\Delta E^{\ddagger}/RT) \quad (2)$$

Here k is Boltzmann's constant, h is Planck's constant, κ is the transmission coefficient and $\Delta S^{\ddagger}$ and $\Delta E^{\ddagger}$ are the entropy and energy of activation, respectively. Following the usual practice of assuming that κ equals unity, we find that $\Delta S^{\ddagger}$ equals -8.1 e. u./mole at 200°, *i. e.*, the activated complex is poorer in entropy by 8.1 units than the normal reactant molecule.

Two structures for the activated complex seem possible. The γ carbon atom on the allyl group might be expected to start to form a bond with the carbon atom ortho to the oxygen simultaneously with the breaking of the carbon–oxygen bond. A second mechanism is one in which the slow step is the breaking of the carbon–oxygen bond, the allyl group being split off as a radical or positive ion, although any mechanism in which the allyl group is ever free seems inconsistent

(5) Claisen, *Ann.*, **418**, 69 (1918).

(6) Claisen and Tietze, *Ber.*, **59**, 2344 (1926); Bartz, Miller and Adams, THIS JOURNAL, **57**, 371 (1935).

(7) Hurd and Schmerling, *ibid.*, **59**, 107 (1937).

(8) Eyring, *J. Chem. Phys.*, **3**, 107 (1935).

with the findings of Hurd and Schmerling,[7] who rearranged a mixture of allyl ethers without finding mixed products. The ring closure mechanism would be expected to involve a considerably larger entropy decrease than is observed here, while in the absence of strong solvation effects the second mechanism should involve an entropy *increase* on the formation of the activated complex. Since it seems impossible to prove the exact mechanism from the data available at present, further discussion will be deferred until later papers of this series.

Summary

1. The rate of the rearrangement of allyl *p*-tolyl ether in diphenyl ether solution has been measured at 214.7, 200.6, and 185.8°, the reaction being followed by determination of the phenol formed by quantitative acetylation with pyridine and acetic anhydride.

2. Over this temperature range and for a five-fold change in concentration the reaction is unimolecular, and the initial rate of the rearrangement in the pure liquid is the same as in solution.

3. The rate is not appreciably affected by the addition of 10% of dimethylaniline, 1% of acetic acid, or by the presence of air or oxygen.

4. The energy of activation is 33.1 kcal./mole, the data for the one normal solutions being represented by the expression $k = 1.60 \times 10^{11} \exp(-33.1/RT)$.

5. The rearrangement has been shown to be at least 95% quantitative at 200° in solution.

ROCHESTER, N. Y. RECEIVED AUGUST 14, 1939

[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY, THE UNIVERSITY OF CHICAGO]

Sulfonation Reactions with Sulfuryl Chloride

BY M. S. KHARASCH AND ALICE TANNER READ[1]

Introduction

In a recent paper[2] chlorination reactions with sulfuryl chloride were discussed, and it was shown that many types of organic molecules can be chlorinated with this reagent by the use of a peroxide catalyst. If the mechanism which was postulated for that reaction is correct, namely, a chain reaction involving the formation of chlorine atoms and SO_2Cl free radicals, then sulfonation as well as chlorination should take place, by the direct action of the SO_2Cl radical on the hydrocarbon, *i. e.*, sulfuryl chloride should, under the proper conditions, be a sulfonating as well as a chlorinating agent. Although no sulfonation products are isolated from the peroxide-catalyzed reaction, even when the sulfuryl chloride is added slowly (a procedure which minimizes any inhibitory effect of sulfuryl chloride itself), other catalysts have been found which, in the light, give both sulfonated and chlorinated products, the proportion of each being dependent upon the type of catalyst and the conditions used. With the exception of peroxides, which yield only the chlorinated hydrocarbons both in the dark and in the light, none of the catalysts investigated were very active in complete darkness. If the reaction were allowed to continue for some time, a small yield of chlorinated product could be obtained, but in no case did we obtain in the absence of light more than a trace of sulfonated product.

Discussion

Since a free-radical mechanism has been demonstrated in the addition of mercaptans to unsaturated molecules in the presence of oxygen,[3] the mercaptan type of compound seemed a likely catalyst for reactions with sulfuryl chloride. A number of such compounds were tried in preliminary test-tube experiments and found to be effective in starting the reaction. The most promising of these were studied on a larger scale with cyclohexane, which was selected as a suitable hydrocarbon because all the hydrogen atoms in this molecule are equivalent, and the products, cyclohexyl chloride and cyclohexylsulfonyl chloride, are easily separated and identified. In all the reactions in which the mercaptan type of catalyst was used, sulfonation as well as chlorination took place. In order to ascertain the op-

(1) When the experimental part of this work was almost complete, but before it was written up, Mrs. Read died suddenly. Her cheerful coöperation in many problems in this Laboratory, her delightful sense of humor, her enthusiasm and devotion to duty, will long be cherished by her associates.—(M. S. K.)

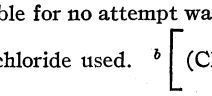
(2) Kharasch and Brown, THIS JOURNAL, **61**, 2142 (1939).

(3) Kharasch, Read and Mayo, *Chemistry and Industry*, **57**, 752 (1938).

TABLE I

CATALYZED REACTION BETWEEN SULFURYL CHLORIDE AND CYCLOHEXANE

Expt.	Catalyst	Conditions	% Yield[a] Chlorination	% Yield[a] Sulfonation	Ratio RSO_2Cl/RCl
1–3	2-Mercaptothiazoline	Dark, in absence and presence of O_2 and SO_2	6.7–15.8	0.0–6.8	0.0–0.43
4–12	2-Mercaptothiazoline	Irradiated, in absence and presence of O_2, SO_2, and H_2O	45.1–58.9	11.0–20.1	0.19–0.35
13	2-Mercaptothiazoline	Irradiated, C_6H_6 as solvent	28.6	34.0	1.2
14–17	Selenide[b]	In diff. light, and irradiated	5.1–51.8	0.0–7.7	0.0–0.15
18–20	Thiourea, thiosinamine, thiourea, resp.	Irradiated	20.2–52.2	0.0–14.9	0.0–0.29
21–24	Tuads[c]	In diff. light, and irradiated	24.6–51.2	8.8–18.2	0.21–0.41
25–26	Thionex[d]	In diff. light, and irradiated	20.2–44.4	5.9–17.8	0.29–0.40
27–36	2.6-Diaminopyridine	Irradiated, with and without filters in presence and absence of O_2 and SO_2	26.9–54.9	3.5–28.5	0.12–0.67
37	2,6-Diaminopyridine	Irradiated; C_6H_6 as solvent[e]	20.9	46.3	2.2
38–41	Pyridine	Irradiated	23.6–44.8	11.0–51.5	0.3–2.2
42	Pyridine	Irradiated; C_6H_6 as solvent[e]	9.4	54.8	5.3
43–50	Nicotinamide, pyridinum acetohydrazide, phenanthroline, aniline, ethanolamine, metal, *p*-phenylenediamine, dimethylstearylamine oxide, resp.	Irradiated[e]	10.8–70.7	0.0–33.8	0.0–0.87
51–56	Quinoline, quinaldine, piperidine, morpholine, cyclohexyldimethylamine stearylamine, resp.	Irradiated[e]	25.3–36.7	37.7–47.1	1.1–1.6
57–58	Diphenylamine, Triphenylamine, resp.	Irradiated[e]	No reaction		...
59–60	Triphenylamine + pyridine	Irradiated[e]	24.6–29.0	42.5–46.3	1.5–1.9
61	None	Irradiated[e]	42.1	...	...

[a] Yields recorded do not represent the maximum, obtainable for no attempt was made to trap material carried off by escaping gases. Yields are calculated on basis of sulfuryl chloride used. [b]  [c] Tetramethylthiuram disulfide. [d] Tetramethylthiuram monosulfide. [e] Sulfuryl chloride added dropwise.

timum conditions for sulfonation, the effects of light, oxygen, sulfur dioxide, water, and concentration of sulfuryl chloride were investigated. The results are given in Table I.

Since even under the optimum conditions the mercaptan-catalyzed reaction gave low yields of cyclohexylsulfonyl chloride, other catalysts for the reaction were sought. In preliminary experiments, a number of anthroquinonesulfonic acids were found to initiate the reaction in the light, but were without effect in the dark. Of these, the potassium salt of anthraquinone-1-sulfonic acid was tried on a larger scale with cyclohexane and gave a 64% yield of the chloride and 4% of the sulfonyl chloride.

Many types of organic nitrogen compounds were tried as catalysts, and in all cases sulfonation as well as chlorination was obtained, except in the presence of those compounds which are bromination and oxidation inhibitors (diphenylamine, *p*-phenylenediamine, etc.) in which case either no reaction at all, or a small amount of chlorination, took place (Table I). Of all the catalysts studied, by far the most effective for sulfonation are the aromatic nitrogen ring compounds, the pyridines and quinolines. With these catalysts, under the proper conditions, the extent of chlorination is greatly reduced and good yields of cyclohexylsulfonyl chloride are obtained.

In Table II are given the results of experiments with hydrocarbons other than cyclohexane. In all aliphatic or aromatic compounds with an aliphatic side-chain, sulfonation in the aliphatic part of the molecule took place. A notable exception is toluene. Attempts to prepare benzylsulfonyl chloride from toluene and sulfuryl chloride, using optimum conditions for sulfonation, and operating at a low temperature (55–60°), were unsuccessful. However, that sulfonation of aliphatic side-chains is possible by this method, is demonstrated by the formation of phenethylsulfonyl chloride in small yields from ethylbenzene,

TABLE II

REACTIONS BETWEEN SULFURYL CHLORIDE AND HYDROCARBONS

Expt.	Hydrocarbon	Catalyst	% Yield[a] Chlorination	Sulfonation	Ratio RSO_2Cl/RCl
62–65	Toluene	2-Mercaptothiazoline, mercaptobenzothiazole, anthraquinone-1-sulfonic acid,[b] resp.	26.5–65.6	...	...
66–67	Ethylbenzene	Selenide, 2-mercaptothiazoline, resp.	33.9–48.6	...	...
68	Ethylbenzene	Quinoline	74.6	12.4	0.17
69–71	*n*-Heptane	Pyridine[c,e] quinoline,[d] resp.	28.0–56.0	17.3–31.0	.31–1.1
72	Benzene	Pyridine[f]	12.0	...	...
73	*t*-Butylbenzene	Pyridine[e]	22.0	39.0	1.8
74	Methylcyclohexane	Pyridine[e]	21.0	44.0	2.1

[a] Yields are based on the sulfuryl chloride added. [b] The potassium salt was used. The reaction was carried out in strong light. [c] The reaction was carried out in strong light at the boiling point of the hydrocarbon, 99°. [d] The reaction was carried out in strong light; the temperature was kept between 60 and 70°. [e] Benzene was used as a solvent; the reaction was carried out in strong light and the sulfuryl chloride was added dropwise. [f] The reaction mixture was refluxed in strong light.

and of fair yields of 2-phenyl-2-methyl propylsulfonyl chloride from *t*-butylbenzene.

It is fairly well established that in the peroxide-catalyzed chlorinations with sulfuryl chloride the aliphatic side-chain of the aromatic hydrocarbon is always the point of attack. We now find the same is true of sulfonation reactions with this reagent. Heretofore, sulfuryl chloride has been used in conjunction with halogen carriers, as an agent for chlorination, and with the aid of aluminum chloride for sulfonation of aromatic nuclei. The above experiments indicate that when the reaction takes place through a free radical mechanism, the aliphatic type of molecule is attacked much more readily than the aromatic. This brings out the striking difference between reagents which can share an electron pair, and act exclusively upon the aromatic nucleus, and reagents, such as atoms and free-radicals, which preferentially attack aliphatic molecules. In this connection it should be noted that benzene, itself, is attacked by sulfuryl chloride in strong light when a catalyst is used, but the only product obtained is hexachlorobenzene. However, when an equimolecular mixture of benzene and cyclohexane is allowed to react with sulfuryl chloride under the same conditions, the benzene is not attacked and good yields of cyclohexylsulfonyl chloride are obtained.[4]

An examination of the foregoing tables discloses the fact that the catalyst, more than any other one factor, determines the course of the reaction. Under similar conditions of light and low sulfuryl chloride concentration, peroxides, as already has been stated, give chlorination exclusively; anthraquinonesulfonic acids give almost entirely chlorination; mercaptans and organic nitrogen compounds give chlorination and sulfonation in varying amounts, the best yields of sulfonation product being obtained with the aromatic nitrogen ring compounds. With any one catalyst, the most favorable conditions for sulfonation are strong light and a low concentration of sulfuryl chloride in the reaction mixture at any one time. Oxygen, which might be expected to inhibit chlorination, inhibits both reactions in diffused light, and has no appreciable effect in strong light, except in the case of the pyridine type of catalyst, where chlorination is somewhat inhibited, but the yield of cyclohexylsulfonyl chloride is not increased. Sulfur dioxide, which, in excess, favors sulfonation when a mixture of sulfur dioxide and chlorine is used as the sulfonating agent,[5] has no effect with sulfuryl chloride in strong light, and inhibits both chlorination and sulfonation in diffused light. The effect of temperature can be seen in the experiments with *n*-heptane (Table II); when the reaction is carried out at the boiling point of the hydrocarbon the proportion of heptylsulfonyl chloride is considerably less than when the temperature is kept at 70°. This is accounted for readily by the fact that sulfuryl chloride is largely dissociated at temperatures above its boiling point, into sulfur dioxide and chlorine[6] and, consequently, some of the reaction takes place through the action of molecular chlorine, rather than through a free-radical mechanism.

(4) With 2-mercaptothiazoline as a catalyst, the yield of sulfonation product was greatly increased by the use of benzene as a solvent, instead of excess cyclohexane, but the effect of benzene as a diluent was not appreciable when the reaction was catalyzed by pyridine.

(5) Reed, U. S. Patent 2,046,090; Kharasch and Alsop, unpublished work.

(6) Trautz, *Z. Elektrochem.*, **14**, 534 (1908).

Although the number of compounds sulfonated by this method is not large, there is little doubt that the reaction is quite general for aliphatic hydrocarbons, and has been extended to alkyl halides and many other types of molecules. Since sulfuryl chloride can now be used either as a sulfonating or a chlorinating agent with aliphatic compounds, it should prove a useful reagent in organic chemistry. The primary purpose of the present investigation, however, was to demonstrate that sulfonation should and does take place when sulfuryl chloride reacts with aliphatic hydrocarbons through a free-radical mechanism.

Experimental Part

The cyclohexane (0.5 mole) and sulfuryl chloride (0.25 mole) were introduced into a 125-cc. round-bottomed flask connected by a ground-glass joint to a Hopkins-type condenser, and brought to a gentle reflux. A small amount of catalyst (0.02–0.12 g.) was added, and the reaction mixture was heated over a low flame until no more gas was evolved. The progress of the reaction was followed by means of a bubble counter attached by a rubber tube to the top of the condenser. No attempt was made to trap any of the reactants swept over with the gases, and in cases where oxygen or sulfur dioxide was bubbled through the mixture during the reaction, the losses were appreciable. After the reaction was complete, the mixture was filtered through a glass-wool plug, and the excess cyclohexane was removed by distillation through an indented column 45 cm. long. The solution was then transferred to a 50-cc. Claisen flask, and the rest of the distillation was carried out at reduced pressure. Cyclohexyl chloride was identified by its boiling point, and cyclohexylsulfonyl chloride by its boiling point and anilide.

The experiments in which the sulfuryl chloride was added slowly, or in which gases were passed through the solution, were carried out in a 125-cc. round-bottomed flask into which was sealed a capillary delivery tube reaching to the bottom of the flask and sealed to a wide neck which held a dropping funnel and gas delivery tube. The flask was connected to the condenser by a ground-glass joint.

The source of illumination was a 2000-watt lamp placed about twelve inches (31 cm.) from the reaction flask. The cyclohexane used was Eastman Kodak Co. practical grade, dried over sodium. The sulfuryl chloride was obtained from the Hooker Electrochemical Company and was not purified further.

The identification of *n*-heptylsulfonyl chloride, and phenethylsulfonyl chloride was made by conversion to the amides.

Summary

1. Simultaneous chlorination and sulfonation of aliphatic hydrocarbons with the aid of sulfuryl chloride, a catalyst, and light is recorded.

2. It is shown that aromatic nitrogen ring compounds when used as catalysts in this reaction, favor the formation of the aliphatic sulfonyl chlorides.

3. The mechanism of the reaction is discussed.

CHICAGO, ILLINOIS RECEIVED AUGUST 10, 1939

[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY, THE UNIVERSITY OF CHICAGO]

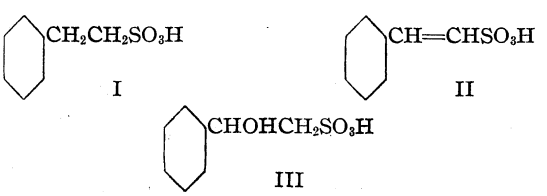
The Peroxide Effect in the Addition of Reagents to Unsaturated Compounds. XXIII. The Reaction of Styrene with Bisulfite

BY M. S. KHARASCH, REMSEN TEN EYCK SCHENCK AND F. R. MAYO

A recent paper from this Laboratory discussed the addition of bisulfite to various olefins.[1] The unique behavior of styrene suggested further study of this reaction.

The Interaction of Styrene and Bisulfite

The formation, by the oxygen-catalyzed reaction between ammonium bisulfite and styrene, of benzoic acid, 2-phenylethanesulfonic acid (I), and 2-phenylethylenesulfonic acid (II) has been confirmed qualitatively. The material isolated in greatest amount, however (about 65% of the total yield in most instances), was found to be not II, as observed by the workers cited, but a new compound, 2-hydroxy-2-phenylethanesulfonic acid (III). This substance, on treatment with phosphorus pentachloride and then with ammonia, loses the elements of water to form the same amide as II, and can be identified in a mixture of the two only by fractional crystallization of the sodium or potassium salt from dilute alcohol. It is not surprising that the previous workers in the field did not suspect its presence since they for the most part converted the crude salts directly into amides without previous puri-



(1) Kharasch, May and Mayo, *J. Org. Chem.*, **3**, 175 (1938); a summary of the earlier literature is given in this article.

fication. The few attempts that were made to work up the products by crystallization from water as the barium salts met with no success, since striking solubility differences between the various components do not exist under such circumstances.

The extent to which styrene will react with bisulfite, and hence the efficiency of the process, has been found to depend somewhat on the *p*H of the original aqueous salt solution, provided no further additions of material capable of altering the hydrogen ion concentration are made during the course of the reaction. The addition occurs, furthermore, under more extreme conditions of acidity and alkalinity than was formerly believed; such variations, however, are ineffective in causing appreciable changes in the ratio of products formed.

A small but reproducible variation in the proportion of the final products has been observed between two main classes of bisulfites: salts of the ammonium group, including all the alkylamines tested, give rise to somewhat greater amounts of the substitution product (II) at the expense of the addition product (I) than do those of the alkali metals. A number of examples of each type are given in Table I. The anomalous behavior of dimethylanilinium sulfite is probably attributable to the effect of the strongly electronegative phenyl radical, but confirmation of this hypothesis was hindered by the inability of diphenylamines, because of their greatly lowered base strength, to form sulfites at all. Much the same sort of difficulty was encountered in an attempt to relate the variations between ammonium and alkali metal salts to base strength—the alkaline earths, for instance, form water-insoluble sulfites. Dimethylaniline possesses the additional peculiarity of furnishing extraordinarily high yields, apparently as a result of its properties as a mutual solvent together with its ability, when present in excess, to keep the solution at all times very close to neutrality. The behavior of pyridine, which has similar characteristics, was found to be practically identical.

The rate of reaction was found to be effectively independent of the salt employed, but to be closely related to the oxygen concentration. Only the roughest of quantitative observations were made, but even these sufficed to indicate that the speed at which oxygen is consumed increases with its partial pressure. Conversely, the over-all yield of organic sulfonates shows an inverse relationship to the oxygen tension. Increasing oxygen pressure, furthermore, results in favoring the substitution reaction, where it occurs to any appreciable extent, as with the ammonium group of salts already referred to, at the expense of the addition reaction. The small amounts of substitution encountered in the use of alkali metal bisulfites are independent of oxygen concentration, as is the ratio of hydroxysulfonate (III) in all oxygen-promoted experiments. The yield of the latter, in fact, remained substantially constant regardless of any alteration of experimental conditions.

The possible effect of bisulfite concentration was investigated in one experiment conducted according to the method of Kolker and Lapworth,[2] as amended by Ashworth and Burk-

TABLE I

THE ADDITION OF BISULFITE TO STYRENE[a]

Cation of bisulfite used	Oxygen tension, mm.	*p*H Initial	*p*H Final	Total % yield on sulfite reacted	% of total yield present as I[b]	II[c]	III[d]
Sodium	760	6.23	2.47	25	28	12	60
Sodium	152	6.23	8.92	43	20	12	68
Sodium	30	6.23	9.81	58	29	11	60
Ammonium	760	6.52	6.90	30	8	28	64
Ammonium	152	6.52	7.40	40	16	14	70
Ammonium	30	6.52	8.72	68	20	7	73
Methylammonium	152	6.55	6.50	32	17	28	55
Dimethylammonium	760	5.97	2.00	29	21	17	62
Trimethylammonium	760	6.40	3.13	30	12	18	70
Ethylenediammonium	152	7.02	7.95	33	8	10	82
Dimethylanilinium	760	[e]	[e]	54	16	5	79
Pyridinium	760	[f]	[f]	66	23	20	57
Ammonium	0[g]	7.81	1.43	15	50	0	50
Ammonium	0[h]	4.87	7.72	20	20	0	80
Sodium	0[i]	4.74	7.11	25	35	0	65

[a] The results herein tabulated are representative examples of a group of 60 consistent experiments. [b] Calculated by difference. [c] By permanganate assay. [d] Weighed as such. [e] *p*H not measured, maintained approximately constant near neutrality by excess dimethylaniline in second phase. [f] *p*H not measured, maintained approximately constant near neutrality by excess pyridine employed as solvent. [g] Oxygen excluded, catalyzed by 0.68 mole of ammonium persulfate per mole of sulfite reacted, added over a period of three and one-half hours. [h] Oxygen excluded, catalyzed by 0.3 mole of ammonium nitrite per mole of bisulfite reacted, added over a period of twelve and one-half hours. [i] Oxygen excluded, catalyzed by 0.3 mole of sodium nitrite per mole of bisulfite reacted, added over a period of six and one-half hours.

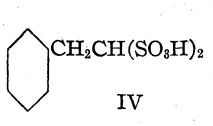
(2) Kolker and Lapworth, *J. Chem. Soc.*, **127**, 307 (1925).

hardt[3] to include styrene. The use of $M/6$ bisulfite solution in place of the usual $M/1$, in a procedure precluding rate comparisons, gave the same products in about the customary yield.

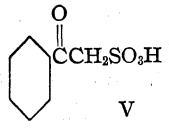
Replacement of oxygen by nitrite or perdisulfate ion as reaction promoter results in complete suppression of the substitution reaction, the proportion of both the addition product and the hydroxysulfonate being at the same time slightly increased. Over-all yields are here to some extent influenced by the rate at which the oxidant is introduced, but even when the latter is added at the minimum convenient speed they are no better than those resulting from use of oxygen at one atmosphere pressure.

Nitrate ion has been found to be of very slight value as an oxidant in bisulfite additions in comparison with the three foregoing materials. The observable effect, in fact, readily may be ascribed not to the nitrate itself but to the few per cent. of nitrite generally present as impurity in nitrates.

Since we have been totally unable to convert any of the three major products into any other by any means comparable to conditions existing during the reaction or the subsequent isolation of the resulting sulfonates, we have concluded that each is a primary reaction product. For instance, a pure sample of each of the three compounds in turn was treated first with hot acid, then with hot alkali, and finally with sodium bisulfite and oxygen. With one exception the starting materials were in every case recovered unchanged, and in that single instance not one of the previously known substances but a new compound was obtained. Specifically, the action of bisulfite and oxygen upon the substitution product results in the addition of another molecule of bisulfite to the double bond with the production in good yields of 2-phenylethane-1,1-disulfonic acid (IV). From the fact that this compound is never formed during treatment of styrene with bisulfite, even in those experiments in which subsequent analysis shows the unsaturated acid to have been present, it is evident that its formation is prevented by the presence of excess styrene.



IV



V

It was anticipated after discovery of the hydroxysulfonate (III) that benzoylmethanesulfonic acid (V) might also logically be included among the products of the reaction, as a result of further oxidation of the former substance. No trace of it, however, has thus far been isolated. It furthermore has been observed in this connection that the hydroxy compound, in view of its structure as a water-soluble secondary alcohol, is surprisingly resistant to oxidation. It is stable to both acid and alkaline permanganate in the cold, and even at 90–100° the oxidation is relatively slow.

This observation was made the basis of an attempt to determine yields of unsaturated sulfonate without separation of the crude mixtures into their components. Accurately weighed samples were treated with cold neutral permanganate in excess, the solution freed from precipitated manganese dioxide, and added to excess acid potassium iodide solution. By titrating the liberated iodine with thiosulfate a measure of the unreacted permanganate was obtained. Under such conditions the substitution product is quickly and completely oxidized. The reaction, however, does not follow any predictable stoichiometric course, and as a result it is necessary to standardize the permanganate against a sample of unsaturated sulfonate or sulfonamide of known purity rather than against any of the usual inorganic standards. As a further qualification, it was found that while pure hydroxysulfonate (III) is not attacked by the oxidizing agents employed, it does react to a varying extent when present in a mixture of products and thus leads to extremely inconsistent results. Its removal is very conveniently effected, fortunately, leaving only addition and substitution products in the remainder. These are nearly impossible to separate, but since the former, unlike the hydroxy derivative, is uniformly inert, assay of the latter with permanganate standardized as described gives highly reproducible results.

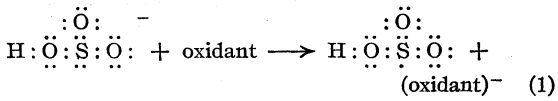
Mechanism

The data herein presented are entirely in accord with the thesis of Kharasch, May, and Mayo[1] that the reaction proceeds through a free-radical intermediate. The evidence for this hypothesis lies in the facts that reagents capable of oxidizing bisulfite are necessary for any interaction to occur and that the products (aside from the benzoic acid arising probably from the direct oxidation of styrene) are exclusively those ac-

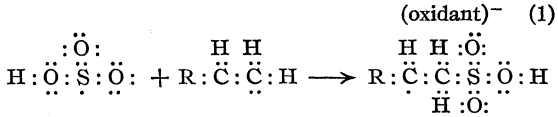
(3) Ashworth and Burkhardt, *J. Chem. Soc.*, 1791 (1928).

countable for by "abnormal" addition to the double bond. Our observations furthermore provide a more quantitative basis for the conclusion that the favored reactions between bisulfite and styrene are unlike those which occur with other olefins in that chains are apparently not important in this particular case. It is true that a chain reaction best accounts for the simple addition products (I), but this class of compound, which constitutes the main product of most unsaturated hydrocarbons, is formed to only a very limited extent from styrene. Reference to the footnotes to Table I will show the comparatively large amounts of oxidant consumed in the addition of bisulfite to the latter olefin, indicating a stoichiometric rather than a chain reaction. In addition, the proportion of sulfite lost as sulfate is not compatible with a self-propagating reaction.

The first steps, wherein a bisulfite free radical, produced by the oxidant[4] capturing an electron from a bisulfite ion, is absorbed by a styrene molecule, have previously been postulated by Kharasch, May, and Mayo.[1] They are reproduced below as equations 1 and 2.



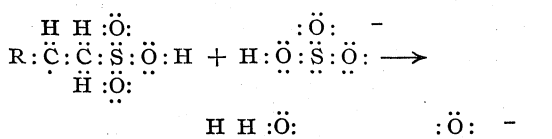
(1)



(2)

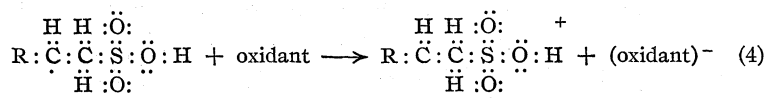
The resulting free-radical complex is then subject to three types of further change, each giving rise to a different product.

1. The simplest case is that in which a hydrogen atom is acquired by collision with another bisulfite ion, as in equation 3, with the formation of 2-phenylethanesulfonic acid and regeneration of sulfite-ion free radical.

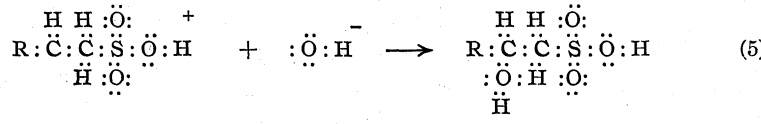


(3)

2. The intermediate may collide with the oxidant and in doing so lose to the latter its unpaired electron. The positively charged molecule thus created readily combines with a negative ion from the solution to form 2-hydroxy-2-phenylethanesulfonic acid.

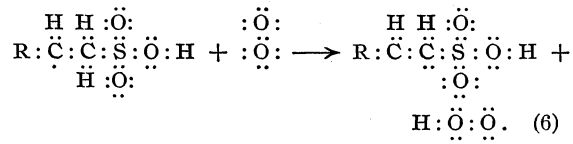


(4)



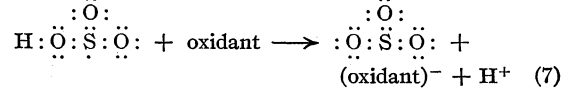
(5)

3. The third type of impact, that which is responsible for the substitution reaction and the formation of 2-phenethylenesulfonic acid, occurs only in the presence of oxygen. For this reason the nature of the oxidant in equation 6 is specified.



(6)

Finally, bisulfite free radicals are transformed to sulfate by a second collision with oxidant, before they can effect combination with styrene, as in equation 7.



(7)

The loss of the second electron to the oxidant has been written, when it takes place (reactions 4 and 6), as a separate step for several reasons. In the first place the removal of both charges at once from sulfite ion results in molecular sulfur trioxide, which in aqueous solution would at once stabilize itself as totally unreactive sulfate ion. Furthermore, if it were possible for sulfur trioxide to exist in dilute solution long enough for it to share the free-electron pair of styrene, the ensuing formation of hydroxysulfonates would be a general property of bisulfite addition instead of being peculiar to styrene, as observed. Lastly, the method employed permits each equation to follow in simple sequence from a common foundation, whereas the introduction of a two-electron transfer would require the retention of both species of inorganic free radical.

It is significant that the apparent relative stabilities of the substituted ethanesulfonate

(4) The term "oxidant" as used in this paper refers to any molecule, atom or free radical capable of accepting an electron or a hydrogen atom from either bisulfite ion, bisulfite free radical, or the organic free-radical complex.

free radicals fall in the same order as those of the corresponding substituted methyl free radicals. The latter, arranged according to increasing ability to independent existence, are methyl, phenylmethyl, diphenylmethyl, and triphenylmethyl. Of the former, the alkylethanesulfonate free radicals are relatively short-lived and are the most reactive with the result that practically every collision with bisulfite is effective, and the products are mainly simple addition compounds. Arylethanesulfonate free radicals, on the other hand, are probably of much greater stability. Reaction of these with bisulfite may be assumed to require an appreciable activation energy. Consequently, fruitful impacts are largely with the oxidant and lead to substitution or the introduction of hydroxyl groups in a large proportion of the intermediate free radicals. The observed phenomena thus follow predictions based on consideration of the probable electron patterns as defined by the theory of electronegativity.[5]

Experimental

Materials.—Styrene, obtained through courtesy of Bakelite Corp., was used both as received (containing small amounts of hydroquinone) and freshly distilled *in vacuo*. No difference between the two kinds was perceptible in any bisulfite addition. Baker monohydrated ammonium sulfite of 71% purity and General Chemical Co. ammonium bisulfite solution, 25% sulfur dioxide, were employed, together with Merck Reagent sodium bisulfite and Mallinckrodt Analytical sodium sulfite, anhydrous, assaying 79% sodium bisulfite and 86% sodium sulfite, respectively. Ethylenediamine sulfite was prepared by diluting the Eastman Kodak Co. Technical base (60% $(CH_2NH_2)_2$ in water) with two volumes of alcohol and saturating with sulfur dioxide. The granular white precipitate, after collection on a filter, an alcohol and ether wash, and air-drying, melted at 176°. Iodine titration of a sample for sulfur dioxide showed the material to be 99% pure $(CH_2NH_3)_2SO_3$. The yield was nearly quantitative. Concentrated stock solutions of substituted ammonium bisulfites were made up by absorbing the maximum of sulfur dioxide in 25–35% solutions of base in water as supplied by Commercial Solvents Corp. Pyridine was diluted with one-fourth its weight of water and sulfur dioxide introduced until its concentration was approximately molar. This reagent was used without further dilution. Dimethylaniline was suspended in water and treated with sulfur dioxide until the mixture became homogeneous. More water was added to the resulting solution to reduce its sulfite content to molar before use.

Procedure for Reaction

Buffered solutions of highly reproducible *p*H for oxygen-promoted runs were prepared by mixing weighed quantities of sulfite and bisulfite, or of solutions of bisulfite and free base, and diluting until molar in total sulfurous acid salts. Reaction was carried out on a high-speed shaker in ordinary round-bottomed flasks with wired-in rubber stoppers, pierced by inlet tubes leading to a graduated reservoir of pure oxygen collected over water. The oxygen tension in the atmosphere over the reaction mixture in the vessel was fixed by using the undiluted gas, air, or a mixture of air with four volumes of nitrogen. In any case the concentration of the promoter was automatically kept constant by replacement with pure oxygen from the reservoir as fast as consumed. Over-all pressure was maintained at atmospheric within narrow limits by never permitting the water level to rise far inside the cylinder. Back diffusion was negligible because of the steady flow of oxygen into the flask. Oxygen runs were continued until iodine titration of an aliquot showed that only a negligible quantity of bisulfite remained, or until extreme *p*H changes greatly reduced the rate of reaction.

Solutions of bisulfite alone were used in nitrite-catalyzed, of sulfite alone in persulfate-catalyzed additions. The sole change necessary in the apparatus was substitution for the gas inlet tube of two stopcocks. Air was displaced from the flask and liquid by passing in carbon dioxide rapidly for fifteen to twenty minutes before shaking was commenced and excluded thereafter, within the limitations of the method, by introducing the oxidant through the stopcocks. The oxidant was added as a 2.5–5 *M* solution at the rate of 10 mmole. per mole of sulfite or bisulfite every half-hour. Samples for assay of unreacted sulfite were withdrawn in a capillary pipet from time to time by the same route without permitting ingress of appreciable oxygen. This type of run was stopped when the sulfite concentration had fallen to such a point (0.15 *M*) that fresh portions of oxidant caused a much smaller drop in the reducing power of the solution than at the start of the experiment.

The proportion of styrene present was in all instances the same: mole for mole with the total sulfurous salts. Since even at best a large part of the latter are oxidized to sulfate, the styrene is always actually in excess.

Among the solvents tested, two, 95% alcohol and liquid ammonia, failed to produce any evidence of reaction whatever. Dimethylaniline was the base employed in the former trial, and in the latter the solvent itself functioned as proton acceptor. This second run was made by bubbling through air under stirring in place of the usual technique of shaking in a closed system. The action of nitrite on either of these mixtures was not investigated. Water proved to be a generally reliable medium. The most desirable results were obtained in 80% aqueous pyridine, in which a much more nearly homogeneous solution is attainable than with water. Even under high oxygen pressures the ratio of sulfonate to sulfate formed in such a run is unusually favorable.

Analysis of Reaction Mixture.—Completed reaction mixtures were separated and the aqueous portion clarified by ether extraction or filtration through a little carbon. After potentiometric *p*H determination and iodine titration of an aliquot to measure the unused sulfite, the salt solution was evaporated to dryness in an open dish on the steam-bath: directly if from an oxygen- or persulfate-sodium sulfite addition, and after mixing with 0.55 mole of sodium carbonate for every gram atom of

(5) Kharasch and Reinmuth, *J. Chem. Educ.*, **8**, 1703 (1931); Kharasch and Flenner, THIS JOURNAL, **54**, 674 (1932).

nitrogen contained if from any other type, whether the nitrogen as originally added was contained in the base or in nitrite or nitrate ion (which are reduced by bisulfite to ammonia or hydroxylamine). Heating of the residue, when nitrogen was present, was continued as long as escape of any ammoniacal fumes could be detected. Small variations in this procedure were desirable in several special cases: for instance, pyridine was not evaporated off freely but was recovered by distilling from the salts *in vacuo*, after addition of aqueous sodium carbonate solution to cause separation of excess styrene. Dimethylaniline was separable mechanically from the alkalinized solution.

The salt residues from these evaporations were finely ground and extracted with 1 liter of boiling 70% alcohol per mole of sulfite consumed. The solution was filtered from the inorganic insolubles and the filtrate taken to dryness as before. The organic residue was then treated with 10 cc. of 90% alcohol per gram, the mixture boiled, cooled to room temperature, and filtered. The residue from this step consists of nearly pure hydroxyphenethyl sodium sulfonate, which may be efficiently recrystallized from 70% alcohol as pearly white platelets. From the filtrate may be obtained, by evaporation to dryness, a mixture of phenethyl and phenethylene sodium sulfonates. These may be recrystallized from 85–90% alcohol or from saturated aqueous salt solutions, but the former solvent often leads to difficultly filterable pastes and the latter to products contaminated with inorganic salts. A much more satisfactory procedure is to convert the sodium to the barium salts by metathesis with barium bromide and recrystallize from water. The sodium salts of both these compounds are obtained as small, shiny white plates from alcohol or as coarse, thin, transparent plates from brine. The barium salts crystallize from water as tiny, white scales, containing one molecule of water of crystallization. Either of the materials may be obtained in a pure state by any of the above methods from a mixture with the other in which it preponderates. The saturated sulfonate also may be freed from any proportion of the unsaturated by destroying the latter with potassium permanganate. No scheme has yet been devised for the separation of both components of an approximately equimolar mixture, or for the isolation of small amounts of unsaturated sulfonate from a mixture rich in the saturated.

Preparation of Sulfonamides.—Sulfonamides were prepared from both the saturated and unsaturated salts in the manner described by Kharasch, May and Mayo.[1] That obtained from the former melted at 124° and from the latter at 143° as they reported. In neither case did a mixed melting point with an authentic specimen show any depression.

Anal. (1) Sodium 2-phenylethanesulfonate. Calcd. for $C_8H_9SO_3Na$: C, 46.15; H, 4.36; Na, 11.05. Found: C, 45.80; H, 4.26; Na, 11.01.

Anal. (2) Barium 2-phenylethylenesulfonate monohydrate. Calcd. for $(C_8H_7SO_3)_2Ba\cdot H_2O$: C, 36.83; H, 3.09; Ba, 26.32. Found: C, 37.00, H, 3.27, Ba, 26.64.

Anal. (3) Sodium 2-hydroxy-2-phenylethanesulfonate. Calcd. for $C_8H_9SO_4Na$: C, 42.85; H, 4.05; Na, 10.26. Found: C, 42.69; H, 4.05; Na, 10.24.

Establishment of Structure of Sodium 2-Hydroxy-2-phenylethane Sulfonate.—The analytical data reproduced above for this salt correspond to those calculated for sodium 2-phenethylenesulfonate containing one molecule of water per mole. We have never been able to prepare such a hydrate, however (it is only the barium salt which forms a stable hydrate). Furthermore, a sample of the material was observed to have lost no weight after standing for a week over phosphorus pentoxide *in vacuo*. The stability of the compound to cold permanganate shows the material to be saturated, and the fact that when it is oxidized under more vigorous conditions only benzoic acid (identified by its mixed melting point of 123° with a known sample) can be isolated in high yield, indicates that all substituents are in the side-chain. Treatment with phosphorus pentachloride in the cold resulted in a vigorous exothermic reaction, accompanied by the evolution of much hydrogen chloride and yielding a sulfonyl chloride which was transformed by the action of ammonia into the unsaturated amide of melting point 143°. The over-all conversion of the salt into amide was about 70%. This reaction, together with the stability of the salt to both acid and base (no inorganic sulfur was liberated even on long boiling), demonstrated the absence of sulfate ester and the position of the sulfonic group as beta to the phenyl. The hydroxyl cannot also be beta to the phenyl group, since compounds having a hydroxyl on the same carbon atom as a sulfonic acid group are known to be easily decomposed by either acid or base into sulfur dioxide and an aldehyde. The configuration thus arrived at has been shown to be correct by synthesis from styrene bromohydrin (see below).

The hydroxyl group here present exhibits none of the reactions characteristic of its class. All attempts to esterify it uniformly failed. No treatment with reagents designed to replace it with halogen was successful: either the salt was recovered unchanged or only the unsaturated derivative was obtained.

Styrene bromohydrin was prepared according to Read and Reid,[6] although it was not found possible to reproduce the high (95–98%) yield reported. Under the best circumstances only 80 to 85% of the bromine employed added as hypobromous acid, the remainder forming styrene dibromide, while as little as 60% of the theoretical quantity of bromohydrin was isolated from larger runs. The two products were efficiently separated by thoroughly cooling the crude oil in the icebox and filtering the still-liquid bromohydrin from the crystallized dibromide.

Styrene iodohydrin was prepared by the method of Brunel.[7]

Styrene dibromide was obtained both as a by-product in the manufacture of the bromohydrin and in the manner of Evans and Morgan.[8]

Sodium 2-hydroxy-2-phenylethanesulfonate resulted from treatment of styrene bromo- or iodohydrin with aqueous sodium sulfite according to the procedure of Houlton and Tartar[9] for alkyl halides in general. It was found to be identical in all its properties, physical and chemical, with that fraction of the reaction products analytically identified as such.

Phenylhydrazinium 2-hydroxy-2-phenylethanesulfonate

(6) Read and Reid, *J. Chem. Soc.*, 1487 (1928).
(7) Brunel, *Ann. chim.*, (viii) **6**, 219 (1905).
(8) Evans and Morgan, THIS JOURNAL, **35**, 56 (1913).
(9) Houlton and Tartar, *ibid.*, **50**, 544 (1938).

was prepared by the method of Latimer and Bost[10] from samples of hydroxysulfonate resulting from both addition to styrene and metathesis of the bromohydrin. It crystallized from alcohol as small yellowish plates, very soluble in water and melting sharply at 180–181° with decomposition. Mixtures from the several sources showed no depression of the melting point.

Sodium 2-phenethylenesulfonate was produced in high yield from the hydroxysulfonate by grinding with excess phosphorus pentachloride, drowning in water and refluxing the resulting water-insoluble sulfone chloride with excess saturated aqueous sodium carbonate solution to complete disappearance of the oily layer. On cooling the unsaturated salt separated as a loose mass of large, thin, transparent plates.

Sodium Benzoylmethanesulfonate.—This salt was prepared also according to Houlton and Tartar,[9] and crystallized from 85% alcohol as soft, asbestos-like fibers. No amide could be obtained from this material, nor was any fraction even remotely resembling it in any of its properties ever isolated from our various reaction products.

Addition of Sodium Bisulfite to Substitution Product.—Ten grams (0.05 mole) of sodium 2-phenethylenesulfonate, from either direct substitution or the hydroxysulfonate as above, was dissolved in a solution of 10.5 g. (0.1 mole) of sodium bisulfite and 25 g. (0.2 mole) of sodium in 250 cc. of water and shaken with oxygen in the same apparatus used for styrene additions until absorption of the gas ceased. The solution was evaporated to dryness on the steam-bath and the residue finely ground. It was then exhaustively extracted with boiling 70% alcohol and the soluble salts isolated by evaporation of the filtrates. The product separated from smaller volumes of dilute alcohol as a pulpy mass of soft, silky needles grouped in rosets. This material no longer gave a positive permanganate test for unsaturation, but was still oxidizable by more powerful reagents to benzoic acid, showing that the additional molecule of bisulfite indicated by the analysis had added to the double bond to form a side-chain disulfonate. Treatment with phosphorus pentachloride eliminates a sulfonic group and causes extensive decomposition. The only amide isolable, and that in extremely small yield, proved to be the β-phenethylene sulfonamide of melting point 143°.

Anal. Disodium 2-phenylethane-1,1-disulfonate dihydrate. Calcd. for $C_8H_8S_2O_6Na_2 \cdot 2H_2O$: Na, 13.28; H_2O, 9.54. Found: Na, 13.12; H_2O, 9.22.

Disodium 2-phenylethane-1,2-disulfonate was prepared from styrene dibromide by Houlton and Tartar's[9] procedure. It crystallized from 70% alcohol as small, elongated prisms totally unlike the needles described immediately above. The action of phosphorus pentachloride and ammonia, however, on this disulfonate was practically identical with that on the addition compound, only a very small quantity of the same unsaturated amide resulting.

Phenylhydrazinium 2-phenylethane-1,2-disulfonate, synthesized according to the instructions of Latimer and Bost,[10] melted sharply at 187–188° with decomposition. It crystallizes from alcohol as microscopic yellowish scales, very soluble in water.

Phenylhydrazinium 2-phenylethane-1,1-disulfonate was prepared in the same manner as the above from the addition product disulfonate. This salt possesses the lowest water solubility of any organic phenylhydrazinium derivative thus far studied by us. It may be recrystallized from water as tiny yellowish scales, and melts at no definite temperature. In a slowly heated bath it darkens at 173° and sinters at 180–185° with decomposition to brownish-black products which thereafter are infusible. When introduced into a pre-heated bath at 195–200°, it visibly melts with evolution of gas and transformation into the same dark residue.

We have been unable to prepare by unambiguous synthesis the β,β-disulfonate we assume the above addition product to be. However, we have shown (1) that both groups are in the chain, (2) that one at least must be terminal, and (3) that the compound is not identical with the α,β-disulfonate of known structure. By elimination, then, the configuration must be that represented by formula (IV), 2-phenylethane-1,1-disulfonic acid.

Summary

1. Previous findings on the production of 2-phenylethanesulfonic acid and 2-phenethylenesulfonic acid by the oxygen- or nitrite-promoted reaction of styrene with bisulfite have been qualitatively confirmed.

2. The interaction of styrene with bisulfite yields mainly 2-hydroxy-2-phenylethanesulfonic acid.

3. A mechanism involving oxygen has been proposed to explain the substitution of bisulfite in styrene, and one independent of the nature of the oxidant to account for the formation of the hydroxy derivative.

4. Four new sulfonic acids, namely, 2-hydroxy-2-phenylethanesulfonic acid, 2-phenylethane-1,2-disulfonic acid, 2-phenylethane-1,1-disulfonic acid, and benzoylmethanesulfonic acid have been prepared, together with derivatives of each of the first three named.

CHICAGO, ILLINOIS RECEIVED AUGUST 16, 1939

(10) Latimer and Bost, THIS JOURNAL, **59**, 2500 (1937).

[CONTRIBUTION FROM THE SUN OIL COMPANY, EXPERIMENTAL DIVISION]

Isolation of 2,2-Dimethylbutane from Natural Gas and Determination of its Physical Properties[1]

BY MILDRED M. HICKS-BRUUN, JOHANNES H. BRUUN AND W. B. MASON FAULCONER

1. Introduction.—In previous publications,[2,3] the authors have reported the isolation of pure samples of four isomeric hexanes: *n*-hexane b. p. 68.7°, 3-methylpentane b. p. 63.2°, 2-methylpentane b. p. 60.19° and 2,3-dimethylbutane b. p. 57.93°. While the fifth of the isomeric hexanes, 2,2-dimethylbutane b. p. 49.7° has been prepared synthetically,[4–8] it seems that no one has ever isolated this compound in a pure condition from any naturally occurring product such as petroleum or natural gas. In our recent investigation[3] of the 55–66° cut from Clendenin Gas Field in West Virginia, we found that approximately 7.4% of this cut, when fractionated in our 100-plate bubble cap stills,[9,10] distilled between 38 and 58°. A subsequent refractionation of this low boiling cut resulted in a definite flat break between 49 and 50° of the distillation curve. The refractive index of the material distilling within this range, however, was too high to correspond to 2,2-dimethylbutane alone and it was concluded that it was mixed with cyclopentane, b. p. 49.2°. Because of the relatively small amounts of this fraction available in the 55–66° cut we were unable at that time to isolate the missing isomer of hexane in a pure condition. The distillation served to indicate, however, that a complete separation might be possible provided the investigation was started with larger amounts of the material boiling as near 49–50° as possible. Inasmuch as the isolation of the 2,2-dimethylbutane would supply complete data on the natural occurrence of the isomeric hexanes in petroleum, it was thought advisable to complete this work.

2. Raw Material Used.—From the Viking Distributing Company, 20 gallons (76 liters) of the 38–55° cut from the natural gas originating in the Clendenin Field in West Virginia has been obtained. This cut was reported to be present to the extent of 18 gallons (68 liters) of liquid per 1000 cubic feet (28,317 liters) of the natural gas measured at a pressure of 14 pounds per square inch (1 atm.).

3. Isolation of the 2,2-Dimethylbutane.—About 37 liters of the raw material was extensively fractionated in two semi-automatic all-glass stills having bubble cap columns of 100 plates each and still pots of 3 and 5 liters capacity. The reader is referred to previous publications for a complete description of these stills.[9,10]

The first distillation consisted of 11 separate runs with charges of either 2500 or 4500 ml. each. The stills were operated at a reflux ratio of about 20:1 and the distillates were collected at a rate of about 0.8 ml. per minute between 26 and 40° and of about 0.1 ml. per minute in the range between 40 and 50°. The temperature–volume relationships of these runs were exactly identical and are given in Fig. 1. As shown in this figure, over 50% of the raw material consisted of *n*-pentane (boiling point 36°) while the 2,2-dimethylbutane fractions (refractive index, $n^{20}D$ averaged 1.380) represented about 10% of the original 38–55° cut. It is noted that the true boiling range of the 38–55° commercial cut varied from about 26 to above 60°.

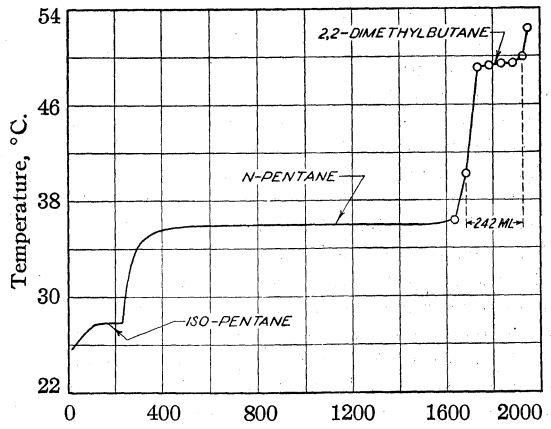


Fig. 1.—First distillation of the raw material.

For the second distillation all of the cuts from the first distillation having boiling ranges of 40–50° were combined and recharged into one of the 100-plate stills which in this case was operated at about 75:1 reflux ratio while the distillate was being collected at a rate of 0.1 ml. per minute. During this run about 80% of the charge distilled between 49.2 and 49.8°.

The third distillation consisted in mixing all fractions from the second distillation boiling at about 49.7° and having refractive indices corresponding to that of the 2,2-dimethylbutane and then subjecting them to a final fractionation in the 100-plate still. The final charge consisted

(1) Paper presented before the Petroleum Division of the American Chemical Society Meeting in Boston, Mass., September, 1939.

(2) (a) J. H. Bruun and M. M. Hicks-Bruun, *Bur. Standards J. Research*, **5**, 933–942 (1930); (b) J. H. Bruun and M. M. Hicks-Bruun, *ibid.*, **6**, 869–879 (1931).

(3) J. H. Bruun, M. M. Hicks-Bruun and W. B. Mason Faulconer, THIS JOURNAL, **59**, 2355–2360 (1937).

(4) J. Timmermans, *Bull. soc. chim. Belg.*, **31**, 389 (1922).

(5) H. v. Risseghem, *ibid.*, **31**, 65 (1922).

(6) J. Smittenberg, H. Hoog and R. A. Henkes, THIS JOURNAL, **60**, 17 (1938).

(7) C. R. Noller, *ibid.*, **51**, 594 (1929).

(8) P. L. Cramer and M. J. Mulligan, *ibid.*, **58**, 373 (1936).

(9) J. H. Bruun, *Ind. Eng. Chem., Anal. Ed.*, **8**, 224 (1936).

(10) J. H. Bruun and W. B. Mason Faulconer, *ibid.*, **9**, 192 (1937).

TABLE I

PHYSICAL CONSTANTS OF 2,2-DIMETHYLBUTANE

		Bruun, Hicks-Bruun Faulconer[a]	H. v. Risseghem[b]	Cramer and Mulligan[c]	J. Timmermans[d]	J. Smittenberg H. Hooge R. A. Henkes[e]	A. v. Grosse[f]
Boiling point, °C.		49.72 ± 0.03	49.73 ± 0.02	49.80 to 49.82	49.7 ± 0.02	49.7	.....
Freezing point, °C.		−98.7 ± 0.2[g]	−98.2	....	−98.2	−100.5	.....
1st transition point, °C.		−99.7[g] (?)	....	....	....	....	.....
2nd transition point, °C.		About −146[g]	....	....	....	About −146	.....
Specific gravity	d^{20}_4	0.6494	0.6491	0.6493	....	....	.....
	d^{25}_4	.64475	....	....	....	....	.....
	dd/dt	.00093	....	....	....	....	.....
Refractive index	$n^{15}D$		1.37518	....	....	....	.....
	$n^{20}D$	1.3689	....	1.3692	....	1.3691	1.36883
	$n^{25}D$	1.36615	....	....	....	....	.....
	dn/dt	0.00055	....	....	....	....	.....

[a] Present investigation. [b] *Bull. soc. chim. Belg.*, **31**, 65 (1922). [c] THIS JOURNAL, **58**, 373 (1936). [d] *Bull. soc. chim. Belg.*, **31**, 389 (1922). [e] THIS JOURNAL, **60**, 17 (1938). [f] U. O. P. Bull. 219, 1938, p. 21. [g] *In vacuo.*

of only 760 ml. of material and the total boiling spread of this charge was found to be 0.1°. The two best samples of about 40 ml. each obtained from the upper end of this distillation had a boiling spread of 0.01° in the 100-plate column.

4. Determination of the Physical Constants of 2,2-Dimethylbutane.—The freezing point, boiling point, the refractive index and the specific gravity of the isolated 2,2-dimethylbutane were determined by using the same apparatus and technique as that employed for the other isomeric hexanes.[3]

The boiling point was determined by means of a Cottrell boiler and the conventional corrections have been applied to the value given in Table I. A Valentine Abbe type refractometer which reads to the fifth decimal place was used to determine the refractive index. Its calibration was checked with pure distilled water and pure *n*-hexane.

The freezing point was determined under vacuum. The 25-ml. sample was placed in a small unsilvered Pyrex vacuum flask, of which the vacuum chamber was equipped with a manometer and stopcock. This arrangement enabled the operator to vary the rate of cooling by changing the vacuum around the sample. A stirrer and a 5-junction copper–constantan thermocouple were provided in order to stir and to read the temperature of the sample. The thermocouple was calibrated by the National Bureau of Standards. The vacuum sample tube was surrounded by a bath of liquid nitrogen which was contained in an unsilvered Pyrex thermos flask.

The specific gravity was determined in a 5-ml. pycnometer specially designed and loaned by S. S. Kurtz, Jr., of the Development Division of this Company. The values were corrected for buoyancy effect and are believed to be accurate to the fourth decimal place.

All of the final corrected values are listed in Table I, together with the best available data on the synthetic hydrocarbon.

5. Discussion of the Results.—From the close agreement of the physical constants, as well as the freezing behavior, it has been concluded that a very pure sample of 2,2-dimethylbutane can be obtained from petroleum by efficient distillation alone.

In Table I, the physical constants are given for the best fraction of 2,2-dimethylbutane which has been obtained in this Laboratory. For direct comparison, the best values from the literature of the physical constants of the pure synthetic hydrocarbon are also included. It can be seen that they are in close agreement with the best of the values except for the freezing point. The freezing behavior proved to be very interesting. The best values found in the literature were those of Timmermans[4] and of van Risseghem,[5] which were both −98.2°, while Smittenberg, Hoog and Henkes[6] found −100.5° and a transition point of −146°. The latter authors were unable to obtain a flat horizontal portion of the curve during the time that freezing took place. They concluded that the substance was pure but the crystallization was inadequate to maintain the temperature at a constant point over the period of freezing.

In the present investigation, in which 25 ml. of 2,2-dimethylbutane was frozen *in vacuo* in concentric transparent vacuum flasks, certain unusual freezing characteristics could be observed. In a normal freezing process supercooling occurs, followed by the formation of white crystals and a horizontal plateau on the time–temperature cooling curve. From the curve in Fig. 2, it can be seen that the first white crystals appeared and a flat portion was obtained about one degree below the point at which the material began to solidify. Thus at −98.7 ± 0.2°, the liquid, without the change in viscosity, which usually occurs if it becomes a glass, began to solidify but remained

transparent. By the time the temperature had dropped one degree, the 2,2-dimethylbutane was almost solid, but still clear. At this point small groups of white crystals began to form and spread rapidly throughout the mass, while the temperature became stationary. This behavior could be duplicated, although it sometimes happened that the white crystals began to form directly at about −99°. In such cases, the temperature did not remain stationary but fell gradually. This behavior gave a time–temperature curve such as that described by Smittenberg, Hoog and Henkes.[6] Whether the first solidification to a transparent mass, with the subsequent change to a white crystalline mass, is evidence of a definite transition point or merely that the first crystals are exceedingly small has not been established. As the main purpose of this investigation has been only to isolate the 2,2-dimethylbutane in a pure condition, no further work has been done on this point. However, due to the rapid change in temperature when the material began to freeze, it is somewhat difficult to establish conclusively the exact temperature of the initial freezing point. The heat of fusion of 2,2-dimethylbutane is 111 cal.$_{15°}$ per mole,[11] which is very low. Calculated from this value, if the freezing point of −98.2° found by Timmermans[4] and van Risseghem[5] is correct and the one for the present sample is 0.5° lower, the purity of the latter is still 99.91%.

A transition point of about −146° has been reported.[6,11] Stull measured the heat of transition at this temperature and found it to be 1095 cal.$_{15°}$ per mole[11] or about ten times the heat of fusion. In the present sample, considerable supercooling (about 20°) occurred before the transition took place. However, the transition point of −146° has been confirmed in this Laboratory.

6. Percentage of the Various Isomeric Hexanes in the Natural Gas.—In Table II, the authors have listed the approximate relative quantities in which the isomeric hexanes are present in the natural gas.

(11) D. R Stull, THIS JOURNAL, **59**, 2726–2733 (1937).

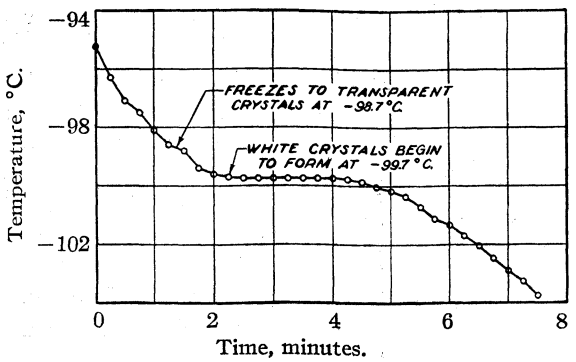


Fig. 2.—Time–temperature cooling curve of 2,2-dimethylbutane.

TABLE II

CALCULATED AMOUNTS OF ISOMERIC HEXANES IN NATURAL GAS

Compound	Boiling point, °C.	Minimum amount present, ml. of liquid per cu. m. natural gas
2,2-Dimethylbutane	49.72	168
2,3-Dimethylbutane	57.93	74[3]
2-Methylpentane	60.19	420[3]
3-Methylpentane	63.2	196[3]

Summary

2,2-Dimethylbutane, the only isomeric hexane that has never been separated from natural sources, has been isolated in a pure condition from natural gas. A careful study of the freezing behavior of 2,2-dimethylbutane has revealed that the compound froze to transparent solid crystals at −98.7° without resulting in a flat portion in its time–temperature cooling curve. One degree lower at −99.7° white crystals began to form and a horizontal plateau appeared on the freezing curve. No attempt has been made to establish whether this behavior is due to the initial formation of very fine crystals or to a definite transition point between two crystal modifications.

The isolated compound is present in natural gas to the extent of 168 ml. per cu. m., and is thus next to 2,3-dimethylbutane, the least predominant isomer of hexane.

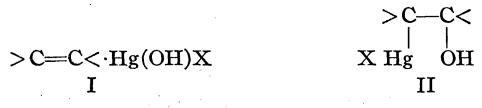
NORWOOD, PENNA. RECEIVED JULY 17, 1939

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, No. 730]

The Coördination Complexes of Mercuric Ion with Cyclohexene

BY H. J. LUCAS, F. R. HEPNER AND S. WINSTEIN

The formation of compounds from olefins and mercuric salts has been studied very extensively since 1900. Hofmann, Sand and co-workers[1] showed that ethylenic compounds combined with mercuric salts in aqueous solution to yield compounds designated by the formula types I or II.



I II

Manchot[2] mainly because of the ease of regenerating the olefin from its addition compound claimed that such products are merely molecular compounds and are best represented by formulas of type I. Considerable discussion has appeared in the literature as to the relative validity of the formula types I and II and later investigators[3] on the basis of various sorts of evidence have established the idea that such compounds are formed by real addition to the double bond and are to be represented by formulas of type II.

There have been indications, however, that there may exist coördination compounds of olefins and mercuric salts (type I) in addition to products of type II. Thus, Sand and Breest,[1d] studying the rate of establishment of equilibrium between ethylene, mercuric chloride and ethanol mercuric chloride and not being able to fit the data very well, thought it possible that an equilibrium existed between compounds of the types I and II. Also, Wright[3d] found a serious downward drift in the bimolecular rate constants for the mercuration of several ethylenic compounds. Wright also found that in testing for completeness of the reaction of mercuration of an ethylenic compound, thiocyanate ion would indicate considerable unused mercuric salt when hydroxide ion failed to indicate any. Further, it was found[4] in this Laboratory that isobutene hydrated incompletely in the presence of mercuric nitrate, the residual isobutene being analyzable by bromination and equivalent to the mercuric nitrate.

Recently it was shown by the distribution method that coördination with silver ion[5] is a general property of ethylenic compounds and we have felt that mercuric ion should act analogously to silver ion. We have now investigated by the distribution method possible complex formation between cyclohexene and mercuric ion in aqueous solution and have found that mercuric ion does indeed complex strongly with cyclohexene. In this paper are presented the results of this investigation and some comments on their significance.

Notation.—For the sake of convenience the symbols to be employed together with their definitions are here listed together. The notation used here is as much as possible nearly identical with the notation previously used in connection with the coördination of silver ion with ethylenic compounds.[5b]

B = unsaturated substance, in this case cyclohexene

(Bt) = total concentration of B in the aqueous phase, moles/liter

(B) = concentration of uncomplexed B in the aqueous phase, moles/liter

$(B)_c$ = concentration of B in carbon tetrachloride, moles/liter

(Hg^{++}) = concentration of uncomplexed mercuric ion in the aqueous phase, moles/liter

(Hgt) = total concentration of Hg in aqueous phase, moles/liter

(BHg^{++}) = concentration of the species, BHg^{++} in the aqueous phase, moles/liter

$(BHgOH^{+})$ = concentration of the species, $BHgOH^{+}$ in the aqueous phase, moles/liter

(HNO_3) = concentration of added nitric acid, moles/liter

(H^{+}) = concentration of total acid in the aqueous phase, moles/liter

μ = ionic strength = normality

$K_D = (B)_c/(B)$ = distribution ratio of cyclohexene between carbon tetrachloride and 1 N potassium nitrate = 4305[5b]

$$K_E = \frac{(Bt) - (B)}{(B)_c[(Hgt) - (Bt) + (B)]} = \text{evaluated constant} = \frac{(Bt)}{(B)_c[(Hgt) - (Bt)]}$$ with negligible error

(1) (a) Hofmann and Sand, *Ber.*, **33**, 1340, 2692 (1900); (b) Sand, *ibid.*, **34**, 1385, 2906 (1901); (c) Sand and Yenssler, *ibid.*, **36**, 3705 (1903); (d) Sand and Breest, *Z. physik. Chem.*, **59**, 424 (1907).

(2) Manchot, *Ber.*, **53**, 984 (1920).

(3) (a) Adams, Roman and Sperry, THIS JOURNAL, **44**, 1781 (1922); (b) Sanborn and Marvel, *ibid.*, **48**, 1409 (1926); (c) Griffith and Marvel, *ibid.*, **53**, 789 (1931); (d) Wright, *ibid.*, **57**, 1994 (1935); (e) Hugel and Hibon, *C. A.*, **23**, 3898 (1929); (f) Nesmejanow and Freidina, *Ber.*, **69B**, 1631, 2019 (1936).

(4) Lucas and Eberz, THIS JOURNAL, **56**, 460 (1934).

(5) (a) Eberz, Welge, Yost and Lucas, *ibid.*, **59**, 45 (1937); (b) Winstein and Lucas, *ibid.*, **60**, 836 (1938).

$K_N = \frac{(B \cdot Hg^{++})}{(B)\ (Hg^{++})}$ = coördination constant of mercuric ion for the formation of the complex BHg^{++} (neutral from the acid base standpoint)

$K_B = \frac{(BHgOH^+)(H^+)}{(B)\ (Hg^{++})}$ = coördination constant of mercuric ion for the formation of the basic complex $BHgOH^+$

$K_0 = K_N/K_D$

$K_0' = K_B/K_D$

Procedure and Analysis.—The procedure followed was essentially that described previously in the silver work,[5] with some modifications. Of these, the most important was in the method of preparing the solutions and of taking the samples, so as to eliminate the presence of oxygen. This was a more serious complication than in the silver case, mainly because the presence of oxygen accelerated the separation of some sort of solid organo-mercuric compound. The cyclohexene was distilled from sodium in an atmosphere of nitrogen, weighed into a volumetric flask filled with nitrogen and made up to the mark with carbon tetrachloride. This solution or one diluted with carbon tetrachloride was used for the distributions.

The apparatus for the distribution measurements as shown in Fig. 1 was kept in a thermostat at 25.0 ± 0.03°. The flask, 200 ml., was filled with nitrogen; the materials were pipetted into the flask through the 10-mm. vertical glass tube which usually was kept closed with rubber tubing. A stream of nitrogen, flowing through the stopcock into the atmosphere, was directed into the flask whenever material was introduced into or taken from the flask. The sampling was done with a pipet having a sealed on 3-way stopcock.[4]

There were three stock solutions, *viz.*, (a) 0.286 *M* in mercuric nitrate and 0.142 *N* in added nitric acid, (b) 1 *N* potassium nitrate and (c) 1 *N* nitric acid. Since all three of these have ionic strength $\mu = 1$, solutions of different concentrations, but of same ionic strength, could be obtained easily by mixing.

The mercuric nitrate stock solution was standardized by titration with potassium thiocyanate. The acid concentration (HNO_3) in this solution was found to be 0.147 *N* and not 0.142 *N* as was intended because of nitric acid in the solid mercuric nitrate. The acid concentration was obtained by precipitating the mercury as mercuric sulfide with hydrogen sulfide, and titrating the acid in the filtrate after removal of excess hydrogen sulfide by boiling.

The length of time allowed for the separation of the two phases was much shorter than that allowed in the silver work,[5b] because in this work the concentrations of cyclohexene in the two phases were of the same order of magnitude.

In connection with possible side reactions it was necessary to know how the hydration product of cyclohexene behaved during the bromination procedure. Cyclohexanol, m. p. 22°, purified and distilled, did not react with bromine according to the analytical procedure, in the presence or absence of carbon tetrachloride.

The analytical method has been described previously.[6]

(6) Lucas and Pressman, *Ind. Eng. Chem., Anal. Ed.*, **10**, 140 (1938).

In the presence of mercuric ion, the bromate–bromide method of analysis gave satisfactory results with attention to some precautions. It was desirable to allow sufficient time, five minutes, for the initial liberation of bromine and at least five minutes between the addition of sodium chloride and potassium iodide solutions. This time interval could be increased to eleven minutes, without causing differences greater than 0.1%. The excess of bromate–bromide solution could be varied from 15 to 65% without introducing an error greater than ±0.5%. When analyzing the carbon tetrachloride phase, the mercuric ion concentration was made comparable to that in the aqueous phase by the addition of 5 ml. of 0.286 *M* mercuric nitrate.

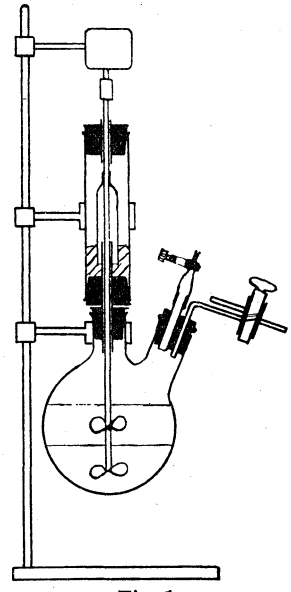


Fig. 1.

The extent to which mercury compounds dissolve in the carbon tetrachloride while cyclohexene is being distributed between carbon tetrachloride and aqueous mercuric nitrate was shown to be less than 0.01 mmol. per liter. This was done by evaporating 50 ml. of the organic phase, after the system had stood for twenty-four hours, taking up the residue (none was visible) in 6 *N* nitric acid, diluting with an equal volume of water, adding saturated hydrogen sulfide solution, and comparing the color with that from known amounts of mercury.

Nature of the Reactions of Cyclohexene in Mercuric Nitrate Solution.—When cyclohexene was distributed between carbon tetrachloride and mercuric nitrate solution containing nitric acid, K_E was much higher than in the case of the silver work[5b] but it varied with time when the acid concentration was low. For about twenty minutes, which seemed to be the time necessary with the present apparatus for establishment of equilibrium between the phases, K_E increased and then it gradually decreased. Thus, when (Hgt) = 0.1907 and (HNO_3) = 0.0980, K_E is 76 at zero time (extrapolated), about 70 after two hours and finally 54 in about twenty hours. At higher acid concentrations this drift seems to be eliminated, K_E varying only as much as would be expected from experimental errors. K_E varies markedly with the acid concentration.

Cyclohexene dissolves readily in aqueous mercuric nitrate. When it does so acid is produced. Under conditions where K_E drifts, there is also a slow further production of acid. These facts are

TABLE I

CHANGE IN pH[a] OF MERCURIC NITRATE BY CYCLOHEXENE

Initial (Hgt)	Initial pH	pH with cyclohexene added: Initial	After 3 hrs.
0.0954	1.55	1.16	1.04
.1907	1.30	1.07	0.77
.1907	1.19	0.92	0.77[b]

[a] Determined by use of Beckmann pH meter. [b] After two hours.

illustrated in Table I. Under conditions where K_E drifts, the apparent mercury concentration as given by thiocyanate titration decreases with time. Thus, when two ml. of cyclohexene is dissolved in 100 ml. of the 0.286 M mercuric nitrate stock solution, the thiocyanate consumption at the beginning is the theoretical value for all the mercury but it drops a few per cent. per hour at the start and some 27% in thirteen hours. The apparent amount of unsaturation as given by bromination is within experimental error of the theoretical for about one and one-half hours under these conditions and then increases at an accelerating rate so that it is some 3% high after three hours and some 40% high after seventeen hours. In time a solid product separates. When cyclohexene dissolves in mercuric nitrate solution, the odor of cyclohexene is not apparent but it becomes so as thiocyanate is added.

The ready solubility of cyclohexene in aqueous mercuric nitrate with loss of cyclohexene odor, the initial production of acid, the initial theoretical consumption of thiocyanate ion, and the variation of K_E with acid concentration in the distribution measurements indicate the rapid coördination of cyclohexene with mercuric ion to give some sort of compound of the formula type I mentioned previously, accompanied by the production of acid. The secondary effects observed at the lower acid concentrations such as the decrease in apparent mercury concentration, the drift of K_E with time, the further production of acid, the increase in the apparent unsaturation after a time, and the separation of a solid indicate that secondary reactions, not as yet completely understood, are taking place. One of the secondary reactions would seem to be the production of a compound of the formula type II. This would produce acid and decrease the consumption of thiocyanate since compounds of type II consume only half as much thiocyanate as mercuric ion does.[3d] These secondary reactions were not investigated further because our chief interest at this time was the study of the coördination type of reaction involving mercuric ion.

At higher acid concentrations, K_E is evaluated easily because the coördination process proceeds with essentially no side reactions. At the lower concentrations a simple extrapolation is sufficient to give K_E quite accurately since the secondary reactions are relatively slow.

Equilibria and Equilibrium Constants.—Distributions were made under conditions in which the concentrations of cyclohexene, mercuric nitrate and nitric acid were changed. The data are summarized in Table II. In each case three independent distributions were made, in duplicate, and the stirring times were 0.5, 1.0 and 1.5 hours, respectively. The evaluated constant K_E for each condition was obtained by averaging the three values of K_E or by extrapolating to zero time when there was a systematic decrease of K_E with time.

TABLE II

VALUES OF K_E OBTAINED BY DISTRIBUTION AT 25° OF CYCLOHEXENE BETWEEN CCl_4 AND $Hg(NO_3)_2 + HNO_3 + KNO_3$ AQ. AT $\mu = 1$

(Hgt)	Extrapolated $(B)_c$	(Bt)	(HNO_3)	K_E: 0.5 hr.	1 hr.	1.5 hr.	Extrap.
0.0477	0.0320	0.0271	0.2731	41.4	41.6	40.6	41.2
.0954	.0135	.0558	.0490	108.5	105.8	103.2	111.2
.0954	.0153	.0529	.0963	83.6	81.2	79.5	85.6
.0954	.0209	.0449	.2740	42.4	42.2	42.5	42.4
.0954	.00805	.0256	.2740	45.6	44.5	46.5	45.5
.0954	.00364	.0137	.2740	45.0	46.3	46.5	45.9
.0954	.0252	.0376	.5490	24.9	25.8	26.3	25.7
.1907	.0158	.1040	.0980	74.4	72.5	71.0	76.0
.1907	.01001	.0606	.2756	45.5	47.7	47.4	46.8

K_E is relatively insensitive to changes in (Hgt) and $(B)_c$ indicating the formation of a complex ion from one molecule of cyclohexene and one mercuric ion. The large variation of K_E with (HNO_3) speaks against the description of the coördination process by equation 1, which one would write

$$C_6H_{10} + Hg^{++} \overset{K_N}{=\!=} C_6H_{10}Hg^{++} \quad (1)$$

$$C_6H_{10} + Hg^{++} + HOH \overset{K_B}{=\!=} C_6H_{10}HgOH^+ + H^+ \quad (2)$$

on the basis of strict analogy between mercuric and silver[5] ions. If reaction 1 were the only one to be considered, K_E would equal K_0 and no variation with (HNO_3) would be observed. Reaction 2 suggests itself as being very important.

If we assume that the reaction of cyclohexene with mercuric ion proceeds entirely in the sense of equation 2, the total acid concentration (H^+) is given, with negligible error, by equation 3 as the sum of the acid present in

$$(H^+) = (HNO_3) + (Bt) \quad (3)$$

the mercuric nitrate solution and that produced by reaction 2. Also, according to equation 4,

K_0' the product of (H^+) and K_E, should be a constant. The values of K_0' which are obtained in

$$K' = K_B/K_D = (H^+)\,K_E = \frac{(BHgOH^+)(H^+)}{(B)_c(Hg^{++})} \quad (4)$$

this way are given in the last column of Table III. K_0' is seen to be reasonably constant, varying only between 11.7 and 15.7, with 13.7 ± 1.2 as the mean value. The conclusion can be drawn, therefore, that the reaction between cyclohexene and mercuric ion proceeds predominantly in the sense of equation 2 to produce a complex ion $C_6H_{10}\cdot HgOH^+$.

TABLE III

VALUES OF K_0' USING EQUATIONS 3 AND 4

(Hgt)	$(B)_c$	(Bt)	K_E	(HNO_3)	$(H^+) = (Bt) + (HNO_3)$	$K_0' = (H^+)K_E$
0.0477	0.0320	0.0271	41.2	0.2731	0.3002	12.4
.0954	.0135	.0558	111.2	.0490	.1048	11.7
.0954	.0153	.0529	85.6	.0963	.1492	12.8
.0954	.0209	.0449	42.4	.2740	.3189	13.5
.0954	.00805	.0256	45.5	.2740	.2996	13.5
.0954	.00304	.0137	45.9	.2740	.2877	13.0
.0954	.0252	.0376	25.7	.5490	.5866	15.1
.1907	.0158	.1040	76.0	.0980	.2020	15.4
.1907	.01001	.0606	46.8	.2756	.3362	15.7
					Mean	13.7
					Mean deviation	±1.2

On the assumption that reaction proceeds according to both equations 1 and 2 the data can be correlated somewhat better than on the basis of only the one reaction. From equation 5

$$K_E = \frac{(BHg^{++}) + (BHgOH^+)}{(B)_c(Hg^{++})} \quad (5)$$

and the definitions of K_0 and K_0', the relation between K_E, K_0, K_0' and (H^+) is given by equation 6.

$$K_E = K_0 + K_0'/(H^+) \quad (6)$$

A first approximation to K_0 can be obtained from the series of runs in which (Hgt) = 0.0954 by plotting K_E against $1/(H^+)$, using (H^+) from Table III. The first approximation was five. Then this value of K_0 was used to obtain a better approximation to the total acid concentration with the relation shown in equation 7

$$(H^+) = (HNO_3) + (Bt)(K_E - K_0)/K_E \quad (7)$$

where $(K_E - K_0)/K_E$ represents the fraction of (Bt) in the form of $(BHgOH^+)$. When K_E was plotted against the corrected (H^+) as shown in Fig. 2, the value of K_0 by this second approximation was five also.

On recalculating K_0' by means of equation 6 using the corrected (H^+) values and the value of $K_0 = 5$, K_0' varies only from 10.9 to 11.9 (Table IV) with 11.6 ± 0.3 as the mean value. The agreement is even better, if the result at the very lowest acid concentration is neglected.

TABLE IV

CORRECTED K_0' VALUES, WITH (Hgt) = 0.0954, $K_0 = 5$ USING EQUATION 6

$(B)_c$	(Bt)	K_E	(HNO_3)	(H^+) equation 7	$K_0' = (K_E-5)(H^+)$
0.0135	0.0558	111.2	0.0490	0.1023	10.9
.0153	.0529	85.6	.0963	.1461	11.8
.0209	.0449	42.4	.2740	.3136	11.7
.00805	.0256	45.5	.2740	.2968	11.9
.00304	.0137	45.9	.2740	.2862	11.7
.0252	.0376	25.7	.5490	.5793	11.8
				Mean	11.6
				Mean deviation	±0.3

From the data of Table IV it can be concluded that when mercuric ion coördinates with cyclohexene, there are two one-to-one complexes formed, *viz.*, $C_6H_{10}Hg^{++}$ and $C_6H_{10}HgOH^+$. The respective equilibrium constants, $K_N = K_0K_D$ and $K_B = K_0'K_D$ are 2.2×10^4 and 5.0×10^4, respectively, when (Hgt) is approximately 0.1 *M*.

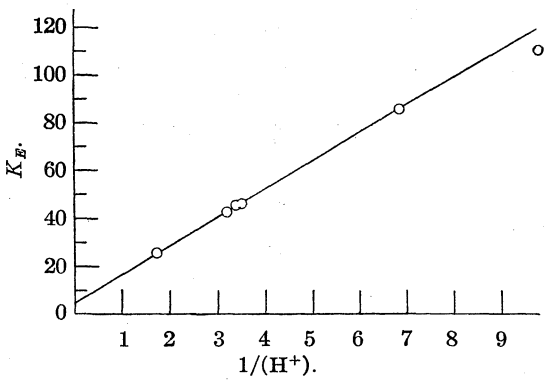


Fig. 2.—Change of K_E with $1/(H^+)$ at (Hgt) = 0.0954 *M*. (H^+) is obtained from equation 7.

There would appear to be a drift in K_0' as (Hgt) is varied. If the assumption is made that K_0 does not change, then K_0' as calculated from equations 6 and 7 varies with (Hgt) as shown in Table V. K_0 may and probably does change somewhat with (Hgt) but since it is so small compared to $(K_E - K_D)$, such a variation can hardly affect very much the trend in K_0' in Table V.

TABLE V

EFFECT OF CHANGE IN (Hgt) ON K_0', WHEN $K_0 = 5$

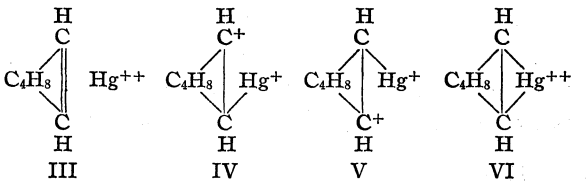
(Hgt)	$K_0' = (H^+)(K_E-5)$
0.0477	10.6
.0954	11.6[a]
.1907	13.7[b]

[a] Average K_0' value, Table IV. [b] Average of two values, 13.8 and 13.6.

A similar but somewhat smaller trend in the constant with the proportion of the various salts making up the total ionic strength of unity was

observed previously in the olefin–silver work.[5] These trends must be due to the fact that even though in the silver work the ionic strength was kept at unity and in the present work it was kept at unity except for changes due to reaction 2, the activity coefficients of the various ionic species change as silver or mercuric nitrate is substituted for potassium nitrate or nitric acid.

Structures.—The coördination complexes of mercuric ion with cyclohexene can be formulated much like the silver–olefin[5] or the positive bromo-olefin complexes.[7] The resonating forms of the cyclohexenemercurinium ion[8] can be represented as III, IV, V and VI and the cyclohexenemercurinium hydroxide ion $C_6H_{10}\cdot HgOH^+$ can be represented similarly with the difference that the mercury atom holds one hydroxyl radical.



The values of K_B and K_N which have been obtained indicate the very extensive hydrolysis of the species $C_6H_{10}Hg^{++}$. In fact, the value for the ionization constant of the base $C_6H_{10}\cdot HgOH^+$ which is given by K_B and K_N is approximately 5×10^{-15}. One would rather expect a low value for the ionization constant of this base, especially if structure VI is at all important, for this form involves an increase in the effective charge on the mercury atom and a consequent decrease in the strength of the corresponding base.

Significance of Mercurinium Complexes.—From a theoretical point of view these coördination complexes of mercury are of great importance. They may be regarded as typical examples of the rather large group of poorly defined substances which are recognized as intermediates in chemical changes, but which usually cannot be isolated.

The process of mercuration of an olefin with production of stable reaction products would appear to be analogous to the *trans* addition of bromine or of bromine derivatives to the double bond. Negative ions or various solvent molecules can attack the substituted ethylenebromonium ions to give dibromides, bromohydrins, etc.[7] Just so are the substituted ethylenemercurinium ions thought to give compounds of the formula type II. One difference is that the mercury complex is so much less reactive that it can be studied directly. In reactivity the mercury complexes would appear to be intermediate between the silver ion and positive bromine analogs. Because of the analogy between bromination and mercuration, we would expect *trans* addition in mercuration also. Actually the mode of addition is uncertain but there is plenty of evidence that mercuration does not proceed by two concurrent reactions, *i. e.*, *cis* addition and *trans* addition[3] to the double bond.

Solid mercury–olefin coördination complexes, comparable to the known solid silver–olefin coördination complexes,[5b] would be expected to exist. It may be that some of the products which have been obtained by workers in the past were actually of the coördination type.

With the finding of coördination complexes of an olefin and mercuric ion the state of the reaction of mercuration has been somewhat complicated. It is known that the mercuration reaction proceeds in some cases to a measurable equilibrium.[1d,3d] Now it would appear that equilibria between the olefin, mercuric salt, compound of type I and compound of type II are involved. In many reactions of mercurated olefins it remains to be seen to what extent these equilibria play a role.

Summary

Coördination complexes of mercuric ion with cyclohexene have been studied chiefly by the distribution of cyclohexene between carbon tetrachloride and aqueous solutions containing mercuric nitrate, nitric acid and potassium nitrate at ionic strength of $\mu = 1$.

The data indicate that two rapid reactions take place: $C_6H_{10} + Hg^{++} \rightleftarrows C_6H_{10}Hg^{++}$ and $C_6H_{10} + Hg^{++} + H_2O \rightleftarrows C_6H_{10}HgOH^+ + H^+$. The equilibrium constant K_N for the first reaction is 2.2×10^4 and K_B, for the second reaction, is 5.0×10^4.

Secondary slower reactions proceed concurrently with the other two.

The significance of mercury–olefin complexes for mercuration phenomena is discussed briefly.

PASADENA, CALIF. RECEIVED AUGUST 25, 1939

(7) (a) Roberts and Kimball, THIS JOURNAL, **59**, 947 (1937); (b) Winstein and Lucas, *ibid.*, **61**, 1576 (1939).

(8) The similarly constituted complex, $C_2H_4Br^+$, has been named the ethylenebromonium ion; Winstein and Lucas, *ibid.*, **61**, 2845 (1939).

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF EMORY UNIVERSITY]

A Study of Organic Parachors. IV. Constitutive Variations of the Parachors of a Series of Tertiary Chlorides[1]

BY OSBORNE R. QUAYLE, KATHERINE OWEN AND ELLINGTON M. BEAVERS[2]

The concept of the highly constitutive nature of parachor has grown out of the fact that it has been shown that many irregularities between observed and calculated values are due, not to experimental error as first believed, but to differences in molecular volume arising from the variations within the molecule. Isomeric compounds show that the additive nature of this constant is modified by constitutive effects. The branching of the chain in hydrocarbons[3,4] causes a lowering of the parachor from that of the value for the straight chain.

Any explanation of the difference in chemical behavior of two carbon atoms in the same general type of structure ultimately must be resolved to a postulation of differences in the extent of consumption of the valence forces of the two, caused by the influences of spatial arrangement and minor differences in adjacent groups. Since the effective volume of an atom is dependent upon its electrical forces, an accurate atomic and molecular volume property should vary slightly from compound to compound because of constitutive influences. On the assumption that the parachor is such a property, most observed deviations are explainable. The validity of this assumption has been tested by comparing the parachors of regular series of compounds.

Beck, Macbeth and Pennycuick[5] measured the parachors of a series of malonic esters, noting the effect of lengthening the ester chain and that of alkyl substitution in the malonic residue. The differences between the observed and calculated parachors showed a regular, depressive constitutive effect, the depression increasing with the length of the alkyl ester chain and apparently reaching a limiting value with the butyl group.

In a study of a series of alkylbenzenes, Buehler, Gardner and Clemens[6] found that the CH_2 parachor value decreased in a very regular manner through the butyl substitution, the amyl rising to the normal value.

In a previous paper,[7] the authors pointed out the influence of varying the length of normal straight chains attached to a tertiary carbon atom jointed to an hydroxyl group. Using trimethylcarbinol as a standard, the effect of substitution in the alcohol was most constitutive with the first CH_2 units added and approached the CH_2 constant of Mumford and Phillips[8] as the length of the chains approached five. These values gave a closer agreement between calculated and observed parachors than those of previous determinations.

This paper is concerned with the measurement of the parachors of the corresponding tertiary chlorides[9] and the resulting extension of the knowledge of the constitutive constants of the compounds containing branching of the tertiary type. As with the alcohols, the chain branching of the chlorides used is limited to the tertiary carbon atom. The values obtained from these compounds afford a second series of position values in tertiary branching. Since chlorides are generally non-associated these values also would indicate any large effect of association that had distorted the values previously recorded for the alcohols.

For the lower molecular weight chlorides densities (Table I) were determined at 15, 25, 50 and 65° with the exception of trimethylchloromethane which boils at 51°. The densities of the higher molecular weight chlorides were determined at 25, 50 and 75°. Extrapolation from the curves shown in Fig. 1 was used to obtain all values at 0°. The surface tensions (Table II) were measured at 0, 25 and 50° for the lower molecular weight compounds and at 25, 50 and 75° for those of higher weight. The estimated experimental precision of the surface tension determinations by

(1) The authors wish to express their gratitude to Prof. E. Emmet Reid, research consultant to the department, for his continued interest in the problem and for his kindness in supplying the chlorides studied.

(2) Abstracted from material presented by Ellington M. Beavers to the graduate faculty of Emory University in partial fulfilment of the requirements for the degree of Master of Science, June, 1939.

(3) G. Edgar and G. Calingaert, THIS JOURNAL, **51**, 1540 (1929).

(4) T. W. Richards, C. L. Speyers and E. K. Carver, *ibid.*, **46**, 1196 (1924).

(5) A. B. Beck, A. K. Macbeth and S. W. Pennycuick, *J. Chem. Soc.*, 2258 (1932).

(6) C. A. Buehler, T. S. Gardner and M. L. Clemens, *J. Org. Chem.*, **2**, 167 (1937).

(7) K. Owen, O. R. Quayle and E. M. Beavers, THIS JOURNAL, **61**, 900 (1939).

(8) S. A. Mumford and J. W. C. Phillips, *J. Chem. Soc.*, 2112 (1929).

(9) The chlorides used were those prepared and described by J. D. Pollard, Johns Hopkins University, Thesis, 1934.

TABLE I

THE DENSITIES OF SIXTEEN TERTIARY CHLORIDES AT VARIOUS TEMPERATURES

Chloromethane	Temperature for densities 0°	15°	25°	50°	65°	75°
Methylmethylmethyl	0.8619	0.8457	0.8347			
Methylmethylethyl	.8876	.8702	.8589	0.8327		
Methylethylethyl	.8949	.8811	.8720	.8488	0.8365	
Ethylethylethyl	.9065	.8946	.8862	.8645	.8527	
Ethylethylpropyl	.9018	.8894	.8813	.8604	.8480	
Ethylpropylpropyl	.8963	.8843	.8765		.8441	
Propylpropylpropyl	.8897	.8780	.8703	.8507		0.8308
Methylmethylpropyl	.8766	.8608	.8523	.8288	.8145	
Methylpropylpropyl		.8741	.8658	.8447	.8322	
Methylethylpropyl	.8915	.8783	.8698	.8477	.8346	
Methylmethylbutyl			.8566	.8342		.8104
Methylmethylhexyl			.8538	.8334		.8124
Methylethylhexyl			.8638	.8442		.8241
Methylpropylhexyl			.8621	.8431		.8236
Methylbutylhexyl			.8612	.8426		.8237
Methylamylhexyl			.8578	.8395		.8206

the maximum bubble pressure method employed is 0.2%. In the case of these chlorides, the surface tensions are evidently a linear function of temperature (Fig. 2).

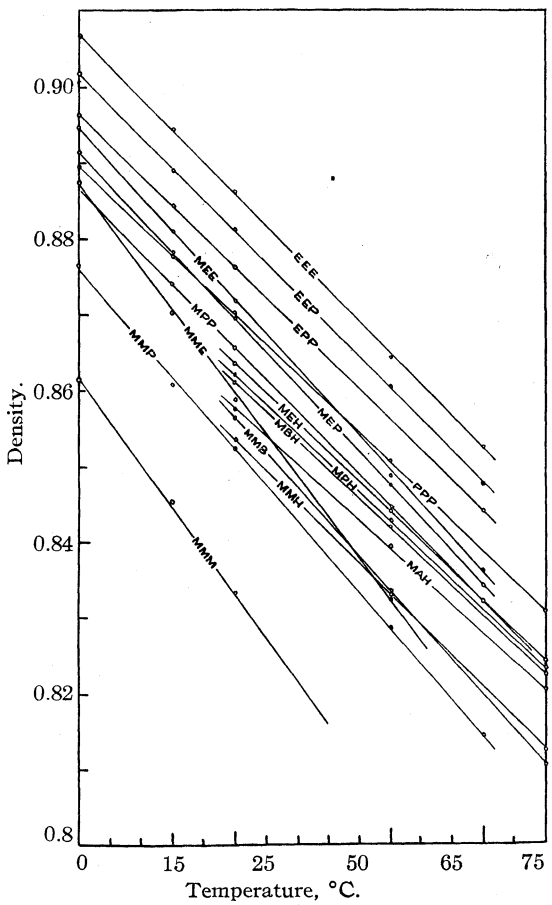


Fig. 1.—Variation of density with temperature for sixteen tertiary chlorides.

TABLE II

THE SURFACE TENSIONS OF SIXTEEN TERTIARY CHLORIDES

Chloromethane	Temperature for surface tensions 0°	25°	50°	75°
MMM	21.35	18.30		
MME	25.39	21.38	18.67	
MEE	26.55	23.46	20.93	
EEE	27.76	25.46	22.82	
EEP	28.06	25.43	23.03	
EPP	28.17	25.76	23.52	
PPP		25.94	23.58	21.25
MMP	25.00	22.37	19.80	17.31
MPP		24.75	22.41	
MEP	26.88	24.32	21.90	
MMB		23.69	21.15	18.80
MMH		25.38	23.00	20.60
MEH		26.37	24.03	21.67
MPH		26.50	24.20	21.97
MBH		27.05	24.83	22.53
MAH		27.01	24.94	22.72

The parachors of the chlorides (Table III) decrease with the exception of ethylpropylpropylchloromethane, in a linear manner with temperature (Fig. 3). The rate of this decrease is less than 0.2% per 10° rise in temperature. The experimental precision of measurement was approximately 0.1%. The parachors were calculated from the mathematical expression[10] $P = \gamma^{1/4} M/D$ where M is the molecular weight, γ is the surface tension, and D is the density of the liquid.

Since the parachor values for the series vary in an essentially regular manner with temperature, comparisons would be essentially the same at any temperature within the range studied. The com-

(10) The more exact expression $P = \gamma^{1/4} M/(D - d)$ includes the value of d the density of the vapor at same temperature. The omission of d introduces an error of less than 0.05% and the shorter expression has been used throughout.

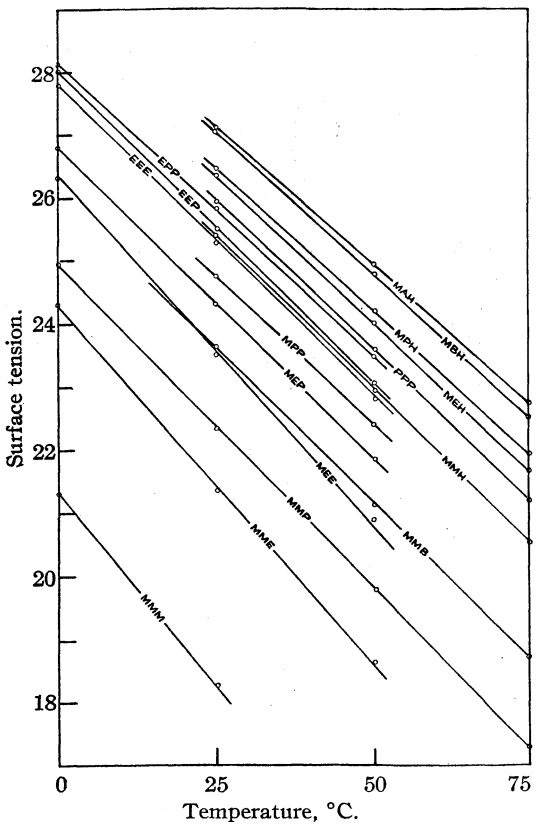


Fig. 2.—Variation of surface tension with temperature for sixteen tertiary chlorides.

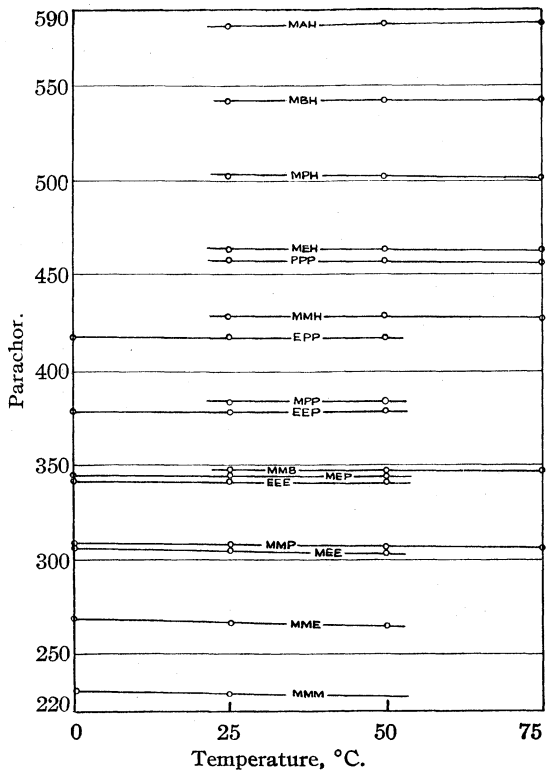


Fig. 3.—Parachors of sixteen tertiary chlorides at various temperatures.

TABLE III

THE PARACHORS OF SIXTEEN TERTIARY CHLORIDES

Chloromethane	Temperature for parachors 0°	25°	50°	75°
MMM	230.9	229.4		
MME	269.6	266.9	265.4	
MEE	306.0	304.4	303.9	
EEE	341.0	341.3	340.6	
EEP	379.4	378.8	378.5	
EPP	418.2	418.2	418.6	
PPP		458.3	457.8	456.8
MMP	307.7	307.6	307.0	305.6
MPP		383.0	382.9	
MEP	343.9	343.8	343.6	
MMB		346.8	346.2	346.0
MMH		427.7	427.5	426.7
MEH		463.6	463.5	462.7
MPH		502.0	501.8	501.4
MBH		542.3	542.5	541.7
MAH		581.5	582.5	582.1

parisons recorded are for convenience made at 25°. Trimethylchloromethane was taken as an observed base for the purpose of making comparisons. The value of the $\rangle$C–Cl group was obtained by subtracting the value of the three methyl groups from the total value. By assuming this basic value, the effect of uniformly lengthening the chains on the value of the $\rangle$C–Cl group may be observed (Table IV).

The effect is of the same order of magnitude as that obtained for the tertiary carbinols. The first several additions to the chains cause the greatest crowding and adsorption of any residual forces on the tertiary carbon.

The effect of substitution at different distances from the tertiary carbon atom has been calculated for the CH_2 values (Table V), and is quite comparable to those obtained in a similar manner for the tertiary carbon in the carbinol series.[8]

The curves of Fig. 4 showing the results of the study of the chlorides, while in no sense identical with those obtained with the corresponding carbinols, are unmistakably of the same general shape.

While by the very nature of the postulate of the extreme constitutive nature of the parachor, the values for the various CH_2 units would not be expected to be identical in the two series, the main structural feature of both series is the same, the varying tertiary carbon atom, and it is of interest to substitute in the chloride series the average

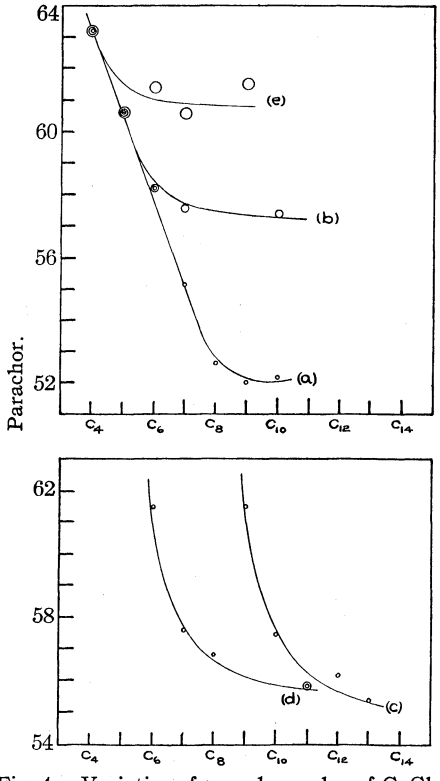


Fig. 4.—Variation of parachor value of C–Cl groups in series.

CH_2 values as obtained from the two series (Table VI).

TABLE IV

VARIATION OF C–Cl GROUP IN SERIES

(Basic value C–Cl assumed 63.2)

Chloromethane	Parachor C–Cl group	Parachor decrease	% decrease from basic C–Cl
	Series a		
MMM	63.2	0.0	0
MME	60.7	2.5	4
MEE	58.2	5.0	8
EEE	55.1	8.1	13
EEP	52.6	10.6	17
EPP	52.0	11.2	18
PPP	52.1	11.1	18
	Series b		
MEM	60.7	2.5	4
MEE	58.2	5.0	8
MEP	57.6	5.6	9
MEB	No determination		
MEA	No determination		
MEH	57.4	5.8	9
	Series c		
MHM	61.5	1.7	3
MHE	57.4	5.8	9
MHP	55.8	7.4	12
MHB	56.1	7.1	11
MHA	55.3	7.9	13
	Series d		
MPM	61.4	1.8	3
MPE	57.6	5.6	9
MPP	56.8	6.4	10
MPB	No determination		
MPA	No determination		
MPH	55.8	7.4	12
	Series e		
MMM	63.2	0.0	0
MME	60.7	2.5	4
MMP	61.4	1.8	3
MMB	60.6	2.6	4
MMA	No determination		
MMH	61.5	1.7	3

TABLE V

VALUE OF THE CH_2 GROUP

In first ethyl position	37.5
second ethyl position	36.5
third ethyl position	35.7
In first propyl position	39.2
second propyl position	39.0
third propyl position	39.9
In first butyl position	39.2
second butyl position	40.3
third butyl position	40 +
In first amyl position	40.7
second amyl position	40 +
third amyl position	40 +
In first hexyl position	40.7
second hexyl position	40 +

TABLE VI

COMPARISON OF OBSERVED AND CALCULATED VALUES FOR THE PARACHORS

M and P values are obtained from the constants as given by Mumford and Phillips. BOQ′ values are obtained from the study of the tertiary chlorides. Average values are obtained from the average value of the CH_2 position of the alcohols and chlorides.

Chloromethane	Obsd. *P* 25°	Calcd. *P* M and P	% diff.	Calcd. *P* BOQ′	% diff.	Calcd. *P* average	% diff.
MME	266.9	270.4	1.4	266.9	0.0	266.9	0.0
MEE	304.4	310.4	2.0	303.4	.3	303.4	.3
EEE	341.3	350.4	2.6	339.1	.6	339.2	.6
EEP	378.8	390.4	3.0	378.3	.1	378.5	.1
EPP	418.2	430.4	2.8	417.3	.2	417.3	.2
PPP	458.3	470.4	2.6	457.2	.2	456.6	.4
MMP	307.6	310.4	0.9	306.1	.5	306.2	.5
MPP	383.0	390.4	1.9	381.6	.4	381.5	.4
MEP	343.8	350.4	1.9	342.6	.4	342.7	.4
MEH	463.6	470.4	1.4	463.2	.1	462.6	.3
MMH	427.7	430.4	0.6	426.7	.2	426.1	.4
MPH	502.0	510.4	1.6	502.2	.0	501.4	.2
MBH	542.3	550.4	1.5	542.5	.0	540.8	.3
MAH	581.5	590.4	1.5	582.5	.2	580.1	.3
MMB	346.8	350.4	1.0	354.3	.4	354.3	.4
		Average % diff.	1.8		0.2		0.3

The average error using the previous most satisfactory values is approximately three times the maximum error of that using these newer values. Still more exact values for the various CH_2 positions of this series as indicated in Table V may be calculated from the chloride values here reported

and when applied show an average error of 0.2%. If averages be found between these two sets of values, the new set would describe both the alcohols and the chlorides with an average error of 0.3% when applied to the chlorides.

The constitutive effect is strikingly brought out by comparing homologs. The maximum CH_2 value from methylethylhexylchloromethane to ethylpropylpropylchloromethane would be 14.8 units or 45% higher than the minimum value in comparing propylpropylpropylchloromethane and methylmethylhexylchloromethane.

Summary

1. The densities, surface tensions and parachors of sixteen tertiary chlorides have been determined.

2. The parachors show a decrease with temperature of approximately 0.2% per 10° rise in temperature.

3. The effect of substitution in trimethylchloromethane has been found to be of the same order as that with trimethylcarbinol.

4. Values for the individual CH_2 groups in the tertiary chlorides have been determined and found to be of approximately the same value as those obtained for the corresponding CH_2 groups in the tertiary carbinols.

5. The similarity of the values obtained for the chlorides and alcohols indicates that association is not an important factor in the parachor values of the alcohol series.

6. The values for the tertiary branching give closer agreement between the calculated and observed values than the values previously used.

EMORY UNIVERSITY, GA. RECEIVED AUGUST 18, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF YALE UNIVERSITY]

The Second Ionization Constant of Oxalic Acid from 0 to 50°

BY HERBERT S. HARNED AND LESLIE D. FALLON

From the electromotive forces of the cells

$$H_2 \mid NaHC_2O_4(xm_1), Na_2C_2O_4(xm_2), NaCl(xm_3) \mid AgCl\text{–}Ag$$

the ionization constant of $HC_2O_4^-$ has been determined at 5° intervals from 0 to 50°.

The observed electromotive forces are given in Table I. The concentrations of the most concentrated solution, m_1, m_2 and m_3, are given. The concentrations of all other solutions are given by xm_1, xm_2 and xm_3 where x is less than unity. The concentrations were known with an accuracy greater than 0.1%. The reproducibility of the measurements was of the order of ±0.05 mv.

The Determination of the Ionization Constant.—By applying the method of Harned and Ehlers[1] in the manner used by Nims[2] for the second ionization constant of phosphoric acid, the electromotive force of the cell may be expressed by

$$\frac{(E - E_0)F}{RT} + \log \frac{m_{Cl}\, m_{HC_2O_4}}{m_{C_2O_4}} + \frac{2u\sqrt{\mu}}{1 + A\sqrt{2\mu}} = -\log K_2 + f(\mu) = -\log K_2' \quad (1)$$

where the symbols have their usual significance. This differs from the equation of Nims by including the Debye and Hückel factor containing A which allows for the effect of the mean distance of approach of the ions. In order to determine the ionization constant, K_2, it is necessary to evaluate

(1) Harned and Ehlers, THIS JOURNAL, **54**, 1350 (1932).
(2) Nims, *ibid.*, **55**, 1946 (1933).

TABLE I

ELECTROMOTIVE FORCES OF THE CELLS

$H_2 \mid NaHC_2O_4(xm_1), Na_2C_2O_4(xm_2), NaCl(xm_3) \mid AgCl\text{–}Ag$

$m_1 = 0.04945$; $m_2 = 0.02600$; $m_3 = 0.03782$

t	x.....1	0.8546	0.7263	0.5617
0	0.51317	0.51736	0.52217	0.52939
5	.51595	.52029	.52510	.53245
10	.51860	.52319	.52806	.53551
15	.52147	.52609	.53110	.53869
20	.52410	.52903	.53416	.54135
25	.52723	.53207	.53724	.54510
30	.53014	.53511	.54035	.54840
35	.53302	.53814	.54353	.55162
40	.53594	.54126	.54664	.55486
45	.53909	.54446	.54999	.55833
50	.54201	.54753	.55330	.56159
t	x...0.4684	0.4050	0.3210	0.1737
0	0.53459	0.53851	0.54465	0.56180
5	.53767	.54187	.54823	.56570
10	.54096	.54504	.55167	.56935
15	.54416	.54836	.55504	.57308
20	.54739	.55172	.55849	.57691
25	.55073	.55509	.56206	.58066
30	.55412	.55856	.56570	.58461
35	.55741	.56202	.56925	.58850
40	.56090	.56554	.57285	.59244
45	.56431	.56915	.57662	.59654
50		.57275	.58016	.60054

the left side of this equation and extrapolate to zero ionic strength. The ionization constant is of the order of 5×10^{-5} and this is great enough to require a small correction to the ratio of $m_{HC_2O_4}$ to $m_{C_2O_4}$ in the term containing these quantities. This correction was made by arithmetical approximation using the expression for the thermodynamic ionization constant and the Debye and Hückel equation for the activity coefficient. At the lowest concentration the correction amounts to 0.007 in $-\log K_2$ and at the higher concentrations it is negligible. In Fig. 1, various extrapolations are shown. The upper plots represent the

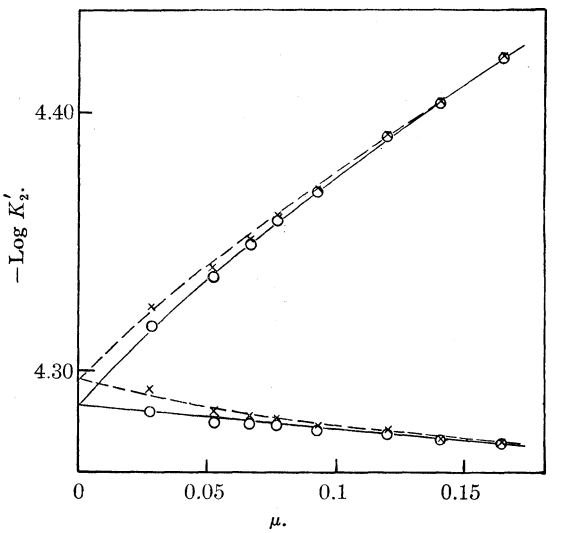


Fig. 1.—Extrapolation at 25°: crosses, uncorrected extrapolation function; circles, extrapolation function corrected for hydrogen ion concentration; upper plots, limiting law; lower plots, limiting equation with term for "mean distance of approach of ions"; diameter of circles equals 0.2 mv.

extrapolation when the Debye and Hückel term, $2u\sqrt{\mu}$, is employed. The lower plots represent the extrapolation when the complete Debye and Hückel expression is used. A was taken to be unity. From the character of these graphs, it is apparent that the latter function yields the better extrapolation. The crosses are the values of the left side of equation (1) uncorrected for hydrogen ion concentration, while the circles represent the values of this quantity when the ratio of $m_{HC_2O_4}$ to $m_{C_2O_4}$ has been corrected. The uncorrected function (dashed lines) leads to a higher value of $-\log K_2$. The corrected function (lowest plot) is a straight line and is easy to extrapolate. The uncertainty in the evaluation of $-\log K_2$ is about 0.002.

Parton and Gibbons[3] and Parton and Nicholson[4] have used a similar cell in which the hydrogen electrode was replaced by the quinhydrone electrode for the determination of K_2. The plots of their results lie very close to ours. At 25°, they obtained 4.300 for $-\log K_2$ at 25° but they did not make the hydrogen ion correction. The present results lead to a value of 4.297 under these circumstances which is excellent evidence of the experimental accuracy of both series of results. Our corrected value is 4.286 at 25°. The same remarks also apply to their results at 30 and 35°.

Heat Content and Heat Capacity of the Ionization Reaction.—Results have been obtained at a sufficient number of temperatures to permit the evaluation of the thermal data from the values of $(-\log K_2)$ given in Table II. The equation of

TABLE II

THE IONIZATION CONSTANT, K_2, HEAT CONTENT AND HEAT CAPACITY OF THE REACTION $HC_2O_4^- \rightleftharpoons H^+ + C_2O_4^{--}$

t	$-\text{Log } K_2$, obsd.	$-\text{Log } K_2$ calcd.	$K_2 \times 10^5$	$-\Delta H$	$-\Delta C_p$
0	4.228	4.229	5.91	278	43
5	4.235	4.234	5.82	501	46
10	4.244	4.243	5.70	739	49
15	4.255	4.254	5.55	993	52
20	4.268	4.269	5.40	1264	56
25	4.286	4.286	5.18	1551	59
30	4.308	4.308	4.92	1856	63
35	4.331	4.331	4.67	2178	66
40	4.356	4.358	4.41	2519	70
45	4.388	4.387	4.09	2877	74
50	4.417	4.420	3.83	3256	77

Constants of equation (2): $\log K_m = \bar{5}.774$; $\Theta = -6.8°$; $p = 6 \times 10^{-5}$.

Harned and Embree[5]

$$\log K_2 = [\log K_m - p\Theta^2] + 2p\Theta t - pt^2 \quad (2)$$

was found to fit the data very accurately if p has the value of 6×10^{-5}. In this equation, K_m is the value of K_2 at its maximum, and Θ is the temperature at which K_2 is a maximum. In most cases of uni-univalent electrolytes, a value of 5×10^{-5} for p is suitable. In the present case, the higher value is somewhat better. K_m was found to be 5.94×10^{-5} at $-6.8°$. Substitution of these values in equation (2) leads to the convenient numerical equation

$$\log K_2' = \bar{5}.771 - 0.000816t - 6 \times 10^{-5} t^2 \quad (3)$$

The agreement between the observed results and those calculated by this equation is shown in the

(3) Parton and Gibbons, *Trans. Faraday Soc.*, **35**, 542 (1939).
(4) Parton and Nicholson, *ibid.*, **35**, 546 (1939).
(5) Harned and Embree, THIS JOURNAL, **56**, 1050 (1934).

second and third columns of Table II. The maximum deviation is 0.003 at 50° and the average deviation is only 0.001.

The changes in heat content and heat capacity accompanying the ionization reaction are given by the equations

$$\Delta H = -5.69 \times 10^{-4}\, T^2(t - \Theta) \quad (4)$$

$$\Delta C_p = -5.49 \times 10^{-4}\, T(T + 2(t - \Theta)) \quad (5)$$

which are derived by differentiation of equation (1). Values of these quantities are contained in the last two columns of Table II.

Summary

1. By means of suitable cells without liquid junction, the second ionization constant of oxalic acid, K_2, has been determined at 5° intervals from 0 to 50°.

2. The equation $\log K_2 = \bar{5}.771 - 0.000816t - 6 \times 10^{-5}\, t^2$ expresses the observed values of $\log K_2$ with an average accuracy of ± 0.001.

3. Values of the heat content and heat capacity of the ionization reaction have been tabulated.

NEW HAVEN, CONN. RECEIVED AUGUST 31, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF YALE UNIVERSITY]

Properties of Electrolytes in Mixtures of Water and Organic Solvents. IV. Transference Numbers of Hydrochloric Acid in Water and Dioxane–Water Mixtures from 0 to 50°

BY HERBERT S. HARNED AND EDWIN C. DREBY[1]

In conjunction with the extensive study of the thermodynamic properties of hydrochloric acid in water and in media covering a wide range of the dielectric constant by measurements of the electromotive force of cells of the type

$$\mathrm{Pt/H_2/HCl}(m), \text{ dioxane}(X), \mathrm{H_2O}(Y)/\mathrm{AgCl\text{–}Ag} \quad (1)$$

it was considered appropriate to investigate the phenomenon of transference for this acid in the same media by means of the cells with transference of the type

$$\mathrm{Ag\text{–}AgCl/HCl}(m), \text{ dioxane}(X), \mathrm{H_2O}(Y)/\mathrm{HCl}(r), \text{ dioxane}(X), \mathrm{H_2O}(Y)/\mathrm{AgCl\text{–}Ag} \quad (2)$$

Very extensive measurements were made which covered the acid concentration range from 0.005 to 3 M, a temperature range from 0 to 50° in solvents consisting of 0, 20, 45 and 70% dioxane–water mixtures. Results of less accuracy were also obtained in 82% dioxane–water mixtures ($D \sim 10$).

The transference number which has been calculated is that defined by the well-known thermodynamic relation

$$T^+ = \mathrm{d}E_t/\mathrm{d}E \quad (3)$$

where the transference number, T^+, at any particular concentration is the slope at the corresponding point on the plot of E_t, the electromotive force of the cell with transference, versus E the electromotive force of the cell without transference.

This is by far the most extensive study of the transference number of an electrolyte as a function of its concentration, the temperature and solvent composition. It is well known that this method is not so accurate as the moving boundary method, but it is reliable, rapid and therefore suitable for an extensive survey of the subject.

Experimental Procedure

A diagram of the cell used is shown in Fig. 1. It consisted of two half-cells connected by means of a stopcock at

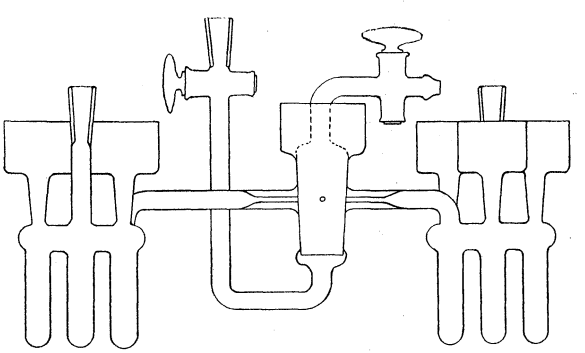


Fig. 1.—Transference cell.

which the liquid junction was formed. Each half-cell contained three legs into which the silver–silver chloride electrodes were inserted. Interchangeable ground glass joints were used between cell and electrode to give air-tight

(1) This communication contains material from a dissertation presented by Edwin C. Dreby to the Graduate School of Yale University in partial fulfilment of the requirements for the degree of Doctor of Philosophy, June, 1939.

(2) Harned and Donelson, THIS JOURNAL, **60**, 339 (1938).

(3) Harned and Ehlers, *ibid.*, **55**, 2179 (1933).

(4) Harned and Morrison, *ibid.*, **58**, 1908 (1936); *Am. J. Sci.*, **33**, 161 (1937).

(5) Harned and Donelson, THIS JOURNAL, **60**, 2128 (1938).

(6) Harned and Walker, *ibid.*, **61**, 48 (1939).

(7) Harned, Donelson and Calmon, *ibid.*, **60**, 2133 (1938).

joints which would not contaminate the dioxane mixtures with grease or rubber. The side arm on each half-cell was used for filling purposes. The junction stopcock consisted of a three-way hollow core with one-inch (2.5-cm.) capillaries leading to the half-cells. The three way stopcock was essential in filling the cells and between measurements the stopcock was set at an intermediate position to prevent diffusion between the two half-cells.

The vacuum technique used in electromotive force work in this Laboratory was not applicable in this case. The procedure was to insert the electrodes and the filling vessels in their respective holes and evacuate the apparatus through the junction stopcock. It was then filled with hydrogen and reëvacuated. This process was carried out three times, finally leaving the whole apparatus under a slight pressure of hydrogen. The solution was then allowed to run in, forcing out the atmosphere of hydrogen. The solutions had previously been saturated with hydrogen and were air free.

The preparation of the solutions and electrodes and the method of measurement was identical with that described by Harned and Morrison.[4] The arrangement of having three electrodes in each half-cell permitted the checking of the electrodes against each other, thus facilitating the detection of faulty electrodes.

Electromotive Forces

In order to obtain reproducible and consistent results, it was found advisable to keep the acid activity ratio in the transference cells less than ten to one. This made it impossible to use the same reference concentration in every cell measured. Instead, a series of cells, interrelated, was measured over the concentration range, and the results were combined in such a manner as to give values of the electromotive force over the entire acid concentration range all referred to one reference concentration

The procedure was to least square the original experimentally determined values of the electromotive force to fit the equation

$$E = E_{25} + a(t - 25) + b(t - 25)^2 \qquad (4)$$

These equations were then combined so as to give the electromotive forces in terms of the reference concentration. The resultant constants were then smoothed concentration-wise. Table I gives values of the constants E_{25}, a and b at the measured concentrations for water, 20, 45 and 70% dioxane–water mixtures.

The average deviations listed in the last column of Table I are the differences in millivolts between the values calculated by equation (4) and the original experimental values, averaged over the temperature range for each cell. The values with the asterisk obviously are associated with poor experimental results and these were not included in

TABLE I

SMOOTHED CONSTANTS OF EQUATION (4) EXPRESSING EXPERIMENTAL ELECTROMOTIVE FORCES. RANGE OF VALIDITY IS 0 TO 50°

m	E_{25}	$a \times 10^4$	$b \times 10^6$	$\Delta_{av.}$
	Water, m_r = 0.100313			
2.99000	0.16695	2.50	−0.62	0.07
1.69357	.12844	2.15	− .51	.05
0.97192	.09787	1.78	− .41	.04
.55472	.07131	1.38	− .31	.03
.31804	.04711	0.93	− .21	.04
.179939	.02351	.48	− .11	.01
.100313	.00000	.00	.00	.00
.058486	− .02171	− .44	.10	.01
.018028	− .06885	−1.38	.31	.01
.0061880	− .11217	−2.25	.51	.03
.0047006	− .12341	−2.48	.56	.01
.0018611	− .16120	−3.41	.73	.01
			Mean $\Delta_{av.}$	.03
	20% Dioxane, m_r = 0.038278			
2.78348	0.20077	3.10	−1.69	0.08
1.49548	.15870	2.67	−1.07	.07
0.70003	.11908	2.13	−0.66	.07
.33243	.08634	1.60	− .46	.03
.165267	.05796	1.10	− .29	.09
.080510	.02935	0.59	− .15	.26*
.038278	.00000	.00	.00	.00
.018333	− .02900	− .58	.15	.76*
.0085061	− .05954	−1.19	.29	.02
.0038779	− .09090	−1.82	.44	.28*
.0020142	− .11700	−2.47	.64	.17
			Mean $\Delta_{av.}$	.07
	45% Dioxane, m_r = 0.037604			
2.99791	0.20336	2.35	−1.32	0.31*
2.44143	.18579	2.36	−1.26	.04
1.50730	.15212	2.29	−1.11	.04
0.68931	.11058	1.86	−0.87	.06
.29646	.07540	1.32	− .62	.03
.16490	.05313	0.95	− .44	.14*
.076748	.02546	.45	− .20	.04
.037604	.00000	.00	.00	.00
.018603	− .02516	− .44	.19	.07
.0084476	− .05442	− .95	.34	.08
.0035521	− .08765	−1.74	.44	.03
			Mean $\Delta_{av.}$	.04
	70% Dioxane, m_r = 0.036576			
1.30623	0.12916	1.76	−1.62	0.03
0.91788	.11065	1.57	−1.42	.13
.63909	.09225	1.39	−1.23	.15
.35639	.06796	1.10	−0.92	.08
.33140	.06499	1.08	− .91	.69*
.15798	.04211	0.71	− .57	.05
.077959	.02090	.37	− .28	.08
.036576	.00000	.00	.00	.00
.0199096	− .01673	− .28	.17	.10
.0085917	− .03905	− .60	.31	.16
.0038857	− .06200	− .82	.40	.03
			Mean $\Delta_{av.}$	.08

computing the over-all $\Delta_{av.}$ listed at the bottom of the column. The experimental results were the average of at least four readings. The spread in these readings was, in the majority of cases, less than 0.1 mv. Only in the higher dioxane mixtures was it impossible to keep within this limit, and here the average was taken from a greater number of readings. The values obtained are believed to be correct within ± 0.05 mv. The $\Delta_{av.}$ listed in Table I would indicate that the quadratic formula is adequate for expressing the data.

Interpolated values of the measurements of these cells at 25° in aqueous solutions by Shedlovsky and MacInnes agree to within 0.1 mv. or less with our results.[8]

Computation of the Transference Number

From equation (3), it is seen that it is necessary to construct a graph of E_t, the electromotive force of the cell with liquid junction, against E, the electromotive force of the cell without liquid junction. The range of values of E_t and E, however, is so large that graphing them directly would cause the loss of significant figures necessary for the accurate determination of the slope. A method was devised whereby values of E at equally spaced intervals of E_t were determined without the loss of significant figures. Furthermore, the results in this form made it possible to determine the slope analytically and hence improve the accuracy.

Deviation functions, defined by the relations

$$X = E + 2k \log m/m_r;\ X_t = E_t + 2k \log m/m_r$$

gave values of X_t and X corresponding to the values of E_t and E where k is defined by $2.303\ RT/F$. These values of X_t and X covered a very small range, so they could be plotted very accurately and with no loss of significant figures. Values of X_t were interpolated graphically to the round concentrations for which values of X existed. These data were used to make a plot of $X - X_t$ *versus* X. It is to be noted that $X - X_t$ is simply $E - E_t$. From this graph, values of $X - X_t$ were read off for values of X_t corresponding to values of E_t spaced at equal intervals of 0.01 v., the latter being obtained from a plot of E_t against X_t. Adding together the appropriate values of $X - X_t$ and E_t gave the desired results, namely, values of E for values of E_t spaced at intervals of 0.01 v. The data were then in a form for the analytical determination of the slope, which is the transference number.

A derivative function derived by Rutledge[9] was employed for the determination of the transference number. It is of the form

$$\frac{dE}{dE_t}(E) = \frac{1}{12h}(C_{-2}E_{-2} + C_{-1}E_{-1} + C_0E_0 + C_1E_1 + C_2E_2)$$

where $(dE/dE_t)(E)$ is the slope at a value, E, of the dependent variable; h is the magnitude of the chosen interval in the independent variable; E_{-2}, E_{-1}, etc., are consecutive values of the dependent variable; and C_{-2}, C_{-1}, etc., are constants. There are three sets of constants, the choice of any one being dependent on whether the slope is to be determined at E_{-1}, E_0 or E_1. Except at the extremes, the values of the slope were determined by taking the average of the results obtained by placing the Rutledge formula in the three possible positions.

This method, as well as any other method used for the determination of slopes, has decreased accuracy at the extremes of the curve. Beside this difficulty, there is also the added fact that data in the more dilute regions are less accurate because of greater experimental difficulties. Thus, in subsequent handling of the data, less stress is laid on the values of the transference number below 0.03 M than on the values at the higher concentrations.

The values of the transference number obtained by application of the Rutledge formula to the data were smoothed by plotting them against values of E_t and reading back values of T^+ for values of E corresponding to round concentrations. Typical of such plots is that shown in Fig. 2 for water at 25°. This is, of course, a concentration-wise smoothing. Subsequently a temperature-wise smoothing was also performed but not until the limiting value of the transference number had been evaluated.

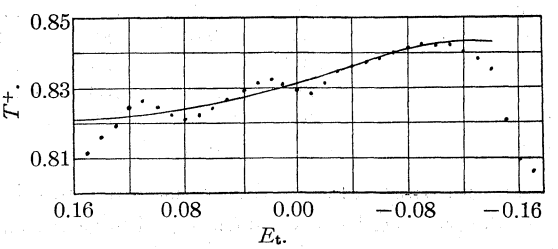


Fig. 2.—Smoothing of transference numbers. Solvent is water.

(8) Shedlovsky and MacInnes, THIS JOURNAL, **58**, 1970 (1936).

(9) Rutledge, *J. Math. Phys. M. I. T.*, **8**, 1 (1929); *Phys. Rev.*, **40**, 262 (1932).

TABLE II

TRANSFERENCE NUMBERS OF HYDROCHLORIC ACID IN WATER AND DIOXANE–WATER MIXTURES

m	0°	5°	10°	15°	20°	25°	30°	35°	40°	45°	50°
					Water						
		0.842	0.837	0.831	0.826	0.821	0.816	0.811	0.806	0.801	0.796
0.005		.844	.840	.834	.829	.824	.819	.814	.809	.804	.799
.01		.845	.841	.835	.830	.825	.821	.816	.811	.806	.801
.02		.846	.842	.836	.832	.827	.822	.818	.813	.808	.803
.05		.848	.844	.838	.834	.830	.825	.821	.816	.811	.806
.1		.850	.846	.840	.837	.832	.828	.823	.819	.814	.810
.2		.851	.847	.843	.839	.835	.830	.827	.823	.818	.814
.5		.854	.850	.846	.842	.838	.834	.831	.827	.822	.819
1.0		.855	.852	.848	.844	.841	.837	.833	.829	.824	.821
1.5		.857	.853	.849	.845	.842	.839	.835	.830	.825	.822
2.0		.857	.853	.849	.846	.843	.839	.835	.831	.826	.822
3.0		.858	.854	.850	.846	.843	.840	.836	.832	.827	.823
					20%						
	0.856	0.851	0.846	0.841	0.836	0.831	0.825	0.821	0.816	0.810	0.805
0.005	.861	.855	.850	.845	.840	.835	.829	.825	.820	.814	.809
.01	.862	.857	.851	.846	.841	.836	.831	.827	.821	.816	.811
.02	.865	.859	.853	.848	.843	.838	.833	.829	.824	.818	.813
.05	.867	.861	.856	.851	.846	.841	.837	.832	.827	.822	.816
.1	.868	.862	.857	.852	.848	.843	.839	.834	.829	.823	.818
.2	.869	.863	.858	.853	.849	.844	.840	.835	.830	.825	.820
.5	.867	.862	.857	.852	.847	.843	.838	.833	.829	.823	.818
1.0	.864	.860	.854	.849	.844	.840	.836	.831	.826	.821	.816
1.5	.862	.857	.852	.847	.842	.838	.834	.829	.824	.819	.814
2.0	.860	.855	.850	.845	.841	.836	.832	.828	.823	.818	.813
3.0	.856	.852	.847	.842	.838	.833	.829	.825	.820	.816	.811
					45%						
	0.828	0.824	0.820	0.816	0.811	0.806	0.801	0.796	0.791	0.787	0.783
0.005	.833	.829	.825	.821	.816	.811	.807	.801	.797	.793	.788
.01	.835	.830	.827	.823	.818	.813	.809	.804	.799	.795	.790
.02	.838	.833	.829	.825	.820	.816	.811	.807	.802	.798	.793
.05	.842	.837	.833	.829	.824	.820	.816	.812	.807	.803	.798
.1	.845	.840	.836	.831	.827	.823	.819	.816	.811	.807	.803
.2	.849	.844	.840	.834	.830	.826	.823	.820	.816	.812	.807
.5	.851	.846	.842	.836	.833	.829	.826	.822	.819	.815	.811
1.0	.851	.846	.841	.836	.832	.828	.825	.822	.819	.815	.811
1.5	.850	.845	.840	.835	.832	.828	.824	.821	.818	.814	.810
2.0	.849	.844	.839	.835	.831	.827	.824	.820	.817	.813	.809
3.0	.847	.843	.838	.833	.830	.825	.822	.817	.814	.810	.807
					70%						
		0.772	0.768	0.764	0.760	0.755	0.750	0.746	0.742	0.738	0.734
0.005		.781	.778	.774	.770	.766	.761	.757	.753	.750	.747
.01		.783	.780	.777	.773	.769	.764	.760	.756	.753	.751
.02		.786	.783	.779	.776	.772	.767	.763	.760	.757	.755
.05		.788	.785	.782	.778	.774	.770	.766	.763	.760	.758
.1		.789	.786	.783	.780	.775	.771	.768	.765	.762	.759
.2		.789	.786	.784	.780	.776	.771	.768	.765	.762	.759
.5		.789	.786	.783	.779	.774	.770	.766	.764	.760	.757
1.0		.788	.785	.782	.777	.772	.768	.764	.762	.758	.754
1.5		.788	.784	.781	.776	.771	.766	.763	.760	.757	.752

The limiting value of the transference number was determined by the method of Longsworth.[10] This consisted in plotting the function

$$T_0^{+\prime} = \frac{T^+\Lambda' + \beta\sqrt{c}}{\Lambda' + 2\beta\sqrt{c}}$$

where

$$\Lambda' = \Lambda^0 - (\alpha\Lambda^0 + 2\beta)\sqrt{c}$$

against the concentration c and extrapolating to $c = 0$ to give the value of the limiting transference number, T_0^+. In this equation, T^+ is the transference number at concentration c in moles per

(10) Longsworth, THIS JOURNAL, 54, 2741 (1932).

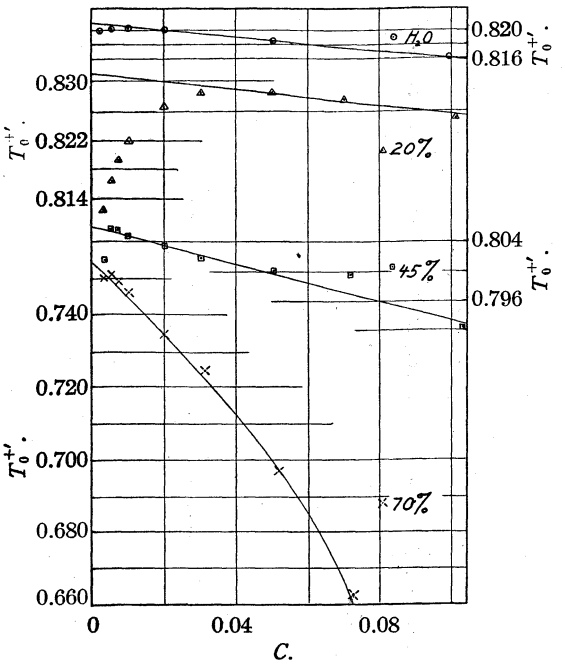


Fig. 3.—Extrapolations for limiting transference numbers.

liter, Λ^0 is the equivalent conductance at infinite dilution and α and β are the constants of the Onsager conductance theory. This function worked very well for water, 20% and 45% dioxane–water mixtures, giving practically straight lines. It began to fail in the 70% mixture, but the curvature was not great enough to seriously affect the extrapolation. Figure 3 shows the nature of these extrapolations in water, 20, 45 and 70% dioxane–water mixtures at 25°. We note that at concentrations below 0.03 *M*, particularly with the 20% dioxane mixtures, the points do not fall on the line used for the extrapolation. We attribute this behavior to the previously mentioned difficulty of obtaining slopes of a curve at the extreme end of the curve, and to a somewhat greater uncertainty in the measurements in the 20% dioxane mixtures.

With the values of the transference number at infinite dilution and the computed values of the transference number smoothed over the concentration range, plots were now made of the transference number *versus* the square root of the concentration and the values for the whole temperature range were plotted on the same sheet of paper. In drawing any one curve the points on either side corresponding to the next higher and lower temperature interval, respectively, were considered. This resulted in a temperature-wise smoothing. In every case but one, the deviations of the drawn curve from the plotted points were well within the expected limit of error. Values of the transference number at round concentrations and at 5° intervals for water, 20, 45 and 70% dioxane–water mixtures are listed in Table II.

Discussion of Errors

From a consideration of the Rutledge derivative function, it can be shown that an error of 0.00001 in E produces an error of 0.001 in T^+. The mean deviations in Table I give, in all probability, a close approximation to the expected error in E from which the error in T^+ can be determined. Also, the average of the deviations of the plotted points from the smooth curve in Fig. 2 will give the order of magnitude of the expected error in the transference number. The results obtained by the first method lead to expected errors of 3, 7, 4 and 8 and the second method of 2, 5, 4 and 8 units in the third place of the transference number for water, 20, 45 and 70% dioxane–water mixtures, respectively. The consistency

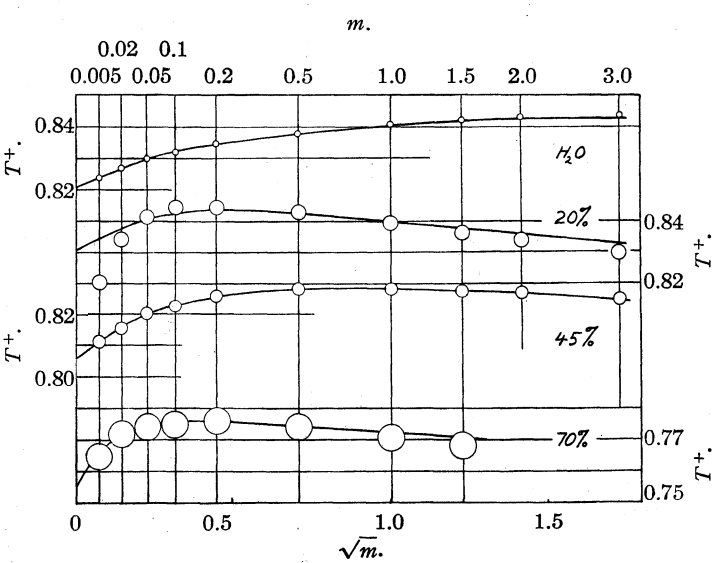


Fig. 4.—Smoothed transference numbers and degree of error.

in the plotted points from which Table II was formed would lead one to believe the error is well within these limits.

A comparison of the transference numbers at 25° for the various solvents with the limit of error

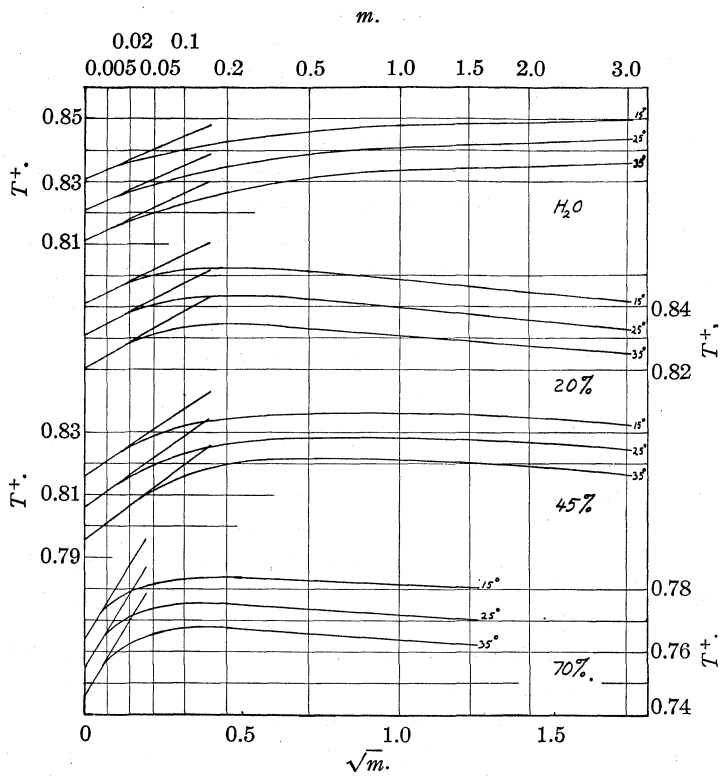


Fig. 5.—Transference numbers and theoretical limiting slopes.

as determined by the second method listed above is shown in Fig. 4. The diameters of the circles represent the size of the error. The circles are drawn about the points determined by the smoothing process of Fig. 2. The lines are drawn through the points listed in Table II.

Limiting Slopes for the Transference Numbers.—The Onsager conductance theory leads to an expression for the limiting slope

$$\text{slope} = \frac{(2T_0^+ - 1)\beta}{\Lambda^0}\sqrt{d_0}$$

where T_0^+ is the limiting value of the transference number, Λ^0 is the limiting equivalent conductance, β is the constant from the Onsager conductance theory and d_0 is the density of the pure solvent. This is the slope for T^+ versus the $\sqrt{m}$. Table III gives the values of the slope in water, 20, 45 and 70% dioxane–water mixtures.

Figure 5 shows plots of the transference numbers at 15, 25 and 35° with the limiting slopes drawn in for water, 20, 45 and 70% dioxane–water mixtures. It is to be noted that, even where the slope is steep as is the case for the higher dioxane mixtures, there is a tendency for the curve to fall rapidly into the limiting slope from 0.02 *M* on down.

Comparison with Other Methods.—Extensive work has not been carried out previously on the determination of the transference numbers of hydrochloric acid over wide concentration and temperature ranges by any one method. Table IV gives values for the transference number of hydrochloric acid in water determined by the three principal methods: electromotive force, Hittorf,

TABLE III

LIMITING SLOPES

	H_2O	20%	45%	70%
15°	0.04278	0.04906	0.06773	0.1629
25°	.04509	.05195	.07186	.1642
35°	.04714	.05507	.07492	.1664

TABLE IV

TRANSFERENCE NUMBERS OF HCl IN WATER AS LISTED IN "INTERNATIONAL CRITICAL TABLES"

c = Concentrations in moles per liter

c	0.005	0.010	0.020	0.050	0.100	0.500	1.00
10°: Hitt.	0.840	0.840	0.841				
	(.840)[b]	(.841)	(.842)				
18°: Hitt.	.832	.833	.833	0.834	0.835	0.840	0.844
M. b.			.835		.835		
E. m. f.	.832	.832	.832	.832	.832		
	(.831)	(.832)	(.834)	(.836)	(.838)	(.843)	(.845)
30°: Hitt.		.822	.822	.822			
M. b.				.828	.832		
		(.821)	(.822)	(.825)	(.828)		
50°: Hitt.		.801					
		(.801)					
25°[a]: M. b.	.8239	.8251	.8266	.8292	.8314		
	(.824)	(.825)	(.827)	(.830)	(.830)		

[a] Longsworth, THIS JOURNAL, **54**, 2741 (1932). [b] Results of present investigation are in parentheses.

and moving boundary, as listed in the "International Critical Tables." The values found in this investigation are listed within parentheses for comparison. On the whole, the agreement is satisfactory.

The most accurate method for the determination of transference numbers is the moving boundary method, particularly in its refined form as developed at the Rockefeller Institute. Longsworth[10] has determined the transference number of hydrochloric acid in water with great precision at 25°. The values determined in this investigation are compared with his in the last two rows of Table IV. The excellent agreement obtained is good confirmation that the method used in computing the transference number from the electromotive forces is a sound one.

Transference Numbers in 82% Dioxane.—The difficulties in obtaining the electromotive forces of the cells with liquid junction for the 82% dioxane–water mixture were not easy to overcome. There was a much greater tendency for diffusion of the electrolyte at the junction and the low conductivity of the solutions made it difficult to make measurements of the electromotive force. A cell was used similar to that in Fig. 1 but without the capillary tubing. It was necessary to have reservoirs of the solutions in the side arms to flush out the junction tubes whenever the junction stopcock had been opened for any length of time. Furthermore, the electrodes took considerable time to come to equilibrium and they did not remain constant over long periods of time.

The electromotive forces of the cells with transference are listed in Table V. The large deviations, particularly in the lower concentrations, indicate that the transference numbers cannot be determined with great precision for the dilute acid solutions. Figure 6 shows the final smoothed values of the transference number at 15, 25 and 35°, represented by the heavy curved lines.

The Longsworth method was not very satisfactory in determining the limiting value of the transference number but the accuracy of the data did not warrant the search for another method. With full knowledge that these values are probably incorrect but that they do give the order of magnitude, the theoretical limiting slopes were calculated. These are shown in Fig. 6 by the heavy straight lines drawn into the origin.

The dashed lines in Fig. 6 show what is believed to be nearer the correct values for the transference number in the dilute region, since they approach the theoretical limiting slopes in a logical manner. It is not unreasonable to assume this when it is considered that, in this region of concentration, the error must be of the order of 10 or 15 units in the third place of the transference number. Despite the possible justification for these assumptions, the transference numbers for the 82% dioxane–water mixtures are listed in Table VI from 0.05 to 0.5 M only, the region in which reliable

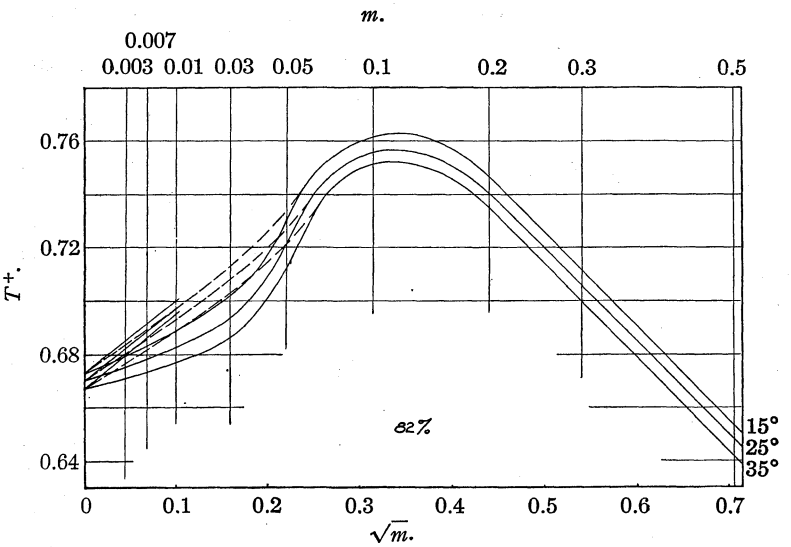


Fig. 6.—Transference numbers in 82% dioxane.

TABLE V

SMOOTHED EXPERIMENTAL RESULTS OF THE CELLS WITH TRANSFERENCE IN 82% DIOXANE–WATER

m	m'	E_{25}	$a \times 10^4$	$b \times 10^6$	$\Delta_{max.}$	Δ_{mean}
0.041369	0.0048874	0.04355	0.428	−0.29	0.15	0.08
.041369	.0097702	.02920	.293	− .24	.50	.31
.041369	.025017	.01035	.108	− .11	.70	.32
.041369	.19080	.03820	.306	− .48	.09	.05
.46526	.041369	.06830	.418	− .50	.21	.18
.46526	.073747	.05505	.298	− .28	.25	.09
.46526	.10492	.04625	.228	− .17	.20	.10

TABLE VI

TRANSFERENCE NUMBERS OF HYDROCHLORIC ACID IN 82% DIOXANE–WATER MIXTURES

m	5°	10°	15°	20°	25°	30°	35°	40°	45°
0.0	0.677	0.675	0.673	0.672	0.670	0.668	0.667	0.665	0.663
.05	.742	.735	.730	.726	.722	.717	.712	.708	.702
.1	.767	.764	.762	.759	.756	.754	.752	.750	.747
.2	.755	.751	.747	.744	.740	.738	.735	.732	.729
.3	.718	.715	.711	.708	.705	.702	.699	.696	.693
.5	.660	.657	.654	.651	.648	.645	.642	.639	.637

values for the electromotive force were obtainable. The extrapolated values of the transference number used in the calculation of the limiting slope are listed in the first row of the table.

Summary

1. Electromotive forces of the cells Ag–AgCl/HCl (m), dioxane (X), $H_2O(Y)$/HCl(r), dioxane (X), $H_2O(Y)$/AgCl–Ag have been obtained for 0, 20, 45, 70 and 82% dioxane solutions at 5° intervals from 0 to 50° and from 0.005 to 3.0 M acid concentration.

2. The cation transference number has been calculated over these ranges of temperature and concentration from these results and previous measurements of the cells without liquid junction.

3. The limiting transference number has been determined by extrapolation for all the solutions over the entire temperature range.

4. Agreement with the limiting law of the Onsager conductance theory was observed in the water, 20, 45 and 70% dioxane–water mixtures.

5. Results obtained with the mixtures containing 82% dioxane were less accurate. They have a value, however, since no transference number data in media of as low a dielectric constant ($D_{25} = 9.57$) are available.

NEW HAVEN, CONN. RECEIVED AUGUST 31, 1939

[CONTRIBUTION FROM THE MORLEY CHEMICAL LABORATORY, WESTERN RESERVE UNIVERSITY]

Phosphoryl Bromofluorides

BY HAROLD SIMMONS BOOTH AND CHARLES GEORGE SEEGMILLER[1]

It has been found in this Laboratory that phosphoryl trichloride can be fluorinated stepwise to yield phosphoryl chlorofluorides[2a] by means of antimony trifluoride with antimony pentachloride as catalyst, and that phosphorus tribromide likewise can be fluorinated stepwise by means of antimony trifluoride but with bromine as the catalyst.[2b]

While the phosphoryl chlorofluorides were quite stable, the compounds $PBrF_2$ and PBr_2F decomposed on standing to PF_3 and PBr_3. Hence it was of interest to learn whether phosphoryl bromide could be similarly fluorinated stepwise and whether the fluorobromides so produced were stable.

Experimental

Phosphoryl tribromide[3] was prepared by the reaction between phosphorus pentabromide and phosphorus pentoxide: $P_2O_5 + 3PBr_5 = 5POBr_3$. The phosphoryl tribromide was fluorinated at a pressure of 25 to 50 mm. by the slow addition of sublimed antimony trifluoride[4] in the generator as described by Booth and Bozarth.[5] During the early stages, the reaction was vigorous at 60°, but in its later stages it became quite slow, so that it was found advantageous to raise the temperature gradually to 100°. It was unnecessary to add a catalyst, perhaps due to traces of bromine left in the phosphoryl tribromide.

The product consisted of about 60% phosphoryl trifluoride, 10% phosphoryl monobromodifluoride, and 30% phosphoryl dibromomonofluoride. The products were separated and purified and their physical constants established, as described by Booth and Bozarth.[6] It was found in the case of the $POFBr_2$ and POF_2Br that an ice–salt mixture made a satisfactory refrigerant for the acetone which was circulated by an automatically actuated centrifugal pump through the fractionating column head.

Analysis.—The phosphoryl trifluoride was established by approximate boiling points obtained from a thermocouple in the fractionating column head, by molecular weight determinations by a gas density balance,[6] and by chemical analysis for phosphorus.

Samples of the phosphoryl bromofluorides were condensed in glass bulbs connected to the apparatus by conical joints as previously described[2a] and absorbed in an excess of potassium hydroxide. They reacted energetically with the solution on warming and were completely dissolved. The solution was then heated on a steam-bath for fifty hours to ensure completion of the reaction. Bromine was determined gravimetrically as silver bromide, and phosphorus

TABLE I

ANALYSES

	Phosphorus		Bromine	
	Calcd.	Exptl.	Calcd.	Exptl.
POF_2Br	18.81	18.81	48.45	48.51
		18.67		48.45
$POFBr_2$	13.73	13.47	70.76	70.54
		13.70		70.85

(1) From a portion of a thesis submitted by Charles George Seegmiller in partial fulfilment of the requirements of the degree of Doctor of Philosophy in Chemistry to the Graduate School of Western Reserve University, May, 1939.

(2) (a) Booth and Dutton, THIS JOURNAL, **61**, 2937 (1939); (b) Booth and Frary, *ibid.*, **61**, 2934 (1939).

(3) See "Inorganic Syntheses," Vol. II, for details of this preparation.

(4) Kindly furnished by the Harshaw Chemical Company, Cleveland, Ohio.

(5) Booth and Bozarth, THIS JOURNAL, **61**, 2927 (1939).

(6) Booth and Bozarth, *Ind. Eng. Chem.*, **29**, 470 (1937).

by precipitation as the phosphomolybdate and direct weighing as such. One set of samples was reprecipitated as magnesium ammonium phosphate and ignited to the pyrophosphate, and was found to be in good agreement with the above method.

Physical Properties.—The determination of the vapor pressure of phosphoryl monobromodifluoride was made by direct observation of the vapor pressure of the liquid held in a small glass bulb immersed in a thermostat, in the manner described by Booth and Bozarth.[6] Two separate samples, A and B, were run; as an extra check, a small portion was distilled out of each sample after a set of readings had been taken, at a pressure different from the pressure of the original distillation of the substance, and a few more points then determined. The temperature was observed with a Leeds and Northrup resistance thermometer calibrated by the United States Bureau of Standards.

The vapor pressure data for phosphoryl dibromomonofluoride, which is a liquid at room temperature, were determined in an isoteniscope,[7] as was that small portion of the curve for phosphoryl monobromodifluoride which was run above room temperatures (Sample C). Here again, for the phosphoryl dibromomonofluoride, two separate samples A and B were run, and small portions were pumped off and more points run as a further check of purity.

The freezing points of phosphoryl dibromomonofluoride and phosphoryl monobromodifluoride were observed in the glass melting point apparatus which is standard in this Laboratory. The rate of cooling was observed on the Micromax recording potentiometer actuated by a three-junction thermocouple which had been calibrated against a platinum resistance thermometer standardized by the United States Bureau of Standards. The freezing points obtained were sharp and easily reproducible. Both compounds showed supercooling under favorable experimental conditions, sometimes as much as 15°.

The liquid density of the phosphoryl bromofluorides at 0° was determined using a pycnometer as described by Booth and Herrmann.[8]

Discussion

Phosphoryl tribromide was found to yield the expected intermediate fluorination products as well as phosphoryl trifluoride. No catalyst was found to be necessary, possibly due to traces of bromine in the phosphoryl tribromide, although Schumb and Gamble[9] found a catalyst was unnecessary in the fluorination of $SiBr_4$ by SbF_3. No tendency toward decomposition of the intermediate compounds to the completely brominated and completely fluorinated end-products was observed at any temperature used, in which the phosphoryl bromofluorides resemble the phosphoryl chlorofluorides and not the fluorobromophosphines.

(7) Booth, Elsey and Burchfield, THIS JOURNAL, **57**, 2064 (1935).
(8) Booth and Herrmann, *ibid.*, **58**, 63 (1936).
(9) Schumb and Gamble, THIS JOURNAL, **58**, 994 (1936).

TABLE II

VAPOR PRESSURE OF $POFBr_2$

$$\log p = (-1642.9/T) + 7.1687$$

	Temp., °C.	P, mm. Obsd.[b]	P, mm. Calcd.[c]	Deviation, mm. Hg
A	27.0	51.8	49.2	− 2.6
A[a]	40.0	78.7	83.2	4.5
B	43.6	96.6	99.9	3.3
A	47.3	107.6	109.3	1.7
A	59.6	165.4	169.4	4.0
B	62.8	191.3	188.9	− 2.4
A[a]	66.6	212.2	214.4	2.2
B	73.1	261.0	263.8	2.8
A[a]	75.1	285.9	280.9	− 5.0
B	81.0	338.8	337.3	− 1.5
A	85.4	372.5	384.5	12.0
B[a]	90.7	453.4	447.8	− 5.6
A	96.8	527.7	532.0	4.3
A	102.4	612.3	619.5	7.2
B	103.8	653.6	643.1	−10.5
B[a]	107.0	715.4	714.7	1.5
A	109.1	736.8	739.5	2.7
B	110.2	769.2	760.7	− 8.5
A	111.5	787.6	786.5	− 1.1

VAPOR PRESSURE OF POF_2Br

$$\log p = \frac{-1550.0}{T} + 7.9662$$

A	−53.1	8	8.3	0.3
B	−36.5	25	25.8	0.8
A	−34.6	29	29.2	− 0.2
A	−30.3	40	38.0	− 2.0
B[a]	−26.7	47	47.6	0.6
A	−22.1	63	61.3	− 1.7
B	−16.4	87	84.3	− 2.7
B[a]	−12.1	107	105.9	− 1.1
B	− 9.3	125	122.3	− 2.7
A	0.7	206	201.0	− 5.0
B[a]	3.6	233	230.3	− 2.7
A	6.5	270	263.1	− 6.9
B[a]	10.2	314	311.5	− 2.5
A	12.6	353	346.3	− 6.7
B	16.4	414	408.6	− 5.4
C	26.4	626	616.5	− 9.5
C	30.7	717	729.0	12.0
C[a]	31.7	751	758.0	7.0
C	33.2	791	802.5	11.5

[a] Indicates check run after part was distilled out. [b] Observed pressures have been corrected to 0° and standard gravity according to the "International Critical Tables." [c] Calculated values were determined by the use of the above equations.

The properties of the phosphoryl bromofluorides lie between those of the tribromide and the trifluoride. When pure, both phosphoryl bromofluorides are colorless in all states. They hydrolyze and fume in moist air, and react violently with water. They attack nichrome wire only slightly or not at all. In order to investigate the possibility of determining critical constants,

samples of the two intermediates were sealed up with mercury in glass capillary tubes and heated to their approximate critical temperatures as estimated by the "three-halves" rule. The mercury was badly attacked in both cases, so that the critical constants could not be determined.

TABLE III

PHYSICAL PROPERTIES

	POF_2Br	$POFBr_2$
Boiling point,[a] °C.	30.5 ± 0.1	110.1 ± 0.1
Freezing point, °C.	− 84.8 ± .2	−117.2 ± .2
Liquid density (at 0°)	2.099	2.568
Gas density observed	166	
Theoretical	165	
Heat of vapn.,[b] cal.	7093	7518
Trouton's constant	23.4	19.6

[a] From a plot of the vapor pressure data. [b] Calculated by the Clausius–Clapeyron equation.

Summary

The fluorination of phosphoryl tribromide with antimony trifluoride yields three products, a gas, phosphoryl trifluoride, first described by Moissan, and two new, stable, volatile liquids, phosphoryl monobromodifluoride and phosphoryl dibromomonofluoride. All three have been isolated and purified. The boiling points, vapor pressure data, gaseous and liquid densities of the two phosphoryl bromofluorides have been determined and recorded along with some of their chemical properties.

CLEVELAND, OHIO RECEIVED AUGUST 30, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF BROWN UNIVERSITY AND OF THE UNIVERSITY OF ILLINOIS]

(I) The Reaction of Gallium with Perchloric Acid and (II) the Preparation and Properties of Gallium Perchlorate Hydrates

BY LAURENCE S. FOSTER

I. Reaction of Gallium with Perchloric Acid

Metallic gallium dissolves very slowly in the common mineral acids. Sebba and Pugh[1] reported recently that concentrated nitric acid was the most rapid reagent but, when it was kept near the boiling point, even it dissolved only 5 g. of the metal in ten hours. The rate was somewhat increased by alternately heating and cooling the mixture. They found, in addition, that because of the pronounced passivity of gallium, it was possible to free it from many metallic impurities with little loss of gallium by allowing it to remain in contact with concentrated nitric acid.

Perchloric acid and mixtures of perchloric acid with other acids have been used to dissolve many ordinarily very resistant alloys, particularly "stainless steels."[2] These same reagents have now been shown to dissolve gallium more rapidly than any used hitherto.

Experimental

Reaction of Gallium with Perchloric Acid.—A small piece of gallium (0.5 g.) was heated with 20 ml. of perchloric acid (72%) in an Erlenmeyer flask (250 ml.) equipped with a Smith refluxing head.[2] A vigorous reaction took place and the metal was dissolved completely within fifteen minutes. In another experiment 5 g. of gallium was dissolved in 60 ml. of the acid within an hour. The gallium perchlorate formed is moderately soluble in the hot concentrated acid, but as soon as the mixture is cooled slightly, hexa-aquo gallium perchlorate separates in the form of coarse, white crystals. The remaining acid, recovered by filtration through a sintered-glass funnel, contains almost no gallium.

Reaction of Gallium with Mixed Perchloric–Sulfuric Acids.—The reaction of gallium with a mixture containing two-thirds sulfuric acid (98%) and one-third perchloric acid (72%) was found to be more rapid than that with perchloric acid alone. Gas evolution started as soon as the cold acid mixture came in contact with the metal and proceeded very rapidly when it was warmed. Five grams of gallium was dissolved in 60 ml. of the mixture in about one-half hour. The reaction product was not so soluble in the mixed acids as in perchloric acid alone, however, and separated immediately as a finely divided, white precipitate. Its presence did not interfere with the progress of the reaction, and after the metal had disappeared the excess perchloric acid was removed by distillation with no "bumping" until sulfur trioxide fumes began to escape. At this point, "bumping" became severe. By dissolving the cooled mixture in water, a clear solution of gallium sulfate, containing excess sulfuric acid, was prepared. The entire process was accomplished in less than an hour.

Reaction of Gallium (III) Oxide with Perchloric Acid.—The soluble form of gallium oxide was found to dissolve readily in perchloric acid, but the insoluble form did not

(1) Sebba and Pugh, *J. Chem. Soc.*, 1373 (1937). For a more complete survey of the literature concerning the reaction of gallium with various reagents, see Gmelin's "Handbuch der anorganischen Chemie," 8th ed., no. 36, 1936, pp. 42–45.

(2) Smith and Getz, *Ind. Eng. Chem., Anal. Ed.*, **9**, 378 (1937); *cf.* G. F. Smith, "Mixed Perchloric, Sulfuric, and Phosphoric Acids and their Application in Analysis," G. F. Smith Chemical Co., Columbus, Ohio, 1935.

react. The latter dissolves fairly rapidly in hot hydrochloric acid, however, and after the mixture has become clear, the excess hydrogen chloride may be removed by heating with perchloric acid. Hexa-aquo gallium perchlorate separates when the solution is cooled.

II. Preparation of Gallium Perchlorate Hydrates

Aluminum perchlorate forms crystalline compounds containing 15, 12, 9 and 6 moles of water. It has been reported that a basic aluminum perchlorate, $2Al(ClO_4)_3 \cdot Al_2O_3$, is formed when the nonahydrate is heated rapidly.[3] With indium, the only perchlorate which has been prepared has the formula $In(ClO_4)_3 \cdot 8H_2O$.[4] It has now been found that gallium perchlorate is stable only when extensively hydrated. The following hydrates have been identified: $Ga(ClO_4)_3 \cdot 6H_2O$ and $Ga(ClO_4)_3 \cdot 9^1/_2H_2O$. Basic gallium perchlorates of indeterminate composition are formed when the hydrated crystals are heated.

Experimental

Preparation of Hexa-aquo Gallium Perchlorate.—Ten grams of pure gallium, or an equivalent amount of the soluble form of gallium sesquioxide, is allowed to react with excess perchloric acid (72%) as described in a previous section. If the volume of acid used is larger than 150 ml., the product is entirely soluble at the boiling point of the mixture (200°) and the observation of the disappearance of the last small globules of the metal is facilitated. If less acid is used, the gallium perchlorate formed separates as a coarsely crystalline precipitate, but it does not interfere with the course of the reaction. Heating is continued after the metal has all reacted to remove water and the perchloric acid reduction products (Cl_2, etc.). The characteristic fumes of constant boiling perchloric acid soon appear, and heating is discontinued. When the mixture has cooled, the product may be collected by suction filtration on a sintered glass Büchner funnel and pressed dry with a glass or porcelain spatula. (The small amount of gallium in the filtrate is recovered separately.) The entire process does not require much more than an hour.

NOTE.—The moist crystals must not be allowed to come in contact with any organic material such as filter paper or a horn spatula. Because of the removal of water, due to the formation of hydrated crystals, the perchloric acid adhering to the product is more highly concentrated than 72%.

The remaining excess acid may be removed from the crystals by heating them *in vacuo* at 125° for about an hour in a glass tube, sealed at one end and large enough to hold the porcelain boat containing the product, and exhausted through a glass connection held in a rubber stopper. The tube may be heated conveniently in a thermostated electric drying oven. It should be long enough (2 ft., 61 cm.) to afford an opportunity for the perchloric acid which is volatilized to condense and cool before it reaches the rubber stopper, and it is desirable to expand a section of the tube to provide a bulb into which the condensate may run. If a mechanical pump is used, it should be protected from the acid fumes by a trap containing solid sodium hydroxide.

The hexa-aquo gallium perchlorate thus prepared is a dry, free running powder. Large crystals of hexa-aquo gallium perchlorate may be prepared by slow evaporation, over concentrated sulfuric acid in a vacuum desiccator, of an aqueous solution of gallium perchlorate which contains excess perchloric acid.

Analysis.—Since the hydrates of gallium perchlorate were found to be very soluble in alcohol, it was possible to carry out analyses on a single sample for both the perchlorate ion and the gallium, and by difference to compute the percentage of water. Potassium perchlorate, precipitated by the addition of an excess of an alcohol solution of potassium thiocyanate, was weighed in a sintered glass filtering crucible, after having been dried for an hour at 120°. Water was added to the filtrate and after the alcohol had been removed by distillation, the gallium was precipitated by means of tannin.[5]

Anal. Calcd. for $Ga(ClO_4)_3 \cdot 6H_2O$: Ga, 14.64; ClO_4, 62.65. Found: (A. Crystals heated *in vacuo* for six hours at 120°), Ga, 14.8 (av.); ClO_4, 62.5 (av.). (B. Large crystals from perchloric acid solution, dried quickly on filter paper), Ga, 14.24; ClO_4, 61.8, 61.7.

Properties of Hexa-aquo Gallium Perchlorate.—After it has been freed of excess perchloric acid, the hexa-aquo complex is a dry crystalline meal. It is very deliquescent, extremely soluble in water, forming a clear solution, and very soluble in alcohol and glacial acetic acid. The crystals which are deposited by slow evaporation from a perchloric acid solution are large, regular octahedra. In polarized light they are seen to be isotropic and may be classified as *cubic*. At atmospheric pressure, the hexa-aquo complex decomposes at 175° and *in vacuo* at 155°, yielding gaseous products and basic gallium perchlorate residues of indefinite composition. At still higher temperatures, it is finally converted to the insoluble form of gallium oxide.

Since hexa-aquo gallium perchlorate is readily prepared from either the metal or the oxide and readily freed from the excess acid, it serves admirably as the starting material for the synthesis of other gallium compounds. Conversely, Willard and Fogg[6] electrolyzed a solution of gallium perchlorate for the preparation of the pure metal.

Preparation and Properties of Gallium Perchlorate. $9^1/_2$ Hydrate.—A concentrated aqueous solution of hexa-aquo gallium perchlorate, containing only a slight contamination of free perchloric acid, was allowed to evaporate in a vacuum desiccator over concentrated sulfuric acid. The very large crystals, 3 cm. × 5 mm. × 2 mm., which formed were shown to contain 9.5 moles of water by the analytical method previously described.

(3) Gmelin's "Handbuch der anorganischen Chemie," 8th ed., no. 35, Part B, 1934, p. 217.

(4) Mathers and Schuederberg, THIS JOURNAL, **30**, 212 (1908).

(5) Moser and Brukl, *Monatsh.*, **51**, 325 (1929); Sebba and Pugh, *Trans. Roy. Soc. S. Africa*, **25**, 392 (1938).

(6) Fogg, *Trans. Electrochem. Soc.*, **66**, 107 (1934); Willard and Fogg, THIS JOURNAL, **59**, 1197 (1937).

Anal. Calcd. for $Ga(ClO_4)_3 \cdot 9^1/_2H_2O$: Ga, 12.93; ClO_4, 55.33. Found: Ga, 12.92 (av.); ClO_4, 55.63 (av.).

A known weight of the $9^1/_2$-hydrate, in the form of a single, large, clear crystal still slightly moist with mother liquor and contained in an uncovered wide-form weighing bottle, was heated at 120° at atmospheric pressure. After thirty-six hours, the loss in weight corresponded to the loss of about one mole of water, and although the crystal had become translucent and somewhat deformed, it had not lost completely its original contours. The sample continued to lose water only very slowly. After a few days, the weighing bottle was transferred to a vacuum desiccator and at the end of six weeks the loss in weight indicated a conversion of the original material to the hexa-aquo derivative. The composition of the product was confirmed by analysis.

Anal. Calcd. for $Ga(ClO_4)_3 \cdot 6H_2O$: Ga, 14.64; ClO_4, 62.65. Found: Ga, 14.80; ClO_4, 62.32.

The behavior of crystal fragments when heated in small melting point tubes was quite different. Under these circumstances the $9^1/_2$-hydrate underwent a transition, at about 80°, to a mixture of the hexa-aquo complex in equilibrium with a small amount of saturated solution. Evidently, when it is heated in an open vessel, water evaporates rapidly enough to coat the surface with an adherent film sufficiently strong to permit the entire mass to retain substantially its original shape.

The $9^1/_2$-hydrate usually crystallized in large, colorless, transparent, pseudo-hexagonal prisms terminated in clinodomes, but occasionally it appears as a mass of fine needles. Both forms are monoclinic and exhibit parallel extinction in the prismatic region, and seem to be identical except for size. The substance is very soluble in water, alcohol and glacial acetic acid and is very deliquescent.

Thermal Decomposition of Hexa-aquo Gallium Perchlorate.—When hexa-aquo gallium perchlorate is heated in an evacuated Pyrex tube in an electric furnace, it begins to undergo decomposition at about 155°. Above that temperature it crumbles and some particles are swept out of the container in the stream of evolved gases, giving the appearance of sublimation. This product, however, is not volatile and upon analysis is seen to be a basic gallium perchlorate. Analyses of the residues in the container show the composition to be variable and dependent upon the duration of heating and the temperature attained. Some of the products corresponded fairly closely to the formulas $2Ga(ClO_4)_3 \cdot 3Ga_2O_3$, and $3Ga_2O_3 \cdot Ga(ClO_4)_3$. Others showed intermediate compositions. Only once, when the heating was not prolonged, did the analysis of the residual material correspond at all closely to that of anhydrous gallium perchlorate, $Ga(ClO_4)_3$.

Due to the insolubility of the basic perchlorates in alcohol, the method of analysis used with the hydrated perchlorates could not be followed. Attempts were made to determine the amount of perchlorate ion by precipitating methylene blue perchlorate[7] from a solution of the basic salt in dilute acids, but the results were unreliable. The precipitate was hard to filter and analyses of aliquot parts of a solution differed by as much as 50% due to incomplete precipitation. It was found practicable, however, to prepare an alcoholic solution of the sample by moistening it with glacial acetic acid and allowing it to stand for two hours or more to convert it to a soluble acetate. When alcohol was then added, a clear solution usually resulted. Potassium perchlorate was precipitated and weighed, and the gallium was determined as gallium oxide after precipitation by means of tannin as before.

A sample of a basic perchlorate, the formula of which corresponded fairly closely to $3Ga_2O_3 \cdot Ga(ClO_4)_3$, was heated in a covered porcelain crucible over a Meker burner. The product was the insoluble form of gallium oxide.

Anal. Calcd. for $2[3Ga_2O_3 \cdot Ga(ClO_4)_3] \rightarrow 7Ga_2O_3$: loss, 29.5%. Found: 32.7%.

Acknowledgment.—The author wishes to acknowledge his indebtedness to the University of Illinois for the use of laboratory facilities and materials and to the members of the Chemistry Staff, particularly Professors G. F. Smith and J. C. Bailar, Jr., for their advice and coöperation.

Summary

1. Gallium has been found to dissolve rapidly in hot concentrated perchloric acid and in perchloric–sulfuric acid mixtures.

2. Two hydrates of gallium perchlorate, containing 6 and 9.5 molecules of water of crystallization, have been prepared and characterized.

3. The conditions of stability of the hydrates have been investigated and their conversion at elevated temperatures to basic perchlorates of indefinite composition and finally to the insoluble form of gallium oxide has been established.

URBANA, ILLINOIS RECEIVED MAY 11, 1939

(7) Atack, *J. Soc. Dyers and Col.*, Jan., Sept. and Oct., 1913; *Can. Chem. Metallurgy*, **9**, 201 (1925); Hofmann, Hartmann and Hofmann, *Ber.*, **58**, 2748 (1925); *Z. anal. Chem.*, **69**, 305 (1926); Bolliger, *ibid.*, **94**, 403 (1933).

[A CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF WISCONSIN]

The Effect of Hydrochloric Acid Concentration on the Reduction of Molybdate in the Silver Reductor

BY C. F. HISKEY,[1] V. F. SPRINGER AND V. W. MELOCHE

In the course of a series of studies associated with an investigation of the thiocyanate complex of molybdenum, it was necessary to prepare relatively pure solutions of quinquevalent molybdenum. Among the various methods for preparing this substance there are three common quantitative procedures available. In all cases, a molybdate is reduced with moderately strong reducing agents in solutions approximately 2 normal with hydrochloric acid. Lang and Gottlieb[2a] used stannous chloride solution, Birnbaum and Walden[2b] used the silver reductor, and Furman and Murray[3] used metallic mercury. Because of certain requirements in our experiments, we selected the silver reductor for our investigations. In earlier studies, Walden, Hammett and Edmonds[4] obtained erratic results when they used silver for the reduction of molybdate. However, Birnbaum and Walden showed later that by regulating the normality of the acid, the rate of flow through the reductor tube and the temperature, molybdate was reduced completely to the quinquevalent state.

It will be recalled that high acid concentrations exert a pronounced effect upon quinquevalent molybdenum solutions as well as upon the reduction of molybdate.[5,6] A solution of five-valent molybdenum in 2 normal hydrochloric acid is amber in color while one in 8 normal hydrochloric acid is green. However, if molybdate is reduced with such vigorous agents as the Jones reductor (Zn) in 2 normal sulfuric acid solutions, the molybdenum is trivalent and the solution is green.[7] When molybdate is reduced electrolytically in 8 normal hydrochloric acid solutions, trivalent molybdenum is formed but the solution is pink instead of green.[8] The work of these authors has been summarized in Latimer's "Oxidation Potentials"[9] in the following scheme

$$Mo^{3+}\ (green) \xrightarrow{+0.25v.} Mo^{5+} \xrightarrow{-0.53v.} Mo^{6+}$$
$$Mo^{3+}\ (red) \xrightarrow{-0.11v.} \uparrow$$

Relative stability of solutions of quinquevalent and trivalent molybdenum is another important consideration. It will be remembered that when molybdenum is reduced in the Jones reductor, the reduced solution of trivalent molybdenum is usually caught in ferric alum, or else the solution is protected from the air by an atmosphere of carbon dioxide. Solutions of quinquevalent molybdenum are much more stable. Furman and Murray have indicated that a solution of quinquevalent molybdenum can be titrated with ceric sulfate without any special precautions. In fact, the quantitative procedure for the estimation of molybdenum by means of the silver reductor depends on the fact that if some trivalent molybdenum is formed in the course of the reduction enough air will be dissolved in the solution to oxidize the molybdenum back to the quinquevalent state.

Reductor Technique.—Since we were interested in the true extent of the reduction, it was necessary to prevent oxidation by air. To this end, a one-liter flask was provided with a three-holed stopper and this was arranged in such a manner that it could be attached to the reductor and the air could be displaced in the attached flask by a stream of carbon dioxide before and during the reduction. In a regular procedure, the reductor was heated by passing through it about 200 ml. of boiling hot hydrochloric acid of the same concentration as that of the molybdate sample which was to be reduced. Following the warming process, a one-liter receiving flask was attached and the air displaced by a rapid stream of carbon dioxide. About 40 ml. of 0.02482 molar molybdate which was 8 normal to hydrochloric acid was diluted with the appropriate amount of boiled distilled water to bring the acid concentration to the desired value. This hot solution was passed through the reductor at a rate of about 60 drops per minute. The reductor was then washed with 100 ml. of hot hydrochloric acid which had the same concentration as that of the sample. The reduced solution was received in a molybdate solution which contained about four times as much molybdate as did the original sample. After suitable dilution to

(1) This paper is part of a thesis offered in fulfilment of the requirements for the degree of Doctor of Philosophy.

(2) (a) Lang and Gottlieb, *Z. anorg. Chem.*, **49**, 148 (1906); (b) Birnbaum and Walden, THIS JOURNAL, **60**, 64 (1938).

(3) Furman and Murray, *ibid.*, **58**, 1689 (1936).

(4) Walden, Hammett and Edmonds, *ibid.*, **56**, 350 (1934).

(5) Foerster, Fricke and Hausswald, *Z. physik. Chem.*, **146**, 81 (1930).

(6) Foerster, Fricke and Hausswald, *ibid.*, **146**, 177 (1930).

(7) Hillebrand and Lundell, "Applied Inorganic Analysis," John Wiley and Sons, Inc., New York, N. Y., 1929.

(8) Foerster and Fricke, *Z. anal. Chem.*, **36**, 458 (1923).

(9) Latimer, "Oxidation Potentials," Prentice-Hall, New York, N. Y., 1938.

bring the whole solution to such a volume that the hydrochloric acid concentration was 2 normal, it was titrated with 0.07217 *N* ceric sulfate. Orthophenanthroline-ferrous complex was used as an internal indicator.

Results.—Table I shows the data for a series of samples which represent different acid concentrations. The extent of the reductions is indicated by the calculation of equivalent valence changes. A better picture of the trend of these reductions is shown in the graph in which acid concentration of the various samples is plotted against valence change.

TABLE I

All titrations were corrected by suitable blanks.

Normality HCl	Av. ml. of 0.02482 *M* MoO_4 taken	Av. ml. of 0.07217 *N* Ce^{++++} used	Av. calcd. valence change	Deviation in valence change
2	40.03	13.95	1.013+	±0.012
3	40.50	25.40	1.823	± .028
3.5	40.05	38.88	2.823	± .002
4	40.13	41.13	2.980+	± .030
4.5	40.61	42.30	3.028	.....
5	40.11	41.90	3.037	.....
6	40.02	42.04	3.055	± .050
7	40.09	42.30	3.068	.....
8	40.02	42.44	3.083	± .030
8.6	40.11	42.53	3.090+	± .030
10.0	40.03	42.63	3.097	± .025
10.5	40.08	42.65	3.097	.....

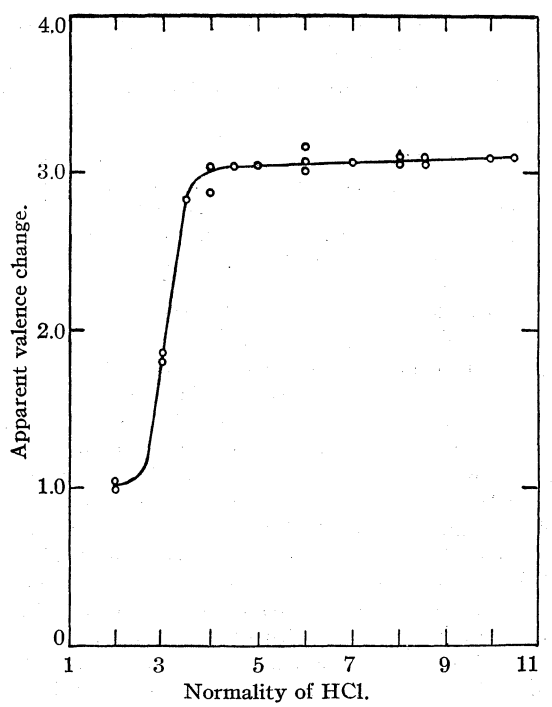


Fig. 1.

Examination of the results indicates that under the conditions of these experiments, a trace of molybdenum is reduced below the five-valent state even in 2 normal hydrochloric acid. Above 4 normal, the molybdate appears to be reduced quantitatively to the trivalent state and the possibility exists that part of the molybdenum is being reduced to an even lower valence state.

In order to see whether such values as those obtained with the 2 normal acid were really due to a reduction of traces of quinquevalent molybdenum to the trivalent state, several samples were treated according to the Birnbaum–Walden procedure without using boiled water or the protective atmosphere of carbon dioxide. The reduced solutions were not caught in molybdate solution. Under such conditions the results obtained showed a valence change of one unit. Typical results for the apparent valence changes were 1.000, 0.9995 and 1.001.

Concerning the fact that in higher acid concentrations the reduction apparently produces a valence change of as much as 3.1, a possible interpretation is that some divalent molybdenum is being formed. The irregularity cannot be due to the titration since all of the titrations were performed in solutions 2 normal to hydrochloric acid. It seemed desirable to compare this behavior with that of Jones reductor under similar conditions. To this end, samples were reduced in the Jones reductor, care being used to avoid all possible oxidation by the air. Titrations were performed in the same manner as those in conjunction with the silver reductor. Some of the data obtained, when this type of reduction was used, are shown in Table II.

TABLE II

Normality HCl	Ml. of MoO_4 0.02482 *M*	Ml. of Ce^{++++} 0.07217 *N*	Apparent valence change
3	39.99	41.30	3.006
	40.00	41.30	3.005
4	40.00	41.30	3.005
	40.03	41.34	3.006
6	40.05	41.41	3.013
	40.06	41.30	3.002

Although extremely high acid concentrations were not used, it is evident that the hydrochloric acid concentration does not affect the degree of reduction in the Jones reductor, at least up to 6 normal. One would want more substantial evidence before concluding that the effect in the silver reductor was due to reduction to a valence state lower than 3.

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Summary

1. It has been shown that when the reduction of molybdate is performed according to the method of Birnbaum and Walden in 2 normal hydrochloric acid, using a silver reductor, their conclusions are substantiated. Although traces of trivalent molybdenum may be formed in the process, exposure to the air oxidizes it to the quinquevalent state before the sample is titrated with ceric sulfate. Therefore their procedure produces quantitative reduction of the molybdate to the quinquevalent state.

2. When reduction of molybdate in 2 normal hydrochloric acid is performed in the silver reductor, using special precautions to avoid air oxidation, the reduction corresponds to slightly more than 1 equivalent in valence change of the molybdenum. If the acid concentration is greater than 4 normal, molybdenum in the molybdate is reduced mainly to the trivalent state. In high acid concentrations such as 10 normal, the reduction shows an apparent valence change as high as 3.1.

3. When reduction of molybdate is performed in a Jones reductor using precautions to prevent air oxidation, the apparent change of valence for molybdenum is not greater than three even though the acid concentration is as high as 6 normal.

MADISON, WISCONSIN RECEIVED JULY 21, 1939

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

Internal Rotation in 1,1,2-Trichloroethane[1]

BY ANTHONY TURKEVICH AND J. Y. BEACH

The problem of the freedom of rotation around the carbon–carbon single bond in halogen substituted ethanes recently has been attacked by the electron diffraction method. Studies have been made of ethylene chloride,[2] ethylene chlorobromide,[3] and ethylene bromide.[3] In all three cases it was found that the *trans* configuration was the stable configuration and that the potential barrier to internal rotation was 5 kcal./mole or greater. In this paper we shall report an electron diffraction investigation of the freedom of internal rotation in 1,1,2-trichloroethane.

The compound used was an Eastman Kodak Co. product, purified by fractional distillation in a 30-inch (76-cm.) column on which the reflux ratio could be controlled. The electron diffraction apparatus was similar to the one described by Brockway.[4] The electron wave length was 0.0590 Å. and the distance from the photographic plate to the nozzle was 12.19 cm. The photographs, taken with the compound warmed to about 65°, show seven irregularly spaced maxima. The fourth maximum is weaker than the third or fifth. The observed values of $s(=(4\pi \sin \theta/2)/\lambda)$ and the visually estimated intensities, I, of the maxima and minima are tabulated in Table I.

TABLE I

VALUES IN PARENTHESES NOT INCLUDED IN THE AVERAGE

Max.	Min.	I	C	s_0	s^a	s^a/s_0	s^b	s^b/s_0
1		15	20	2.937	2.85	(0.907)	3.12	(1.062)
	2	−13	−35	3.993	3.76	(.942)	3.86	(0.967)
2		20	44	4.835	4.82	.997	4.89	1.011
	3	−12	−51	6.851	6.08	.887	6.15	0.898
3		16	51	7.654	7.61	.994	7.64	.998
	4	− 2	− 9	8.645	8.59	.994	8.63	.998
4		8	29	9.387	9.18	.978	9.24	.984
	5	− 7	−35	10.92	10.17	.931	10.21	.935
5		12	48	11.85	11.86	1.001	11.87	1.002
	6	− 5	−24	12.88	13.06	1.014	13.07	1.015
6		3	14	13.65	13.95	1.022	14.03	1.028
	7	− 3	−14	14.59	14.45	0.990	14.45	0.990
7		2	14	15.29	15.08	.986	15.10	.988
					Average	0.981		0.986
					C–Cl	1.73 Å.	C–Cl	1.74 Å.

[a] Calculated for a model in which the interactions are assumed to be electrostatic plus exchange. [b] Calculated for a model in which the interactions are assumed to be electrostatic plus "corrected" exchange.

The photographs were interpreted by the radial distribution method[5] and the usual visual method.[6] Two radial distribution functions are shown in Fig. 1. Curve A was calculated by a method somewhat improved over the original one[5]

(1) These results were presented to the American Chemical Society at the Boston, Mass., meeting, September, 1939.

(2) J. Y. Beach and K. J. Palmer, *J. Chem. Phys.*, **6**, 639 (1938).

(3) J. Y. Beach and Anthony Turkevich, THIS JOURNAL, **61**, 303 (1939).

(4) L. O. Brockway, *Rev. Modern Phys.*, **8**, 231 (1936).

(5) L. Pauling and L. O. Brockway, THIS JOURNAL, **57**, 2684 (1935).

(6) L. Pauling and L. O. Brockway, *J. Chem. Phys.*, **2**, 867 (1934).

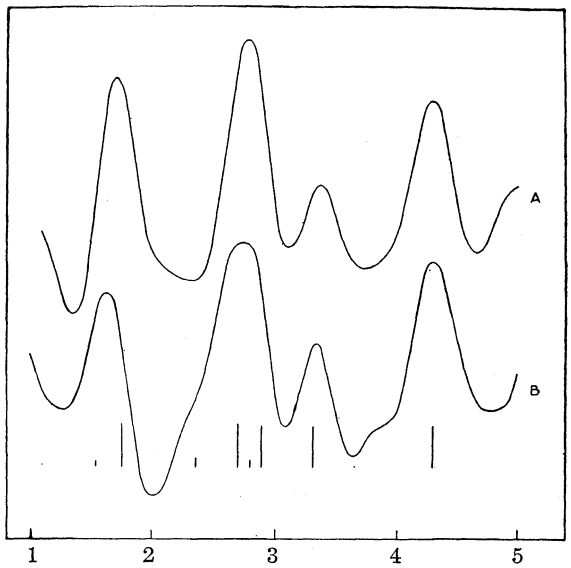


Fig. 1.—Radial distribution functions for 1,1,2-trichloroethane. In curve A the coefficients of the (sin ls)/ls terms are $s^2e^{-as^2}$ times the visually estimated intensities of the maxima. The minima are not used. a is determined by setting e^{-as^2} equal to 0.1 for the largest ring. Curve B is calculated according to the method of Schomaker. Both maxima and minima are used. The C's in Table I are the coefficients of the (sin ls)/ls terms.

and has been called the modified radial distribution method in several previous publications.[7] Curve B was calculated by a procedure suggested by Schomaker[8] in which both maxima and minima are used in a slightly different way. The first peak at about 1.70 Å. represents the carbon–chlorine bond distance together with the carbon–carbon distance. The broad peak at 2.77 Å. represents the short chlorine–chlorine distance and the long carbon–chlorine distance. The two peaks at 3.36 and 4.30 Å. must represent distances between chlorine atoms bonded to different carbon atoms, and the interpretation of these two peaks leads to the most important result of the investigation—the most stable configuration of the molecule. In designating the internal configuration we shall use the relative azimuthal angle of the two ends of the molecule, ϕ. ϕ is 0° when the molecule is *cis* and 180° when it is *trans*. The *cis* and *trans* configurations are the only ones which possess a plane of symmetry. If, as might have been expected at first, the *trans* configuration were the most stable, the radial distribution function should possess a single maximum at 3.95 Å. in place of the two at 3.36, 4.30 Å. In the *trans* configuration the atoms involved in the long chlorine–chlorine distances are at an angle of 120° with respect to each other. The peaks at 3.36 and 4.30 Å. correspond to distances between chlorine atoms separated by angles of about 70 and 180°, respectively. These immediately are seen to be the angles involved in a model for which ϕ is about 130°. The radial distribution function shows, therefore, that the most stable configura-

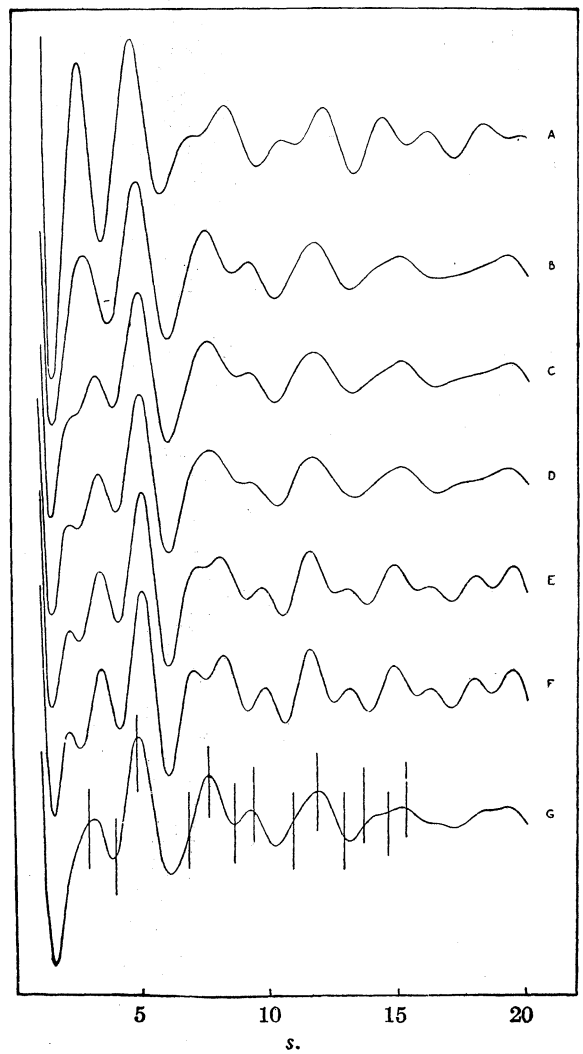


Fig. 2.—Theoretical intensity curves for 1,1,2-trichloroethane. Curve A, *cis* model. Curve B, freely rotating model. Curve C, model having a sinusoidal potential barrier of 5 kcal./mole, the *trans* configuration being the most stable. Curve D, same as for C except that the barrier is 10 kcal./mole. Curve E, same as for C except that the barrier is 20 kcal./mole. Curve F, *trans* model. Curve G, calculated for a model in which the potential barrier is taken to be the sum of the electrostatic interactions and the exchange repulsions.

(7) L. O. Brockway and J. Y. Beach, THIS JOURNAL, **60**, 1836 (1938); J. Y. Beach and Anthony Turkevich, *ibid.*, **61**, 299 (1939).

(8) V. F. H. Schomaker, paper presented to the American Chemical Society at Baltimore, Md., April, 1939.

tion of the molecule is not the *trans* but is *rotated about 50°* from the *trans* configuration. In making this argument it was assumed that the interatomic distances in the molecule are those given by the table of covalent radii,[9,10] and that the bond angles on the carbon atoms are tetrahedral.

In interpreting the photographs by the usual visual method, theoretical intensity curves were first calculated for a rigid *cis* and a rigid *trans* model. These curves are shown in Fig. 2, curves A and F, respectively. In calculating these curves and curves for the other models considered, the interatomic distances in the molecule were taken to be those given by the table of covalent radii.[9] All the bond angles were assumed to be tetrahedral except the Cl–C–Cl angle which was taken to be 111°, the value found in chloroform.[11] Other values for this angle were tried but gave unsatisfactory results. The *cis* curve shows the fourth maximum to be higher than the third or fifth, while the photographs show it to be weaker than the third or fifth. The *cis* model is, therefore, ruled out. The *trans* curve does not resemble the photographs in that it shows extra maxima that are not observed on the photographs. This is easily seen by examining the positions of the observed maxima and minima and curve F in Fig. 2.

If the interaction of the chlorine atoms on the two ends of the molecule is assumed to produce a sinusoidal potential barrier, then the two such interactions in 1,1,2-trichloroethane, when added together, will give again a sinusoidal potential barrier, the stable configuration being the *trans*. Although this result has been shown to be not valid by the radial distribution function, we shall consider it in calculating theoretical intensity curves. Theoretical curves were calculated for sinusoidal potentials having heights of zero, 5, 10 and 20 kcal./mole. These curves are shown in Fig. 2. The curve for zero barrier corresponds to completely free rotation. This curve is unsatisfactory because it shows only one maximum instead of the sixth and seventh. The 5 and 10 kcal./mole curves are unsatisfactory for the same reason. The 20 kcal./mole curve resembles the *trans* curve in showing too many maxima and therefore is not acceptable. We have thus reached the same conclusion as was reached by examination of the radial distribution function—the most stable configuration is not the *trans* configuration.

In calculating these curves the same procedure was followed as in the case of the disubstituted ethanes.[2,3] For the disubstituted ethanes curves were calculated for molecules having all possible configurations differing by 30°. These curves were then added together using the Boltzmann factor as a weighting factor. For 1,1,2-trichloroethane it was found necessary to include molecules having values of ϕ differing by 10° instead of by 30°, except for the steeper barriers.

A potential barrier to internal rotation can be calculated in the following manner. The nine electrostatic interactions can be evaluated by the use of the individual bond moments. These moments have been tabulated by Smyth.[12] In making this calculation it was assumed that the bond moments were due to charges at the centers of the atoms involved in the bond. The sums of these interactions are tabulated in Table II as a function of the angle ϕ. The exchange repulsions also must be considered. We have evaluated the nine exchange repulsions by the method of Eyring.[13] The Morse curve was assumed to be 20% coulombic in each case. These totals are tabulated in Table II as a function of ϕ. The sums of the electrostatic and exchange interactions are tabulated in Table II and shown in Fig. 3, curve A. It is seen that the stable configuration of the molecule is about 60° removed from the *trans* configuration. This is in agreement with the result deduced from the radial distribution function.

TABLE II

ELECTROSTATIC AND EXCHANGE INTERACTIONS AS A FUNCTION OF THE INTERNAL CONFIGURATION, KCAL./MOLE

Interactions	0°	30°	60°	90°	120°	150°	180°
Electrostatic	2.64	2.60	2.43	1.83	1.15	0.55	0.34
Exchange	13.31	14.28	15.56	14.83	14.25	15.36	16.11
"Corrected" exchange	16.09	17.42	19.19	17.53	15.78	16.16	16.70
Electrostatic plus exchange, $E(\phi) - E(\text{min.})$	0.55	1.48	2.59	1.26	0	0.51	1.05
Electrostatic plus "Corrected" exchange, $E(\phi) - E(\text{min.})$	2.02	3.31	4.91	2.65	0.22	0	0.3

In treating the disubstituted ethanes,[2,3] it was found necessary to apply a correction to the halogen–halogen exchange repulsions to obtain agreement with the photographs.[2] When this method is used to get the chlorine–chlorine exchange re-

(9) L. Pauling and M. L. Huggins, *Z. Krist.*, **87A**, 205 (1934).

(10) L. Pauling and L. O. Brockway, THIS JOURNAL, **59**, 1223 (1937).

(11) L. E. Sutton and L. O. Brockway, THIS JOURNAL, **57**, 473 (1935).

(12) C. P. Smyth, *J. Phys. Chem.*, **41**, 209 (1937).

(13) H. Eyring, THIS JOURNAL, **54**, 3191 (1932).

pulsions in 1,1,2-trichloroethane, we obtain the "corrected" exchange repulsions collected in Table II. The sums of the "corrected" exchange repulsions and the electrostatic interactions are given in Table II and shown in Fig. 3, curve B.

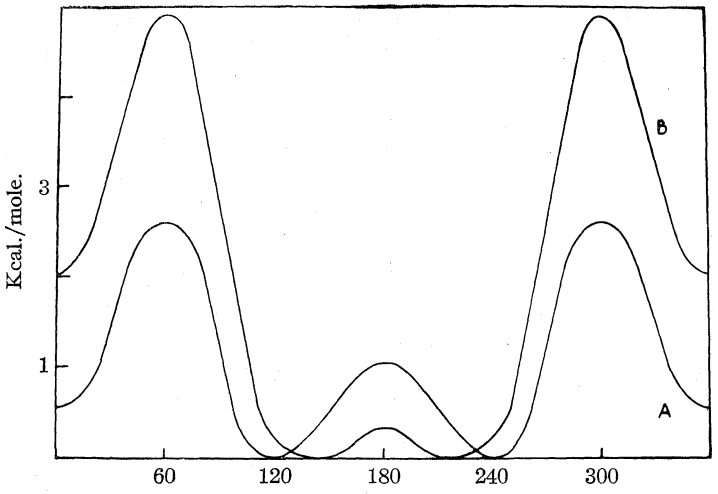


Fig. 3.—The potential barrier to internal rotation. Curve A, the electrostatic interactions plus the exchange interactions, assuming the Morse curve to be 20% coulombic. Curve B, the electrostatic interactions plus the "corrected" exchange interactions.

The shape of the potential curve is changed somewhat but the most stable configuration is essentially the same.

Theoretical intensity curves were calculated for the potential functions shown in Fig. 3. These two curves are practically indistinguishable to the eye so only one of them (curve G) has been included in Fig. 2.

Both curves are quantitatively compared with the photographs in Table I. Curve G resembles the photographs more closely than any other curve calculated. The vertical lines represent the positions of the observed maxima and minima. The incomplete resolution of the sixth and seventh maxima would probably be remedied if the temperature factor had been included and the Z approximation had not been made.

The vertical lines in Fig. 1 indicate the position and importance in the scattering function of the finally determined interatomic distances. The values shown for the long chlorine–chlorine distances are those for a model in the most stable configuration—when ϕ is 130°. The oscillation about this position will, of course, smear these points to some extent.

The radial distribution function and the qualitative and quantitative comparison of the photographs with the calculated intensity curves lead to the final results.

Summary

From an electron diffraction investigation it has been shown that 1,1,2-trichloroethane is not a rigid molecule in the *cis* or the *trans* configuration, nor does it have a sinusoidal potential barrier to internal rotation with the *trans* configuration the most stable. The most stable configuration is rotated about 50° from the *trans* position. A potential barrier calculated from electrostatic (dipole) and exchange interactions is in agreement with the experiments. The C–Cl distance is 1.75 ± 0.03 Å. The Cl–C–Cl angle is 111° 30 ± 2°. The C–C and C–H distances were assumed to be 1.54 and 1.09 Å., respectively.

PRINCETON, N. J. RECEIVED SEPTEMBER 6, 1939

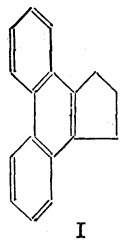
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF DUKE UNIVERSITY]

Synthesis of Phenanthrene Derivatives. IV.[1] 9,10-Cyclopenteno- and 9,10-Cyclohexenophenanthrene

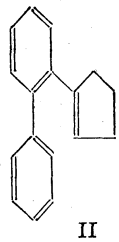
BY CHARLES K. BRADSHER

The first synthesis of 9,10-cyclopentenophenanthrene (I) was that by Bachmann and Kloetzel[2] who obtained this hydrocarbon, together with the isomeric 5,6-benzo-2,3-dihydrobenzonaphthene, upon reduction of the mixture of ketones formed by the cyclization of β-(9-phenanthryl)-propionic acid.

A more convenient route, and one which suggested itself to the aforementioned authors, is that through the cyclization of 1-(2-biphenyl)-cyclopentene-1 (II). They found, however, that the cyclopentene (II), upon treatment with



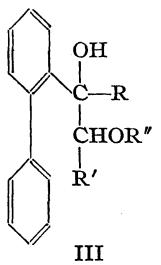
I



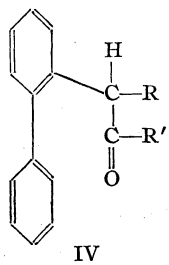
II

aluminum chloride, gave not the desired 9, 0-cyclopentano-9,10-dihydrophenanthrene, but the corresponding spiran.

In the preceding papers of this series, we have described a general method for the synthesis of 9- and 9,10-substituted phenanthrene hydrocarbons. This method involves the cyclization of carbinols of type III by hydrobromic acid.



III

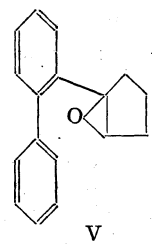


IV

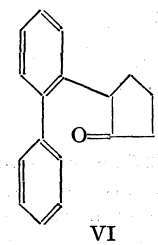
(R′ = alkyl, aryl, or H)

Although the evidence does not as yet amount to a demonstration, it has appeared increasingly probable that a carbonyl compound of type IV, or its enol form, is an intermediate in this cyclization. It should then follow that any carbonyl compound of type IV, or any substance capable of being converted by acids to such a carbonyl compound, would undergo cyclization to give a phenanthrene derivative.

For our purposes, the most satisfactory compound fulfilling the latter requirement seemed to be the cyclopentene oxide (V).



V



VI

Such a compound could be formed readily by the action of monoperphthalic acid on the cyclopentene and would be expected to isomerize under the influence of acids to give 2-(2-biphenyl)-cyclopentanone-1 (VI). Whether or not this was the mechanism of the reaction, when 1-(2-biphenyl)-cyclopentene-1 (II) was oxidized with monoperphthalic acid, and the crude oxide (V) thus afforded refluxed with a mixture of acetic and hydrobromic acids, 9,10-cyclopentenophenanthrene was obtained.

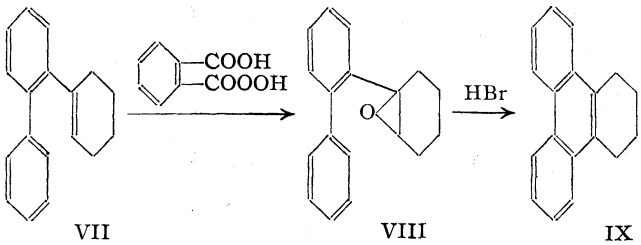
The synthesis of 9,10-cyclohexenophenanthrene (1,2,3,4-tetrahydrotriphenylene (IX)) has been accomplished previously by Bergmann and Blum-Bergmann[3] both by partial dehydrogenation of dodecahydrotriphenylene and by the reduction of the ketone obtained when γ-(9-phenanthryl)-butryic acid was cyclized.

The hydrocarbon (IX) was synthesized by us in a manner analogous to that employed in the case of 9,10-cyclopentenophenanthrene. The Grignard reagent from 2-iodobiphenyl was treated with the cyclohexanone and the crude carbinol dehydrated with potassium bisulfate to give 1-(2-biphenyl)-cyclohexene-1 (VII). The cyclohexene (VII) was treated with monoperphthalic acid to give the corresponding oxide (VIII) and the crude oxide cyclized to 1,2,3,4-tetrahydrotriphenylene by the action of hydrobromic acid.

(1) For the preceding paper of this series see THIS JOURNAL, **61**, 2184 (1939).

(2) Bachmann and Kloetzel, *ibid.*, **59**, 2207 (1937). Weizmann, Bergmann, and Berlin likewise prepared this hydrocarbon by a similar method, *ibid.*, **60**, 1331 (1938).

(3) Bergmann and Blum-Bergmann, *ibid.*, **59**, 1441 (1937).



VII VIII IX

The yield of the hydrocarbon from the cyclohexene was 30%.

The importance of this method is that it is applicable to the synthesis of alkyl tetrahydrotriphenylenes which would be expected to give alkyltriphenylenes upon dehydrogenation.

The author is indebted to Dr. W. E. Bachmann for the gift of a sample of 9,10-cyclopentenophenanthrene.

Experimental

1-(2-Biphenyl)-cyclopentene-1 (II).—A Grignard reagent was prepared from 30.8 g. of 2-iodobiphenyl and 3.74 g. of magnesium. To this was added 8.4 g. of cyclopentanone in ethereal solution. The mixture was refluxed for a half hour and then decomposed by the addition of a 20% solution of ammonium chloride. The ether layer was dried, the ether distilled off and the residue heated for one hour at 160° with 30 g. of powdered potassium bisulfate. At the end of this period, water and benzene were added. The benzene layer was separated, concentrated to a small volume and the residue distilled under reduced pressure. After a large fore-run, consisting chiefly of biphenyl, the desired cyclopentene (II) came over as a colorless oil, b. p. 150–159° (5 mm.); yield 4.0 g.

Monoperphthalic acid was prepared by the action of an alkaline solution of hydrogen peroxide on phthalic anhydride by a method essentially that of Böhme.[4] We found, however, that satisfactory yields of the acid could be obtained only when the alkaline solution of hydrogen peroxide was stirred vigorously with a mechanical stirrer and when the solution was cooled by the addition of crushed ice. In every case the yields of monoperphthalic acid obtained were verified by iodimetric titration.

9,10-Cyclopentenophenanthrene (I).—The cyclopentene (II) (2 g.) was dissolved in ether, cooled in an ice-bath and poured into an ice-cold ether solution containing 0.019 mole of monoperphthalic acid. The mixture was allowed to stand for twelve hours at room temperature, after which the acids were extracted from the solution with sodium bicarbonate solution. The ether was evaporated off and the crude cyclopentene oxide (V) was dissolved in 25 cc. of acetic acid. To this was added 25 cc. of 34% hydrobromic acid and the mixture refluxed for twenty-four hours. Upon cooling, the hydrocarbon solidified, but contained some resinous material which made crystallization impossible. The hydrocarbon was, therefore, purified by vacuum sublimation. The sublimation product, once recrystallized from acetic acid, was obtained pure as long slender needles, m. p. 150–151°; yield, 0.31 g. It showed no depression of melting point when mixed with an authentic sample of 9,10-cyclopentenophenanthrene.

Anal. Calcd. for $C_{17}H_{14}$: C, 93.5; H, 6.5. Found: C, 93.5; H, 6.4.

The picrate prepared in alcohol was obtained as red needles, m. p. 164–165° (Bachmann,[2] 161.5–162°).

1-(2-Biphenyl)-cyclohexene-1 (VII).—A Grignard reagent was prepared from 14 g. of 2-iodobiphenyl and 4.9 g. of cyclohexanone added. The mixture was decomposed with ammonium chloride solution and the crude carbinol dehydrated as in the preparation of the corresponding cyclopentene (II). Upon distillation, 3.4 g. (29%) of a yellowish oil was obtained, b. p. 183–193° (23 mm.).

9,10-Cyclohexenophenanthrene (IX).—The cyclohexene (VII) (3.4 g.) obtained above was dissolved in ether and oxidized with an ether solution containing 0.024 mole of monoperphthalic acid. After sixteen hours, the acids were extracted with bicarbonate solution, the ether evaporated and the crude oxide (VIII) cyclized by refluxing for twenty-four hours in a mixture of hydrobromic and acetic acids. Upon cooling, the hydrocarbon crystallized from the solution. Twice recrystallized from acetic acid, it was obtained as pure, colorless needles, m. p. 122–123° (Bergmann,[3] 120–121°); yield, 1.0 g. (30%).

Anal. Calcd. for $C_{18}H_{16}$: C, 93.1; H, 6.9. Found: C, 92.9; H, 6.9.

Summary

By the use of a new modification of the ring closure, 9,10-cyclopenteno- and cyclohexeno-phenanthrene have been synthesized.

DURHAM, N. C. RECEIVED AUGUST 16, 1939

(4) Böhme, *Ber.*, **70**, 379 (1937).

[CONTRIBUTION FROM THE HAVEMEYER CHEMICAL LABORATORIES, COLUMBIA UNIVERSITY]

Secondary Alpha Furfuryl Amines

BY J. E. ZANETTI AND J. T. BASHOUR

Little has been published on secondary furfuryl amines. The methyl and ethyl furfuryl amines were first prepared by Schwabbauer,[1] by the reduction of the condensation products of methyl and ethyl amine with furfural. This work was repeated by Litterschied.[2] No further work was done on these compounds until 1921 when von Braun and Braunsdorf[3] stated that they had prepared the furfurylethylamine by the action of furfuryl bromide on ethylamine but did not describe their procedure. The Goodyear Tire and Rubber Company[4] took a patent in 1934 for a method of preparing secondary furfuryl amines by reducing the corresponding condensation products of amines and furfural with hydrogen under pressure but although their claims extend to a large number of amines, the only product described was the di-α-furfurylamine which had been prepared by Zanetti and Beckmann[5] by the action of furfuryl bromide on ammonia.

In connection with a study of furfuryl bromide already published in part it seemed of interest to study its reactions on amines which had been but briefly touched upon by von Braun and Braunsdorf. In this study we employed the ether solution of α-furfuryl bromide since as we have demonstrated the pure product is so unstable as to be unmanageable.[6]

The action of the bromide on a primary amine in ether solution is rapid. In a few minutes a crystalline precipitate appears which we thought at first was the hydrobromide of the secondary amine but proved to be the hydrobromide of the primary amine, the action proceeding according to the equation

$$2RNH_2 + BrCH_2C_4H_3O \longrightarrow RNHCH_2C_4H_3O + RNH_2HBr$$

The secondary amine being a much weaker base than the primary amine is released from its hydrobromide formed by the addition of the furfuryl bromide, by the primary compound. In order, therefore, to make the addition complete mole with mole we carried the reaction in the presence of potassium hydroxide, which proved to be a satisfactory method. The yields were only fair, varying from 50 to 65% assuming the yield of the bromide to be 70% of theoretical. In all cases varying amounts of what appears to be the tertiary amines were formed but these condensation products have not yet been investigated.

The secondary amines are colorless liquids turning yellowish in a few days as do most furan compounds, except α-furfurylphenylamine, which is yellow even when repeatedly distilled. They are soluble in ethanol, ether, acetone, carbon tetrachloride, but only slightly soluble in boiling petroleum ether. The specific gravities and the indices of refraction of these compounds, none of which has been previously reported, are given in Table I.

TABLE I

Amine	B. p. °C.	Mm.	Sp. gr., 25/25	n^{20}	M. p. of hydrochloride, °C
α-Furfurylmethyl	149–149.5	761	0.992	1.4729	144–146
α-Furfurylethyl	165–167	761	.963	1.4688	127–128
α-Furfuryl-*n*-butyl	198–200	768	.935	1.4669	189–191
α-Furfuryl-*n*-amyl	214–216	756	.927	1.4668	185–188
α-Furfurylphenyl	109–110	0.5	1.110	1.5834	150–151, dec.

The amines decompose slightly when boiled under ordinary atmospheric pressure but distil readily under reduced pressure. The boiling point of the phenylamine derivative could not be determined as at atmospheric pressure decomposition is too great.

These amines readily form hydrochlorides and the aliphatic ones also form picrates. The furfurylphenylamine, however, did not form a picrate.

Experimental

General Procedure.—The ethereal furfuryl bromide solution was added at once to the ethereal solution of the amine standing over crushed potassium hydroxide. The mixture was stirred continuously from one to two hours and then allowed to stand overnight. After filtration and washing of the potassium hydroxide and bromide with ether, the ether was distilled off and products separated by fractional distillation *in vacuo*.

Furfurylmethylamine, $C_4H_3OCH_2NHCH_3$.—Methylamine was generated from the hydrochloride (81 g.) by the addition of 50% potassium hydroxide solution. The

(1) Schwabbauer, *Ber.*, **35**, 410 (1902).
(2) Litterschied, *Ann.*, **335**, 368 (1904).
(3) Von Braun and Braunsdorf, *Ber.*, **54**, 2081 (1921).
(4) Brit. Pat. No. 412,914, July 2, 1934.
(5) Zanetti and Beckmann, THIS JOURNAL, **50**, 2031 (1928).
(6) Zanetti and Bashour, *ibid.*, **61**, 2249 (1939).

vapors were driven through an upright water-cooled condenser, a long drying tube containing potassium hydroxide pellets into a receiver containing crushed potassium hydroxide (80 g.) covered with dry ether, the receiver being immersed in a dry-ice–ethylene trichloride bath. Heating was continued until the bulk of the amine had distilled over. Furfuryl bromide solution (prepared according to the method of Zanetti[7] from 38 g. of furfuryl alcohol) was cooled to minus 10° and siphoned into the solution of the amine. The mixture was rocked for several minutes, then removed from the bath and shaken frequently for two hours. It was then allowed to stand overnight. After filtration, the ether was removed by distillation and the product was fractionally distilled *in vacuo*. The fraction boiling 50–57° at 16.5–18 mm. was redistilled; yield, 15 g. (50% of theoretical, assuming 70% yield of bromide). As this amine had been prepared before no analysis was made.

Furfurylethylamine, $C_4H_3OCH_2NHC_2H_5$.—Ethylamine was generated from the hydrochloride (50 g.) in an apparatus consisting of the following train: an ordinary distilling flask equipped with a dropping funnel, a long slightly inclined drying tube containing potassium hydroxide pellets, a water-cooled condenser, and the same receiver as in the preparation of the methylamine. The ethereal furfuryl bromide solution prepared from 25 g. of furfuryl alcohol and precooled to minus 10° was introduced by siphon as before, and the product separated as in the preceding case. The fraction boiling at 63–65° at 17–18 mm. was redistilled; yield, 13 g. (58% on basis of 70% yield of the bromide). This amine having been prepared previously no analysis was made.

Furfurylbutylamine, $C_4H_3OCH_2NHC_4H_9$.—Twenty-five grams of normal butylamine, previously dried over potassium hydroxide and distilled, was added at once to a 20-g. batch of the ethereal furfuryl bromide solution over 50 g. of crushed potassium hydroxide. The whole was stirred for one hour and then allowed to stand overnight. After filtration and removal of the ether, the fraction boiling at 92–95° at 16–18 mm. was redistilled; yield, 13 g. (60% on basis of 70% yield of furfuryl bromide).

Anal. Calcd. for $C_9H_{14}ON$: C, 70.58; H, 9.80; N, 9.15. Found: C, 70.40; H, 9.96; N, 9.29.

Furfurylamylamine, $C_3H_3OCH_2NHC_5H_{11}$.—The procedure was similar to the preceding: 8 g. of amylamine and a 4-g. batch of the furfuryl bromide solution were used. The fraction boiling at 108–111° at 16–18 mm. was redistilled; yield, 3.0 g. (65% on basis of 70% yield of bromide).

Anal. Calcd. for $C_{10}H_{17}ON$: N, 8.48. Found: N, 8.66.

Furfurylphenylamine, $C_4H_3OCH_2NHC_6H_5$.—Forty-five grams of aniline and a 20-g. batch of furfuryl bromide were used in this case. On distillation, the main fraction came over at 113–120° at approximately 1 mm. On redistillation this fraction boiled at 109–110° under 0.5 mm.

Anal. Calcd. for $C_{11}H_{11}ON$: C, 76.30; H, 6.36; N, 8.09. Found: C, 76.51; H, 6.47; N, 8.26.

Summary

1. The action of α-furfuryl bromide in ether solution on primary amines has been studied and found to form secondary amines.

2. The methyl, ethyl, butyl, amyl and phenyl α-furfuryl amines have been prepared by the above method and their properties reported.

NEW YORK, N. Y. RECEIVED SEPTEMBER 7, 1939

(7) Zanetti, THIS JOURNAL, **49**, 1065 (1927).

[CONTRIBUTION FROM THE BIOCHEMICAL RESEARCH FOUNDATION OF THE FRANKLIN INSTITUTE]

Derivatives of Aminomethanethiol

BY ARTHUR BINZ AND LELAND H. PENCE

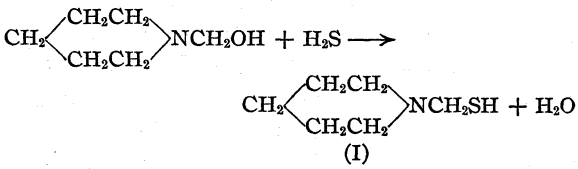
Hydroxymethanethiol, $HOCH_2SH$, was assumed by Baumann[1] to be formed as an unstable intermediate on treating formaldehyde with hydrogen sulfide, and he showed that the reaction proceeds to insoluble trithioformaldehyde, $HCHO + H_2S \longrightarrow HOCH_2SH \longrightarrow (CH_2S)_3$. Since trithioformaldehyde because of its low solubility and reactivity is of no particular interest for biochemical research, it was considered advantageous to investigate hydroxymethanethiol, either as such or in the form of easily soluble and reactive products obtained from it. For these reasons Binz, Räth, and Walter[2] attempted to isolate hydroxymethanethiol by reducing formaldehyde-sulfoxylate with hypophosphorous acid, $HOCH_2SO_2H \longrightarrow HOCH_2SH$, and obtained a product which appeared to be the desired thiol, but the yield was very small.

In taking up this work again we endeavored to obtain a derivative of the corresponding aminomethanethiol which would be stable, by first condensing formaldehyde-sulfoxylate with piperidine and then reducing the product with hypophosphorous acid in the presence of hydriodic acid according to the reaction $C_5H_{10}NCH_2SO_2H \longrightarrow C_5H_{10}NCH_2SH$. Hydrogen sulfide was also used as a reducing agent, but in both cases the yields of a compound showing the reactions of a thiol were very small.

(1) Baumann, *Ber.*, **23**, 1869 (1890).

(2) Binz, Räth and Walter, *ibid.*, **57**, 1398 (1924).

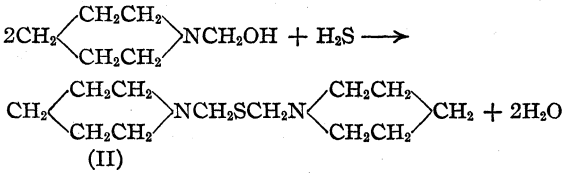
Another method, however, was successful. When piperidine was added to formaldehyde and the 1-piperidinemethanol thus obtained treated with hydrogen sulfide, a vigorous reaction with strong evolution of heat set in and 1-piperidinemethanethiol (I) was obtained in good yield



(I)

It is a clear oil at room temperature, crystallizing in the icebox.

When the reaction was conducted with cooling, 1,3-di-(1′-piperidine)-2-thiapropane (II)[3] was formed:

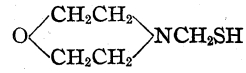


(II)

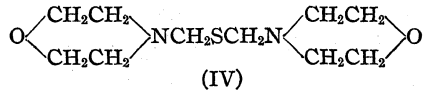
It is probable that the latter reaction is the primary one and that the thiol (I) is produced from the splitting of the sulfide (II) by excess hydrogen sulfide at a higher temperature.

Compound (II) has been obtained by LeFèvre and LeFèvre[4] by saturating an aqueous solution of piperidine with hydrogen sulfide and then adding formaldehyde. These authors had to keep the piperidine at 0° in order to dissolve the necessary amount of hydrogen sulfide and for this reason obtained only the monosulfide (II), not the thiol (I). Furthermore, experiments carried out in this Laboratory by Dr. F. E. Reinhart have shown that our method, even in the case of monosulfides, is more generally applicable than the LeFèvre method, since an excess of hydrogen sulfide must be used in some cases. This is possible only if a stream of the gas is applied to the previously formed aminomethanol.

The application of our procedure to morpholine gave results which closely correspond to those obtained with piperidine. Treatment of morpholine with formaldehyde and hydrogen sulfide yielded 4-morpholinemethanethiol (III); when the reaction was carried out with cooling 1,3-di-(4′-morpholine)-2-thiapropane (IV) was formed.

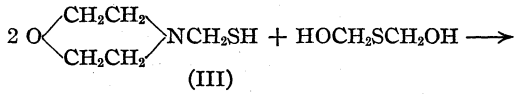


(III)

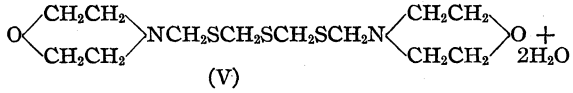


(IV)

One difference in comparison with piperidine was that the formation of compound (III) required the presence of hydrochloric acid. This was unexpected because the addition compounds of amines and aldehydes are sensitive to acids. A greater difference, however, was that compounds (III) and (IV) did not appear as the only reaction products. Simultaneously with (III) was formed 1,7-di-(4′-morpholine)-2,4,6-trithiaheptane (V); apparently di-(hydroxymethyl) sulfide was formed during the reaction and condensed with some of the (III)

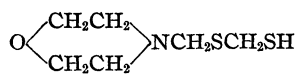


(III)



(V)

Compound (V) was formed as the chief product, if, instead of equivalent amounts of morpholine and formaldehyde, an excess of the latter was added before the introduction of hydrogen sulfide. Simultaneously with compound (IV), 3-(4′-morpholine)-2-thiapropanethiol (VI) was formed as a by-product.



(VI)

Compounds (V) and (VI) are white flocculent precipitates which show no sharp melting points, and cannot be purified by crystallization. The fact that these compounds are quite soluble in the usual organic solvents precludes the possibility that they are mere mixtures of the amine and trithioformaldehyde.

This tendency to form polymerized thioformaldehyde derivatives was still more pronounced when diethanolamine was treated with formaldehyde and then with hydrogen sulfide. A white flocculent mass (VII) was obtained which according to analysis contained 7 molecules of thioformaldehyde bound to 1 molecule of diethanolamine, although the reaction mixture contained no excess of formaldehyde. This means that some primary compound, perhaps the mono-

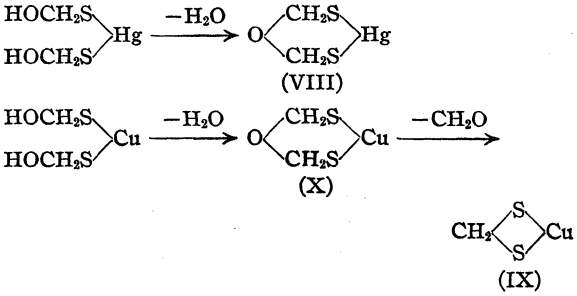
(3) This nomenclature is in conformity with that published in *C. A.* **31**, 9486 (1937), and specifically with Rule 16, THIS JOURNAL, **55**, 3912 (1933).

(4) LeFèvre and LeFèvre, *J. Chem. Soc.*, 1142 (1932).

sulfide $[(HOCH_2CH_2)_2NCH_2]_2S$, has undergone further changes during the reaction. In fact, an oily compound corresponding to this formula was obtained by conducting the reaction between methanoldiethanolamine and hydrogen sulfide at zero degrees. This oil decomposes with water to a white solid mass.

The result of analysis of compound (VII) suggests the formula, $(HOCH_2CH_2)_2N(CH_2S)_7H$. Although this formula might indicate the presence of $2(CH_2S)_3$, trithioformaldehyde could not be extracted with any solvent, nor could it be obtained by sublimation when the compound was heated *in vacuo*.

Most of the compounds give precipitates with the salts of heavy metals. Some of these precipitates have been investigated, and it was found that both 1-piperidinemethanethiol (I) and 4-morpholinemethanethiol (III) with mercuric chloride in alcoholic solution yield the same precipitate, which, according to analysis, appears to be mercuric di-(mercaptomethyl) ether (VIII), $Hg(SCH_2)_2O$. Under the same conditions copper acetate reacts with either (I) or (III) to give a precipitate, the analysis of which indicates it to be cupric methylene dimercaptide (IX), CuS_2CH_2. Perhaps the primary reaction is: $2R_2NCH_2SH + HgCl_2 \longrightarrow (R_2NCH_2S)_2Hg + 2HCl$, a corresponding one occurring with copper acetate. Then the piperidine and morpholine are split off and further changes ensue



We do not consider these conclusions final, as the compounds could not be redissolved and purified. For that reason the possible existence of an equimolecular mixture of the usual cuprous salt of a thiol, in this case $CuSCH_2SCu$, and CH_2S_2 cannot be excluded entirely; this assumption, however, does not appear justified since it would require the two components to have the same high degree of insolubility in order to account for the analytical results obtained (1Cu: 2S).

Many of the compounds are lethal. From an investigation carried out under the direction of Dr. J. O. Ely, of our Cytological Department, we submit the following data. 1-Piperidinemethanethiol (I) and 1,3-di-(1′-piperidine)-2-thiapropane (II) in 0.04% water solution killed paramecia immediately, and daphnia in twenty minutes. Lethal doses of 4-morpholinemethanethiol (III), 1,3-di-(4′-morpholine)-2-thiapropane (IV), compound (VII), 1-piperidinemethanethiolhydrochloride (XI), and 1,3-di-(1′-piperidine)-2-thiapropane dihydrochloride (XII), are, respectively, 0.025, 0.021, 0.165, 0.05, and 0.083 mg. per g. of body weight when injected intravenously into mice. The lethal doses of piperidine, 1-methylpiperidine, 1-ethylpiperidine, and coniine, injected subcutaneously into rabbits, have been reported[5] to be 0.5, 0.4, 0.3, and 0.09 mg. per g. body weight, respectively. Thus most of these sulfur compounds are even more poisonous than coniine, without possessing the latter's characteristic side chain. Thioacetic acid, which was tested in comparison, has a lethal dose of 0.125 mg. per g. body weight when injected intravenously in mice, and is tolerated better than our compounds.

It was difficult to obtain several of the compounds analytically pure, as many of them were either insoluble, amorphous, or unstable.

Experimental

1-Piperidinemethanethiol (I).—Piperidine (10 g.) was poured gradually and with cooling into 37% aqueous formaldehyde (20 cc.), and shaken with anhydrous potassium carbonate (10 g.). The 1-piperidinemethanol, $C_5H_{10}N-CH_2OH$, thus formed[6] was separated from the aqueous layer, placed in a large test-tube, weighed, and gassed with hydrogen sulfide. The temperature rose spontaneously to 68°. After fifteen minutes an oily turbidity appeared, and at the end of two and one-half hours the hydrogen sulfide uptake was 3.3 g. The mixture was shaken with 10% sodium hydroxide (25 cc.) to remove unreacted hydrogen sulfide, and the oil was extracted with ether (75 cc.). After separating, drying with sodium sulfate, and evaporating the ether *in vacuo* at room temperature (to prevent decomposition), there remained 13.6 g. (yield, 88%) of 1-piperidinemethanethiol. The oil solidified in the icebox to colorless crystals; m. p. 12.5–15°. It is soluble in the ordinary organic solvents and dilute acid, but insoluble in alkaline solutions.

Anal. Calcd. for $C_6H_{13}NS$: N, 10.68; S, 24.44. Found: N, 9.55; S, 22.65; $n^{21}D$ 1.5552.

Although the analytical results showed a ratio of nitrogen to sulfur of 1:1.03, the values were too low because of the difficulty in removing the last traces of ether from the

(5) Wolffenstein and Wolffenstein, *Ber.*, **34**, 2403 (1901).
(6) L. Henry, *Bull. soc. chim.*, [3] **14**, 157 (1895).

oil at room temperature. A sample of the oily base was therefore converted into the solid hydrochloride for analysis.

1-Piperidinemethanethiol Hydrochloride (XI).—After dissolving 1-piperidinemethanethiol (2.3 g.) in toluene (15 cc.), hydrogen chloride gas was introduced through an inverted funnel with stirring and cooling. The white, solid hydrochloride, which precipitated immediately, was filtered and washed with ether: yield 2.5 g.; m. p. 195–205°.

Anal. Calcd. for $C_6H_{14}NSCl \cdot {}^1/_2H_2O$: N, 7.93; S, 18.15; Cl, 20.07. Found: N, 7.35; S, 18.18; Cl, 20.25.

After dissolving the hydrochloride in water and adding 10% sodium carbonate solution, the oily 1-piperidinemethanethiol was reprecipitated.

It was not possible to purify the 1-piperidinemethanethiol by distillation. On heating 1-piperidinemethanethiol (10 g.) at 4 mm. pressure and 150–170° bath temperature, the main fraction distilled at 75–81° and proved to be di-(1-piperidyl)-methane, $C_5H_{10}NCH_2NC_5H_{10}$, contaminated with a small amount of a sulfur compound.

Anal. Calcd. for $C_{11}H_{22}N_2$: N, 15.4. Found: N, 15.9; S, 0.24; $n^{15}D$ 1.4891.

Putochin[7] found $n^{15}D$ 1.4883 for di-(1-piperidyl)-methane. Piperidine has $n^{15}D$ 1.4538. The residue in the distillation flask consisted of 2.4 g. of a brittle brownish mass; m. p. 228–231°; S found, 58.4%.

1-Piperidinemethanethiol (10 g.) refluxed with dilute hydrochloric acid (25 cc.) at 90° for two hours gradually deposited needles of trithioformaldehyde. The total yield after repeating several times with the filtrate was 3 g.; theoretical, 3.5 g.; m. p. 216–218°. An analogous decomposition had been observed by LeFèvre and LeFèvre[4] with compounds obtained from reactions between dimethyl- and diethylamines, hydrogen sulfide and formaldehyde.

To 1-piperidinemethanethiol (1.3613 g.) dissolved in ethyl alcohol (10 cc.) there was added mercuric chloride (1.409 g.) dissolved in ethyl alcohol (39.2 cc.). A flocculent dark yellow precipitate of mercuric di-(mercaptomethyl) ether (VIII) appeared, which was filtered and washed with absolute ethanol: yield 97%; decomposition at 95–105°. The compound is very insoluble. When hydrogen sulfide gas was passed through an aqueous suspension of this mercury derivative, mercuric sulfide was precipitated immediately, this reaction being characteristic of mercuric mercaptans.

Anal. Calcd. for $HgS_2C_2H_4O$: Hg, 64.97; S, 20.77; C, 7.77; H, 1.31. Found: Hg, 64.51; S, 20.10; C, 6.34, 6.34; H, 1.19, 1.22.

To 1-piperidinemethanethiol (1.8201 g.) dissolved in ethyl alcohol (125 cc.) there was added a saturated alcoholic solution of cupric acetate until a permanent blue color was established. The resulting yellow-tan flocculent precipitate was centrifuged and washed five times with absolute ethanol (150 cc. each), and dried at room temperature *in vacuo;* yield 0.8964 g., (91% based on cupric methylene dimercaptide (IX)); decomposes at 105–110°. Sodium sulfide solution produced a coating of black copper sulfide on the surface of the compound, which hydrogen sulfide would not accomplish. The high insolubility of the compound prevented any further purification.

Anal. Calcd. for CuS_2CH_2: Cu, 44.86; S, 45.24. Found: Cu, 43.74, 43.90; S, 44.09 (Ratio, 1.000 N; 1.995 S).

1,3-Di-(1′-piperidine)-2-thiapropane (II).—1-Piperidinemethanol, prepared from piperidine (10 g.), was treated with hydrogen sulfide at 0° for one and one-half hours, 2.6 g. of the gas being absorbed. The reaction product was extracted with ether (100 cc.), shaken with 10% sodium hydroxide (50 cc.), separated, and dried with calcium chloride. On evaporation of the ether an oil was obtained which crystallized on cooling: yield, 3.2 g.; m. p. 48.5–50.5°. The compound is soluble in the ordinary organic solvents and dilute acid, but insoluble in alkaline solutions.

Anal. Calcd. for $C_{12}H_{24}N_2S$: N, 12.27; S, 14.04. Found: N, 12.38, 12.45; S, 14.56.

1,3-Di-(1′-piperidine)-2-thiapropane Dihydrochloride (XII).—1-Piperidinemethanol, prepared as before from piperidine (10 g.), was dissolved in concd. hydrochloric acid (10 cc.), cooled, and treated with hydrogen sulfide for one hour. The colorless, crystalline mass of 1,3-di-(1′-piperidine)-2-thiapropane dihydrochloride was filtered and washed with acetone; yield, 4.2 g.; m. p. 171–175°, with decomposition.

Anal. Calcd. for $C_{12}H_{26}N_2SCl_2 \cdot H_2O$: N, 8.77; S, 10.04; Cl, 22.21. Found: N, 8.70, 8.60; S, 10.24, 10.33; Cl, 22.01.

An aqueous solution of the hydrochloride, treated with 10% sodium carbonate, yielded a precipitate of the free base (II); m. p. 50–53°.

4-Morpholinemethanethiol (III).—To morpholine (17.5 cc.) there was added slowly with cooling 37% aqueous formaldehyde (18 cc.), followed by concd. hydrochloric acid (17 cc.); *p*H 3.5. On treatment with hydrogen sulfide at 55° for two hours, the solution absorbed 5.1 g. of the gas (calcd., 6.8 g.). The reaction mixture was treated with 10% sodium hydroxide (100 cc.), and extracted with ether (200 cc.). The extract, which was dried with calcium chloride, and concentrated, deposited crystals of 4-morpholinemethanethiol; yield 8 g. Recrystallization from methanol (15 cc.) gave 5.3 g. of fine prisms; m. p. 86–88°. Cooling below room temperature during the recrystallization was avoided to prevent the precipitation of the by-product (V) of the reaction.

Anal. Calcd. for $C_5H_{11}NSO$: N, 10.52; S, 24.07. Found: N, 10.46, 10.50; S, 24.14, 24.08.

When the thiol (1.85 g.) was refluxed for one hour with concd. hydrochloric acid (25 cc.), trithioformaldehyde (0.6 g. or 94%) was obtained; m. p. 219°. S, calcd. 69.6; found, 69.0.

To 4-morpholinemethanethiol (1.3309 g.) dissolved in ethyl alcohol (30 cc.) there was added mercuric chloride (1.3575 g.) dissolved in ethyl alcohol (37.7 cc.). A flocculent canary-yellow precipitate of mercuric (di-mercaptomethyl) ether (VIII) appeared immediately. After purification by washing with absolute ethanol and centrifuging several times, the precipitate was dried: yield 94%; decomposition at 110–115°. When an aqueous suspension of the compound was treated with hydrogen sulfide, mercuric sulfide was precipitated.

(7) Putochin, *Ber.*, **55**, 2749 (1922).

Anal. Calcd. for $HgS_2C_2H_4O$: Hg, 64.97; S, 20.77; C, 7.77; H, 1.31. Found: Hg, 65.08, 65.10; S, 20.70; C, 5.26, 5.27; H, 1.03, 1.04.

To 4-morpholinemethanethiol (0.6655 g.) dissolved in ethyl alcohol (15 cc.) there was added a saturated alcoholic solution of cupric acetate until a permanent blue color was imparted to the solution. The flocculent yellow precipitate was purified as much as possible by washing several times with absolute ethanol, centrifuged, and dried at room temperature: yield, 94% based on cupric methylene dimercaptide (IX); decomposition at 100–110°. When suspended in sodium sulfide solution the compound immediately acquired a black coating of copper sulfide; hydrogen sulfide had no effect.

Anal. Calcd. for CuS_2CH_2: Cu, 44.86; S, 45.24; C 8.47; H, 1.43. Found: Cu, 45.79; S, 43.71; C, 5.98, 6.08; H, 1.78, 1.60.

In these cases also the mercury and copper derivatives were too insoluble for further purification, and the values found for carbon are too low, presumably because of the difficulty of obtaining complete combustion.

The ether filtrate obtained after removal of the 8 g. of crude 4-morpholinemethanethiol (III) was cooled to 0°, yielding 5 g. of an amorphous white compound. The latter was purified by dissolving in hot ethanol and cooling, followed by two similar treatments from acetone, and gave a precipitate which melted at 72–80°. This is apparently the same compound which is formed when the reaction between morpholine, formaldehyde, and hydrogen sulfide is carried out without hydrochloric acid, but with twice as much formaldehyde as was previously used. Morpholine (8.75 g.) was added gradually with cooling to 37% formaldehyde (18 cc.), followed by benzene (40 cc.). Hydrogen sulfide was then passed in, with moderate cooling, until 5 g. was absorbed. After the reaction mixture was shaken with 10% sodium hydroxide (25 cc.), the benzene layer was separated, washed with water, concentrated, and cooled to 0°. A colorless, amorphous solid (7.6 g.) was obtained; m. p. 67–78°. Successive purifications with hot methanol, and acetone, raised the melting point to 77–84°.

Anal. Calcd. for $C_{12}H_{24}N_2S_8O_2$: N, 8.64; S, 29.60. Found: N, 8.88, 8.78; S, 30.21.

According to this analysis the compound is probably 1,7-di-(4′-morpholine)-2,4,6-trithiaheptane (V).

1,3-Di-(4′-morpholine)-2-thiapropane (IV).—Morpholine (35 cc.) was added gradually with cooling to 37% formaldehyde (36 cc.). The reaction mixture was shaken with anhydrous potassium carbonate (20 g.), to give an upper layer of 4-morpholinemethanethiol which was separated and treated with hydrogen sulfide at 0°. The crystalline precipitate of 1,3-di-(4′-morpholine)-2-thiapropane formed almost at once. After fifteen minutes the yield of filtered crystals was 12.8 g. The filtrate on treatment with hydrogen sulfide gave a second crop of 11.6 g. and a third crop of 2.6 g. After recrystallizing the product twice from acetone and once from ether the 1,3-di-(4′-morpholine)-2-thiapropane separated as colorless, cube-like crystals, melting at 107–108°.

Anal. Calcd. for $C_{10}H_{20}N_2SO_2$: N, 12.06; S, 13.80. Found: N, 12.16; S, 13.85.

In preparing 1,3-di-(4′-morpholine)-2-thiapropane, a certain amount remains dissolved in the aqueous filtrate after the crystals have been removed. This filtrate on standing deposits a white flocculent precipitate which appears to be identical with a compound obtained from 1,3-di-(4′-morpholine)-2-thiapropane directly by dissolving 3.7 g. in 75 cc. of water at room temperature. After twenty-four hours 0.15 g. of a white precipitate had formed, m. p. 72–82°. The filtrate after warming on the water-bath gave an additional 1.6 g.

Anal. Calcd. for $C_6H_{13}NS_2O \cdot {}^1/_2H_2O$: N, 7.44; S, 34.06. Found: N, 7.41; S, 33.58, 33.51.

According to this analysis the compound is probably 3-(4′-morpholine)-2-thiapropanethiol (VI), $OC_4H_8NCH_2SCH_2SH$.

The Reaction between Diethanolamine, Formaldehyde, and Hydrogen Sulfide.—According to German Patent 564,787 (1931) (I. G. Farbenindustrie), diethanolamine and formaldehyde, when warmed for one-half hour at 50°, form hydroxyethyloxazolidine. We have added diethanolamine to formaldehyde[8] in the cold, thus avoiding the formation of the oxazolidine ring, and have treated the resulting methanoldiethanolamine with hydrogen sulfide.

Gradually and with cooling diethanolamine (5.2 g.) was poured into 37% aqueous formaldehyde (4.5 cc.). Hydrogen sulfide was passed into the solution and within one-half hour a white mass filled the test-tube. The entire reaction mixture was digested with boiling ethanol, in which it did not dissolve, and was then filtered and washed with alcohol and ether: yield, 3.3 g. of compound (VII); m. p. 224–226°.

Anal. Calcd. for $(HOCH_2CH_2)_2N(CH_2S)_7H$: N, 3.28; S, 52.47. Found: N, 3.03; S, 52.39.

Compound (VII) can be dissolved in 20 parts of boiling diethanolamine and remains in solution on addition of water. Since the melting point is near that of trithioformaldehyde (216°) the question arises, whether trithioformaldehyde (S calcd. 69.7) has formed during the reaction and become part of the compound. This is doubtful, as trithioformaldehyde when dissolved in 20 parts of boiling diethanolamine is precipitated by adding water.

Another preparation made from diethanolamine (21 g.) and aqueous formaldehyde (18 cc.) was treated with hydrogen sulfide for one hour. The absorbed gas amounted to 6.8 g. when the tube began to fill with the white semi-solid mass. This was boiled in acetone (600 cc.), in which most of it dissolved. The filtrate on cooling gave 6.7 g. of (VII) as a white precipitate, m. p. 218–221°. When the compound was placed in a bath at 170° it melted immediately to a clear liquid, then solidified, and remelted at 218–228°.

Anal. Calcd. for $(HOCH_2CH_2)_2N(CH_2S)_7H$: N, 3.28; S, 52.47. Found: N, 3.46, 3.43, 3.37; S, 52.00.

We tried to ascertain whether it was possible to obtain the same compound by using the components in the ratio suggested by the above formula. Into 37% formaldehyde (18 cc.) was poured diethanolamine (3 g.). In order to

(8) The reaction between diethanolamine and formaldehyde has been studied by Lyubomudrov, *Ukrain. Khem. Zhur.*, **11**, Wiss. Tl. 119 (1936); *C. A.*, **30**, 5957 (1936).

keep the resulting compound more dispersed, water was added (175 cc.), and the hydrogen sulfide was passed into the suspension at 65°. Within one hour 7.4 g. of the gas had been absorbed. The resulting suspension of white precipitate was made alkaline with 10% sodium hydroxide (20 cc.) and then washed with water by centrifuging. After drying *in vacuo* a yield of 7 g. was obtained; m. p. 220–224°. When placed in the bath at 180°, the compound did not melt until 230–233° Found: N, 1.56; S, 51.08.

This compound (XIII) has a ratio N:S = 1:14.4, which shows that this preparation is different from the one mentioned above.

However, as in the case of (VII), it is not likely that this compound (XIII) is a molecular combination of diethanolamine with trithioformaldehyde. Both are much less soluble in acetone, ether, absolute alcohol, and benzene, and far more soluble in hot diethanolamine than the trithioformaldehyde. Furthermore, the three substances show a marked difference when submitted to sublimation, as is shown in the table.

	100°	230°
$(CH_2S)_3$	Started to sublime	Completely sublimed
(VII)	Slight sublimation with subsequent melting of sublimate	Residue melted with decomposition
(XIII)	Nothing sublimed	Residue unchanged

The analyses were done by Dr. H. K. Alber of our Microchemical Department.

Summary

Piperidine, morpholine, and diethanolamine were treated with aqueous formaldehyde to form the corresponding aminomethanols.

The 1-piperidinemethanol, 4-morpholinemethanol, and methanoldiethanolamine were treated with hydrogen sulfide under varying conditions, yielding 1-piperidinemethanethiol, 1,3-di-(1-piperidine)-2-thiapropane, 4-morpholinemethanethiol, 1,3-di-(4′-morpholine)-2-thiapropane, and polymerized thioformaldehyde derivatives of methanoldiethanolamine, respectively.

The lethal doses of the sulfur derivatives of piperidine, morpholine, and diethanolamine were determined by intravenous injections in mice.

PHILADELPHIA, PENNA. RECEIVED JULY 20, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING OF THE UNIVERSITY OF PENNSYLVANIA]

The Alkylation of α-Sulfonylamides[1]

BY AUSTIN POMERANTZ[2] AND RALPH CONNOR

A number of α-sulfonyl-α-alkylacetamides recently were prepared[3] by the alkylation of α-sulfonylacetamides. While this method was adequate for the compounds previously investigated, continuation of the earlier work disclosed that in certain cases the yields were low and the products difficult to purify. Since the alkylation products were of some interest as hypnotics,[4] a more complete study of this reaction was undertaken. The discussion will be limited to the ethylation of α-*n*-butylsulfonylacetamide (I) but examples of other alkylations will be given in the experimental part.

In several ethylations of α-*n*-butylsulfonylacetamide under the conditions previously used (sodium ethoxide and an alkyl halide in alcohol solution), a considerable amount of unchanged I was always present and consequently the purification of the product (α-*n*-butylsulfonyl-*n*-butyramide, II) was very difficult. The recovered starting material was not present in the reaction mixture as unreacted sodium derivative, for the solution was refluxed until it became neutral. It therefore seemed likely that the methylene group of I was not sufficiently activated to compete successfully for the sodium with the large excess of alcohol that was present[5] and that the true situation might be represented according to the equations[6]

(1) This communication is constructed from a thesis submitted by Austin Pomerantz in partial fulfilment of the requirements for the degree of Doctor of Philosophy at the University of Pennsylvania in June, 1939.

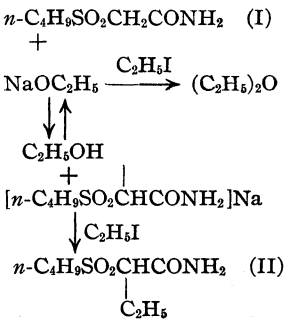
(2) Harrison Fellow in Chemistry, 1938–1939; Harrison Scholar in Chemistry, 1937–1938.

(3) d'Ouville and Connor, THIS JOURNAL, **60**, 33 (1938).

(4) A pharmacological examination of the compounds reported in this paper is being made under the direction of Dr. Robert S. Shelton of the Wm. S. Merrell Company and will be reported elsewhere.

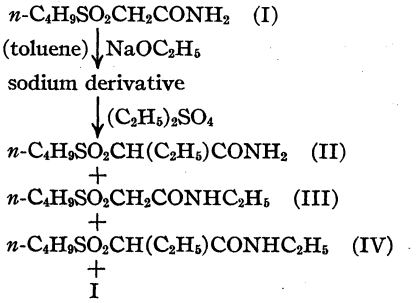
(5) Tröger and Lux [*Arch. Pharm.*, **247**, 618 (1909)] reported that α-phenylsulfonylacetamide ($C_6H_5SO_2CH_2CONH_2$) formed no sodium derivative with alcoholic sodium ethoxide. However, the alkylations of α-*p*-tolylsulfonylacetamide previously reported[3] were carried out in alcoholic solution and appeared to be more satisfactory than the alkylation of I.

(6) The weak acidity of the methylene group of I is not surprising in view of the fact that both the sulfone and carbonamide groups are generally considered to be relatively weak labilizing groups.[5,7] It is interesting to note, however, that when a methylene group

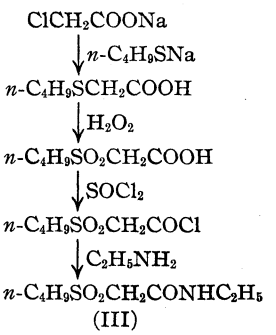


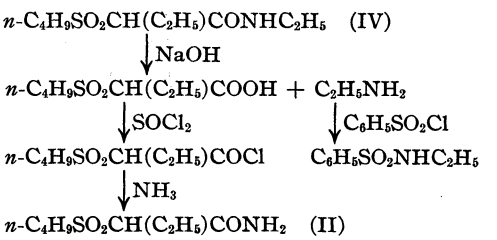
In order to avoid the effect of a high concentration of alcohol upon the above equilibrium the alkylation was next carried out in dry benzene and in dry toluene containing sodium ethoxide prepared by the reaction of sodium with the theoretical amount of alcohol. The equivalent of alcohol liberated by the reaction of I with sodium ethoxide was insufficient to interfere with the alkylation reaction since similar results were obtained whether or not this alcohol was removed before alkylation. Under these conditions the sodium derivative of I was formed quantitatively and precipitated from the hot solution as a yellow-orange oil which dried to a yellow powder. By acidification of the sodium derivative unchanged I was recovered in an amount which showed that no side reaction had occurred as a result of the sodium ethoxide treatment. The sodium derivative reacted very slowly with alkyl halides and a bromide analysis after refluxing for twenty-five hours in toluene with five equivalents of *n*-butyl bromide showed that 56% of the theoretical amount of sodium bromide had been formed. Treatment of the sodium derivative in boiling benzene with six equivalents of ethyl iodide gave a reaction mixture which was alkaline after refluxing for fifty-five hours. With ethyl sulfate the reaction was much more rapid and the alkylation mixture was neutral after refluxing for three hours. Analysis showed that the theoretical amount of sodium ethyl sulfate had been formed.

The reaction of the sodium derivative of I with ethyl sulfate in toluene gave, in addition to unchanged I, the expected *α*-*n*-butylsulfonyl-*n*-butyramide (II) and also *α*-*n*-butylsulfonyl-N-ethylacetamide (III) and *α*-*n*-butylsulfonyl-N-ethyl-*n*-butyramide (IV). The pure products were isolated in yields of 30, 7 and 0.04%, respectively. Separation was difficult, however,



and these figures do not show the relative amounts of the three compounds actually formed. It was estimated that the ratio of II to III was near to 2:1. The structure of III was established by comparison with a sample prepared by a conventional synthetic method and the identity of IV was shown by the isolation and identification of its hydrolysis products.





The results of these alkylations may be rationalized by recalling that amides undergo many reactions analogous to those generally considered typical of active methylene compounds. It may therefore be considered that in I there are two activated groups, —CH_2— and —NH_2. The data indicate that while the methylene group is somewhat the more active, their relative activity is such that both groups undergo alkylation. This possibly involves two different types of sodium derivatives, V and VI,[10] which could be interconverted by a prototropic change and which

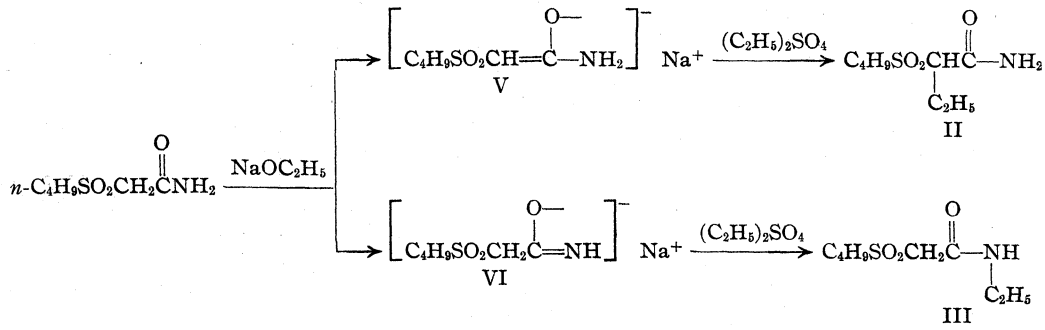
is activated by two sulfone groups[8] or by two carbonamide groups,[9] alkylation in alcoholic solution is apparently more successful than in the case of I.

(7) Gilman, "Organic Chemistry," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1938, p. 1709; Tröger and Nolte, *J. prakt. Chem.*, **101**, 136 (1920).

(8) Shriner, Struck and Jorison, THIS JOURNAL, **52**, 2060 (1930).

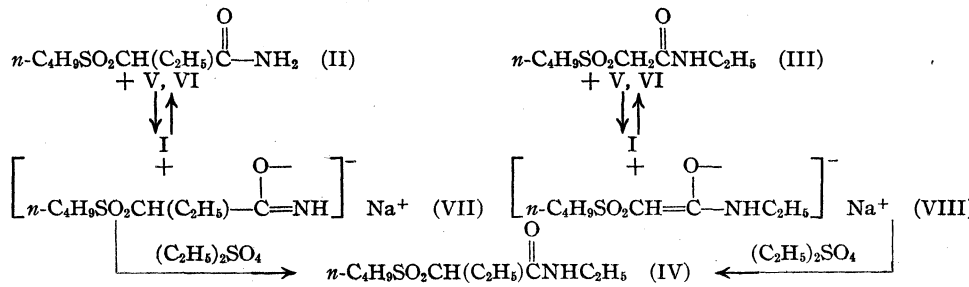
(9) Meyer, *Monatsh.*, **28** 1 (1907); Conrad and Schulze, *Ber.*, **42**, 729 (1909).

(10) Various other structures might be written for these sodium derivatives. Since a consideration of such possibilities adds nothing to the present discussion, V and VI have been arbitrarily selected to show that in one case the methylene group is involved and in the other case the —NH_2.



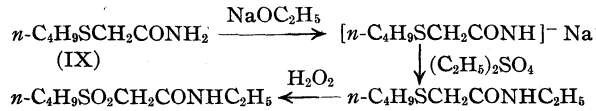
might be in dynamic equilibrium. It is also possible that the equilibrium is modified by the insolubility of the sodium derivatives; the slow rate of reaction with ethyl iodide might be construed as an indication that VI is present and not readily converted to V.[11]

The formation of a dialkylation product, IV, obviously occurred by the reaction of the monoalkylation products (II and III) with V and VI to give I and the sodium derivatives (VII and VIII) of II and III.



In the above equations the formation of only one sodium derivative from each monoalkylation product has been shown. The basis for this is the fact that the alkylation both of pure II and of pure III gave IV.[12] Furthermore, this is in accord with the view that in the system $-CH_2-\overset{O}{\overset{\|}{C}}-NH_2$ the $-CH_2-$ and $-NH_2$ are activated to approximately the same extent. Substitution of an ethyl group would change the relationship by decreasing the activity of the group to which it was attached, not only because of steric factors but also due to the fact that an alkyl group has an effect opposite to that of the common labilizing groups.[13] Therefore in II the H of $-NH_2$ is more active than that of $-CH(C_2H_5)-$ while in III the H of $-CH_2-$ is more active than that of $-NHC_2H_5$ and the formation of sodium derivatives and their alkylation should proceed as shown above.

To compare the influence of the RS— and RSO_2— groups, the alkylation of α-(*n*-butylthio)-acetamide (IX) was investigated. The reaction of IX with sodium ethoxide in dry toluene gave a gelatinous sodium derivative. In this case an unknown side reaction apparently occurred, since only 70% of the starting material was recovered after acidification. With ethyl sulfate the sodium derivative gave an oil which was oxidized to III. It seems fairly certain that



no alkylation occurred on carbon and hence that the sodium derivative was an amide salt. Therefore, the RS— group, as would be expected, is not a labilizing group so far as this reaction is concerned. The yield of III was too low to make this a promising synthetic method.

(11) While it is well known that the sodium derivatives of amides may be converted to N-alkyl amides by the action of alkylating agents, Titherly [*J. Chem. Soc.*, **79**, 391 (1903)] observed that alkyl halides were unreactive in such syntheses while potassium alkyl sulfates reacted satisfactorily.

(12) Theoretically, II might give α-*n*-butylsulfonyl-α,α-diethylacetamide and III might give α-*n*-butylsulfonyl-N,N-diethylacetamide. Possibly these are formed in small amounts. No evidence was obtained for the former reaction. However, the crude material remaining in the mother liquors from the recrystallizations of the product from the alkylation of III was hydrolyzed and the detection of traces of diethylamine showed that alkylation of the $-NHC_2H_5$ group had occurred to a slight extent.

(13) Watson, "Modern Theories of Organic Chemistry," Oxford Press, 1937, pp. 40, 70.

Experimental Part

All melting points are uncorrected unless otherwise specified. The absolute alcohol used was the commercial material which had been further dried over lime and then treated with sodium and ethyl phthalate. Benzene and toluene were dried over sodium ribbon. The ligroin used was the fraction boiling at 70–90°.

I. Alkylation in Alcohol Solution

α-*n*-Butylsulfonyl-*n*-butyramide (II).—The reaction of α-*n*-butylsulfonylacetamide[3] (I) with ethyl bromide and sodium ethoxide was carried out using 0.05 molar quantities and the conditions previously[3] described. The diluted reaction mixture was concentrated under reduced pressure and chilled. The impure product weighed 7.1 g. and after repeated recrystallization from water gave 1.17 (11%) of the alkylation product (II), m. p. 124–125°. Repeated recrystallization of the residues obtained by evaporation of the aqueous mother liquors gave 1.78 g. (20%) of slightly impure starting material (I), m. p. 114–117°.

α-*n*-Butylsulfonyl-*n*-caproamide.—Using 0.03 molar quantities of the reagents and 125 ml. of alcohol as a solvent, the reaction of (I) with *n*-butyl bromide and sodium ethoxide was carried out as in the ethylation reaction. The reaction mixture was not neutral after refluxing for eight hours. Dilution with water gave no precipitate and the solution was concentrated, first under reduced pressure and then at atmospheric pressure. Several fractions of impure solid were obtained and when combined weighed 2.78 g., m. p. 104–115°. Recrystallization from water gave 1.06 g. (15%) of alkylation product, m. p. 104–105°, which was not purified further. The preparation of the pure compound is described below.

II. Alkylations with Alkyl Halides in Inert Solvents

Sodium ethoxide was prepared by the method of Cox and McElvain[14] with four modifications: (1) benzene or toluene were used instead of ether, (2) approximately 2–5% excess of absolute alcohol was used, (3) the reaction was carried out at room temperature and the completion of the reaction assured by allowing the mixture to stand overnight before use and (4) the air in the apparatus was displaced by dry nitrogen to avoid discoloration of the sodium ethoxide and a slow stream of dry nitrogen passed through the apparatus during the course of the reaction. The theoretical quantity of α-sulfonylamide was then added and the reaction mixture refluxed in an oil-bath until the formation of the insoluble sodium derivative was complete (one-half to two hours). In some cases the hot solvent was then decanted from the oily sodium derivative and replaced by fresh solvent in order to remove any unreacted starting material as well as the alcohol liberated in the reaction. However, the results did not differ in comparable runs in which decantation was omitted, so that this was not adopted as a general procedure. Evaporation of the decanted solvent in several experiments showed that the unreacted starting material was negligible and hence that the formation of the sodium derivative was complete.

An excess of the alkyl halide was then added and the reaction mixture refluxed in an oil-bath with stirring for periods up to fifty-five hours. In no case did the solution become neutral to moist litmus. The mixture was filtered through a fluted filter while hot to remove sodium halide and unreacted sodium derivative. The filtrate was concentrated and chilled to obtain the α-sulfonylamides. Further concentration of the mother liquors gave in all cases a small amount of an oil which was not successfully crystallized, although in some cases there appeared to be solid present. Since the oil was apparently a mixture of compounds similar to those described later in the discussion of the reaction of ethyl sulfate, no further attempts at characterization were made.

α-*n*-Butylsulfonyl-*n*-butyramide (II).—The sodium derivative from 6.46 g. (0.036 mole) of α-*n*-butylsulfonylacetamide (I) in 150 ml. of benzene was refluxed with 34.0 g. (0.22 mole) of ethyl iodide for fifty-five hours and the reaction product isolated as described above. From the benzene filtrate was obtained 1.8 g. (24%) of impure II, m. p. 117–120°. Recrystallization from water gave 1.4 g. (19%) of the pure material, m. p. 124–124.5°.

The alkaline, benzene-insoluble residue obtained by filtration of the reaction mixture was suspended in acetone, neutralized with glacial acetic acid and the solvent removed on the steam-bath. The residue was extracted repeatedly with small amounts of benzene and the extracts chilled. The first extracts appeared to consist mainly of II and the last of I. They were therefore divided into two portions; recrystallization of the less soluble portion from benzene gave a small amount of I. Recrystallization of the other fraction from water gave 1.1 g. (15%) of II, bringing the total yield of alkylation product to 2.5 g. (33% of the theoretical).

α-*n*-Butylsulfonyl-*n*-caproamide.—The sodium derivative from 4.48 g. (0.025 mole) of *n*-butylsulfonylacetamide (I) in 100 ml. of toluene was refluxed for twenty-five hours with stirring with 17.1 g. (0.125 mole) of *n*-butyl bromide. Isolation of the product by the general method described above gave 2.3 g. of impure solid, m. p. 85–95°. Recrystallization from water gave 1.1 g. (19%) of impure α-*n*-butylsulfonyl-*n*-caproamide, m. p. 107–108°. The product was very difficult to purify further but repeated recrystallizations from dilute alcohol gave analytically pure material, m. p. 110.5–111° (corr.).

Anal. Calcd. for $C_{10}H_{21}O_3NS$: N, 5.95; S, 13.62. Found: N, 5.90, 5.91; S, 13.74, 13.35.

The toluene-insoluble solid isolated by filtration of the reaction mixture was dissolved in dilute nitric acid and a solution of silver nitrate added. The silver bromide formed weighed 2.6 g., indicating 56% reaction.

α-*p*-Tolylsulfonyl-*n*-caproamide.—The sodium derivative from 9.45 g. (0.044 mole) of α-*p*-tolylsulfonylacetamide[3] in 150 ml. of dry toluene was refluxed with stirring for nineteen hours with 24.3 g. (0.18 mole) of *n*-butyl bromide. The product was 5.05 g. of impure material, m. p. 128–138°. Several recrystallizations from dilute alcohol gave 3 g. (25%) of the pure alkylation product, m. p. 165.5–166° (corr.).

Anal. Calcd. for $C_{13}H_{19}O_3NS$: N, 5.20; S, 11.90. Found: N, 5.18, 5.15; S, 11.93, 11.60.

α-Benzyl-α-*p*-tolylsulfonylacetamide.—The sodium derivative from 14.62 g. (0.07 mole) of a α-*p*-tolylsulfonylacetamide in 200 ml. of dry toluene was refluxed with

(14) Fieser, "Organic Syntheses," John Wiley and Sons, Inc., New York, N. Y., 1937, Vol. XVII, p. 54.

stirring for eighteen hours with 15.4 g. (0.12 mole) of benzyl chloride. The impure product weighed 4.3 g. but was separated by repeated recrystallization from dilute methanol into the starting material, α-*p*-tolylsulfonylacetamide, and 1.6 g. of the alkylation product.

The toluene-insoluble material was washed with dilute hydrochloric acid, dried and recrystallized from dilute alcohol. The weight of α-benzyl-α-*p*-tolylsulfonylacetamide from this source was 7.6 g., making the total yield of the product 9.2 g. (44%), m. p. 203–204° (corr.).

Anal. Calcd. for $C_{16}H_{17}O_3NS$: N, 4.62; S, 10.57. Found: N, 4.61, 4.58; S, 10.47.

III. Alkylations with Ethyl Sulfate in Toluene

Ethylation of α-*n*-Butylsulfonylacetamide (I).—The sodium derivative prepared from 76.7 g. (0.43 mole) of I in 700 ml. of dry toluene by the procedure mentioned above was refluxed with stirring with 72.6 g. (0.47 mole) of freshly distilled ethyl sulfate. The reaction mixture became neutral after three and one-half hours but heating was continued until the total reaction time was seven hours. At the end of this time the solution was no longer alkaline to moist litmus and the sodium ethyl sulfate obtained by filtering the hot solution weighed 62.0 g. (98% of the theoretical). The filtrate was concentrated and chilled, giving 43.9 g. of impure material, m. p. 100–108°. Repeated recrystallization from water gave 27.0 g. (30%) of pure α-*n*-butylsulfonyl-*n*-butyramide (II). The water was evaporated from the combined filtrates from these recrystallizations and the residue recrystallized repeatedly from a mixture of benzene and alcohol. While the separation of I from mixtures with II was very difficult, this procedure gave a considerable amount of unchanged I.

Further concentration of the toluene filtrate of the original reaction mixture gave a thick oil which could not be crystallized. The solvent was removed completely and the residue distilled under reduced pressure in a modified Claisen flask. The fraction (29 g.) boiling at 168–177° (2 mm.) was a viscous liquid which partly solidified in the receiver but which could not be crystallized by ordinary methods. However, using methanol as a solvent and a cooling bath of dry-ice–acetone, 9.3 g. of impure solid was isolated. Recrystallization of this product from a mixture of benzene and ligroin gave 6.2 g. (7%) of α-*n*-butylsulfonyl-N-ethylacetamide (II), m. p. 73–73.5° (corr.), which was identical with the synthetic material described later. The methanol solution obtained by filtration after the dry-ice–acetone treatment stood for some time at room temperature and a crystal growth of α-*n*-butylsulfonyl-N-ethyl-*n*-butyramide (IV), 0.4 g. (0.04%), m. p. 63–64°, was formed. This was identical with the definitely characterized material described later. Attempts to crystallize the remainder of the material were unsuccessful but it appeared to be a mixture of III and IV. In other experiments repeated attempts to separate III and IV satisfactorily were unsuccessful; small amounts were separated by crystallization and none at all by distillation.

Ethylation of α-*n*-Butylsulfonyl-N-ethylacetamide (III).—Thirty-one grams (0.15 mole) of III (prepared as described later in this paper) was refluxed with stirring for two and one-half hours in 400 ml. of dry toluene containing one equivalent of sodium ethoxide. The sodium derivative precipitated as a white granular solid. There was then added 28.2 g. (0.18 mole) of freshly distilled ethyl sulfate and the mixture refluxed in an oil-bath with stirring for two and one-half hours. This alkylation was relatively rapid; the reaction mixture had become neutral to litmus within one hour. The hot solution was filtered to remove the sodium ethyl sulfate which, when dry, weighed 20.0 g. (91% of the theoretical). The filtrate was concentrated and chilled but there was no crystallization. Removal of all of the solvent gave a thick oil which was distilled in a modified Claisen flask. The fraction (31.0 g.) boiling at 174–178° (3 mm.) was a viscous liquid boiling almost entirely at 174° (3 mm.). This distillate remained an oil for two weeks but solidified when seeded with α-*n*-butylsulfonyl-N-ethyl-*n*-butyramide (IV) isolated from the above ethylation. Recrystallization was very difficult but was accomplished by using methanol as a solvent and dry-ice in acetone as a cooling bath. The pure product weighed 16.4 g. (47%), m. p. 64–65°. Evaporation of the methanol gave an oil from which no additional pure solid was obtained. The hydrolysis of 4.9 g. of this impure material was carried out by refluxing with 60 ml. of 17% sulfuric acid for fifty hours. The solution was made alkaline, steam-distilled, and the distillate collected in dilute hydrochloric acid. A Hinsberg separation was carried out on the distillate, using *p*-toluenesulfonyl chloride.[15] There were isolated 1.5 g. of N-ethyl-*p*-toluenesulfonamide, m. p. 59–60°, and 0.15 g. of N,N-diethyl-*p*-toluenesulfonamide, m. p. 56–58°. These products did not depress the melting points of authentic samples of the proper amides.

The structure of the pure IV was established by refluxing 1.8 g. of the product for twenty-two hours with 35 ml. of 10% sodium hydroxide solution. The ethylamine evolved was absorbed in dilute hydrochloric acid and converted to N-ethylbenzenesulfonamide,[15] m. p. 56–57°. The saponification mixture was acidified with dilute hydrochloric acid, extracted with ether, and the extracts dried over sodium sulfate. The ether was removed by evaporation and the crude acid converted to the acid chloride and then the amide,[16] m. p. 124–124.5°. The identities of both derivatives were confirmed by mixed melting points with synthetic samples.

Ethylation of *n*-Butylsulfonyl-*n*-butyramide (II).—Forty-five grams (0.22 mole) of II[17] was refluxed with stirring for two hours in 400 ml. of dry toluene containing one equivalent of sodium ethoxide. The sodium derivative was soluble in hot and cold toluene. There was then added 36.9 g. (0.24 mole) of freshly distilled ethyl sulfate and the mixture refluxed in an oil-bath with stirring for eight and one-half hours. The reaction mixture was neutral; it was filtered while hot to remove the sodium ethyl sulfate which, when dry, weighed 30.0 g. (93% of the theoretical). The filtrate was concentrated and cooled and 4.67 g. (10%) of unchanged II, m. p. 117–119°, obtained. The solvent was removed completely and the thick oily residue distilled in a modified Claisen flask. In addition to

(15) Hickinbottom, "Reactions of Organic Compounds," Longmans, Green and Company, London, 1936, p. 263.

(16) Shriner and Fuson, "Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1935, p. 144.

(17) The material used in this reaction was identical with that obtained by alkylation but was prepared by a method to be described in a later paper.

the customary fore-run of ethyl sulfate, there was obtained 40.8 g., b. p. 172–178° (3–4 mm.), which solidified when seeded with α-*n*-butylsulfonyl-N-ethyl-*n*-butyramide (IV). Recrystallization from a mixture of benzene and ligroin gave 30.5 g. (60%) of impure IV, m. p. 58–61°. Several recrystallizations gave 24 g. (47%) of the pure material, m. p. 64.5–65° (corr.), which did not depress the melting points of the material obtained by the ethylation of III or that obtained as one of the products from the ethylation of I.

Anal. Calcd. for $C_{10}H_{21}O_3NS$: N, 5.95; S, 13.62. Found: N, 5.91, 5.90; S, 13.72, 13.68.

Ethylation of α-(*n*-Butylthio)-acetamide.—The sodium derivative was prepared by refluxing with stirring 74.7 g. (0.51 mole) of α-(*n*-butylthio)-acetamide[3] for two and one-half hours in 800 ml. of dry toluene containing an equivalent amount of sodium ethoxide. The sodium derivative was soluble in hot toluene but precipitated as a gelatinous mass on cooling. The sodium derivative was refluxed with stirring for eight and one-half hours with 82.5 g. (0.54 mole) of freshly distilled ethyl sulfate. At the end of this period the reaction mixture was neutral to moist litmus. The sodium ethyl sulfate obtained by filtration of the hot solution weighed 70 g. (93% of the theoretical). The filtrate was concentrated and the oily residue distilled in a modified Claisen flask. Fraction 1, 12.7 g., distilled at 73–81° (4–6 mm.). Ethyl sulfate was shown to be present in this mixture by the formation of barium sulfate. Another component of the fraction was probably ethyl α-(*n*-butylthio)-acetate[18] which is reported[19] to boil at 89–90° (10 mm.). Fraction 2, 47.5 g., distilled at 122–125° (4 mm.). Considerable decomposition occurred during distillation and the residue was large. The entire fraction was dissolved in 270 ml. of 1:1 acetic acid–acetic anhydride mixture and treated with 70 ml. of 30% hydrogen peroxide according to the method already described.[3] At the end of the oxidation period the excess peroxide was decomposed by manganese dioxide and the solvent removed under reduced pressure. The residue was an oil which dissolved in hot benzene and was precipitated as a solid by the addition of ligroin. The product thus obtained weighed 41.11 g., corresponding to approximately 75% of the theoretical for the oxidation step. Crystallization from benzene gave 5 g. of I, m. p. 117–118°, and the addition of ligroin to the filtrate gave 24.1 g. of impure III, m. p. 65–67° (23% of the theoretical, based on α-(*n*-butylthio)-acetamide). Since the separation of I and III in other experiments was fairly easy, it seems safe to say that the product of the oxidation was III contaminated with relatively small amounts of I. Several recrystallizations of the impure III raised its melting point to 72°.

IV. Reactions of Amides with Sodium Ethoxide

The general procedure was to prepare sodium ethoxide in benzene by the method already described, add an equivalent amount of the amide and reflux in an oil-bath for the periods of time stated below. Glacial acetic acid was then added in 10% excess of the theoretical amount and heating continued until the mixture was neutral to moist litmus.

α-*n*-Butylsulfonylacetamide (I).—To 150 ml. of benzene containing sodium ethoxide was added 4.05 g. (0.023 mole) of I and the mixture refluxed for two and one-half hours. After treatment with glacial acetic acid as described above, the hot solution was filtered, concentrated and chilled. The amount of I recovered was 3.40 g. (84%), m. p. 116–117°. Considering the mechanical losses that might be expected, it seems safe to say that no appreciable side reactions arise from the action of sodium ethoxide on I. Evidence for the complete conversion of I to the sodium derivative has been mentioned earlier in the experimental part.

α-(*n*-Butylthio)-acetamide (IX).—To 100 ml. of benzene containing sodium ethoxide was added 6.01 g. (0.041 mole) of the amide and the mixture refluxed for five hours. After treatment with glacial acetic acid as described above, the hot solution was filtered, concentrated, and the amide precipitated by the addition of ligroin. The recovery was 4.16 g. (69%), m. p. 55–56°. The poor recovery and the large residue after distillation of the alkylation product as mentioned above both suggest that the reaction of sodium ethoxide with α-(*n*-butylthio)-acetamide gives other products in addition to the sodium derivative.

V. Preparation of α-*n*-Butylsulfonyl-N-ethylacetamide

α-(*n*-Butylthio)-acetic Acid.[20]—This compound was prepared from sodium chloroacetate and sodium *n*-butylmercaptide.[21] An aqueous solution of sodium chloroacetate was prepared by mixing a concentrated aqueous solution containing 66.2 g. (0.7 mole) of chloroacetic acid with a concentrated aqueous solution containing 28 g. (0.7 mole) of sodium hydroxide and diluting with water to a total volume of 150 ml. The solution was placed in a 1-liter, three-necked, round-bottomed flask equipped with a mechanical stirrer and a dropping funnel and immersed in an ice–salt bath. A solution of 75.5 ml. (63.1 g., 0.7 mole) of *n*-butyl mercaptan and 28.0 g. (0.7 mole) of sodium hydroxide in 110 ml. of water was added, with stirring, over a period of one and one-half hours. The reaction mixture was allowed to come to room temperature as the freezing bath melted and after standing overnight was heated on the steam-bath for three hours. The solution was transferred to a separatory funnel, an excess of concentrated sulfuric acid added and the oily upper layer separated. The aqueous layer was extracted with two 100-ml. portions of ether, the extracts added to the original acid layer and the solution dried over calcium chloride. The ether was removed on the steam-bath and the residue distilled in a modified Claisen flask. The product weighed 93.4 g. (90%), b. p. 125–130° (5–6 mm.).

α-*n*-Butylsulfonylacetic Acid.[20]—A solution of 93.4 g. (0.63 mole) of α-(*n*-butylthio)-acetic acid in 630 ml. of 1:1 acetic acid–acetic anhydride mixture was chilled in an ice–salt bath and a one-third excess (172 ml.) of 30% hydrogen

(18) In the alkylation of the α-sulfonylamides, as well as in this case, it often was noted that a fraction corresponding to the ethyl ester was present unless freshly dried alcohol was used. Apparently the slightest traces of moisture cause saponification and the salt formed is converted to the ester by the ethyl sulfate: $RSO_2CH_2CONH_2 \xrightarrow{NaOH} RSO_2CH_2COONa \xrightarrow{(C_2H_5)_2SO_4} RSO_2CH_2COOC_2H_5$.

(19) Uyeda and Reid, THIS JOURNAL, **42**, 2385 (1920).

(20) The conditions for these reactions were worked out in this Laboratory by Mr. Gordon Urquhart.

(21) This reaction had been described previously by Uyeda and Reid.[19] Since certain modifications were made in their directions and higher yields obtained, our method has been described in detail.

peroxide solution added slowly to the cold mixture. The solution was allowed to come to room temperature as the ice-bath melted and stand at room temperature overnight.[22] Manganese dioxide[23] was added, the solution transferred to a Claisen flask and the solvent removed under reduced pressure. The solid residue was dissolved in a mixture of ether and acetone, dried over sodium sulfate and the solvent removed on the water-bath. The yield of crude product was 88 g. (77%), m. p. 59–62°. Recrystallization from toluene gave the pure acid, m. p. 67.5–68.5° (corr.).

Anal. Calcd. for $C_6H_{12}O_4S$: S, 17.79. Found: S, 17.76, 17.91.

α-*n*-Butylsulfonyl-N-ethylacetamide (III).—Crude α-*n*-butylsulfonylacetic acid (40.5 g., 0.225 mole) was placed in an Erlenmeyer flask which was connected by a wide rubber tube to the neck of a three-necked, round-bottomed flask. The acid chloride was prepared by adding the solid acid slowly to thionyl chloride and treating according to the method described for *n*-butyryl chloride.[24] Ethylamine, generated from the hydrochloride by the addition of concentrated alkali and heating, was passed through a tube of soda-lime and bubbled into 250 ml. of dry ether in a 1-liter, three-necked, round-bottomed flask surrounded by an ice–salt bath. When the increase in weight of the ethereal solution was 26 g. (0.58 mole of ethylamine) the flask was fitted with a reflux condenser, a mercury-sealed stirrer and a dropping funnel, kept in the cooling bath, and the acid chloride added dropwise. The reaction mixture stood overnight and the ether then distilled on the steam-bath and replaced by dry benzene during the distillation. The resulting benzene solution was filtered while hot through a fluted filter, concentrated, and the product precipitated by the addition of ligroin and chilling. The product weighed 37.6 g. (81%), m. p. 60–65°, but was contaminated with *n*-butylsulfonylacetic acid. It was dissolved in cold benzene, washed with a saturated solution of sodium bicarbonate, dried over sodium sulfate and recrystallized from a benzene–ligroin mixture. The pure product so obtained weighed 17.4 g., m. p. 73–73.5° (corr.). Concentration of the mother liquor gave an additional 7.4 g., m. p. 70–71°, making the total yield of product 24.8 g. (53%).

Anal. Calcd. for $C_8H_{17}O_3NS$: N, 6.76; S, 15.47. Found: N, 6.69, 6.71; S, 15.36, 15.55.

(22) A longer oxidation period would probably give better results.

(23) Manganese dioxide was used in small amounts, since it formed a manganese salt of the product. Nevertheless, it appeared to assist in the decomposition of the excess peroxide and was always used.

(24) Gilman, "Organic Syntheses," John Wiley and Sons, New York, N. Y., 1932, Coll. Vol. I, p. 142.

Summary

The alkylationi n alcohol of α-alkylsulfonylamides ($RSO_2CH_2CONH_2$) was complicated by the fact that the compounds were not acidic enough to form sodium derivatives satisfactorily in the presence of a considerable amount of alcohol. In inert solvents alkyl halides were not very reactive but ethyl sulfate reacted readily with the sodium derivative of α-*n*-butylsulfonylacetamide (I). The products of this reaction were, in addition to unchanged starting material, α-*n*-butylsulfonyl-*n*-butyramide (II), α-*n*-butylsulfonyl-N-ethylacetamide (III) and α-*n*-butylsulfonyl-N-ethyl-*n*-butyramide (IV). Under similar conditions both II and III gave IV. The results may be interpreted as evidence that in the system —CH_2—CO—NH_2 of this series, two types of sodium derivatives are formed and that the —CH_2— and —NH_2 are activated to about the same extent. Introduction of an alkyl substituent on either —CH_2— or —NH_2 decreases the relative reactivity of the group to which the alkyl substituent is attached and subsequent alkylation occurs on the other active group.

PHILADELPHIA, PENNA. RECEIVED AUGUST 8, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

The Reductive Alkylation of Aromatic Primary Amines. II[1]

BY WILLIAM S. EMERSON AND W. D. ROBB

In view of earlier success with the reductive alkylation of aniline[1] it seemed advisable to test the generality of this reaction with other aromatic primary amines. For this purpose we selected *p*-toluidine, *p*-anisidine and α- and β-naphthylamines.

Using the procedure previously described[1] ethyl-α-naphthylamine was prepared in 88% yield, ethyl-, *n*-butyl- and benzyl-β-naphthylamine, and ethyl- and *n*-butyl-*p*-toluidine in 50 to 64% yields. These amines were identified by the formation of known salt or amide derivatives.

The new substances, N-*n*-butyl-α-naphthylamine and N-ethyl- and N-*n*-butyl-*p*-anisidine, were also prepared by this method. Their properties, as well as those of the new benzamide of benzyl-α-naphthylamine, are given in Table I.

N,N-Dialkylarylamines.—In the alkylation of *p*-toluidine and *p*-anisidine with *n*-butyraldehyde, a high boiling fraction was obtained. Three grams of this material was boiled with 20 cc. of acetic

(1) For paper I, see Emerson and Walters, THIS JOURNAL, 60, 2023 (1938).

TABLE I

PROPERTIES OF AMINES

Amine	N-*n*-Butyl-α-naphthylamine	N-Ethyl-*p*-anisidine	N-*n*-Butyl-*p*-anisidine	Benzyl-α-naphthylamine
Yield, %	80	51	65	24
B. p. °C.	155–167	135–140	142–145	..
B. p. Mm.	8	20	6	..
d^{20}_{20}	1.004	1.017	0.963	..
$n^{20}D$	1.5963	1.5444	1.5207	..
Derivative	HCl	*p*-Br-Bz-sulfonamide	HCl	Benzamide
Deriv. m. p., °C.	151–152	113–114	187.5–188	103–104
Anal. Calcd. C, %	71.4	48.7	61.3	N, 4.16
Anal. Calcd. H, %	7.64	4.32	8.36	
Anal. Found C, %	71.4	49.3	61.5	N, 4.21
Anal. Found H, %	8.07	4.50	8.60	

anhydride for one-half hour and then diluted with water. After neutralization with sodium carbonate the mixture was boiled until all the tertiary amine had distilled. Upon extraction of the oil from the filtrate with ether and evaporation of the ether the alkylations were found to have produced a 19% yield of N,N-di-*n*-butyl-*p*-toluidine and a 25% yield of N,N-di-*n*-butyl-*p*-anisidine.

Summary

The method for preparing N-alkylanilines by reducing an alcoholic solution of aniline and an aldehyde with hydrogen in the presence of Raney nickel and sodium acetate has been extended to four other aromatic primary amines from which ten N-alkylarylamines have been obtained in 24 to 88% yield.

URBANA, ILLINOIS RECEIVED AUGUST 14, 1939

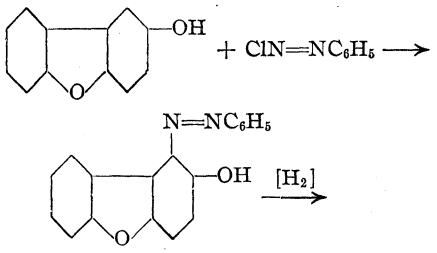
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

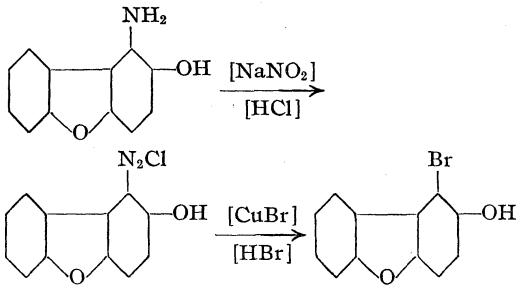
Dibenzofuran. XIV. Diazo Coupling of 2-, 3-, and 4-Hydroxy Compounds[1]

BY HENRY GILMAN AND MARIAN WESTON VAN ESS

Introduction

The recent availability of authentic specimens of some bromohydroxydibenzofurans[2] has made possible the determination of structure of the benzeneazo-hydroxydibenzofurans formed by diazo coupling with the 2-, 3-, and 4-hydroxydibenzofurans. The following transformations illustrate the general procedure used for proof of structure of the coupling products.





The 3-hydroxydibenzofuran also coupled in an ortho position to give 2-benzeneazo-3-hydroxydibenzofuran; but the 4-hydroxydibenzofuran coupled in a para position to give 1-benzeneazo-4-hydroxydibenzofuran. These general directions of coupling are consistent with early observations on phenols.[3] However, there are two available ortho positions for diazo coupling of the 2- and the 3-hydroxydibenzofurans. On general grounds, it might have been predicted that 3-hy-

(1) Paper XIII, Gilman, Parker, Bailie and Brown, THIS JOURNAL, **61**, 2836 (1939).

(2) Gilman and P. R. Van Ess, *ibid.*, **61**, 1365 (1939).

(3) Chattaway and Hill, *J. Chem. Soc.*, **121**, 2756 (1922).

droxydibenzofuran would couple predominantly in the 2-position rather than in the 4-position, because (other than by metalation) the 4- and the 6-positions are generally not susceptible to the introduction of substituents.[1]

The problem of selective ortho diazo coupling is not without some interest in connection with the relative fixation of possible bond structures in dibenzofuran. It is quite likely that diazo coupling and bromination of both phenols and aliphatic enols are intimately associated, and that each involves an enolic double bond.[4] From the experimental evidence presented at this time, it appears that there is no preferential stabilization of one of the bond structures for the isomeric hydroxydibenzofurans. If there were marked rigidity, a condition that would be unusual in the simple monosubstituted types, then the observed coupling in the 1-position of 2-hydroxydibenzofuran would indicate double bonds between the 1- and 2- and between the 3- and 4-positions. However, a fixed double bond between the 3- and 4-positions would lead one to expect that 3-hydroxydibenzofuran would couple in the 4-position, and not in the 2-position as was the case.

The solubilities of the coupling products in alkali conform with related types in the naphthalene series. The azo dyes derived from the 2- and 3-hydroxydibenzofurans were found to be insoluble in dilute alkali, even when heated, whereas the dye derived from 4-hydroxydibenzofuran was easily soluble in cold alkaline solution. 1-Hydroxy-2-benzeneazonaphthalene[5] and 1-benzeneazo-2-hydroxynaphthalene[6] are insoluble in alkali, and 1-hydroxy-4-benzeneazonaphthalene[6] is readily soluble.

Experimental Part

1-Benzeneazo-2-hydroxydibenzofuran.—The general procedure for the coupling reaction was adapted from that used by Werner and Frey[7] in preparing the benzeneazo derivative of 10-hydroxyphenanthrene. The 2-hydroxydibenzofuran, 3.68 g. (0.02 mole), was dissolved in 15 cc. of 15% potassium hydroxide solution, and subsequently diluted with 60 cc. of water, then cooled to 0° in a 200-cc. three-necked flask equipped with a stirrer, dropping funnel, and thermometer. The diazonium solution was prepared by adding 5 cc. of concd. hydrochloric acid to a mixture of 1.86 g. (0.02 mole) of aniline and 15 g. of finely cracked ice, then adding dropwise a solution of 1.46 g. (0.021 mole) of sodium nitrite in a few cc. of water, until a slight but permanent test for nitrite ion was indicated by a test with starch–potassium iodide paper. The diazonium solution was added dropwise to the cold solution of 2-hydroxydibenzofuran through the chilled dropping funnel. The temperature was maintained at 0° by means of an ice-bath. A red precipitate formed at once. To ensure complete reaction the mixture was stirred for thirty minutes after addition was completed. The product was then removed by filtration and washed well with water. Acidification is not necessary since the desired product is insoluble in alkali. The yield was almost quantitative. The crude product melted at 161–164°, and two recrystallizations from alcohol gave red needles melting at 165.5–166°.

Anal. Calcd. for $C_{18}H_{12}O_2N_2$: N, 9.72. Found: N, 9.84 and 9.98.

2 - Benzeneazo - 3 - hydroxydibenzofuran.—The 3-hydroxydibenzofuran was coupled with benzenediazonium chloride in exactly the manner described above for 2-hydroxydibenzofuran. It was found to be advantageous, however, to run the reaction at a slightly lower temperature (−5°). The mixture was filtered at the close of the reaction without previous acidification. The yield from 3.68 g. (0.02 mole) of 3-hydroxydibenzofuran was 4 g. or 73% of the theoretical. The product after twice crystallizing from alcohol, and once from ethyl acetate, and once from a mixture of ethyl acetate and alcohol melted at 177–178°. It crystallized in minute lustrous golden-brown plates.

Anal. Calcd. for $C_{18}H_{12}O_2N_2$: N, 9.72. Found: N, 9.70 and 9.83.

1 - Benzeneazo - 4 - hydroxydibenzofuran.—The 4-hydroxydibenzofuran was coupled with benzenediazonium chloride by the procedure described for 2-hydroxydibenzofuran. In this case the resulting azo compound formed a salt which separated in very fine orange crystals. Direct acidification of the reaction mixture gave purplish material which turned green upon drying and was difficult to purify. In order to obtain a pure sample it was necessary either to filter out the potassium salt from the reaction mixture and then acidify, or to crystallize the purplish material obtained by acidification of the reaction mixture at once from dilute alcohol without allowing it to stand. The purified product which separated in yellow-orange needles from dilute alcohol melted at 174–175°.

Anal. Calcd. for $C_{18}H_{12}O_2N_2$: N, 9.72. Found: N, 9.77 and 9.99.

Conversion of 1-Benzeneazo-2-hydroxydibenzofuran to 1-Bromo-2-hydroxydibenzofuran.—The method described by Pschorr[8] for the reduction of 9-hydroxy-10-benzeneazophenanthrene was used as a basis for the reduction of the hydroxyazodibenzofurans. One gram (0.0045 mole) of 1-benzeneazo-2-hydroxydibenzofuran was dissolved in 40 cc. of boiling glacial acetic acid, and a solution of 2.0 g. of stannous chloride hydrate in 15 cc. of concd. hydrochloric acid added gradually. The color of the solution quickly faded to yellow. The solution was then cooled, whereupon fine white needles separated out. These crystals

(4) Mills and Nixon, *J. Chem. Soc.*, 2510 (1930); Fieser and Lothrop, THIS JOURNAL, **58**, 2050 (1936); and Fieser in Chap. 2 of Gilman, "Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1938.

(5) McPherson, *Ber.*, **28**, 2418 (1895).

(6) Liebermann, *ibid.*, **16**, 2860 (1883).

(7) Werner and Frey, *Ann.*, **321**, 303 (1902).

(8) Pschorr, *Ber.*, **35**, 2734 (1902).

proved to be the hydrochloride of 1-amino-2-hydroxydibenzofuran. A quantitative yield was obtained. The compound had a tendency to oxidize in air, hence it was used at once to prepare the corresponding bromohydroxy compound.

The diazotization of all of the hydroxyaminodibenzofurans proved rather difficult owing to their marked sensitivity to oxidation. The procedure finally used was based on a patented process for the diazotization of *o*-aminonaphthols.[9] The hydrochloride of 1-amino-2-hydroxydibenzofuran was suspended in ether and treated with an equivalent amount of sodium carbonate solution. The ether layer was washed with water, dried over sodium sulfate and the amine hydrobromide precipitated by passing in dry hydrogen bromide.[10] The hydrobromide, 0.45 g. (0.0025 mole), was suspended in 30 cc. of water at 0° and poured gradually into a similarly cooled solution of 0.12 g. (0.0017 mole) of sodium nitrite and 0.08 g. of copper sulfate hydrate in 10 cc. of water. A light brown precipitate formed. Fifteen minutes was allowed for the completion of the diazotization, whereupon the mixture was poured into a suspension of 0.81 g. (0.0021 mole) of cuprous bromide in 20 cc. of water, and 13 cc. of 40% hydrobromic acid was added gradually. As soon as the evolution of gas ceased, the mixture was boiled for a few minutes. Some very dark precipitate was filtered from the hot solution. The filtrate on cooling deposited grayish needles, 0.015 g., melting at 115–116°. When decolorized with charcoal and crystallized from dilute alcohol, the melting point was 121.5–122° and was not depressed by mixture with an authentic sample of 1-bromo-2-hydroxydibenzofuran.

Conversion of 2-Benzeneazo-3-hydroxydibenzofuran to 2-Bromo-3-hydroxydibenzofuran.—The 2-benzeneazo-3-hydroxydibenzofuran was reduced according to the procedure described for the 1-benzeneazo-2-hydroxydibenzofuran. In the case of the 3-hydroxy derivative, the hydroxy-amine formed a complex with the tin salt and hence did not precipitate out directly as the hydrochloride upon cooling the reaction mixture. In order to break up the complex, the solution obtained after reduction was complete was cooled in an ice-bath and treated with small portions of 30% sodium hydroxide solution until the precipitated tin hydroxide had redissolved, then made barely acid with hydrochloric acid, and finally slightly basic with ammonium hydroxide. The solution was then extracted with ether, the ether layer dried over sodium sulfate, and the amine hydrobromide precipitated with dry hydrogen bromide.

The conversion of the hydrobromide to 2-bromo-3-hydroxydibenzofuran was accomplished by the method employed for the hydrobromide of 1-amino-2-hydroxydibenzofuran. From 0.45 g. (0.0025 mole) of the hydrobromide the yield was 0.04 g. of crude product, which after decolorizing and crystallizing from dilute alcohol melted at 111–112°. A mixed melting point determination with authentic 2-bromo-3-hydroxydibenzofuran showed no depression.

Conversion of 1-Benzeneazo-4-hydroxydibenzofuran to 1-Bromo-4-hydroxydibenzofuran.—The 1-benzeneazo-4-hydroxydibenzofuran was reduced in the same manner as described for 1-benzeneazo-2-hydroxydibenzofuran. The amine hydrochloride did not form a complex with the tin salt, but separated out at once in greenish-gray crystals. The hydrochloride was converted to the hydrobromide, diazotized, and the diazonium group replaced by bromine as previously outlined for 1-amino-2-hydroxydibenzofuran. From 0.45 g. (0.0025 mole) of the hydrobromide, a crude yield of 0.015 g. of bromohydroxydibenzofuran melting at 145–146° was obtained. By decolorizing and crystallizing from dilute alcohol, white needles were produced melting at 150°. Identification of the compound as 1-bromo-4-hydroxydibenzofuran was completed by a mixed melting point determination.

Miscellany.—In some orienting experiments we have so far not succeeded in coupling dibenzofuran with benzenediazonium chloride in alcohol solution in the presence of potassium acetate, nor with the more active 2,4-dinitrobenzenediazonium chloride[11] in acetic acid. 2-Amino- or 2-acetaminodibenzofuran also failed to couple with benzenediazonium chloride under conditions which give quantitative yields with β-naphthylamine.[12] The principal present difficulty in this case appears to be the greater insolubility of the amine or the acetamino compound in the alcoholic reaction medium even when the reaction is run at a somewhat higher temperature.

Summary

Coupling of 2-, 3-, and 4-hydroxydibenzofurans with benzenediazonium chloride gives, respectively, 1-benzeneazo-2-hydroxydibenzofuran, 2-benzeneazo-3-hydroxydibenzofuran, and 1-benzeneazo-4-hydroxydibenzofuran. The non-isolation of any 4-benzeneazo-3-hydroxydibenzofuran from the coupling with 3-hydroxydibenzofuran indicates absence of fixed bond structures in these simple types.

AMES, IOWA RECEIVED SEPTEMBER 1, 1939

(9) German Patent 172,446 [*J. Chem. Soc.*, **90**, 908 (1906)].

(10) Hydrogen bromide gas was prepared by the method of Ruhoff, Burnett and Reid, "Organic Syntheses," Vol. XV, 35 (1935).

(11) Meyer, *Ber.*, **47**, 1747 (1914), reported that 2,4-dinitrobenzenediazonium chloride couples with mesitylene and acenaphthene under these conditions.

(12) Bamberger and Schieffelin, *ibid.*, **22**, 1376 (1889).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

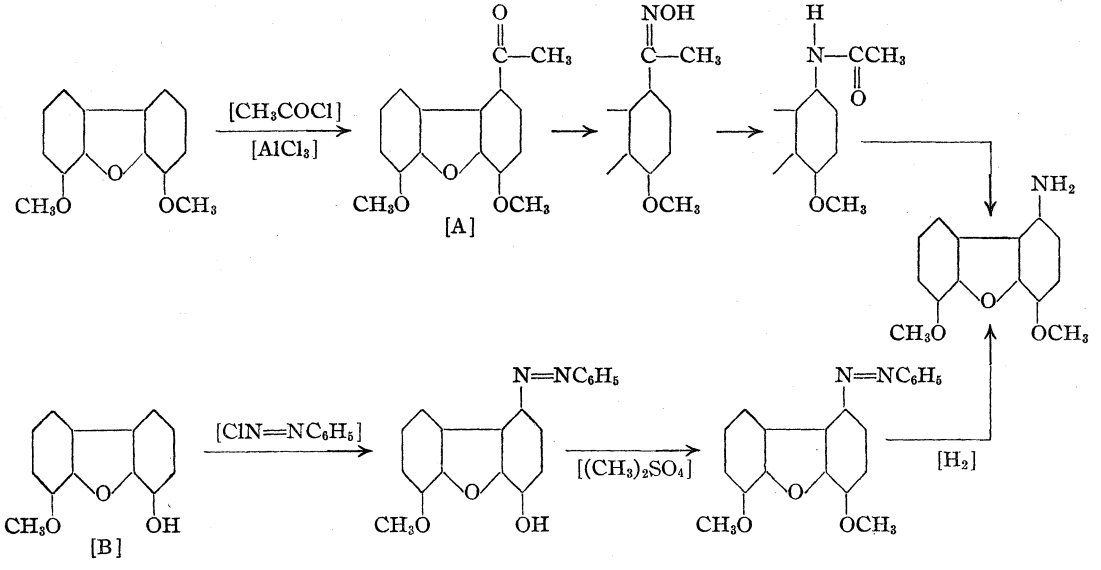
Dibenzofuran. XV. 1,4- and 1,4,6-Derivatives[1]

BY HENRY GILMAN AND LEE C. CHENEY

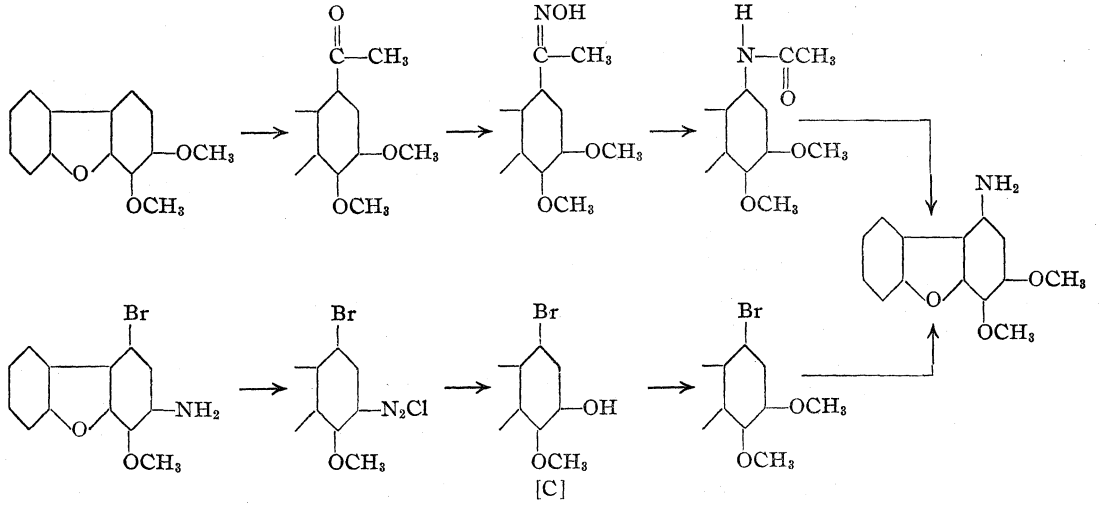
Introduction

Bridging of the 1,9-positions in dibenzofuran undoubtedly will be facilitated by the presence in the 4- and 6-positions of strong ortho-para directing groups. The recent availability of procedures for the introduction of such substituents, as well as some authentic reference compounds having a substituent in the 1-position,[2] now permits the synthesis of desirable 1,4- and 1,4,6-derivatives.

Friedel–Crafts Acylations.—Acetylation of 4,6-dimethoxydibenzofuran gave 1-acetyl-4,6-dimethoxydibenzofuran, the structure of which was established by the following sequence of reactions



The diazo coupling reaction with 4-hydroxy-6-methoxydibenzofuran [B] undoubtedly involved the nucleus containing the phenolic hydroxyl group. It was shown recently[1] that diazo coupling with 4-hydroxydibenzofuran goes para to the hydroxyl to yield 1-benzene-azo-4-hydroxydibenzofuran.

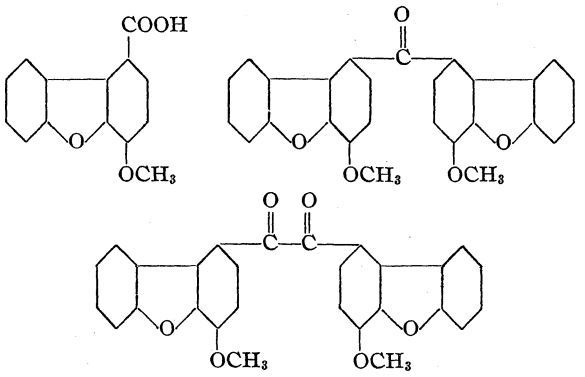


(1) Paper XIV is Gilman and M. W. Van Ess, THIS JOURNAL, **61**, 3146 (1939).

(2) Gilman and P. R. Van Ess, *ibid.*, **61**, 1365 (1939).

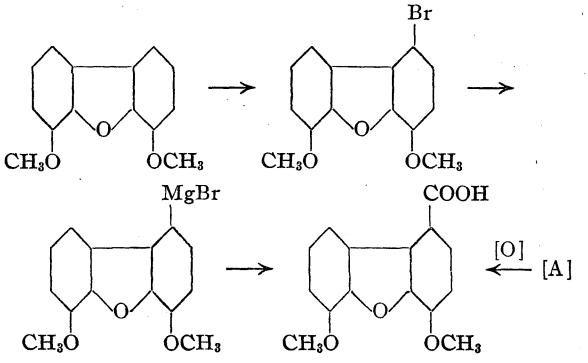
The recent proof of structure of 1-bromo-3-amino-4-methoxydibenzofuran[3] provided the essential compound for establishing the constitution of the acetylation product of 3,4-dimethoxydibenzofuran by the transformations shown.

Oxalyl chloride, aluminum chloride and 4-methoxydibenzofuran gave the following three products: 4-methoxy-1-dibenzofurancarboxylic acid, di-(4-methoxy-1-dibenzofuryl) ketone, and bi-(4-methoxy-1-dibenzofuroyl), all of which owe their formation to initial acylation in the 1-position.



The same three types (acid, ketone and benzil analog) resulted from interaction of 4,6-dimethoxydibenzofuran with oxalyl chloride.

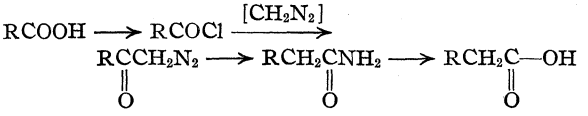
Bromination.—The structure of the monobromination product of 4,6-dimethoxydibenzofuran was established as follows



Dibromination of 4,6-dimethoxydibenzofuran gave 1,9-dibromo-4,6-dimethoxydibenzofuran. The same dibromo compound resulted on dibromination of 4,6-dihydroxydibenzofuran with subsequent methylation. However, dibromination of 4-hydroxy-6-methoxydibenzofuran followed by methylation produced a dibromo-4,6-dimethoxydibenzofuran which, unexpectedly, proved to be unlike the compound obtained by dibromination of 4,6-dimethoxydibenzofuran. This isomer is probably 1,3-dibromo-4-hydroxy-6-methoxydibenzofuran. It would be interesting to establish the course of dibromination of 1-hydroxy-8-methoxy-naphthalene.

Bromination of 3,4-dimethoxydibenzofuran yielded 1-bromo-3,4-dimethoxydibenzofuran. The proof of structure of this product was established by first preparing 1-bromo-3-hydroxy-4-methoxydibenzofuran [C] from the authentic 1-bromo-3-amino-4-methoxydibenzofuran by means of the diazo reaction. Then the 3-hydroxy-4-methoxydibenzofuran was brominated to give the same 1-bromo-3-hydroxy-4-methoxydibenzofuran, and this on methylation yielded 1-bromo-3,4-dimethoxydibenzofuran, identical with the product of bromination of 3,4-dimethoxydibenzofuran.

4,6-Dimethoxy-1-dibenzofurylacetic Acid.—In the synthesis of this compound, 4,6-dimethoxy-1-dibenzofurancarboxylic acid (used as the starting material) was prepared by two procedures: oxidation of 1-acetyl-4,6-dimethoxydibenzofuran, and carbonation of the Grignard reagent prepared from 1-bromo-4,6-dimethoxydibenzofuran. The transformations of the acid were as follows, where R = 4,6-dimethoxy-1-dibenzofuryl.



1,2,3,4-Tetrahydro-6-aminodibenzofuran.—Reduction of 4-aminodibenzofuran by sodium and alcohol was shown to involve the nonsubstituted nucleus, for the resulting tetrahydro-6-aminodibenzofuran formed no carbonate, but did undergo diazotization and subsequent coupling with β-naphthol.

Experimental Part

4,6-Dihydroxydibenzofuran.—Refluxing a solution of 8.56 g. (0.04 mole) of 4-hydroxy-6-methoxydibenzofuran with 20 ml. of hydrobromic acid (sp. gr. 1.49) in 50 ml. of acetic acid gave a 91.6% yield of 4,6-dihydroxydibenzofuran. The compound crystallized in needle form from dilute methanol, and melted at 200–202°. This melting point is higher than that reported for the dihydroxy compound obtained by two other procedures.[4]

4,6-Dimethoxydibenzofuran.—Methylation was effected by an adaptation of the procedure of Stevens and Tucker.[5] From 24.5 g. (0.115 mole) of 4-hydroxy-6-methoxydibenzofuran, 0.345 mole of dimethyl sulfate, 39 ml. of 60%

(3) Gilman, Parker, Bailie and Brown, THIS JOURNAL, **61**, 2836 (1939).

(4) Gilman and Young, *ibid.*, **57**, 1121 (1935).

(5) Stevens and Tucker, *J. Chem. Soc.*, **123**, 2140 (1923).

potassium hydroxide, and acetone as a solvent, the yield of 4,6-dimethoxydibenzofuran was practically quantitative. The compound crystallized from petroleum ether (b. p. 60–68°) as pearly plates melting at 128–129°.

Anal. Calcd. for $C_{14}H_{12}O_3$: methoxyl, 27.2. Found: methoxyl, 26.4.

The picrate of 4,6-dimethoxydibenzofuran was obtained as deep yellow needles, melting at 161–162° after crystallization from alcohol. Under corresponding conditions of preparation, the isomeric 3,4-dimethoxy compound did not form a picrate.

Anal. Calcd. for $C_{14}H_{12}O_3 \cdot C_6H_3O_7N_3$: N, 9.19. Found: N, 9.11.

1-Acetyl-4,6-dimethoxydibenzofuran.—Admixture of reagents was effected in the cold between 17.35 g. (0.0761 mole) of 4,6-dimethoxydibenzofuran, 5.97 g. (0.0761 mole) of acetyl chloride, and 10.18 g. (0.0761 mole) of aluminum chloride in 100 ml. of nitrobenzene. When addition of aluminum chloride was complete, the contents of the flask were allowed to come slowly to room temperature, and stirring was continued for twenty hours. Subsequent to hydrolysis, and removal of the nitrobenzene by steam distillation, there was isolated 12.35 g. (a 60% yield) of 1-acetyl-4,6-dimethoxydibenzofuran which melted at 178.5–179.5° after crystallization from alcohol or dilute acetone.

Anal. Calcd. for $C_{16}H_{14}O_4$: C, 71.10; H, 5.22. Found: C, 71.18 and 71.30; H, 4.93 and 5.08.

Oxime of 1-Acetyl-4,6-dimethoxydibenzofuran and its Beckmann Rearrangement Product.—By using the procedure for the preparation of the oxime of 1-acetyl-4-methoxydibenzofuran,[3] there was obtained an 88% yield of the oxime of 1-acetyl-4,6-dimethoxydibenzofuran which crystallized from alcohol as plates melting at 203–204°.

Anal. Calcd. for $C_{16}H_{15}O_4N$: N, 4.91. Found: N, 5.02.

Rearrangement of a benzene suspension of the oxime by phosphorus pentachloride gave a 76.4% yield of **1-acetamino-4,6-dimethoxydibenzofuran,** which crystallized from benzene as fine needles melting at 244–245°.

Anal. Calcd. for $C_{16}H_{15}O_4N$: N, 4.92. Found: N, 4.93.

Hydrolysis of the acetamino compound by heating an alcohol–concd. hydrochloric acid solution gave a 94.5% yield of 1-amino-4,6-dimethoxydibenzofuran hydrochloride, obtained as needles melting at 286–287°. The hydrochloride and ammonium hydroxide gave 1-amino-4,6-dimethoxydibenzofuran melting at 162–162.5° after crystallization from methanol, and identical (mixed m. p.) with the amine obtained by reduction of 1-benzeneazo-4,6-dimethoxydibenzofuran.

1 - Benzeneazo - 4 - hydroxy - 6 - methoxydibenzofuran.—The extreme insolubility of the potassium salt of 4-hydroxy-6-methoxydibenzofuran necessitated a modification of the procedure used for the coupling of 4-hydroxydibenzofuran.[1]

The alkaline solution of the phenol prepared from 4.28 g. (0.02 mole) of 4-hydroxy-6-methoxydibenzofuran, 15 ml. of 15% potassium hydroxide solution, and 385 ml. of water, was placed in a one-liter three-necked flask equipped with stirrer, low-temperature thermometer and dropping funnel. The diazonium salt solution was prepared from 2.58 g. (0.02 mole) of aniline hydrochloride in 15 ml. of water, 15–25 g. of cracked ice, 3.4 ml. of concd. hydrochloric acid, and 1.46 g. (0.021 mole) of sodium nitrite in 15 ml. of water. This ice-cold benzenediazonium chloride solution was added to the cold, stirred, alkaline solution of the phenol at such a rate that the temperature did not rise above 3°. A beautiful orange precipitate formed at once. After addition was complete, the reaction mixture was stirred for forty-five minutes, and the coupling product filtered off and dried. Two crystallizations from alcohol yielded rust-colored needles of 1-benzeneazo-4-hydroxy-6-methoxydibenzofuran, m. p. 175°. The yield was 3.6 g. or 56.6%.

Anal. Calcd. for $C_{19}H_{14}O_3N_2$: N, 8.84. Found: N, 8.89.

1-Benzeneazo-4,6-dimethoxydibenzofuran and its Reduction to 1-Amino-4,6-dimethoxydibenzofuran.—Methylation of 1.59 g. (0.005 mole) of 1-benzeneazo-4-hydroxy-6-methoxydibenzofuran by dimethyl sulfate and potassium hydroxide in acetone gave an 88% yield of deep orange prisms, melting at 170° when crystallized from benzene.

Anal. Calcd. for $C_{20}H_{16}O_3N_2$: N, 8.44. Found: N, 8.51.

The 1-benzeneazo-4,6-dimethoxydibenzofuran (1 g.) was reduced in essential accordance with the procedure described for the reduction of 1-benzeneazo-4-hydroxydibenzofuran.[1] The yield of 1-amino-4,6-dimethoxydibenzofuran was 0.24 g. (32.8%).

Anal. Calcd. for $C_{14}H_{13}O_3N$: N, 5.77. Found: N, 5.88.

Friedel–Crafts Reaction with 4-Methoxydibenzofuran and Oxalyl Chloride.—Into a solution of 9.90 g. (0.05 mole) of 4-methoxydibenzofuran and 7.0 g. (10% excess over 0.05 mole) of oxalyl chloride in 75 ml. of nitrobenzene contained in a three-necked flask equipped with stirrer and condenser topped with a calcium chloride tube, was gradually added 14.7 g. (10% excess) of anhydrous aluminum chloride. Throughout the addition an ice-bath cooled the reaction mixture, which was then allowed to come slowly to room temperature. After twenty-eight hours, the red-brown mixture was hydrolyzed with ice and hydrochloric acid, the nitrobenzene was removed with steam, and the amorphous solid boiled with 5% sodium hydroxide solution and filtered. The dried acidification product from the filtrate (0.7 g.), after crystallization from acetic acid, melted at 276–277° and was shown to be **4-methoxy-1-dibenzofurancarboxylic acid** by mixed melting point.

The dried, amorphous, alkali-insoluble solid was extracted with 100 ml. of acetic acid. From the cold filtrate was obtained 1.9 g. (18%) of **di-(4-methoxy-1-dibenzofuryl) ketone** in the form of colorless needles, m. p. 234°.

Anal. Calcd. for $C_{27}H_{18}O_5$: C, 76.8; H, 4.29. Found: C, 76.1; H, 4.37.

The acetic acid insoluble residue, which proved to be **bi-(4-methoxy-1-dibenzofuroyl)**, crystallized from nitrobenzene in the form of pale yellow needles, m. p. 329°. The yield was 3.9 g. or 34.6%.

Anal. Calcd. for $C_{29}H_{22}O_7$: C, 72.2; H, 4.62. Found: C, 72.3; H, 4.68.

Friedel–Crafts Reactions of 4-Methoxydibenzofuran with Chloroacetyl Chloride and Ethyl Chloroglyoxalate.—From 12.5 g. (0.063 mole) of 4-methoxydibenzofuran, 7.9 g. (0.07 mole) of chloroacetyl chloride, 8.5 g. (0.0635 mole) of aluminum chloride and 60 ml. of nitrobenzene there was obtained 6.3 g. or a 53.2% yield of **1-chloroacetyl-4-methoxydibenzofuran** which crystallized from alcohol as needles melting at 165–166°.

Anal. Calcd. for $C_{15}H_{11}O_3Cl$: Cl, 12.92. Found: Cl, 13.12 and 13.05.

From a corresponding reaction between 9.9 g. (0.05 mole) of 4-methoxydibenzofuran, 7.5 g. (10% excess) of ethyl chloroglyoxalate, 8.0 g. (20% excess) of aluminum chloride and 60 ml. of nitrobenzene there resulted 6.4 g. (43%) of **1-ethoxalyl-4-methoxydibenzofuran** which melted at 113° after crystallization from alcohol.

Anal. Calcd. for $C_{17}H_{14}O_5$: C, 68.4; H, 4.73. Found: C, 68.0; H, 4.82.

Hydrolysis of 1 g. of 1-ethoxalyl-4-methoxydibenzofuran by refluxing with 15% sodium hydroxide gave (subsequent to acidification) 0.43 g. of **4-methoxy-1-dibenzofuryl-α-oxoacetic acid** which crystallized from alcohol as pale yellow needles melting at 187°.

Anal. Calcd. for $C_{15}H_{10}O_5$: C, 66.64; H, 3.73. Found: C, 66.39; H, 3.75.

Concentrated sulfuric acid colored the keto acid deep red. Oxidation of the keto acid by alkaline permanganate gave 4-methoxy-1-dibenzofurancarboxylic acid (mixed m. p.). The **semicarbazone of 4-methoxy-1-dibenzofuryl-α-oxoacetic acid** melted at 211.5–212° with decomposition after crystallization from alcohol.

Anal. Calcd. for $C_{16}H_{13}O_5N_3$: N, 12.84. Found: N, 12.83.

Friedel–Crafts Reaction with 4,6-Dimethoxydibenzofuran and Oxalyl Chloride.—The procedure described for the reaction of 4-methoxydibenzofuran and oxalyl chloride was used. Into an ice-cold solution of 4.56 g. (0.02 mole) of 4,6-dimethoxydibenzofuran and 2.8 g. (10% excess over 0.02 mole) of oxalyl chloride in 50 ml. of nitrobenzene, was slowly added 6.42 g. (20% excess over 0.04 mole) of powdered, anhydrous aluminum chloride. Addition required one and three-fourths hours, after which the reaction mixture was allowed to come to room temperature, stirring being continued for twenty hours. Hydrolysis was effected with ice and hydrochloric acid, after which the nitrobenzene was removed with steam. The remaining gray solid was extracted with 200 ml. of 10% sodium hydroxide solution to remove any acids. Acidification of the filtrate furnished 0.37 g. of **4,6-dimethoxy-1-dibenzofurancarboxylic acid,** m. p. 297–298°.

The gray solid residue was extracted (Soxhlet apparatus) with 100 ml. of acetic acid to yield 0.5 g. (10.4%) of **di-(4,6-dimethoxy-1-dibenzofuryl) ketone,** m. p. 254–255°.

Anal. Calcd. for $C_{29}H_{22}O_7$: C, 72.17; H, 4.62. Found: C, 72.31 and 71.54; H, 4.93 and 4.68.

The pale yellow, extremely insoluble residue from the acetic acid extraction crystallized from nitrobenzene in the form of very small needles, m. p. above 300°. Analysis showed the compound to be **bi-(4,6-dimethoxy-1-dibenzofuroyl)**. The yield was 3.1 g. (60.7% of the theoretical).

Anal. Calcd. for $C_{30}H_{22}O_8$: C, 70.65; H, 4.35. Found: C, 70.94 and 70.63; H, 4.60 and 4.69.

3,4-Dihydroxydibenzofuran and 3,4-Diacetoxydibenzofuran.—An 88% yield of 3,4-dihydroxydibenzofuran was obtained by refluxing an acetic acid solution of 8.56 g. (0.04 mole) of 3-hydroxy-4-methoxydibenzofuran with hydrobromic acid (sp. gr. 1.49). Recrystallization from hot water gave needles melting at 164–164.5°.

Anal. Calcd. for $C_{12}H_8O_3$: C, 71.98; H, 4.03. Found: C, 71.56; H, 4.21.

From 3,4-dihydroxydibenzofuran (1.95 g.), acetic anhydride and a drop of concd. sulfuric acid was obtained a 74.1% yield of 3,4-diacetoxydibenzofuran which melted at 104–105° after crystallization from methanol.

Anal. Calcd. for $C_{16}H_{12}O_5$: C, 67.5; H, 4.28. Found: C, 67.6; H, 4.21.

3,4-Dimethoxydibenzofuran.—Methylation of 49.2 g. (0.39 mole) of 3-hydroxy-4-methoxydibenzofuran by dimethyl sulfate and 10% sodium hydroxide gave an 81% yield of 3,4-dimethoxydibenzofuran, which crystallized from petroleum ether (b. p. 28–38°) as needles melting at 60–61°.

Anal. Calcd. for $C_{14}H_{12}O_3$: methoxyl, 27.2. Found: methoxyl, 26.8.

1-Acetyl-3,4-dimethoxydibenzofuran.—Acetylation of 13.7 g. (0.06 mole) of 3,4-dimethoxydibenzofuran by the procedure used with the 4,6-dimethoxy compound gave a 55.5% yield of 1-acetyl-3,4-dimethoxydibenzofuran which crystallized from alcohol as needles melting at 90.5–91°.

Anal. Calcd. for $C_{16}H_{14}O_4$: C, 71.10; H, 5.22. Found: C, 71.11 and 70.54; H, 5.41 and 5.42.

Some demethylated phenol also was isolated.

Oxime of 1-Acetyl-3,4-dimethoxydibenzofuran and its Rearrangement to 1-Acetamino-3,4-dimethoxydibenzofuran.—The oxime of 1-acetyl-3,4-dimethoxydibenzofuran (84% yield) was crystallized from alcohol as needles melting at 156–157°.

Anal. Calcd. for $C_{16}H_{15}O_4N$: N, 4.91. Found: N, 5.11.

A Beckmann rearrangement of a benzene solution of the oxime by phosphorus pentachloride gave a 94% yield of 1-acetamino-3,4-dimethoxydibenzofuran which crystallized from alcohol (to which several drops of acetic anhydride were added) as needles melting at 196–196.5°.

Anal. Calcd. for $C_{16}H_{15}O_4N$: N, 4.92. Found: N, 5.02.

Hydrolysis of 1 g. of 1-acetamino-3,4-dimethoxydibenzofuran by alcoholic potash gave a 48% yield of 1-amino-3,4-dimethoxydibenzofuran (m. p., 162.5–163°) which showed no depression in a mixed m. p. determination with the compound obtained by amination of 1-bromo-3,4-dimethoxydibenzofuran.

1-Amino-3,4-dimethoxydibenzofuran.—A mixture of 7.5 g. (0.0244 mole) of 1-bromo-3,4-dimethoxydibenzofuran, 15 g. of powdered cuprous bromide, and 130 ml. of concd. ammonium hydroxide was heated in a bomb for fourteen and one-half hours at 220–230°. After working up in a customary manner there was obtained a 10% yield of 1-amino-3,4-dimethoxydibenzofuran which crystal-

lized from dilute methanol as needles melting at 162.5–163°.

Anal. Calcd. for $C_{14}H_{13}O_3N$: N, 5.76. Found: N, 5.94.

Bromination of 4,6-Derivatives.—Bromination of 22.8 g. (0.1 mole) of 4,6-dimethoxydibenzofuran in 600 ml. of acetic acid by the dropwise addition of 100 ml. of a molar solution of bromine in acetic acid gave a 73% yield of 1-bromo-4,6-dimethoxydibenzofuran which crystallized from a large volume of alcohol as plates melting at 152°. In addition, 3.7 g. (12%) of product melting at 144–147° was isolated.

Anal. Calcd. for $C_{14}H_{11}O_3Br$: Br, 26.01. Found: Br, 26.23.

From 3.0 g. (0.0132 mole) of 4,6-dimethoxydibenzofuran in 120 ml. of acetic acid and 52.7 ml. of a 0.5 molar solution of bromine in acetic acid was obtained a 74% yield of **1,9-dibromo-4,6-dimethoxydibenzofuran** which crystallized from acetic acid as needles melting at 167–168°.

Anal. Calcd. for $C_{14}H_{10}O_3Br_2$: Br, 41.42. Found: Br, 41.60.

Instantaneous decolorization was noted when 40 ml. of a 0.5 molar solution of bromine in acetic acid was added to a solution of 2.0 g. (0.01 mole) of 4,6-dihydroxydibenzofuran in 20 ml. of acetic acid. The yield of **1,9-dibromo-4,6-dihydroxydibenzofuran** was essentially quantitative. The melting point after crystallization from xylene was 239–240° (with decomposition).

Anal. Calcd. for $C_{12}H_6O_3Br_2$: Br, 44.66. Found: Br, 44.77.

Methylation by dimethyl sulfate converted the dibromodihydroxy compound quantitatively to 1,9-dibromo-4,6-dimethoxydibenzofuran, identical with the dibromination product of 4,6-dimethoxydibenzofuran.

Decolorization was less rapid when 40 ml. of a 0.5 molar solution of bromine in acetic acid was added to 2.14 g. (0.01 mole) of 4-hydroxy-6-methoxydibenzofuran in 20 ml. of acetic acid. The dibromo compound, probably **1,3-dibromo-4-hydroxy-6-methoxydibenzofuran,** crystallized from acetic acid as needles melting at 177–178°; yield, 2.17 g. (58.6 %).

Anal. Calcd. for $C_{13}H_8O_3Br_2$: Br, 42.98. Found: Br, 43.10.

The dibromo-4-hydroxy-6-methoxydibenzofuran was methylated in the usual manner (using acetone as part of the medium) to give a quantitative yield of what is probably **1,3-dibromo-4,6-dimethoxydibenzofuran.** This compound crystallized from acetic acid as needles melting at 173.5–174°.

Anal. Calcd. for $C_{14}H_{10}O_3Br_2$: Br, 41.42. Found: Br, 41.68.

Bromination of 3,4-Derivatives.—Decolorization proceeded rapidly when 13.4 ml. of a 0.5 molar solution of bromine in acetic acid was added slowly and with shaking to 1.5 g. (0.0066 mole) of 3,4-dimethoxydibenzofuran in 15 ml. of acetic acid. Crystallization from alcohol gave an 88.5% yield of **1-bromo-3,4-dimethoxydibenzofuran** in the form of fine needles which melted at 108°.

Anal. Calcd. for $C_{14}H_{11}O_3Br$: Br, 26.03. Found: Br, 26.11.

To a stirred solution of 4.28 g. (0.02 mole) of 3-hydroxy-4-methoxydibenzofuran in 50 ml. of acetic acid was slowly introduced 40 ml. of a 0.5 molar solution of bromine in acetic acid. The decolorization was almost instantaneous. Dilution of the reaction mixture, followed by filtration, furnished 5.65 g. of substance which melted at 130–149°, indicating that isomers were probably present. After one crystallization from 30% alcohol and three recrystallizations from benzene, white fluffy needles of **1-bromo-3-hydroxy-4-methoxydibenzofuran,** m. p. 161–162°, were obtained. The yield was 3.1 g. or 54.6% of the theoretical. No attempt was made to isolate the more soluble isomer.

Anal. Calcd. for $C_{13}H_9O_3Br$: Br, 27.28. Found: Br, 27.32.

An intimate mixture of this compound and authentic 1-bromo-3-hydroxy-4-methoxydibenzofuran prepared from the known 1-bromo-3-amino-4-methoxydibenzofuran showed no melting point depression.

1-Bromo-3,4-dimethoxydibenzofuran, m. p. 108°, was prepared by methylating 0.5 g. of 1-bromo-3-hydroxy-4-methoxydibenzofuran at room temperature with 3 ml. of dimethyl sulfate and 5 ml. of 10% sodium hydroxide solution. The compound obtained by direct bromination of 3,4-dimethoxydibenzofuran was proved identical with this by a mixed melting point determination.

Conversion of 1-Bromo-3-amino-4-methoxydibenzofuran to 1-Bromo-3-hydroxy-4-methoxydibenzofuran.—An iced diazonium solution prepared from 0.95 g. (0.00325 mole) of 1-bromo-3-amino-4-methoxydibenzofuran, sodium nitrite and sulfuric acid was added dropwise to a boiling solution of 75 g. of copper sulfate in 250 ml. of water contained in a distilling flask fitted with a condenser. The white solid which steam-distilled was dissolved in 5% sodium hydroxide solution, treated with Norite, filtered, and acidified. The white needles of authentic 1-bromo-3-hydroxy-4-methoxydibenzofuran thus obtained, m. p. 161–162°, weighed 0.2 g. (21% yield). No depression in melting point was observed when this compound was mixed with the bromination product of 3-hydroxy-4-methoxydibenzofuran.

4-Bromo-6-hydroxydibenzofuran.—A suspension of 0.5 g. of 4-bromo-6-methoxydibenzofuran in 5 ml. of hydriodic acid (sp. gr. 1.67) was heated to give a 19% yield of 4-bromo-6-hydroxydibenzofuran which crystallized from water as needles melting at 138–139°. An alcoholic solution of this phenol gave a green color with ferric chloride solution.

Anal. Calcd. for $C_{12}H_7O_2Br$: Br, 30.39. Found: Br, 30.47.

4-Amino-6-methoxydibenzofuran and 4-Amino-6-hydroxydibenzofuran.—An intimate mixture of 5 g. (0.018 mole) of 4-bromo-6-methoxydibenzofuran and 6 g. of freshly prepared cuprous bromide was placed in a large test-tube, covered with 150 ml. of concd. ammonium hydroxide, and electrically heated in a steel bomb at 100° for ten hours. The temperature was then raised to 215° and held constant for eight hours. The **hydrochloride** of **4-amino-6-methoxydibenzofuran,** isolated in a 51% yield by customary procedures, crystallized from water as fine needles melting at 235–236° with discoloration. The **4-amino-6-methoxydibenzofuran,** m. p. 109°, was obtained

in the form of needles by adding ammonium hydroxide to a hot solution of the hydrochloride.

Anal. Calcd. for $C_{13}H_{11}O_2N$: N, 6.57. Found: N, 6.53.

To 2.35 g. (0.0094 mole) of 4-amino-6-methoxydibenzofuran, dissolved in 25 ml. of glacial acetic acid, was added 25 ml. of hydrobromic acid (sp. gr. 1.49), and the mixture was refluxed for nine hours. The hydrobromide, which precipitated on cooling, was dissolved in hot water and the hydrochloride, in the form of small plates melting at 265–266° dec., was precipitated from this solution by passing in dry hydrogen chloride. The free 4-amino-6-hydroxydibenzofuran, crystallizing as needles which melted at 191.5–192.5°, was not discolored by atmospheric oxygen.

Anal. Calcd. for $C_{12}H_9O_2N$: N, 7.03. Found: N, 7.15.

4,6-Diaminodibenzofuran and 4,6-Diacetoxydibenzofuran.—In each of four Carius tubes, a mixture of 1.0 g. (0.005 mole) of 4,6-dihydroxydibenzofuran, 7.5 g. of sodium bisulfite dissolved in 15 ml. of water, and 15 ml. of concd. ammonium hydroxide was sealed. The tubes were then heated at 185–195° in an electric furnace for twenty hours. The cooled mixtures were combined and extracted thrice with a total volume of 400 ml. of ether. The ether solution was washed thoroughly with 10% sodium hydroxide solution and then with water. The **4,6-diaminodibenzofuran dihydrochloride,** m. p. 297–298° with decomposition, was precipitated from the dried ether solution by the introduction of dry gaseous hydrogen chloride. The yield was 4.4 g. or 81% of the theoretical. The hydrochloride was dissolved in about 25 ml. of hot water, digested with Norite, filtered and precipitated again with gaseous hydrogen chloride to give needles which melted at 298° with decomposition.

Anal. Calcd. for $C_{12}H_{12}ON_2Cl_2$: N, 10.33. Found: N, 10.52.

The free **4,6-diaminodibenzofuran,** liberated by the addition of ammonium hydroxide to a solution of the hydrochloride, crystallized from the methanol in the form of colorless prisms, m. p. 152°. This compound has been obtained recently by the reduction of 4,6-dinitrodibenzofuran, which in turn was prepared by a biphenyl ring closure.[6a]

The **picrate of 4,6-diaminodibenzofuran** crystallized from alcohol as shiny, red-brown plates which melted at 213° with pronounced decomposition.

Anal. Calcd. for $C_{12}H_{10}ON_2 \cdot C_6H_3O_7N_3$: N, 16.40. Found: N, 16.28.

The **4,6-diacetaminodibenzofuran,** prepared in quantitative yield from the 4,6-diamino compound and acetic anhydride, crystallized from acetic acid as needles melting at 297–298°.

Anal. Calcd. for $C_{16}H_{14}O_3N_2$: N, 9.93. Found: N, 9.92.

Yamasiro[6a] has reported a melting point of 322.5–323.5° for this compound. In the same paper are reported 4-aminodibenzofuran, m. p. 118–119°, and 4-acetaminodibenzofuran, m. p. 235–236°. The melting points observed in this Laboratory for these two compounds were 84.5–85.5° and 172.5°, respectively.[6b]

4,6-Diacetoxydibenzofuran (prepared in 53% yield from 4,6-dihydroxydibenzofuran, acetic anhydride and a drop of concd. sulfuric acid) crystallized from methanol as small, shiny plates melting at 177°.

Anal. Calcd. for $C_{16}H_{12}O_5$: C, 67.5; H, 4.28. Found: C, 67.4; H, 4.31.

Coupling of Benzenediazonium Chloride with 4,6-Dihydroxydibenzofuran.—A cold benzenediazonium chloride solution prepared from 7.75 g. (0.06 mole) of aniline hydrochloride was added to a cold solution of 6.0 g. (0.03 mole) of 4,6-dihydroxydibenzofuran in aqueous potassium hydroxide to give 5.1 g. of a very dark brown microcrystalline product which melted at about 224° with decomposition. Recrystallization from acetic acid raised the melting point to 228° with decomposition. The product dissolved in acetone with a brilliant red color and, because the nitrogen analyses were nearly one per cent. low for 1,3,9-tribenzeneazo-4,6-dihydroxydibenzofuran, the impurity may be a dibenzeneazo derivative. Methylation imparted stability to the molecule, and a pure compound was isolated by methylating in acetone to give a 77% yield of what is probably **1,3,9-tribenzeneazo-4,6-dimethoxydibenzofuran.** Crystallization from acetic acid gave a red-orange product melting at 191–193°. The structure assigned the compound is based largely on our present knowledge of diazo coupling of hydroxydibenzofurans.

Anal. Calcd. for $C_{32}H_{24}O_3N_6$: N, 15.56. Found: N, 15.52.

4,6-Dimethoxy-1-dibenzofurancarboxylic Acid. A.—Oxidation of 1 g. of 1-acetyl-4,6-dimethoxydibenzofuran by the procedure of Fuson and Tullock[7] (iodine–potassium iodide, sodium hydroxide and dioxane) gave a 55.2% yield of 4,6-dimethoxy-1-dibenzofurancarboxylic acid which melted at 297–298° after crystallization from acetic acid.

Anal. Calcd. for $C_{12}H_{12}O_5$: C, 66.45; H, 4.45. Found: C, 66.21; H, 4.53.

B.—The filtered Grignard reagent prepared from 22.5 g. (0.073 mole) of 1-bromo-4,6-dimethoxydibenzofuran in a 1:1 ether-benzene solution, was carbonated by solid carbon dioxide to give the same 4,6-dimethoxy-1-dibenzofurancarboxylic acid (m. p. 297–298°). Mixed melting point determinations were made not only with the two acids from (A) and (B), but also with the methyl esters from each of these acids.

The **methyl 4,6-dimethoxy-1-dibenzofurancarboxylate,** prepared in a quantitative yield from the acid and diazomethane, melted at 163°.

Anal. Calcd. for $C_{16}H_{14}O_5$: C, 67.11; H, 4.93. Found: C, 67.2; H, 5.11.

Diazomethyl 4,6-Dimethoxy-1-dibenzofuryl Ketone.—The directions used were those of Arndt and Eistert,[8] adapted to dibenzofurans. The required acid chloride was prepared by refluxing 11.5 g. (0.042 mole) of 4,6-dimethoxy-1-dibenzofurancarboxylic acid with 80.0 g.

(6) (a) Yamasiro, *J. Chem. Soc. Japan,* **59,** 945 (1938) [*C. A.,* **33,** 603 (1939)]; (b) Kirkpatrick and Parker, THIS JOURNAL, **57,** 1123 (1935).

(7) Fuson and Tullock, *ibid.,* **56,** 1638 (1934).

(8) Arndt and Eistert, *Ber.,* **68,** 200 (1935); see, also, ref. 3.

(0.672 mole) of thionyl chloride for two and one-half hours, during which time the solid acid slowly dissolved to produce a clear red solution. The excess thionyl chloride was distilled off at diminished pressure at a temperature of 100° (water-bath). The crude pink acid chloride, after crystallization from dry benzene, melted over a wide, indefinite range which indicated incomplete conversion. Purification was effected by boiling the substance with petroleum ether (b. p. 77–115°). The acid chloride dissolved and 5.2 g. of impure, unconverted acid was removed by filtration. The colorless product which separated from the cooled solution melted at 147–150°. The yield was 6.2 g. or 50.5% of the theoretical.

To a stirred solution of diazomethane prepared from 20 ml. of ethyl N-nitroso-N-methylcarbamate was introduced, in several portions, 6.2 g. (0.0213 mole) of 4,6-dimethoxy-1-dibenzofurancarboxylic acid chloride. After five minutes of stirring, 100 ml. of anhydrous dioxane was added to effect solution. The ice-bath was removed and the clear yellow reaction mixture was allowed to stand overnight. The pale yellow crystals of diazomethyl 4,6-dimethoxy-1-dibenzofuryl ketone, melting at 151° with gas evolution, were filtered from solution. The yield was 1.34 g. or 21.2% of the theoretical.

Anal.[9] Calcd. for $C_{16}H_{12}O_4N_2$: N, 9.46. Found: N, 9.51.

4,6-Dimethoxy-1-dibenzofurylacetamide.—A solution of 1.25 g. (0.0042 mole) of diazomethyl 4,6-dimethoxy-1-dibenzofuryl ketone in 75 ml. of dioxane was placed in a 250-ml. flask fitted with reflux condenser and mechanical stirrer. With efficient stirring, 15 ml. of concd. ammonium hydroxide was added followed by 5 ml. of 10% silver nitrate solution. Heating on the steam-bath and stirring were continued for forty-five minutes. Then 5 ml. more of concd. ammonium hydroxide was added, and the stirred solution was heated for thirty minutes longer.

The hot solution was filtered and diluted to a volume of 300 ml. with water. Cooling in the refrigerator precipitated 0.82 g. (66% yield) of the gray amide, m. p. 206–207°. Pure 4,6-dimethoxy-1-dibenzofurylacetamide crystallized from alcohol, after digestion with Norite, in the form of needles, m. p. 210–211°. The yield of pure compound was 0.62 g. or 51.6%.

Anal. Calcd. for $C_{16}H_{15}O_4N$: N, 4.91. Found: N, 4.86.

4,6-Dimethoxy-1-dibenzofurylacetic Acid.—A mixture of 0.5 g. (0.00175 mole) of 4,6-dimethoxy-1-dibenzofurylacetamide, 25 ml. of 15% sodium hydroxide solution and 5 ml. of alcohol was refluxed for thirteen hours before a clear solution was realized. The reaction mixture was diluted with 50 ml. of water, gently boiled with a pinch of Norite, and filtered. Acidification of the solution precipitated the crude acid in nearly quantitative yield, m. p. 204–205°. Two crystallizations from alcohol gave colorless needles of 4,6-dimethoxy-1-dibenzofurylacetic acid, m. p. 205.5–206.5°. The yield was 0.36 g. or 71.7%.

Anal. Calcd. for $C_{16}H_{14}O_5$: C, 67.11; H, 4.93. Found: C, 67.0; H, 4.98.

(9) The authors are grateful to Messrs. L. D. Apperson and T. H. Cook for help with some of the nitrogen analyses.

3-Hydrazinodibenzofuran.—In essential accordance with the directions of Fischer,[10] 9.2 g. (0.05 mole) of 3-aminodibenzofuran was diazotized, and the suspension of diazonium chloride was reduced by stannous chloride.

The white **3-hydrazinodibenzofuran hydrochloride** was filtered off and crystallized from a large volume of water. It melted with decomposition at 242–243°. The yield was 10.3 g. or 87.3%.

Anal. Calcd. for $C_{12}H_{11}ON_2Cl$: N, 11.94. Found: N, 11.98.

The free 3-hydrazinodibenzofuran was obtained by decomposing a hot solution of the hydrochloride with sodium acetate. The base readily dissolved in hot alcohol, crystallizing from this solvent in the form of small pale yellow needles, m. p. 174–175°, which turned orange in color in contact with the atmosphere.

Anal. Calcd. for $C_{12}H_{10}ON_2$: N, 14.14. Found: N, 14.09.

A melting point of 225° for the hydrochloride, and 152° for the free base, have been reported.[11]

1,2,3,4-Tetrahydro-6-aminodibenzofuran.—Two and five-tenths grams (0.0136 mole) of 4-aminodibenzofuran was dissolved in 100 ml. of absolute alcohol contained in a three-necked flask equipped with stirrer and reflux condenser. A nitrogen atmosphere was used throughout the reduction. While the solution was stirred vigorously, the sodium (8.0 g.) was added in small pieces through the top of the condenser. After the addition, which required twenty-five minutes, the solution was boiled gently to dissolve the remaining sodium. A noticeable amount of ammonia was evolved during the reduction.

The hot reaction mixture was poured promptly into ice and hydrochloric acid in sufficient quantity to render the resulting solution acid to litmus. After removal of the alcohol by steam distillation, the mixture was immersed in a freezing mixture, made alkaline with 10% sodium hydroxide, and extracted thrice with a total volume of 400 ml. of ether. This red solution was dried over anhydrous sodium sulfate, and, following filtration, gaseous hydrogen chloride was introduced. The solid was filtered off and repeatedly washed with sodium-dried ether to remove a red resinous impurity adhering to the shiny pink plates of the hydrochloride. The yield was 1.9 g. or 62%. The salt was dissolved in water, digested with Norite, and filtered. Gaseous hydrogen chloride precipitated small pink plates which commenced to darken at 214° and melted at 228° with decomposition. Attempts to prepare a solid free base were unsuccessful, the product remained as an oil at 0°. The low hydrogen values indicated that some unreduced amine may have been present as an impurity.

Anal. Calcd. for $C_{12}H_{14}ONCl$: C, 64.4; H, 6.31. Found: C, 64.4 and 64.4; H, 6.06 and 5.99.

In experiments to determine which ring had been reduced, the observation was made that a dry ether solution of the tetrahydro-6-aminodibenzofuran would not form a carbonate, although carbon dioxide was bubbled into the solution for an hour.

The following coupling reaction definitely established the aromatic nature of the reduced amine. Five milli-

(10) Fischer, *Ann.*, **232**, 237 (1885).

(11) Borsche and Bothe, *Ber.*, **41**, 1940 (1908).

liters of dilute (6 *N*) hydrochloric acid was added to a solution of 0.1 g. (0.00045 mole) of the tetrahydro-6-aminodibenzofuran hydrochloride in 15 ml. of water. Diazotization was effected by cautiously adding a 5% solution of sodium nitrite to the ice-cold, well-stirred solution until cadmium iodide–starch paper immediately turned blue when moistened with the stirring rod. After the clear yellow diazonium solution had stood for thirty minutes, it was slowly added to a cold solution of 0.1 g. of β-naphthol in 25 ml. of 10% sodium hydroxide. A brilliant carmine red dye, m. p. 199–201°, immediately precipitated in quantitative yield (0.15 g.).

Summary

Incidental to studies concerned with the bridging of the 1- and 9-positions in dibenzofuran types, series of 1,4- and 1,4,6-derivatives have been synthesized. In these compounds the 4- and the 4,6-substituents are strong ortho–para directors. Among other compounds described are 4,6-dimethoxy-1-dibenzofurylacetic acid and 1,2,3,4-tetrahydro-6-aminodibenzofuran.

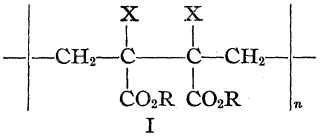
AMES, IOWA RECEIVED SEPTEMBER 1, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

The Structure of Vinyl Polymers. IV.[1] The Polymers of the Methyl α-Haloacrylates

BY C. S. MARVEL AND JOHN CHARLES COWAN[2]

The polymers of the α-haloacrylates are especially suitable for a study of the arrangement of the structural units in the polymeric chain, since the reactions of the simple 1,2- and 1,3-dihalogen esters which correspond to the two most probable arrangements (I and II) of the structural units in these polymers are well known.



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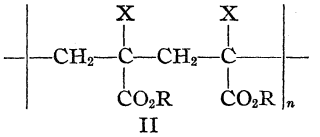
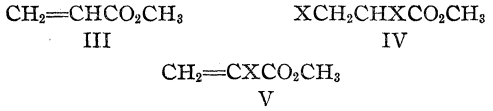


II

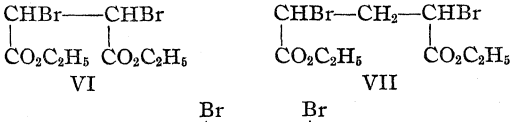
The polymer of methyl α-chloroacrylate has been described[3] but the corresponding bromo compound apparently has not been prepared previously. In the present work the α,β-dihalopropionates (IV) were treated with quinoline to give the α-haloacrylates (V).



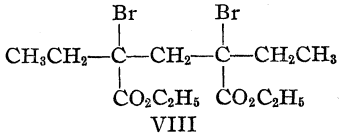
III IV V

The monomeric esters polymerized readily on standing or more rapidly on warming in the presence of peroxides. The polymers could be obtained either as clear, pale amber glassy solids or as white powders. They were readily soluble in dioxane and acetone. Viscosity measurements on 0.606% (0.0368 molar, based on monomeric unit) solutions indicated a molecular weight of about 11,500. One sample of methyl α-chloroacrylate which polymerized slowly at room temperature over a period of nine months gave a polymer insoluble in acetone, benzene and dioxane; this insolubility indicates a very high molecular weight.

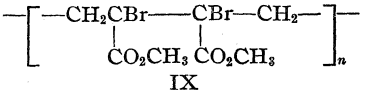
When either the chloro or bromo polymer was treated with potassium iodide in peroxide-free acetone or dioxane, iodine was liberated. This reaction is characteristic for 1,2-dihalogen compounds[4] and indicates that the methyl α-haloacrylate polymers have structure I above and thus do not have the usual 1,3-distribution of the functional groups which has been accepted as the structural feature of most vinyl polymers. A comparison of the amount of iodine liberated from potassium iodide by ethyl α,α′-dibromosuccinate (VI), ethyl α,α′-dibromoglutarate (VII),



VI VII



VIII



IX

(1) For the third communication in this series, see THIS JOURNAL, **61**, 1682 (1939).

(2) Du Pont Special Research Assistant in Chemistry, 1937–1939.

(3) British Patent 411,860; *C. A.*, **28**, 6956 (1934).

(4) Davis and Heggie, *J. Org. Chem.*, **2**, 470 (1937).

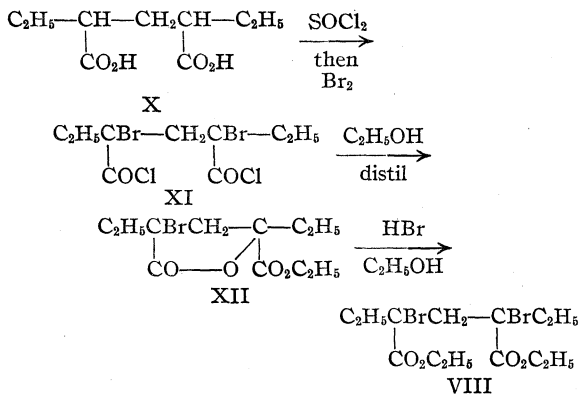
ethyl α,α′-dibromo-α,α′-diethylglutarate (VIII) and the polymer of methyl α-bromoacrylate (IX) is given in Table I.

TABLE I

LIBERATION OF IODINE FROM POTASSIUM IODIDE BY VARIOUS DIBROMO ESTERS

Ester used	% iodine liberated: Acetone soln. 24 hr. 25°	Boiling acetone soln. 24 hr.	Dioxane 24 hr. 25°	Boiling dioxane 72 hr.
Polymer of methyl α-bromoacrylate	30	49	24	92
Ethyl α,α′-dibromosuccinate	33	53	26	96
Ethyl α,α′-dibromoglutarate	4	6	4	21
Ethyl α,α′-dibromo-α,α′-diethylglutarate	2	5	..	..

The comparison with ethyl α,α′-dibromo-α,α′-diethylglutarate seemed to be desirable in order to be sure that a substituted bromoglutarate of this type did not react with potassium iodide. This ester was prepared by the reactions indicated. The starting acid (X) was prepared by methods described in earlier literature.[5]



Evidence to support the "head to head, tail to tail" formulation of these α-haloacrylate polymers (I) was obtained by the use of zinc. This reagent readily removed 97% of the bromine from the bromo polymer, an amount far above that which could be removed from a 1,3-dibromopolymer as shown by the calculation of Flory.[6]

Additional evidence supporting the 1,2-dihalogen structure was found in a comparison of the effect of heat on the polymer of methyl α-bromoacrylate, ethyl α,α′-dibromosuccinate (VI), and ethyl α,α′-dibromo-α,α′-diethylglutarate (VIII). The polymer and the succinate (VI)[7] lost hydrogen bromide at a much lower temperature than did the glutarate (VIII). During the preparation of the glutarate (VIII), it was noticed that the ester on distillation under reduced pressure lost ethyl bromide. During the pyrolysis of the polymer of methyl α-bromoacrylate, methyl bromide was formed but only after the appearance of hydrogen bromide. Heating the polymer of methyl α-bromoacrylate with quinoline removed half of the bromine as hydrogen bromide.

Further evidence supporting the 1,2-dihalogen structure (I) for the polymers was obtained by a comparison of the ultraviolet absorption spectra of the polymers of methyl α-bromoacrylate, ethyl α,α′-dibromosuccinate and ethyl α,α′-dibromoglutarate. Figure 1 shows the absorption curves for these compounds.

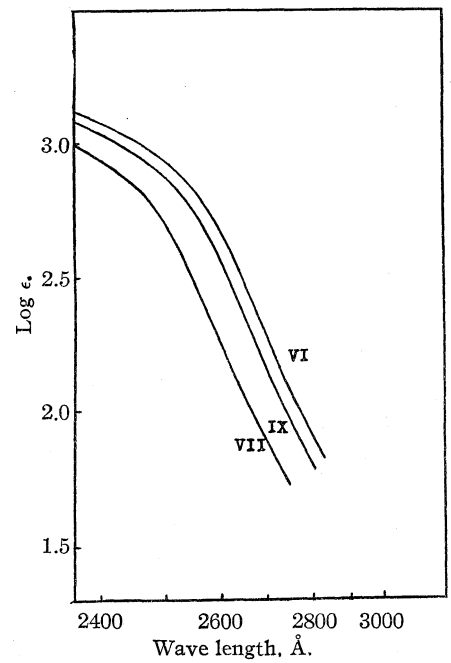
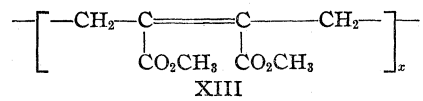


Fig. 1.—Absorption spectra.

The unsaturated polymeric ester (XIII) which undoubtedly results from the action with potassium iodide apparently undergoes some further polymerization to give a cross-linked product, as the debrominated compound is insoluble.



XIII

However, it does decolorize aqueous potassium permanganate solution slowly, thus indicating

(5) Dressel, *Ann.*, **256**, 185 (1889); Redeman and Lucas, *Ind. Eng. Chem., Anal. Ed.*, **9**, 521 (1937).

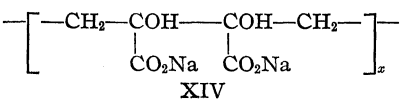
(6) Flory, THIS JOURNAL, **61**, 1518 (1939).

(7) Anschütz, *Ber.*, **12**, 2282 (1879).

unsaturation. All attempts to isolate definite products from the oxidation have been unsuccessful.

When zinc reacts with the bromo polymer there is apparently some cross-linking. This would account for the fact that not quite all of the halogen is eliminated from the polymer. For each halogen which is used up in the cross-linking reaction, an isolated halogen will remain in the polymer after the reaction is complete. The debrominated product is again an insoluble product as would be expected if cross-linking had occurred.

The polymers on alkaline hydrolysis yielded the salt of a 1,2-dihydroxy dibasic acid (XIV). The



XIV

product (XIV) reduces periodic acid to iodic acid in approximately forty-eight hours. This oxidation is characteristic of 1,2-glycols.[8] Reduction of the iodic acid also occurs; this observation has also been noted by Jackson and Hudson[9] in a study of the oxidation of cellulose. The amount and rate of oxidation varied with different samples of the polymers, but in every test some oxidation occurred.

Experimental

Methyl α-Bromoacrylate.—In a 250-cc. modified Claisen flask was placed 73 g. (0.3 mole) of methyl α,β-dibromopropionate (prepared by addition of bromine to methyl acrylate)[10] and 39 g. (0.3 mole) of freshly distilled quinoline.[11] The methyl α-bromoacrylate was distilled out of this mixture at once. The yield was 40 g. (82% of the theoretical amount) of a colorless liquid which boiled at 72.5–74° (78 mm.); d^{20}_{20} 1.61; $n^{20}D$ 1.4840.

Anal. Calcd. for $C_4H_5O_2Br$: Br, 48.48. Found: Br, 47.90.

Methyl α-Chloroacrylate.—The same method was used for the preparation of methyl α-bromoacrylate.[10,11] The yield from 47 g. (0.3 mole) of methyl α,β-dichloropropionate was 33 g. (73% of the theoretical amount). The ester boiled at 57–59° (55 mm.); d^{20}_4 1.189; $n^{20}D$ 1.4400.

Anal. Calcd. for $C_4H_5O_2Cl$: Cl, 29.43. Found: Cl, 29.02.

Synthesis of Ethyl α,α′-Dibromo-α,α′-diethylglutarate.—Ethyl propane-1,1,3,3-tetracarboxylate[12] was treated with sodium ethoxide and ethyl iodide[5] to form ethyl heptane-3,3,5,5-tetracarboxylate. The latter was hydrolyzed with potassium hydroxide in diethylene glycol[5] and decarboxylated by refluxing in dilute hydrochloric acid.[5]

The crude diethylglutaric acid (33 g.) was warmed (60–80°) with thionyl chloride for twenty-four hours, and the excess thionyl chloride was removed by distillation. Dried bromine (21 cc.) was added to the residual acid chloride and the mixture was heated at 70° for five hours. The bromine treatment was repeated with 15 cc. of dried bromine. The bromination mixture was allowed to stand for two days, and the bromo acid chloride was poured into absolute ethyl alcohol. This solution was distilled and after the removal of all the low-boiling material a fraction boiling at 134–138° (3 mm.) was obtained as the main product: d^{20}_{20} 1.358; $n^{20}D$ 1.4775. The yield was 25 g. (48% of the theoretical amount). The analysis showed that this product was the bromo-lactone (XII).

Anal. Calcd. for $C_{11}H_{17}O_4Br$: C, 45.05; H, 5.71. Found: C, 45.14; H, 5.98.

The bromo-lactone (25 g.) was dissolved in absolute ethyl alcohol and saturated with dry hydrogen bromide.[13] The reaction mixture was allowed to stand for twenty-four hours. All low-boiling material was removed from the reaction mixture under diminished pressure. Analysis showed the residue was mainly the ethyl α,α′-dibromo-α,α′-diethylglutarate.

Anal. Calcd. for $C_{13}H_{22}O_4Br_2$: Br, 39.81. Found: Br, 38.70.

Polymerization of the Methyl α-Haloacrylates.—The monomers were polymerized either without solvent or in dioxane or toluene solution. Forty grams of methyl α-bromoacrylate was allowed to stand in a glass container at room temperature for three weeks; the liquid gradually became viscous and finally turned to a clear, pale amber, brittle solid.

Anal. Calcd. for $(C_4H_5O_2Br)_n$: C, 29.09; H, 3.03; Br, 48.48. Found: C, 29.20; H, 3.20; Br, 47.88.

Twenty grams of methyl α-bromoacrylate was dissolved in 100 cc. of dry dioxane and 0.48 g. of benzoyl peroxide was added. The solution was warmed at 35° for forty-eight hours and the addition of benzoyl peroxide repeated. After an additional forty-eight hours at 35°, the reaction mixture was diluted with approximately 500 cc. of ether and the polymer was precipitated as a white powder. It was collected on a filter, washed with ether, and dried; the yield was 15 g. When toluene was used as a solvent for polymerization, the yields were lower than when dioxane was used.

The methyl α-chloroacrylate gave a clear, pale amber, brittle solid when the monomer was allowed to stand in a glass container for one month. The methyl α-chloroacrylate also polymerized in dioxane or toluene solution. Ten grams of the methyl α-chloroacrylate was dissolved in 100 cc. of toluene, and 0.5 g. of benzoyl peroxide was added. The solution was warmed at 35° for twenty-four hours and the polymer precipitated as a white powder by the addition of approximately 500 cc. of ether. The yield was 3 g.

Anal. Calcd. for $(C_4H_5O_2Cl)_n$: C, 39.85; H, 4.19; Cl, 29.43. Found: C, 39.51; H, 4.48; Cl, 27.26.

(8) Malaprade, *Compt. rend.*, **186**, 382 (1928); Fleury and Boisson, *ibid.*, **204**, 1264 (1937).

(9) Jackson and Hudson, THIS JOURNAL, **59**, 2049 (1937).

(10) Moureu, Murat and Tampier, *Ann. chim.*, **15**, 221 (1921).

(11) Crossley, *J. Chem. Soc.*, **85**, 1416 (1904).

(12) "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1932, p. 284.

(13) Noyes, *Am. Chem. J.*, **22**, 258 (1899).

Both the bromo and chloro polymers were soluble in acetone and dioxane when freshly prepared. Both polymers were insoluble in ether, ethyl alcohol, and carbon tetrachloride. One sample of methyl α-chloroacrylate which stood for ten months gave a polymer that did not dissolve when shaken with dioxane for forty-eight hours. This insolubility indicates that the polymer had a very high molecular weight.

The molecular weight of one sample of methyl α-bromoacrylate was determined by viscosity measurement. The sample which was used was prepared in dioxane with benzoyl peroxide at 35°. The relative viscosity of a 0.0368 molar dioxane solution (molarity based on the monomeric unit) was found to be 1.11. Using 2.6×10^{-4} for the value of K_m[14] in the equation $N_{sp}/C = K_m M$, the molecular weight was found to be approximately 11,500.

Study of the Reaction of Potassium Iodide with the Polymers of α-Haloacrylates and with the Esters of Dibromosuccinic and Dibromoglutaric Acids.—Standard solutions of the polymers and the esters were prepared in peroxide-free dioxane or acetone and to each of these solutions was added a measured amount of an aqueous solution of potassium iodide. Each of the reaction mixtures was placed in an all-glass apparatus and subjected to conditions as shown in Table II.

The iodine liberated was determined with standard thiosulfate. In some of the determinations, the procedure was modified further by using an acetone solution of potassium iodide instead of an aqueous solution. The results are summarized in Table II.

TABLE II

LIBERATION OF IODINE FROM POTASSIUM IODIDE BY HALOGENATED ESTERS

Compound	Molality in dioxane	Treatment Time, hr.	Treatment Temp., °C.	Molality of iodine liberated	Conversion, %
Polymer of methyl α-bromoacrylate	0.0171[a]	1	100	0.0061	36
	.0171	72	100	.0157	92
Ethyl α,α′-dibromosuccinate (VI)	.0290	1	100	.0115	40
	.0135	72	100	.0130	96
Ethyl α,α′-dibromoglutarate (VII)	.0304	1	100	.0009	3
	.0142	72	100	.0029	20
	In acetone				
Polymer of methyl α-bromoacrylate	0.0098	16	25	0.0029	30
	.0049	21	55	.0024	49
Ethyl α,α′-dibromosuccinate (VI)	.0101	16	25	.0033	33
	.0051	21	55	.0027	53
Ethyl α,α′-dibromoglutarate (VII)	.0127	16	25	.0005	4
	.0085	21	55	.0005	6
Ethyl α,α′-dibromo-α,α′-diethylglutarate (VIII)	.0114	24	25	.0002	2
	.0114	24	55	.0005	5

[a] Based on the polymeric unit I.

A 0.0084 molal acetone solution of the polymer of methyl α-chloroacrylate was heated to 90° for five days in a sealed tube with aqueous potassium iodide and approximately 58% of the calculated amount of iodine was liberated. The amount of iodine liberated in this experiment was determined colorimetrically.

Debrominated Polymers from the Polymer of Methyl α-Bromoacrylate.—The debrominated polymers were obtained by the action of potassium iodide and by the action of zinc dust on the polymer of methyl α-bromoacrylate.

To a solution of 3 g. of the polymer in 100 cc. of peroxide-free dioxane was added 10 cc. of 30% aqueous potassium iodide. The mixture was warmed at 80–85° for three days. The solution became deeply colored by the liberation of iodine, and a polymeric precipitate formed in the reaction flask. It was isolated, washed with water and alcohol and dried. Analysis showed that 93% of the bromine had been removed.

Anal. Calcd. for $(C_8H_{10}O_4)_n$: C, 56.47; H, 5.88. Found: C, 52.10; H, 4.36; Br, 3.77.

This debrominated polymer decolorized an aqueous solution of potassium permanganate in a period of about forty-eight hours. A 5-g. sample of the polymer of methyl α-bromoacrylate was dissolved in 100 cc. of dioxane and 4 g. of purified zinc dust was added. The mixture was refluxed gently for forty-eight hours. After the solution cooled, the unreacted zinc and the precipitated organic material were separated from the dioxane by filtration.

The filtrate gave a positive test for halogen ion, indicating that the zinc had reacted. The residue was suspended in dilute hydrochloric acid for forty-eight hours in order to dissolve the zinc. The residue was collected on a filter and washed thoroughly with water. It burned with a smoky flame, decolorized aqueous permanganate at room temperature within forty-eight hours, and gave a slight test for halogen. The yield was 2 g.

Anal. Calcd. for $(C_8H_{10}O_4)_n$ (XIII): C, 56.47; H, 5.88. Found: C, 50.61; H, 5.24; Br, 3.20. A portion of the polymer which had precipitated on the sides of the flask and which was not contaminated with zinc was analyzed. Found: C, 53.52; H, 5.62; Br, 1.42.

Effect of Heat on the Polymers of Methyl α-Bromoacrylate, Methyl α-Chloroacrylate, and on the Esters of Halogenated Succinic and Glutaric Acids.—The materials were heated in 50-cc. Erlenmeyer flasks and the vapors passed into water and then through a trap immersed in a dry-ice–acetone bath. The liberation of hydrogen bromide was noted by an indicator (congo red) which was placed in the water, and the dry-ice–acetone trap was used to catch any low-boiling substances which were liberated. The polymer of methyl α-bromoacrylate began to lose hydrogen bromide when heated to 110°, and the reaction was rapid between 120 and 150°. The hydrogen bromide appeared before any loss of methyl bromide was noticed. Finally, the polymer was heated to 220° to give a shiny, dark brown residue.

Anal. Calcd. for $(C_7H_6O_4)_n$: C, 54.50; H, 3.90. Found: C, 55.18; H, 4.00.

The ethyl α,α′-dibromosuccinate (VI) lost hydrogen bromide at 130–170°, which is in agreement with observations recorded in the literature.[7] The ethyl α,α′-dibromo-α,α′-diethylglutarate (VIII) began to lose hydrogen bromide at approximately 175°, the major portion of the decomposition occurring at 190–200°.

The polymer of methyl α-chloroacrylate was heated to 330° under pressure of 3 mm. for one hour. The residue was a shiny dark brown material which was very brittle. It burned with a smoky flame, contained no chlorine, and was insoluble in organic solvents.

Anal. Calcd. for $(C_4H_4O_2)_n$: C, 57.10; H, 4.76. Found: C, 59.37; H, 4.65.

(14) Staudinger and Schwalbach, *Ann.*, **488**, 8 (1931).

Reaction of the Polymer of Methyl α-Bromoacrylate with Quinoline.—One and one-half grams of methyl α-bromoacrylate was dissolved in 100 cc. of dried dioxane and 3 g. of quinoline was added. The reaction mixture was warmed at 60° for eight hours. It was diluted with 300 cc. of ether and a polymeric material was precipitated. The precipitate was washed alternately with water and alcohol to remove impurities. Analysis of the polymer showed that a molecule of hydrogen bromide had been removed for each unit (see formula IX).

Anal. Calcd. for $(C_8H_9O_4Br)_n$: C, 38.50; H, 3.61; Br, 32.10. Found: C, 39.10; H, 3.94; Br, 30.40.

Absorption Spectra.—The spectra were taken on a Bausch and Lomb ultraviolet spectrograph. A hydrogen discharge tube operating on 15,000 volts was used as the source of ultraviolet light and the hydrogen lines were used to calibrate the wave length scale. The absorption coefficients were determined by comparing the absorption of the compounds with the absorption of a 10^{-4} molal naphthalene solution. Dioxane, which had been carefully purified, was used as the solvent.[15] The results are shown in Fig. 1.

Hydrolysis and Subsequent Oxidation of the Polymer of Methyl α-Bromoacrylate.—A 14-g. sample of the polymer of methyl α-bromoacrylate was warmed with 150 cc. of aqueous sodium hydroxide (8 g. of sodium hydroxide) for twenty hours. The polymer dissolved slowly to give a dark brown solution. This was cooled and the alkali neutralized with hydrochloric acid. The solution was inclosed in parchment paper and dialyzed for seventy hours, when the solution gave a negative test for halogen ion. The solution was evaporated to dryness on a steam-bath to give a brown residue. This residue burned with a luminous flame and gave a white residue on ignition. The white residue when dissolved in water gave an alkaline reaction. Analysis of the material indicated that it was the sodium salt of a polymeric hydroxy acid (XIV).

Anal. Calcd. for $(C_3H_3O_2Na)_n$: C, 32.80; H, 2.73; Na_2O, 28.20; Na_2O_2, 35.45. Found: C, 35.20; H, 3.31; ash, 34.50.

A 0.5375-g. sample of the brown residue was dissolved in 50 cc. of water and the solution was cooled to 17°. To this solution was added 50 cc. of periodic acid solution containing 5 cc. of dilute hydrochloric acid, and the mixture was immersed in a water-bath at 17°. A 25-cc. sample was removed immediately and titrated with standard sodium thiosulfate. This value was used to determine the normality of the periodic acid (0.75 *N*) in the reaction mixture. After thirty minutes, another 25-cc. sample was titrated. The difference in titrations was 3.00 (35.50–32.50) cc. of 0.528 *N* sodium thiosulfate. This difference amounts to 33.8% reduction of the periodic acid to iodic acid.

A 7.095-g. sample of the polymer of methyl α-bromoacrylate was treated with hot dilute alkali for twenty-four hours. The solution was acidified with an excess of dilute hydrochloric acid and the volume diluted to 250 cc. After cooling the solution to 16°, 100 cc. of periodic solution (cooled to 16°) was added. Throughout the oxidation the mixture was kept at 16°. A 25-cc. sample was immediately titrated. Table III gives the change in titration in cubic centimeters of 0.269 *N* sodium thiosulfate with time.

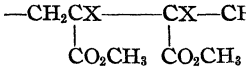
TABLE III

Time	Cc. of 0.269 *N* $Na_2S_2O_3$ per 25 cc. sample	% reduction of HIO_4
0	41.20	0
15 min.	40.98	3.1
47 min.	40.05	11.9
107 min.	39.85	14.0
6.5 hours	37.95	33.8
46.5 hours	31.30	103
52.5 hours	30.45	..
53.5 hours	30.30	..
71.5 hours	28.25	..

At the end of approximately forty-six hours all of the periodic acid had been reduced to iodic acid but the titration value in terms of thiosulfate slowly decreased, indicating that the iodic acid was being reduced further.

Summary

The structures of the polymers of methyl α-chloroacrylate and methyl α-bromoacrylate have been determined. The structural unit present in these polymers has been shown to be



URBANA, ILLINOIS RECEIVED JULY 7, 1939

(15) Oxford, *Biochem. J.*, **28**, 1325 (1934).

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Hydrogen Bonding by S–H. VII.[1] Aryl Mercaptans

BY M. J. COPLEY, C. S. MARVEL AND EMANUEL GINSBERG

It has been commonly held that hydrogen bonding is restricted to hydrogen atoms attached to fluorine, oxygen, or nitrogen. Recently, however, large masses of data involving diverse types of physical measurements (polarization measurements,[2] solubility,[3,4] heat of mixing,[1,5] infrared absorption,[6,7] and viscosity[8]) have shown definitely that a hydrogen attached to a highly negatively substituted carbon atom, for example, $CHCl_3$, $CHCl_2F$, CH_2Cl_2, or $C_6H_5C{\equiv}CH$, will bond to an unshared pair of electrons on an oxygen or a nitrogen atom in an organic molecule. Infrared absorption measurements by Buswell, Rodebush and Roy[6] and by others[9] have also shown that the ether–hydrogen chloride complex is another case of hydrogen bonding.

These results have suggested to the authors that hydrogen bonding is more common than hitherto believed, and that whenever a hydrogen is attached to another atom by a sufficiently ionic link, it will further bond to an unshared pair of electrons on a donor atom. To test this hypothesis, the heats of mixing of an alkyl mercaptan and of an aryl mercaptan with some donor solvents have been measured. The method followed in making the measurements has been described in a previous publication.[5] In Table I are tabulated the heat effects on mixing equimolar quantities of *n*-heptyl or phenyl mercaptan with four organic solvents. For comparison, corresponding heats of mixing of chloroform and phenylacetylene[1] are included where available. Where the statement "No heat" is made, either a slight cooling or inappreciable heating was observed. In Fig. 1 the complete heat of mixing curves are shown for phenyl mercaptan with the three donor solvents, N,N-dimethylacetamide, ethyl ether, and acetone.

TABLE I

HEATS OF MIXING IN CALORIES PER MOLE OF SOLUTION AT 3° FOR EQUIMOLAR MIXTURES

	n-Heptyl mercaptan	Phenyl mercaptan	Phenyl-acetylene	Chloro-form
N,N-dimethyl-acetamide	No heat	572	644	920[a]
Ethyl ether	No heat	173	272	700[b]
Acetone	No heat	150	200	. . .
Benzene	No heat	No heat	No heat	No heat

[a] Unpublished data obtained in this Laboratory. [b] McLeod and Wilson, *Trans. Faraday Soc.*, **31**, 596 (1935).

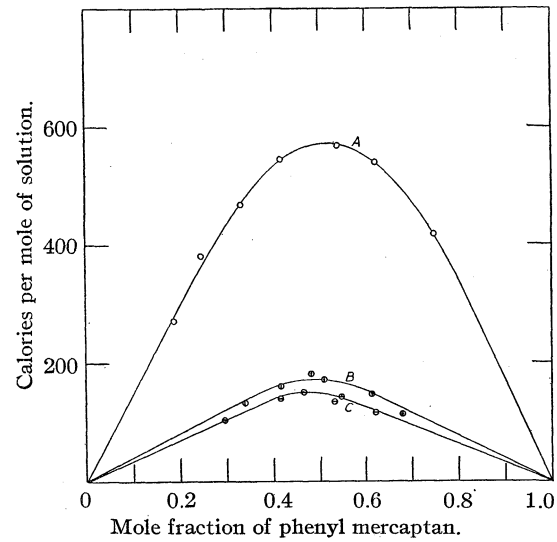


Fig. 1.—The heat evolved per mole of solution at 3° *versus* the mole fraction of phenylmercaptan: A, N,-N-dimethylacetamide, B, ethyl ether, and C, acetone.

The data show that whereas *n*-heptyl mercaptan gives no evidence of hydrogen bonding, the more acidic phenyl mercaptan bonds to the donor atoms, oxygen or nitrogen. The location of the maxima at 0.5 mole fraction suggests the formation of an equimolar complex in each case. From the magnitude of the heats of mixing alone, it appears that the S–H←O or N bonds are considerably weaker than the C–H←O or N bonds formed by chloroform, and slightly weaker than the C–H←O or N bonds formed by phenylacetylene; however, it must be remembered that if weak S–H←S bonds are present in phenyl mercaptan they would lead to lower heats of mixing.

In Table II the boiling points of methyl mercaptan, methyl sulfide, phenyl mercaptan, and phenylmethyl sulfide along with their oxygen analogs are listed. Methyl mercaptan has a lower

(1) For the sixth communication in this series see Copley and Holley, THIS JOURNAL, **61**, 1599 (1939).
(2) Glasstone, *Trans. Faraday Soc.*, **33**, 200 (1937).
(3) Zellhoefer, Copley and Marvel, THIS JOURNAL, **60**, 1337 (1938).
(4) Copley, Zellhoefer and Marvel, *ibid.*, **60**, 2666, 2714 (1938).
(5) Zellhoefer and Copley, *ibid.*, **60**, 1343 (1938).
(6) Buswell, Rodebush and Roy, *ibid.*, **60**, 2528 (1938).
(7) Gordy, *ibid.*, **60**, 605 (1938); *J. Chem. Phys.*, **7**, 163 (1939).
(8) Ewell, *ibid.*, **5**, 967 (1937).
(9) Gordy and Martin, *Phys. Rev.*, **52**, 1075 (1937); *J. Chem. Phys.*, **7**, 99 (1939).

TABLE II

	B. p., °C.
Methyl mercaptan	7.2
Methyl sulfide	38
Phenyl mercaptan	169.5
Phenylmethyl sulfide	188
Methyl alcohol	64.5
Methyl ether	− 24.9
Phenol	182
Anisole	155.8

boiling point than methyl sulfide; similarly phenyl mercaptan has a lower boiling point than phenylmethyl sulfide; on the other hand, the reverse is true for the oxygen analogs. This indicates that phenyl mercaptan as well as alkyl mercaptans is unassociated or at most forms very weak S–H←S bonds. This is in agreement with previous work[3] which showed that a sulfur atom is an extremely poor donor atom for the bonding of a hydrogen on a carbon.

Summary

The heats of mixing of *n*-heptyl and phenyl mercaptans with N,N-dimethylacetamide, ethyl ether, acetone, and benzene have been measured. The results afford evidence of hydrogen bonding to donor oxygen and nitrogen atoms by phenyl mercaptan, but not by *n*-heptyl mercaptan. The failure of aryl mercaptans to show association is a result of the weak donor ability of the sulfur atom for hydrogen bonding and not from any lack of acceptor ability on the part of the hydrogen of the S–H link. It is pointed out that whenever a hydrogen is attached to another atom by a sufficiently ionic link, hydrogen bonding is possible.

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[CONTRIBUTION FROM THE RESEARCH LABORATORY, GENERAL ELECTRIC CO.]

Electrical Characteristics of Molecular Films

BY FRANCIS J. NORTON

1. Introduction

It has been shown by Blodgett and Langmuir[1,2] that single layers of molecules on water surfaces can be transferred to polished metal slides by dipping the slide through the water surface. When one molecular layer goes on the slide as it is dipped downward, but none as the slide is withdrawn, this transferred layer is called an X film. When one layer is transferred on the down dip and one on the up dip, they are called Y films.

Porter and Wyman[3,4] found that X films of calcium and barium stearates, deposited from baths of *p*H above 9, possess a potential which increases with the number of molecular layers. The Y films of calcium and barium stearates, on the other hand, do not show this growth of potential with successive dips.

The experimental results of Porter and Wyman have been repeated and confirmed, using both the vibrating plate method and also a polonium–air electrode to measure surface potential. The interpretation of certain of our experiments indicates, according to the theory given by Langmuir,[5] that the principal portion of the charge on calcium and barium stearate X films may be due, not to molecular orientation within the films, but to a surface electrification.

(1) Blodgett, THIS JOURNAL, **57**, 1007 (1935).
(2) Blodgett and Langmuir, *Phys. Rev.*, **51**, 964 (1937).
(3) Porter and Wyman, THIS JOURNAL, **59**, 2746 (1937).
(4) Porter and Wyman, *ibid.*, **60**, 1083 (1938).
(5) Langmuir, *ibid.*, **60**, 1190 (1938).

2. Apparatus

The vibrating plate method is that described by Zisman[6] and Porter.[7] A beat frequency oscillator (RCA type TMV 134–A) was used to produce the audio frequency which was amplified and fed to a loud speaker element in a sturdy support. This element vibrated an insulated polished nickel disk just above the film. When a potential exists between the disk and film, this vibration plate condenser feeds an alternating current into an audio-frequency amplifier. An opposing potentiometer and voltmeter was used to balance out the surface potential to a minimum of sound in earphones.

The polonium–air electrode affords an independent method of measuring surface potentials. The use of radioactive material for measuring contact potentials was described by Lord Kelvin shortly after the discovery of radioactivity. The polonium method has been used by Guyot, Frumkin, Rideal and others. Old radon tubes were crushed and soaked in 4 *N* hydrochloric acid. A buffed disk of nickel 0.5 cm. in diameter, 0.025 cm. (10 mils) thick was welded to a nickel wire. When this is rotated for a few minutes in hydrochloric acid extract from radon tubes, polonium is deposited on the nickel disk. The disk was then washed in distilled water and dried.

(6) Zisman, *Rev. Sci. Instruments*, **3**, 367 (1932).
(7) Porter, THIS JOURNAL, **59**, 1883 (1937).

The polonium ionizes the air in the neighborhood, and this polonium–air electrode can be used to explore the potentials existing between the disk and the metal slide, or the surface of thin insulating films on the slide.

One essential feature of the method was a guard sleeve around the disk, so the ionized air was confined to the immediate region of the film being measured, and stray currents did not flow to other parts of the apparatus. The slide was held on a small adjustable table. It was brought 2 mm. from the polonium disk and 1 mm. from the protecting sleeve. The whole was enclosed in a grounded metal box, as was the amplifier and lead to the grid of the tube.

By a d-c. amplifier using an FP-54 tube[8] the small ionization currents were amplified and put into a photoelectric recording micro-ammeter.[9] This had a coil resistance in the primary galvanometer element of 1200 ohms, and a damping resistance of 20,000 ohms across the meter terminals. By putting various known values of grid resistances, from $R_g = 10^8$ to $R_g = 10^{11}$ ohms, into the amplifier circuit, currents down to 10^{-13} ampere could be continuously recorded. The resistors were made by the S. S. White Dental Mfg. Company. Care was taken not to touch the resistor element with the fingers, and the air in the amplifier box containing resistor and tube was kept at low humidity by phosphorus pentoxide. The usual grid resistor used was 10^9 ohms, which was near the value of resistance of the ionized air constituting the polonium–air electrode. Where these two resistances are of the same order, best sensitivity is obtained. The usual range of current was 10^{-8} to 10^{-11} ampere. As shown in Fig. 1, a potentiometer and voltmeter enabled various potentials to be applied so as to bring the current to zero on the recording microammeter, and the surface or contact potentials existing between the film surface and the nickel–polonium disk could thus be determined. The calibration of the recording galvanometer to give actual currents was made by putting a known high resistance externally in place of the polonium–air electrode. Then various voltages were applied by the external potentiometer, and for each applied voltage a reading was obtained on the galvanometer. A circulating current is obtained in the circuit: external resistance, voltmeter, ground, grid resistor. The galvanometer reading represents the amplification of this current. Knowing the values of voltage and of the two resistors in the circuit, the value of the current for each galvanometer reading can be calculated from Ohm's law.

The procedure for obtaining the resistance of the polonium–air contact was as follows. The nickel slide was buffed so as to offer the same type of surface as the small polonium coated disk. After a time, the value of surface potential between disk and slide became nearly zero as measured on the external potentiometer circuit. Then various values of voltage were applied by the potentiometer to give various readings on the galvanometer. These were translated into current readings by the calibration described in the preceding paragraph, and the value of total resistance obtained in the circuit: polonium–air electrode, voltmeter, ground, grid resistor. Knowing the value of the grid resistor, and using various resistors as a check, the resistance of the polonium–air electrode was calculated. It was found to be ohmic in the range of voltages used.

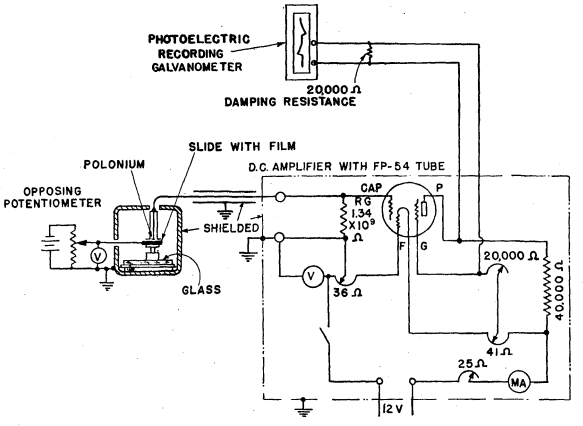


Fig. 1.

The two methods, vibrating plate and polonium–air electrode, gave substantial agreement in values of surface potential. The obvious difference is that a film left in the ionized air loses its charge, as the surface is continually short-circuited. This behavior is discussed later.

The principal baths used were:

Solution 1: for Ca stearate Y films *p*H 7, 10^{-4} *m* $CaCl_2$, 3×10^{-4} *m* $KHCO_3$

Solution 2: for Ca stearate X films *p*H 10, 10^{-4} *m* $CaCl_2$, 10^{-3} *m* $KHCO_3$, raise *p*H by adding NH_4OH

Solution 3: Ba baths like Ca

Solution 4: for Cu stearate Y *p*H 5.0, 10^{-4} *m* Cu acetate, 3×10^{-5} *m* HCl

Solution 5: for Pb stearate X *p*H 5.7, 10^{-4} *m* $PbCl_2$, 2×10^{-6} *m* HCl

Solution 6: for Pb stearate Y *p*H 5.7, 10^{-4} *m* $PbCl_2$, 2×10^{-6} *m* HCl, 10^{-5} *m* $SnCl_2 \cdot 2H_2O$

The *p*H values were measured by a glass electrode *p*H meter.

Effect of *p*H of Bath.—The surface potential of calcium stearate films put on by 20 round-trip dips was found to vary with the bath *p*H in the manner shown in Fig. 2. At *p*H 9, the layers are definitely of the X type; at *p*H 7, definitely Y. The transition region may give a mixture.

It is interesting to note that the region where charged X films are formed on dipping is one of change in sign of electrical potential of stearic acid films on the bath surface. When stearic acid is spread on a water of *p*H 6, the surface becomes more positive by +250 mv.[10] At *p*H 7 this change is about +160 mv., but near *p*H 9, spreading stearic acid on water causes no change in its surface potential. Above 9 the surface becomes negative with respect to the clean water surface, and it is in this region that the greatest surface charges on the transferred films are found.

(8) Metcalf and Thompson, *Phys. Rev.*, **36**, 1489 (1930).

(9) LaPierre and Carson, *Gen. Elec. Rev.*, **36**, 271 (1938).

(10) Porter, THIS JOURNAL, **59**, 1883 (1937).

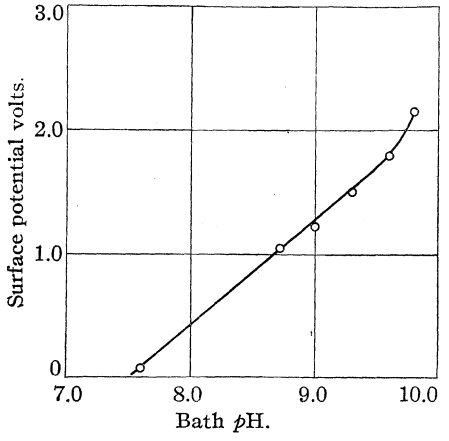


Fig. 2.

Age of Film on Bath Surface.—Another factor influencing the voltage acquired by calcium stearate X films on dipping is the age of the stearic film spread on water. If the film is transferred immediately after spreading, a higher charge per dip results than if an interval of ten or twenty minutes elapses between the time of spreading and the time of dipping. This is illustrated in Fig. 3 and was observed many times. The data of this figure also confirm the result of Porter and Wyman—that one Y dip will take away the charges resulting from X dips.

Various Types of Films.—Dr. Blodgett has found that stearic acid ($C_{17}H_{35}COOH$) spread on a bath 10^{-4} molal in lead chloride, *p*H 5.5, will yield an X type film when transferred to metal. If arachidic acid ($C_{19}H_{39}COOH$) is used on this same bath a Y type of film results. This affords an excellent opportunity to find out if the surface potential depends on the film type.

Surface type	Potential volts	ΔE
Bare Cr	+0.25	
55 mol. layers Pb arachidate Y films	+ .38	+0.13
Bare Cr	+ .43	
40 mol. layers Pb stearate X films	+ .55	+ .12

This would indicate that X films of lead stearate do not possess the high surface charge which calcium and barium X films show, or else lose the charge much more quickly.

Another test involving X and Y films deposited from a bath at the same *p*H is afforded by Dr. Blodgett's discovery that adding a small amount of stannous chloride (10^{-5} molal in bath) to a lead bath of *p*H 5.5, causes Y films to be deposited, whereas without the tin, X films are deposited.

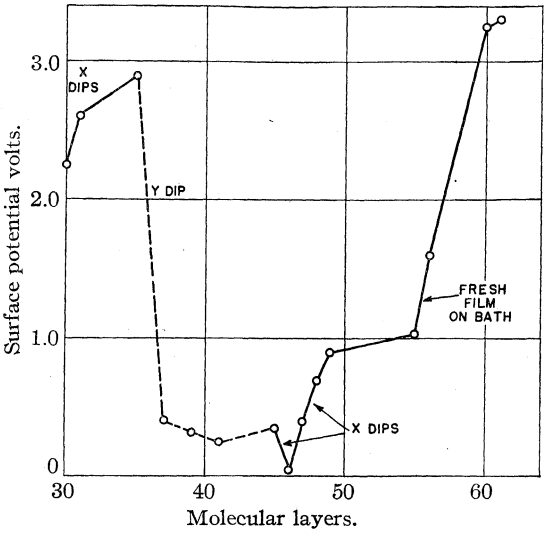


Fig. 3.

When this was tried, the measurements being made within a minute of completing the film transfer, the results indicated two things: first, lead stearate X films can build up an initial potential at about a tenth of the rate for calcium stearate X films; second, these lead X films have this potential even though they are made from a bath of *p*H 5.5, whereas Y films do not have the charge. The stannous chloride enabled both X and Y films to be made from a bath of the same *p*H.

Experiments to be presented in detail in a subsequent publication indicate that lead stearate films have lower electrical resistance than calcium stearate films and hence do not hold their surface charges so well.

Dipping into Various Solutions

The effect of dipping various films into clean water at different *p*H values indicated the composition of the bath and especially *p*H governed the magnitude of the charge developed on the surface.

A calcium stearate X film, 30 round-trip dips in bath *p*H 8.8, with stearic acid spread on it, gave 31 molecular layers (counting the initial layer on the rubbed slide) and a surface potential $E = +2.20$ volts, measured by the vibrating plate method. This was then dipped into baths which had no stearic film on. The successive changes in surface potential upon successive dips are:

Bath	*p*H	Δ*E*
		+2.20 as made
Clean Ca bath	9.4	+2.40
Clean Ca bath	8.25	+2.30
Distilled water	6.7	+1.70
Distilled water	6.1	+0.50
Clean Ca bath	9.4	+1.30

Successive dips into a bath of *p*H 9.4 will, as Porter and Wyman report, make the X films more negative after the first dip. On the other hand, Y films became consistently more negative on dipping into an alkaline bath, as shown below.

Δ*E*	Dips	
+0.27		Bare Ni surface
+ .08		37 Ca stearate Y layers, bath *p*H 7.5
+ .046	1	Clean Ca bath *p*H 9.5
+ .022	2	Clean Ca bath
− .15	7	Clean Ca bath
		Left in Po to discharge
0	..	Start
− .20	1	Clean Ca bath *p*H 9.5
− .22	2	Clean Ca bath
− .54	7	Clean Ca bath

These films all came out dry. If they are dipped into solutions containing aluminum or thorium ions, the surfaces are made hydrophilic, they emerge wet and the surface charge is near zero.

Solutions were made from sodium chloride, barium chloride, aluminum sulfate, thorium nitrate and hydrochloric acid with the *p*H values given below; 21 calcium stearate X layers were then dipped and held for thirty seconds in each with the results shown in Table I.

TABLE I

21 CA STEARATE X LAYERS ON NICKEL

Bath 0.001 *N*	*p*H	Δ*E* Initial	Δ*E* 1st dip	Δ*E* 2nd dip	Surface emerged
Na	6.1	+1.2	+1.0	..	Dry
Ba	5.95	+1.7	+1.15	+0.85	Dry
Al	4.5	+1.45	0	0	Wet
Th	3.4	+1.15	+0.13	− .15	Wet
HCl	3.45	+1.0	+1.15	+ .78	Dry

This illustrates the importance of the composition of the solution on changes of surface potential on dipping. In every case it has been found that when the film surface comes out wet, the surface charge has been lost. Sometimes the drying takes place very quickly as the film is being raised out of the water.

Surface Potential of Films on Glass.—To find out whether the metal surface on which Y films were deposited was essential to their possessing a surface potential, the following experiment was devised. A glass electrode was made from very thin special glass of high conductivity such as is used in *p*H electrodes. A portion was made flat, and on this X films of Ca stearate were deposited. The interior of the glass electrode was filled with 0.1 *N* hydrochloric acid and contact made to this by a platinum wire. This flat thin glass with calcium stearate film on the top surface and hydrochloric acid beneath was then made the lower plate, and the surface potential measured by the vibrating plate method.

It was found at the start that the clean glass had a potential relative to the vibrating nickel plate of near zero, ±0.005 v. This was raised to +0.80 v. by 25 X dips of calcium stearate on glass and with more layers finally a potential of +1.5 v. was attained. This value was checked by the ionized air method.

Through ionized air, 10 v. was applied, so the surface potential of these calcium stearate X films was raised to +6.2 v. The surface was then taken out of the ionized air and the next day was +3.3 v. Upon dipping the glass with the film into a solution of citrate–phosphate buffer of *p*H 7, the film was displaced from the glass and floated on the solution as iridescent fragments.

Application and Decay of Surface Potential in Ionized Air.—As described, the air–polonium electrode was so arranged that voltage could be applied with a potentiometer arrangement, and the small current resulting recorded continuously. Upon applying and maintaining a voltage, a relatively high initial current flows. This then decays exponentially, as the charges accumulate on the insulating surface film. These charges create an opposing potential, the magnitude of which is given by Equation 2, in Langmuir's paper[5]

$$V = 4\pi\sigma et/D$$

where σ = surface intensity of electrification
e = elementary charge = 4.77×10^{-10} e. s. u.
t = thickness of film = 24×10^{-8} cm. per layer
D = dielectric constant = 2.56

If the film is a good insulator, the initial charging current drops to zero, if a poor insulator, to a constant value of current, the conduction current of the insulator. The automatic record is shown in Fig. 4. At "*a*," 5.0 v. were applied to 41 calcium stearate X layers. The initial current was "*b*" which decayed to "*c*." At "*c*" the external voltage was taken off and the current "*d*" resulted from the surface charge. This then decayed along "*de*."

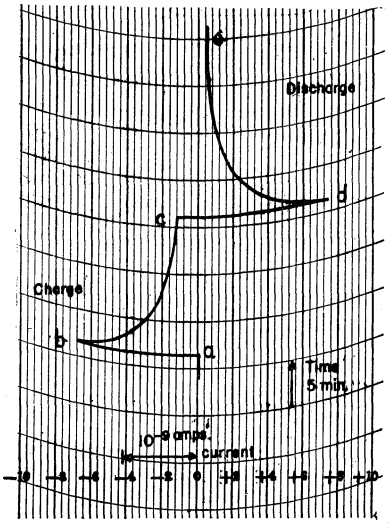


Fig. 4.

Thus when a charged film is put into ionized air, with no voltage applied, but the nickel slide and polonium electrode grounded, the ionized air short circuits the charges on the film surface, and the voltage decays exponentially to zero.

The magnitude of surface intensity of electrification is interesting, especially when considered as number of charges relative to the number of surface molecules.

On 41 calcium stearate Y layers a surface potential was built up by putting it into the ionized air beneath the polonium–air electrode and applying 0.5 v. for sixteen minutes. On taking off the voltage, a surface potential of 0.48 v. was found. This, left in the ionized air, decayed to $1/e^{\text{th}}$ of its value in one hundred and eighty seconds.

First can be calculated σ from the equation given above, remembering to convert the ordinary volts to e. s. u. and putting in the proper film thickness. The surface intensity comes out 7×10^{10} elementary charges per square centimeter. The cross sectional area of the stearate molecule is 20 square Ångströms, or 20×10^{-16} sq. cm., a total of 5×10^{14} molecules per sq. cm. Hence to produce the surface potential of 0.48 v., there need be only one elementary charge per 7000 surface molecules, and if distributed in a square array, two charges would be separated by some 84 molecules.

The 7×10^{10} elementary charges per sq. cm. amount to 1.11×10^{-8} ampere-second, or coulomb, per sq. cm. Since the area of the polonium–air electrode is 3.14 sq. cm., the total amount of electricity in that area is 3.5×10^{-8} coulomb. The recording meter gives amperes $\times$ seconds, so by graphically integrating the area under the decay curve, the total amount of electricity discharged is found. This integration gave 5.3×10^{-8} coulomb, compared to the 3.5×10^{-8} calculated from the voltage equation. This discrepancy undoubtedly is due to a difference between the actual effective area of the polonium–air electrode and that calculated from its dimensions.

The capacitance of this 3.14 sq. cm. of charged film is $C = AD/4\pi t$ (where A is the area) $= 6.5 \times 10^4$ cm. or 7.2×10^{-8} farad. The time constant of a condenser discharge in seconds is $\tau = CR$. The resistance in this circuit is the polonium–air gap, of 0.9×10^9 ohms, and that of the grid resistor, 1.34×10^9 ohms. Hence

$$\tau = 7.2 \times 10^{-8} \times 2.24 \times 10^9 = 161 \text{ sec.}$$

This is to be compared to the observed value of 180 sec.

From these calculations three results emerge which seem to indicate that the surface potential on molecular films can be regarded as a surface electrification.

(1) The value of σ, the surface intensity of electrification, is reasonable, and when thought of in relation to the total number of molecules on the surface, it is surprising what a low density of charge population will account for the observed surface potentials.

(2) The total amount of electricity as observed in the charge decay curve is approximately the same as that calculated from the voltage equation of Langmuir's paper.

(3) The time constant of decay observed is near that calculated, regarding the charged film simply as a charged condenser.

By the corona discharge from a spark coil leak tester, a surface potential of 4.0 v. was put on 5 molecular layers of calcium stearate X films. This is a gradient through the film of 3,300,000 v./cm., and the surface intensity of electrification can be calculated as 4.7×10^{12} elementary charges per sq. cm. There is thus one charge for a hundred molecules on the surface, and this represents some type of saturation value for this particular film.

Application of Surface Potential by Corona Discharge.—The sharp point of a portable spark coil leak tester was held 7 cm. above a film on a grounded nickel slide, so a corona discharge but not actual sparks occurred in the air just above the film. It became charged to a value

which depended on the number of molecular layers in the film, and on the time in the corona atmosphere, up to saturation. This is shown in Table II.

TABLE II

EFFECT OF CORONA

Mol. layers Ca stearate X	After ½	1	1½	2
	Minutes in corona, surface potential is volts			
2	+0.685	1.1	1.2	1.25
3	1.5	2.0	2.3	2.3
5			3.85	4.0
10				9.3

The gradient in these films of various thicknesses is high, and of the same order of magnitude, as Table III shows.

TABLE III

CA STEARATE X, CHARGE PUT ON BY CORONA

Mol. layers	Surface potential, v.	Volts per layer	Gradient volts/cm.
2	1.25	0.63	2,600,000
3	2.3	.77	3,200,000
5	4.0	.80	3,300,000
10	9.3	.93	3,700,000
50	23.5	.47	2,000,000

Corona was also produced by high voltage d. c., and it was found that the film collected a positive charge on its surface when the underlying nickel slide was made negative relative to the sharp point from which the corona was proceeding. With the nickel slide positive, a negative charge accumulated on the surface of the insulating film, presumably the negative ions attracted to the positively charged slide.

As discussed in a communication by Norton and Langmuir[11] corona from high voltage a. c., as near an unlighted Coolidge X-ray tube, caused a negative charge to accumulate on the surface film of a grounded slide, as though there were a preponderance of negative ions in the neighborhood or a higher mobility of the negative ions. The film becomes negative, even though there are no X-rays. Experiments involving X-rays will be presented in a subsequent paper. The results are, briefly, that when air is rendered conducting by X-rays, surface charges of either sign can be put on the film by applying the appropriate field.

Loss of Charge in Air.—As Porter and Wyman have indicated, calcium stearate X films can maintain their surface potentials for a surprisingly long time. I have found that the charges put on by ionized air, as well as the potentials on the film by dipping, persist after a rapid initial drop.

The fact that the charge stays on for weeks must mean that the calcium stearate films are extremely good insulators. How then is the loss of charge to be explained? An examination of the rate is of interest.

One film of 71 molecular layers had a surface potential of 1.22 v. at twelve days, and 0.97 v. at forty-eight days, a loss of 0.25 v. in thirty-six days when kept out in the air, away from radioactive material. From the voltage equation, it can be calculated that this represents a loss of 6750 elementary charges per second from each square centimeter, or a current of

$$6750 \times \frac{4.77 \times 10^{-10}}{3 \times 10^{9}} = 1.07 \times 10^{-15} \text{ ampere per sq. cm.}$$

In an article on "Ionization of the Atmosphere" Koller[12] states that for the gradient existing in the earth's atmosphere of some 100 v./m., the air conductivity leads to a current of 2×10^{-16} amp./sq. cm. constantly flowing toward the earth. It will be observed that this is near the order of magnitude of the leakage of charge from the molecular films, where a similar gradient exists to the bare metal near-by.

Similarly, Porter and Wyman[4] find on a 245-layer film a potential 6.02 v. at four days and 5.19 v. at nine days, a leakage of 0.16 v./day. This represents a loss from each sq. cm. of 3.9×10^{4} elementary charges per second or 6.2×10^{-15} amp./sq. cm. Since the voltage gradient is about six times greater on Porter and Wyman's slide, their results reduce to the same value as mine, 1×10^{-15} amp./sq. cm., and the loss of charge can be explained as being due to normal air conductivity.

The following three examples illustrate the loss of charge in the air, away from radioactive material. These surface potentials were all measured by the vibrating plate method.

(1) On 20 Ca stearate Y layers were put 51 Ca stearate X layers, a total of 71 molecular layers on a nickel slide

Time, days	0	4	12	15	18	22	23	48
Potential	+3.20	+1.90	+1.22	+1.40	+1.15	+1.08	+1.07	+0.97

(2) 21 Ca stearate X layers. Slide made positive and 90 volts applied through air ionized by Po for half an hour, then slide taken out

Time	0	30 min.	5 days	8	11	15 days
Potential	−6.88	−4.3	−2.42	−2.25	−2.25	−2.17

(3) 21 Ca stearate X. Slide made negative and 90 volts applied through air ionized by Po, 15 min. then slide taken out

(11) Norton and Langmuir, THIS JOURNAL, **60**, 1513 (1938).

(12) Lewis R. Koller, *Jour. Franklin Inst.*, **214**, 543 (1932).

Time, min.	0	2	5	14	24
Potential	+6.9	+6.5	+6.2	+5.5	+5.0
Time, hr.	1½	4	5		
Potential	+4.0	3.3	3.0		
Time, days	5	8	11	15	
Potential	+1.74	+1.65	+1.51	+1.45	

It is apparent that the usual potentials acquired by dipping, or potentials of either sign put on by ionized air, all behave in a similar manner.

Summary

Surface potentials can be put on X or Y stearate multi-films by applying a voltage while the films are in a conducting medium as air ionized by polonium. With voltage off, the films lose their charge exponentially. The coulombs represented by the area under the automatically registered discharge curve agree with Langmuir's equation which calculates potential resulting from surface charges.

The slow leakage of charge from X films left in ordinary air can be explained by the natural electrical conductivity of air.

Surface potentials were found to exist on calcium stearate X films deposited on glass.

SCHENECTADY, NEW YORK RECEIVED JULY 8, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

Magnetic Measurements on Hexaphenyldigermane

BY P. W. SELWOOD[1]

The molecular weight of hexaphenyldigermane has been reported by Morgan and Drew[2] as 560 to 566 determined ebullioscopically in benzene. They interpret this as evidence for "no recognizable dissociation" although the value obtained is slightly lower than the molecular weight (606.8) computed for the compound.

A sample of this compound was obtained through the courtesy of Professor Warren C. Johnson of the University of Chicago.

Experimental Part

Magnetic Measurements.—The magnetic susceptibilities were measured by means of the Gouy balance previously described.[3] The only modifications were (1) the use of a magnetically damped microbalance, and (2) a modified temperature control. In previous work the temperature of the sample had been maintained through careful injections of liquid air into a lead block surrounding the sample. In the present work oxygen was liquefied by passing it through a condenser surrounded by liquid nitrogen. The oxygen was then allowed to fall, drop by drop, into the lead block. Through control of the rate of flow of oxygen into the condenser, a high degree of temperature control was possible.

All measurements were referred to freshly boiled distilled water, the specific susceptibility of which was assumed to be -0.7200×10^{-6} at 20°.

Preparation of Materials.—Measurements were made on powdered hexaphenyldigermane and on a solution of the digermane in benzene. Some rather interesting experiences were encountered in preliminary tests on the powder, and are described.

The substance gave evidence of having a magnetic susceptibility markedly dependent on field strength. The apparent susceptibility varied from $+1.45 \times 10^{-6}$ at 1000 oersteds to -0.10×10^{-6} at 11,000 oersteds. This behavior strongly suggested the presence of a ferromagnetic impurity. The digermane was therefore recrystallized from benzene, after which the susceptibility became normal, that is, constant, from about 1000 to 17,000 oersteds. A small insoluble residue was found to contain a very few almost microscopic specks of some highly magnetic substance, presumably magnetic oxide of iron. These results are illustrated in Fig. 1 in which Δw, the apparent change in weight on application of the field, is plotted against i, the current through the magnet. While these results have no bearing on the main problem, yet they do show the extraordinary sensitivity of the magnetic method for detecting ferromagnetic impurities and the necessity for excluding iron-bearing laboratory dust from samples under investigation.

The benzene solution used in this work was prepared by shaking the powdered digermane with redistilled thiophene-free benzene. No effort was made to exclude air. The solution was analyzed by evaporating to dryness at 125° and weighing the residue. The density was determined pycnometrically.

Results

The susceptibility of the powdered hexaphenyldigermane at several temperatures is given in Table I.

These results follow the relationship $\chi = A + (C/T + \Delta)$ where χ is the susceptibility, A is the constant diamagnetic part of the susceptibility, C is the Curie constant of the paramagnetic part, T is the absolute temperature, and Δ is the "molecular field constant." In the above relationship $A = -0.47 \times 10^{-6}$ and this is believed

(1) The author is indebted to the National Research Council for funds for the construction of a magnet, and to the National Academy of Sciences for a research grant from the Joseph Henry Fund.

(2) Morgan and Drew, *J. Chem. Soc.*, **127**, 1760 (1925).

(3) Haller and Selwood, THIS JOURNAL, **61**, 85 (1939).

TABLE I

SUSCEPTIBILITY AT FIELD STRENGTH 13,100 OERSTEDS

Temp., °C.	Susceptibility per gram, $\chi \times 10^6$
20	−0.436
0	− .431
−20	− .423
−40	− .410
−60	− .390
−80	− .357

to be the magnetic susceptibility of undissociated hexaphenyldigermane. The Curie constant is 5.0×10^{-3} and $\Delta = -150°$.

The temperature dependence of the measured susceptibility may be interpreted as evidence for slight dissociation or for the presence of a paramagnetic impurity in very small amount. If triphenylgermanium exists, it may be expected to have a molar paramagnetic susceptibility of about 1270×10^{-6}, corresponding to a single unpaired electron spin.[4] About 1% of dissociation would then account for the results. However, this is considered improbable because the molecular field constant, Δ, would not be expected to approach $-150°$ for such a compound having, as is likely, no orbital contribution to the susceptibility. On the other hand, molecular field constants of $-150°$ are not unusual for such highly paramagnetic oxides as might be present as impurities to the extent of a few thousandths of a per cent.

Further, if dissociation actually takes place it may be expected to increase sharply with rise in temperature. The data do not indicate such an effect.

The measurements on the powder therefore set an upper limit of 1% as to the extent of dissociation in the solid. The weight of evidence is that no dissociation takes place.

Hexaphenyldigermane is not very soluble in benzene at room temperature. Measurements had therefore to be made as accurately as possible.

TABLE II

Field strength, oersteds	Pure benzene $\chi \times 10^6$	0.00387 M soln. $\chi \times 10^6$
11,450	−0.7024	−0.7017
16,080	− .7027	− .7033
17,100	− .7019	− .7018
Averages	− .7023	− .7023

(4) Van Vleck "Electric and Magnetic Susceptibilities," Oxford University Press, New York, N. Y., 1932, p. 274.

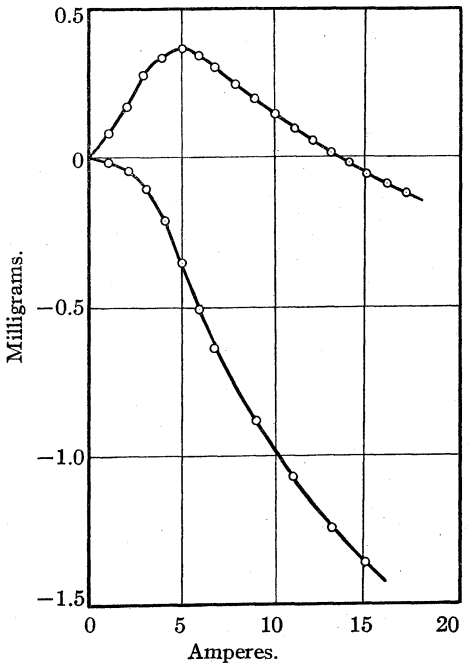


Fig. 1.—Apparent change in weight, Δw, plotted against current through magnet: upper curve, original sample; lower, recrystallized sample.

A single solution 0.00387 M in digermane was investigated at 25°. Measurements were made at several field strengths. The results are given in Table II.

The susceptibility of the solution, assuming no dissociation, may be calculated to be -0.7022×10^{-6}, using Wiedemann's law and the observed susceptibility of the solid. On the other hand, the susceptibility of the solution, assuming complete dissociation, may be calculated to be -0.7012×10^{-6}. It is therefore evident that nothing approaching complete dissociation takes place. It is probable that as little as 20% dissociation would have been detected.

Summary

Magnetic measurements on hexaphenyldigermane set upper limits of dissociation at 1% in the solid and 20% in a nearly saturated benzene solution at 25°. It is considered improbable that any dissociation takes place under these conditions.

EVANSTON, ILLINOIS RECEIVED SEPTEMBER 18, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, CARNEGIE INSTITUTE OF TECHNOLOGY]

A Thermodynamic Study of the Zinc–Antimony System. The Thermodynamic Properties of the Intermetallic Compounds: ZnSb, Zn_3Sb_2 and Zn_4Sb_3

BY BERNARD DEWITT AND HARRY SELTZ

In a previous paper[1] the authors have reported the results of an electromotive force study of liquid cadmium–antimony solutions and have calculated the thermodynamic properties of the intermetallic compounds CdSb and Cd_3Sb_2. By similar methods, zinc–antimony solutions have now been investigated and the thermodynamic properties of the three intermetallic compounds, ZnSb, Zn_3Sb_2 and Zn_4Sb_3, which appear as stable, solid phases, have been determined. The equilibrium diagram (Fig. 1a) for this system has been established accurately by the exhaustive studies of Takei,[2] and his solubility curves have been used in this work.

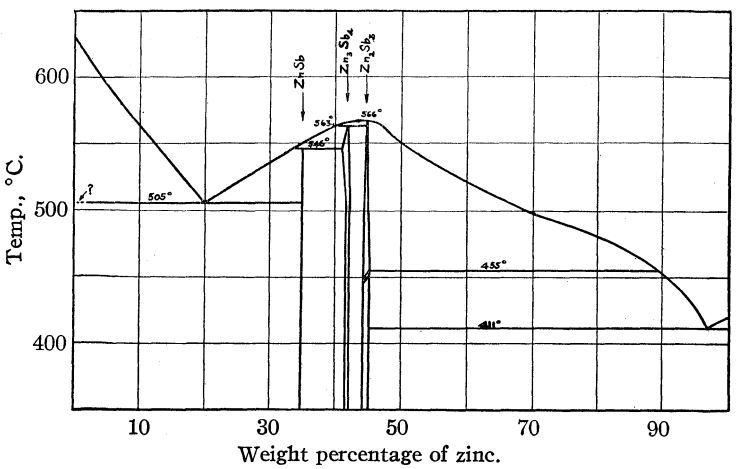


Fig. 1a.—Equilibrium diagram for the zinc–antimony system.

Experimental Results

The electromotive force measurements were made on evacuated cells of the type

$Zn(l)/ZnCl_2$ in LiCl + KCl(l)/Zn (in Zn–Sb liquid solutions)

and the results are given in Table I along with the calculated activities of zinc, a_1, and relative heat contents, $\bar{L}_1$.

From these a_1 and $\bar{L}_1$ values for zinc the corresponding a_2 and $\bar{L}_2$ values for antimony have been calculated along with the ΔH of formation of a mole of the liquid melts from the pure liquid metals. These results are given at round number mole fractions in Table II, and the activities are plotted in Fig. 1 and the $\bar{L}$ and ΔH values in Fig. 2.

The activity curves show deviations from Raoult's law similar to those encountered in the cadmium–antimony system, except that here they are even more pronounced. The a_1 values at higher mole fractions of zinc exhibit definite positive deviations and at lower mole fractions very marked negative deviations. As stated elsewhere,[3] in the binary systems of which antimony is a component there seem to be opposing influences at work, one tending to produce positive and the other negative deviations. A theoretical explanation of this behavior is not as yet forthcoming. The abnormal forms of the $\bar{L}$ and ΔH curves also are worthy of note.

TABLE I

N_1	E. m. f. at 823.1°K., mv.	a_1 823.1°K.	$dE/dT \times 10^5$ volt/°C.	$\bar{L}_1$, cal.	Temp. range, °C.
0.9198	1.68	0.954	0.58	142	480–560
.7871	4.74	.875	1.35	295	510–585
.6973	9.49	.765	3.91	1049	540–610
.6451	14.67	.661	4.60	1070	555–610
.5826	25.23	.491	4.18	425	565–620
.4940	44.11	.288	2.38	−1031	565–620
.3893	63.24	.168	2.97	−1788	535–595
.2741	81.73	.100	6.06	−1468	530–590
.1507	107.45	.048	11.27	− 679	580–620

TABLE II

	At 823.1°K.						
N_1	a_1	a_1/N_1	a_2	a_2/N_2	$\bar{L}_1$	$\bar{L}_2$	ΔH, cal./mole
1.0	1.0	1.0	0	0.400	0	850	0
.9	0.949	1.054	0.036	.356	140	400	166
.8	.883	1.104	.053	.264	275	− 645	91
.7	.770	1.100	.079	.264	1030	−2870	−140
.6	.525	0.875	.152	.381	600	−2205	−522
.5	.292	.584	.324	.647	− 950	− 275	−613
.4	.179	.448	.485	.808	−1730	390	−458
.3	.113	.377	.621	.887	−1660	375	−235
.2	.062	.310	.751	.939	− 960	150	− 72
.1	.024	.240	.884	.982	− 230	25	0
.0	.000	.170	1.0	1.0	+ 220	0	0

(1) Seltz and DeWitt, THIS JOURNAL, **60**, 1305 (1938).

(2) Takei, *Sci. Rep. Tohoku Univ.*, **16**, 1031 (1927).

(3) Seltz and DeWitt, THIS JOURNAL, **61**, 2594 (1939).

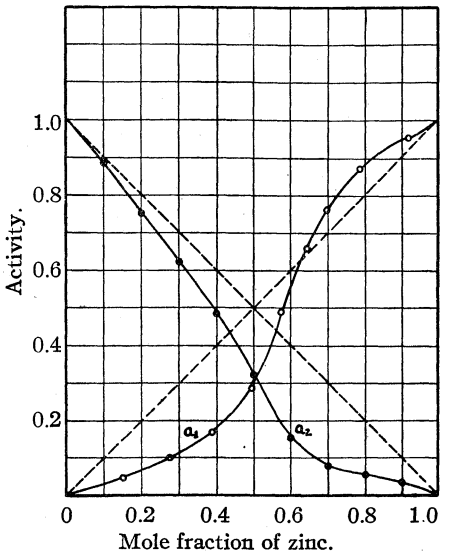


Fig. 1.—Activity curves at 823.1°K.: ○, experimental; ●, calculated.

Calculations

In the calculations which follow, the heats and free energies of fusion of antimony and zinc at various temperatures are required. Equations for these quantities have been set up from the fusion and heat capacity data recommended by Kelley[4] and are given below

$$\text{Sb(s)} = \text{Sb(l)}$$

$$\Delta H = 4015 + 1.64T - 0.89 \times 10^{-3}T^2 \quad (1)$$

$$\Delta F^\circ = 4015 - 1.64T \ln T + 0.89 \times 10^{-3}T^2 + 5.914T \quad (2)$$

$$\text{Zn(s)} = \text{Zn(l)}$$

$$\Delta H = 555 + 2.34T - 1.075 \times 10^{-3}T^2 \quad (3)$$

$$\Delta F^\circ = 555 - 2.34T \ln T + 1.075 \times 10^{-3}T^2 + 13.49T \quad (4)$$

The Solid Solubility of Zinc in Antimony.—From equation 2 the activity of pure solid antimony, a_2(s), relative to pure liquid as standard state, can be calculated at any temperature by the relation, $\Delta F^\circ = -RT \ln a_2$(s). From the solubility or freezing point curve[2] the activity of antimony in the equilibrium liquid at a given temperature is calculated from the experimental a_2 and $\bar{L}_2$ values corresponding to this composition. The $\bar{L}_2$ values are considered constant over the temperature range. If the a_2(s) and a_2 values thus determined are equal, the equilibrium solid phase is pure antimony. If, however, the value of a_2 is less than a_2(s), the equilibrium solid must be a solid solution of zinc in antimony. For small solubilities the solid solution can be considered ideal, as shown for the Pb–Bi system,[5] and the mole fraction composition, N_2(s), is given by the relation $N_2(s) = a_2/a_2(s)$. In Table III the data and solubilities are given at temperatures between the melting point and the eutectic.

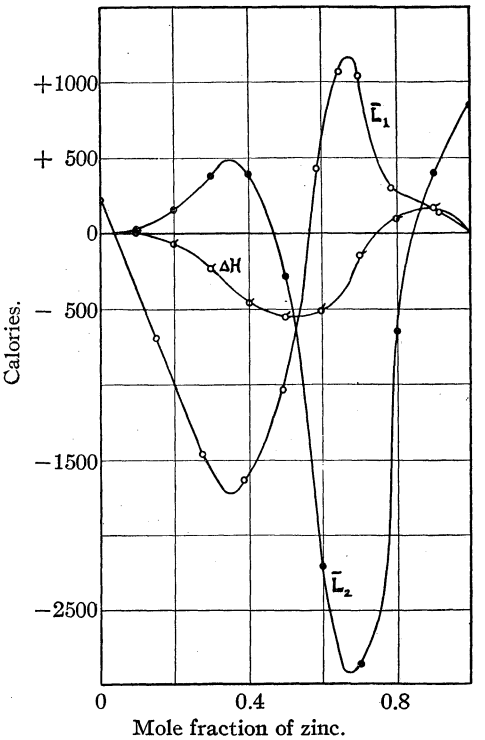


Fig. 2.—Relative heat content and heat of formation.

TABLE III

Temp., °K.	N_2 Equil. liq.	a_2(s)	a_2	N_2(s) Equil. solid soln.
865.1	0.900	0.890	0.883	0.992
823.4	.800	.773	.751	.972
784.6	.800	.670	.627	.936
778.1 (eutectic)	.682	.653	.609	.933

Thermodynamic Properties of ZnSb, Zn_3Sb_2 and Zn_4Sb_3.—At any temperature where a liquid phase is in equilibrium with a solid intermetallic compound such as ZnSb, we can write for the equilibrium constant

$$K_{ZnSb} = \frac{1}{a_1 \times a_2}$$

where a_1 and a_2 are the activities of zinc and antimony in the equilibrium liquid and where the activity of the solid is unity. Hence, for the formation of the compound from the two pure liquids, we write

$$\text{Zn(l)} + \text{Sb(l)} = \text{ZnSb(s)}; \quad \Delta F^\circ = -RT \ln \frac{1}{a_1 \times a_2}$$

(4) Kelley, Bureau of Mines Bulletins 383 (1935) and 393 (1936).

(5) Strickler and Seltz, THIS JOURNAL, 58, 2084 (1936).

Similarly for the Zn_3Sb_2 and Zn_4Sb_3

$$3Zn(l) + 2Sb(l) = Zn_3Sb_2(s);\ \Delta F^\circ = -RT \ln \frac{1}{a_1^3 \times a_2^2}$$

$$4Zn(l) + 3Sb(l) = Zn_4Sb_3(s);\ \Delta F^\circ = -RT \ln \frac{1}{a_1^4 \times a_2^3}$$

Using the solubility curves of Takei and the experimental activities and relative heat contents from this investigation, the values of ΔF° of formation of the compounds at different temperatures are given in Table IV. For Zn_3Sb_2 and Zn_4Sb_3 the

TABLE IV

Temp., °K.	Solubility N_1	a_1	a_2	ΔF°
	Zn(l) + Sb(l) = ZnSb(s)			
778.1	0.318	0.117	0.609	− 4,085
791.4	.375	.153	.528	− 3,957
804.1	.425	.195	.452	− 3,881
810.3	.450	.225	.410	− 3,838
816.7	.475	.259	.369	− 3,815
	3Zn(l) + 2Sb(l) = Zn_3Sb_2(s)			
837.1	0.610	0.551	0.152	− 9,243
823.1	.655	.682	.103	− 9,314
806.0	.700	.780	.076	− 9,449
774.2	.800	.892	.052	− 9,625
760.1	.850	.938	.045	− 9,762
	4Zn(l) + 3Sb(l) = Zn_4Sb_3(s)			
819.1	0.485	0.272	0.350	−13,604
823.1	.502	.300	.317	−13,515
826.1	.513	.320	.298	−13,445
829.4	.525	.341	.283	−13,335
832.3	.538	.362	.266	−13,294
836.1	.558	.410	.233	−13,183

slight solid solubilities are negligible; their activities are taken as unity at each temperature.

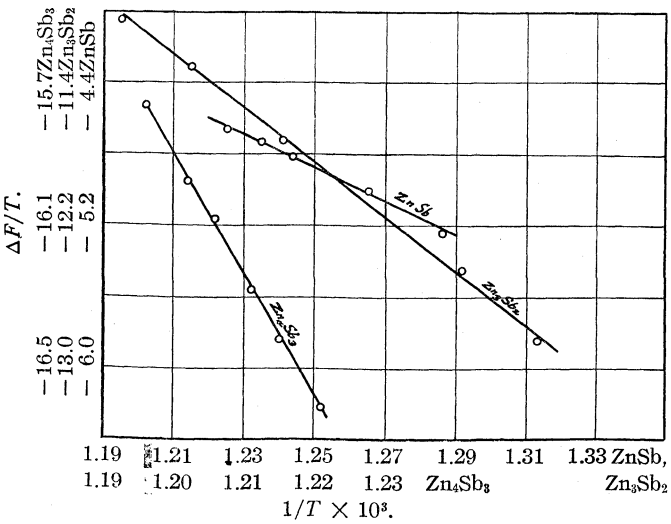


Fig. 3.—Plots of $\Delta F^\circ/T$ against $1/T$.

Plots of $\Delta F^\circ/T$ against $1/T$ for the three compounds are shown in Fig. 3, where it is seen that the points lie satisfactorily on straight lines, the slopes of which give directly the ΔH values of the reactions. Taking the mid-temperature for each compound the following relations obtain

$Zn(l) + Sb(l) = ZnSb(s);\ \Delta F^\circ_{804.1} = -3881;$
$\Delta H_{804.1} = -9570$ cal.

$3Zn(l) + 2Sb(l) = Zn_3Sb_2(s);\ \Delta F^\circ_{806} = -9449;$
$\Delta H_{806} = -14{,}800$ cal.

$4Zn(l) + 3Sb(l) = Zn_4Sb_3(s);\ \Delta F^\circ_{826.1} = -13{,}445;$
$\Delta H_{826.1} = -34{,}400$ cal.

Combining these values with those calculated from equations (1), (2), (3) and (4) at the corresponding temperatures, and calculating to 298.1°K. by the usual thermodynamic methods, with the assumption that ΔC_p is zero, we obtain

$Zn(s) + Sb(s) = ZnSb(s);\ \Delta F^\circ_{298.1} = -3361;$
$\Delta H_{298.1} = -3069;\ \Delta S_{298.1} = 0.98$ e. u.

$3Zn(s) + 2Sb(s) = Zn_3Sb_2(s);\ \Delta F^\circ_{298.1} = -3700;$
$\Delta H_{298.1} = -51;\ \Delta S_{298.1} = 12.25$ e. u.

$4Zn(s) + 3Sb(s) = Zn_4Sb_3(s);\ \Delta F^\circ_{298.1} = -13{,}581;$
$\Delta H_{298.1} = -13{,}095;\ \Delta S_{298.1} = 1.63$ e. u.

These values of $\Delta S_{298.1}$ with the entropies of Sb(s) and Zn(s)[6] lead to the following entropies for the compounds

ZnSb(s), $S_{298.1} = 21.43$ e. u.; Zn_3Sb_2(s); $S_{298.1} = 63.65$; Zn_4Sb_3(s); $S_{298.1} = 73.48$ e. u.

It should be noted that these thermodynamic quantities refer to the forms of the solid Zn_3Sb_2 and Zn_4Sb_3 as they exist at temperatures of the liquid–solid equilibria and do not consider any transformations which have been reported at lower temperatures. There is still some uncertainty as to the nature of these changes and no thermal data are available for them.

Of the three compounds, Zn_3Sb_2 is the only one which melts congruently and the heat of fusion can be evaluated from the $\bar{L}$ values and the heat of formation. For the change

$3Zn(l) + 2Sb(l) = Zn_3Sb_2$(liq. soln. $N_1 = 0.6$)

$\Delta H = 3\bar{L}_1(N_1 = 0.6) + 2\bar{L}_2(N_1 = 0.6) = 3 \times 600 + 2(-2205) = -2610$ cal.

Combining this value with the ΔH of formation of the compound from the pure liquid metals, we obtain the heat of fusion

$Zn_3Sb_2(s) = Zn_3Sb_2(l);\ \Delta H = 12{,}190$ cal.

Summary

1. The activities and partial molal relative heat contents of zinc and antimony in their liquid melts have been determined over the entire concentration range.

(6) K. K. Kelley, Bureau of Mines Bulletin 394.

2. The solid solubility of zinc in antimony has been calculated.

3. The free energies and heats of formation and the entropies of ZnSb, Zn_3Sb_2 and Zn_4Sb_3 have been evaluated.

4. The heat of fusion of Zn_3Sb_2 has been calculated.

PITTSBURGH, PENNA. RECEIVED SEPTEMBER 1, 1939

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORY OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, No. 727]

The Electron Diffraction Investigation of the Molecular Structures of the *meso* and Racemic 2,3-Dibromobutanes[1]

BY D. P. STEVENSON[2] AND VERNER SCHOMAKER

The recent electron diffraction investigations of the structures of some ethylene halides by Beach[3] and co-workers have provided considerable information regarding the magnitude of the repulsive forces acting between halogen atoms attached to adjacent carbon atoms. In order to extend the work of Beach to the study of the interactions of the methyl group with other methyl groups and with bromine atoms attached to adjacent carbon atoms, *meso* and racemic 2,3-dibromobutane were selected for electron diffraction investigation. It was hoped that the quite different chemical properties of this pair of molecules[4] might result from an appreciable difference in the relative orientations of the "isopropyl bromide" groups about the 2,3 carbon–carbon single bond, inasmuch as these molecules would be expected to show structural differences in only this respect.

Experimental.—The *meso* and racemic 2,3-bromobutanes used in this research were portions of samples prepared for another investigation.[5] It was estimated by Dr. Winstein that neither compound contained more than 2% of the other and that both were otherwise very pure. Inasmuch as the racemic and *meso* compounds are structurally very similar, such a quantity of one in the other would have no effect on the electron diffraction photographs.

The electron diffraction apparatus used in this investigation has been described by Brockway.[6] The wave length of the electrons, determined in the usual way from transmission photographs of gold foil, was 0.0611 Å. Photographs were taken with two camera distances, 10.86 and 20.21 cm.

As the compounds are not very volatile (b. p. *ca.* 150°), it was necessary to use the high temperature nozzle[7] in order to obtain sufficient gas pressure. Photographs were taken with the liquid in the boiler at 100 to 130°.

Interpretation.—The photographs of each molecule showed 13 rings, and were practically identical qualitatively. Only small quantitative differences of doubtful reality were found. Curve C of Fig. 2, to be discussed below, gives a good representation of the appearance of the photographs. The observed values of $s\left(s_0 = \frac{4\pi}{\lambda}\sin\frac{\vartheta}{2}\right)$ for the maxima and minima as well as the visually estimated intensities, I, are given in Table I.

Radial distribution functions[8] were calculated using the formulas

$$D(l) = \sum_n C_n \frac{\sin s_n l}{s_n l} \qquad (1)$$

$$C_n = f(I_n, s_n) \qquad (2)$$

The values of C_n were chosen in accordance with the recommendations of Schomaker[9] and are given in column 4 of Table I.

The curves of Fig. 1 are plots of the radial distribution functions calculated from the measurements of the maxima and the minima for the *meso* and the racemic compounds. The two curves for each compound are in satisfactory agreement with respect to the two peaks at ~2.8 and ~4.6 Å., the precise location being for the *meso*-maxima curve, 2.83 and 4.61 Å., the *meso*-minima 2.85 and 4.62, the racemic-maxima 2.82 and 4.58 Å., and the racemic-minima 2.87 and

(1) The results of this investigation were presented at the meeting of the A. A. A. S. in Stanford, June, 1939.

(2) National Research Fellow.

(3) (a) J. Y. Beach and J. K. Palmer, *J. Chem. Phys.*, **6**, 639 (1938); (b) J. Y. Beach and A. Turkevich, THIS JOURNAL, **61**, 303 (1939).

(4) The rates with which the *meso* and the racemic dibromobutanes react with iodide ion are very different: *cf.* Dillon, Young and Lucas, *ibid.*, **52**, 1953 (1930), and Young, Pressman and Coryell, *ibid.*, **61**, 1640 (1939).

(5) S. Winstein, D. Pressman and W. G. Young, *ibid.*, **61**, 1645 (1939).

(6) L. O. Brockway, *Rev. Modern Phys.*, **8**, 231 (1936).

(7) L. O. Brockway and K. J. Palmer, THIS JOURNAL, **59**, 2181 (1937).

(8) L. Pauling and L. O. Brockway, *ibid.*, **57**, 2684 (1935).

(9) Verner Schomaker, A. C. S. meeting, Baltimore, Md., April, 1939.

TABLE I

Values in parentheses have been omitted from the averages

Max.	Min.	I_0	C_n	meso s_0	dl s_0	s_c[a]	meso s_c/s_0	dl s_c/s_0
	1	− 6	−1.4	1.86	1.71	2.01	(1.081)	(1.176)
1		7	2.5	2.93	2.99	2.93	(1.000)	(0.980)
	2	−10	−4.2	3.73	3.72	3.80	1.019	1.021
2		10	5.9	4.65	4.57	4.65	1.000	1.016
	3	− 4	−2.2	5.07	5.15	...	...	...
3		3	2.2	5.68	5.84	...	...	...
	4	−10	−6.9	6.35	6.44	6.33	0.996	0.984
4		9	7.4	7.16	7.26	7.22	1.008	.995
	5	−65	−5.5	7.90	8.06	8.06	1.022	1.000
5		2	2	8.62	8.80	8.80	1.021	1.000
	6	− 5.5	−5.2	9.24	9.26	9.28	1.005	1.002
6		8	8.4	9.79	9.82	9.93	1.014	1.011
	7	− 7	−7	10.53	10.59	10.64	1.011	1.005
7		5	5.4	11.30	11.43	11.42	1.011	0.999
	8	− 2.5	−2.6	11.91	12.14	12.15	1.019	1.001
8		4.5	5.1	12.60	12.83	12.80	1.017	0.992
	9	− 3.5	−3.8	13.19	13.40	13.20	1.001	.985
9		4.75	5.5	13.89	13.87	14.04	1.011	1.013
	10	− 5.5	−6.2	14.66	14.50	15.00	(1.023)	(1.034)
10		3	3.4	15.35	15.35	...	...	...
	11	− 1	−1.1	15.94	15.97	...	...	...
11		3	3.3	16.53	16.44	16.80	1.016	1.021
	12	− 4	−4.3	17.23	17.10	17.51	1.017	1.024
12		3	2.8	18.07	17.87	18.22	1.009	1.021
	13	− 3	−3	18.88	18.71	19.06	1.010	1.018
13		2	2	20.07	19.40	20.02	0.998	(1.032)
						Average	1.011 ± 0.006	1.007 ± 0.011

[a] Calculated with C–Br = 1.91 Å., C–C = 1.54 Å., ∠C–C–C = 110.5°, ∠C–C–Br = 108.5° and "*trans*" configuration (Curve C).

4.60 Å. The pronounced peaks at lesser values of l are unreliable as is indicated by the disagreement between the two distribution curves calculated for each compound. For a model with tetrahedral angles, C–C and C–Br bond distances of 1.54 and 1.91 Å. (the covalent values),[10] respectively, and a "*trans*" configuration with respect to the bromines, the shorter non-bonded carbon–bromine distance is 2.82 Å., and the bromine–bromine distance is 4.57 Å. An increase of less than 1° in the carbon–carbon–bromine angle brings the calculated distances into agreement with those indicated by the radial distribution curves.

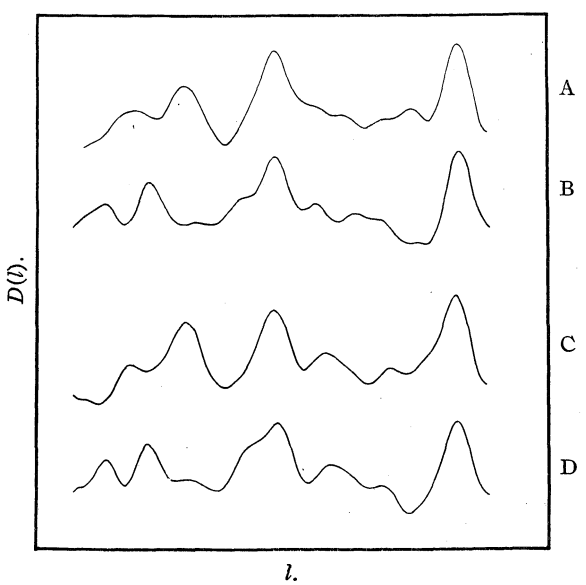


Fig. 1.—Radial distribution function $D(l)$ against l: Curve A, *meso*, maxima; Curve B, *meso*, minima; Curve C, racemic, maxima; Curve D, racemic, minima.

Three theoretical intensity curves were calculated using equation (3). The Z's are the atomic

$$I(s) = \sum\sum \frac{(Z_i - f_i)(Z_j - f_j)}{(Z_C - f_C)^2} \frac{\sin l_{ij}\, s}{l_{ij}\, s} \qquad (3)$$

numbers, the f's the atomic scattering factors,[11] and the l_{ij}'s the interatomic distances involving the ith and j^{th} atoms. It was assumed that the ends of the molecule are like isopropyl bromide[12]

(10) L. Pauling and L. O. Brockway, THIS JOURNAL, **59**, 1234 (1937); H. A. Levy and L. O. Brockway, *ibid.*, **59**, 1662 (1937).

(11) L. Pauling and J. Sherman, *Z. Krist.*, **81**, 1 (1932).

(12) J. Y. Beach and D. P. Stevenson, THIS JOURNAL, **61**, 2463 (1939).

with respect to angles and distances, and that the bromines are "*trans*" to each other, as is indicated by the radial distribution functions. Only one group of curves was calculated, since for the "*trans*" configuration there are, in $I(s)$, only unimportant terms which are different for the *meso* and racemic compounds. These terms, involving the methyl–methyl distances, have such small coefficients that they may be discarded without appreciably affecting $I(s)$. Furthermore, the terms involving hydrogen atoms, which are dependent on the orientation of the methyl groups with respect to their carbon–carbon bonds, were omitted because of their small coefficients and their undoubtedly severe temperature factors.

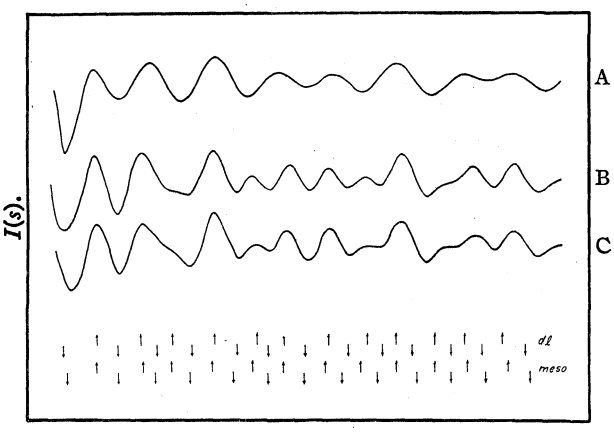


Fig. 2.—Theoretical intensity curves: Curve A, C–Br = 1.91 Å., C–C = 1.54 Å., C–C–C = 110.5°, C–C–Br = 108.7°. Terms dependent on rotational orientation omitted. Curve B, Curve A plus terms dependent on orientation, *trans* configuration. Curve C, Curve A plus bromine–bromine term, *trans* configuration.

In the calculation of curve A, Fig. 2, all of the terms which depend on the orientation about the 2,3-bond were omitted. Curve B includes these terms, with the exceptions indicated in the preceding paragraph. Curve C, which is in best agreement with the photographs, includes all the terms of B except that involving the bromine to methyl–carbon distance. The better agreement obtained when the methyl–carbon to bromine term is omitted indicates that the amplitude of libration is sufficiently large to make the temperature factor in the coefficient of this term severe, but that it is not large enough to cause an effective temperature factor in the coefficient of the bromine–bromine term. An average displacement of about 20 to 30° from the "*trans*" configuration is consistent with these observations.

Dielectric constant measurements[13] on liquid *meso* and racemic 2,3-dibromobutane show these molecules to have considerable dipole moments. This is possible only if the amplitude of libration is considerable, in agreement with the results of our investigation.

The quantitative comparison of the photographs with curve C is given in Table I. The agreement between the curve and the photographs of the racemic and *meso* compounds is quite satisfactory, indicating that the assumption of isopropyl bromide angles and distances is justified. Our final results are Br–Br = 4.60 ± 0.03 Å., C–Br = 2.83 ± 0.02 Å., ∠ C–C–Br = 109.5 ± 2°, C–Br = 1.91 Å. (assumed), C–C = 1.54 Å. (assumed), ∠ C–C–C = 110.5° (assumed).

Discussion.—The results of the studies of the deviations of the bond angles from the tetrahedral value in substituted methanes[10b,12,14] may be summarized by the following set of inequalities, $R_{CH_3-CH_3} > R_{CH_3-X}$, $R_{X-X} > R_{X-H}$, R_{CH_3-H}, where R is the repulsion between the groups indicated by the subscripts and X represents a chlorine or bromine atom.

The data available at present are insufficient to set up a similar set of inequalities for substituted ethanes. On the basis of several fairly reasonable assumptions, however, it is possible to draw some conclusions regarding the interaction of nonbonded groups in substituted ethanes. We are interested in only that part of the total potential energy of an ethane-like molecule which depends on the internal rotation. This potential we regard as the sum of the interaction potentials of pairs of groups and a symmetrical three-fold potential similar to that of ethane. The three-fold potential drops out in any consideration of the relative energies of orientations differing by 120°. We designate the interaction potentials of the groups i and j in an ethane-like molecule for the two orientations of Fig. 3 by V_A and V_B and their differences $V_A - V_B$, by X_{ij}.

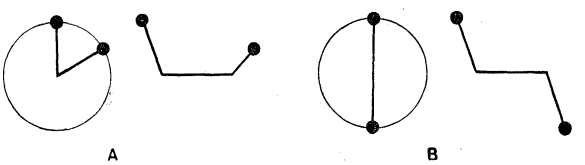


Fig. 3.

(13) S. Winstein and R. Wood, private communication.

(14) R. E. Sutton and L. O. Brockway, THIS JOURNAL, **57**, 413 (1935); J. Y. Beach and D. P. Stevenson, *ibid.*, **60**, 475 (1938).

The heat contents of *meso* and racemic 2,3-dibromobutane are practically the same[15] and both molecules have the "*trans*" configuration; hence it follows that

$$X_{CH_3-CH_3} + X_{H-H} - 2X_{CH_3-H} = 0 \quad (a)$$

and from the results of Beach and Turkevich[3b] we have

$$X_{Br-Br} + X_{H-H} - 2X_{Br-H} > 2.5 \text{ kcal./mole}) \quad (b)$$

while from the "*trans*" configuration of racemic 2,3-dibromobutane

$$X_{Br-Br} + X_{CH_3-CH_3} - 2X_{Br-CH_3} > 0 \quad (c)$$

It is interesting to note that while additivity obtains for the X's involving methyl groups and hydrogen atoms, (a), it does not hold for the X's involving bromine atoms in substituted ethanes.

From equation (a) it follows that the three staggered configurations of *n*-butane have approximately the same energy, in agreement with the assumption of Pitzer.[16]

The authors would like to express their thanks to Dr. Saul Winstein of the Institute for the samples of the compounds used in this research, as well as for information regarding the properties and purity of the compounds.

Summary

From electron diffraction photographs it has been found that both racemic and *meso* 2,3-dibromobutane have "*trans*" configurations with respect to the bromine atoms, the bromine–bromine distance being 4.60 ± 0.03 Å. It has been shown further that a model for the structure of this pair of compounds, based on the known structure of isopropyl bromide, gives a theoretical scattering curve which is compatible with the photographs. Evidence for considerable torsional oscillation about the equilibrium "*trans*" configuration is presented.

(15) J. B. Conn, G. B. Kistiakowsky and E. A. Smith, THIS JOURNAL, **60**, 2770 (1938).

(16) K. S. Pitzer, *J. Chem. Phys.*, **6**, 473 (1937).

PASADENA, CALIF. RECEIVED SEPTEMBER 6, 1939

[CONTRIBUTION FROM THE COATES CHEMICAL LABORATORY, LOUISIANA STATE UNIVERSITY]

The Homogeneous Decomposition of Ethyl Chlorocarbonate

BY A. R. CHOPPIN, H. A. FREDIANI AND G. F. KIRBY, JR.

Though a number of homogeneous decomposition reactions in the gas phase are reported in current literature, the number of such reactions which are not complicated as to order or mechanism is comparatively small. From a series of compounds which have been investigated in this Laboratory, ethyl chlorocarbonate was chosen for more complete study since it appeared to have the characteristics of a member of this somewhat select group. Ethyl chlorocarbonate was found to undergo homogeneous, unimolecular decomposition to ethyl chloride and carbon dioxide between 150 and 200°.

Experimental

The ethyl chlorocarbonate used in this series of experiments was obtained from the Eastman Kodak Company. The commercial product was purified as follows: 250 ml. of the substance was placed in a round-bottomed flask, fitted with a 90-cm. fractionating column and distilled. The first and last 100 ml. were discarded, the intermediate 50 ml. retained. This intermediate portion was refractionated. The first 20 ml. was discarded and the next 10 ml., having a boiling range of 0.01°, was used for study.

The thermostat employed had a capacity of five gallons (20 liters), was insulated with filter-cell set in a plaster of paris mold, and employed as a bath medium hydrogenated cottonseed oil circulated by means of a turbine stirrer. After a short period of use the oil darkened in color, cracking became less pronounced, and the bath was serviceable at temperatures as high as 250°.

Three specially wound resistance coils capable of a total heat input of 1200 watts constituted the permanent heater. In addition to this heating unit, two 250-watt hairpin type heaters were connected to the line through a 460-ohm rheostat to give a partial regulation of the heat input. These two sets of heaters were so adjusted as to maintain the bath within one degree of the desired temperature.

Exact temperature regulation was obtained by means of a 200-watt light bulb operated by the thermoregulator, which consisted of a Leeds and Northrup reflecting galvanometer connected to a platinum resistance thermometer through a Wheatstone bridge. The circuit was so arranged that light reflected from the galvanometer turned on the light heater at zero scale reading through a photoelectric cell. An unbalanced circuit through a resistance change in the platinum resistance thermometer caused the light to swing away from the cell a distance of 10 cm. for a change of less than 0.01°. The temperature of the bath was constant to 0.01°.

The reaction was followed by a static method in an all-glass system. Reaction vessels were constructed of

Pyrex glass, and the pressure was balanced through a diaphragm actuating platinum contacts, as described by Daniels.[1] Small bulbs containing the reactant were introduced through a side-arm and broken at the proper time by a glass enclosed, solenoid-operated hammer. A mercury relay was actuated by the completion of the diaphragm circuit. This relay was in turn connected to a power relay, the arm of which was placed opposite the tip of an automatic valve sealed into the outside system. Completion of the relay circuit by an unbalanced condition of the diaphragm resulting from a pressure increase inside the reaction vessel caused the arm of the power relay to tap the valve at a rate of about 300 times per minute, admitting air into the outside system. In this way automatic pressure regulation was secured by practically continuous balancing of the outside pressure with the pressure inside the reaction vessel. The changes in pressure were followed by means of a mercury manometer which fell smoothly during the course of a reaction. For experiments in which the initial pressure was 100 mm. or greater, a vertical mercury manometer reading to 0.5 mm. was used. In those experiments in which the initial pressure was below this value, a Fisher vacuum gage and a calibrated inclined mercury manometer were sealed into the line. Each of these gave pressure readings directly to an accuracy of 0.05 mm. of mercury.

The diaphragms employed in the system were flexed to a constant zero point before use. This required about half an hour of automatic flexing with a slightly reduced pressure inside the reaction vessel and the vacuum pump working only on the outside system.

Before use cells were boiled with cleaning solution, rinsed with fuming nitric acid and finally with distilled water. There was no opportunity for contact with stopcock grease, mercury or other foreign materials and no dead space correction was necessary.

To test the homogeneity of the reaction runs were made at the same temperature and approximately the same pressure with the unpacked vessel and with a vessel having an increased surface. The increase in surface was obtained by packing the vessel with ground glass, quartz or with glass wool.

A bulb of ethyl chlorocarbonate was chosen to give approximately the desired pressure and sealed into the side arm of the reaction cell. The vessel was evacuated to a pressure of 0.001 mm. of mercury, rinsed with nitrogen, and this process repeated several times. Pressures on each side of the diaphragm were equalized by drawing gas from the cell through a small side tube which was sealed off immediately preceding a run. After the final evacuation and sealing of the cell, the bulb of reactant was broken by the solenoid operated hammer and the bath quickly raised by means of a hydraulic jack to immerse the vessel. The initial pressure was taken as one-half the final constant pressure eventually reached and this value was checked against the value calculated from the weight of the sample and the volume of the cell, which was determined with distilled water.

The final products were analyzed for ethyl chloride gravimetrically and for carbon dioxide by means of a Fisher apparatus. In order to obtain large amounts of material for analysis, a special type of vessel was used. A sealed bulb containing from 0.1 to 0.5 g. of ethyl chlorocarbonate was introduced into the vessel, after which the vessel was rinsed with nitrogen and sealed. The bulb was broken by shaking and the vessel submerged in the thermostat. At the end of the time required for complete decomposition it was removed from the thermostat, packed in dry ice–acetone, and the ethyl chloride collected as a liquid. Silver nitrate was used to precipitate the chloride and the carbon dioxide was absorbed in 40% potassium hydroxide. The analysis of carbon dioxide was accurate within 2% and the more accurate gravimetric determination of chloride checked the theoretical within 0.5%.

No chemical evidence of products other than ethyl chloride and carbon dioxide has been obtained. No test for chlorine could be obtained upon allowing the decomposition products to come in contact with a potassium iodide–starch solution. Spectroscopic work being done on the compound at present should give a more positive answer as to the possibility of the presence of small amounts of substances other than those determined chemically. Typical examples of the data taken from chemical analyses of the products are shown in Table I.

TABLE I

Sample, g.	Carbon dioxide, cc. Found	Carbon dioxide, cc. Calcd.	Silver chloride, g. Found	Silver chloride, g. Calcd.
0.3125	62.9	64.9	0.4031	0.4105
.4311	90.1	89.4	.5648	.5663
.2104	44.2	43.6	.2761	.2763
.1071	22.0	22.2	.1423	.1409

Experimental Results

Since the only products of the reaction found by the analytical methods employed thus far are carbon dioxide and ethyl chloride, the equation for the reaction is

$$C_2H_5OCOCl = CO_2 + C_2H_5Cl$$

Since the decomposition of one mole of reactant results in an increase of one mole in the total number of moles of gases present, the pressure increase upon decomposition may be taken as directly proportional to the change in concentration of the reactant. Thus the concentration of undecomposed ethyl chlorocarbonate is given by the equation

$$p = 2P_1 - P_t$$

where P_1 is the initial pressure, P_t the pressure at any time t and p the partial pressure of undecomposed ethyl chlorocarbonate. The apparent simplicity of the reaction does not seem to be general for the chlorocarbonates.[2]

The curves obtained by plotting pressure against time are the typical log curves of a first order reaction. The number of these curves which have been plotted over the normal pres-

(1) Daniels, "Chemical Kinetics," Cornell University Press, Ithaca, N. Y., 1938, p. 59.

(2) Lessig, *J. Phys. Chem.*, **36**, 2325 (1932).

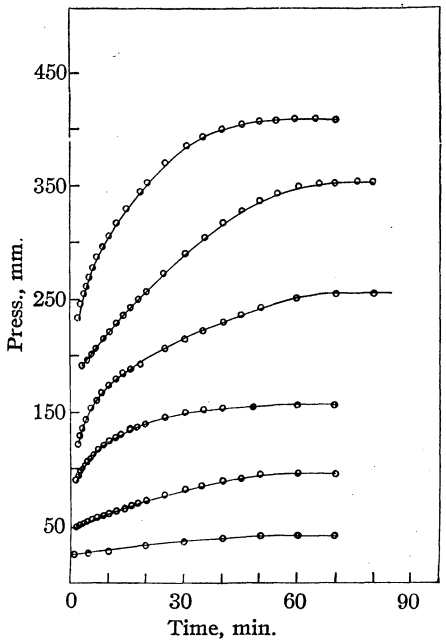


Fig. 1.—Typical ethyl chlorocarbonate decomposition curves: pressure *vs.* time at 175°.

sure range gives ample evidence of the smooth and regular rate of decomposition (Figs. 1 and 2).

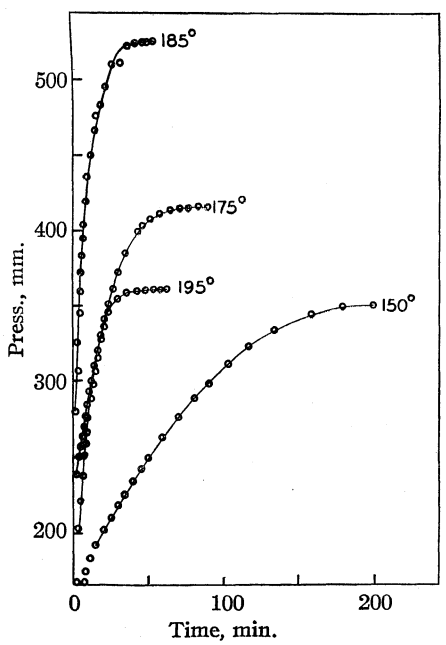


Fig. 2.—High pressure curves.

The specific reaction rate was determined from the slopes of the lines in Fig. 3. In these curves the log of $2P_1 - P_t$ has been plotted against time. The slope in each case was determined by the method of least squares and this value was

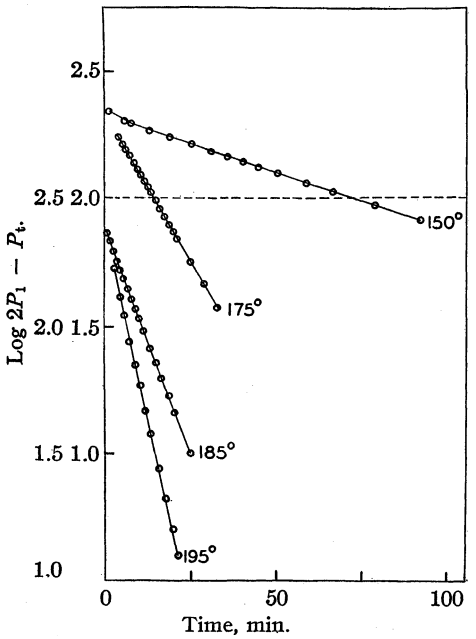


Fig. 3.—Plot of log of concentration against time.

TABLE II

P_1, mm.	k, min.	k/k_0
Temperature 150°; k_0 = 0.00780		
325	0.00769	0.986
177[a]	.00787	1.009
125	.00481	0.617
115	.00749	.960
105	.00472	.605
Temperature 175°; k_0 = 0.0451		
246[a]	0.0449	0.995
212	.0446	0.998
177	.0459	1.017
176[a]	.0406	0.899
152[a]	.0348	.771
131	.0366	.811
126[a]	.0338	.759
102	.0301	.677
85	.0278	.612
45	.0263	.583
37	.0204	.450
24	.0127	.286
18	.0156	.377
Temperature 185°; k_0 = 0.0899		
260[a]	0.0894	0.994
176	.0904	1.005
158	.0691	0.768
76.5	.0600	.667
Temperature 195°; k_0 = 0.1815		
179	0.183	1.008
175	.180	0.991
151	.138	.760
85	.114	.628
20	.102	.562

[a] Vessel packed.

multiplied by 2.303 according to the conventional first order rate equation

$$-\log c = kt/2.303 + C$$

The values of the specific rate constant k determined by this method have been reported in Table II. The value of k_0 in this table was taken as the average value of the velocity constants of the high pressure runs.

The increase in the high pressure decomposition rate with temperature is shown in Fig. 4. The

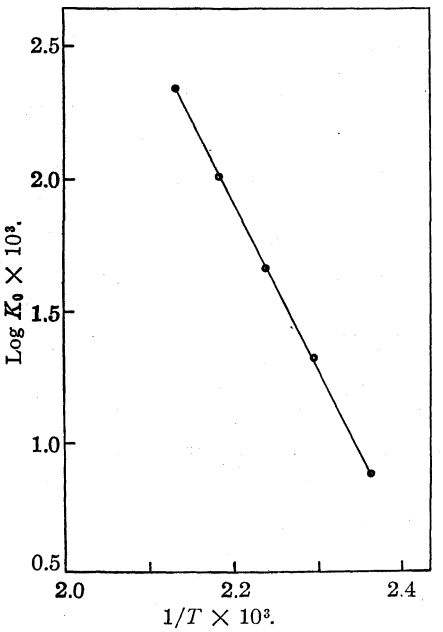


Fig. 4.

energy of activation calculated from the simple Arrhenius equation using this straight line is 29,410 cal. per mole. From this value are calculated the values of the frequency factor s in the expression $k = se^{-E/RT}$ as recorded in Table III.

TABLE III

T, °K.	423	448	468	478
$s \times 10^{-10}$	5.943	5.254	5.225	5.403

The rate of reaction, then, may be obtained from the equation

$$k = 5.5 \times 10^{10} e^{-29,410/RT}$$

The magnitude of s, while smaller than similar values obtained in most unimolecular reactions,[3] has been calculated over the active temperature range and an average value taken as suggested by Rice and Gershinowitz.[4]

Brearly, Kistiakowsky and Stauffer[5] observed

(3) Kistiakowsky, *Chem. Rev.*, **17**, 47 (1935).

(4) Rice and Gershinowitz, *J. Chem. Phys.*, **3**, 479, 490 (1935).

(5) Brearly, Kistiakowsky and Stauffer, THIS JOURNAL, **58**, 43 (1936).

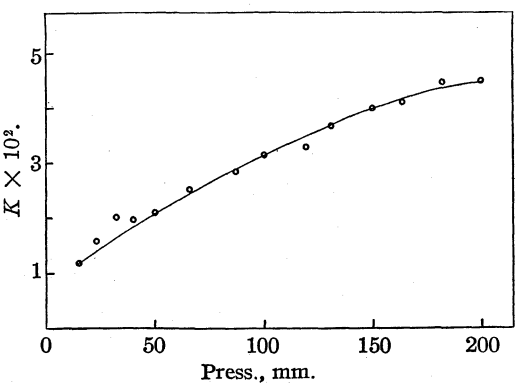


Fig. 5.—Variation of k with initial pressure.

that in experiments with t-butyl chloride much more reproducible results were obtained with coated walls. A similar effect has been reported by Daniels[6] in the decomposition of ethyl bromide. In view of the negligible influence of packing on the decomposition of ethyl chlorocarbonate, no appreciable surface catalysis was expected. However, pressure measurements of decomposition in clean vessels were observed to fluctuate slightly, with this effect disappearing and the pressure increasing smoothly after about two runs with the same vessel.

The exact effect of pressure[7] on the specific rate constant of unimolecular reactions is still

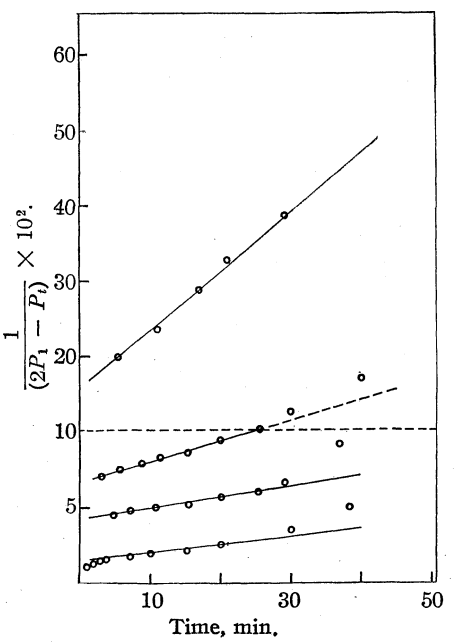


Fig. 6.—Low pressure approach to a second order rate.

(6) Daniels and Veltman, *J. Chem. Phys.*, **7**, 756 (1939).

(7) Kassel, *J. Chem. Phys.*, **32**, 1065 (1928); "The Kinetics of Homogeneous Gas Reactions," The Chemical Catalog Co., New York, N. Y., 1932, Chapters V and VI.

controversial. Recent statements by Pease[8] and Daniels[9] have shown that some investigators are far from satisfied with the present theories of quasi-unimolecular mechanisms. Reactions which throw light on this situation are still of great value, and the present series of experiments seems to have definite possibilities in this connection. The effect of pressure on rate has been studied at several temperatures, and more closely at 175°. The observed effects are shown graphically in Fig. 5 in which k is plotted against P_1. The fall off in rate has been found to begin appreciably above the expected value of about 40 mm.

The low pressure approach to a second order rate is demonstrated in Fig. 6. The reciprocal of reactant pressure has been plotted against time for several runs having initial pressures lower than 100 mm.

(8) Pease, *J. Chem. Phys.*, **7**, 749 (1939).
(9) Ref. 1, pp. 71, 72; ref. 5, p. 100.

The effect of foreign materials has been investigated quite thoroughly. An account of this effect will be published in the next paper of the present series.

Summary

1. Ethyl chlorocarbonate has been found to decompose homogeneously and by a unimolecular mechanism between 150 and 195° and over a pressure range from 10 to 700 mm. of mercury.

2. The specific reaction rate may be obtained from the equation

$$k = 5.5 \times 10^{-10} e^{-29,410/RT}$$

3. A slight effect has been observed in the comparison of runs in coated and uncoated vessels.

4. It has been found that at low pressures the rate constant falls appreciably and that the reaction approaches a second order rate.

BATON ROUGE, LA. RECEIVED AUGUST 3, 1939

[FROM THE DEPARTMENT OF PHYSIOLOGY AND BIOCHEMISTRY IN THE MEDICAL COLLEGE AND THE DEPARTMENT OF DAIRY INDUSTRY IN THE NEW YORK STATE COLLEGE OF AGRICULTURE, CORNELL UNIVERSITY]

Molecular Weight and Association of the Enzyme Urease

BY DAVID B. HAND

Introduction

The osmotic pressure of crystalline urease solutions corresponds to an average particle weight of 700,000[1] but the diffusion rate, when measured by activity, establishes the presence of active particles of 17,000 or less. Although much is known about the particle weights of proteins in general, there is yet no knowledge of the size of the smallest units which can exist with unaltered specific properties. In the case of the protein urease, it is possible to prove that smaller particles than those predominating in the solution possess enzyme activity.

Osmotic Pressure Measurements

An apparatus has been designed for measuring the osmotic pressure in a 1.0 ml. sample of solution. Even with these small volumes the expense and difficulty of obtaining the urease were considerable. The apparatus, which has proved convenient, is shown in Fig. 1. The collodion sack is mounted on the outer portion of a universal glass joint, thus making the filling of the sack very simple. Mineral oil is used as a manometer fluid and can be added through the side arm after the apparatus is set up. Equilibrium is reached rapidly since only 0.5 ml. of outer solution are needed. The details of the method are essentially those described by other workers.[2,3,4] Figure 2 gives the measurements of osmotic pressure which were made at pH 7.0 in 0.01 M citrate buffer and at pH 6.3 in 0.001 M phosphate. It is impossible to work nearer the isoelectric point of 5.0[5] or to increase the buffer concentration because of the lower solubility of urease under these conditions.[6] It was found that osmotic pressures were high in 0.001 M buffer due to unequal distribution of ions, but that this effect was repressed in 0.01 M buffer (see Fig. 3).

Mineral oil above both the inner and the outer solutions was allowed to rise in capillary tubes so that a value for osmotic pressure was obtained directly from the difference in the height of the oil in the two capillary tubes. The capillary tube for the outer solution is not illustrated in Fig. 1. The density of the oil was 0.842. In a typical experiment 32 lots of jack bean meal of 100 g. each were extracted with a total volume of 16 liters of 31.6% acetone by the method of Sumner and the urease allowed to crystallize. After centrifuging, washing and recrystallizing, the urease was dissolved in 4.0 ml. of water at 0°.

(1) Paper read before the American Chemical Society, New York City, April, 1935.

(2) Adair, *Proc. Roy. Soc.* (London), **A109**, 292 (1925); **A120**, 573 (1928); **A126**, 16 (1929).
(3) Krogh and Nakazawa, *Biochem. Z.*, **188**, 241 (1927).
(4) Weber and Stöver, *ibid.*, **259**, 269 (1933).
(5) Sumner and Hand, THIS JOURNAL, **51**, 1255 (1929).
(6) When the concentration of citrate is increased, the urease crystallizes in octahedra which are better defined and larger than those obtained with 32% acetone.

The clear solution contained 77.3 mg. of urease per cc. To 1.0 ml. of the urease solution was added 0.1 ml. of 0.1 *M* citrate buffer, *p*H 7.0. The osmotic pressure of this solution at 3° was found to be 4.1 cm. of oil.

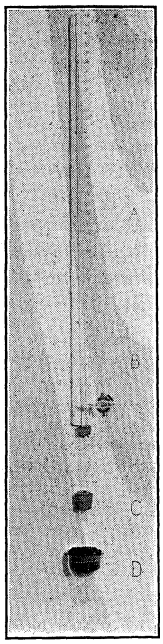


Fig. 1.—Osmometer for measuring osmotic pressure of protein solutions: A, scale and manometer tube; B, side tube for adding mineral oil; C, collodion sack mounted on interchangeable joint; D, outer vessel.

The curve for the variation of osmotic pressure with concentration of urease is not a straight line, so the calculation of particle weight has to be made by extrapolation. Particle weights are calculated from the osmotic pressure at the various concentrations and these values are extrapolated to zero concentration. When this is done the particle weight is found to be 700,000. This is a minimum value for the average particle weight depending on how completely the unequal distribution of ions was suppressed. The apparatus and method have been checked with hemoglobin which is known to be homogeneous with particle weight of 68,000.

Diffusion Measurements

The rate of diffusion of urease through a porous glass membrane was determined by the method of Northrop and Anson[7] as simplified by Dawson.[8] The urease was crystallized once and dissolved in 0.1 molar glycine, *p*H 6.0, to protect against destruction in the outer solution due to extreme dilution. The concentrations in the inner and outer solutions were determined by allowing aliquot portions to act on urea in phosphate buffer and then aerating off the ammonia into standard acid.[9] The rates of diffusion of oxyhemoglobin and hydrochloric acid were also determined with the same cell, for comparison with the urease and calculation of the cell constant. The diffusion of hemoglobin was measured colorimetrically by comparison of the outer solution with the original inner solution. Tables I, II, and III give the experimental data together with the calculated values of diffusion rate. For convenient calculation of diffusion coefficient the rate of diffusion was expressed in cubic centimeters of inner solution diffusing per hour.[7] The diffusion rate of the proteins decreased during the first two or three days, but then remained constant. The final value found for hemoglobin is in agreement with those of other workers using cells either with sintered glass membranes[7,10] or without membranes.[11,12]

No error is introduced by the fact that the diffusion rates of urease and hemoglobin decrease during the first few days in the diffusion cell since calculation of particle weight is made by comparison of the two proteins. Both

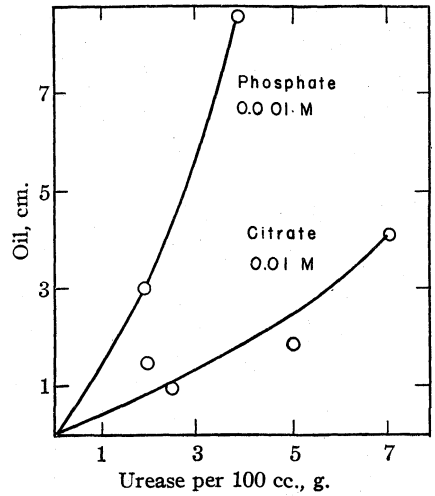


Fig. 2.—Osmotic pressures of urease solutions at 3°.

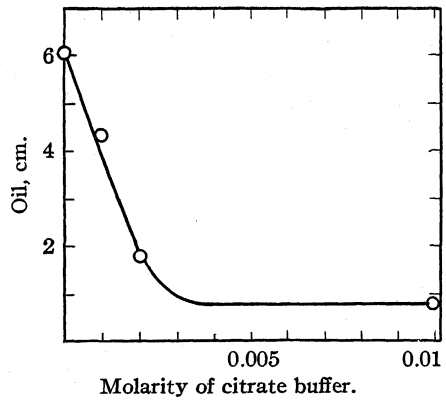


Fig. 3.—Effect of buffer concentration on the osmotic pressure of urease.

TABLE I

DIFFUSION OF UREASE

0°, 0.10 g. per 100 cc. in 0.1 molar glycine; cell no. 1, inner volume 21.0 cc., outer volume 20.4 cc., amount of urease in inner solution at start, 2850 units.

Run	Duration (in hr.)	Amt. diffusing per run (in urease units)	Amt. left in inner soln. at middle of run (in urease units)	Diffusion rate (in cc. inner soln. per hr.)
0	....	*ca.* 7	2848	.....
1	20.5	38.4	2826	(0.0139)
2	20.0	36.7	2789	(.0138)
3	8.0	13.8	2754	(.0132)
4	15.0	21.0	2737	.0107
5	23.25	31.0	2711	.0103
6	9.25	12.8	2689	.0108
7	15.0	18.5	2674	.0097
8	26.0	*ca.* 35	....	.....
				.0104

(7) Northrop and Anson, *J. Gen. Physiol.*, **12**, 543 (1928–1929).
(8) Dawson, THIS JOURNAL, **55**, 432 (1933).
(9) Sumner and Hand, *J. Biol. Chem.*, **76**, 149 (1928).
(10) Zeile, *Biochem. Z.*, **258**, 347 (1933).
(11) Tiselius and Gross, *Kolloid-Z.*, **66**, 11 (1934).
(12) Svedberg and Nichols, cited by Nichols, *Coll. Symp. Monograph*, **6**, 287 (1928).

TABLE II

DIFFUSION OF HEMOGLOBIN

0°, 2.93 g. per 100 cc. in *M*/15 phosphate, *p*H 7.0, cell no. 1, inner volume 21.0 cc., outer volume 20.4 cc., amount of hemoglobin in inner solution at start, 615 mg.

Run	Duration (in hr.)	Amt. diffusing per run (in mg.)	Amt. left in inner soln. at middle of run (in mg.)	Diffusion rate (in cc. inner soln. per hr.)
1	20.0	4.88	613	(0.00836)
2	23.0	4.86	608	(.00728)
3	23.25	4.43	604	.00661
4	22.5	4.06	599	.00632
5	23.25	4.39	595	.00664
				.00650

TABLE III

DIFFUSION OF HYDROCHLORIC ACID

0°, 0.979 normal, cell no. 1, inner volume 21.0 cc., outer volume 20.4; HCl in inner solution at start equivalent to 2900 cc. $Ba(OH)_2$; *N*, 0.0071.

Run	Duration (in hr.)	Amt. diffusing per run (in cc. $Ba(OH)_2$)	Amt. left in inner soln. at middle of run (in cc. $Ba(OH)_2$)	Diffusion rate (in cc. inner soln. per hr.)
1	1.0	41.8	2880	0.305
2	1.0	39.6	2860	.291
3	0.5	19.8	2830	.294
4	.517	20.1	2810	.290
5	.5	19.7	2790	.297
				.295

proteins behaved in the same way and the same value is obtained when either the initial or final rates of diffusion are compared. The decrease in diffusion rate was found not to be due to denaturing of the proteins because there was no measurable loss of native protein in the inner cell except that accounted for by diffusion. The decrease in diffusion rate was also shown not to be due to a progressive clogging of the pores during the experiment. No clogging of the pores occurred during the diffusion experiments. An independent measure of the clogging of the pores can be obtained from the rate of flow of solution through the membrane under a given hydrostatic pressure. During the flow of protein solution, but not during the diffusion, the pores become clogged so that the rate of flow for a given pressure becomes progressively slower. Even after the pores have been so completely clogged that the flow of liquid is practically prevented, the rate of diffusion through the cell is unchanged. Zeile[10] has reported a decrease in the rate of diffusion of hemoglobin during the course of the experiment and he has attributed this to a change in concentration gradient.

Calculations of diffusion coefficients are based on a value of 1.655×10^{-5} cm.^{2} per sec. for the diffusion coefficient of molar hydrochloric acid at 0°.[10,13,14,15] The diffusion coefficient of urease, when measured by activity, is 5.83×10^{-7} cm.^{2} per sec. and that of hemoglobin is 3.67×10^{-7} cm.^{2} per sec.

The diffusion rate of urease activity is thus 59% faster than that of hemoglobin under the same conditions. Particle weights of proteins calculated from diffusion by the Einstein equation[16] are larger than the true weights if the particles are hydrated or non-spherical. Polson has proposed a method for obtaining the shape of protein particles from viscosity data and has found, for all the proteins investigated, that the diffusion coefficients are about 0.7 as great as they would be for spherical particles and also that the hydration factor is approximately the same for all the proteins.[17] This relationship might reasonably be expected to hold for crystalline proteins which yield solutions of similar and comparatively low viscosity.[18] Insofar as these relationships hold, a very satisfactory value for the particle weight of a given protein can be obtained by comparison of the diffusion rate with that of some known protein such as hemoglobin. Particle weights are inversely proportional to the third power of the diffusion coefficients. The particle weight so obtained is equal to the weight of the diffusing particle only if the solution is homogeneous with respect to particle size. Otherwise the calculated value is somewhat larger than the smallest, most rapidly diffusing particle. Thus by comparison with hemoglobin it can be calculated that a maximum value for the weight of the diffusing particle of urease is 17,000.

The experiments described in this paper to determine the particle weight of urease[1] are not in disagreement with the later measurements of sedimentation and diffusion velocity[19] by Sumner, Gralén and Eriksson-Quensel in Svedberg's laboratory. It was shown by these workers that urease solutions (twice crystallized) could be prepared which consisted of two to five components. In all the solutions the component with particle weight 483,000 predominated. In the most homogeneous solutions all but 15% of the protein consisted of this component. For the urease solution containing five components of different particle weights, the relative amounts of the components and the activity of this preparation were not reported. No experiments were made to determine whether the enzyme activity was restricted to a single particle size.

Diffusion experiments with other enzymes have not indicated any dissociation or association of the particles. The diffusion rate for the activity is the same as the diffusion rate for protein material with pepsin[20] and chymotrypsin.[21] The results reported for catalase are uncertain. Stern's experiments[22] on the diffusion of catalase by activity measurements indicate a particle weight somewhere between 8500 and 500,000 with an average of 68,900, while Zeile finds a destruction of the catalase during diffusion.[10] By physical measurements the catalase particle is found to have a weight of 250,000.[23,24,26] In the case of horse antibody, Kabat[25] has reported that many lots could be prepared which were inhomogeneous in

(13) Öholm, *Z. physik. Chem.*, **50**, 309 (1904–1905).
(14) McBain and Liu, THIS JOURNAL, **53**, 59–74 (1931).
(15) Anson and Northrop, *J. Gen. Physiol.*, **20**, 575 (1936–1937).
(16) Einstein, *Z. Elektrochem.*, **14**, 235 (1908).
(17) Polson, *Nature*, **137**, 740 (1936).
(18) Hand, *J. Gen. Physiol.*, **18**, 847 (1934–1935).
(19) Sumner, Gralén and Eriksson-Quensel, *J. Biol. Chem.*, **125**, 37 (1938).
(20) Northrop, *J. Gen. Physiol.*, **13**, 739 (1929–1930).
(21) Kunitz and Northrop, *ibid.*, **18**, 433 (1934–1935).
(22) Stern, *Z. physiol. Chem.*, **217**, 237 (1933).
(23) Stern and Wyckoff, *Science*, **87**, 18 (1938).
(24) Sumner and Gralén, *J. Biol. Chem.*, **125**, 33 (1938).
(25) Kabat, *J. Exp. Med.*, **69**, 103–118 (1938).
(26) Agner, *Biochem. J.*, **32**, 1702 (1938).

amounts up to 65% of the total protein present. He found that the "degraded components" possessed antibody activity. Frampton and Saum have found that the particle weight of tobacco mosaic virus protein as determined from diffusion and viscosity is decreased in 6 molar urea solution to 100,000 without any decrease in biological activity.[27]

Discussion

Although it has been shown by the diffusion rate of urease that particles of a weight as low as 17,000 can carry the activity, it has not been proved that urease exists in this dissociated form at the time that it exerts its catalytic action. The particles may associate again under the conditions in which the activity is measured. Similarly the associated fractions, as separated in the ultracentrifuge, might dissociate in the test solution. There is no evidence to show that dissociation or association has any effect on the activity of urease. Incidentally, urease activity is determined in a solution which is very dilute with respect to protein and which contains 1.5% urea. Both of these conditions are known to be favorable to the dissociation of proteins.

However, in the case of enzymes other than urease, the conditions for measurement of activity might not be so favorable to complete dissociation. It is conceivable that the state of aggregation might have a considerable influence on the activity per gram. This may account for the enzyme preparations which have been reported to be more active than the same enzymes in crystalline preparations. Furthermore, a slow dissociation and association might well give rise to one or more forms of the same enzyme similar to the lyo- and desmo-enzymes of Willstätter.

The weight of the smallest particle of active enzyme is perhaps of more interest than the weight of the associated particles. Theoretically the aggregate dissociates by breaking very weak bonds under such influences as the presence of urea or a shift in *p*H. However, a final unit is reached which cannot be further dissociated except by breaking strong bonds, as for example by peptic or acid hydrolysis. Any further breakdown of this basic unit is accompanied by loss of enzyme activity. Although the term molecular weight has been justifiably applied to the aggregate, it probably would be less confusing to chemists if molecular weight referred only to the smallest particle still possessing enzyme activity, and the term associated molecular weight were used for the aggregates. For example, the molecular weight of acetic acid is 60, although it is known to associate. In this sense the molecular weight of urease is no greater than 17,000, and the average associated molecular weight is 700,000.

Acknowledgment.—The author is indebted to Professor J. B. Sumner for valuable criticism and advice during the course of the work; to Dr. J. S. Kirk for the synthesis of the glycine; and to Dr. S. F. Howell for the purification of the buffer solutions.

Summary

1. From the osmotic pressure the average particle weight of crystalline urease solutions is found to be 700,000.

2. From the rate of diffusion, particles with a weight as low as 17,000 are shown to possess urease activity.

3. There is no evidence to show in which form urease exists at the time that it exerts its catalytic action.

(27) Frampton and Saum, *Science*, **89**, 84 (1939).

ITHACA, NEW YORK RECEIVED FEBRUARY 10, 1939

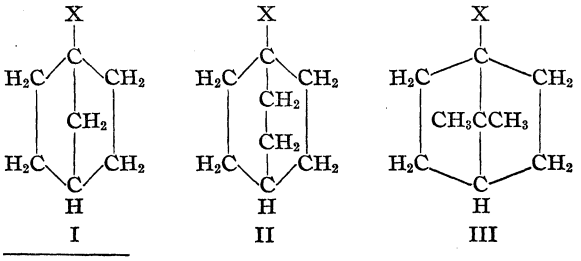
[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

Bicyclic Structures Prohibiting the Walden Inversion. Replacement Reactions in 1-Substituted 1-Apocamphanes[1]

BY PAUL D. BARTLETT AND LAWRENCE H. KNOX

Many replacement reactions at a saturated carbon atom are known to proceed with Walden inversion, many with racemization, and a few with retention of configuration. Recent research has resulted in great emphasis on the first of these groups. Indeed, some workers in this field[2] have proposed that one negative substituent cannot replace another at a saturated carbon atom without a Walden inversion, and that retention of configuration in such a reaction necessarily means that two successive steps each involving inversion have occurred. The present work was undertaken to test this hypothesis of the universality of the Walden inversion with respect to the replacement of the amino group by hydroxyl and by halogen, and to the interchange of hydroxyl groups and halogen atoms in a saturated compound.

A derivative of bicyclo-[2,2,1]-heptane (I) or bicyclo-[2,2,2]-octane (II) with a substituent on the bridge-head is incapable of reacting by the currently favored mechanism of negative substitution with Walden inversion. In the first place, no negative ion or other nucleophilic reagent can approach carbon atom 1 from the side opposite to the substituent and get within bond-forming distance, because carbon atoms 3, 4, 5, and 7 or 8 form a cage around it. In the second place, the three carbon atoms directly bound to the bridge-head (carbons 2, 6, and 7) are not free to alter their positions as required for an inversion of configuration. Both these restrictions apply whether there is optical activity present in the system or not. Hence we may work with an optically inactive series of compounds and still be sure that the mechanism of reaction which, in optically active compounds, underlies the Walden inversion, is excluded.



I II III

Compounds of this type containing the readily replaceable amino or hydroxyl group or halogen on the bridge-head are exceedingly rare. As the most available starting material we have chosen 1-apocamphanecarboxylic acid (III, X = COOH), which can be prepared by the reduction of ketopinic acid by the Wolff–Kishner or, better, by the Clemmensen method as modified by Martin.[3] The yields by these two methods are 62 and 50%, respectively, of purified acid melting at 217–218°. The greater convenience of the Clemmensen procedure for large quantities offsets its slightly lower yield.

In conformity with the experience of Houben and Pfankuch[4] with dihydrocamphene-4-carboxylic acid, we found that the amide of 1-apocamphanecarboxylic acid, treated with methyl alcoholic alkaline solution of bromine, readily gave the Hofmann reaction to methyl 1-apocamphylcarbamate, obtained in 60% yield. This urethan melted, after recrystallization from petroleum ether, at 93–94°. Though quite resistant to hydrolysis, it could be converted in 82% yield into 1-apocamphylamine, m. p. 175°, by refluxing for forty-three hours with concentrated potassium hydroxide in methanol–water solution. The amine yielded an acetyl derivative, m. p. 132°, which could not be hydrolyzed by twenty-four hours of boiling with 8 *N* potassium hydroxide in 80% ethyl alcohol. Since N-*t*-butylacetamide proved similarly resistant, this property is not to be attributed to the special character of the apocamphane ring system.

Treatment of 1-apocamphylamine with four equivalents of sulfuric acid and two equivalents of sodium nitrite in concentrated aqueous solution resulted in a quantitative evolution of nitrogen and a 66% yield of an alcohol melting at 161–162° which we believe to be apocamphanol-1 on the basis of the following evidence. The analysis

(1) Presented before the Organic Division of the American Chemical Society at Boston, September 12, 1939.

(2) See, for example, Olson, *J. Chem. Phys.*, **1**, 418 (1933); Olson and Voge, THIS JOURNAL, **56**, 1690 (1934); Ogg, *ibid.*, **61**, 1946 (1939).

(3) Martin, *ibid.*, **58**, 1440 (1936).

(4) Houben and Pfankuch, *Ann.*, **489**, 193 (1931).

for carbon and hydrogen is that of an apocamphanol. After standing for twenty-four hours at 25–30° with chromic anhydride in glacial acetic acid, it had produced no color change and the alcohol was recovered in 51% yield. The loss seems likely to have been manipulative, since a sample of only 0.115 g. was used in this experiment. This resistance to oxidation indicates a tertiary alcohol. In agreement with this, its esterification was very slow, the *p*-toluenesulfonate (m. p. 93°) being obtained in only 34% yield from the reaction of the alcohol with the acid chloride in anhydrous pyridine for twenty hours on the steam-bath.

In spite of being a tertiary alcohol, this compound dissolves reversibly and with no evidence of polymerization in concentrated sulfuric acid. A pale yellow color, which turns to red on standing, is produced in the solution but is discharged by the addition of water, which precipitates the original alcohol. This suggests that dehydration, and molecular rearrangements leading to it, are prohibited in this compound. This is what we should expect from Bredt's rule[5] and the considerations concerning rearrangements discussed later in this paper, if our alcohol is in fact apocamphanol-1 (III, X = OH). We have not succeeded in establishing this structure in any more direct way.

We attempted to replace the hydroxyl group of this tertiary alcohol with halogen by a number of standard methods, all with negative results. As was expected, 1-apocamphyl *p*-toluenesulfonate was recovered (in 91% yield) from refluxing with a saturated acetone solution of lithium iodide for twenty-three hours. This type of replacement reaction, when it occurs, always involves Walden inversion, and we tried this experiment merely for the sake of completeness. More surprising is the failure of thionyl chloride, which has been credited by Hughes, Ingold, and their co-workers[6] with the ability to replace certain hydroxyl groups by chlorine without the occurrence of any configurative inversion. On the addition of apocamphanol-1 to excess thionyl chloride, a vigorous reaction occurred, after which the mixture was refluxed on the steam-bath for fifteen hours. From the product, after pouring on ice, a white solid could be obtained, melting at 95–98°, which contained no halogen and which was slowly hydrolyzed to apocamphanol by dilute sodium hydroxide in 50% ethyl alcohol in the cold. This product was clearly a sulfite.

From the reaction of apocamphanol-1 with phosphorus pentachloride a white solid was obtained having the properties and composition of a loose molecular compound between two molecules of the alcohol and one of hydrogen chloride. Its melting point was not reproducible, ranging between 157 and 168°. It depressed the melting point of apocamphanol-1 slightly, but did not depress the melting point of camphor in an attempted molecular weight determination. This is consistent with the structure of an oxonium salt, insoluble in camphor. The proposed composition recalls the "dipinacol hydrobromide" of Ayers.[7]

The passage of gaseous hydrogen bromide into a petroleum ether solution of apocamphanol-1 deposited an oil which crystallized and yielded a product of melting point 83–84° which appeared to be the bromine counterpart of the hydrochloride just described. Water decomposed it immediately into hydrogen bromide and apocamphanol-1, as did mere standing in a desiccator over calcium chloride for several weeks. Its bromine content corresponded approximately to a diapocamphanol hydrobromide.

The treatment of N-apocamphylbenzamide with phosphorus pentachloride, a method successfully used by von Braun[8] for the conversion of an amine into a chloride, yielded only starting material and tars.

These experiments with apocamphanol-1 indicate clearly that this tertiary alcohol lacks a necessary structural feature for the direct replacement of its hydroxyl group by halogen. The obvious method remaining to be tried for the preparation of the chloride was the reaction between 1-apocamphylamine and nitrosyl chloride. The addition, in ether at −10°, of pure nitrosyl chloride to the amine resulted in a smooth evolution of nitrogen and a solid product which proved to be a mixture of the desired chloride with the alcohol, apocamphanol-1. This mixture could be separated completely by extraction of the petroleum ether solution with 95% sulfuric acid, which removed the alcohol. The resulting chloride was a white, very volatile, solid melting at 154–156°. Allowance being made for recovered amine, the yield of the chloride was 45%.

(5) Bredt, *ibid.*, **437**, 1 (1924).

(6) Cowdrey, Hughes, Ingold, Masterman and Scott, *J. Chem. Soc.*, 1267 (1937).

(7) Ayers, THIS JOURNAL, **60**, 2959 (1938).

(8) Von Braun, *Ber.*, **65B**, 880 (1932).

All attempts to replace the chlorine of 1-chloroapocamphane failed. After refluxing for twenty-one hours with 30% potassium hydroxide in 80% ethanol, 70% of the chloride was recovered unchanged and no apocamphanol could be obtained by a sulfuric acid extraction. The attack of the alkali upon the glass made the detection of small amounts of chloride ion impracticable. To escape this limitation an experiment was tried in which the chloride was refluxed with silver nitrate in aqueous ethanol solution for forty-eight hours. At the end of this time the solution was perfectly clear, with no opalescence, and 60% of the original 0.1-g. sample of chloride was recovered unchanged. All recovered products were identified by mixed melting points in these experiments. Taking the solubility product of silver chloride in this alcoholic medium to be the same as in water, a concentration of silver chloride as small as 2.4×10^{-10} should have been detectable by opalescence. If the concentration was less than this, then the bimolecular velocity constant (time in hours) for the reaction of silver nitrate with 1-chloroapocamphane is less than 1.7×10^{-10} at about 85°.

We were unable, by the use of ordinary dry ether and the usual methods and precautions, to prepare 1-apocamphylmagnesium chloride, but we are not ready to make this the basis of any theoretical conclusions.

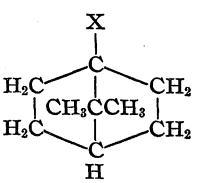
We then considered the possibility that some structural feature of the apocamphane derivatives other than location of the functional group on the bridgehead of a caged ring system might be responsible for the remarkable inertness of these compounds toward replacement reactions. One obvious suggestion is that the substituent X in Formula III, though on a tertiary carbon atom, has "neopentyl" character, that is, it is situated on a carbon atom which is adjacent to a quaternary carbon atom. Neopentyl alcohol is inert to ordinary methods of replacing the hydroxyl group, and the possibility is not to be ignored that apocamphanol-1 might owe some of its inertness to the same cause as neopentyl alcohol, whatever that cause may be. Accordingly we prepared *t*-butyldiethylcarbinol and its chloride (IV, X = OH and Cl) identical with III except for the replacement of two ring-closures remote from the functional group by four hydrogen atoms. This carbinol is converted into the chloride instantly by gaseous hydrogen chloride, and the resulting chloride reacts in ethyl alcohol–water much faster than *t*-butyl chloride. In 80% ethanol at 25° in eight hours, 98% of the possible hydrogen chloride has been liberated. We tried to estimate the amount of olefin formed in this reaction as was done by Hughes and his co-workers.[9] Unfortunately, in the present case variations in the time of the bromine titration produced continuous changes in the apparent fraction of olefin, up to well over 100% of the calculated. Evidently this nonene cannot be reliably titrated with bromine. There is, of course, a possibility that all the appearance of hydrogen chloride was due to elimination and none to direct replacement of halogen. However, this seems unlikely in view of the figures in Table I, where it appears that the actual rate of replacement is much greater in *t*-amyl than in *t*-butyl chloride despite the greater molecular size of the former. The experimental figures on these two chlorides are those of Hughes and his co-workers.

TABLE I

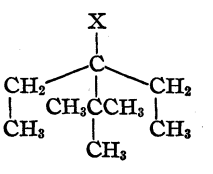
UNIMOLECULAR VELOCITY CONSTANTS AT 25° IN 80% ALCOHOL FOR THE FORMATION OF HYDROCHLORIC ACID (k_{HCl}) AND FOR SOLVOLYSIS (k_s) BY TERTIARY ALKYL CHLORIDES

Chloride	k_{HCl}	% Olefin in product	k_s
t-Butyl	0.0329	15	0.028
t-Amyl	.324	42	.19
α,α-Diethylneopentyl	.42	..	...

Another possibility to be reckoned with is that a rearrangement may have occurred in the reaction of nitrosyl chloride with 1-apocamphylamine. Past experience, and current theories, would not lead us to expect such rearrangements, and the behavior of our apocamphanol toward oxidizing and dehydrating agents seems to exclude them in its case. Nevertheless, it seemed well to make a comparison of the behavior of our chloroapocamphane with that of a similarly constituted and rather inert secondary chloride, bornyl chloride (V), which incidentally also contains a neopentyl system.

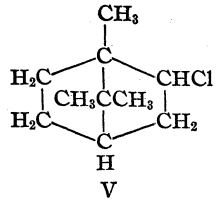


III



IV

(9) Hughes, Ingold and Shapiro, *J. Chem. Soc.*, 225 (1936).



V

At room temperature, in 75% (by volume) ethanol–water solution, neither bornyl chloride nor chloroapocamphane gave any hydrochloric acid. However, with silver nitrate, under the identical conditions of the negative experiment with chloroapocamphane, bornyl chloride lost 22% of its chlorine in five minutes and 84% in an hour. The latter figure corresponds to a bimolecular velocity constant (time in hours) for the reaction between silver nitrate and bornyl chloride of 11.25, thus certainly at least ten powers of ten greater than the corresponding constant for 1-chloroapocamphane. From all these experiments it appears that apocamphanol-1 and 1-chloroapocamphane are unique among known alcohols and saturated chlorides in their resistance to replacement of their functional groups, and that this uniqueness can be associated only with the location of these groups on the bridge-head of a bicyclic ring system.

Interpretation of Results

The reasoning out of which this work arose—that the Walden inversion is prohibited in replacement reactions among compounds of the type III—allows only positive results to be interpreted with certainty. We can now say quite definitely that no inversion, or series of inversions, need be involved in the Hofmann rearrangement of an amide or in the reaction of an amine with nitrous acid or nitrosyl chloride. All three of these reactions proceed as smoothly and rapidly when the Walden inversion is prohibited as when it is possible. It is still a question whether these reactions proceed by concerted intramolecular processes or through the intermediate formation of a practically free ion with its charge on carbon. In the case of the Hofmann rearrangement, such an ion, if formed, would carry a negative charge,[10] while the intermediate ions, if any, in the reaction of amines with nitrous acid and nitrosyl chloride would be positively charged. There are difficulties in both types of mechanism which are not resolved by the present work. In view of the considerations brought forward below, the purely intramolecular mechanism now seems the more probable for those cases of this reaction which proceed without inversion. This does not exclude the existence of a competing negative replacement reaction with inversion in compounds capable of inversion.

In the case of the reactions which fail to occur—reciprocal replacement of the hydroxyl group and halogen atom—the interpretation runs into complications. To be sure, the lack of any dehydration or elimination of hydrogen chloride is readily explained if we consider the large amount of strain which the formation of the resulting cycloolefin would necessarily entail. The impossibility of a double bond at the bridge-head of a bicyclo-[2,2,1]-heptane often has been discussed theoretically and supported experimentally.[11] Likewise, the failure of the system to rearrange into one capable of olefin formation can be correlated with the observation that the rearrangement of certain cyclic alcohols and chlorides is attended by inversion at the carbon atom originally holding the functional group.[12] The back side of carbon atom 1 in 1-apocamphanol can no more be attacked by a migrating radical or hydrogen atom than it can by an extraneous reagent, and hence the Wagner–Meerwein rearrangement is among the processes of which this compound is incapable.

With regard to the failure of replacement reactions in this alcohol and halide, the first explanation to present itself is that these reactions cannot proceed without Walden inversion, and that any racemization observed in them is ordinarily due to mobile inversions in the solvated cation (conjugate acid of the alcohol) reacting with the solvent. This may indeed be the correct explanation, but if it is it means the discarding of some very satisfactory features of the theory of the dual mechanism of solvolytic reactions of halides. Hughes and his co-workers have shown[13] that halides can be broadly divided into those in which the rate of replacement of the halogen atom by hydroxyl or alkoxyl is influenced by the concentration of the hydroxyl or alkoxyl ion, and which therefore react by a bimolecular mechanism, and those in which this rate of replacement is independent of the hydroxyl or alkoxyl ion concentra-

(10) See the discussion by Whitmore, THIS JOURNAL, **54**, 3281 (1932).

(11) For historical references, see ref. 5.

(12) Bartlett and Pöckel, THIS JOURNAL, **59**, 820 (1937); Bartlett and Bavley, *ibid.*, **60**, 2416 (1938).

(13) For a review of this field see Watson in "Annual Reports of the Chemical Society for 1938," Vol. XXXV, pp. 208–226.

tion, and which therefore may be said to react by a unimolecular or pseudo-unimolecular mechanism. Both these mechanisms are presumably possible in all halides, and in certain cases the presence of both has been demonstrated. Now, any theory which makes the attack of a nucleophilic reagent on the back side of the halogenated carbon atom necessary to the occurrence of replacement thereby postulates that the bimolecular and pseudo-unimolecular mechanisms are exactly alike except that in the former case a strongly basic ion, and in the latter case a weakly basic solvent molecule, does the attacking. It seems out of all reason that the hydroxyl ion should be the most powerful reagent for a primary chloride, but the water molecule the most powerful reagent for a tertiary chloride, as is actually observed, if the fundamental mechanism is exactly the same in both cases. The insertion of other solvent molecules in the activated complex, some of which may have an acceptor, rather than a donor, function, does nothing to resolve this difficulty since it would seem that with any halide an activated complex involving a powerful donor in the position where a donor is needed should have a lower activation energy for reaction than an otherwise identical one involving a weaker donor in the donor position.

This difficulty is avoided completely if we may assume, with Hughes and Ingold, that in the unimolecular mechanism there is no donor molecule contributing at all to the energy of the transition state, but that the rate-determining step is entirely a "pull" which removes the halogen leaving a carbonium ion.[14] Such an assumption is consistent, though not uniquely so, with observations of the catalytic effect of acceptor ions and molecules on the solvolysis of halides.[15] To make this assumption compatible with the facts about 1-chloroapocamphane, what we need is some reason why the 1-apocamphyl positive ion cannot be formed while the *t*-butyldiethylcarbonium ion can be. In this direction we have one suggestion to make.

Evidence has long been accumulating that carbonium ions either have a permanently planar arrangement of the three bonds attached to the unsaturated carbon atom, or oscillate rapidly between what may be called the *d*- and *l*-tetrahedral configurations. Recent evidence from electron diffraction[16] has shown that in the molecule of trimethylborane the boron and carbon atoms all lie in the same plane. The boron atom in this compound is the nearest analog in a stable compound to the carbon atom with an open sextet, and the situation here suggests that a permanently planar arrangement is the only possible one for any carbonium ion. If this is so, then it is to be expected that the formation of the 1-apocamphyl positive ion will be attended by considerable strain. In order to bring carbon atoms 2, 6, and 7 of the bicyclo-[2,2,2]-octane ring system into the same plane with carbon atom 1 a total strain of at least 58°24′ would be distributed among three valence angles, and for the apocamphane ring system the strain would be considerably greater. A strain of 19°28′ per CH_2 group is present in cyclobutane, and a comparison of the heat of combustion of cyclobutane with that of cyclohexane gives 7.5 kcal. per methylene group as the approximate translation of this strain into heat units. This suggests that the energy of activation for the unimolecular solvolysis of 1-chlorobicyclo-[2,2,2]-octane (assuming the ionization mechanism) should be higher than that of an acyclic analog by at least $3 \times 7.5 = 22.5$ kcal. This corresponds to a factor of more than 10^{14} in the rates of reaction at 350°K. and hence is an important enough effect to take account of the experimental observations. Incidentally, this 22.5 kcal. is the same approximate amount by which such a bicyclic compound with a double bond at the bridge-head would be more strained than an isomer with the double bond in the 2-position. Bredt's rule is thus seen to embody a high degree of probability in thermodynamic terms.

There exists, therefore, an hypothesis which would reconcile our present results with the general theory of solvolytic reactions which postulates ionization of the tertiary halide as a rate-controlling step. The evidence for this hypothesis is obviously far from complete, but we feel that the absolute rates of solvolysis of the tertiary halides in alcohol–water mixtures are not without significance in this connection. When a model of *t*-butyldiethylcarbinyl chloride is constructed out of atomic calotte models according

(14) The semiquantitative arguments recently presented by Ogg (ref. 2) against this mechanism apply only to methyl and, less strongly, to ethyl halides. These and other primary halides, of course, are the very ones which *do not* hydrolyze by the unimolecular or pseudo-unimolecular mechanism in the presence of basic ions.

(15) For example, the work of Roberts and Hammett, THIS JOURNAL, 59, 1063 (1937).

(16) Levy and Brockway, *ibid.*, 59, 2085 (1937).

to H. A. Stuart,[17] even the most favorable orientation of the atoms seems to offer little opportunity for a solvent molecule to approach within bond-forming distance of the central carbon atom on the side opposite to the halogen. If this kind of participation of the solvent is necessary to solvolysis, we should expect this compound to occupy a position intermediate between *t*-butyl chloride and 1-chloroapocamphane with respect to its ease of solvolysis. Instead, it gives no indication that mere hindrance to the back side of the central carbon atom, unattended by restriction of the bond angles, is of the slightest inhibitory influence in the solvolytic reaction. Another case in point is that of dimesitylchloromethane.[18] It is impossible to make a Stuart model of a transition state in which both the chlorine atom of this compound and the oxygen of an alcohol molecule are within bond-forming distance, and on opposite sides, of the central carbon atom, assigning to the atoms their commonly accepted interference radii. Nevertheless, the chlorine of dimesitylchloromethane is replaced by alkoxyl as readily as would be expected in a substituted benzhydryl chloride. This case is free from the possibility of an olefinic intermediate. Thus the balance of the present evidence seems to us in favor of the ionization mechanism for the solvolysis of tertiary chlorides and its reverse reaction, with the carbonium ion having a planar arrangement of its central carbon atom with the three atoms attached to it.

Experimental

dl-**Ketopinic acid** was prepared by the direct oxidation of *dl*-camphor-10 sulfochloride. This eliminates a step in the procedure of Wedekind and Weindand[19] without loss in yield. The use of racemic camphor as the starting material is advantageous, as the racemic forms of compounds in this series have better crystallizing properties than the optically active forms. The camphorsulfochloride (100 g.) was added in three portions with stirring to 1000 g. of a 10% solution of sodium carbonate, heated on the steam-bath, together with the three corresponding portions of a hot solution of 100 g. of potassium permanganate in 600 cc. of water. Heating was continued for an hour, after which the excess permanganate and manganese dioxide were destroyed with bisulfite. Long needles of ketopinic acid separated when the clear solution was cooled. The remainder of the acid was obtained by ether extraction of the cold solution. Recrystallization from water yielded 28–32 g. of the pure acid (38.4–42.7% of the theoretical) melting at 233–234°.

Anal. Calcd. for $C_{10}H_{14}O_3$: C, 65.89; H, 7.75. Found: C, 65.95, 66.20; H, 8.21, 8.03.

The reduction of ketopinic acid to apocamphane-1-carboxylic acid was carried out by both the Wolff–Kishner method[20] and the method of Clemmensen as modified by Martin.[3] The latter method is preferable for working in quantity. From 50 g. of ketopinic acid the product, after four recrystallizations from water, amounted to 28 g. (60.4%) and melted at 217–218°.

Anal. Calcd. for $C_{10}H_{16}O_2$: C, 71.39; H, 9.58. Found: C, 71.00; H, 9.53.

A mixed melting point with the acid obtained by the Wolff–Kishner method showed no depression.

Amide of Apocamphane-1-carboxylic Acid.—The acid (28 g.) was refluxed with thionyl chloride (80 g.) for one hour. After removal of the excess thionyl chloride under diminished pressure the acid chloride was taken up in dry ether and ammonia gas passed in. The yield of amide, after crystallization from ligroin, was 25.5 g. (92.1%). The melting point was 185°.

Anal. Calcd. for $C_{10}H_{17}NO$: C, 71.81; H, 10.23. Found: C, 71.67; H, 10.12.

Methyl 1-Apocamphylcarbamate.—To a solution of 7 g. of sodium in 385 cc. of methyl alcohol was added 25 g. of the amide. To the ice-cold solution 24 g. of bromine was added dropwise with stirring. The mixture was refluxed on the steam-bath for fifteen minutes, cooled, and diluted with a liter of water. A white solid precipitated which was separated by three extractions with 100-cc. portions of petroleum ether. After drying with anhydrous sodium sulfate and removal of the solvent, the urethan was obtained as an oil which crystallized on cooling. The yield was 8.3 g. (60.2%). Recrystallization from petroleum ether gave a product melting at 93–94°.

Anal. Calcd. for $C_{11}H_{19}O_2N$: C, 66.95; H, 9.71. Found: C, 66.97; H, 9.39.

1-Aminoapocamphane was obtained in 82.7% yield (8.5 g.) by refluxing the urethan (14.5 g.) with a solution of 50 g. of potassium hydroxide in 117 cc. of methyl alcohol and 33 cc. of water for forty-three hours. The product was isolated by diluting with water, extracting with petroleum ether, and purifying through the hydrochloride. The amine is very volatile and melts at 175° in a sealed tube.

Anal. Calcd. for $C_9H_{17}N$: C, 77.64; H, 12.28. Found: C, 77.69; H, 12.79.

The hydrochloride began to discolor at 235–240°, but did not melt below 320°.

N-Acetyl-1-apocamphylamine crystallizes from ligroin in long, slender needles melting at 132°.

Anal.[20a] Calcd. for $C_{11}H_{19}ON$: C, 72.88; H, 10.56. Found: C, 73.09; H, 10.79.

After refluxing 0.7 g. of this amide with 15 g. of potassium hydroxide in 25 cc. of 80% aqueous ethyl alcohol for twenty-four hours, we recovered 0.6 g. (85.7%) of the amide. There was an odor of the amine, but none could be isolated.

(17) Stuart, *Z. physik. Chem.*, **27B**, 354 (1934). Models of this type are now obtainable from the Fisher Scientific Co.

(18) Nauta and Wuis, *Rec. trav. chim.*, **56**, 535 (1937).

(19) Wedekind and Weindand, *Ber.*, **55**, 946 (1922).

(20) Wedekind, *ibid.*, **57**, 664 (1924).

(20a) Starred analyses (*) were performed by H. S. Wight.

N-Benzoyl-1-apocamphylamine melts at 112° after crystallization from ligroin.

Trimethylacetamide, m. p. 154–156°, was prepared in 73.5% yield by the procedure of Whitmore and Langlois.[21]

***t*-Butylamine,** b. p. 46.4°, was prepared in 64% yield (as the hydrochloride) by the action of aqueous sodium hypobromite on the amide at 0°.

N-*t*-Butylacetamide, prepared from the amine and acetic anhydride, melted at 97°, was volatile with steam and very hygroscopic. A mixture of 25 cc. of a 25% aqueous solution of potassium hydroxide and 2.32 g. of the amide was heated to reflux in an apparatus with a trap for collecting vapors of the amine which might escape. After twenty and one-half hours 1.7 g. of the amide was recovered and 0.11 g. of *t*-butylamine hydrochloride was isolated from the trap.

Reaction of 1-Aminoapocamphane with Nitrous Acid.—In dilute solution no reaction of 1-aminoapocamphane with nitrous acid could be detected even on long standing at room temperature. In an experiment carried out at 80°, in which the nitrogen evolved could be estimated quantitatively, 0.0039 mole of amine hydrochloride was used, 0.0021 mole was recovered, and 0.0018 mole of nitrogen was evolved (calcd., 40.30 cc.; found, 40.00 cc., at S. T. P.). The apocamphanol-1 isolated from this experiment amounted to 0.0011 mole.

Apocamphanol-1.—To a solution of 5 g. of 1-apocamphylamine in 70 cc. of 10% sulfuric acid (five times the calculated amount) 5 g. of sodium nitrite (twice the calculated amount) in concentrated aqueous solution was added. When the vigorous reaction had abated, the reaction flask was warmed for ten to fifteen minutes on the steam-bath. After cooling, the product was isolated by ether extraction and recrystallization from petroleum ether. The yield was 1.58 g. (66.6% of the unrecovered material) of silky white needles melting at 161–162° in a sealed tube and subliming readily.

*Anal.** Calcd. for $C_9H_{16}O$: C, 77.03; H, 11.50. Found: C, 76.80; H, 11.44.

By making the mother liquor from the diazotization alkaline and extracting with ether, 2.63 g. of the free amine was recovered.

1-Apocamphyl *p*-toluenesulfonate, crystallized from 50% ethanol, melts at 93°.

*Anal.** Calcd. for $C_{16}H_{22}O_3S$: C, 65.27; H, 7.53. Found: C, 65.36; H, 7.52.

Behavior of Apocamphanol-1 toward Hydrogen Bromide.—Dry hydrogen bromide was passed into a solution of 1 g. of the alcohol in 75 cc. of dry ether, cooled in an ice-bath. Evaporation after half an hour yielded a yellow oil from which crystals slowly deposited. Both the oil and the crystals were insoluble in petroleum ether, but in contact with water a white solid was formed immediately which proved identical with the alcohol and amounted to 0.7 g.

In another experiment, hydrogen bromide was passed into a petroleum ether solution of the alcohol for two hours. After several hours of standing the oil which was at first deposited solidified. By decantation of the mother liquor the solid residue of brittle crystals was isolated. These fumed strongly in air and melted at 83–84°. A further crop was deposited slowly from the mother liquor.

Anal. Calcd. for $C_{18}H_{33}O_2Br$: Br, 22.14. Found: Br, 24.46.

The sample was stored in a desiccator over anhydrous calcium chloride. The melting point rose from day to day, and after several weeks it had reached 157–160° and this melting point was not lowered by mixture with apocamphanol-1. In contact with water, this alcohol was immediately produced, as shown by a mixed melting point.

Behavior of Apocamphanol-1 toward Phosphorus Pentachloride.—A solution of 1 g. of the alcohol in 40 cc. of petroleum ether (b. p. 20–40°) was treated with 2 g. of phosphorus pentachloride. The mixture was allowed to stand overnight in a glass-stoppered Erlenmeyer flask and was then washed carefully with ice water and the petroleum ether solution was dried and evaporated. Since we expected to get the chloride, the solid residue was next sublimed. The sublimed material melted unreliably between 157 and 168°.

*Anal.** Calcd. for $C_{18}H_{33}O_2Cl$: C, 68.21; H, 10.49; Cl, 11.19. Found: C, 67.79; H, 10.49; Cl, 11.04.

An attempt to determine the molecular weight of this substance by the Rast method was unsuccessful, since no depression of the melting point of camphor was obtained.

Nitrosyl Chloride.—Dry sulfur dioxide was passed for several hours into 150 cc. of fuming nitric acid cooled in ice. The resulting crystalline mass was freed of adhering liquid by suction filtration and stored in a desiccator over sulfuric acid. Equivalent amounts of this nitrosylsulfuric acid and sodium chloride were warmed gently and the nitrosyl chloride condensed in a U-tube surrounded by dry-ice. A stream of dry nitrogen was passed through this liquid to remove as much dissolved hydrogen chloride as possible. The nitrosyl chloride was stored in the dark.

1-Chloroapocamphane.—A solution of 5 g. of 1-aminoapocamphane in 100 cc. of dry ether was cooled below −10° in a 250-cc. three-necked flask fitted with a mercury-sealed stirrer, dropping funnel, and gas exit tube for collecting the gaseous products of the reaction over water. An ethereal solution of nitrosyl chloride was added dropwise until the orange-yellow color of the reagent persisted and nitrogen ceased to be evolved. The volume of nitrogen collected was roughly estimated at between 450 and 500 cc. When the reaction mixture had come to room temperature a little cold water was added to dissolve the amine hydrochloride precipitated by the hydrogen chloride remaining in the reagent. The ether layer was removed, dried, and concentrated. The yellow, semi-solid residue was taken up in 25 cc. of low-boiling petroleum ether and extracted with three 5-cc. portions of 95% sulfuric acid. The petroleum ether solution was then washed with cold water, dried with sodium sulfate, and concentrated. White crystals (1.7 g.) were obtained melting at 154–156°. Mixture with apocamphanol-1 depressed the melting point to 145–148°.

Anal. Calcd. for $C_9H_{15}Cl$: C, 68.13; H, 9.53; Cl, 22.35. Found: C, 67.71; H, 9.72; Cl, 21.95.

1-Aminoapocamphane (1.8 g.) was recovered from the aqueous extract from the original reaction by the addition of sodium hydroxide and extraction with ether. The yield

(21) Whitmore and Langlois, THIS JOURNAL, **54**, 3438 (1932).

of 1-chloroapocamphane, based upon the amount of amine consumed, was 45% of the theoretical. Its great volatility may have been responsible for some loss in isolation.

Attempted Hydrolysis of 1-Chloroapocamphane.—A solution of 0.096 g. of the chloride and 1.5 g. of potassium hydroxide in 5 cc. of 80% ethyl alcohol by volume was refluxed for twenty-one hours. The solution became discolored. It was diluted with water and extracted with several portions of petroleum ether. The aqueous extract was acidified with pure nitric acid and an excess of 10% silver nitrate solution added. A brownish opalescence was produced. After standing for thirty-six hours the mixture was filtered, yielding 0.0256 g. of solid having the appearance of discolored glass. This was digested with concentrated aqueous ammonia and again filtered. A colorless glassy precipitate remained, weighing 0.0221 g., which was evidently not silver chloride. These residues were dried at 120°. Acidification of the ammoniacal solution gave a precipitate weighing 0.0020 g. Extraction of the petroleum ether solution with concentrated sulfuric acid removed no organic matter which could be precipitated by dilution; hence no detectable amounts of alcohol or ether were produced. From the petroleum ether extract 0.067 g. of unchanged chloride was recovered, which depressed the melting point of the alcohol and not that of the chloride.

Behavior of 1-Chloroapocamphane toward Silver Nitrate.—A solution of 0.1 g. of the chloride and 0.54 g. of silver nitrate in 2 cc. of water and 7 cc. of absolute ethyl alcohol was refluxed for forty-eight hours. At the end of this time the solution was still perfectly clear, and remained free of opalescence on cooling to room temperature. By the usual procedure 60% of the chloride was recovered and its identity checked by mixed melting points with both pure 1-chloroapocamphane and apocamphanol-1.

Behavior of Bornyl Chloride toward Silver Nitrate.—A solution of 0.10 g. of bornyl chloride and 0.54 g. of silver nitrate in 2 cc. of water and 7 cc. of absolute ethyl alcohol was refluxed for a measured length of time and the precipitate of silver chloride collected on a sintered glass funnel and weighed. Three such samples were run for different lengths of time, with the following results.

Weight of bornyl chloride	Time of reflux, min.	Weight of AgCl	% reaction
0.10	5	0.0182	22
.1013	10	.0256	30
.1021	60	.0711	84

An approximate calculation of the bimolecular velocity constant k, neglecting any heterogeneous reaction or autocatalysis, on the basis of the sixty minute point, gives

$$k = \frac{2.3}{0.3542} \log_{10} \frac{0.3648 \times 0.0658}{0.0106 \times 0.420} = 11.25$$

time being expressed in hours.

2,2-Dimethyl-3-ethylpentanol-3 (*t*-butyldiethylcarbinol) was prepared from ethylmagnesium bromide and trimethylacetyl chloride, as described by Whitmore and coworkers.[22] The yield was supplemented by oxidizing the *t*-butylethylcarbinol produced in the reaction and treating the ketone again with the ethyl Grignard reagent. In the preparation of trimethylacetyl chloride use was made of the excellent method described by Brown.[23] The *t*-butyldiethylcarbinol, obtained in 22.9% yield from the direct reaction of Grignard reagent and acid chloride, boiled at 118–119.6° under 160 mm. pressure.

2,2-Dimethyl-3-ethyl-3-chloropentane.—Dry hydrogen chloride was passed into 20 g. of the carbinol at 0° until no further increase in the water layer was apparent. The water layer was then removed and the organic layer again saturated with hydrogen chloride. After washing and drying of the chloride it was distilled, giving 12.5 g. of colorless liquid boiling at 53–54° under 6 mm. pressure.

Anal. Calcd. for $C_9H_{19}Cl$: Cl, 21.97. Found: Cl, 21.54.

In an earlier preparation the distillation of the product under 150 mm. pressure yielded a considerable amount of olefin, boiling at 80.6–81° (150 mm.).

*Anal.** Calcd. for C_9H_{18}: C, 85.64; H, 14.36. Found: C, 85.09; H, 14.46.

Hydrolysis of the Acyclic Chloride.—A kinetic study of the hydrolysis at 25° in 80% ethyl alcohol by volume was carried out in order to have results comparable with those in the literature on other tertiary chlorides. The chloride (0.6220 g.) was weighed into a glass-stoppered Erlenmeyer flask and diluted to 50 cc. with the solvent, which had already been brought to temperature in a thermostat bath. Five-cc. portions were removed at suitable intervals, swirled with carbon tetrachloride, and the acid in the aqueous layer titrated with sodium hydroxide solution. The logarithms of the molar concentrations of the remaining chloride were plotted against time, yielding a fairly good straight line. From the slope of this line the unimolecular velocity constant was found to be 0.4206 (time in hours).

Summary

Apocamphane-1-carboxylic acid amide has been converted by the Hofmann reaction into 1-aminoapocamphane. Although the amino group is so situated that it cannot possibly be replaced in any reaction involving a Walden inversion, this compound readily reacts with nitrous acid to yield apocamphanol-1 and with nitrosyl chloride to yield 1-chloroapocamphane. This alcohol and chloride cannot be interconverted. The alcohol forms loose molecular compounds with hydrogen chloride and hydrogen bromide, while the 1-chloroapocamphane withstands forty-eight hours of boiling with silver nitrate in water–alcohol solution without producing any opalescence.

It is concluded from the reactions of the amide and amine that the Walden inversion, in which one negative substituent replaces another on the opposite side of the same carbon atom, is not a universal necessity for the occurrence of a "negative substitution" reaction.

(22) Whitmore, Meyer, Pedlow and Popkin, THIS JOURNAL, **60**, 2788 (1938).

(23) H. Brown, *ibid.*, **60**, 1325 (1938).

The inertness of the bridge-head hydroxyl group and chlorine atom may be interpreted as indicating either (1) that a Walden inversion is absolutely necessary in the replacement of these groups, or (2) that in a carbonium ion the central carbon atom and the three atoms forming bonds with it must be coplanar. Certain drawbacks to the former of these interpretations are pointed out.

CAMBRIDGE, MASSACHUSETTS
RECEIVED SEPTEMBER 16, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NEW HAMPSHIRE]

Synthesis of α-2-Methoxyphenyl-β,β,β-triphenylethane

BY H. A. IDDLES, K. S. FRENCH AND E. F. MELLON

In 1932 Parsons and Porter[1] reported a synthesis of the methyl ether of α-2-hydroxyphenyl-β,β,β-triphenylethane (m. p. 172°) and used the product in establishing the probable structure for the methylation product (m. p. 172°) which they had prepared from Schorigin's[2] so-called "kryptophenol." Schorigin had obtained this rearrangement product as a by-product during the synthesis of triphenylmethyl *o*-tolyl ether and by a direct rearrangement of the ether when it was heated with metallic sodium. He postulated a structure, α-2-hydroxyphenyl-β,β,β-triphenylethane, from a somewhat analogous case in which benzyl *o*-tolyl ether was rearranged to give *o*-hydroxydibenzyl[2] by heating with metallic sodium. Van Alphen[3] also reported results on the preparation and rearrangement of this triphenylmethyl *o*-tolyl ether but gave no proof of structure of the product obtained.

However, the work of Boyd and Hardy[4] has questioned the unusual and special interpretation of Schorigin[2,5,6] which postulates the migration of the triphenylmethyl group to the side chain of *o*-cresol. They distilled the triphenylmethyl rearrangement products from the three cresols and phenol with soda lime, obtaining triphenylmethane in each case, and warmed each product with sulfuric acid, producing triphenylcarbinol. Consequently they conclude there is no evidence for postulating a different constitution for the ortho derivative.

To aid in clarifying these opposing points of view, further syntheses of "kryptophenol" as its methyl ether have been carried out. This seemed particularly desirable since the one direct synthesis of Parsons and Porter[1] has one unusual step in which the hydrolysis of the Grignard addition compound gave a hydrocarbon instead of the expected secondary alcohol.

For use in two separate syntheses, *o*-methoxybenzyl chloride was prepared by methylation of salicylic acid, electrolytic reduction to methoxybenzyl alcohol and treatment of the alcohol with thionyl chloride. In the first method the methoxybenzyl chloride was treated with triphenylmethylsodium in an atmosphere of nitrogen according to the procedure of Schlenk and Marcus,[7] who similarly produced unsymmetrical tetraphenylethane from triphenylmethylsodium and benzyl chloride. The product melted at 142–143°. In a second sequence a Grignard reagent was prepared from the *o*-methoxybenzyl chloride and this was coupled with triphenylchloromethane following an analogous reaction of Gomberg and Cone,[8] who reported an almost quantitative yield of unsymmetrical tetraphenylethane from benzylmagnesium bromide and triphenylchloromethane. The product in this case melted at 140–142° and there was no depression in a mixed melting point of the two synthetic products. However, neither agreed with the m. p. of 172° recorded by Parsons and Porter[1] for their synthetic product and a depression in melting point occurred when each of these synthetic samples was mixed with the methylated rearranged product of m. p. 162–163°.

The non-agreement between these synthetic samples and the methylated rearranged compound supports the interpretation of mechanism of Boyd and Hardy[4] which maintains that the original rearrangement of the triphenylmethyl group involves a ring position instead of the side

(1) Parsons and Porter, THIS JOURNAL, **54**, 363 (1932).
(2) Schorigin, *Ber.*, **58**, 2028 (1925); **59**, 2502 (1926).
(3) Van Alphen, *Rec. trav. chim.*, **46**, 287 (1927).
(4) Boyd and Hardy, *J. Chem. Soc.*, 630 (1928).
(5) Porter, "Molecular Rearrangements," Chemical Catalog Co., New York, N. Y., 1928, p. 118.
(6) Houben, "Die Methoden der organischen Chemie," Vol. III, 1930, p. 184.
(7) Schlenk and Marcus, *Ber.*, **47**, 1664 (1914).
(8) Gomberg and Cone, *ibid.*, **39**, 1461 (1906).

chain of *o*-cresol as first postulated by Schorigin.[2] Further work is in progress to determine the actual course of this rearrangement.

Experimental

Preparation of Rearranged Compound from *o*-Cresol.—Approximately the condensation method of Baeyer and Villiger[9] was followed in which 15 g. of triphenylcarbinol, 50 g. of *o*-cresol and 360 g. of glacial acetic acid were mixed and 75 g. of concentrated sulfuric acid was gradually added. After standing for two days or longer, an orange precipitate appeared whereupon the reaction mixture was poured into water. The crystals and oily layer were extracted with ether and this extract repeatedly washed with 10% sodium hydroxide solution. After drying and evaporation of the ether, the residue was taken up in ligroin (b. p. 70–90°) and this solution was extracted with Claisen's solution (equal parts of 50% aqueous potassium hydroxide and methyl alcohol). Upon acidification of the alkaline extract, the product precipitated and was purified by recrystallization from ethyl alcohol. The yields of colorless product (m. p. 182–183°) averaged 70%.

Preparation of Methyl Ether of Rearranged Compound.—Ten grams of the phenolic rearranged compound was suspended in a solution of 250 ml. of 2 *N* sodium hydroxide and 37.5 g. of dimethyl sulfate was added with constant stirring. After stirring for three or four hours, 10 g. of sodium hydroxide was added and the mixture was refluxed for one hour to hydrolyze excess dimethyl sulfate. The reaction mixture was then cooled, neutralized with hydrochloric acid, and the insoluble material filtered from the aqueous solution and dried. The dried solid was dissolved in a mixture of 10% ether and 90% ligroin (70–90°) and the solution extracted with Claisen's solution to remove unchanged phenolic compound. The residue from evaporation of the dried ether layer was recrystallized from alcohol, yielding 3.6 g. of product of m. p. 162–163°. Since 5.2 g. of unchanged phenol was recovered, this was a yield of 73%.

Anal. Calcd. for $C_{27}H_{24}O$: C, 88.97; H, 6.64. Found: C, 88.93; H, 6.66.

This product agrees satisfactorily with the product obtained by Boyd and Hardy[4] by two independent syntheses and to which they assign the m. p. 165°. However, there is considerable discrepancy between these two closely agreeing melting point values and that of 172° reported by Parsons and Porter,[1] who methylated by means of methyl iodide and silver oxide.

Preparation of *o*-Methoxybenzoic Acid.—One hundred grams of salicylic acid was methylated according to the directions of Graebe,[10] producing 98.6 g. or a 89.5% yield of methoxybenzoic acid, m. p. 96–98°.

Electrolytic Reduction of *o*-Methoxybenzoic Acid to *o*-Methoxybenzyl Alcohol.—The *o*-methoxybenzoic acid was electrolytically reduced according to the directions of Tafel[11] and Mettler.[12] *o*-Methoxybenzyl alcohol, 49.2 g., was recovered, boiling from 120–122° at 12 mm. pressure, a yield of 54.7%.

(9) Baeyer and Villiger, *Ber.*, **35**, 3013 (1902).
(10) Graebe, *Ann.*, **139**, 137 (1866).
(11) Tafel, *Ber.*, **33**, 2209 (1900).
(12) Mettler, *ibid.*, **39**, 2933 (1906).

Preparation of *o*-Methoxybenzyl Chloride.—*o*-Methoxybenzyl alcohol, 34 g., in 50 ml. of ether was dropped into 50 g. of concentrated hydrochloric acid in 50 ml. of ether according to Quelet and Allard.[13] From the reaction 27.5 g. of product was obtained, boiling at 111–113° at 14 mm. pressure.

Preparation of α-2-Methoxyphenyl-β,β,β-triphenylethane.—A Grignard reagent was prepared by adding 10.7 g. of freshly distilled *o*-methoxybenzyl chloride, dissolved in 300 ml. of anhydrous ether, to 1.58 g. of magnesium turnings. After refluxing and stirring for four hours, the solution was decanted from a trace of unreacted magnesium and a solution of 6 g. of triphenylchloromethane in 50 ml. of dry benzene was added. This mixture was refluxed for two hours, causing the formation of a yellow precipitate.

To prevent subsequent formation of triphenylcarbinol from the hydrolysis of any unreacted triphenylchloromethane with the resulting contamination of the product, 5 g. of zinc dust was added to the reaction mixture to form free triphenylmethyl. After filtering the solution from the zinc, oxygen was passed through the mixture, but no triphenylmethyl peroxide precipitated, indicating complete reaction of the triphenylchloromethane with the Grignard reagent.

The ether–benzene solution was then evaporated to dryness on the steam-bath, leaving a dark oil which was recrystallized from alcohol. Three grams of pure crystals was obtained, m. p. 140–142°. This material was not identical with the methyl ether prepared from the rearranged triphenylmethyl ether of *o*-cresol, m. p. 162–163°.

Anal. Calcd. for $C_{27}H_{24}O$: C, 88.97; H, 6.64. Found: C, 88.79; H, 6.68.

Reaction between Triphenylmethylsodium and *o*-Methoxybenzyl Chloride.—The triphenylmethylsodium was prepared by the method of Schlenk and Ochs[14] from 200 g. of 2% sodium amalgam and 10 g. of triphenylchloromethane suspended in ether and protected by an atmosphere of nitrogen. When the triphenylmethylsodium had formed, as evidenced by the deep red color, 5.6 g. of *o*-methoxybenzyl chloride, dissolved in ether, was added. The mixture was allowed to stand until the red color disappeared. It was aerated for several hours with dry air to convert any free triphenylmethyl to the peroxide, then filtered and the ether evaporated. A heavy viscous brown oil remained which, after recrystallization from alcohol, gave 4 g. Several recrystallizations gave 2.2 g. of colorless crystals, m. p. 142–143°. A mixed melting point proved this product was identical with that prepared by the Grignard reaction. It was not identical with the methylated rearranged compound.

Anal. Calcd. for $C_{27}H_{24}O$: C, 88.97; H, 6.64. Found: C, 88.48; H, 6.87.

Summary

1. α-2-Methoxyphenyl-β,β,β-triphenylethane, m. p. 142–143°, has been prepared by two direct syntheses. This compound is not identical with the methylated rearranged compound obtained

(13) Quelet and Allard, *Bull. soc. chim.*, [v] **4**, 1468 (1937).
(14) Schlenk and Ochs, *Ber.*, **49**, 608 (1916).

from rearrangement of the triphenylmethyl ether of *o*-cresol, m. p. 162–163°.

2. This study supports the evidence of Boyd and Hardy,[4] who conclude the migrating radical has not entered the side chain when triphenylmethyl *o*-tolyl ether undergoes rearrangement.

DURHAM, NEW HAMPSHIRE
RECEIVED SEPTEMBER 28, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY]

The Utilization of Aliphatic Nitro Compounds. (I) The Production of Amines and (II) The Production of Oximes[1]

BY KENNETH JOHNSON WITH ED. F. DEGERING

The nitroparaffins were studied by a number of investigators following their first production by Victor Meyer[2] in 1872. The preparation of these compounds, however, was such that not very large amounts were available for experimentation and in many cases the investigators were not very thorough. With the work of Hass, Hodge and Vanderbilt,[3] begun in 1930, a process was perfected whereby the paraffin hydrocarbons were nitrated directly, making the nitroparaffins available at a lower cost and in greater abundance. The possibility of industrial development of this process brought about renewed interest in the study of nitroparaffins and their derivatives and a broad investigation was begun. The work reported here is a part of that much larger work.

I. Reduction of Nitroparaffins to Amines

A number of investigators[3,4] have reported the reduction of nitroparaffins with different reagents and under different experimental conditions, but in every case the yields of isolatable products have been small.

(a) **Reduction with Iron and Hydrochloric Acid.**—After several preliminary experiments the following apparatus and procedure were adopted: a three-necked flask is equipped with a mercury-seal stirrer (motor driven) and a reflux condenser. A trap containing standard hydrochloric acid is arranged to absorb any amines which might pass through the condenser. To 35 g. of 40-mesh iron filings are added 75 ml. of water and 10 ml. of concd. hydrochloric acid. After the evolution of hydrogen has stopped, one-sixth of a mole of the nitroparaffin is added and, with rapid stirring, the mass is heated at 100° for thirteen to fifteen hours. The solution is then made alkaline and the amine distilled out into standard hydrochloric acid. The conversion is calculated from the amount of hydrochloric acid required for neutralization. In another series of experiments, 1 g. of ferric chloride was added to the reaction mixtures.

The reaction mixture was evaporated to dryness, and the hydrochlorides of the amines extracted with butanol. No ammonium chloride remained as a residue. The amine hydrochlorides were further identified by titration with silver nitrate, from which data the molecular weight was calculated, and by a Van Slyke determination of amino nitrogen.

(b) **Catalytic Hydrogenation.**—These nitroparaffins were also reduced with hydrogen to give yields of 92–98% of the theoretical, by dissolving 0.25–0.33 mole of nitroparaffin in 175 ml. of methyl or ethyl alcohol and treating with hydrogen in a Parr bomb under 6–110 atmospheres over 7.5 g. of Raney nickel[5] for two to five hours, at 40–50°, with rocking. The non-formation of ammonia and the identity and yields of the amines were established as in the reductions with iron and hydrochloric acid.

Other catalysts were studied, but the results were unsatisfactory.[6]

The following nitro compounds were reduced in this way: nitromethane, nitroethane, 1- and 2-nitropropane, 1- and 2-nitrobutane, and 1- and 2-nitro-2-methylpropane. Percentage conversions of 82–94% were obtained in the absence of, and 93–97% in the presence of, ferric chloride. The titration gave the calculated molecular weight with an average deviation of only 1% and with an extreme deviation of 2.3%, while the amino nitrogen was found in every case to be either the exact amount required by the formula or within 1% thereof.

II. Reduction of Nitroparaffins to Oximes

The partial reduction of primary and secondary nitroparaffins produces oximes.[7,8] A number of reducing agents were tried, but the procedure adopted is: to 100 ml. of glacial acetic acid and 15 ml. of 1-nitropropane, add 35 g. of zinc dust, stir, and reflux for six hours. Hydrolyze the oxime by adding 25 ml. of water, then 5 ml. of concd. sulfuric acid, and heating. Distil the aldehyde and

(1) Abstracted from a portion of a Thesis submitted to the Faculty of Purdue University by Kenneth Johnson in partial fulfilment of the requirements for the degree of Doctor of Philosophy, June, 1937. This research project was sponsored by The Commercial Solvents Corporation under the general supervision of Jerome Martin and H. B. Hass. Presented before the Division of Industrial Engineering Chemistry of the American Chemical Society at the Baltimore meeting, April 3–7, 1939.

(2) Victor Meyer, *Ber.*, **5**, 203, 514, 1029, 1034 (1872).

(3) Hass, Hodge and Vanderbilt, *Ind. Eng. Chem.*, **28**, 339 (1936).

(4) Meyer, *Ann.*, **171**, 1 (1874); Kahn and Meyer, *Chem. Abs.*, **21**, 3205 (1927).

(5) Covert and Adkins, THIS JOURNAL, **54**, 4116 (1932).

(6) Adkins and Connor, *ibid.*, **53**, 1091 (1931).

(7) Konowaloff, *J. Chem. Soc.*, **76**, 733 (1899).

(8) Ponzio, *ibid.*, **82**, 334 (1902).

identify by its reaction with $H_2NOH \cdot HCl$. The conversion to aldehyde is 43%.[9]

Summary

All the nitroparaffins available from the nitration of propane, butane, and isobutane have been reduced to the corresponding amines by the use of iron and hydrochloric acid and catalytic hydrogenation. These processes produce good yields of easily purified products and require only simple technique. The results indicate that primary, secondary, and tertiary nitroparaffins can be reduced to give almost quantitative yields of the corresponding amines.

The conversion of nitroparaffins to oximes gives, in general, rather low yields because of the simultaneous formation of the amines.

LAFAYETTE, INDIANA RECEIVED APRIL 28, 1939

(9) Pemberton, Card and Craven, *J. Soc. Chem. Ind.*, **54**, 163T (1935).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF SWARTHMORE COLLEGE]

Preparation and Cyclization of Monoacylethylenediamines. II

BY SAMUEL R. ASPINALL

It has been shown[1] that the best method of preparing 2-substituted-4,5-dihydroimidazoles is by dehydrating monoacylated ethylenediamines.

$$RCOOEt + NH_2CH_2CH_2NH_2 \longrightarrow RCONHCH_2CH_2NH_2 \xrightarrow{-H_2O} RC\begin{matrix}N{-}CH_2\\ \diagup\quad\ \diagdown\\ NHCH_2\end{matrix}$$

The investigation herein reported was undertaken to determine the extent of the applicability of this method. As a result of this and previous work[1] it is shown that an ester may be converted to the corresponding 4,5-dihydroimidazole in an over-all yield of about 75% when R is any one of such divergent groups as: CH_3—, C_2H_5—, *n*-C_5H_{11}—, $(C_2H_5)_2CH$—, (iso-C_5H_{11})$_2$CH—, C_6H_5—, *p*-$CH_3C_6H_4$—, or $C_6H_5CH_2$—. The yield of 2-diphenylmethyl-4,5-dihydroimidazole from ethyl diphenylacetate was considerably lower. Because reaction conditions for this series of experiments were more or less arbitrarily fixed in order to give comparable data, the yield reported for any given experiment is not necessarily the best obtainable.

Two slight changes in the procedure heretofore employed[1] have resulted in simplification and generally higher yields. (a) The reaction of ethylenediamine and esters of six or more carbon atoms which are branched in the alpha position requires higher temperatures than heretofore used. This effect is presumably due to the condition usually described as steric hindrance. (b) If the mixture of monoamide and diamide resulting from the reaction of ethylenediamine and an ester is treated in the usual way with lime, the yields are somewhat higher than those obtained by dehydrating the isolated monoamide with lime. This fact is in accord with earlier observations[2] that ethylenediamides yield some 4,5-dihydroimidazole when heated at a high temperature with acid binding materials.

A typical experiment is now carried out as follows: **2-diethylmethyl-4,5-dihydroimidazole.** Forty-eight grams (1/3 mole) of ethyl diethylacetate and 60 g. (1 mole) of ethylenediamine are heated at 215° for twenty-four hours, and the low boiling material consisting of ethyl alcohol and excess ethylenediamine removed at diminished pressure. The remaining 39 g. of monoamide and diamide is heated with 94 g. (5/3 mole) of calcium oxide at 225° for fifteen hours in an atmosphere of nitrogen. The organic products are extracted from the lime with alcohol, the solvent removed, and the product distilled at low pressure. 2-Diethylmethyl-4,5-dihydroimidazole, which distils as a pure white oil, solidifies immediately on cooling and is obtained as glistening white needles from petroleum ether.

It was earlier[1] pointed out that although the lower aliphatic monoacylethylenediamines are distillable under ordinary laboratory vacuum conditions, the corresponding aromatic derivatives are not, because the latter dehydrate to the 4,5-dihydroimidazole configuration at a temperature below that required for their distillation. It has now been found the behavior of the higher and phenylated aliphatic derivatives upon distillation is somewhat variable and depends upon structural features. (a) A higher aliphatic monoacylethylenediamine containing an alkyl group branched in the alpha position may be smoothly distilled at constant temperature to yield a distillate whose purity and homogeneity were demonstrated by quantitative conversion to simple derivatives. Presumably the steric factors which inhibit the initial reaction between the ester and

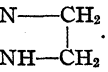
(1) Hill and Aspinall, THIS JOURNAL, **61**, 822 (1939).

(2) Chitwood and Reid, THIS JOURNAL, **57**, 2424 (1935).

TABLE I

REACTION OF ESTERS WITH ETHYLENEDIAMINE, CYCLIZATION TO 4,5-DIHYDROIMIDAZOLES AND PROPERTIES OF THEIR DERIVATIVES

Reacting ethyl ester	Product	M. p., °C. corr.	B. p., °C.	Mm.	Yield, %	% N Calcd.	% N Kjeld.[a]	Picrate[b] M. p., °C. corr.	Picrate[b] % N Calcd.	Picrate[b] % N Kjeld.[a]	Hydrochloride[c] M. p., °C. corr.	Hydrochloride[c] % N Calcd.	Hydrochloride[c] % N Kjeld.[a]	Phenylureido derivative[d] M. p., °C. corr.	Phenylureido derivative[d] % N Calcd.	Phenylureido derivative[d] % N Kjeld.[a]
Caproate	C_5H_{11}—$C_3H_7N_2O$[e]	...	...	.	80[f]	...	...	93	18.09	18.16	141	14.40	14.47	171	15.16	15.22
Caproate	C_5H_{11}—$C_3H_5N_2$	54[g]	108	7	75	20.00	19.98	127[h]	18.97	18.89	[i]	...	...	...	...	...
Diethylacetate	$(C_2H_5)_2CH$—$C_3H_7N_2O$	...	113	7	60	...	...	123	18.09	18.09	133	14.40	14.44	179[k]	15.16	15.26
Diethylacetate	$(C_2H_5)_2CH$—$C_3H_5N_2$	86	97	9	70	20.00	19.98	106	18.97	19.02	245	15.86	15.90	133	16.22	16.20
Diisoamylacetate	$(C_5H_{11})_2CH$—$C_3H_5N_2$	103	123	6	75	12.50	12.48	125	15.45	15.44	[i]	...	...	82[j]	12.24	12.22
Phenylacetate	$C_6H_5CH_2$—$C_3H_7N_2O$[e]	...	...	.	80[f]	...	...	133	17.20	17.21	142	13.05	13.16	191	14.14	14.09
Phenylacetate	$C_6H_5CH_2$—$C_3H_5N_2$	68	134	6	75	17.50	17.45	149	18.00	17.94	174	17.94	17.96	...	...	...
Diphenylacetate	$(C_6H_5)_2CH$—$C_3H_5N_2$	137	[l]	.	35	11.86	11.90	185	15.05	15.00	[i]	...	...	...	...	...

[a] Reported analytical results are the average of two determinations whose maximum absolute deviation from theoretical is less than 0.15%. [b] Picrates are made in the usual way in water, alcohol or dilute alcohol and recrystallized from alcohol or dilute alcohol. [c] All hydrochlorides are made by passing dry hydrogen chloride into an absolute alcohol–absolute ether solution of the base, and are recrystallized from absolute alcohol or absolute alcohol–absolute ether mixtures. All hydrochlorides are extremely soluble in water, warm alcohol and acetone. Insoluble in absolute ether. [d] Usually made in benzene and recrystallized from alcohol or acetone. [e] Reaction temperature, 100°. Isolated by solvent extraction. See Hill and Aspinall, THIS JOURNAL, **61**, 822 (1939). [f] Crude product. [g] Literature 38.8°, *ibid.*, **57**, 2424 (1935). [h] Literature 128°, *ibid.*, **57**, 2424 (1935). [i] The spaces so marked indicate that the hydrochloride is unsuitable for characterization because it is liquid or excessively hygroscopic. In these cases the hydrochlorides may be converted to well-defined chloroplatinates which may be accurately analyzed for platinum by ignition, provided extreme care is exercised to prevent spattering. The derivatives have no sharp melting points but char and melt with decomposition at a temperature dependent upon the rate of heating. A typical analysis: Calcd. for (iso-$C_5H_{11})_2CHC$  $\cdot{}^1/_2H_2PtCl_6$: Pt, 22.78; found 22.75. [j] Made in and recrystallized from petroleum ether. [k] This derivative apparently exists in dimorphic forms. When a sample is slowly heated there is a definite slight shrinking at 150° (corr.) after which no further change occurs until the sample melts sharply at 179° (corr.). If, however, a sample is introduced into a melting point bath at any temperature between 150 and 179° there is an immediate and complete fusion followed in a few seconds by an equally rapid and complete solidification, after which no change is evident until the sample permanently remelts at 179°. A sample once melted always remelts at 179°. [l] Undistillable. After extraction with alcohol 2-diphenylmethyl-4,5-dihydroimidazole was isolated as follows: the alcohol was removed the solid residue dissolved in dilute hydrochloric acid, boiled with charcoal, filtered, and reprecipitated with sodium carbonate. The white product so obtained was recrystallized from acetone.

ethylenediamine likewise prevent cyclization to the 4,5-dihydroimidazole configuration. (b) On the other hand, a monoacylethylenediamine derived from an ester containing five or more carbon atoms and not branched in the alpha position does undergo a slow dehydration at the temperature required to distil it at ordinary laboratory vacuum or if too high reaction temperature is used. When monocaproylethylenediamine is distilled, the temperature is originally at 135° (7 mm.), but slowly falls during the course of the distillation to 108° (7 mm.). The lower temperature is the boiling point of 2-*n*-amyl-4,5-dihydroimidazole and the higher temperature is probably the boiling point of monocaproylethylenediamine.[3] That dehydration proceeds during distillation was definitely proved by the fact that derivatives of both the cyclic and acyclic bases were isolated from the distillate.

The higher and phenylated aliphatic 4,5-dihydroimidazoles are well-defined white solids which may be recrystallized from petroleum ether, ethyl acetate or benzene. They react readily with picric acid, hydrogen chloride and phenyl isocyanate, although the derivatives formed are not suitable for characterization in all cases. The author is indebted to Miss Bettina Meyerhof for preparing some of the esters used in this work. Further investigations dealing with monoacylated aliphatic polyamines are in progress.

(3) The boiling point of any 2-alkyl-4,5-dihydroimidazole has been found to be invariably lower than the boiling point of the corresponding monoacylethylenediamine from which it is derived.

Summary

1. The preparation of 2-substituted-4,5-dihydroimidazoles from monoacylethylenediamines has been shown to proceed in excellent yields for many types of hydrocarbon substituents.

2. Refinements in previous experimental procedure have been introduced.

3. A study of the ease of dehydration of monoacylethylenediamines has been made.

4. The cyclic and acyclic bases prepared in this study have been fully characterized as picrates, hydrochlorides, chloroplatinates and phenyl ureas.

SWARTHMORE, PENNA. RECEIVED JUNE 26, 1939

[CONTRIBUTION FROM THE NAVAL STORES RESEARCH DIVISION, BUREAU OF AGRICULTURAL CHEMISTRY AND ENGINEERING, U. S. DEPARTMENT OF AGRICULTURE]

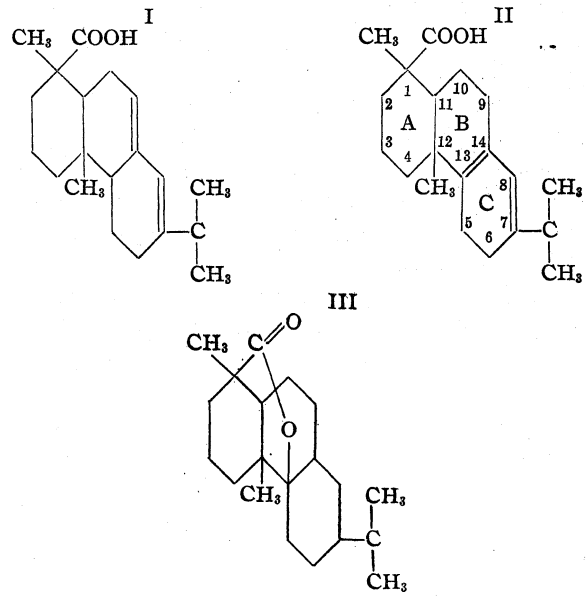
Lactonization of Dihydro-*l*-abietic and Dihydro-*l*-pimaric Acids

BY ELMER E. FLECK AND S. PALKIN

As is well known in the pine resin acid series, isolation of the individual isomers, because of pronounced isomorphism, is attended with considerable difficulty. Similar difficulties are encountered in isolating the individual isomers from dihydro mixtures obtained on hydrogenating *l*-abietic or *l*-pimaric acid. Thus there are reported in the literature dihydroabietic acids ranging from $[\alpha]_D$ −23 to +108°, and melting points of 141 to 218°, and dihydro-*l*-pimaric acids from $[\alpha]_D$ +24 to +35°, and melting points of 135 to 144°.

Ruzicka and co-workers[1] first showed that dihydroabietic acid, $[\alpha]_D$ −12°, m. p. 167–168°, may be converted with strong mineral acids into a completely saturated lactone, $C_{20}H_{32}O_2$. It has now been found possible to prepare this same lactone from the high-rotating dihydro-*l*-abietic acid, $[\alpha]_D$ +108°,[2] and from dihydro-*l*-pimaric acid, $[\alpha]^{20}_D$ +35°. This raises the question as to the identity of the dihydro acid shown to exist in pine oleoresin and in rosin,[3] since the dihydro acid was isolated as the lactone and therefore may be any one or a mixture of the three dihydro compounds shown to give this lactone.

Up to the present time there has been little evidence as to the point of lactonization in lactonized dihydroabietic acid. The C-10 position has been suggested[4] and seemed possible on the basis that the positions of the double bonds in *l*-abietic acid I are such that, on hydrogenation to the dihydro compound, lactonization could occur on the residual double bond in ring B, with the postulation of a shift to the 9,10-position, thus forming a five-membered lactone. There are, however, other possibilities for this lactone that appear more plausible.



l-Pimaric acid II[5] is now represented as containing a system of conjugated double bonds confined to ring C. *l*-Abietic acid I[5] is represented as having a conjugated system of double bonds distributed in rings B and C. An inspection of the structure of *l*-pimaric acid and *l*-abietic acid indicates the $\Delta^{13,14}$ for dihydro-*l*-pimaric acid, and $\Delta^{9,14}$ for dihydro-*l*-abietic acid, assuming hydrogenation to take place at the $\Delta^{7,8}$ position in both cases, that is, under the simplest possible conditions. A 1:4 addition to the conjugated system of either *l*-pimaric or *l*-abietic acid would produce a $\Delta^{14,8}$ dihydro derivative.

On saturation of one of the double bonds of either acid, formation of a series of isomeric dihydro-*l*-pimaric and dihydro-*l*-abietic acids which have the residual double bond in any one of the positions, 14,13, 14,9, 14,8 and 7,8 would seem quite possible.

It may be shown how the three possible positions of the double bond in dihydro derivatives

(1) Ruzicka and Meyer, *Helv. Chim. Acta*, **5**, 333 (1922); Ruzicka, Waldmann, Meier and Hösli, *ibid.*, **16**, 178 (1933).

(2) Fleck and Palkin, THIS JOURNAL, **60**, 2621 (1938).

(3) Fleck and Palkin, *ibid.*, **61**, 1230 (1939).

(4) Hasselstrom and McPherson, *ibid.*, **60**, 2340 (1938).

(5) Fieser and Campbell, *ibid.*, **60**, 159 (1938).

(14,13, 14,9, 14,8) might conceivably give rise to the same lactone at C-14, but this would necessitate an assumption of a 7-membered lactone. A more probable view would be lactonization at C-13, with formation of a six-membered lactone, such as shown in formula III. This is possible by assuming a shift of the double bond from the 9,14 or 8,14 to the bridge-head position, 13,14, a reasonable assumption, when these acids are under the influence of strong mineral acids. Lactonization on C-10, as previously suggested,[4] would, on the other hand, necessitate a much greater shift of double bonds, and hence becomes less probable.

An effort was made to obtain additional information on the point of lactonization by the preparation of typical derivatives and by oxidation experiments with tetrahydrohydroxyabietic acid obtained by hydrolysis of the lactone. Of the three possible points of lactonization two, C-9 and C-10, should yield secondary hydroxyl groups when the lactone is opened. Either of these should yield a ketone on oxidation. The third possibility, C-13, would give rise to a tertiary hydroxyl group and should be stable against oxidation. Actually, the oxidation experiments led to no ketone and, while such evidence would tend to support the assumption of a tertiary hydroxyl and consequently the C-13 position for lactonization, the weakness of such negative evidence is recognized. Moreover, the strong tendency of tetrahydrohydroxyabietic acid and even its methyl ester to lactonize further complicated the oxidation experiments and the attempts to prepare derivatives.

The tetrahydrohydroxyabietic acid was prepared by an improved procedure involving fusion of lactonized dihydroabietic acid III with potassium hydroxide and subsequent acidification of the reaction mass. This acid was methylated with diazomethane to obtain a crystalline tetrahydrohydroxyabietic methyl ester, m. p. 50–51°, $[\alpha]^{20}D$ + 21°. The methyl ester could be distilled unchanged and showed the usual stability against alkaline hydrolysis. In warm acetic acid, however, the methyl ester was rapidly converted into the lactone. All attempts to acetylate the methyl ester with acetic anhydride and sodium acetate, acetyl chloride and acetic anhydride gave only the lactone. No benzoate was obtained by the pyridine and benzoyl chloride method. Attempts to oxidize the methyl ester with chromic anhydride in acetic acid at room temperature and above yielded only the lactonized dihydroabietic acid. The hydroxy methyl ester was completely stable against potassium permanganate in acetone solution. Similarly alkaline potassium permanganate at room temperature for twenty hours did not materially affect tetrahydrohydroxyabietic acid.

Experimental Part

Lactonization of Dihydro-*l*-pimaric Acid.—One gram of dihydro-*l*-pimaric acid, m p. 144–146°, $[\alpha]^{20}D$ +35°,[6] was added to 10 cc. of concentrated sulfuric acid cooled to −5 to −10°. Stirring and cooling was continued for forty-five minutes. The light yellow-colored solution was poured on ice and the resulting mixture was extracted with ether. The ether solution was washed with water, then 0.25 *N* sodium hydroxide and finally with water until neutral to phenolphthalein. When the ether was distilled and the residue dried in vacuum at 80°, 1 g. of crystalline material was obtained that melted at 127–129°. The product when recrystallized from alcohol melted at 131–132°, $[\alpha]^{20}D$ −4°. *Anal.* Calcd. for $C_{20}H_{32}O_2$: C, 78.88; H, 10.60. Found: C, 78.91; H, 10.87. No depression of melting point was observed when this compound was mixed with lactonized dihydroabietic acid.[3]

Tetrahydrohydroxyabietic Acid from Lactonized Dihydroabietic Acid.—A solution of 0.3 g. of the lactone from dihydro-*l*-pimaric acid, in 10 cc. of 10% *n*-butyl alcoholic potassium hydroxide, was hydrolyzed as previously outlined.[2] The resulting acid melted at 164–165° with effervescence. When the melt was cooled and allowed to crystallize, it remelted at 130–131°. *Anal.* Calcd. for acid, $C_{20}H_{34}O_3$: C, 74.47; H, 10.63. Found: C, 74.48; H, 10.79. There was no lowering of the melting point when the acid was mixed with tetrahydrohydroxyabietic acid.

Lactonization of High-Rotating Dihydroabietic Acid Isomer.—Two cc. of concentrated sulfuric acid was cooled to −5 to −10° and 50 mg. of dihydroabietic acid, $[\alpha]D$ +108°,[2] was added. Stirring and cooling were continued for forty-five minutes. The reaction mass was poured on ice and worked up as described for dihydro-*l*-pimaric acid. Twenty-five mg. of neutral residue was obtained. Stout prisms were obtained from methyl alcohol that melted at 130–131°. No lowering of melting point was observed when mixed with authentic lactonized dihydroabietic acid. Owing to the small amount of material available and the difficulty involved in preparing more of the dihydro-isomer, no further characterization of the product was feasible.

Tetrahydrohydroxyabietic Methyl Ester.—Six grams of lactonized dihydroabietic acid was hydrolyzed with *n*-butyl alcoholic 10% potassium hydroxide.[2] The resulting tetrahydrohydroxyabietic acid was esterified with diazomethane in the usual manner. The methyl ester was crystallized as needles from methyl alcohol by slow addition of water. When dried in vacuum at room temperature the methyl ester melted at 50–51°, $[\alpha]^{20}D$ +21°.[6] *Anal.* Calcd. for $C_{21}H_{36}O_3$: C, 74.94; H, 10.79; OCH_3, 9.22. Found: C,

(6) The specific rotations recorded in this publication were all taken on 2% absolute alcoholic solutions.

74.92; H, 10.94; OCH_3, 9.20. The Zerewitinoff test showed 5.38% OH; calcd. for $C_{21}H_{36}O_3$, 5.06.

Saponification with 0.1 *N* sodium hydroxide in alcoholic solution for four hours at reflux temperature: Calcd.: 4.34 cc. of 0.1 *N* sodium hydroxide; found, 0.23 cc.

One gram of the methyl ester distilled at 175–180° at 2 mm. Found: C, 75.06; H, 10.92; OCH_3, 9.16.

Fusion of Lactonized Dihydroabietic Acid with Potassium Hydroxide.—Four grams of 88% potassium hydroxide was melted and heated to 200° in a nickel crucible. To this one gram of lactonized dihydroabietic acid was added. The mixture was stirred and the heating was continued for fifteen minutes. As the reaction proceeded the insoluble potassium salt separated as a white powder that floated on the surface of the caustic. The fusion mass was cooled and dissolved in 200 cc. of water and shaken with ether to remove any unchanged lactone. The alkaline solution was made acid to litmus with 10% acetic acid. The tetrahydrohydroxyabietic acid that separated as pearly plates was filtered and washed with water. When dried in vacuum the acid melted at 164–165° with effervescence and showed no depression with tetrahydrohydroxyabietic acid prepared by the *n*-butyl alcoholic hydrolysis. When the melted acid was allowed to cool and crystallize, it remelted at 130–131°.

Summary

Dihydro-*l*-pimaric acid and dihydro-*l*-abietic acid, $[\alpha]_D$ +108°, have been lactonized to form lactones identical with lactonized dihydroabietic acid.

Formulations for these dihydro compounds have been advanced to show how they may all yield the same lactone.

Oxidation and acylation experiments have been shown to indicate the C-13 position as a more probable point of lactonization than C-10.

A rapid method for hydrolysis of lactonized dihydroabietic acid by caustic fusion has been developed.

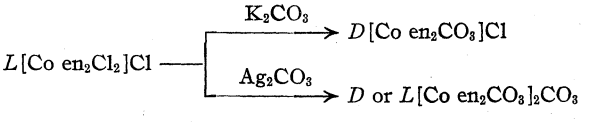
WASHINGTON, D. C. RECEIVED AUGUST 28, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

The Stereochemistry of Complex Inorganic Compounds. V. The Reaction of Carbonates with Dichloro-dipropylenediamine Cobaltic Chloride. A New Method of Determining Relative Configurations

BY JOHN C. BAILAR, JR., AND J. P. MCREYNOLDS[1]

The reaction of dichloro-diethylenediamine cobaltic chloride with potassium and silver carbonates yielded the first example of the Walden inversion in the field of optically active inorganic complex compounds.[2] Bailar, Jonelis and Huffman[3] found that either enantiomorph of the resulting carbonato compound could be produced by the action of silver carbonate, depending upon the conditions under which the reaction took place.



Mathieu[4] checked the Walden inversion reaction of Bailar and Auten[2] and from circular dichroism measurements came to the conclusion that the carbonato diethylenediamine cobaltic salt resulting from the use of potassium carbonate was the non-inverted form.

It was thought that the use of rotatory dispersion curves for closely related compounds might lead to valuable information in respect to this reaction. Lowry, Pickard and Kenyon[5] found that the rotatory dispersion curves for a series of secondary alcohols showed similarities as to dispersion ratios. The rotatory dispersion curves for a large number of diethylenediamine cobaltic complexes are given by Mathieu.[6] A comparison of these curves with those of analogous members of the di-levo-propylenediamine (*l*-pn) cobaltic series was undertaken as a method of attacking the Walden inversion problem.

Evidence has been presented to show that cobaltic complexes containing optically active diamines do not exist in all of the possible stereochemical forms, but only in certain preferred configurations. Hürlimann,[7] working with dinitrodipropylenediamine cobaltic compounds, could isolate only half of the calculated number of *cis* forms. Jaeger,[8] using active cyclopentylenediamine, observed the same result. He assigned

(1) Taken from a portion of the doctorate thesis of J. P. McReynolds, 1938. Presented at the Baltimore meeting of the American Chemical Society, April, 1939.

(2) Bailar and Auten, THIS JOURNAL, **56**, 774 (1934).

(3) Bailar, Jonelis and Huffman, THIS JOURNAL, **58**, 2224 (1936).

(4) Mathieu, *Bull. soc. chim.*, [5] **3**, 497 (1936).

(5) Lowry, Pickard and Kenyon, *J. Chem. Soc.*, **105**, 94–102 (1914).

(6) Mathieu, *Bull. soc. chim.*, [5] **3**, 463–475 (1936).

(7) Hürlimann, Dissertation, Zurich, 1918.

(8) Jaeger, *Rec. trav. chim.*, **38**, 170 (1919).

the structures $[Co_D(l\text{-cptd})_2X_2]^+$ and $[Co_L(d\text{-cptd})_2X_2]^+$ to the two isomers stable enough to be isolated. It was supposed from this that $[Co(l\text{-pn})_2Cl_2]^+$ and $[Co(l\text{-pn})_2CO_3]^+$ would each exist in only one form, so that the conversion of the former into the latter could not produce a Walden inversion. It has been found, however, that the carbonato salt can exist in both possible configurations. One of these is much more stable than the other, however, so the principle involved evidently can be used to determine configurations.

Upon comparison of the rotatory dispersion curves of *cis*-dichloro-diethylenediamine cobaltic chloride[6] and *cis*-dichloro-di-*l*-propylenediamine cobaltic chloride it was found that the general shape of the curves, the maxima, the minima and the points of zero rotation were essentially the same (Fig. 1). The absorption curves for the two

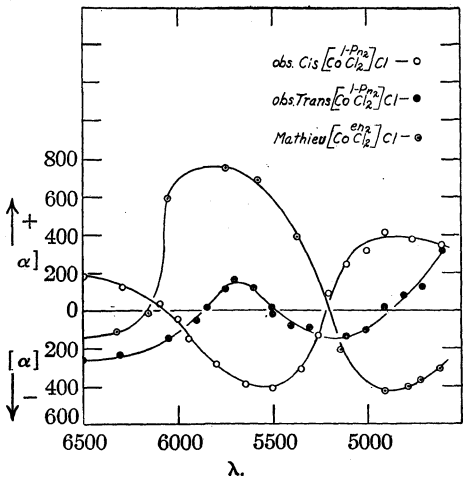


Fig. 1.

compounds (not shown here) were also found to be almost identical. Comparison of the rotatory dispersion curve for carbonato diethylenediamine cobaltic chloride[6] with those for the two diastereoisomeric forms of carbonato di-*l*-propylenediamine cobaltic carbonate shows one of these forms to give a curve very similar to that of the diethylenediamine compound while the other form shows a curve of markedly different characteristics (Fig. 2). The form of the carbonato di-*l*-propylenediamine complex which showed the marked dissimilarity as to dispersion characteristics was easily converted to the other diastereoisomeric form by heating in solution. Using Jaeger's convention[8] for the stable form, the starting material is assigned the structure $[Co_D(l\text{-pn})_2Cl_2]^+$, the more stable product $[Co_D(l\text{-pn})_2CO_3]^+$ and the less stable form $[Co_L(l\text{-pn})_2CO_3]^+$.

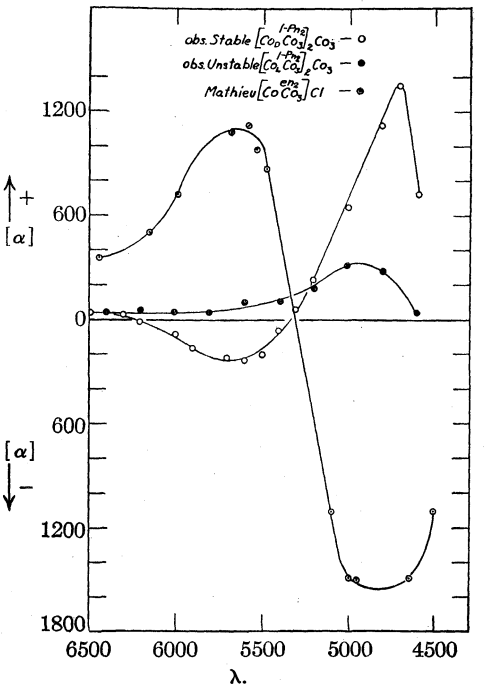


Fig. 2.

In the di-*l*-propylenediamine series the inversion can be brought about by either silver carbonate alone or potassium carbonate alone by varying the conditions under which the reaction is carried out. Under the conditions similar to those by which Bailar, Jonelis and Huffman[3] produced the inversion with silver carbonate alone, analogous results are obtained. With potassium carbonate alone they were unable to produce an inversion in the diethylenediamine series. In the di-*l*-propylenediamine series such an inversion is produced easily. The stable diastereoisomeric form is produced by either reagent when conditions are favorable for a slow reaction. The assignment of inverted and non-inverted forms in the diethylenediamine series as made by analogy with the di-*l*-propylenediamine series agrees with that of Mathieu.[4]

In the course of the preparation of the diastereoisomeric carbonato di-*l*-propylenediamine complexes an explanation of the apparent effect of large excesses of insoluble silver carbonate was found. In every case in which the unstable diastereoisomer was produced, it was observed that the change from the purple dichloro starting material to the red carbonato compound was ex-

tremely rapid, while in the cases in which the stable diastereoisomer resulted the change was rather slow. The *cis*-dichloro-di-*l*-propylenediamine cobaltic chloride undergoes aquation when allowed to stand in solution. This reaction proceeds at a fairly rapid rate, so that it seemed probable that the stable or non-inverted form resulted from a series of reactions. That this postulate was true was shown by allowing a solution of the dichloro-di-*l*-propylenediamine compound to stand until aquation was complete and then treating with silver carbonate. This procedure led to the production of the stable carbonato compound. The inverted form evidently is produced when conditions are such that the substitution of the carbonato group for the chloride ions in the complex proceeds directly, while the non-inverted form is produced by the stepwise displacement of chloride ions by water molecules and the subsequent displacement of the water molecules by the carbonato group.

Since this mechanism rests entirely upon the relative speeds of the aquation and the substitution reactions, the possibility of producing an inversion in the diethylenediamine series by the use of potassium carbonate alone was investigated further. It was found that the aquation rate in this series is more rapid than in the di-*l*-propylenediamine series and was markedly catalyzed by the addition of an alkaline reagent. To avoid the effect of an alkaline solution solid dichloro-diethylenediamine cobaltic chloride was ground with a large excess of dry potassium carbonate. After intimate grinding, water was added. The change to the carbonato compound was almost instantaneous and the product showed a rotation of opposite sign to that obtained by reaction with potassium carbonate in solution. This seems to substantiate the mechanism set up for the Walden inversion reactions discussed.

Experimental

Preparation of Compounds.—*l*-Propylenediamine was prepared by resolving commercial propylenediamine with tartaric acid by the method of Baumann[9] as modified by Bailar, Stiegman, Balthis and Huffman.[10] The dichloro-di-*l*-propylenediamine cobaltic chloride was prepared according to the directions of Bailar, Stiegman, Balthis and Huffman.[10]

The stable diastereoisomeric form of carbonato di-*l*-propylenediamine cobaltic carbonate was prepared by adding a 20% excess of silver carbonate to a solution of *cis*-dichloro-di-*l*-propylenediamine cobaltic chloride and allowing the reaction to progress slowly until no purple color remained and no more silver chloride was formed. The solution was then filtered and evaporated until a red waxy mass remained. This mass was dried by extraction with a mixture of equal parts of absolute alcohol and absolute ether. The resultant product was crystalline but was too soluble in water to be purified by recrystallization. The same product was also obtained by allowing a solution of dichloro-di-*l*-propylenediamine cobaltic chloride to stand for twenty-four hours (to allow aquation to proceed to completion) and then adding an excess of silver carbonate. After silver chloride ceased to be precipitated, the product was isolated as before. The stable diastereoisomer could be obtained with potassium carbonate only when the amount of potassium carbonate added was much below the theoretical amount needed to produce the carbonato carbonate. Best results were obtained when an amount just in excess of the theoretical amount to produce carbonato chloride was added to the solution. This product was not isolated from solution due to the fact that its great solubility prevented a successful separation from the potassium salts. The solutions resulting from all three methods gave specific rotations of $-170°$ when read in a 0.1% solution at the sodium D line.

The unstable diastereoisomeric form of the carbonato complex was prepared by adding the dry dichloro complex to a paste of silver carbonate with grinding. Best results were obtained by using an excess of at least five times the amount of silver carbonate necessary to produce the carbonato-carbonate and adding the dichloro compound in very small quantities over a period of an hour or more, with constant grinding. To isolate the compound it was necessary to filter out the silver chloride and evaporate the solution to a waxy mass at room temperature, since heating converts the product rapidly to the more stable form. The unstable form was prepared but not isolated by the action of an excess of potassium carbonate upon a solution of the dichloro complex.

Analyses for total carbon dioxide content were made upon the stable diastereoisomer obtained by the action of silver carbonate upon the fresh solution (no. 1), upon the stable diastereoisomer obtained by the action of silver carbonate upon the completely aquated solution (no. 2) and upon the stable diastereoisomer obtained by heating a solution of the unstable diastereoisomer (no. 3). These were carried out by displacing the carbonate radicals with hot sulfuric acid and absorbing the evolved carbon dioxide upon ascarite. Since the compounds could not be purified by recrystallization and the samples used were quite small, the checks obtained were not very satisfactory. For this reason the theoretical percentages for the other products which might reasonably be expected from such a reaction are included for comparison.

Anal. Found: CO_2, no. 1, 21.4; no. 2, 19.8; no. 3, 19.9. Calculated: $[Co(l\text{-pn})_2CO_3]_2CO_3$, 22.2; $[Co(l\text{-pn})_2(OH)H_2O]CO_3$, 14.5; $[Co(l\text{-pn})_2(OH)_2]_2CO_3$, 8.2; $[Co(l\text{-pn})_2(H_2O)_2]_2(CO)_3$, 19.7.

It seems quite improbable that the diaquo salt could be formed under the conditions used, for it is definitely acid. To establish this point definitely, however, samples

(9) Baumann, *Ber.*, **28**, 1179 (1895).

(10) Bailar, Stiegman, Balthis and Huffman, THIS JOURNAL, **61**, 2402 (1939).

of the stable isomer (prepared from the aquated dichloro salt and silver carbonate) and the unstable isomer, were analyzed for the ratio of ionic to non-ionic carbonate. Samples of about 0.5 g. were treated with calcium nitrite in excess. After standing for an hour the precipitated calcium carbonate was filtered out. The filtrate was heated on the steam-bath for several hours to effect the reaction

$$[Co(l\text{-pn})_2CO_3]^+ + 2NO_2^- \longrightarrow [Co(l\text{-pn})_2(NO_2)_2]^+ + CO_3^=$$

(which requires several weeks at room temperature), and the calcium carbonate was again filtered out. Making allowance for the slight amount of silver carbonate which goes into solution (determined by a blank) the ratios of ionic to non-ionic carbonate were found to be: stable isomer, 0.51; unstable isomer, 0.47; calculated, 0.50.

Rotatory Dispersion Curves.—The polarimeter readings for the rotatory dispersion curves were made with a Schmidt–Haensch polarimeter using an ordinary 1000-watt tungsten filament projection bulb as a light source. The wave lengths reported are not strictly monochromatic but represent an intensity average for a band of approximately 100 Å. obtained with a monochromator. All data represent an average of at least four readings and for the most part six or more readings were made. The polarimeter was scaled to read to 0.001° but the accuracy obtainable in this work was of the order of ±0.01° in the regions of high transparency and much less in the regions of high absorption.

TABLE I

cis-DICHLORO-DI-*l*-PROPYLENEDIAMINE COBALTIC CHLORIDE (FIG. 1)

The solution used contained 0.05 g. of complex in 100 cc. of water.

Wave length, Å.	Observed rotation, °	Specific rotation, °
6500	+0.09	+180
6300	+ .06	+120
6100	+ .02	+ 40
6000	− .02	− 40
5800	− .12	−240
5650	− .19	−380
5500	− .20	−400
5350	− .15	−300
5250	− .06	−120
5200	+ .05	+100
5100	+ .13	+260
5000	+ .16	+320
4900	+ .21	+420
4750	+ .19	+380
4600	+ .18	+360

Due to the rapid aquation of these compounds, it was found necessary to prepare a fresh solution for every four wave lengths, or at time intervals of about every thirty minutes. The readings above represent data taken upon at least two different solutions at each wave length.

In this series aquation did not affect the stability of the solution so that the same solution could be used for all the readings.

Extension of the Mechanism to Inversion of the Diethylenediamine Complex by Potassium Carbonate.—Forty grams of potassium carbonate was ground with 0.2830 g. of dry *l*-*cis*-dichlorodiethylenediamine cobaltic chloride for one and one-half hours. Sufficient water was then added to give a solution containing 0.1% of the carbonato complex. An immediate reaction took place giving a product which showed a rotation of −0.03°. Normally the potassium carbonate reaction leads to a dextro product if allowed to proceed through the aquation intermediate. The levo rotation indicated that the inverted form was produced in excess. To check the effect of the presence of such large excesses of potassium carbonate upon the rotation of the carbonato complex, a 0.1% solution of carbonato diethylenediamine cobaltic carbonate was prepared having a rotation of −0.24°. To 20 cc. of this solution sufficient potassium carbonate was added to give the same concentration as was used above. The resultant solution had a volume of 22 cc. and a rotation of −0.21°. The effect of the large excess of potassium carbonate is evidently very slight.

TABLE II

STABLE CARBONATO DI-*l*-PROPYLENEDIAMINE COBALTIC CARBONATE (FIG. 2)

Wave length, Å.	Observed rotation, °	Specific rotation, °
6500[a]	+0.04	+ 40
6300[a]	+ .02	+ 20
6200[a]	− .02	− 20
6000[a]	− .10	− 100
5900[a]	− .18	− 180
5700[a]	− .22	− 220
5600	− .12	− 240
5500	− .11	− 220
5400	− .04	− 80
5300	+ .03	+ 60
5200	+ .10	+ 200
5000	+ .32	+ 640
4800	+ .56	+1120
4700	+ .66	+1320
4600	+ .36	+ 720

[a] These wave lengths were read upon a solution containing 0.1 g. of complex in 100 cc. of water, the remainder upon a solution containing 0.05 g. of complex in 100 cc. of water.

TABLE III

UNSTABLE CARBONATO DI-*l*-PROPYLENEDIAMINE COBALTIC CARBONATE (FIG. 2)

Wave length, Å.	Observed rotation, °	Specific rotation, °
6400[a]	+0.04	+ 40
6200[a]	+ .06	+ 60
6000[a]	+ .04	+ 40
5800[a]	+ .04	+ 40
5600[a]	+ .10	+100
5400[a]	+ .10	+100
5200	+ .09	+180
5000	+ .16	+320
4800	+ .14	+280
4600	+ .02	+ 40

[a] These wave lengths were read upon a solution containing 0.1 g. of complex in 100 cc. of water. The other readings were made upon a solution containing 0.05 g. of complex in 100 cc. of water.

Summary

1. Two diastereoisomeric forms of carbonato di-*l*-propylenediamine cobaltic carbonate have been prepared by a Walden inversion method. The inverted form is unstable in hot water, being converted to the more stable non-inverted form.

2. Rotatory dispersion curves have been made for *cis*-dichloro-di-*l*-propylenediamine cobaltic chloride and for the two diastereoisomeric forms of carbonato di-*l*-propylenediamine cobaltic carbonate. By comparison of these curves with those for analogous compounds in the diethylenediamine series, it has been possible to determine which of the two carbonato forms is obtained by an inversion about the central cobalt atom in the latter case.

3. A mechanism for the production of the two forms of the carbonato complex has been advanced. The non-inverted form is produced through the preliminary displacement of the chloride ions in the *cis*-dichloro-di-*l*-propylenediamine cobaltic chloride by water molecules, followed by the displacement of the water molecules by carbonato groups. The inverted form is produced by direct substitution of the carbonato group for the chloride ions within the complex. It was found possible by varying the reaction conditions on the basis of this mechanism to produce either form with either silver carbonate alone or potassium carbonate alone. Further it was found possible to produce the inverted form of carbonato diethylenediamine cobaltic carbonate with potassium carbonate for the first time.

URBANA, ILLINOIS RECEIVED AUGUST 31, 1939

[CONTRIBUTION FROM THE DIVISION OF PHYSICAL CHEMISTRY OF THE STATE UNIVERSITY OF IOWA]

Kinetics of the Thermal Decomposition of Ethyl Formate

BY R. F. MAKENS[1] AND W. G. EVERSOLE

The vapor phase decomposition of ethyl formate in the absence of catalysts, other than the glass used as containers, has not been investigated extensively. Sabatier and Mailhe[2] found no appreciable decomposition when ethyl formate was passed through a glass tube at 400°. At 300° in a sealed flask the decomposition of this ester was reported by Engler and Grimm.[3] Hurd[4] states, "The esters with the general formula $RCOOCH_2CH_2R$ should decompose into free acid and olefin." If this explanation is correct, ethyl formate should yield formic acid or its decomposition products and ethylene. The gases found by Engler and Grimm[3] were in accord with this theory; however, the amounts of the various constituents which they found varied greatly from those required by the reaction. Sabatier and Mailhe,[2] Pearce and Wing[5] and others have shown that this reaction does not predominate in the presence of any one of several different catalysts. Sabatier and Mailhe[2] found that the vapors of formic esters may decompose in two ways

$$2HCOOC_nH_{2n+1} \longrightarrow HCHO + CO_2 + (C_nH_{2n+1})_2O \quad (1)$$

$$HCOOC_nH_{2n+1} \longrightarrow CO + C_nH_{2n+1}OH \quad (2)$$

This paper reports quantitative data on the thermal decomposition of ethyl formate. The data permit the calculation of the order of the principal primary reaction and its energy of activation. Evidence of the other associated reactions including those given above also is presented.

Experimental

Materials.—Ethyl formate (Eastman Kodak Co.) was dried and distilled in a packed column, and the resultant product was redistilled. It was found that the middle portion, which was the part used in the investigation, boiled at 54.20–54.26° (corr.). The density was d^{25}_4 0.9055 and the refractive index $n^{25}D$ 1.3582.

Apparatus and Procedure.—The apparatus, a modification of that used by Thompson and Frewing,[6] was of the static type. The reaction vessel consisted of a 220-cc. Pyrex flask. For the rapid removal of gaseous decomposition products a large Toepler pump was provided. Liquid products were condensed by passing through a carbon dioxide–acetone trap and subsequently allowing the temperature to reach −10°. The resulting vapor was added to the main gas sample, while the remainder of the liquid was analyzed by micro-methods. A mercury vapor pump backed by a Hyvac oil pump comprised the evacuation equipment. Pressures in the system were reduced

(1) Present address: The Michigan College of Mining and Technology, Houghton, Michigan.

(2) Sabatier and Mailhe, *Compt. rend.*, **154**, 49–52 (1912).

(3) Engler and Grimm, *Ber.*, **30**, 2922 (1897).

(4) Hurd, "Pyrolysis of Carbon Compounds," Chemical Catalog Company, New York, N. Y., 1929, p. 525.

(5) Pearce and Wing, *J. Phys. Chem.*, **36**, 709 (1932).

(6) Thompson and Frewing, *J. Chem. Soc.*, 1444 (1935).

to 0.2 micron or less before each run. During a run the pressures were read on an ordinary manometer connected through a heated capillary manometer to the reaction flask.

The furnace was controlled to ±0.3° by a circuit described by Zabel and Hancox.[7] A modified Orsat apparatus equipped with a flushing manifold was used for the gas analysis.

Cleaning of the reaction flask was effected by hot concentrated nitric acid and water followed by drying and evacuation at 450°.

Results

The decomposition of ethyl formate was very slow at 300°. Two runs were made; one at an initial pressure of 39.05 cm. and one at 39.86 cm. In the first run the pressure increase in thirty hours was 2.83 cm. and the volume of gaseous products was 5.85 ml.; in the second run the pressure increase was 2.92 cm., and the volume of gaseous products was 5.70 ml. The same gaseous decomposition products were present at all temperatures. The liquid product gave a very weak aldehyde test with Schiff reagent. Fractional distillation of the liquid product according to Emich and Schneider[8] permitted the identification of ethyl formate and water.

At 375° the decomposition rate was satisfactory, but at 350° it was much too slow. Table I shows the data for two duplicate series of decompositions made without disturbing the reaction flask.

TABLE I

GASEOUS PRODUCTS FROM ETHYL FORMATE DECOMPOSITIONS AT 375°

Time, hours	2	4	6	8	10	30
Ml. of CO_2	1.5	2.6	3.7	4.0	4.1	11.0
Ml. of higher unsatd.	0.2	0.3	0.5	0.7	0.6	1.6
Ml. of C_2H_4	14.8	23.5	27.8	31.4	33.3	34.2
Ml. of H_2	0.8	1.7	2.3	3.2	3.7	10.2
Ml. of CO	3.6	10.6	16.2	21.8	25.3	32.1
Ml. of CH_4	0.3	0.6	0.4	0.4	0.5	0.5
Ml. of C_2H_6	0.1	0.2	0.2	0.2	0.1	0.5
Ml. of total gas	21.3	39.4	51.3	61.7	67.6	90.1
Initial pressure	38.8	38.0	37.8	38.8	38.5	37.9
Final pressure	51.3	61.0	68.9	75.5	78.2	86.3
Ml. of C_2H_4 formed[a]	15.0	24.3	29.2	32.4	34.3	37.7
$(a - x)$[b]	22.7	13.4	8.5	5.3	3.4	0.0

[a] Corrected for an average initial pressure of 38.3 cm. [b] Maximum volume of ethylene formed minus the volume formed in the time interval given.

The polymerization of ethylene to butylene, noted by Storch,[9] no doubt accounts for the presence of the higher unsaturates. Thus the total ethylene originally formed would equal the volume found plus twice the volume of higher unsaturates.

The production of ethylene conforms to a first order reaction as shown by plotting the logarithms of the values of $(a - x)$ in Table I against time. The liquid products contained ethyl formate, water, formic acid, and a small amount of some aldehyde. After distilling off and discarding the more volatile portion, the formic acid was identified in the residue by forming the cerous derivative and observing these crystals under crossed nicols.[10] The presence of an aldehyde was established by the use of Schiff reagent, which produced a weak reaction.

In like manner, without disturbing the reaction flask, two duplicate series of runs were made at 425°. The data reported in Table II are the average of these duplicate runs.

The production of ethylene at 425° conforms to a first order reaction as was shown in the previous instance. At 425° and at 375° the liquid decomposition products were also qualitatively identical. The specific velocity constants calculated from the data in Tables I and II are $K_{375°} = 0.824 \times 10^{-4}$ and $K_{425°} = 7.61 \times 10^{-4}$. The energy of activation calculated by substitution of these constants in the Arrhenius equation is 40,010 cal. The value of K from four duplicate runs made at 400° is 2.441×10^{-4}. Log K plotted against the reciprocal of the absolute temperature produces a straight line.

Preliminary work proved that the method of cleaning the reaction flask had a very decided effect on the rate of formation of carbon monoxide, carbon dioxide and hydrogen, but had no effect on the rate of formation of ethylene. This observation is in agreement with Hinshelwood, Hartley and Topley[11] who noted that the decomposition of formic acid varied with the nature of the glass surface. To avoid the difficulty the data were all obtained without disturbing the reaction flask.

Discussion

The principal primary reaction in the decomposition of ethyl formate produces ethylene by a reaction which is represented by the first order

(7) Zabel and Hancox, *Rev. Sci. Instruments*, **5**, 28 (1934).

(8) Emich and Schneider, "Microchemical Laboratory Manual," John Wiley and Sons, Inc., New York, N. Y., 1932, pp. 34–38.

(9) Storch, THIS JOURNAL, **57**, 2601 (1935).

(10) Emich and Schneider, "Microchemical Laboratory Manual," John Wiley and Sons, Inc., New York, N. Y., 1932, p. 121.

(11) Hinshelwood, Hartley and Topley, *Proc. Roy. Soc.* (London), **A100**, 575–577 (1922).

TABLE II

GASEOUS PRODUCTS FROM ETHYL FORMATE DECOMPOSITION AT 425°

Time, hours	0.25	0.50	0.75	1	1.333	2	4	8
Ml. of CO_2	1.8	2.3	5.0	4.4	4.6	8.6	9.0	13.7
Ml. of higher unsatd.	0.4	0.6	0.6	1.0	1.1	1.1	1.4	2.0
Ml. of C_2H_4	18.4	30.2	34.0	35.6	36.7	38.4	37.8	36.9
Ml. of H_2	0.8	1.5	3.5	2.7	3.3	6.4	6.6	11.7
Ml. of CO	2.3	8.0	10.6	14.7	17.2	21.0	28.3	29.5
Ml. of CH_4	0.4	0.6	0.4	0.7	0.7	0.8	0.7	0.9
Ml. of C_2H_6	.1	.1	.2	.3	.3	.3	.7	1.0
Total	24.2	36.1	54.3	59.4	63.9	76.6	84.5	95.7
Initial pressure	38.3	39.8	39.3	38.0	38.6	39.2	38.9	39.6
Final pressure	55.9	66.4	72.1	75.9	78.8	84.6	89.7	94.6
Ml. of C_2H_4 formed[a]	19.5	30.7	34.8	38.4	39.2	40.3	40.6	40.4
$(a - x)$[b]	20.9	9.7	5.6	2.0	1.2	0.0	0.0	0.0

[a] Corrected to an average initial pressure of 38.9 cm. [b] Maximum volume of ethylene formed minus the volume formed in the time interval given.

equation. The greater part of the carbon monoxide and carbon dioxide must be produced by secondary reactions, as can be seen by an inspection of Fig. 1. (A similar curve is obtained by plotting the corresponding data from Table II.) Since the curves do not pass through the zero point, as shown by plotting according to the method of least squares, and since the final ratio of carbon monoxide and carbon dioxide to ethylene is greater than one, one or more minor primary reactions simultaneous with the principal primary reaction are present. The fact that the ratio of carbon dioxide to carbon monoxide was greater at the earlier stages of the decomposition suggests that at least one of these minor reactions produces carbon dioxide.

The reaction suggested by Hurd[4] in which the ethyl formate decomposes to form ethylene and formic acid is confirmed. Formic acid was identified in the liquid products; the production of carbon monoxide, carbon dioxide and hydrogen paralleled the decomposition of formic acid as observed by Hinshelwood, Hartley and Topley,[11] and by Nelson and Engelder.[12]

The minor primary reactions are probably those designated (1), (2) in this paper. Sabatier and Mailhe,[2] Senderens[13] and Pearce and Wing[5] have shown that these products are formed when ethyl formate is passed over various heated catalysts. These reactions and their secondary decomposition products account for the excess of carbon monoxide plus carbon dioxide over ethylene in the final runs, for part of the pressure change, for the small amounts of methane formed, and for the higher ratio of carbon dioxide to carbon monoxide in the shorter than in the longer runs.

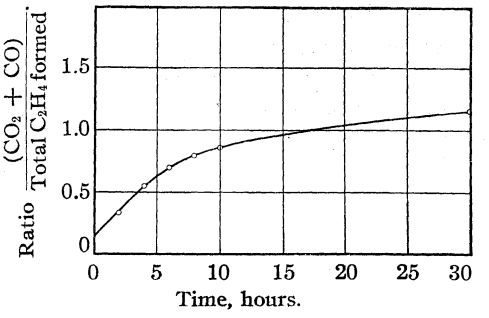


Fig. 1.—The ratio of carbon monoxide plus carbon dioxide to the total ethylene formed at 375°.

If the principal reactions continued to completion and if no other reactions were present, the pressure theoretically would be tripled and the ratio of carbon monoxide plus carbon dioxide to ethylene formed would be one. Several factors contributed to a pressure ratio lower than would be predicted by these assumptions. The dead space in the apparatus used was about 2.3%. This would alter the theoretical pressure ratio from 3.0 to less than 2.9 when calculated on the basis of the equation developed by Allen.[14] The minor primary reactions postulated would produce less than three moles of product per mole of ethyl formate. Figure 1 indicates that the decomposition of the formic acid may not have been complete; the acid reaction of the final liquid decomposition products supports this assumption.

Summary

1. The decomposition of ethyl formate has been shown to be very slow at 300°. At 375,

(12) Nelson and Engelder, *J. Phys. Chem.*, **30**, 470 (1926).

(13) Senderens, *Compt. rend.*, **196**, 979 (1933).

(14) Allen, THIS JOURNAL, **56**, 2053 (1934).

400, and at 425° the reaction rates were determined for the principal primary reaction. Evidence is presented concerning the other reactions involved.

2. The principal primary reaction is shown to be

$$HCOOC_2H_5 \longrightarrow C_2H_4 + HCOOH$$

This is followed by the decomposition of formic acid

$$HCOOH \longrightarrow CO + H_2O$$
$$HCOOH \longrightarrow CO_2 + H_2$$
$$2HCOOH \longrightarrow CO_2 + HCHO + H_2O$$

3. Evidence is presented that minor primary reactions occur, and the nature of these reactions is suggested.

4. Calculated from the present data, the energy of activation of the reaction producing ethylene is 40,010 cal.

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Vapor–Liquid Equilibrium. IV. Carbon Tetrachloride–Cyclohexane Mixtures[1]

BY GEORGE SCATCHARD, S. E. WOOD AND J. M. MOCHEL

In the third paper of this series,[2] we showed that benzene–cyclohexane mixtures have an entropy increase on mixing which is larger than that of an ideal solution even at constant total volume, and which we attributed tentatively to some lack of randomness in at least one of the pure liquids. Since earlier calculations[3] had given no indication of such an effect for benzene–carbon tetrachloride mixtures, and since cyclohexane has an unusually small entropy of fusion, we have next studied carbon tetrachloride–cyclohexane mixtures. Although there is a slight excess entropy of mixing at constant total volume, it is less than a tenth of that for benzene–cyclohexane mixtures. Mixtures of cyclohexane with carbon tetrachloride agree with simple theory in every respect more closely than do those with benzene.

The cyclohexane was purified as in III. Merck C. P. carbon tetrachloride was refluxed for eleven hours with an aqueous solution 10% in potassium permanganate and 10% in sodium hydroxide. The carbon tetrachloride was distilled off, dried with calcium chloride and rectified in the column described in Paper III. The boiling points of the products and of the rejected portions were measured in a small Cottrell apparatus with a five-junction thermocouple. The normal boiling points, which should be used for relative values only, are:

	CCl_4	Product		76.69
Tops	75.93	76.54	76.67	76.69
Bottoms	76.72	76.69	76.68	
	C_6H_{12}	Product		80.73
Tops	79.29	80.41	80.69	80.68
Bottoms	82.64	80.99	80.74	

(1) Presented before the Division of Physical and Inorganic Chemistry of the American Chemical Society, September 14, 1939.

(2) I and II are published in THIS JOURNAL, **60**, 1275, 1278 (1938), and III in *J. Phys. Chem.*, **43**, 119 (1939).

(3) George Scatchard, *Trans. Faraday Soc.*, **33**, 160 (1937).

The gas heater for the equilibrium still was replaced by an electrical heater with a Variac control which greatly increased the accuracy of the regulation of the boiling. To prevent direct radiation to the thermometer, the bottom of the glass still is painted with black stovepipe enamel which is renewed when necessary. A hood of aluminum foil is placed over the top of the still, and for temperatures of 60° or higher a shield of aluminum foil is placed around the still. This protection prevents the increase of material in the inner boiler during the runs at high temperatures, but does not affect the decrease during the low temperature runs.

The thermocouple was recalibrated from 60 to 100° as before by measuring the vapor pressure of water and determining the temperature from this pressure by the equation of Smith, Keyes and Gerry,[4] and the low temperature calibration was checked by a determination of the transition point of sodium sulfate decahydrate. Measurements of the vapor pressure of cyclohexane agreed with those with the gas heated still except at 30 and 35°. Apparently there had been radiation from the flame to the thermometer which cancelled out at those temperatures at which the calibration had also been carried out in the still. So the measurements for benzene at 30, 35 and 40° were repeated, and new equations were derived for cyclohexane and benzene. The equations are

$$CCl_4: \quad \log p_1 = 6.68148 - 1045.022/T - 99{,}577/T^2$$
$$C_6H_{12}: \quad \log p_2 = 6.65859 - 1040.641/T - 104{,}865/T^2$$
$$C_6H_6: \quad \log p_3 = 6.66457 - 1007.742/T - 116{,}197/T^2$$

($T = t + 273.16$.) The standard (root mean square) deviations are 0.5, 1.3 and 1.5 × 10^{-4}, respectively. The normal boiling point of carbon tetrachloride is 76.68₇°. Timmermans and Martin[5] give 76.75. The new boiling points of cyclohexane and benzene are 80.73₉ and 80.10₅°, which are 0.004 lower and 0.005° higher than our former values. The values of the vapor pressures of these three substances at rounded temperatures are given in Table II.

(4) L. B. Smith, F. G. Keyes and H. T. Gerry, *Proc. Am. Acad. Arts and Sci.*, **69**, 137 (1934).

(5) J. Timmermans and F. Martin, *J. chim. phys.*, **23**, 747 (1926).

The compositions were determined from the densities at 25°, which are given by the equation

$$d = (0.77383 + 0.81031\, z_1)/(1 + z_1 z_2/150) \quad (1)$$
$$z_1 = 1 - z_2 = 1/(1 + w_2 d_1/w_1 d_2) \quad (2)$$

in which w_1 is the weight of carbon tetrachloride, d_1 its density, and z_1 its volume fraction, and w_2, d_2 and z_2 are the corresponding quantities for cyclohexane. In Table I are given the weight fractions and mole fractions of carbon tetrachloride, the measured densities, the difference of these densities from those calculated by equation 1, and the measured values of $100V^M/V^0$. V is the volume of the mixture, V^0 that of the unmixed components, and $V^M = V - V^0$. From equation 1, it follows that

$$V^M/V^0 = z_1 z_2/150 \quad (3)$$

TABLE I

DENSITIES OF CYCLOHEXANE–CARBON TETRACHLORIDE MIXTURES AT 25°

Weight fraction CCl_4	Mole fraction CCl_4	Density	Deviation from eq. 1	$100V^M/V^0$
0.0000	0.0000	0.77383	.....	...
.2053	.1238	.86401	−0.00003	0.069
.3744	.2466	.95609	+ .00008	.108
.5177	.3699	1.05106	+ .00011	.140
.6369	.4897	1.14605	+ .00016	.151
.6434	.4968	1.15162	+ .00006	.161
.7530	.6251	1.25638	− .00018	.175
.7530	.6251	1.25646	− .00010	.168
.8458	.7500	1.36199	− .00009	.139
.9268	.8738	1.47019	+ .00010	.078
1.0000	1.0000	1.58414	.....	...

There is a systematic error in these results which corresponds to a loss of 2–4 mg. of the component first weighed out, and which we confirmed later as the approximate loss by evaporation between the two weighings. Since this corresponds to only 0.01–0.02% in the composition, it was not considered worth while to repeat these measurements with a different technique, but we have used equation 1 to determine the equilibrium compositions.

Vapor–liquid equilibrium measurements were made at intervals of approximately one-eighth in the mole fraction at 40 and 70° and for a single mixture, about 50 mole per cent., at 30, 50 and 60°. For mixtures containing more than 40% carbon tetrachloride, nitrogen replaced helium as the confining gas. The measurements at 40° are shown in Fig. 1, in which the curves are determined from equations 6, 7, 14 and 15 and the circles are the individual experimental points. The top curve gives the equilibrium pressure as ordinate and the liquid composition as abscissa. The curve just below it and the flagged circles have the vapor composition as abscissa, and the two lower curves are the derived partial pressures with the liquid composition as abscissa. The broken lines are the Raoult's law lines for the total and partial pressures *vs.* liquid composition.

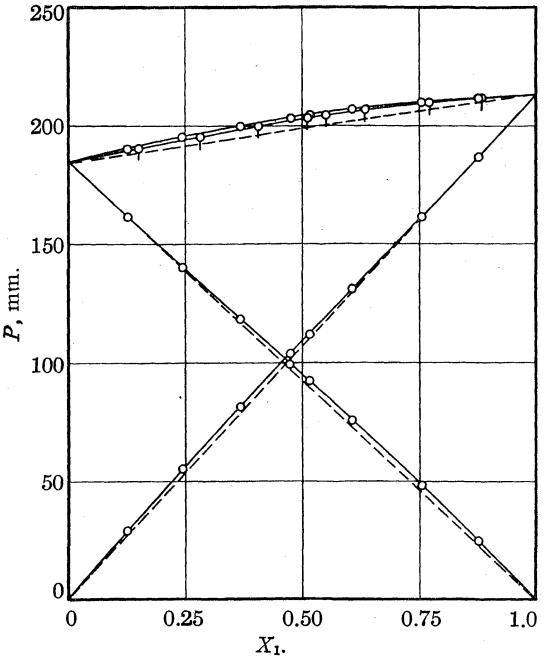


Fig. 1.—Vapor pressure *vs.* mole fraction for carbon tetrachloride–cyclohexane at 40°.

TABLE II

VAPOR PRESSURES OF PURE SUBSTANCES

Temp., °C.	Carbon tetrachloride, mm.	Cyclohexane, mm.	Benzene, mm.
30	141.55	121.60	119.16
40	213.34	184.61	182.70
50	312.04	271.80	271.34
60	444.28	389.29	391.66
70	617.43	543.95	551.03
80	....	743.27	757.56

The measurements are reported in detail in Table III as mole fraction of carbon tetrachloride in the liquid and in the vapor, equilibrium pressure, and the derived excess free energy of mixing. After each of the last three is given the deviation of the corresponding quantity from that calculated by equations 6, 7, 14 and 15.

After the measurements with mixtures there was a distinct odor of phosgene which was stronger from the condensate than from the liquid and which increased after each measurement. Therefore three approximately equimolal mixtures

TABLE III

VAPOR PRESSURES OF MIXTURES

t	Mole fr. of CCl_4 Liquid (x_1)	Vapor (y_1)	Dev. in y_1	Pressure P	Dev. in P	F_x^E	Dev. in F_x^E
40°	0.1262	0.1515	−0.0006	190.62	±0.00	6.77	+0.05
	.2453	.2822	− .0008	195.62	+ .01	11.50	+ .10
	.3669	.4066	− .0008	200.08	+ .02	14.62	+ .18
	.4739	.5103	− .0010	203.40	− .06	15.61	− .13
	.5151	.5474	− .0029	204.59	− .05	15.90	+ .09
	.4753	.5116	− .0010	203.45	− .05	15.65	− .07
	.6061	.6341	− .0008	206.97	− .06	15.16	− .11
	.7542	.7702	− .0004	210.15	− .03	12.01	− .06
	.8756	.8822	− .0002	212.04	− .03	7.10	− .09
70°	.1248	.1458	− .0002	558.78	+ .06	5.98	+ .10
	.2468	.2787	+ .0002	571.59	+ .05	10.19	+ .04
	.3640	.3981	− .0003	582.59	+ .17	13.03	+ .02
	.4836	.5150	− .0003	591.97	− .11	13.89	− .10
	.5153	.5473	+ .0017	594.42	± .00	13.90	− .15
	.4796	.5113	± .0000	591.73	− .05	13.92	− .06
	.6074	.6320	− .0004	600.52	− .09	13.48	− .08
	.7535	.7680	− .0001	608.79	+ .05	10.79	+ .06
	.8757	.8818	− .0001	613.97	+ .10	6.50	+ .12
30°	.4728	.5114	− .0010	134.73	± .00	16.38	+ .10
50°	.4829	.5173	− .0006	298.44	+ .01	15.23	+ .07
60°	.4810	.5137	− .0006	425.34	− .04	14.57	± .00

were studied at 40 and at 70°. The first was the last of a series which included all those preceding it, the third was the last of a series which included all those following it run in the order opposite to that of the table, and the second was made up fresh from the components. The first and third check extremely well, and the deviations of the third are in opposite directions at the two temperatures. A test with *p*-dimethylaminobenzaldehyde[6] indicated less than 0.005% phosgene. This confirms the evidence from the equilibrium measurements that the effect of the phosgene is negligible.

In II it was shown[2] that, if the liquid and vapor volumes are given, respectively, by

$$V/(N_1 + N_2) = V_1x_1 + V_2x_2 \quad (4)$$

$$V'/(N_1 + N_2) = RT/P + \beta_1y_1 + \beta_2y_2 \quad (5)$$

the excess chemical potentials and other excess thermodynamic functions are given by

$$\mu_1^E = RT \ln Py_1/P_1x_1 + (\beta_1 - V_1)(P - P_1) \quad (6)$$

$$\mu_2^E = RT \ln Py_2/P_2x_2 + (\beta_2 - V_2)(P - P_2) \quad (7)$$

$$F_x^E = F^E/(N_1 + N_2) = x_1\mu_1^E + x_2\mu_2^E \quad (8)$$

$$S_x^E = -(\partial F_x^E/\partial T)_{p,N} \quad (9)$$

$$H_x^E = H_x^M = F_x^E + TS_x^E \quad (10)$$

in which N_1 and N_2 are the numbers of moles of the two components, x_1 and x_2 are the mole fractions in the liquid, y_1 and y_2 the mole fractions in the vapor, P is the vapor pressure of the solution, P_1 and P_2 are the vapor pressures of the components, V_1 and V_2 are the molal volumes of the liquid components, and β_1 and β_2 are functions of the temperature, each characteristic of one of the components. The effect on the subsequent equations of the deviations from equation 4 is entirely negligible, and the effect of deviations from equation 5 may probably be neglected.

For β_1 and β_2 we have used 0.9 the value calculated by the theory of corresponding states from the equation of Keyes, Smith and Gerry[7] for water vapor. The values for carbon tetrachloride are one-sixth to one-third larger than those measured by Eucken and Mayer,[8] but their measurements with carbon tetrachloride do not seem consistent with those on other gases.

These results may be expressed by the equations

$$F_x^E = (1.3335 - 0.0022916T)V_x^0z_1z_2 \quad (11)$$

in which $V_x^0 = x_1V_1 + x_2V_2 = V^0/(N_1 + N_2)$

$$H_x^M = 1.3335\ V_x^0z_1z_2 \quad (12)$$

$$S_x^E = 0.0022916\ V_x^0z_1z_2 \quad (13)$$

$$\mu_1^E = (1.3335 - 0.0022916T)V_1z_2^2 \quad (14)$$

$$\mu_2^E = (1.3335 - 0.0022916T)V_2z_1^2 \quad (15)$$

The calculated results from which the deviations in Table III are calculated are from equation 11 for F_x^E, and from the combination of equations 6, 7, 14 and 15 for P and y_1.

The constants are chosen to give the average of F_x^E at 40 and 70° and a linear variation of F_x^E with the temperature. The average deviation is 0.07% in y_1 and about 0.01% in P. Although the equation is simpler than that of III, the agreement is considerably better than in that paper. There is no indication that a more complicated function of the composition or of the temperature would be preferable. The solutions are far from regular. The ratio of the temperature coefficient of equation 11 to the constant term is 0.0017. The corresponding coefficient for benzene–cyclohexane mixtures is 0.0019.

For theoretical purposes we are interested in the mixing process at constant total volume.[3] We will designate the functions calculated for this process with a subscript $_v$, and the values measured at constant pressure with a subscript $_p$. We apply the equations as in III, using for the coefficients of thermal expansion and of compressibility and their ratio at 25°

$$\alpha_0 = 1.228(1 - 0.018z_2) \times 10^{-3}$$

$$\beta_0 = 1.10(1 + 0.009z_2) \times 10^{-4}$$

$$(\alpha_0/\beta_0) = 11.16(1 - 0.027z_2)$$

$(\mathrm{d} \ln \beta)/\mathrm{d}T = 0.0076$, which is its value for carbon tetrachloride as well as for benzene.

$$V_x^0 = 97.111/(1 - 0.10706z_2) \text{ cc./mole}$$

(6) L. Rosenthaler, *Pharm. Acta. Helv.*, **12**, 6 (1937).

(7) F. G. Keyes, L. B. Smith and H. T. Gerry, *Proc. Am. Acad. Arts and Sci.*, **70**, 319 (1936).

(8) A. Eucken and L. Mayer, *Z. physik. Chem.*, **B5**, 452 (1929).

Then at 25°

$$F^E = (V^0/2\beta)(V^M/V^0)^2$$

$$(A^E_v - F^E_p)_x = 0.004891 \times 97.111\, z_1^2 z_2^2/(1 + 0.009 z_2)(1 - 0.10706 z_2) \text{ cal./mole} \quad (16)$$

$$S^E_v - S^E_p = -V^M \alpha_0/\beta_0 + (V^0/2\beta)(V^M/V^0)^2\, \mathrm{d} \ln \beta/\mathrm{d}T$$

$$(S^E_v - S^E_p)_x = -0.001802 \times 97.111(1 - 0.027 z_2) z_1 z_2/(1 - 0.10706 z_2) + 0.0076(A^E_v - F^E_p) \text{ cal./mole °C.} \quad (17)$$

$$(E^M_v - H^M_p)_x = T(S^E_v - S^E_p)_x + (A^E_v - F^E_p)_x \quad (18)$$

In Fig. 2 are shown F^E_{px} at 25° and at 70° from equation 11, H^M_{px} from equation 12, and E^M_{vx} at 25°, calculated from H^M_{px} and equation 18. The difference between A^E_{vx} and F^E_{px} at 25° is less than half the width of the line, so the same curve may serve for both. TS^E_{px} is the difference between the top curve and the third, and TS^E_{vx} is the difference between the second curve and the third. This second difference is less than a quarter of the first, so three-quarters of the deviation from regularity is accounted for by the change in volume on mixing.

These mixtures are so nearly ideal that we should expect the deviations from random distribution to have a very small effect. Using, as in III, Kirkwood's equation[9] for this effect for a mixture of spheres of equal radii, each with eight nearest neighbors, and with the same value of E^M_{vx} for an equimolal mixture as for carbon tetrachloride–cyclohexane, 20.7 cal./mole, we obtain

$$E^M_{vx} = B_{12} x_1 x_2 - (B_{12}^2/4RT) x_1^2 x_2^2 \quad (19)$$

$$20.7 = B_{12}/4 - B_{12}^2/64RT$$

$$B_{12} = 84$$

$$E^M_{vx} - A^E_{vx} = (-84^2/8RT) x_1^2 x_2^2 = -0.09 \text{ cal./mole, when } x_1 = 0.5 \quad (20)$$

This effect is very small compared to the measured difference of +4.0 cal./mole.

The difference of 4 cal./mole is so small that it is well to consider the corresponding difference in the more familiar quantities which are directly measured. The effect on y_1 is very small and may be neglected. In an equimolal mixture the measured pressure is 2.63% greater than that calculated by Raoult's law at 40°, and 2.17% greater at 70°. This decrease of 0.46% would be only 0.18% if the solutions were regular. Of the remaining 0.28%, 0.22% is accounted for by the volume change on mixing, and there is only 0.06% left unexplained. However, our measurements are so precise that we believe that the uncertainty of this figure is less than 0.02% or less than one-third its value.

(9) J. G. Kirkwood, *J. Phys. Chem.*, **43**, 97 (1939).

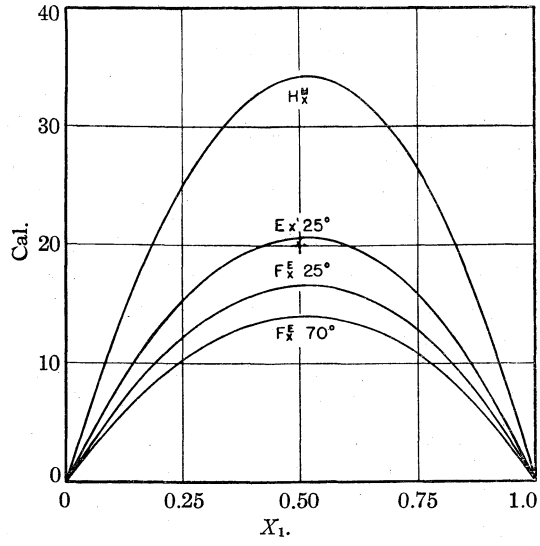


Fig. 2.—Various thermodynamic functions for carbon tetrachloride–cyclohexane.

We are particularly interested in the comparison with benzene–cyclohexane mixtures, for which the unexplained difference is 50 cal. per mole, or thirteen times as great as for carbon tetrachloride–cyclohexane. If the explanation is to be sought in incomplete randomness in one of the component liquids, not more than one-thirteenth is contributed by the cyclohexane unless there are compensating effects in the mixtures of cyclohexane with carbon tetrachloride. However, earlier measurements indicate that benzene–carbon tetrachloride mixtures are almost regular.[3] We are at present making further measurements on this system.

With the assumptions that the cohesive energy density, $a = (E - E_0)/V$, is equal to $-(\partial E/\partial V)_T$ and that S^E_v is zero, E^M_v may be computed from V^M and β by the equation

$$E^M_v = V^M/\beta \quad (21)$$

This leads to a value of 41 cal. per mole for an equimolal mixture, which is approximately twice as great as the directly determined value of 21 cal. per mole and is even larger than the heat of mixing at constant pressure, which is 34 cal. per mole. The absolute difference is not, however, so very great.

From the equations for the vapor pressures of the components, the equations for the deviations from the perfect gas laws, and the densities of the components at 25°, the cohesive energy densities of the components are calculated as $a_{11} = -72.96$ and $a_{22} = -66.54$. The assumption

that the mutual energy per unit volumes, a_{12}, is equal to $\sqrt{a_{11}a_{22}}$ leads to the result

$$E^M_{vx} = -(\sqrt{a_{11}} - \sqrt{a_{22}})^2 V^0_x z_1 z_2 \qquad (22)$$

For an equimolal mixture this yields $E^M_{vx} = 3.8$ cal. per mole instead of the measured 20.7. However, if we calculate $-a_{12}$ from the relation

$$E^M_{vx} = (2a_{12} - a_{11} - a_{22}) V^0 z_1 z_2 \qquad (23)$$

and the measured 20.7 for equimolal mixtures, we obtain $-a_{12} = 69.34$, which is only 0.5% less than $\sqrt{72.96 \times 66.54} = 69.67$. So, quadratic combination gives a very good approximation for a_{12}, and the small error is in the direction predicted by the quantum theory. The treatment of solutions makes too drastic demands for a simple theory in requiring a small difference between large numbers. On the other hand, measurements on solutions afford a correspondingly accurate measure of one of these quantities if the others are known.

Summary

The vapor–liquid equilibrium pressure compositions of carbon tetrachloride–cyclohexane mixtures have been measured at 40 and 70° over the whole composition range, and at 30, 50, and 60° for approximately equimolal mixtures. The densities have been determined at 25°.

These measurements have been expressed analytically, and corresponding equations derived for the thermodynamic functions, including the energy and entropy of mixing at constant total volume.

The dependence upon composition agrees with the predictions of the simple theory. The deviation from regularity is relatively large but most of it is explained by the volume change on mixing.

The unexplained entropy increase on mixing is only one-thirteenth as large as for benzene–cyclohexane mixtures.

CAMBRIDGE, MASSACHUSETTS RECEIVED AUGUST 29, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, STANFORD UNIVERSITY]

Solutions of the Paraffin-Chain Sulfonic Acids as Colloidal Electrolytes

BY EVELYN LAING MCBAIN, WALTER B. DYE AND STEWART A. JOHNSTON

Colloidal electrolytes since their first recognition by McBain in 1913 have received steadily increasing attention, because of their interesting departures from the behavior of ordinary electrolytes and because they embrace such large groups of substances. The soaps originally studied do not lend themselves to precise examination in very dilute solution on account of the prominent effects of hydrolysis. It remained therefore for Lottermoser and Püschel[1] to show that in great dilution many non-hydrolyzable salts of alkyl sulfuric acids conform to the behavior of the Debye–Hückel theory, rather suddenly departing from it at a very low concentration designated, by Bury and collaborators, the critical concentration for micelles. This has been confirmed by many subsequent investigators, and necessitated a modification of the original formulation to conform more closely to later conceptions of interionic attraction. Different authors, however, differ in their formulations. It is desirable to have exact measurements of many different properties of a non-hydrolyzable pure material of simple chemical composition sufficiently soluble that it may be studied over a wide range of concentrations.

The present communication comprises measurements of lowering of freezing point, conductivity, viscosity and density of straight chain sulfonic acids with special emphasis upon dodecyl sulfonic acid. The results for diffusion have been published[2] and a provisional discussion is being given elsewhere,[3] although it is not until our measurements of transport number are completed that a sufficient number of equations will be available for a definitive solution of the problem, except in its principal outlines which are already generally known.

Experimental

An especially pure preparation of laurylsulfonic acid was made by M. E. Synerholm by the method of Noller and Gordon[4]; its equivalent weight by titration was 100.05% of the theoretical, the excess probably being water. The other sulfonic

(1) Lottermoser and Püschel, *Kolloid Z.*, **63**, 175 (1933).

(2) Evelyn Laing McBain, *Proc. Roy. Soc.* (London), **A170**, 415 (1939).

(3) Van Rysselberghe, Colloid Symposium, 1939.

(4) Noller and Gordon, THIS JOURNAL, **55**, 1090 (1933).

acids from C_2 to C_{14} were prepared by F. M. McMillan. The potassium methyl, ethyl and propyl sulfonates were purchased from Kahlbaum, their solutions being filtered before use. The acids were made up by weight on the basis of their titrated value with conductivity water, from a Barnstead still, of specific conductance 0.3 to 0.4×10^{-6} mho.

The conductivity measurements were made with complete Leeds and Northrup Jones–Dike equipment, with an oil thermostat at 25°. Potassium chloride solutions were made up by the Jones and Bradshaw method. The cells were H-shaped with electrode leads from opposite ends, one[5] for use with stronger solutions and another shortened one for the most dilute solutions.

The Conductivity Data

To save space the density and conductivity results obtained by one of us (W. B. D.) for the lower members of the homologous series are given graphically in Figs. 1 and 2, which also include for comparison the "I. C. T." values for hydrochloric acid. Figure 2 also includes the data for the higher homologs and for the potassium salts. It will be noted that the first clear indication of departure from the behavior of ordinary strong electrolytes occurs with C_7 and that in concentration above about 0.4 *N*. There is a slight effect in solutions of C_6 approaching 1 *N*, and it is possible that in still greater concentrations the lower homologs of the free acids would give similar indications.

The conductivity data for the higher homologs are given in Tables I to IV for the sulfonic acids C_9, C_{11}, C_{12}, and C_{14}. The necessary density data by one of us (E. L. M.) were included in a previous publication,[6] except those for nonylsulfonic acid where very little material was available and where the density is so nearly that of water (d^{25}_4 0.9994 for 0.098 *m*) that other concentrations are based upon a linear graph.

TABLE I

EQUIVALENT CONDUCTIVITY OF AQUEOUS SOLUTIONS OF NONYL SULFONIC ACID AT 25°, AT VARIOUS MOLALITIES

m	μ	*m*	μ	*m*	μ
0.0008505	369.3	0.006366	362.5	0.04908	329.7
.001993	367.8	.007159	365.0	.05560	320.1
.002917	366.6	.01270	359.8	.06556	305.8
.003226	366.9	.01984	354.4	.07450	293.1
.003801	365.7	.03032	347.5	.08232	283.9
.004756	364.7	.03610	342.9	.08804	277.1
.005604	363.9				

(5) McBain, Laing and Titley, *Trans. Chem. Soc.*, **115**, 1279 (1919).

TABLE II

SPECIFIC AND EQUIVALENT CONDUCTIVITY OF UNDECYL SULFONIC ACID AT 25°

m	*k*	μ	*m*	*k*	μ
0.0007187	0.0002627	366.7	0.006113	0.002199	361.3
.001486	.0005405	365.0	.006432	.002319	362.2
.001597	.0005820	365.5	.006704	.002410	361.1
.002348	.0008533	364.7	.007233	.002598	360.8
.002515	.0009123	364.0	.008332	.002982	359.6
.003102	.0011237	363.6	.009027	.003236	360.3
.003818	.001382	363.3	.009303	.003523	359.0
.004059	.0014655	362.5	.009860	.003518	358.6
.004552	.001645	362.8	.01732	.006021	350.0
.005175	.001871	363.0			

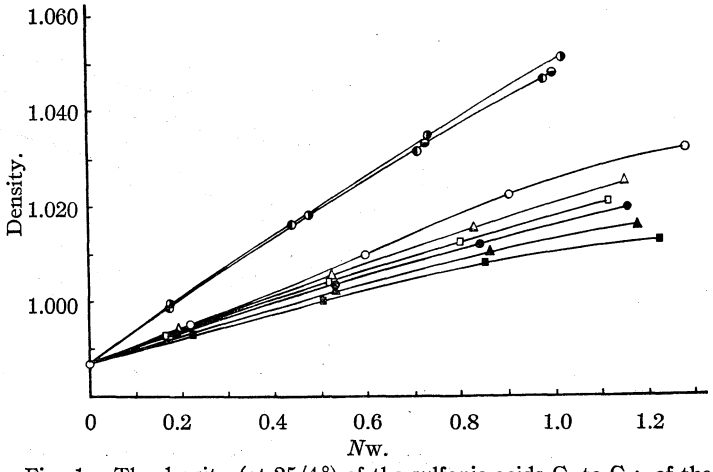


Fig. 1.—The density (at 25/4°) of the sulfonic acids C_2 to C_7: of the potassium sulfonates C_1 to C_8: ◑, CH_3SO_3K; ◐, $C_2H_5SO_3K$; ◒, $C_3H_7SO_3K$; ○, $C_2H_5SO_3H$; △, $C_3H_7SO_3H$; □, $C_4H_9SO_3H$; ●, $C_5H_{11}SO_3H$; ▲, $C_6H_{13}SO_3H$; ■, $C_7H_{15}SO_3H$.

TABLE III

SPECIFIC AND EQUIVALENT CONDUCTIVITY OF DODECYL SULFONIC ACID AT 25°

0.00002466	0.000009135	371.5	0.004630	0.001628	360.8
.00004183	.00001550	371.5	.004677	.001684	361.2
.0001303	.00004816	371.2	.005325	.001924	359.7
.0001462	.00005424	370.8	.005546	.001987	358.6
.0001903	.00007060	372.0	.005867	.002107	359.8
.0003937	.0001462	371.1	.006592	.002347	356.1
.0004098	.0001519	371.2	.007037	.002513	358.0
.0004130	.0001532	371.2	.007920	.002806	355.2
.0004183	.0001550	371.5	.007941	.002821	356.1
.000547	.0002024	371.1	.008067	.002874	356.6
.0006454	.0002395	371.0	.009581	.003188	333.6
.0008925	.0003298	370.5	.01077	.003211	299.1
.001398	.0005185	370.9	.02059	.004345	211.4
.001693	.0006250	369.6	.03018	.005411	180.6
.001828	.0006842	369.1	.0510	.007991	159.8
.002149	.0007861	367.6	.0516	.008098	156.5
.002377	.0008746	367.1	.0705	.01054	146.8
.003473	.001255	362.8	.0958	.01505	147.6
.003750	.001352	362.0			

(6) McBain and Betz, THIS JOURNAL, **57**, 1906 (1935).

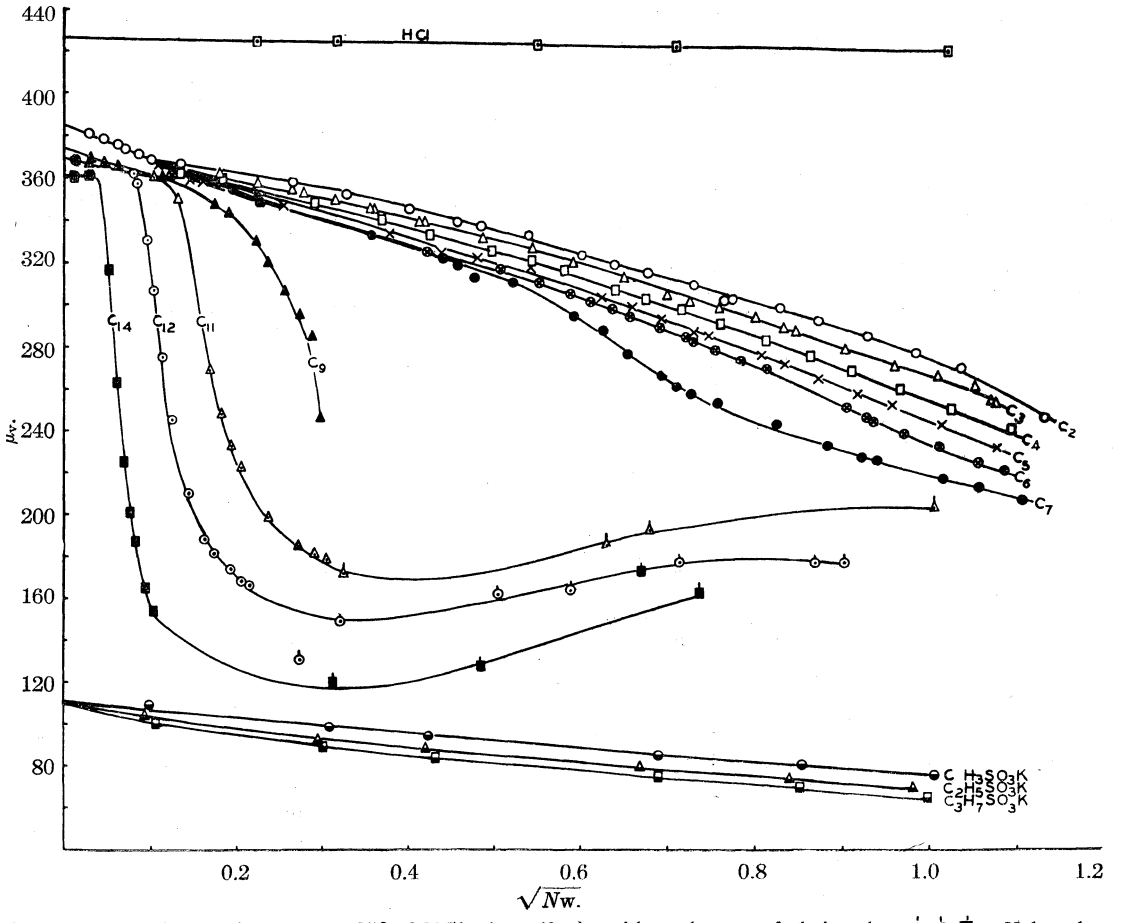


Fig. 2.—The molar conductance at 25° of HCl, the sulfonic acids and some of their salts: △ ⊙ ■. Values by Miss Betz.

TABLE IV

EQUIVALENT AND SPECIFIC CONDUCTIVITY OF TETRADECYL SULFONIC ACID AT 25°

m	k	μ	m	k	μ
0.0001089	0.00003914	360.5	0.002556	0.0008045	315.9
.0001384	.00004968	359.9	.003419	.0008941	262.5
.0001802	.00006464	359.7	.004458	.0009953	224.2
.0002221	.00008002	361.3	.005459	.001089	200.4
.0004878	.0001754	360.6	.006265	.001163	186.5
.0007667	.0002758	360.8	.007110	.001247	176.2
.0010570	.0003806	361.2	.008317	.001365	165.0
.001852	.0006739	359.3	.010065	.001537	153.6

The most interesting portions of the data for the present purpose are those for extreme dilution which are plotted in Fig. 3; the measurements of the most dilute solutions of C_{11} and C_{14} (by W. B. D.) may possibly be affected by some systematic error. Indeed, it was found to be the case in the corresponding measurements of C_{12} (by W. B. D.). However, it does not show in the measurements with C_2 in the same dilutions.

Figure 3 also includes the straight line representing the Onsager slope $\mu_e = \mu_\infty - [0.2274\ \mu_\infty + 59.78]\ \sqrt{N_V}$ for complete dissociation. The limiting equivalent conductances are, for the acids, 385 for C_2, 374 for C_9, 372 for C_{12} and 361 for C_{14}; and for the potassium salts 109, leaving 35.5 for the C_2 anion. From this the limiting mobilities of the anions are, for C_2 35, for C_9 24, and for C_{12} 22. For sodium dodecyl sulfate, Ward[7] obtained $\mu_\infty = 65.46$ at 20°, from which we deduce for the anion 22 to 23 depending upon whether one uses the data for Na^+ from "I. C. T.," Ward or MacInnes, Shedlovsky and Longsworth.[8] Howell and Robinson for the same sulfate had $\mu_\infty = 85.1$ at 25°, but with a systematic error still to be corrected, meanwhile leaving 35.1 mhos for the C_{12} ion. Reed and Tartar had $\mu_\infty = 86$ for the sodium dodecyl sulfonate or 36 mhos for the anion, but their more recent paper[9] contains conductivities for this particular substance that differ by as much as 6 to 20% from their previous paper.

(7) Ward, *J. Chem. Soc.*, 522 (1939).

(8) MacInnes, Shedlovsky and Longsworth, THIS JOURNAL, **54**, 2762 (1932).

(9) Wright, Abbot, Sieverts and Tartar, *ibid.*, **61**, 550 (1939).

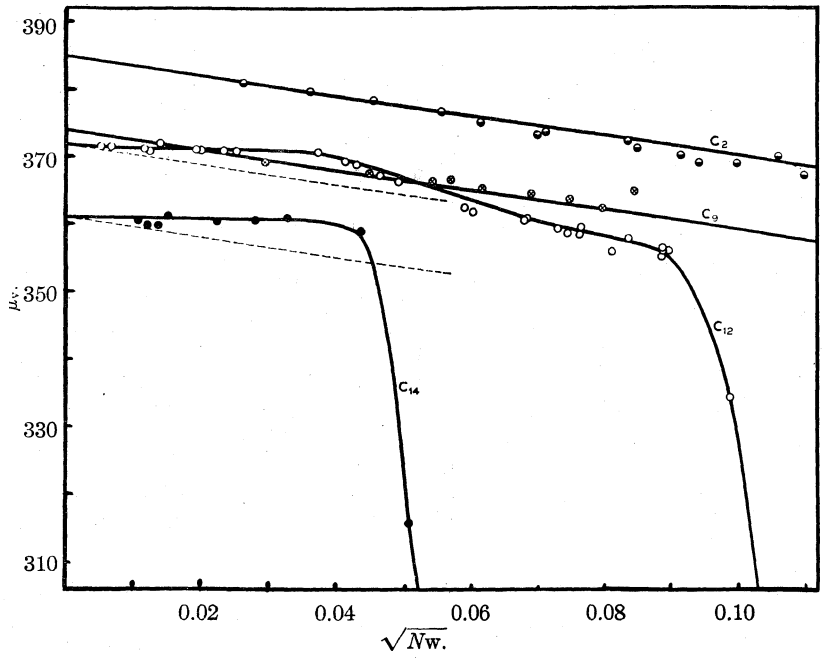


Fig. 3.

Their value for C_{14} at 40° was 2 mhos less. Lottermoser and Püschel obtained $\mu_\infty = 75$ for sodium dodecyl sulfate at 25° (but extrapolating linearly against $\sqrt[3]{N}$) giving 24.5 mhos for this anion, and a value for C_{12} 4 mhos less than C_{14} at 40°. We shall take our own value of 22 mhos as being the most likely for C_{12} anion with 35 mhos for the C_2 anion, which may be compared with the "I. C. T." value of 36.7 mhos for acetate and the MacInnes, Shedlovsky and Longsworth value of 40.87 mhos for the acetate ion.

The slope of the conductivity curve at extreme dilution in Fig. 3 is exactly the Onsager value for C_2 but with the higher members the conductivity of the colloidal electrolyte in this range decreases less than expected with concentration. Tartar's collaborators likewise noted the same effect. For example, for sodium dodecyl sulfonate at 40, 60 and 80°, they obtained slopes of 80, 109 and 140; whereas Onsager's equation would demand 106, 115 and 203, respectively. A noticeable increase of conductivity above that derived by the Onsager equation at infinite dilution could in these great dilutions only be accounted for on the basis of small amounts of highly conducting ionic micelle. Indeed, the fact that in dilutions such as 0.0004 N the conductivity of methylene blue is very greatly above the value for infinite dilution (of the order of 25–30% excess) was explained similarly by Moillet, Collie, Robinson and Hartley. They noted that even when with *m*-benzopurpurin the conductivity slope appeared normal, transport measurements conclusively proved the presence of micelles conducting better than the ions from which they were formed.

The mass law requires that for small micelles or complexes their formation must be gradual and extend over the whole range of concentration. A sharp break in the slope, at the "critical concentration to form micelles," is incompatible with the mass law even for the largest micelles. Writers since Lottermoser and Püschel have tended to overstress the sharpness of this break. Our critical concentrations are C_9 0.04, C_{11} 0.015, C_{12} 0.08 and C_{14} 0.0026 N, as read from the graph of equivalent conductivity, Fig. 3, with slightly different and likewise arbitrary values if read from the graph of specific conductivity, Fig. 4. The value for C_{12} is less than would be expected from those of the sodium salts,[9] whereas that for C_{14} is slightly greater.

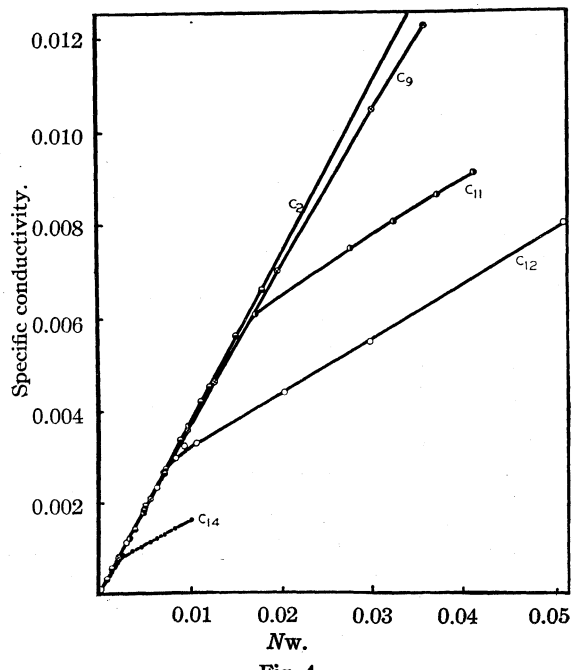


Fig. 4.

Those for the acids of uneven carbon atoms lie likewise at lower concentrations than those predicted for the sodium salts, being more nearly equal to the next highest homolog of even carbon number. The curve is very smoothly rounded for C_9 with increasing abruptness for the higher homologs.

Refractive Index

Refractive index, being essentially a measurement of atomic volumes, is but little affected by change from crystalloid to colloid. Lifshitz and Brandt[10] found that the molar refraction for the soaps as observed in soap solutions agreed with that calculated for ordinary organic chemicals. For this reason refractive index is frequently a valuable method of analysis of soap solutions since with the dipping refractometer and auxiliary prism only 0.03 cc. is required for measurement and the readings at 25° are linear when plotted against % or against equivalent weights in 1000 g. of total solution, as shown in Fig. 5. The slopes for the first four homologs are as shown in the figure 0.0293, 0.0247, 0.0210, and 0.0186, respectively.

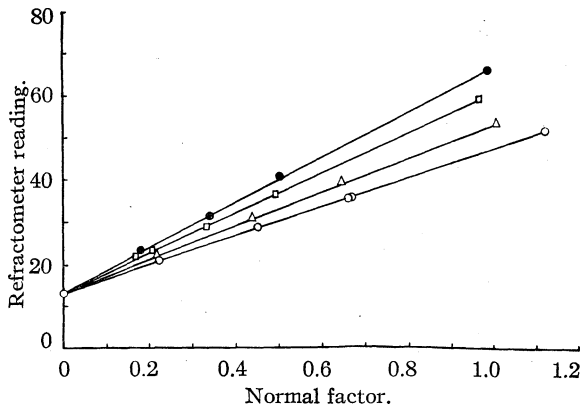


Fig. 5.—The refractometer reading at 25° of the sulfonic acids C_2 to C_5 plotted against the normal factor (equiv./1000 g. of solution): O, $C_2H_5SO_3H$; △, $C_3H_7SO_3H$; □, $C_4H_9SO_3H$; ●, $C_5H_{11}SO_3H$.

Viscosity Data

The following results were obtained (by E. L. M.) for the viscosity of dodecyl sulfonic acid solutions at 25°, taking the value for water as unity, and employing an Ostwald viscometer.

N_W	0.020	0.035	0.050	0.060	0.090	0.105	0.302	0.36
r	1.14	1.19	1.21	1.22	1.26	1.30	1.82	2.01
N_W	0.455	0.565	0.77	0.805	0.95	1.026	1.052	
r	2.28	3.01	4.64	5.04	7.54	10.93	13.4	

The viscosity results are graphed in Fig. 6. The rapid rise in the more concentrated solutions

(10) Lifshitz and Brandt, *Kolloid Z.*, **22**, 142 (1918).

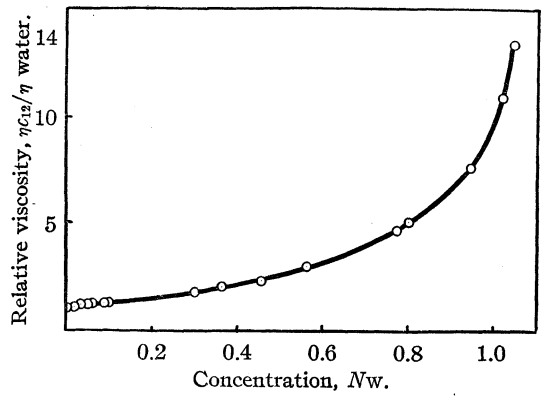


Fig. 6.

corresponds to structural viscosity. Thus the equivalent conductivity throughout the most concentrated range is rising in spite of an increase in viscosity amounting to many fold. Were it not for this, the increase of conductivity with increase of concentration evidently would be still greater. In the most concentrated solutions diffusion and conductivity show definite signs of reduction.

Freezing Point Data (by S. A. J.)

The freezing equipment was modelled after that of Scatchard.[11] The e. m. f. across the twenty-four junction thermocouple is measured by a relatively inexpensive null method designed by Dr. Stuart W. Grinnell, Fig. 8, and sensitive to 5×10^{-5} degree or 5×10^{-8} volt. The voltage divider AB (ratio 1:1627.3), like the galvanometer circuit, is of copper; P is a simple potentiometer to give a fine adjustment.

The thermocouple is calibrated directly by measuring the thermal e. m. f. produced by the freezing point lowering of approximately 0.15 *N* potassium chloride solutions, and calculating the freezing point depression using *g* values obtained by Scatchard.

The freezing point results for dodecylsulfonic acid are assembled in Table V and are shown

TABLE V

Concn.	θ	g	Concn.	θ	g
0.08713	0.05297	0.1636	0.01211	0.03704	0.8231
.07778	.05101	.1765	.01148	.03686	.8638
.05674	.04492	.2130	.01029	.03581	.9367
.05612	.04589	.2200	.009233	.03254	.9483
.05373	.04635	.2321	.006843	.02427	.9543
.03466	.04038	.3135	.005985	.02135	.9599
.02978	.04111	.3714	.005797	.02079	.9649
.02208	.03915	.4772	.004470	.01592	.9584
.02045	.03856	.5074	.003469	.01238	.9604
.01804	.03888	.5799	.002716	.009817	.9726
.01778	.03847	.5822	.002174	.007905	.9785

(11) Scatchard, Jones and Prentiss, THIS JOURNAL, **54**, 2676 (1932).

graphically in Fig. 7. The concentrations are in moles per 1000 g. of water, θ is the number of degrees lowering of freezing point, and g is the Bjerrum osmotic coefficient, $g = \theta/2\ \lambda\ m$, where $\lambda = 1.858°$ and g = van't Hoff's $i/2$ and Lewis and Randall's $l - j$.

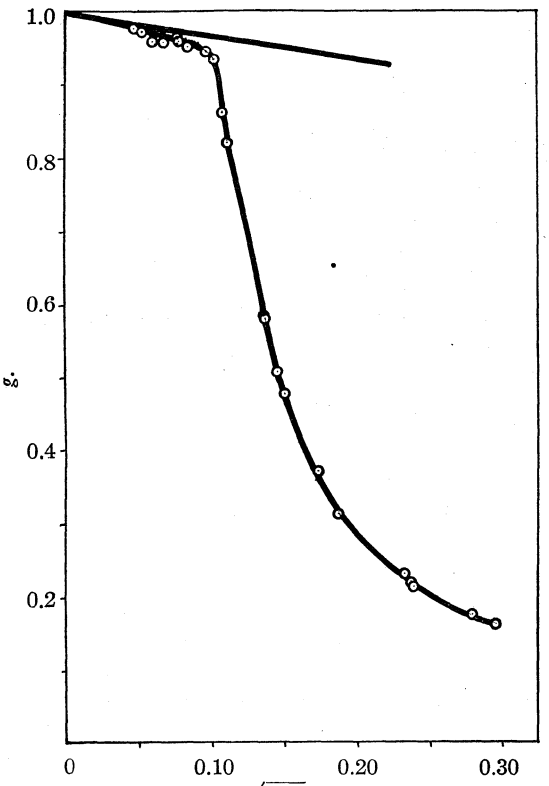


Fig. 7.

Attention may be called to the extremely steep drop in the values of g in the neighborhood of 0.02–0.03 N where the actual freezing point, $-\theta°$, is only just progressively lowered by increase in concentration. In other words, these dilute solutions are almost on the verge of separating into a heterogeneous mixture of two solutions both dilute and within this range. The requirement that θ should increase continuously with concentration to prevent such separation is paralleled by the requirement that $g/N + dg/dN$ must be positive where N is the mole fraction of the solute.

Discussion

The salient features of the data are, first, the regularity within the homologous series showing a gradual transition from typical fully dissociated electrolytes in the lowest members to well characterized colloidal electrolytes in the higher members. In the latter there is the region in extreme dilution corresponding approximately to the Debye–Hückel–Onsager behavior followed by the region of concentration in which conductivity and lowering of freezing point fall to a fraction of their former values, and then after a minimum the third characteristic region where equivalent conductivity and molar lowering definitely increase with increasing concentration.

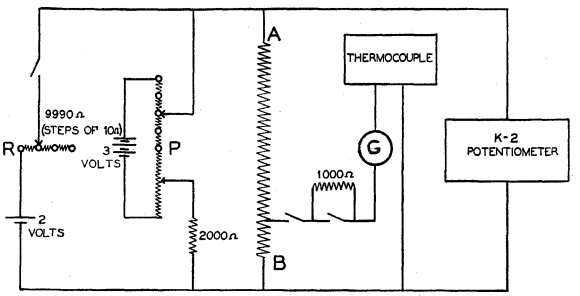


Fig. 8.

The transition from the first to the second region occurs over a very appreciable range of moderately concentrated solutions for heptyl- and nonylsulfonic acids, the transition being very gradual. This transition zone is commonly called the critical concentration for micelles. We believe, as is indeed evident from a comparison with freezing point lowering, that even in the solutions of greater dilution there is at least some ionic micelle that enhances the conductivity. After the transition zone or critical concentration, the much larger micelles of low conductivity like ordinary colloidal particles, which McBain called "neutral colloid," are formed so rapidly that they destroy much of the conductivity and freezing point lowering, in spite of any relatively small increase of highly conducting or ionic micelles. However, after the minimum, the effects due to the latter gain the upper hand by their steady increase, and the conductivity rises again.

Summary

1. Conductivity measurements are presented for the homologous series of straight chain sulfonic acids from two to fourteen carbon atoms, together with data for density and refractive index. The data show the gradual transition from the behavior of fully dissociated electrolytes for the lowest homologs through the intermediate members in higher concentration to the typical behavior of colloidal electrolytes for the higher homologs. The latter approximate to complete

dissociation in extreme dilution, then rather suddenly lose much of their conductivity through association of ion-pairs and ions to form colloidal particles of low conductivity, but after a well-defined minimum in moderately dilute solution, regain some of their conductivity through increasing formation of better conducting or ionic micelles.

2. This interpretation is in agreement with exact freezing point and diffusion data for dodecylsulfonic acid.

STANFORD UNIVERSITY, CALIF. RECEIVED JULY 10, 1939

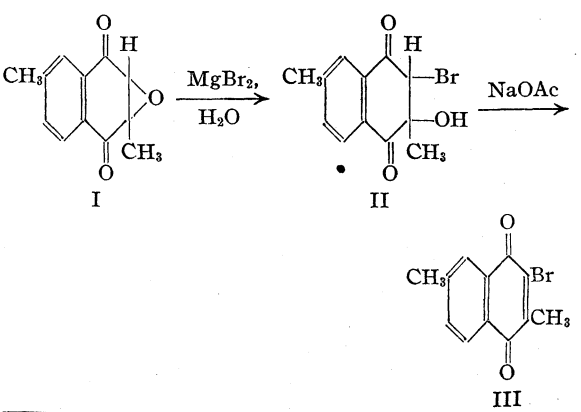
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Naphthoquinones of the Vitamin K_1 Type of Structure[1]

BY LOUIS F. FIESER, WILLIAM P. CAMPBELL, EDWARD M. FRY[2] AND MARSHALL D. GATES, JR.

The synthesis of various allyl derivatives of α-naphthoquinone[3,4] by utilization of the Claisen rearrangement reaction was undertaken to provide model substances of the structural types postulated for vitamins K_1 and K_2. It was recognized that methods involving use of this reaction probably would not be applicable to the synthesis of the vitamins themselves, and the present paper reports attempts to develop methods suitable for accomplishing this second objective.

One scheme tried without success consisted in the attempted addition of a Grignard reagent to a naphthoquinone oxide. The reaction between allylmagnesium bromide and 2,6-dimethyl-1,4-naphthoquinone oxide (I) was studied because addition in the desired direction would lead to 2,6-dimethyl-3-allyl-1,4-naphthoquinone,[3] which was already characterized. The chief product isolated, however, proved to be the bromohydrin II, the structure following from the analysis of the colorless product and from its conversion to a yellow bromodimethylnaphthoquinone of the composition of III. That cleavage of the oxide ring is due, as in comparable cases,[5] to interaction of the oxide with magnesium bromide present in the Grignard solution was established by the observation that the bromohydrin can be obtained in 73% yield from the oxide and magnesium bromide in ether. On attempted coupling of the MgBr derivative of II with allylmagnesium bromide there was isolated a small amount of the oxide, indicating that the cleavage reaction is reversible. When 2-methyl-1,4-naphthoquinone oxide was treated with methylmagnesium chloride and the oily product refluxed with alcoholic hydrochloric acid, a colorless substance resulted which appears to be formed by the addition of the elements of methane and of hydrogen chloride. The investigation was not pursued beyond these unpromising observations. A useful outcome of the brief study is the development of a method of preparing 1,4-naphthoquinone oxides which is much more convenient than Zincke's[6] hypochlorite procedure.



I II III

A few trials were made of the method of introducing a β-unsaturated group by direct C-alkylation of a phenolic salt, and it was observed that a small amount of 2-methyl-3-benzyl-1,4-naphthoquinone can be isolated from the very dark mixture produced by refluxing of 2-methyl-1,4-naphthohydroquinone with benzyl bromide and potassium carbonate in acetone. When the reaction was conducted at room temperature with two equivalents of benzyl bromide the mixture remained light in color and the sole crystalline product was methylnaphthohydroquinone dibenzyl ether (73% yield). With one equivalent

(1) For a preliminary account of a part of this work see Fieser, Campbell, Fry and Gates, THIS JOURNAL, **61**, 2559 (1939).

(2) Du Pont Research Fellow.

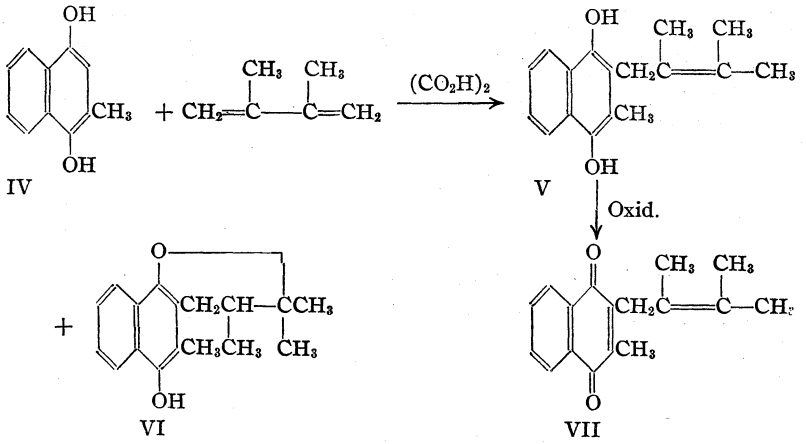
(3) Fieser, Campbell and Fry, THIS JOURNAL, **61**, 2206 (1939).

(4) Fieser, Bowen, Campbell, M. Fieser, Fry, Jones, Riegel, Schweitzer and Smith, *ibid.*, **61**, 1925 (1939).

(5) Gilman, "Organic Chemistry," Vol. I, John Wiley and Sons, Inc., New York, N. Y., pp. 428–429, 1938.

(6) Zincke, *Ber.*, **25**, 3602 (1892).

of the halide at room temperature a part of the starting material remained unchanged and both the mono and dibenzyl ethers were formed, but there was no indication of C-benzylation.



On the basis of the postulated[3] origin of vitamin K_1 in nature it seemed likely that this substance might be obtainable by the direct condensation of phytol with a 2-alkyl-1,4-naphthoquinone in either the oxidized or the reduced form. Trials with 2-methyl-1,4-naphthoquinone were invariably unpromising and attention was directed to use of the hydroquinone. From the investigations of Karrer, L. I. Smith, Todd, and others it is known that alkylated benzohydroquinones having a free nuclear position condense readily with β-unsaturated alcohols or with dienes in the presence of a mineral acid or a zinc halide, or under conditions where a mineral acid is liberated in the course of the initial condensation. The reported condensations invariably are attended by cyclization to compounds of the tocopherol type.[7] For the most direct approach to a substance of the desired vitamin K_1 type, it would appear necessary to avoid the natural disposition for the formation of a structure characteristic of vitamin E. The naphthalene derivatives, moreover, show a high sensitivity to mineral acids not encountered in the benzene series. It seemed desirable to seek a milder and less destructive condensing agent less prone to promote cyclization and other side reactions. Anhydrous oxalic acid fulfils the requirements, and dioxane is a suitable solvent. In isolated experiments successful use was made of trichloroacetic acid as the catalyst and ethylene glycol monomethyl ether as solvent.

On refluxing methylnaphthohydroquinone (IV) with excess 2,3-dimethylbutadiene in dioxane solution in the presence of anhydrous oxalic acid, the starting material was completely consumed in twenty-four hours, and in this time there was no appreciable discoloration or decomposition. The reaction mixture contained both the substituted hydroquinone V and an isomeric substance which probably is a naphthotocopherol of the structure VI, although this product has not been studied in detail. The hydroquinone V can be separated from the mixture by virtue of its sparing solubility in petroleum ether, or it can be extracted with a liberal amount of strong alkali containing sodium hydrosulfite. The naphthotocopherol is considerably more soluble in the hydrocarbon solvent and shows even feebler acidic properties than the hydroquinone. The latter substance, which forms a diacetate, was oxidized in good yield to 2-methyl-3-(β,γ,γ-trimethylallyl)-1,4-naphthoquinone (VII). The spectrum of this crystalline yellow compound in absolute alcohol, kindly determined by Mr. D. M. Bowen, is very similar to that of vitamin K_1 as reported by Dam, Karrer, *et al.*,[8] and shows the following maxima (log E values in parenthesis): 243 mμ (4.23), 249, 264, 270.5 mμ (4.27), 329 mμ (3.43).

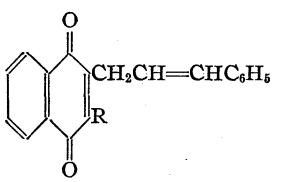
Reductive acetylation of the quinone VII under mild conditions gave the above diacetate, but when the temperature was not suitably controlled a part of the material was converted into a substance of the composition of the naphthotocopherol acetate. A new procedure for the reductive acetylation of quinones which avoids secondary reactions consists in the use of zinc dust, acetic anhydride, and a small amount of pyridine as catalyst. The reaction proceeds rapidly at 0°. In trials with 2-methyl- and 2-ethyl-1,4-naphthoquinone, it was found that reductive benzoylation can be accomplished readily by treating the quinone with zinc dust, pyridine and benzoyl chloride; this constitutes a useful method of preparing crystalline derivatives of low melting quinones.

Under the conditions indicated, the substituted hydroquinone V was obtained in 29% yield and

(7) Professor Lee I. Smith has kindly informed us that the isolation of hydroquinones is reported in papers from his Laboratory which are now in press.

(8) Dam, Geiger, Glavind, P. Karrer, W. Karrer, Rothschild and Solomon, *Helv. Chim. Acta*, **22**, 310 (1939).

the naphthotocopherol VI in 15% yield. Using isoprene as the second component, no condensation was observed at the reflux temperature, but a small amount of product was formed at 180°. Piperylene likewise reacted less readily than 2,3-dimethylbutadiene, but there were indications of condensation at a temperature of 120°. Cinnamyl alcohol reacted rather readily at the reflux temperature with methylnaphthohydroquinone (22% yield), and somewhat less readily with ethylnaphthohydroquinone (9.4% yield). In each case some starting material was recovered by extraction with 1–2% alkali containing hydrosulfite, and the substituted hydroquinone was then separated most conveniently by repeated extraction with 10% alkali-hydrosulfite. The reaction products were readily converted into crystalline quinones of the type VIII. Benzyl



VIII (R = CH_3, C_2H_5)

alcohol combined with methylnaphthohydroquinone only to a minor extent at the boiling point, giving after oxidation 2-methyl-3-benzyl-1,4-naphthoquinone. With allyl alcohol no reaction occurred at 180°. It appears, therefore, that in the presence of anhydrous oxalic acid in dioxane solution certain highly reactive dienes, β-unsaturated alcohols, and aryl carbinols condense to a greater or less extent with alkylnaphthohydroquinones, but that the reaction has distinct limitations. It is significant, however, that with a compound of suitable reactivity, condensation to a hydroquinone with a β-unsaturated side chain can be accomplished without undue cyclization of the primary product.

In the Dam–Karrer[8] test with alcoholic alkali 2-methyl and 2-ethyl-3-cinnamyl-1,4-naphthoquinone give intense blue colors which persist somewhat longer than observed with corresponding allyl compounds.[3] The 3-benzyl compound gives a light purple color, but no purple or blue phase was observed with 2-methyl-3-trimethylallyl-1,4-naphthoquinone (VII). The presence of a substituent on the β-unsaturated carbon atom apparently interferes with the color reaction.

In bio-assays kindly conducted by Dr. W. L. Sampson, 2-methyl-3-benzyl-1,4-naphthoquinone was inactive at a dosage level of 100 γ and the corresponding 3-trimethylallyl compound was inactive at a level of 200 γ. From carefully repeated assays of the compounds described in the early reports from our Laboratory[3,4,9] it is concluded that the only substance in the group previously considered which has appreciable antihemorrhagic activity is 2,3-dimethyl-1,4-naphthoquinone.[3] In addition, 2-methyl-3-cinnamyl-1,4-naphthoquinone has been found active at a dosage of 100 γ but not at 10 γ.

Experimental Part[10]

Preparation of Starting Materials

2-Methylnaphthoquinone (M. D. G.).—Satisfactory results were obtained by a procedure considerably shorter than that of Anderson and Newman.[11] (The yield was much lower when the oxidation was conducted at the reflux temperature as in the preparation of certain dimethylnaphthoquinones.[12]) A solution of 200 g. of β-methylnaphthalene in 2 liters of glacial acetic acid was added in the course of two hours to a well-stirred solution of 800 g. of chromic anhydride in 1.5 liters of 80% acetic acid, cooling the mixture in an ice-bath and keeping the temperature from rising above 20°. At the end of the addition the temperature was allowed to rise slowly; after a few hours cooling was again required to moderate the reaction and keep the temperature from rising above 50–60°. After a total period of thirty-six hours, the solution was poured into water and the precipitated quinone collected and washed and obtained as a good yellow solid (100 g.). This was crystallized directly from methanol (Norite), giving in all 70 g. (29%) of yellow prismatic needles, m. p. 105–106°.

2-Ethyl-1,4-naphthoquinone.—In the preparation of β-ethylnaphthalene the best results were obtained (W. P. C.) using 50 g. of β-acetonaphthalene, 150 cc. of benzene, 300 cc. of methanol, 200 cc. of concentrated hydrochloric acid, and 155 g. of zinc amalgamated with 10 g. of mercuric chloride. The mixture was refluxed vigorously for twenty-four hours with the addition of three 20-cc. portions of fresh acid. About 1.5 liters of water was then added and a little ether was used to facilitate separation of the benzene layer. The latter, combined with an ether extract of the aqueous layer, was dried and the product distilled, giving 29 g. (63%) of colorless β-ethylnaphthalene, b. p. 127–129° at 14 mm. When the reflux period was extended to forty-seven hours the yield was 57%. The yield by the Martin procedure (M. D. G., 57%) was essentially the same as previously reported.[13]

The following oxidation procedure (W. P. C.) is regarded as more convenient than that described for the lower homolog or that of the literature.[14] A solution of

(9) Fieser, Bowen, Campbell, Fry and Gates, THIS JOURNAL, **61**, 1926 (1939).

(10) Microanalyses by Lyon Southworth and Herbert S. Wight.

(11) Anderson and Newman, *J. Biol. Chem.*, **103**, 405 (1933).

(12) Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., Boston, Mass., 1935, p. 230.

(13) Martin, THIS JOURNAL, **58**, 1438 (1936).

(14) Kruber and Schade, *Ber.*, **69**, 1722 (1936).

TABLE I

ALKYL-1,4-NAPHTHOQUINONE OXIDES

Alkyl substituents	Properties M. p., °C.	Cryst. form	Analyses, % Carbon Found	Carbon Calcd.	Hydrogen Found	Hydrogen Calcd.
None	134.5–135.5	Prism. needles	...	...	..	..
2-Methyl	95.5– 96.5	Long needles	70.38	70.20	4.36	4.29
2,6-Dimethyl	97– 98	Prisms	71.23	71.27	5.07	4.99
2,7-Dimethyl	91– 92	Slender needles	71.29	71.27	5.09	4.99

70 g. of chromic anhydride in 30 cc. of water, diluted with 150 cc. of acetic acid, was added in one hour to a stirred solution of 29 g. of β-ethylnaphthalene in 200 cc. of acetic acid while maintaining the temperature at 45–50° by suitable cooling. The exothermic reaction was soon over, and after standing for fifteen hours the mixture was stirred at 60° for one hour and poured into 2 liters of water. The quinone separated as a light yellow solid and crystallization from methanol gave 12.6 g. (39%) of satisfactory material, m. p. 86–87°, in two crops.

2-Methyl-1,4-naphthohydroquinone (L. F. F., M. D. G.) (a) with Stannous Chloride.—A solution of 10 g. of 2-methyl-1,4-naphthoquinone in 100 cc. of hot alcohol was cooled rapidly to room temperature and the resulting paste treated with 40 g. of stannous chloride in 40 cc. of concentrated hydrochloric acid. The quinone dissolved at once giving a transient deep brown color (quinhydrone) rapidly fading to light yellow, and the solution became hot. Water (165 cc.) was added and the hydroquinone which precipitated was brought into solution at the boiling point. The solution was clarified with norite, filtered, diluted with an equal volume of water at the boiling point and set aside to crystallize. The hydroquinone separated as colorless needles and after thorough washing with cold water was dried at 50–60° either in the air or at 20 mm.; yield 9.2–9.5 g. When obtained by this procedure in an initially colorless condition, the material keeps for several days without deterioration.

(b) With Sodium Hydrosulfite.—A solution of 10 g. of the quinone in 50 cc. of hot alcohol was treated with a solution of hydrosulfite (about 30 g.) in water until the color (yellow, then brown) was discharged and the cooled mixture was diluted and the product extracted with ether. The dried, nearly colorless ethereal solution was evaporated nearly to dryness and the residual solid was triturated with petroleum ether and collected. The hydroquinone was obtained as a white powder (9.7 g.). This method is rapid and the product entirely suitable for immediate use, but the material darkens more rapidly on storage than the crystalline product of (a).

The **diacetate**[11] of 2-methyl-1,4-naphthohydroquinone, prepared by reductive acetylation of the quinone using either sodium acetate or pyridine, formed colorless prisms from ether–petroleum ether or ether, m. p. 112.5–113°. The dibenzoate was prepared by adding 1 cc. of benzoyl chloride by drops to a mixture of 0.5 g. of methylnaphthoquinone, 0.5 g. of zinc dust, and 3 cc. of pyridine, while cooling with ice. Reaction occurred at once and after standing at room temperature for ten minutes the pale yellow mixture was heated to boiling, cooled, and the product extracted with ether–alcohol. After washing with dilute acid and with soda solution and concentrating the dried solution to a small volume, the dibenzoate separated as colorless needles (0.6 g.), m. p. 178.5–179.5°. Two crystallizations from alcohol (35 cc.) raised the m. p. to 180–180.5°.

Anal. Calcd. for $C_{25}H_{18}O_4$: C, 78.53; H, 4.75. Found: C, 78.71; H, 4.80.

2-Ethyl-1,4-naphthohydroquinone was prepared by the second procedure described above (b) with similar results; the material softened at 140° and melted at 144–145°, dec. The **diacetate** was obtained by adding 2 drops of pyridine to a suspension of 0.2 g. each of ethylnaphthoquinone and zinc dust in 2 cc. of acetic anhydride. Heat was evolved and the mixture became colorless; acetic acid was added and the mixture filtered at the boiling point, using more acetic acid and water in subsequent extractions of the residue. (A yellow color not connected with the acetylative reduction becomes quite pronounced if the reaction mixture is allowed to stand for some time but the color is easily eliminated in the purification process.) After suitable dilution at the boiling point the product separated in a good condition, m. p. 104–105° (0.20 g.). It forms prism clusters of the same m. p. from ether–petroleum ether or ligroin. The **dibenzoate**, prepared by reductive benzoylation as above, formed short needles from alcohol, m. p. 164–165°.

Alkylnaphthoquinone Oxides (L. F. F.)

In a typical experiment 5 g. of 2-methyl-1,4-naphthoquinone was dissolved in 15 cc. of alcohol and the solution was cooled to 45° and treated with 10 cc. of 30% hydrogen peroxide followed by a solution of 2.5 g. of sodium carbonate in 10 cc. of water. Heat was evolved, the yellow color was discharged, and inorganic salts separated. After five minutes the mixture was diluted well with water, whereupon 2-methyl-1,4-naphthoquinone oxide separated in the form of long colorless needles. One crystallization from dilute alcohol gave 3.6 g. of satisfactory product, m. p. 94.5–95.5°. The properties and analyses of purified samples of this and other oxides are recorded in Table I. The preparations were conducted as described, using sufficient alcohol to keep the quinone in solution at about 45°, and the yields were as reported in the example. The parent substance corresponds to the description of Zincke[6] (m. p. 136°); the 2-methyl derivative had the properties noted by Madinaveitia[15] except that the m. p. is considerably lower (M., 102°). The oxides crystallize well from alcohol, dilute alcohol, or ligroin.

Grignard Reactions with Alkylnaphthoquinone Oxides (E. M. F.)

2,6-Dimethyl-1,4-naphthoquinone Bromohydrin (II), (a) Grignard Reaction of Oxide.—The Grignard reagent obtained from 1.5 cc. of allyl bromide, added in 80 cc. of

(15) Madinaveitia, *Rev. acad. cienc. Madrid*, **31**, 617 (1934).

ether during one and one-half hours to a stirred suspension of 1.4 g. of magnesium in 20 cc. of ether, was added slowly to a solution of 3.16 g. of 2,6-dimethyl-1,4-naphthoquinone oxide in 50 cc. of ether. A white complex separated at once and on displacing most of the ether with benzene and refluxing for one-half hour it turned somewhat red. Decomposition was effected with dilute acetic acid (yellow color), and extraction of an ethereal solution of the reaction product with sodium carbonate (red solution) gave 0.1 g. of 2,6-dimethyl-3-hydroxy-1,4-naphthoquinone,[16] m. p. 192–194.5°, mixed m. p. 193–194.5°. The residual oil when treated with dilute alcohol afforded 0.38 g. of a crystalline product identified as the unchanged oxide and 1.25 g. of 2,6-dimethyl-1,4-naphthoquinone bromohydrin. This crystallized from dilute alcohol in colorless, rectangular plates, m. p. 146–148°.

Anal. Calcd. for $C_{12}H_{11}O_3Br$: C, 50.90; H, 3.92; Br, 28.23. Found: C, 51.05, 51.05; H, 4.24, 4.18; Br, 28.33.

(b) **With Magnesium Bromide.**—A solution prepared from 5.32 g. of bromine and 150 cc. of dry ether was added slowly to a stirred suspension of 0.81 g. of magnesium in ether. A vigorous reaction took place with the separation of a yellow oil turning dark purple at the end. After stirring for twenty minutes, 3 g. of 2,6-dimethyl-1,4-naphthoquinone oxide was added slowly in ether solution. A complex soon formed and eventually separated as a white solid mixed with a little of the dark oil. After stirring for fifteen minutes water was added and the yellowish ether layer was washed, dried, and evaporated. The crystalline residue, washed free of oil with a little ether, amounted to 3.07 g. (73%) and consisted of nearly pure bromohydrin. Recrystallized from dilute alcohol the substance melted at 147–148.5° and showed the properties of the sample obtained in (a).

In a further experiment 3 g. of the bromohydrin was treated in ether with two equivalents of allylmagnesium bromide (2 cc. of the halide). A complex formed at once with evolution of heat; after refluxing for seventeen hours and decomposing with dilute acetic acid, a small amount of acidic material was removed by extraction with 1 *N* alkali and the residual oil afforded 0.4 g. of 2,6-dimethyl-1,4-naphthoquinone oxide (m. p. 96.5–97.5°; no depression on mixing). No other pure product was isolated.

3-Bromo-2,6-dimethyl-1,4-naphthoquinone.—A solution of 0.1 g. of the bromohydrin II and 0.1 g. of sodium acetate in 2 cc. of acetic acid was refluxed for one-half hour, when it had become red, and diluted with water. The precipitated material on crystallization from alcohol gave 0.03 g. of yellow needles, m. p. 114–114.5°. The substance gives a positive Beilstein test and is not soluble in alkali.

Anal. Calcd. for $C_{12}H_9O_2Br$: C, 54.36; H, 3.42. Found: C, 54.64; H, 3.61.

Action of Methylmagnesium Chloride on Methylnaphthoquinone Oxide.—The reagent from 0.51 g. of magnesium was added to a solution of 3.35 g. of 2-methyl-1,4-naphthoquinone oxide in 75 cc. of ether. A complex separated at once and did not appear to undergo change on refluxing for two hours and allowing the mixture to stand overnight. After decomposition with acetic acid and washing the ethereal solution with soda, 0.38 g. of starting material was collected on crystallization from dilute alcohol. The residual oil yielded a solid product only on being refluxed for a few minutes with two volumes of alcohol and 0.5 cc. of concentrated hydrochloric acid. The dark red solution was evaporated in vacuum, and the oil then crystallized from ether–petroleum ether. A total of 1 g. of crude brown product was collected, and crystallization from ether using Norite afforded 0.7 g. of colorless material in the form of parallelograms. The substance decomposes when heated slowly; when immersed in a bath just below the m. p. it melts at 141.5–142° to a colorless liquid which rapidly darkens with gas evolution.

Anal. Calcd. for $C_{12}H_{13}O_2Cl$: C, 59.88; H, 5.45; Cl, 14.73. Found: C, 60.05, 60.16; H, 5.75, 5.67; Cl, 14.99.

Benzylation of Methylnaphthohydroquinone (L. F. F.)

In the most successful preparation of **2-methyl-1,4-naphthohydroquinone dibenzyl ether** a mixture of 2 g. of the hydroquinone, 4 g. of benzyl bromide and 20 cc. of acetone was flushed out with nitrogen, 4 g. of finely powdered potassium carbonate was added, and the vessel was stoppered and shaken at room temperature for twenty-five hours. The solution was orange-red at the start but became light yellow. The mixture was poured into water, extracted with ether, and the extract washed twice with 10% potassium hydroxide, which removed only a trace of phenolic material. Evaporation of the dried ether solution left a yellow oil which went solid on rubbing. Crystallization from 35 cc. of alcohol gave 2.91 g. (72%) of slightly yellow product, m. p. 72–3°. On further purification by crystallization from ligroin (b. p. 60–90°) the ether formed colorless needles, m. p. 74.5–75°.

Anal. Calcd. for $C_{25}H_{22}O_2$: C, 84.71; H, 6.26. Found: C, 84.93; H, 6.33.

The **monobenzyl ether** was isolated along with the diether in an experiment conducted as above but using only one equivalent of benzyl bromide (1 g. of hydroquinone, 1 g. of bromide, 1.5 g. of potassium carbonate, 10 cc. of acetone). The mixture was poured into aqueous sodium hydrosulfite solution, extracted with ether, and the light yellow ethereal solution extracted three times with 2% potassium hydroxide containing hydrosulfite, which removed about 0.2 g. of impure starting material (yellow alkaline liquor). Eight extractions with 10% alkali containing hydrosulfite (total, 200 cc.) then extracted the monobenzyl ether; after acidification this was taken into ether and the solution dried and evaporated. The oily residue yielded a solid on treatment with ether–petroleum ether, and after two recrystallizations from ligroin the substance formed small, colorless plates, m. p. 159–160°, with some previous darkening; yield 3 mg.

Anal. Calcd. for $C_{18}H_{16}O_2$: C, 81.79; H, 6.10. Found: C, 81.81; H, 6.25.

From the neutral fraction there was obtained 0.34 g. of the dibenzyl ether in a crystalline condition. In a qualitative trial the reaction seemed to proceed about the same in boiling ethylene glycol dimethyl ether as in cold acetone.

2-Methyl-3-benzyl-1,4-naphthoquinone was isolated in an exploratory experiment in which 2 g. of the hydroqui-

(16) Fieser and Seligman, THIS JOURNAL, 56, 2690 (1934).

none was refluxed for fifteen and one-half hours with 4 g. of benzyl bromide, 4 g. of potassium carbonate, and 20 cc. of acetone. The very dark reaction mixture was diluted with water and extracted with ether and the extract shaken with dilute alkali-hydrosulfite. The ethereal solution remained very dark brown throughout this and other washings and the residue on evaporation was a dark resin. On distillation in vacuum the bulk of the material came over without decomposition and a part of the distillate solidified. Using this seed and employing ether–petroleum ether as solvent, a crystalline crust was obtained yielding on one crystallization from alcohol 0.3 g. of yellow crystals of the quinone, m. p. 107–108°. After two more crystallizations the substance formed ball-like clusters of bright yellow needles, m. p. 107.5–108°.

Anal. Calcd. for $C_{18}H_{14}O_2$: C, 82.41; H, 5.38. Found: C, 82.50; H, 5.42.

The substance gives a large depression when mixed with methylnaphthoquinone. It yields a colorless hydroquinone on reduction with aqueous hydrosulfite in alcoholic solution, and with 5% alcoholic potassium hydroxide in the cold it gives a light purple color changing through brown to greenish-yellow.

Condensation of Methylnaphthohydroquinone with 2,3-Dimethylbutadiene (L. F. F.)

A solution of 3 g. of 2-methyl-1,4-naphthohydroquinone, 3 g. of anhydrous oxalic acid (prepared by heating the hydrate at 140°), and 10 cc. of 2,3-dimethylbutadiene in 30 cc. of dioxane (purified with sodium) was refluxed for twenty-four hours and the pale orange solution was poured into water and extracted with ether. After washing with water the solution was extracted three times with 1% alkali containing hydrosulfite, each extract being weakly yellow. The alkaline liquor was washed with ether, acidified, and the precipitated solid dissolved in alcohol and treated with ferric chloride solution. This afforded 0.11 g. (m. p. 94–95°) of the quinone VII described below, showing that the starting material had been completely consumed. The ethereal solution was washed, dried, and evaporated to a small volume, and on displacing the ether with petroleum ether and cooling there was obtained 1.18 g. of a nearly colorless crystal powder which proved to be the hydroquinone of VII in an essentially pure condition (total yield, 29%).

On allowing the petroleum ether mother liquor to stand overnight, a few large prisms of the naphthotocopherol VI separated on the walls (0.08 g., m. p. 71.5–72°). To isolate the bulk of this the dark mother liquor was extracted with 4% alkali until this was colorless (five times) to remove traces of the substituted hydroquinone and the light yellow organic layer was dried and evaporated. A rather mobile yellow oil resulted, and when seeded with the above prisms gave a crystalline paste. After rubbing with methanol and cooling well there was collected 0.59 g. of colorless naphthotocopherol, m. p. 71.5–72°; total yield 15%.

When the refluxing time in the preparation was decreased to sixteen hours a significant amount of starting material was unconsumed (removed in one extraction with 1% alkali). In one experiment ethylene glycol monomethyl ether was used as solvent and the reaction was conducted at 70°. Three extractions from ether with 1% alkali-hydrosulfite removed 38% of recovered starting material, identified by conversion to methylnaphthoquinone (m. p. 103–104°), and the yield of substituted hydroquinone based on material not recovered was 15%; some naphthotocopherol was also formed.

2 - Methyl - 3 - (β,γ,γ - trimethylallyl) - 1,4 - naphthoquinone (VII).—On adding a solution of 0.49 g. of ferric chloride crystals in dilute hydrochloric acid to a solution of 0.23 g. of the crude hydroquinone in 2 cc. of alcohol and gradually adding water, the quinone separated in yellow blades, m. p. 94–95° (0.22 g.). Lead tetraacetate gave nearly as good results (0.18 g., m. p. 93–94.5°). A sample for analysis was sublimed at 130–150° (2 mm.) and crystallized twice from methanol, forming bright yellow blades, m. p. 95–95.5°.

Anal. Calcd. for $C_{17}H_{18}O_2$: C, 80.28; H, 7.14. Found: C, 80.33; H, 7.25.

On treating a cold alcoholic solution of the quinone with an equal volume of 10% alcoholic potassium hydroxide, the original yellow color gives place to a faint pinkish coloration changing to dull red when heated. No blue or purple phase has been observed.

2 - Methyl - 3 - (β,γ,γ - trimethylallyl) - 1,4 - naphthohydroquinone Diacetate.—The crude hydroquinone separated from the reaction mixture as described above underwent oxidation on attempted crystallization from ligroin or dilute alcohol and was not obtained pure; the best material was pale rose colored and turned yellow on standing. For characterization the substance was therefore acetylated by warming with acetic anhydride–sodium acetate for a few minutes. The crude product was an oil, but after washing in ether with soda solution, drying, and replacing the solvent with petroleum ether, it was obtained as a white powder. The diacetate then crystallized from ligroin (b. p. 60–90°) in colorless cubes, m. p. (constant) 119–120°.

Anal. Calcd. for $C_{21}H_{24}O_4$: C, 74.09; H, 7.11. Found: C, 74.04; H, 7.23.

A product of the same m. p. and mixed m. p. was obtained by reductive acetylation of the quinone by the pyridine method without application of heat. In an earlier experiment the reaction was conducted with zinc dust, acetic anhydride, and sodium acetate and the mixture was boiled for a few minutes. In this case, after extraction with ether and crystallization from petroleum ether and then twice from ligroin there was obtained, in very poor yield, a substance having the composition of the acetate of the naphthotocopherol VI. The substance forms large, colorless, transparent prisms, m. p. 128.5–129°.

Anal. Calcd. for $C_{19}H_{22}O_3$: C, 76.48; H, 7.43. Found: C, 76.36; H, 7.54.

Naphthotocopherol of Probable Structure VI.—The material separated with methanol as described crystallized most satisfactorily from petroleum ether, in which it is quite soluble, but less so than in methanol. The substance forms large, transparent prisms, m. p. 73–73.5°.

Anal. Calcd. for $C_{19}H_{20}O_2$: C, 79.65; H, 7.87. Found: C, 79.95; H, 7.63.

The substance forms no picrate or trinitrobenzene derivative from alcohol. It is not extracted from ether by 10%

alkali but dissolves in alcoholic alkali with a deep yellow color and precipitates on dilution. No reaction was observed on treating the substance with silver nitrate in methanol, with ferric chloride in alcohol, or with lead tetraacetate in acetic acid.

Other Condensations of Methyl and Ethylnaphthohydroquinone (W. P. C.)

2-Methyl-3-cinnamyl-1,4-naphthoquinone.—A solution of 3 g. of methylnaphthohydroquinone, 1.54 g. of cinnamyl alcohol, and 2 g. of anhydrous oxalic acid in 20 cc. of dioxane was refluxed for twenty-two hours, poured into water and extracted with ether. Starting material was extracted with a total of 150 cc. of 1% sodium hydroxide-hydrosulfite and collected in the form of the quinone, m. p. 100–103° (1.0 g.). The ethereal solution was dried and evaporated and the oily product digested with three 80-cc. portions of petroleum ether. The solution each time was decanted and eventually left 1.55 g. of solid consisting largely of methylcinnamylnaphthohydroquinone. This was dissolved in ether, shaken with 5 g. of silver oxide and anhydrous sodium sulfate (twenty minutes) and the material left on filtering and evaporating the yellow solution was crystallized from ether–petroleum ether and gave 0.8 g. of the quinone, m. p. 124–126° (yield, allowing for recovered material, 22%). Purified by further crystallizations from alcohol the substance formed bright yellow blades, m. p. 127–127.5°. In the test with alcoholic alkali in the cold it gives an intense indigo blue which persists for about fifteen minutes and fades to brown.

Anal. Calcd. for $C_{20}H_{16}O_2$: C, 83.31; H, 5.59. Found: C, 83.63; H, 5.71.

In other runs the methylcinnamylnaphthohydroquinone was separated from the ethereal solution by repeated extraction with 10% alkali containing hydrosulfite, and this seemed more convenient than the above procedure. The extraction method was employed in an experiment paralleling that above but employing trichloroacetic acid (2 g.) in place of oxalic acid as the condensing agent (3 g. of the hydroquinone, twenty-three hours). There was obtained 0.7 g. of quinone, m. p. 126.5–127°, and 0.15 g., m. p. 125–126°; the yield is thus the same as in the above preparation.

The **hydroquinone diacetate** was obtained both from the crude hydroquinone with acetic anhydride and pyridine in the cold and from the quinone, zinc dust, acetic anhydride and pyridine. It crystallized from ether–petroleum ether in fine, silky needles, m. p. 167.5–168°.

Anal. Calcd. for $C_{24}H_{22}O_4$: C, 76.98; H, 5.92. Found: C, 77.17; H, 6.09.

2-Ethyl-3-cinnamyl-1,4-naphthoquinone.—2-Ethyl-1,4-naphthohydroquinone (3 g.) was condensed with cinnamyl alcohol (1.54) exactly as described for the lower homolog (twenty-two hours) and unchanged starting material (1.68 g.) was extracted with three portions of 2% alkali-hydrosulfite. The substituted hydroquinone was then extracted with 10% alkali (five portions) and the yellow liquor washed with ether and acidified. The product was taken into ether and oxidized with silver oxide and the crude quinone (0.38 g.) crystallized three times from alcohol; yield, 0.2 g. (9.4%, based on material consumed). The quinone forms flat needles, m. p. 118–118.5°; the behavior in the test with alcoholic alkali is like that of the methyl compound.

Anal. Calcd. for $C_{21}H_{18}O_2$: C, 83.41; H, 6.00. Found: C, 83.29; H, 6.10.

The **hydroquinone diacetate,** prepared as above by the pyridine method, was obtained from ether–petroleum ether as elongated prisms, m. p. 123.5–124.5°. Recrystallization from methanol did not change the m. p.

Anal. Calcd. for $C_{25}H_{24}O_4$: C, 77.30; H, 6.23. Found: C, 77.23; H, 6.34.

Condensation with Isoprene.—A solution of 2 g. each of methylnaphthohydroquinone, isoprene, and anhydrous oxalic acid in 20 cc. of dioxane was heated in a sealed tube at 180° for fifteen hours. Unchanged hydroquinone was extracted with 1% alkali-hydrosulfite (75 cc.) and yielded 0.6 g. of pure methylnaphthoquinone. Extraction with 100 cc. of 10% alkali-hydrosulfite in four portions and acidification with acetic acid gave 0.3 g. of white solid. This was oxidized with ferric chloride giving the quinone as a yellow oil which failed to crystallize and which was therefore converted by reductive acetylation (sodium acetate) to **2-methyl-3-(γ,γ-dimethylallyl)-1,4-naphthohydroquinone diacetate.** On purification this crystallized from ether–hexane as colorless prisms, m. p. 104.5–105.5°.

Anal. Calcd. for $C_{20}H_{22}O_4$: C, 73.60; H, 6.80. Found: C, 73.52; H, 6.79.

Condensation with Benzyl Alcohol.—The reaction was conducted with methylnaphthohydroquinone (2 g.), benzyl alcohol (1.24 g.), oxalic acid (2 g.), and dioxane (20 cc.) at the reflux temperature (twenty-five hours) and worked up as in the reaction with isoprene. The recovered starting material isolated as the quinone (m. p. 105–106°) amounted to 1.5 g., and oxidation of the product extracted with 10% alkali (75 cc.) afforded a few milligrams of **2-methyl-3-benzyl-1,4-naphthoquinone.** After two crystallizations from ether–petroleum ether this melted at 105–107.5°; a mixture with the sample described above melted at 107–108°, and the m. p. of methylnaphthoquinone was depressed to 73°.

Other Trials.—The starting material was largely recovered (1.4 g., as quinone) on attempted condensation of allyl alcohol (0.8 g.) with methylnaphthohydroquinone (2 g.) at 180° for twenty-four hours under the above conditions. Piperylene did not react readily, but there were indications of partial condensation at 120°. No reaction occurred on refluxing either the diacetate (thirty-six hours) or the dibenzyl ether (twenty-eight hours) of methylnaphthohydroquinone with dimethylbutadiene and oxalic acid in dioxane, the starting materials being recovered unchanged.

Summary

By using a mild condensing agent such as anhydrous oxalic acid in dioxane solution, 2-alkyl-1,4-naphthohydroquinones can be condensed with sufficiently reactive β-unsaturated alcohols, dienes or aryl carbinols, and under these conditions the substituted hydroquinones first formed are only partially cyclized and can be isolated and con-

verted into quinones of the structural type of vitamin K_1.

Another observation of this work is that a typical 2-alkyl-1,4-naphthoquinone oxide is converted into a bromohydrin by the action of magnesium bromide in ether. New methods are described for the preparation of such oxides and for carrying out the reductive acetylation of quinones.

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Quantum Yields and Kinetics of a Photosensitized Production of Reducing Sugars from Sucrose in Aqueous Solutions of Uranyl Sulfate by Visible and Ultraviolet Light

BY LAWRENCE J. HEIDT

Aqueous solutions of sucrose are about as transparent as water in the visible and near ultraviolet to 200 mμ, so light in this region has not been found to produce any measurable effect upon the stability of sucrose dissolved in water. When uranyl ions are added to these solutions, they absorb visible and ultraviolet light; but their extinction coefficients between 470 and 208 mμ are the same as if no sucrose was present. Neither does the uranyl sulfate greatly affect the specific rotation of sucrose, which remains within 0.2% of 66.5° for the D lines of sodium.

Illumination of these sucrose–uranyl solutions with light absorbed by the uranyl ion causes a decrease in their optical activity and the formation of products which reduce the alkaline cupric solutions of Shaffer, Hartmann and Somogyi.[1]

Materials.—The sucrose was U. S. Bureau of Standards sample 17, lot 3650, and the fructose and glucose were recrystallized specimens with the correct rotations.[2] They were stored in vacuum over "Anhydrone" and were kept in the dark as much as possible.

The uranyl salts, oxalic acid, and permanganate were recrystallized and centrifuged specimens like those used previously.[3]

The sodium oxalate used to standardize the permanganate solutions was U. S. Bureau of Standards sample 40c.

All the other chemicals were reagent quality.

Apparatus and Procedure.—Monochromatic light was obtained by means of a prism monochromator using crystal quartz lenses. The 60° cornu prism was 6.5 cm. high and had faces 8 cm. long. It was purchased with a grant from the Warren Fund of the American Academy of Arts and Sciences. The monochromator transmitted in air the 185 mμ line of aluminum and separated the 578 and 546 mμ lines of mercury. In combination with a zinc spark, the energies at 208, 254 and 280 mμ transmitted by the exit slit were about the same as those obtained elsewhere with similar apparatus.[4]

Two reaction cells were used with the monochromator ensemble. One was rectangular, 20 mm. wide and 40 mm. high and held 5 cc. of solution in a 5-mm. layer. The other cell was trapezoidal and held 12 cc. of solution in a 30-mm. layer between the parallel windows. The front window was 10 mm. wide and 20 mm. high and the back window, 20 mm. wide and 40 mm. high. The transparency of the windows of both cells agreed within 2% at 208 mμ.

The source of light at 366 and 436 mμ was an inverted "U" type mercury vapor arc lamp.[5] Its intensity at these wave lengths was increased by reducing to 5 mm. the internal diameter of the quartz tubing containing the arc. This made available behind the exit slit (1 mm. wide × 10 mm. high) 7×10^{17} photons per minute at 366 mμ and 4×10^{17} at 436 mμ, varying less than 1% in twenty hours when the lamp was properly operated.

The amount of monochromatic light at 254 mμ was increased over 200-fold, to 5×10^{19} photons per minute, as described elsewhere.[6] Duplicate cells and stirrers used with this apparatus were made from the same pieces of transparent quartz. Quantum yields were the same whether obtained with this set-up or with the monochromator (see Table I, Expts. 12 and 13). The effectiveness of the light-proof aluminum tube that acted as a shutter was demonstrated in Expt. 9d, Table I, where the values in parentheses are directly proportional to the light flux which would have been incident on the sugar solution had the shutter been removed.

Analytical.—The light flux entering the actinic systems was measured with the uranyl oxalate solutions recommended for use as actinometers.[3,7] The oxalate content of the solutions was determined by electrometric titration with permanganate after proof that the method gave the same values of ϕ as titration to a color end-point. The

(1) Heidt and Purves, THIS JOURNAL, **60**, 1206 (1938), give data when this reagent is used to follow the hydrolysis of sugars.

(2) I am indebted to Professor C. B. Purves for supplying these sugars and to Drs. F. B. Cramer and D. H. Grangaard for recrystallizing the fructose and glucose.

(3) Forbes and Heidt, THIS JOURNAL, **56**, 2363 (1934), and research referred to therein.

(4) Forbes and Brackett, *ibid.*, **53**, 3973 (1931).

(5) Forbes and Heidt, *ibid.*, **53**, 4349 (1931).

(6) Heidt, *Science*, forthcoming publication.

(7) Daniels, *J. Phys. Chem.*, **42**, 701 (1938).

end-point by the electrometric method can be reproduced to 0.04 cc. of 0.0002 molar permanganate (4×10^{-8} equivalent) when the volume of the titrated solution is less than 10 cc. Titrations were made with solutions weighed to 1 mg.

The amount of reducing sugars formed was determined with the Shaffer–Hartmann–Somogyi (S.–H.–S.) reagent, whose composition is given in reference 1. The procedure was modified when the solutions containing reducing sugars were buffered. In the first place, accurately measured aliquots of the buffered sugar solutions were made up to 5 cc. by adding more buffer if necessary. Then they were neutralized with caustic soda solution, before adding 5 cc. of the S.–H.–S. reagent. Second, instead of 5, 10 cc. of 1 *N* sulfuric acid was added to liberate the iodine before titration with approximately 0.002 *M* sodium thiosulfate, hereafter called "hypo." This avoided a fading end-point which occurred when the *p*H of the titrated solution was not low enough.

The calibration plots of mg. reducing sugar *vs.* cc. hypo (equivalent to the cuprous oxide formed) showed that the acetate buffer, the uranyl sulfate, the concentrations of the reducing sugars and sucrose, the dark reaction, and the reoxidation of the cuprous oxide during the heating and at room temperature—all affected the S.–H.–S. titrations. These effects, however, altered less than 10% the estimations of the reducing sugars formed in photolysis, as calculated from the observed difference between the titrations on the samples photolyzed and on those kept in the dark under otherwise similar conditions. The acetate buffer and uranyl sulfate increased slightly the weight of reducing sugar equivalent to a cc. of hypo, and corrections made for these effects were less than 7%. A yellow precipitate formed sometimes when the uranyl sulfate solutions were neutralized, but this did not seem to interfere with the reproducibility of the titrations. The calibration plots of the S.–H.–S. reagents used agreed within 3%.

Both "dark" and illuminated solutions were analyzed at the same time and under the same conditions. In most cases, the dark reaction was less than 2% of the total, but at the highest concentrations of sucrose, the dark reaction and the presence of the sucrose caused a reduction of the S.–H.–S. reagent, equivalent to 0.6 cc. of hypo per cc. of sugar solution.

The range of *p*H was confined between 3 and 6. At lower values, the hydrolysis of sucrose in the dark becomes appreciable.[1] At higher values, the stability of fructose and glucose decreases—the former being most stable at *p*H 3.3.[8] In addition, it was observed that as the *p*H was increased from 6 to 11, a 0.01 *M* solution of uranyl sulfate changed from green to yellow and finally produced a yellow precipitate.

The *p*H values were measured to 0.05 on a vacuum tube *p*H meter which used a glass electrode against a calomel half-cell saturated with potassium chloride.

Stock solutions of sugar always were made up less than an hour before withdrawing a sample and were not used a second day except in experiments covering more than a day. These solutions were made from tared samples of dry sucrose, 0.04 *M* uranyl sulfate, and enough water or 1 or 0.1 molar acetate buffer to complete the solution. Other organic compounds used as buffers between *p*H 3 and 6 absorb light strongly at 254 mμ. Even acetate absorbs 208 mμ and was omitted when working at this wave length. It was omitted also at 366 and 436 mμ because extinction coefficients of the acetate solutions were not available to evaluate the light transmitted. Phosphate buffers precipitated the uranyl ion and left solutions which transmitted through 3 cm. both 254 and 208 mμ, accompanied by a green fluorescence.

(8) Mathews and Jackson, *Bur. Standards J. Research*, **11**, 619 (1933).

Results

Extinction coefficients, k, were measured from 45,000 to 21,000 cm.$^{-1}$ for aqueous solutions of uranyl sulfate at 0.04 and 0.0004 molar and for 0.0365 and 0.000365 *M* uranyl sulfate containing sucrose at 4.02 and 0.0402 *M*, respectively. The null photographic method was used. The presence of the sucrose had no effect upon k and Beer's law was obeyed. These facts strongly suggest that in this part of the spectrum the absorbing species in solutions of uranyl sulfate were not changed when 100 times as much sucrose was added or when concentrations were varied 100-fold.

The observed values of k agreed with the best values in the literature,[9] but the dip in absorption at 366 mμ has a broader minimum on the long wave length side than the values previously obtained by extrapolation between 365 and 405 mμ. The smoothed values of $\log_{10} k$ are 0.6 at 450, 380 and 364 mμ; 0.7 at 445, 385 and 352 mμ; 0.8 at 443, 390 and 351 mμ; 0.9 at 440, 395 and 350 mμ; and 1.0 at 430, 405 and 349 mμ. $k = [\log_{10} (I_0/I)]/cd$ where c is in moles per liter and the depth d of the absorbing layer is in centimeters.

Pringsheim's photographs[10] of the absorption spectrum of 0.05 *M* uranyl sulfate also show a broad minimum about 366 mμ.

No measurements of k were made on solutions containing acetate buffer because absorption of 254 mμ was complete whenever acetate buffer was used. It was observed, however, that the presence of acetate in uranyl sulfate solutions gave rise at 313 mμ and longer wave lengths to a green fluorescence which even defined the variations of the light intensity in the beam. At 254 mμ, the green fluorescence changed to blue. The oxalic acid–uranyl sulfate solutions gave only a very faint, visible fluorescence. An analysis of the visible and near ultraviolet absorption and fluores-

(9) (a) Leighton and Forbes, THIS JOURNAL, **52**, 3139 (1930); and (b) Brackett and Forbes, *ibid.*, **55**, 4459 (1933).

(10) Pringsheim, *Physica*, **4**, 733 (1937).

cent spectra of uranyl salts has been published.[11]

Table I summarizes all the data obtained when reactions were followed with the copper reduction technique. This eliminated any corrections for the mutarotation of the liberated reducing sugars, and was many times more sensitive than following the accompanying change in the optical activity. Even in a 4-dm. tube, a change of 0.01° was equivalent per cc. of solution to nearly 0.5 cc. of hypo, which was reproduced within 0.1 cc.

Column II gives the average of two or more determinations of the reducing sugars formed by light in 1 cc. of the solutions photolyzed. These entries refer to the sensitivity of the S.-H.-S. reagent when reduced one-fourth by a solution containing invert sugar in the presence of 1 M acetate buffer and 0.008 M uranyl sulfate. Under these conditions 1 cc. of hypo was equivalent to 5.8×10^{-5} g. of invert sugar which represented the average of 5.74×10^{-5} g. for glucose alone, and 5.85×10^{-5} g. for fructose alone. This amount of invert sugar could be formed from $5.8 \times 6.06 \times 10^{18}/360 = 9.76 \times 10^{16}$ molecules of sucrose.

Column III gives the average of four or more determinations of the cc. of 0.00179 molar potassium permanganate equivalent to the oxalate particles which disappeared in 1 cc. of the actinometer solution each minute it was photolyzed. One-twentieth to one-fifth of the oxalate was decomposed. At the lowest intensities, the actinometer solutions were photolyzed immediately before and after illuminating the sugar solution; otherwise, the light intensities were determined at the beginning, middle, and end of a day. These values always agreed within 5% and showed no trend, so their average was taken for all experiments that day.

The actinometer was 0.001 M in uranyl sulfate and 0.0067 M in oxalic acid at 208 and 254 mμ, and 0.01 M in uranyl sulfate and 0.067 M in oxalic acid at 366 and 436 mμ. The fraction of an oxalate particle which disappeared per photon absorbed by these solutions at 25° was taken[3,9] as 0.49 at 208 mμ, 0.63 at 254 mμ, 0.49 at 366 mμ and 0.58 at 436 mμ with a ten degree temperature coefficient of 1.03 at all these wave lengths.

The volumes of the actinometer and sugar solutions photolyzed were 11 cc. except when the change in optical activity of the sugar solution was followed; then they were 12 cc. However, when the monochromator was used, the photolyzed samples were only large enough to intercept the diverging beam from the exit slit.

Quantum yields, ϕ, in Table I are equal to a constant, A, multiplied by column II divided by the product of columns I and III.

Light at 208 and 254 mμ was completely absorbed by the sugar and actinometer solutions, so at 25° for 208 mμ, A equals 9.76×10^{16} divided by $(2.72 \times 10^{18}/0.49)$ to give 0.0176; and for 254 mμ, A equals 0.0212 at 10° and 0.0288 at 35°.

Light at 366 and 436 mμ was not completely absorbed by the 30-mm. depths of either the (1) actinometer or (2) sugar solutions. Solution (1) absorbed 72% of the light incident at λ 366 mμ and 60% at λ 436 mμ. Solution (2) absorbed 52% at 366 mμ and 82% at 436 mμ. These percentages include the amount absorbed after reflection from the back window of the cell and were calculated from the data in reference 9a. Therefore, for 366 mμ, $A = 0.0248$; and for 436 mμ, $A = 0.0155$.

The reproducibility of the quantum yields for the sugar solutions was 3% as shown in Table I by Expts. 3 and 4 made six weeks apart, and by 19 and 20 made five weeks apart.

The products of the reaction which reduced the S.-H.-S. reagent were assumed to be equal weights of glucose and fructose commonly called invert sugar. This is, no doubt, too simple an hypothesis during the latter stages of the photolysis when much sucrose has been decomposed. Many attempts were made to test this hypothesis by following the decrease in the optical activity of the solution which accompanied the formation of the reducing sugars. It was impossible, however, to decompose by photolysis enough sucrose to decrease the observed rotations more than a fraction of a degree before the solutions became discolored or a precipitate appeared. Moreover, solutions could not be made alkaline to eliminate corrections for the mutarotation of the liberated reducing sugars because sucrose mutarotates in alkaline solutions containing uranyl salts.[12] Specific rotations, $\alpha^{21.5°}D$, therefore, were obtained for glucose (52.0°), fructose (−91.0°), and sucrose (66.4°) at concentrations covering the range used in the photolysis. The fraction of d-glucose (starting at $\alpha > 100$) that underwent mutarotation each minute at 21.5° varied from 0.026 at pH 3.0 to 0.031 at pH 3.5 in these solutions. The

(11) Van Heel, *Comm. Phys. Lab., Univ. of Leiden*, Supplement No. 55B to Nos. 169–180, 7 (1925).

(12) Grossmann and Rothgiesser, *Ber.*, **43**, 676 (1910).

TABLE I

Data giving the photochemical efficiency, ϕ, of the production by light of reducing sugars in aqueous solutions of sucrose and uranyl sulfate. $\phi = A$ multiplied by column (II)/(I)(III). The appropriate values of A are given in the text. The temperature was 10 ± 1° except as noted in column I. A starred ϕ indicates that the light was isolated by a prism monochromator and accompanying entries in columns II and III, marked "*t*," represent the amount photolyzed (per min. for III) in the total volume illuminated. In the *p*H column, the unmarked values represent solutions buffered with 1 *M* acetate, and values with one star those buffered with 0.1 *M* acetate. The barred w values are for unbuffered solutions and represent the average of the initial and final *p*H, which differed less than 0.1 except in Expt. 15 where the difference was 0.15. Solutions were placed only in glass vessels sterilized at 110° and then cooled to 25° just before being used.

Expt.	G. sucrose in 50 cc.	Moles of UO_2SO_4 per liter	*p*H	I Av. min. photolyzed	II Av. reducing sugars formed measured as cc. hypo/cc.	III Av. light absorbed per min. measured as cc. MnO_4^-/cc.	Av. quantum yields, ϕ
			λ 254 mμ				
1	0.0000	0.008	3.5	102	0.00	0.050	0.000
2 a	.0306	.008	3.5	98	1.86	.048	.008
bcd				58	1.21	.048	.009
3 ab	.1396	.008	3.5	101	7.60	.050	.032
cd				24	2.14	.050	.038
4 abcd	.1406	.008	3.5	14.1	1.75	.075	.036
5 abcd	.1390	.0008	3.5	28.8	2.92	.049	.045
6 abcd	.1373	.008	6.0	30.4	2.74	.050	.039
7 abcd	.1397	.008	5.6*	26.2	2.46	.049	.040
8 abc	.1362	.008	6.0	1040	3.77	.0018	.042
9 ab	.1396	.008	6.0	7 at 35°	3.90	.43	.031
c				1 at 35°	0.70	.43	.037
d				(50) at 35°	.00	(.43)	...
10 ab	.1383	.008	6.0	77 at 35°	1.65	.0135	.037
11	.1405	.0008	$\overline{3.5}$w	3 at 20°	1.45	.137	.077
12 ab	.4173	.008	3.5	8	2.60	.076	.091
cd				4.1	1.44	.076	.098
13 ab	.4090	.008	6.0	68 at 27°	8.45t	.028t	.102*
14 ab	.4100	.008	$\overline{3.5}$w	3.5 at 20°	3.37	.125	.17
cd				1.5 at 20°	1.75	.125	.21
			λ 208 mμ				
15	0.4162	0.008	$\overline{3.4}$w	81 at 27°	23.0t	0.0154t	0.32*
16 ab	.4072	.008	$\overline{3.5}$w	30 at 27°	7.45t	.0145t	.31*
			λ 366 mμ				
17 ab	0.4080	0.0286	$\overline{3.0}$w	35 at 27°	37t	0.088t	0.30*
			λ 436 mμ				
18 abc	0.4030	0.0286	$\overline{3.0}$w	38 at 27°	31t	0.043t	0.29*
			λ 254 mμ				
19 ab	1.3944	0.008	3.5	104	29.5	0.050	0.12
cd				23	9.5	.050	.18
20 abcd	1.3983	.008	3.5	3.25	2.22	.072	.21
21 abcd	1.3909	.0008	3.5	7	3.43	.045	.23
22 abcd	1.3942	.0008	6.0	6.5	2.69	.042	.21

mutarotation of fructose was completed in less than ten minutes. Thus, the small decreases in the optical activities, when no discoloration was evident, were known only within 5% although the rotations were read to 0.02° in a 4-dm. tube. Despite this uncertainty combined with those in the S.–H.–S. method, the experiments showed that the reducing sugars—assuming them to have the same reducing power as invert sugar—produced by the photochemical decomposition of the sucrose had a combined *negative* rotation whose absolute value was not greater than that of invert sugar.

The decreases in the optical activities of the samples kept in the *dark* agreed in every case to ±0.02°, with the S.–H.–S. estimates of invert sugar, and no discoloration or precipitate occurred even when 13% of the sucrose had been inverted in a solution containing 4% sucrose in 0.016 *M* uranyl sulfate buffered with 1 *M* acetate at *p*H 3.0. The invert sugar derived from a gram of sucrose was taken to have an α of 360 (52.0 − 91.0)/2 × 342 = −20.5°.

The dark rates for the inversion of sucrose at 21.5° and *p*H 3.0 to 3.5 were not changed in solutions partially inverted by photolysis.

Subsequent reactions in the early stages of the photolysis affected little the amount of reducing sugar formed. Quantum yields did not change more than corresponded to the depletion of the sucrose when 15% of the sucrose was decomposed in Expt. 2a, Table I, and the molar ratio of sucrose decomposed to uranyl sulfate initially present was less than one as in Expt. 21. Nevertheless, the decrease of 0.05 to 0.15 in the *p*H of the unbuffered solutions can be attributed to a minute amount of direct[13] and also photosensitized decomposition of the reducing sugars initially formed.

Side reactions due to the deactivating effect of the acetate halved the efficiency of the measured reaction as shown by Expts. 12 and 14, Table I. Decreasing the acetate buffer from 1 *M* in Expt. 6 to 0.1 *M* in Expt. 7, however, had no effect, but in both experiments the concentration of the acetate was many times greater than the sucrose or uranyl sulfate. The deactivating effect of acetate, therefore, had reached a limit at 254 mμ before its concentration was ten times greater than the uranyl sulfate.

When sucrose was omitted from an acetate buffered uranyl sulfate solution as in Expt. 1, no substances were produced which reduced the S.–H.–S. reagent[14] nor were they produced when 0.008 *M* uranyl sulfate alone in water absorbed per cc. of solution 3×10^{19} photons of λ 254 mμ. The depletion of uranyl particles[15] also did not change the *p*H of this solution, which remained at 3.5.

In a preliminary experiment, a solution containing 0.14 g. of sucrose in 50 cc. of 0.0008 *M* uranyl sulfate without buffer was photolyzed under its own vapor pressure, and the results showed that the production of the reducing sugars was affected less than 20% by dissolved oxygen from the air which enters the photosensitized oxidation of iodide by uranyl sulfate.[16]

Kinetics of the Photosensitized Reaction.—The primary act is the capture of a photon by a uranyl particle. Part of the activated uranyl particles are sufficiently close to sucrose and the other reactants and properly oriented to initiate the hydrolysis. The fraction of the activated particles so disposed is proportional to ϕ, whereupon

$$\phi = B[UO_2SO_4]^n[\text{sucrose}]^m[H_3O^+]^l \cdots/[UO_2SO_4] \quad (1)$$

where B is the proportionality constant and the sum of the exponents in the numerator equals the number of reactant particles entering the photochemically active cluster. When ϕ cannot exceed a finite value a

$$\phi = a[1 - \exp(-gx)] \quad (2)$$

where x is directly proportional to the right side of (1) and g includes B. At small values of gx equation (2) becomes

$$\phi = agx \quad (3)$$

In this range of values, each exponent except that of the photosensitizer, uranyl sulfate, equals the slope of the plot of log ϕ against the logarithm of the concentration of the corresponding reactant when other variables are fixed. For the photosensitizer, however, n equals one plus the slope. The independence of ϕ upon the concentration of uranyl sulfate between 0.008 and 0.0008 *M* in Expts. 4 and 5, and in 19, 20 and 21, therefore, shows that only one uranyl particle enters the reactive complex. These results also confirm the observed independence of ϕ upon the light intensity, I, in Expts. 6 and 8, and 9 and 10, where I was changed over 200-fold, yet ϕ was not affected. They also show that the stirring adequately prevented the local depletion of reactants in the zones absorbing most of the actinic light, and that the transparent quartz stirrers did not alter the amount of light absorbed by the solutions even when there impinged on the stirrers possibly one-tenth of the light incident on the most dilute solutions of uranyl sulfate.

The points on a plot of log ϕ at 254 mμ. in the buffered solutions against log (sucrose) fell on a curved line that approached unit slope, within experimental error,[17] only when ϕ was less than 0.1. Therefore, the largest observed values of ϕ are too near the maximum value for equation (3) to hold. The approach of the plot to unit slope when ϕ is small, however, shows that $m = 1$. Thus, one molecule of sucrose enters the reaction with each uranyl particle.

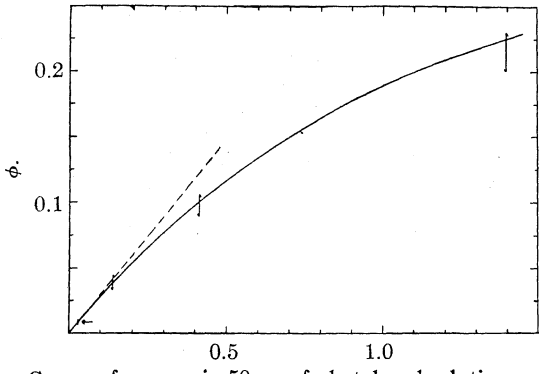
In Fig. 1, the equation for the curve is

$$\phi = 0.3\ [1 - \exp\ (-\ g[\text{sucrose}])\ ] \quad (4)$$

$g = 1$ when, as plotted [sucrose] equals grams in 50 cc. of solution, but for [sucrose] in moles per liter of solution, $g = 0.585$.

(13) Cantieni, *Helv. Chim. Acta*, **18**, 808 (1935).
(14) See also Baur and Rebmann, *ibid.*, **5**, 221 (1922).
(15) Pitzer, Gordon and Wilson, THIS JOURNAL, **58**, 67 (1936).
(16) Schneider, *Z. physik. Chem.*, **28B**, 311 (1935).
(17) A straight line through all the points had a slope of 0.77 calculated by the method of least squares.

The choice of 0.3 for a and of 1 for m was confirmed by a plot of log log $[(a - \phi)a]$ against log [sucrose] in which the points, within the limits of error, fell on a line with unit slope.



Grams of sucrose in 50 cc. of photolyzed solution.

Fig. 1 illustrates, for the initial reaction, the increase of quantum yields, ϕ, at 254 mμ. with [sucrose] in acetate buffered solutions of uranyl sulfate. No other variables needed to be fixed because ϕ was independent of them. Vertical lines represent the spread of all the observed values at pH 3.5 to 6.0 and at 10 to 35°. The curve was calculated from theory. The dotted line gives the linear dependence of ϕ upon [sucrose] as both terms approach zero. The slope of this line equals ag where a is the maximum value of ϕ and g is also a constant.

The factor a equals the maximum value of ϕ at this wave length in these buffered solutions. It is a function of the transfer and utilization of energy within the complex.

The factor g includes the equilibrium constant K for the reaction defined in equation (1). As the stability of the cluster increases, g will increase. When more clusters are formed with increasing temperature, ϕ will approach a, and the temperature coefficient of ϕ will approach zero. The temperature coefficient will also be small for ϕ much less than a when $\mathrm{d}(\ln K)/\mathrm{d}T = -\Delta H/RT^2$ is small. In Expts. 6 and 10, ϕ remained unchanged while the temperature was increased from 10 to 35°, which shows that ΔH is small since these values of ϕ were not near $\phi = a$.

The independence of ϕ upon the pH in Expts. 4 and 6, and 21 and 22, shows that the catalytic effect of the hydrogen ions is replaced by the activated uranyl salts.

In Fig. 2, the plots of wave length against log ϕ for the sugar and actinometer solutions have a dip in the ultraviolet at which ϕ is, roughly, 25% of ϕ at 436 mμ. The values of ϕ for sucrose at 366 and 436 mμ may be slightly high because absorption of light was incomplete and small increases in the concentration of the uranyl sulfate from the values given would increase ϕ measurably, but would hardly be detected in the measurements of the extinction coefficients by the null photographic method. The dip in ϕ at 208 mμ for the actinometer is due to absorption of this wave length by the oxalic acid.[9b]

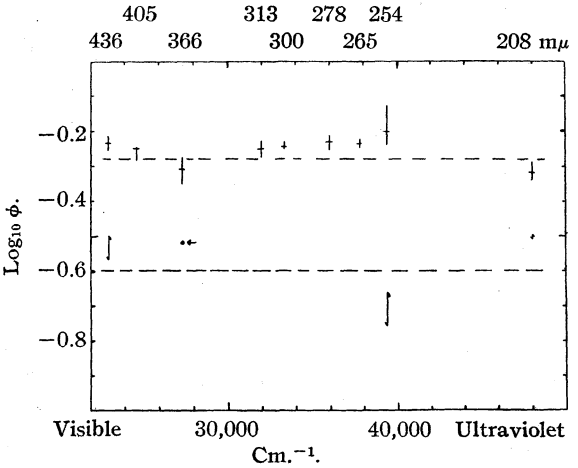


Fig. 2 illustrates the variations in quantum yields with wave length. The dotted lines only serve to emphasize these variations. Vertical lines of equal length give the same percentage spread of the separate, observed values of ϕ included in the average values tabulated. Lines with arrows represent the data for the photolysis of sucrose in the unbuffered solutions of uranyl sulfate given in Table I. Expt. 11 is not included. Lines without arrows represent the maximum values of ϕ at 25° for the oxalic acid–uranyl sulfate actinometer. The points where these lines are crossed give the logarithm of the weighted average values.[9]

It is also seen from Fig. 2 and Table I that blue light, at 436 mμ, is just as efficient as the ultraviolet in the photosensitized production of reducing sugars from sucrose. This suggests that a part of the polysaccharides in plants is converted into simpler sugars by sunlight acting through naturally occurring photosensitizers.

Summary

Reducing sugars have been produced from sucrose by visible and ultraviolet light acting through uranyl salts as photosensitizers.

The decrease in the optical activity which accompanied the formation of the reducing sugars was approximately equivalent to the Shaffer–Hartmann–Somogyi estimations of reducing sugars calculated as invert sugar.

Quantum yields, ϕ, were calculated as molecules

of sucrose decomposed per photon absorbed by the system. The variation in ϕ with the concentration of sucrose was given by $\phi = a[1-\exp(-g[\text{sucrose}])]$. At 254 m$\mu$, $a = 0.3$ and $g = 0.6$ when [sucrose] was expressed in moles per liter and solutions were buffered with acetate. ϕ increased when the solutions were not buffered, but the *p*H then decreased slightly due to subsequent reactions. ϕ was independent of (1) the light intensity over a 200-fold range, (2) the temperature between 10 and 35°, (3) the *p*H between 3 and 6, and (4) the concentration of uranyl sulfate between 0.0008 and 0.008 molar.

The kinetics of the reaction have been discussed.

Extinction coefficients of uranyl sulfate solutions were obtained at intervals of 0.1 in the logarithm and are given for the dip in absorption about 366 mμ. Beer's law was obeyed and sucrose concentrations up to 100 times those of uranyl sulfate did not affect the measurements.

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[CONTRIBUTION FROM THE MALLINCKRODT CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

The Aquation of Carbonato Pentammine Cobaltic Bromide

BY ARTHUR B. LAMB AND ROGER G. STEVENS

Carbonate tetrammine cobaltic salts undergo little or no aquation in pure aqueous solution at ordinary temperatures. In other words, the carbonate group is not readily displaced from the complex ion by molecules of water. This is explained by its firm attachment, presumably by two covalent links.

In carbonato pentammine salts the carbonato group appears to be held by one polar and one covalent link. While the former would permit dissociation, the latter holds the carbonato group firmly, so that it cannot function as a separate ion. In agreement with this, their freshly prepared solutions, like those of the corresponding carbonato tetrammine salts, do not give the characteristic tests for the carbonate ion and exhibit the conductance to be expected of uni-univalent electrolytes.

One might expect, however, that carbonato pentammine salts with but a single covalent link holding the carbonato group, would undergo aquation more readily than the carbonato tetrammine salts. Yet, Werner and Gosling,[1] to whom we owe most of our knowledge of the carbonato pentammines, appear never to have observed any aquation of these substances, and Schwartz and Tede[2] state that dilute solutions of the nitrate are stable both in the dark and when exposed to ultraviolet light, as shown by the constancy of their electrical conductance. Duff,[3] to be sure, found that while dilute solutions of the nitrate showed no change in conductance at 25° by themselves, an increase in conductance took place when the solutions were left in contact with platinum electrodes. Solely on the basis of this evidence he inferred that carbonato pentammine nitrate does not aquate spontaneously, but does so under the catalytic influence of the platinum. The latter part of this inference was and is quite unjustified, because no such catalytic effect on aquation has ever been observed by others, while it has long been recognized that the decomposition of cobalt ammines is markedly accelerated by contact with platinum electrodes.[4]

In this situation it appeared of interest to examine solutions of these carbonato pentammines more particularly for possible aquation, and this we have now done by means of measurements of the conductance of dilute solutions of the bromide at 25 and 0°.

The carbonato pentammine cobaltic bromide was prepared through the nitrate following the methods of Werner and Gosling.[1] The conductances were measured using "dip" electrodes following the procedure previously described in another connection.[5] Duplicate readings were taken over an interval of more than an hour with and without the removal of the electrodes from the solution. Identical changes in conductance took place in each instance indicating that the platinum electrodes exerted no perceptible effect under the circumstances.

(1) Werner and Gosling, *Ber.*, **36**, 2380 (1903).
(2) Schwartz and Tede, *ibid.*, **60**, 65 (1927).
(3) Duff, *J. Chem. Soc.*, **123**, 573 (1923).
(4) Lamb and Larson, THIS JOURNAL, **42**, 2025 (1920); Lamb and Yngve, *ibid.*, **43**, 2354 (1921); Brönsted, *ibid.*, **49**, 439 (1927).
(5) Lamb and Stevens, *ibid.*, **54**, 2643 (1932).

The resulting data are collected in Table I.

TABLE I

CHANGE IN CONDUCTANCE OF A 0.004 *M* SOLUTION OF CARBONATO PENTAMMINE COBALTIC BROMIDE

AQUATION

0°				25°			
Time, min.	Mol. cond. 1/ohm	$a - x$ 1/ohm	$k_1 + k_2$ 1/min.	Time, min.	Mol. cond. 1/ohm	$a - x$ 1/ohm	$k_1 + k_2$ 1/min.
0	(54.8)	(19.7)		0	(102)	(69.2)	
4	55.5	19.0	0.0089	1	108.9	62.2	0.106
5	55.7	18.8	.0094	2	115.8	55.3	.113
7	56.1	18.4	.0097	4	127.2	43.9	.113
10	56.6	17.9	.0097	5	131.4	39.7	.111
11	56.8	17.7	.0097	6	135.5	35.6	.111
15	57.5	17.0	.0099	8	142.0	29.1	.111
16	57.6	16.9	.0097	10	147.3	23.8	.106
25	58.9	15.6	.0092	12	151.8	19.3	.106
50	61.7	12.8	.0085	15	156.0	15.1	.101
101	66.0	8.5	.0083	20	161.9	9.2	.101
145	68.8	5.7	.0085	25	165.4	5.7	.099
205	71.6	2.9	.0084	35	168.6	2.5	.094
	(74.5)	0		60	171.0	0.1	.105
				86	171.1	0	
				444	171.2		
		Average	0.0092 ± .0004			Average	0.106 ± .005

It can be seen that the conductance increases slowly, indicating a slow aquation. A stationary state is reached after about an hour at 25° and after perhaps ten hours at 0°.

It was possible, to be sure, that the observed increase in conductance was caused by a decomposition of the ammine. If this occurred, free ammonia should be present. A current of air was therefore bubbled through a solution of the ammine and thence into Nessler reagent, blank tests having shown that minute amounts of ammonia in a solution can be detected in this way. With the ammine solution at 0° no trace of ammonia was indicated until after an hour's bubbling. At 25° a trace was indicated in thirty minutes and a marked test was obtained in seventy minutes. Since the change in conductance is nearly complete before any decomposition is detectable, the observed change in conductance cannot be ascribed to decomposition.

Tests were also made to confirm the presence of the bicarbonate ions produced by the aquation. For this purpose a weakly ammoniacal solution of barium chloride was added to freshly prepared solutions of the bicarbonato ammine bromide at 0°. At first no indication of carbonate or bicarbonate was obtained, but after the solution had stood for an hour at this temperature a small precipitate was formed. A similar solution kept at 25° for seventy minutes and then cooled to 0° gave an immediate and copious precipitate when the barium hydroxide was added. These results confirm the inference drawn from the conductance measurements that aquation of the carbonato pentammine does indeed take place.

From the data in Table I values of k in the formula for a unimolecular reaction have been computed taking a, the concentration of the reacting substance, as equal to the total change in conductance and $a - x$ as equal to the change in conductance at the time t. Since the final state reached is, on the basis of all our previous studies of aquation, an equilibrium, the constants thus obtained represent the sum of the individual constants for the direct and the reverse reaction, *i. e.*, $k_1 + k_2$. They are given in the last column of Table I and show a reasonable constancy at each temperature.

The Mechanism of the Aquation

Aquation is usually looked upon as a direct replacement of a complexly held anion by a molecule of water. An alternative mechanism would be the primary addition of hydrogen ion to the complexly held anion with the formation of the undissociated acid which is then replaced by a molecule of water. It is, however, unlikely that this latter is the sole mechanism of aquation, because then the anions of weak acids should aquate more rapidly and completely than those of strong acids, and this does not appear to be the case.

This mechanism is, however, presumably operative in the case of the carbonato pentammines. They react rapidly with acids to give carbonic acid and aquo pentammine salts. Direct replacement of the complexly attached carbonato group by water certainly could not account for so rapid a reaction. There can, therefore, be little doubt that the hydrogen ion here combines directly with carbonato group to form the bicarbonato group. The resulting ion, for electrostatic reasons, would aquate much more rapidly than the carbonato ion itself. Indeed, it might aquate with sufficient rapidity to account entirely for the observed aquation of the carbonato ammine.

Aquation and Anation of the Bicarbonato Pentammines.—To ascertain how rapidly and completely the aquation of the bicarbonato pentammine takes place, we have measured the conductance of dilute solutions of its nitrate at 0° and at successive intervals of time. The data are given in the second column of Table II.

It can be seen that a relatively rapid rise in conductance takes place, indicating rapid aquation, a stationary state being reached in about

TABLE II

CHANGE IN CONDUCTANCE OF A 0.00286 *M* SOLUTION OF BICARBONATO PENTAMMINE COBALTIC NITRATE AND BROMIDE AT 0°

AQUATION

Time, min.	Molecular conductance Nitrate, 1/ohm	Molecular conductance Bromide (calcd.), 1/ohm	$a - x$, 1/ohm	$k_1 + k_2$, 1/min.
0	(124.2)	(130.0)	(21.2)	
6	138.1	143.9	7.3	0.177
7	139.4	145.2	6.0	.179
8	141.1	146.9	4.3	.198
9	141.9	147.7	3.5	.200
10	142.5	148.3	2.9	.198
11	143.2	149.0	2.2	.205
12	143.8	149.6	1.6	.214
13	144.2	150.0	1.2	.221
15	144.5	150.3	0.9	.209
18	144.8	150.6	0.6	.198
	(145.4)	(151.2)	0	

Average 0.20 ± 0.01

eighteen minutes. The extrapolated initial molecular conductance, 124.2 1/ohm, is what would be expected from the previously observed[6] conductance of hydroxo pentammine chloride, 132 1/ohm.

To ascertain whether this final stationary state represents an equilibrium, we have also carried out the reverse process, *i. e.*, the anation[7] of the aquo pentammine. For this purpose we added an equivalent weight of aquo pentammine bromide to a solution of sodium bicarbonate and followed the change of the conductance with the time. The resulting data are collected in Table III.

TABLE III

CHANGE OF CONDUCTANCE OF A 0.00286 *M* SOLUTION OF SODIUM BICARBONATE AND OF AQUO PENTAMMINE COBALTIC BROMIDE AT 0°

ANATION

Time, min.	Molecular conductance Observed, 1/ohm	Molecular conductance Corrected, 1/ohm	$a - x$, 1/ohm	$k_1 + k_2$, 1/min.
0		(183.3)	(32.5)	
1	0.6624	174.8	24.0	0.304
2	.6393	166.8	16.0	.318
3	.6261	162.2	11.4	.346
4	.6166	158.9	8.1	.348
5	.6107	156.8	6.0	.337
7	.6029	154.0	3.2	.332
10	.5972	152.0	1.2	.330
18	.5937	150.8	...	
38	.5935	150.8	...	
∞		(150.8)		

Average 0.33 ± 0.005

The observed specific conductances are given in the second column of the table. They exhibit a rapid *decrease*, indicating the formation of the bicarbonato pentammine ion, *i. e.*, anation. To compare these data with those obtained in the previous aquation experiment it was necessary to eliminate the conductance of the sodium bromide present here as shown by the equation

$$(Co(NH_3)_5H_2O)Br_3 + NaHCO_3 \longrightarrow (Co(NH_3)_5HCO_3)Br_2 + NaBr + H_2O$$

and not present in the aquation experiment. This was accomplished by multiplying the observed specific conductance of the sodium bicarbonate solution before the addition of the ammine (0.0001334 1/ohm) by the ratio of the molecular conductances of sodium bromide and sodium bicarbonate at the prevailing concentration, and subtracting the product from the observed specific conductances. The resulting corrected specific conductances were then converted to molecular conductances and were corrected for the diminished conductances, both of the ammine and of the sodium bicarbonate, in the mixture. These corrected molecular conductances are given in the third column of Table III and are shown graphically as the upper curve in Fig. 1. The

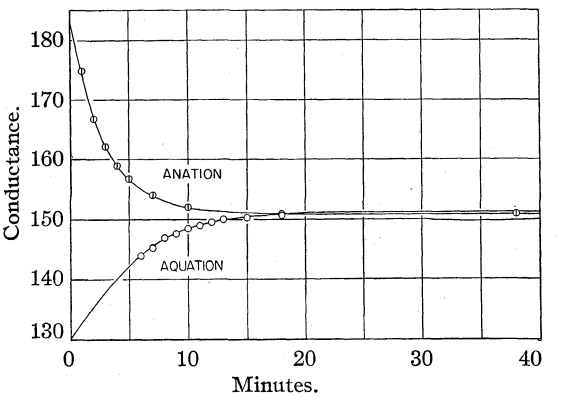


Fig. 1.—Change in conductance (corrected) of a solution of bicarbonatopentammine cobaltic bromide (aquation) and of a solution of aquopentammine cobaltic bromide and sodium bicarbonate (anation) at 0°.

corresponding molecular conductances observed with the bicarbonato pentammine nitrate, corrected to bromide by addition of 5.8 1/ohm for the difference in mobility between two bromide and two nitrate ions, are given in the third column of Table II and are also shown as the lower curve in Fig. 1. It can be seen that these two curves approach each other and after about eighteen minutes become nearly coincident. This indicates that the stationary condition reached both by aquation and anation is indeed an equilibrium.

(6) Lamb and Stevens, ref. 5, p. 2649.

(7) A. B. Lamb, THIS JOURNAL, **61**, 699 (1939).

The composition of the solution of aquo pentammine bromide and sodium bicarbonate at the start, before any bicarbonato pentammine has been formed by anation, can be computed from the known dissociation constants of aquo pentammine ion and carbonic acid. The reactions involved in this equilibrium can be represented as follows

$$(Co(NH_3)_5HCO_3)^{++} \underset{}{\overset{\text{(slow)}}{\rightleftharpoons}} (Co(NH_3)_5H_2O)^{+++} + HCO_3^-$$
$$\downarrow\uparrow\text{(fast)} \qquad\qquad \downarrow\uparrow\text{(fast)}$$
$$(Co(NH_3)_5CO_3)^{+++} \qquad (Co(NH_3)_5OH)^{++} + H_2CO_3$$

Calling Aq^{+++} and Hy^{++} the concentrations of aquo and hydroxo pentammine ions, respectively, and considering solely the above equilibria on the right

$$Hy^{++}/Aq^{+++} = \sqrt{\frac{K_{Aq}}{K_{H_2CO_3}}} = \sqrt{\frac{1 \times 10^{-7}}{4 \times 10^{-7}}} = 1/2$$

That is, $Aq^{+++} = 2Hy^{++}$ at the start.[8] Taking the molecular conductances of the aquo and hydroxo pentammine bromide, sodium carbonate and sodium bromide at 0°, and at the prevailing concentration, as 222, 130, 47.5 and 62.6 1/ohm, respectively, the initial conductances of the system on the right, before any bicarbonato had formed, would be 222 + 47.5 − 62.6, or 206.9 1/ohm, if the pentammine were exclusively aquo, and 130 1/ohm, if exclusively hydroxo. Since, however, $Aq^{+++} = 2Hy^{++}$, the initial conductance should be 206.9 − 1/3(206.9 − 130) = 181.3 1/ohm. This value corresponds closely with the extrapolated value shown in Fig. 1.

The concentrations of the various ions in these solutions at any time during the aquation or anation could likewise be calculated from the observed conductances and the known dissociation constants of aquo pentammine ion and carbonic acid if the dissociation constant for the bicarbonato pentammine ion were also known. From these concentrations velocity constants for aquation and anation could then be directly evaluated with a good deal of certainty. Lacking this information as to the bicarbonato ammine, we have simply assumed, as usual, that the extent of the reaction is proportional to the change in conductance, and since an equilibrium is attained we have taken the total concentration of reacting substance as equal to the amount transformed at equilibrium. The resulting apparent velocity constants for a unimolecular reaction of this sort, $k_1 + k_2$, the sum of the unimolecular velocity constants of the simple aquation and anation reactions, respectively, are given in the final columns of Tables II and III.[7]

It can be seen that the individual values for $k_1 + k_2$ are in each series reasonably constant. The average of the values obtained in the anation measurements is, however, considerably larger than the average obtained in the aquation measurements. This may well be due to a lack of rigor in our assumption of direct proportionality between the change in conductance and the concentrations of the ions undergoing either aquation or anation, or to the failure of the approximate unimolecular formula to represent adequately the bimolecular anation reaction when corrected for the kinetic salt effect.[7]

Aquation in Mixtures of Carbonato and Bicarbonato Pentammine.—We have also made measurements of the change in conductance of solutions of carbonato pentammine bromide to which aliquot amounts of hydrochloric acid have been added. This has afforded a convenient means of obtaining mixtures of the carbonato and bicarbonato ammines. The observed conductances of the ammine immediately upon the addition of the acid and at intervals thereafter are given in Table IV. Velocity constants computed in the same way as for the pure compounds are also given.

It can be seen that the solution to which an equivalent amount of acid was added showed substantially the same initial conductance and the same rate of aquation as a solution of pure bicarbonato pentammine. Solutions containing lesser amounts of acid showed progressively smaller velocities of aquation. Indeed, the velocity constants for the aquation of the several solutions followed closely the formula

$$k_1 + k_2 = 0.214 \frac{(Co(NH_3)_5HCO_3)^{++}}{0.00286}$$

the calculated values for $k_1 + k_2$ when $1/10$ and $1/4$ equivalents of hydrochloric acid were added, being 0.0214 and 0.0535, respectively, whereas 0.0233 and 0.0515 were actually observed.

The application of this formula to the 0.00286 M solution of pure carbonato pentammine bromide where the velocity constant of aquation is 0.0092 1/min. would indicate a concentration of bicarbonato pentammine = 0.0092 × 0.00286/0.214, or 0.00012 M, provided aquation takes

(8) From the data of Brönsted, *Z. physik. Chem.*, **134**, 133 (1928); and MacInnes, THIS JOURNAL, **55**, 2638 (1933); **57**, 1084 (1935), by application of the observed temperature coefficients.

TABLE IV

CHANGE IN CONDUCTANCE OF A 0.00286 *M* SOLUTION OF CARBONATO PENTAMMINE COBALTIC CHLORIDE CONTAINING VARIOUS CONCENTRATIONS OF HCl AT 0°

HCl = 0.000286 *M*				HCl = 0.000715 *M*				HCl = 0.00286 *M*			
Time, min.	Mol. cond. obsd., 1/ohm	$a - x$, 1/ohm	$k_1 + k_2$, 1/min.	Time, min.	Mol. cond. obsd., 1/ohm	$a - x$, 1/ohm	$k_1 + k_2$, 1/min.	Time, min.	Mol. cond. obsd., 1/ohm	$a - x$, 1/ohm	$k_1 - k_2$, 1/min.
0	(64.4)	(27.8)		0	(74.6)	(26.6)		0	(130.0)	(25.3)	
1	65.0	27.2		2	77.2	24.0	0.0516	3	142.0	13.3	0.215
2	65.7	26.5	0.0240	3	78.5	22.7	.0528	4	144.9	10.4	.217
3	66.3	25.9	.0235	4	79.6	21.6	.0521	5	147.3	8.0	.230
4	67.0	25.2	.0244	5	80.7	20.5	.0521	6	149.0	6.3	.232
5	67.5	24.7	.0237	6	81.7	19.5	.0518	7	150.5	4.8	.237
6	68.1	24.1	.0237	7	82.7	18.5	.0518	8	151.5	3.8	.237
7	68.7	23.5	.0240	9	84.5	16.7	.0518	9	152.4	2.9	.240
8	69.3	22.9	.0242	11	86.1	15.1	.0516	10	153.0	2.3	.240
10	70.3	21.9	.0240	13	87.5	13.7	.0512	11	153.3	2.0	.230
12	71.2	21.0	.0235	16	89.4	11.8	.0510	12	153.8	1.5	.235
15	72.7	19.5	.0237	19	91.0	10.2	.0506	14	154.2	1.1	.224
20	74.7	17.5	.0230	22	92.5	8.7	.0510	17	154.5	0.8	.206
25	76.6	15.6	.0230	26	94.1	7.1	.0510		(155.3)	0	
30	78.2	14.0	.0228	31	95.7	6.5	.0510				
35	79.7	12.5	.0228	36	96.9	4.3	.0507				
45	82.1	10.1	.0226	41	97.8	3.4	.0502				
55	84.0	8.2	.0221	51	99.3	1.9	.0516				
70	86.2	6.0	.0219	66	100.4	0.8	.0530				
90	88.4	3.8	.0221		(101.2)	0					
125	90.5	1.7	.0223								
160	91.6	0.6	.0240								
195	91.9	.3	.0233								
	(92.2)										
		Average	0.0233			Average	0.0515			Average	0.228
			± .0006				± .0006				± .007

place exclusively via the bicarbonato ammine, that is, with no direct aquation of the carbonato. This concentration of bicarbonato in equilibrium with the carbonato in pure water would correspond to a dissociation constant of about 4×10^{-10}. A direct determination of this constant would show the actual concentration of bicarbonato in equilibrium with the carbonato and thus permit a decision as to what part of the aquation of the carbonato takes place directly and what part via the bicarbonato pentammine.

Summary

1. It has been found from conductance measurements that carbonato pentammine bromide undergoes a slow aquation to give an equilibrium mixture of bicarbonato, aquo and hydroxo pentammines. Bicarbonato pentammine salts undergo a much more rapid aquation, reaching an equilibrium with the opposing anation reaction by which aquo pentammine is converted into bicarbonato pentammine. The velocities of these aquation and anation reactions have been measured and velocity constants have been computed.

2. Evidence is presented to show that in the equation of the carbonato pentammine salts a rapid, reversible addition of hydrogen ion to the complexly held carbonato group takes place, followed by a relatively slow, but reversible, aquation of the bicarbonato group.

3. It has been pointed out that these measurements, coupled with measurements of the dissociation constant of the bicarbonato pentammine ion would permit an estimate of how much of the aquation of the carbonato pentammine takes place directly and how much through the intermediate formation of the bicarbonato pentammine.

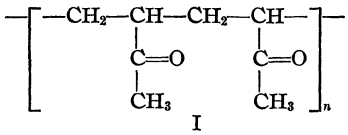
CAMBRIDGE, MASSACHUSETTS RECEIVED JUNE 27, 1939

NOTES

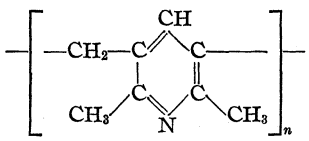
Structure of Vinyl Polymers. V.[1] Some Reactions of the Polymer of Methyl Vinyl Ketone

By C. S. Marvel and Charles L. Levesque[2]

Work from this Laboratory has shown[3] that the polymer of methyl vinyl ketone has a "head to tail" structure (I), and hence contains 1,5-diketone units. However, when this polyketone was treated with hydroxylamine, the corresponding polyketoxime rather than the expected polypyridine (II)[4] was obtained. It has now been found possible to prepare the polypyridine (II) by heating the polyketoxime with alcoholic hydrogen chloride.[5] Flory has shown[6] that no more than 86.47% of the ketoxime groups can participate in this reaction. Analytical results support the conclusion that under the conditions employed in our experiment, the remaining 13.53% of the ketoxime groups were hydrolyzed.

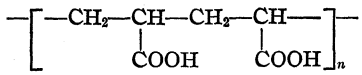


I



II

By treating a dioxane solution of the polymer of methyl vinyl ketone with aqueous sodium hypochlorite,[7] a polyacrylic acid (III) has been obtained. Attempts to compare this polyacid with that obtained by the polymerization of acrylic acid are now in progress.



III

Experimental

Preparation of the Polypyridine.[5]—A solution of 3.2 g. of the oxime of the polymer of methyl vinyl ketone[3] in 50 cc. of concentrated hydrochloric acid was placed in a 1-liter flask and a solution of 135 g. of hydrogen chloride in 500 cc. of alcohol was added. A reflux condenser was attached, and the milky solution was heated to boiling. Enough water to effect complete solution (40 cc.) was added and the mixture was refluxed for nineteen hours. The clear red reaction mixture was concentrated to 15 cc. and neutralized with ammonium hydroxide. The solid which precipitated was collected on a filter and dried under reduced pressure over solid potassium hydroxide. The product was 2.0 g. of light brown powder, readily soluble in acids, but insoluble in aqueous sodium hydroxide.

Anal. Calcd. for 0.4323 mole of C_8H_9N + 0.1353 mole of C_4H_6O: N, 9.94. Found: N, 9.53.

This product may be identical with the basic polymer which Balthis has obtained by the action of ammonia on the polymer of methyl vinyl ketone.[8]

Preparation of the Polyacid.[7]—A solution of sodium hypochlorite was prepared by bubbling chlorine into 160 g. of cold 10% sodium hydroxide until the gain in weight was 12 g. This solution was cooled by an ice-bath and stirred while a solution of 2.8 g. of the polymer of methyl vinyl ketone in 450 cc. of dioxane was added slowly. After the addition was complete, the mixture was stirred at room temperature for six hours. The lower aqueous layer was separated and concentrated under reduced pressure to 35 cc. The concentrate was filtered and the filtrate was acidified with concentrated hydrochloric acid. A white precipitate formed. The mixture of solution and precipitate was placed in a parchment paper sack and dialyzed until freed from chloride ion. The yellow solution remaining in the sack was filtered and the filtrate was evaporated to dryness. The residue was 1.15 g. of brittle, brown solid.

Anal. Calcd. for $(C_3H_4O_2)_n$: C, 50.0; H, 5.55. Found: C, 53.19; H, 5.92. The analysis indicates that about 90% of the methyl ketone groups have been oxidized.

(1) For the fourth communication in this series see This Journal, **61**, 3156 (1939).

(2) Du Pont Fellow in Chemistry.

(3) Marvel and Levesque, This Journal, **60**, 280 (1938).

(4) Knoevenagel, *Ann.*, **281**, 56 (1894).

(5) Blaise and Montagne, *Compt. rend.*, **180**, 1760 (1925).

(6) Flory, This Journal, **61**, 1518 (1939).

(7) Fuson and Tullock, *ibid.*, **56**, 1638 (1934).

(8) Balthis, U. S. Patent 2,122,707 (1938).

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Received July 10, 1939

The Rotatory Power of Zinc Lactate[1]

By W. Dayton Maclay, Raymond M. Hann and C. S. Hudson

In a recent article[2] we published measurements of the specific rotation of pure zinc D-lactate dihydrate in water for the concentrations 3.2 and 5.2%, which indicated that the change in rotation with concentration is a small one. Professor

(1) Publication authorized by the Surgeon General, U. S. Public Health Service.

(2) Maclay, Hann and Hudson, This Journal, **61**, 1666 (1939).

Karl P. Link has kindly informed us that he and Mr. R. J. Dimler have measured the rotation of zinc L-lactate in the course of a research on some derivatives of lactic acid, soon to be published, and have found considerable variation in rotation with concentration. We have repeated and confirmed their measurements and, at their suggestion, now record the two sets of values over the wider range of concentrations from 1.5 to 7.0%. In this range the $[\alpha]_D$ values may be expressed approximately as $[\alpha]^{20}D = -9.2° + 0.4(c)$, in aqueous solution, for zinc L-lactate dihydrate. (The configuration of L-lactic acid is $CH_3-\underset{H}{\overset{OH}{C}}-COOH$.)

TABLE I

VARIATION OF ROTATION WITH CONCENTRATION, AQUEOUS SOLUTIONS OF ZINC L-LACTATE DIHYDRATE (ACCURACY ±0.1°)

Concn. (as dihydrate)	$[\alpha]^{25}D$ (Dimler and Link)	$[\alpha]^{20}D$ (Maclay, Hann and Hudson)
1.5	−8.7°	−8.7°
3.0	−7.9	−7.9
4.0	−7.6	−7.5
5.0	−7.2	−7.1
7.0	−6.7	−6.6

In our article we expressed the opinion that the rotations $[\alpha]^{15}D$ +6.84° (*c*, 5.6) for zinc D-lactate dihydrate and $[\alpha]^{20}D$ −6.83° (*c*, 7.1) for zinc L-lactate dihydrate, found by Irvine,[3] indicated some racemization of the lactic acids. It is now seen, however, that these values fit the new measurements very well, from which it may be concluded that the procedure which Irvine used in preparing the zinc lactates does not cause racemization and is therefore preferable to the more laborious procedure which we employed in order to exclude the possibility of racemization.

(3) Irvine, *J. Chem. Soc.*, **89**, 935 (1906).

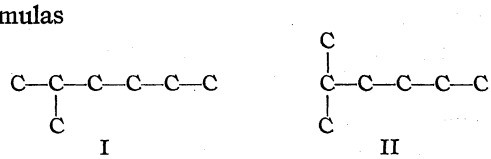
NATIONAL INSTITUTE OF HEALTH
U. S. PUBLIC HEALTH SERVICE
WASHINGTON, D. C. RECEIVED OCTOBER 7, 1939

Molecular Structure of Aliphatic Compounds and their Boiling Points

BY E. NEYMAN-PILAT

On the basis of Walker's formula C. R. Kinney recently[1] has developed a new system correlating molecular structure of organic compounds with their boiling points. In a paper dealing specially with aliphatic compounds, the boiling point numbers (b. p. n.) for carbon and hydrogen as well as for some radicals and characteristic groups have been presented. From these data and the given formula the boiling points at atmospheric pressure of aliphatic compounds may be calculated easily and with fair accuracy.

C. R. Kinney has stated that due to the lack of adequate boiling point determinations recorded in the literature for the branched hydrocarbons, the b. p. n.'s for only the methyl, ethyl, propyl and butyl radicals were calculated and that even those may undergo some alteration when more boiling points will be recorded. This point of view would seem to be open to question, as some of the paraffin hydrocarbons listed in Table I of the quoted paper may be considered as being derivatives of different radicals. For example the 2-methylhexane may be treated as a methyl (I) as well as a butyl derivative (II) according to the structural formulas



I II

In the same way the 3-methyloctane may be regarded as 2-pentylbutane and the 3-methylnonane as 2-hexylbutane, etc.

The calculated B. P. N. obviously must be independent of the way in which the structural formulas are expressed.

Taking as a basis the values of 0.8, 1.0 and 3.05 for C, H and CH_3 as given by Kinney, and calculating the B. P. N. for both formulas of each hydrocarbon, the characteristic values for the alkyl radicals have been established. The values as presented in Table I differ by 2.8 for all the neighboring members of the series, this being in accordance with the value calculated from Kinney's data for the CH_2 group. The calculated b. p. n.'s as seen from Table I are somewhat higher

TABLE I

Alkyl radical	B. p. n. calcd. by Kinney	B. p. n. calcd. by the author
CH_3	3.05	3.05
C_2H_5	5.5	5.85
C_3H_7	7.0	8.65
C_4H_9	9.7	11.45
C_5H_{11}		14.25
C_6H_{13}		17.05
C_7H_{15}		19.85
$C_{10}H_{21}$		28.25
$C_{15}H_{31}$		42.25

than those of Kinney but seem to be more accurate as may be seen from the following examples.

(1) C. R. Kinney, THIS JOURNAL, **60**, 3032 (1938).

(1) The 2-methylhexane with a b. p. of 90° has the calcd. B. P. N. of 20.85. If expressed as 2-butylpropane its B. P. N. calcd. with the new value for the butyl radical 11.45 amounts to 20.85 and with the Kinney value 9.7 to 19.1. The b. p. calcd. from the last value amounts to 72.2° while from the first to 90.4°.

(2) For the 2-methylpentane b. p. 60° with the B. P. N. equal to 18.05, the corresponding values for the second formula 2-propylpropane are 18.05 when based on b. p. n. 8.65, and 16.4 when based on b. p. n. equal to 7.0 for the propyl radical. The corresponding calcd. b. p.'s are 60.7 and 41.7°.

(3) The 3,3-diethylpentane has the obsd. B. P. N. of 26.04, the calcd. by Kinney of 25.00 and the calcd. with the new increment for the ethyl radical (5.85) amounting to 25.70.

(4) The 2-methylheptadecane with a b. p. of 311°[2] has the B. P. N. equal to 51.65 (13.6 + 35 + 3.05 or regarded as 2-pentadecylpropane: 2.4 + 7 + 42.25) and the calcd. b. p. of 314.1°.

Using for alkyl radicals the proposed values of b. p. n. the calculated boiling points are in better agreement with observed b. p. for all the ethyl derivatives quoted by Kinney. However, in the case of propyl derivatives as well as of 5-butylnonane, the Kinney values agree much better than those now proposed. It seems to be very plausible that these discrepancies are due either to inaccurate b. p. determinations or to some other unadditive factors bearing on the boiling phenomena.

Instead of calculating the b. p. n. for all the possible radicals, it seems to be much more advisable to calculate the B. P. N. of a compound as a sum of the atomic b. p. n. and take into account the number and kind of the branching present. The increment for a singular branching in the hydrocarbon series amounts in this system evidently to 0.75 (3.8 − 3.05) and must be subtracted from the total B. P. N. In such a way the B. P. N. for *e. g.*, the 2-ethylpentane (C_5H_{16}) will amount to: $(7 \times 0.8) + (16 \times 1) - 0.75 = 20.85$.

It is possible that the value of 0.75 which is true for a single branching, does not hold good in case of two radicals being attached to one carbon atom in the paraffinic chain, and that this is responsible for the discrepancies found in strongly packed molecules.

In addition to the above, mention should be made that Kinney in his calculations does not take into account the influence of the position of the radicals in relation to the whole molecule, although this considerably affects the boiling points of organic compounds.

(2) G. Egloff, "Physical Constants of Hydrocarbons," Vol. I, New York, N. Y., 1939, p. 103.

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RECEIVED APRIL 20, 1939

The Calculation of the Boiling Point Numbers of Aliphatic Compounds

BY CORLISS R. KINNEY

In Dr. Neyman-Pilat's note, "Molecular Structure of Aliphatic Compounds and their Boiling Points," the view was taken that, "The calculated B. P. N. obviously must be independent of the way in which the structural formulas are expressed." If this means that the B. P. N. (molecular boiling point number) of a compound may be calculated without regard for the relationships between the structural components in the molecule, the statement is misleading and the results obtained are variable and consequently of no value. This is true because the relationships between the atoms and groups in molecules do have an effect upon the boiling point of the substance.

By way of example, Dr. Neyman-Pilat suggested that the B. P. N. of 2-methylhexane may be calculated, considering it as 2-butylpropane, by adding the b. p. n. of the side chain butyl group to the b. p. n.'s for the propane chain. Since this gave erroneous results, a new set of b. p. n.'s for the alkyl radicals were proposed (Table I). However, these values were found by Dr. Neyman-Pilat to give unsatisfactory results for those derivatives in which the higher radicals were attached to a longer chain, which, of course, is of no advantage. Furthermore, these values must be used in a particular way, just as the original b. p. n.'s[1] must. This may be demonstrated as follows. Dr. Neyman-Pilat considered 2-methylhexane as 2-butylpropane and, by assigning a new b. p. n. to the butyl radical, obtained a satisfactory B. P. N. However, 2-methylhexane may also be considered as butyldimethylmethane and, if Dr. Neyman-Pilat's new value of 11.45 be used in calculating the B. P. N. of butyldimethylmethane, the result is 19.35 which is much too low. Therefore, by using Dr. Neyman-Pilat's values in a way in which they were

(1) Kinney, THIS JOURNAL, 60, 3032 (1938).

not designed to be used, just as erroneous results may be obtained as when the original b. p. n.'s are used in an erroneous fashion. Since these calculations also show that it is not possible to obtain universal b. p. n.'s for the alkyl groups as Dr. Neyman-Pilat has attempted, it seems advisable to retain the original values which were obtained on the basis that the alkyl radicals were derivatives of the normal paraffin hydrocarbons and not of the 2-methylparaffins. It is essential that the longest chain in the molecule be considered as the base to which the smallest possible radicals are attached. Following this procedure always gives uniform results. The underlying reason is well known to organic chemists in the fact that the boiling point of a substance is not only dependent upon the kind and number of atoms in the molecule, but is also dependent upon the arrangement of those atoms and especially upon the length of the chain.

Dr. Neyman-Pilat has suggested that a higher b. p. n. for the ethyl group than that given in the original paper would give better results. However, it should be pointed out that this is true particularly for the paraffin hydrocarbons and that the value was adopted because it gave more uniform results with all types of organic compounds.

CONTRIBUTION NO. 56 FROM THE
UNIVERSITY OF UTAH
SALT LAKE CITY, UTAH RECEIVED AUGUST 7, 1939

Parachor of Aluminum Bromide in Benzene

BY ISIDORE POPPICK AND ALEXANDER LEHRMAN

The work described here was carried out with the object of determining if the molecular formula of aluminum bromide when dissolved in benzene is the same as that determined for molten aluminum bromide.[1] The method used was to determine the mean parachor of solutions of aluminum bromide in benzene, and to see whether an extrapolation (assuming that the parachor obeys the straight line mixture law) to 100% solute using the formula of Hammick and Andrew[2] would lead to a value of the parachor of pure aluminum bromide that agrees with the value determined by Sugden.[1]

In this method

$$P_m = M_m\gamma^{1/4}/d$$
$$M_m = M_2(X) + M_1(1 - X)$$

(1) Sugden, *J. Chem. Soc.*, 320 (1929).
(2) Hammick and Andrew, *ibid.*, 754 (1929).

Before many measurements had been made, however, it was noticed that the solutions of aluminum bromide in benzene gradually separated into two layers: one, a dense light red oil which turned dark brown-purple on standing, and a less dense colorless layer. All our measurements were made before the separation into the second phase occurred. B. Menschutkin[3] found that the presence of moisture or the introduction of hydrogen bromide into solutions of aluminum bromide in benzene caused the separation into two layers. In our work no hydrogen bromide had been introduced, so it is probable that some water vapor had reacted with the aluminum bromide in the benzene, liberating hydrogen bromide, which in turn caused the formation of the heavy oil. Norris and Rubinstein[4] investigating the formation of complexes of aluminum bromide with toluene in the presence of hydrogen bromide, found by analysis that the complex was $Al_2Br_6 \cdot 6C_6H_5CH_3$. The oil in the case of benzene is probably $Al_2Br_6 \cdot 6C_6H_6$.

Because of the formation of this oil we were unable to carry on work in more concentrated solutions.

Experimental.—The benzene was allowed to stand for one week over mercury, fractionated three times, and dried over phosphorus pentoxide.

Bromine was purified by the method of P. C. Terwogt.[5]

Aluminum bromide was prepared by the method of Kaveler and Monroe.[6] Samples were distilled directly into weighing vials in an atmosphere of dry carbon dioxide.

Densities were determined with a pycnometer with ground glass caps.

Surface tensions were determined using a slightly modified form of Sugden's apparatus.[7] Successive readings were consistent to within 0.4%.

All measurements were made at 34.90 ± 0.03°.

Table I lists the results obtained when the formula Al_2Br_6 is assumed.

TABLE I

Density of solution, d	Mole fraction Al_2Br_6, X	Mean mol. wt., M_m	Surface tension, γ dyne/cm.	Mean parachor P_m
0.9454	0.01737	84.21	26.55	206.6
1.0035	.03330	93.21	27.07	211.9
1.0250	.04195	97.15	27.45	217.0
1.1070	.06345	106.95	27.64	221.5
1.1173	.08325	115.96	27.74	238.3
Extrapolated value of mean parachor when $X = 1.00$				470.4

When plotted, the mean parachors deviate

(3) Menschutkin, *J. Russ. Phys.-Chem. Soc.*, **41**, 1089 (1909).
(4) Norris and Rubinstein, THIS JOURNAL, **61**, 1163 (1939).
(5) P. C. Terwogt, *Z. anorg. Chem.*, **47**, 203 (1905).
(6) Kaveler and Monroe, THIS JOURNAL, **50**, 2421 (1928).
(7) Sugden, *J. Chem. Soc.*, **125**, 27 (1924).

from a straight line over the region investigated by 1% (the total change in the parachor in this range being 11%).

Sugden[1] had obtained 457.6 as the parachor of molten aluminum bromide, assuming the same formula Al_2Br_6. The value obtained here deviates by 3% from Sugden's value. If Sugden had used the formulas $AlBr_3$ or Al_3Br_9, he would have obtained parachors of 228.8 and 686.4, respectively; in this work the same formulas give values of 232.9 and 703.2 after extrapolation, which represent deviations of a little less than 3%.

Our extrapolation is over a large range, so that any errors made at low concentrations will magnify greatly the error in the final value of the parachor. For this reason, it is somewhat surprising that the extrapolated values for the solution fall so near the values for the molten salt.

Owing to the above uncertainty, we can say only that the results obtained here tend to indicate that the formula of aluminum bromide dissolved in benzene is the same as that for the molten compound.

DEPARTMENT OF CHEMISTRY
COLLEGE OF THE CITY OF NEW YORK
NEW YORK, N. Y. RECEIVED JULY 3, 1939

Preparation of Di-*o*-tolylchloromethane

BY EUGENE B. REID

Incidental to a program of measurement of physical properties, di-*o*-tolylchloromethane was prepared. It has not been described previously in the literature.

o,o'-Dimethylbenzohydrol was prepared by reducing *o,o'*-dimethylbenzophenone with 2% sodium amalgam; m. p. 120.5–121.5°. Boyd and Hatt[1] found 119–119.5°. A benzene solution of the carbinol was kept in contact with a concentrated aqueous hydrochloric acid solution for two days; the two layers were separated, and the benzene solvent evaporated. The di-*o*-tolylchloromethane crystallized from petroleum ether as long prisms; m. p. 70–71°; yield 90%.

Anal. Calcd. for $C_{15}H_{15}Cl$: Cl, 15.37. Found: Cl, 15.44.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF MICHIGAN
ANN ARBOR, MICHIGAN RECEIVED AUGUST 17, 1939

(1) Boyd and Hatt, *J. Chem. Soc.*, 898 (1927).

The Dipole Moment of the Amino Benzoic Acids in Dioxane

BY LLOYD VAN BLARICOM AND E. C. GILBERT

The dipole moments of *o*-, *m*- and *p*-aminobenzoic acid have been determined in water solution[1] in which solvent they occur partially in the zwitter-ion form. In non-polar solvents they should exist in ordinary molecular form but their low solubility has precluded measurements of their moment in such solvents. However, their solubility in dioxane proved upon examination to be sufficiently high to allow satisfactory measurements, which are reported in this paper. Dioxane has an additional advantage in that it does not cause association, in general, and it has therefore been used in the determination of the moments of many acids which associate in the ordinary non-polar solvents.[2]

Apparatus and Method.—The apparatus has been described previously.[3] It is based upon the heterodyne beat method and has been demonstrated to give correct results on substances of known dielectric constant. Refractive index was measured with a Bausch and Lomb dipping refractometer. Densities were determined with a pycnometer designed to avoid evaporation losses.[4] All weights were reduced to vacuum.

Materials.—Eastman Kodak Co. dioxane was refluxed with sodium hydroxide for ten hours and fractionated, discarding the first and last portions. It was then refluxed over sodium metal for another ten hours, and again distilled. That used for the measurements had the following constants: m. p. 11.7°; $n^{25}D$ 1.41990; ϵ^{25} 2.2266; d^{25}_4 1.02681.

The amino acids were Eastman best grade, further recrystallized three times. They were boiled with charcoal when necessary to improve the color and fractionally crystallized. They had the melting points: ortho, 144.5–145°; meta, 173–174°; para, 187–188° (all corrected for emergent stem).

Results

The results are shown in Table I, and summarized in Table II. It is frequently assumed that the dipole moments of acids will be similar to those of their methyl esters. Estermann has determined the moments of the three methyl esters of these acids and they are included in the tables for comparison.[5] In each case the moment of the free acid is greater than that of the ester by a considerable percentage.

Dielectric studies of these acids in aqueous solu-

(1) (a) Hedestrand, *Z. physik. Chem.*, **135A**, 36 (1928); (b) Devoto, *Gazz. chim. ital.*, **63**, 247 (1933).
(2) Wilson and Wenzke, *J. Chem. Phys.*, **2**, 546 (1934).
(3) Frey and Gilbert, THIS JOURNAL, **59**, 1344 (1937).
(4) Gilbert and Stark, *ibid.*, **59**, 1818 (1937).
(5) Estermann, *Z. physik. Chem.*, **1B**, 134 (1928).

TABLE I

POLARIZATION DATA FOR DIOXANE SOLUTIONS OF AMINOBENZOIC ACIDS

Mole fraction	ϵ^{25}	d^{25}_4	$n^{25}D$	P_2
		Ortho		
0.0000	2.23025	1.02689	1.41990	
.00510	2.24795	1.02857	1.42143	90.0
.012868	2.26766	1.03134	1.42356	82.7
.020991	2.28782	1.03406	1.42581	80.3
		Meta		
0.0000	2.22661	1.02681	1.41990	
.002963	2.26603	1.02817	1.42101	188.8
.006905	2.30146	1.02933	1.42181	183.5
.009591	2.32697	1.03029	1.42256	177.6
		Para		
0.0000	2.22661	1.02681	1.41990	
.006280	2.33950	1.02933	1.42190	291.2
.014378	2.47570	1.03234	1.42487	280.1
.019724	2.55689	1.03436	1.42624	267.4

tion have indicated[1,6] that they differ considerably in the extent to which they exist in the polar amphoteric form, the meta acid being the only one which is predominantly of the zwitter-ion type, its solutions showing characteristically different behavior from the others.

(6) Devoto, *Z. Elektrochem.*, **40**, 490 (1934); Halbedel, *Z. physik. Chem.*, **33B**, 83 (1936).

TABLE II

DIPOLE MOMENTS OF AMINOBENZOIC ACIDS (DEBYE UNITS)

Acid	∞P_2	R_2	$P_E + P_A$	μ, obsd.	μ, calcd.	μ, ester
Ortho	91.5	39.7	43.7	1.51	1.73	1.00
Meta	194.5	39.0	42.9	2.70	2.95	2.40
Para	301.5	40.6	44.7	3.51	3.40	3.30

In the non-polar solvent dioxane, on the other hand, it assumes the expected intermediary position between the para- and ortho-. This may be shown by a rough calculation of the moment by the method of Williams involving vector addition,[7] the results of which are shown in Table II, column 4. In making them a value of -1.9 is assigned to the carboxyl group and $+1.5$ to the amino group. Such simple assumptions cannot be applied quantitatively to structures as complicated as these molecules since they neglect the effects of valency angles, rotation, resonance, etc. Qualitatively, however, they are useful in illustrating the effect of polarity of the solvent upon the behavior of the meta acid.

(7) Williams, THIS JOURNAL, **50**, 2350 (1928).

DEPARTMENT OF CHEMISTRY
OREGON STATE COLLEGE
CORVALLIS, OREGON

RECEIVED JULY 10, 1939

NEW BOOKS

Organic Syntheses. An Annual Publication of Satisfactory Methods for the Preparation of Organic Chemicals. Vol. XIX. By JOHN R. JOHNSON, *Editor-in-Chief*, HOMER ADKINS, C. F. H. ALLEN, W. E. BACHMANN, N. L. DRAKE, R. L. SHRINER, LEE IRVIN SMITH and A. H. BLATT, *Secretary*. John Wiley and Sons, Inc., 440 Fourth Ave., New York, N. Y., 1939. vi + 105 pp. 15.5 × 23.5 cm. Price, $1.75.

The present volume, like the preceding one, is in harmony with the contemporary interest in biochemistry. As a reviewer of this volume (G. Bryant Bachman) recorded in a recent number of our News Edition, "it is interesting to note that 17 of the 30 preparations described are of nitrogen compounds." The methods of preparation have all been carefully tested. In a few instances—as in preparations IX, XXII, XXV, and XXX—a brief statement is given concerning the specific usefulness of the compound. Some of us, I am sure, would be glad to see an extension of this desirable feature.

The list of the new preparations is as follows: α-acetaminocinnamic acid, acetylglycine, acridone, 2-amino-4-methylthiazole, benzimidazole, benzohydroxamic acid, ε-benzoylamino-α-bromocaproic acid, ε-benzoylaminocaproic acid, ω-bromoacetophenone, *n*-butyl sulfate, *n*-butyl sulfite, copper chromite catalyst, cyclohexylbenzene, dichloroacetic acid, *p*-dinitrobenzene, ethyl benzoyldimethylacetate, ethyl hydrogen sebacate, hexamethylene glycol, 5-iodoanthranilic acid, iodobenzene, *m*-iodobenzoic acid, *dl*-lysine hydrochlorides, methyl nitrate, *dl*-β-phenylalanine, *o*-phenylenediamine, phenylnitromethane, phenylpyruvic acid, *p*-thiocyanodimethylaniline, 1,2,3-triiodo-5-nitrobenzene, triphenylmethylsodium.

M. GOMBERG

Chemie der Zucker und Polysaccharide. (Chemistry of Sugars and Polysaccharides.) By FRITZ MICHEEL, Professor of Organic Chemistry at the University of Münster (Westfalen). Akademische Verlagsgesellschaft m. b. H., Sternwartenstrasse 8, Leipzig C 1, Germany, 1939. xvi + 399 pp. 16 × 23.5 cm. Price, RM. 26.80; bound, RM. 28.40.

The author, whose important carbohydrate researches are well known, has now published one of the best treatises dealing with this field. The chemistry of the sugars, with

main emphasis on the structural and stereochemical side, is presented thoroughly, logically and concisely, with a wealth of literature references. In addition, there are short chapters concerning starch, cellulose and other polysaccharides, biochemical aspects of carbohydrates, and industrial utilizations. A scholarly selection of those topics in which knowledge is now certain, a thorough but concise and objective presentation of matters which still admit of doubt, combined with a precise yet lucid style of writing, have enabled the author to condense the essentials of the subject into such compass that the book can well be recommended as a text for a one-year course in carbohydrate chemistry. It is also valuable as a reference book because of its clear critical judgments and its literature references.

C. S. HUDSON

Qualitative Organic Chemistry. By NEIL CAMPBELL, Lecturer in Organic Chemistry, University of Edinburgh. D. Van Nostrand Company, Inc., 250 Fourth Avenue, New York, N. Y., 1939. ix + 231 pp. Illustrated. 14 × 20.5 cm. Price, $2.60.

The book is divided into two approximately equal parts. Part A comprises six brief chapters dealing with: (1) Isolation and criteria of purity of pure compounds, (2) Preliminary tests and general procedure for identification of organic compounds, (3) Supplementary and color tests, (4) Choice of derivatives, (5) Preparation of derivatives, (6) Examination of mixtures. It is both interesting and significant that of 57 references cited in the chapter on derivatives 68% are to journals of American origin, while only 3 (*i. e.*, 4%) are to German publications.

Part B consists mainly of 94 pages of tables of compounds. These are arranged by liquids and solids under each of the following headings (numbers indicate the numbers of individual compounds discussed).

Paraffins and cycloparaffins (8), unsaturated hydrocarbons (9), aromatic hydrocarbons (30), halogen derivatives of the hydrocarbons (58), nitro compounds (25), halogen-nitro compounds (18), alcohols (31), phenols (19), halogeno- and nitro-phenols (17), ethers (23), cyclic ethers (3), aldehydes and ketones (52), halogeno- and nitro-carbonyl compounds (12), quinones (8), carbohydrates (14), glycosides (4), carboxylic acids (58), halogeno- and nitro-carboxylic acids (19), acid anhydrides (9), esters (46), esters of inorganic acids (9), acid chlorides (10), amides, imides and ureas (32), nitriles (14), amines (primary and secondary) (39), amines (tertiary) (9), halogen substituted amines (13), nitro amines (14), hydroxy- and alkoxyamines (9), anilides and toluidides (50), amino acids (14), phenylhydrazines (10), nitroso-, azoxy-, hydrazo- and azo-compounds (13), heterocyclic compounds (23), aromatic sulfonic acids (7), substituted sulfonic acids (15), sulfonyl chlorides (6), sulfonamides (6), thioamides (3), and finally isothiocyanates (8).

Part B also includes the usual explanatory material, a general index, author index (136 entries) and an alphabetical index of compounds given in the tables. A count of this last index indicates that 755 compounds have been included. Within each of the solid and liquid sections the compounds are arranged in increasing order of m. p. or b. p., respectively, their values being rounded off to even degrees in each case. For most of the compounds one or two derivatives are suggested (not three for each as stated by the publisher in an extravagantly worded current advertisement); occasionally a very brief remark calls attention to a specific property. For many of the liquids (but by no means all) values of density are given to three figures.

The book is intended primarily for students taking a course in organic qualitative analysis. It will prove useful and stimulating for short elementary courses in this field.

ERNEST H. HUNTRESS

BOOKS RECEIVED

September 15, 1939–October 10, 1939

RALPH E. DUNBAR. "Visual Outline of General Chemistry." Longmans, Green and Co., 114 Fifth Ave., New York, N. Y. 348 pp.

CARL J. ENGELDER. "Calculations of Quantitative Analysis." John Wiley and Sons, Inc., 440 Fourth Ave., New York, N. Y. 174 pp. $2.50.

KARL JELLINEK. "Kurzes Lehrbuch der Physikalischen Chemie." Heft II. N. V. Uitgevers-Maatschappij AE. E. Kluwer, Deventer, Netherlands. 252 pp. Dutch fl. 7.50.

HYMAN LEVY. "Modern Science. A Study of Physical Science in the World Today." Alfred A. Knopf, Inc., 501 Madison Ave., New York, N. Y. 736 pp. $5.00.

FREDERICK GEORGE MANN AND BERNARD CHARLES SAUNDERS. "Introduction to Practical Organic Chemistry." Longmans, Green and Co., 114 Fifth Ave., New York, N. Y. 191 pp. $1.50.

E. H. FRITZMAN, Editor. "D. I. Mendeléeff Literary Heritage." Vol. I. Edition of the Leningrad State University, Leningrad, U. S. S. R. 25 pp.

ARTHUR R. MIDDLETON AND JOHN W. WILLARD. "Semimicro Qualitative Analysis." Prentice-Hall, Inc., New York, N. Y. 446 pp. $3.50.

F. J. MOORE. "A History of Chemistry." Third edition. McGraw-Hill Book Co., Inc., New York, N. Y. 447 pp. $3.00.

WILH. SCHLENK. "Ausführliches Lehrbuch der organischen Chemie." II Band, Franz Deuticke, Vienna, Germany. 896 pp. RM. 30. Bound RM. 33.

"Gmelins Handbuch der anorganischen Chemie." Edited by E. PIETSCH. 1 Ergänzungsband, Teil 1. "Aluminum Legierungen Patentsammlung," by G. Apel. Verlag Chemie G. m. b. H., Berlin W 35, Germany. 880 pp. RM. 72.

"Minerals Yearbook, 1939." H. HERBERT HUGHES, Editor. Superintendent of Documents, Government Printing Office, Washington, D. C. 1422 pp. $2.00.

JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

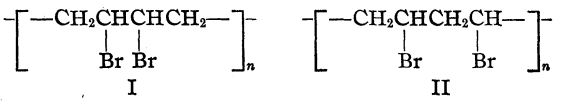
VOLUME 61 DECEMBER 19, 1939 NUMBER 12

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

The Structure of Vinyl Polymers. VI.[1] Polyvinyl Halides

BY C. S. MARVEL, J. H. SAMPLE AND MAX F. ROY

The earliest work on the structure of the polyvinyl halides was that of Ostromysslenski[2] who showed that zinc removes bromine from polyvinyl bromide in chlorobenzene solution. He stated that this reaction showed that polyvinyl bromide had the same structural unit which occurred in the perbromide of polybutadiene (I).



I

II

The properties of the two bromine-containing products were compared and it was stated that they were identical. Somewhat later a patent[3] was granted on the preparation of a caoutchouc-like product by the action of zinc on polyvinyl halides.

Harries[4] made a vigorous attack on the authenticity of Ostromysslenski's work. He pointed out that the perbromide of polybutadiene never can be obtained with the theoretical bromine content of 74.7% corresponding to that of polyvinyl bromide. Actually bromination of polybutadiene gave a product with a bromine content of 62.4 to 71.8%. The difficulties of proving the identity of two polymeric products were pointed out by Harries.

Later Staudinger, Brunner and Feisst[5] studied the reactions of polyvinyl bromide and concluded that it was a 1,3-dihalide (II). They confirmed the observation of Ostromysslenski that zinc removes the halogen from a polyvinyl halide and accounted for this by ring formation. They also noted that zinc alkyls removed bromine from polyvinyl bromide and that reduction produced paraffin-like products.

In the present study of the structure of the polyvinyl halides most of the work has been done with polyvinyl chloride. When a saturated solution in dioxane of this polymer was heated with zinc, an insoluble product still containing most of the halogen was formed. When a very dilute solution of polyvinyl chloride in dioxane was heated with zinc the cross-linking reaction which produced the insoluble material was avoided and a smooth dehalogenation reaction occurred. It was never possible to remove all of the chlorine under the conditions used, but the amount removed under the most favorable conditions varied from 84 to 87%. Similarly, zinc removed 85.9% of the bromine from polyvinyl bromide. These facts are particularly significant, since Flory[6] has shown that random removal of pairs of halogens in a polymeric 1,3-dihalide should take out 86.47% of the halogen and leave 13.53% of the halogen isolated from reactive neighbors and non-removable except by cross-linking of the carbon chains. The polymeric material left after the reaction of polyvinyl chloride with zinc was still soluble in dioxane. It did not decolorize an alkaline solu-

(1) For the fifth communication in this series, see THIS JOURNAL, **61**, 3234 (1939).

(2) Ostromysslenski, *J. Russ. Phys.-Chem. Soc.*, **44**, 204, 240 (1912); *Chem. Zentr.*, **83**, (I), 1980, 1982 (1912).

(3) Ostromysslenski, German Patent 264,123 (1913); *Chem. Zentr.*, **84**, II, 1187 (1913).

(4) Harries, *Ann.*, **395**, 216 (1913).

(5) Staudinger, Brunner and Feisst, *Helv. Chim. Acta*, **13**, 805 (1930).

(6) Flory, THIS JOURNAL, **61**, 1518 (1939).

tion of potassium permanganate if care was taken to avoid contamination with peroxides from the dioxane. Treatment of the dehalogenated polymer with ozone and subsequent hydrolysis in the presence of an oxidizing agent did not give definite products, whereas under the same conditions polybutadiene gave succinic acid.[7] Nitric acid did not attack the dehalogenated polymer readily. Chlorine would attack the dehalogenated polymer and both addition and substitution of chlorine occurred. All of these reactions indicate that the dehalogenated polymer consists of cyclopropane units with occasional isolated —CH_2CHCl— units (III).

$$-CH_2CHCH_2CHCH_2CHCH_2CHCH_2CH- \xrightarrow{Zn}$$
$$-CH_2CHCH_2CHCH_2CHCH_2CHCH_2CH-$$

III

Another fact which supports the 1,3-dihalide structure for the polyvinyl halides is that neither the chloride nor the bromide liberates iodine from a peroxide-free dioxane solution of potassium iodide, a reaction which is characteristic of 1,2-dihalides.[8]

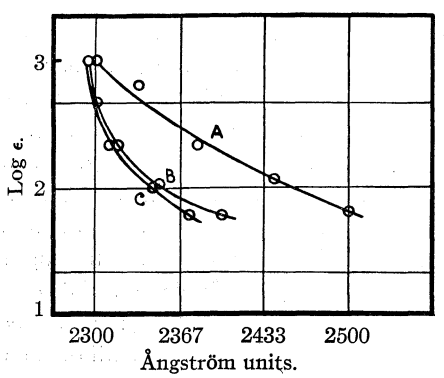


Fig. 1.—Ultraviolet absorption spectra, ϵ = extinction coefficient: A, 2,3-dichloropentane; B, 2,4-dichloropentane; C, polyvinyl chloride.

Further evidence for the 1,3-dihalide structure is obtained by a comparison of the ultraviolet absorption spectra of 2,3-dichloropentane (IV), 2,4-dichloropentane (V) and polyvinyl chloride (VI). The absorption curves are given in Fig. 1.

$CH_3CHCHCH_2CH_3$ (Cl, Cl)

IV

$CH_3CHCH_2CHCH_3$ (Cl, Cl)

V

(7) Ref. 4; also Harries, *Chem. Ztg.*, **36**, 654 (1912).

(8) Davis and Heggie, *J. Org. Chem.*, **2**, 470 (1937).

$$-\left[-CH_2CHCH_2CH-\right]_n-$$
(Cl, Cl)

VI

It is interesting to note that treatment of a "Cellosolve" solution of polyvinyl chloride with potassium hydroxide removes halogen acid and leads to the formation of an insoluble shiny reddish-brown polymer which corresponds to the polymer $(CH)_x$ reported by Ostromysslenski.[3] This product is probably a very long chain polyene (VII). We have not investigated this polymer in any detail.

$$-[-CH=CH-CH=CH-]_n-$$

VII

All of the reactions and properties of the polyvinyl halides are thus best accounted for on the basis of the 1,3-dihalide structure which was first proposed by Staudinger, Brunner and Feisst.[5]

Experimental

The polyvinyl chloride used in this investigation was furnished by the Carbide and Carbon Chemicals Corporation.[9] It had been prepared by the polymerization of vinyl chloride in the presence of peroxides. Its chlorine content was 56.7%. The polymer was stable to boiling water. It was insoluble in most solvents but did dissolve slowly in dioxane.

Reaction of Polyvinyl Chloride with Zinc.—Ordinary zinc dust was purified by treating it with dilute hydrochloric acid to remove oxide and sulfide, then by washing with water to remove acid and with acetone to remove water. The zinc was dried in a desiccator and used without long exposure to air. In the air the zinc became unreactive in about two months.

When a saturated solution of polyvinyl chloride in dioxane was boiled with zinc, a rubbery gray mass separated out. This material contained halogen and a great deal of occluded zinc. It was not soluble in organic solvents and no satisfactory procedure could be devised to separate the organic and inorganic constituents.

When a very dilute solution of polyvinyl chloride in peroxide-free dioxane was boiled with zinc, halogen was

TABLE I

REMOVAL OF CHLORINE FROM POLYVINYL CHLORIDE BY TREATMENT WITH ZINC

Polyvinyl chloride, g.	Peroxide-free dioxane, cc.	Active zinc, g.	Time of reflux, hours	Chlorine removed, %
1.1060	500	6	39.5	57.6
7.6292	3400	37.2	83	67
4.2315	2000	35.6	76	80
1.895	650	7	150	85
0.2899	115	4	155.5	84.5
.4651	150	4	155.5	84
.4719	150	4	155.5	87.2

(9) The authors desire to express their thanks to Mr. H. B. McClure of Carbide and Carbon Chemicals Corporation for his aid in this connection.

removed and the organic residue remained soluble. The dehalogenation reaction proceeded rather slowly and seemed to stop after about one hundred fifty to one hundred sixty hours. The excess zinc could be removed by filtration and the addition of water to the filtrate precipitated a rubbery polymer. Analysis of this polymer and of the remaining solution showed that the zinc treatment had removed about 85% of the chlorine from the polyvinyl chloride. Some typical experiments are listed in the table.

Properties of the Dehalogenated Polymer.—The dehalogenated polymer was precipitated from the dioxane solution as a rubbery mass by the addition of water. This polymer dissolved slowly in carbon tetrachloride. Its dioxane solution did not give a test for unsaturation when shaken with 2% alkaline potassium permanganate solution.

A carbon tetrachloride solution of the rubbery polymer was treated with ozone and then hydrolyzed but no evidence of ozonolysis was obtained. Treatment with nitric acid caused some oxidation but did not yield crystalline products. When the dioxane solution from the zinc treatment was mixed with a solution of chlorine in carbon tetrachloride, it was found that chlorine added again to the polymer but also chlorination occurred as more chlorine was taken up for the solution than had been removed from the polyvinyl chloride by the zinc.

Polyvinyl Bromide and Zinc.—Vinyl bromide was prepared by the method of Kharasch[10] and polymerized by warming it with benzoyl peroxide. The white amorphous powder thus obtained was washed with ether, dilute hydrochloric acid, distilled water, and finally with ethyl alcohol and ether. The bromine content of the polymer was 74.45%.

A solution of 0.0667 g. of polyvinyl bromide in 50 cc. of peroxide-free dioxane was refluxed with a slight excess of active zinc for one hundred and forty-six hours. The solution was filtered and the bromide ion was determined by titration. This treatment removed 85.9% of the bromine from the sample of polyvinyl bromide.

Treatment of Polyvinyl Halides with Potassium Iodide.—Heating a solution of 1.2109 g. of polyvinyl chloride and 9.0227 g. of potassium iodide in 500 cc. of peroxide-free dioxane to boiling under a reflux condenser for two hundred and twenty-three hours did not liberate enough iodine to give a test with starch paste. Similarly heating a solution of 0.2 g. of polyvinyl bromide and excess potassium iodide in 100 cc. of peroxide-free dioxane to boiling under reflux for eighty-two hours liberated only a trace of free iodine.

Action of Potassium Hydroxide on Polyvinyl Chloride.—A solution of potassium hydroxide in "Cellosolve" was added to a solution of polyvinyl chloride in the same solvent and the resulting clear colorless solution was boiled under reflux. Almost immediately it turned a light yellow which quickly changed to dark yellow, to orange, and finally to a reddish-brown with the formation of a brown gelatinous precipitate. On further heating, the color of the solution became darker and the gelatinous precipitate coagulated to a black stringy mass.

After several hours, heating was stopped, the solution was cooled and the black precipitate removed by filtration and discarded. Acidification of the dark reddish-brown filtrate with concentrated nitric acid discharged most of the color, and addition of silver nitrate to the acidified solution gave a copious precipitate of silver chloride.

A mixture of 3.000 g. of polyvinyl chloride in 100 cc. of 5% solution of potassium hydroxide in "Cellosolve" was refluxed for thirty hours. (The solubility of polyvinyl chloride in "Cellosolve" is considerably less than 3 g. in 100 cc. so that most of the polyvinyl chloride was present at the start of the reaction as undissolved polyvinyl chloride.)

As refluxing was started, the color of the solution and of the undissolved solid quickly became a dark reddish-brown and remained so throughout the period of refluxing.

The solution was cooled and the dark red-brown solid was collected on a sintered-glass filter, washed with "Cellosolve" and with water, and dried in a vacuum desiccator over concentrated sulfuric acid for forty-eight hours. During this period the color of the material changed from deep red-brown to deep orange. The weight of the dried material was 1.746 g., indicating a loss in weight of 1.254 g. from the original weight of polyvinyl chloride.

This orange material burned with a smoky flame without any visible melting and, unlike the original polyvinyl chloride, was insoluble in hot dioxane. On further standing the color became lighter and lighter and after two weeks was a faint yellow. Some of the material was heated with concentrated nitric acid on a steam-bath. All of the solid slowly dissolved with the evolution of gas. Evaporation to dryness left no appreciable residue.

The filtrate and washings from the above were combined and the resulting solution was acidified with nitric acid. Silver nitrate solution was then added until no further precipitation of silver chloride occurred. The silver chloride was collected on a sintered-glass filter, dried in a vacuum desiccator over concentrated sulfuric acid, and weighed. The weight of silver chloride was 6.744 g., equivalent to 1.668 g. of chlorine. The original 3.000 g. of polyvinyl chloride (56.73% chlorine) contained 1.702 g. of chlorine which was removed to the extent of 98% by the action of the potassium hydroxide in "Cellosolve" solution.

Ultraviolet Absorption Spectra Studies.—The spectra were taken with a Bausch and Lomb ultraviolet spectrograph. A hydrogen discharge tube operating on 15,000 volts gave a continuous ultraviolet source and the Hα, Hβ, and Hγ lines served to calibrate the wave length scale of the instrument. Eastman Kodak Company D-O-(double coated) Ortho plates were used and the pictures were taken with a slit opening of $10\mu \times 4$ mm. and a 1-cm. quartz cell. Each exposure was for one and one-quarter minutes. The absorption coefficient was determined by comparison with the blackness of a trace in a 10^{-4} molar solution of naphthalene. A concentration of 0.02 M for the dichloropentanes was used. The concentration of the polymer was 0.02 M on the basis of a dimer unit.

Summary

Zinc removes 84–87% of the halogen from polyvinyl halides in dilute solution to yield a rubbery

(10) Kharasch, THIS JOURNAL, **55**, 2521 (1933).

polymer which does not decolorize aqueous potassium permanganate solution. Polyvinyl halides do not liberate iodine from potassium iodide. The ultraviolet absorption spectrum of polyvinyl chloride is very similar to that of 2,4-dichloropentane and somewhat different from that of 2,3-dichloropentane. All of these facts support the view that polyvinyl chloride has the 1,3-dihalide structure.

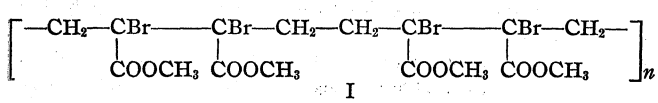
URBANA, ILLINOIS RECEIVED JULY 10, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

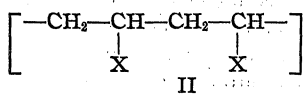
The Structure of Vinyl Polymers. VII. Polyacrylyl Chloride[1]

BY C. S. MARVEL AND CHARLES L. LEVESQUE[2]

Recent work from this Laboratory[3] has shown that the polymers of alkyl α-haloacrylates have a "head to head, tail to tail" structure (I), in contrast to many other vinyl polymers which have a "head to tail" structure (II, X = halogen, OH, $COCH_3$).[4]



I

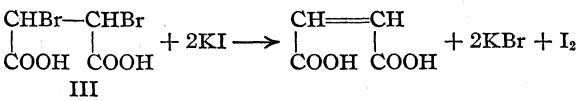


II

Since the vinyl halides are known to form "head to tail" polymers,[4a] this anomalous behavior of the haloacrylates must be due either to the presence of two activating groups attached to the vinyl group, or it must be peculiar to acrylic acid derivatives. The results reported in this paper support the latter explanation.

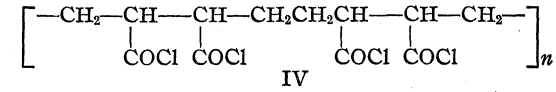
Acrylyl chloride prepared from sodium acrylate and phosphorus oxychloride[5] may be polymerized either by peroxides or ultraviolet light. When thionyl chloride is substituted for the phosphorus oxychloride in the preparation of the acrylyl chloride, the product obtained is polymerizable only by ultraviolet light. It is probable that this acrylyl chloride was contaminated with a little thionyl chloride, which inactivated the peroxide catalyst. The polymers obtained are all brittle, pale yellow solids, soluble in phosphorus oxychloride and dioxane, but insoluble in other common solvents.

By treating a phosphorus oxychloride solution of photopolymerized acrylyl chloride with bromine, it was possible to introduce into the polymer bromine equivalent to one atom for every 3.4 acrylyl chloride units. When this brominated polymer was transformed into the corresponding methyl ester and heated with potassium iodide in acetone solution, free iodine was released. The amount of iodine was equivalent to 46% of the bromine in the polymer. This reaction is characteristic of 1,2-dibromo compounds, especially those in which the bromine atoms are adjacent to a negative group, as in dibromosuccinic acid (III).[6]



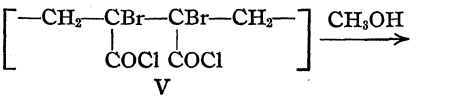
III

The production of 1,2-dibromo units by the bromination of polyacrylyl chloride is most logically explained by assuming a "head to head, tail to tail" structure for this polymer (IV).

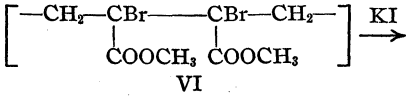


IV

Since bromine readily substitutes in the α-position of an acid chloride, bromination of IV would give rise to 1,2-dibromo units (V). The corresponding methyl ester (VI) would release iodine from potassium iodide, forming an unsaturated ester (VII).



V



VI

(1) For the sixth communication in this series, see THIS JOURNAL, **61**, 3241 (1939).

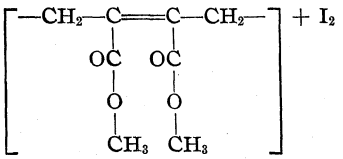
(2) Du Pont Fellow in Chemistry (1938–1939).

(3) Marvel and Cowan, THIS JOURNAL, **61**, 3156 (1939).

(4) (a) Marvel and Sample, *ibid.*, **61**, in press (1939); (b) Marvel and Denoon, *ibid.*, **60**, 1045 (1938); Marvel and Levesque, *ibid.*, **60**, 280 (1938).

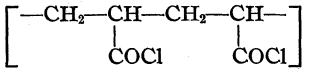
(5) Moureu, *Ann. chim.*, [7] **2**, 145 (1894).

(6) Davis and Heggie, *J. Org. Chem.*, **2**, 470 (1937); see also ref. 3.



VII

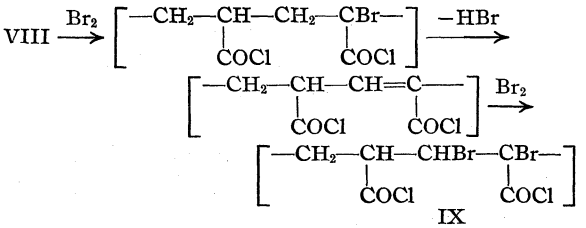
Since only a third of the hydrogen atoms in the α-positions of the polymer were replaced by bromine, the possibility of the presence of some "head to tail" units (VIII) is not excluded. The



VIII

presence of any appreciable fraction of these units, however, would make it quite improbable that the substitution of bromine in only one-third of the α-positions of the polymer would place nearly half of the bromine atoms on adjacent carbon atoms.

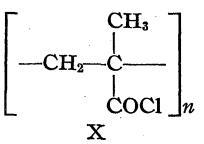
A polyacrylyl chloride having only the "head to tail" structure (VIII) might give rise to 1,2-dibromo units (IX) by the following series of reactions. However, the fact that even in the



IX

presence of bases, ethyl α-bromoglutarate is transformed into glutaconic acid in only very small yields argues against this mechanism.

Although the direct substitution of bromine in other than the α-position of polyacrylyl chloride seemed unlikely, this possibility was investigated. Polymethacrylyl chloride (X) was treated with bromine under conditions identical with those



X

prevailing during the bromination of polyacrylyl chloride. The α-positions of this polymer are not available for substitution and, as expected, no bromination occurred.

From these facts it is evident that at least a part of the units of polyacrylyl chloride are arranged in a "head to head, tail to tail" structure (IV).

Experimental

Preparation of Acrylyl Chloride.—Acrylyl chloride was prepared from phosphorus oxychloride and sodium acrylate.[5] The first crude product was purified by careful fractionation. The yield of acrylyl chloride boiling from 72–73° was 22%. When thionyl chloride was substituted for the phosphorus oxychloride, the yield dropped to 19%.

Polymerization of Acrylyl Chloride by Benzoyl Peroxide.—In a round-bottomed flask connected by a ground joint to a reflux condenser carrying a calcium chloride tube was placed 3 cc. of acrylyl chloride prepared from phosphorus oxychloride, 50 cc. of dry carbon tetrachloride and a few crystals of benzoyl peroxide. The mixture was boiled for four hours. The polyacrylyl chloride separated as a pale yellow solid which adhered to the sides of the flask. The solvent was decanted and the polymer was scraped into a tared evaporating dish. After drying under reduced pressure, it weighed 1.1 g. (45%). The polymer was soluble in phosphorus oxychloride.

Acrylyl chloride prepared from thionyl chloride did not polymerize under similar conditions.

Polymerization of Acrylyl Chloride by Ultraviolet Light.—A solution of 15 g. of acrylyl chloride in an equal volume of dry carbon tetrachloride was placed in a tightly stoppered quartz test-tube and irradiated with light from a mercury vapor arc for thirty hours. The polyacrylyl chloride separated as a brittle, light yellow solid. It was isolated by removing the solvent under reduced pressure in a stream of dried air. It weighed 7.2 g. (48%).

Bromination of Polyacrylyl Chloride.—A solution of 7.2 g. of photopolymerized acrylyl chloride in 90 cc. of phosphorus oxychloride was placed in a 200-cc. round-bottomed flask and 6.3 cc. of bromine was added. A reflux condenser carrying a calcium chloride tube was attached to the flask by a ground joint, and the mixture was irradiated for seven days with light from a 100-watt lamp. Most of the phosphorus oxychloride was removed by distillation under reduced pressure and a mixture of 50 cc. of toluene and 50 cc. of methanol was added to the viscous residue. The mixture was refluxed for one hour. The excess methanol was removed by distillation and the residual toluene solution was filtered through a sintered glass funnel. The brown gel remaining on the funnel was treated with 150 cc. of acetone and most of it dissolved. The acetone solution was filtered and the filtrate was added to the toluene filtrate. The combined filtrates were diluted with four volumes of alcohol and the tacky, brown solid which separated was isolated by decantation. The solid was redissolved in 50 cc. of acetone and reprecipitated with alcohol. The precipitate was collected on a filter. After drying under reduced pressure over sulfuric acid, the product was 5.8 g. of a fibrous, light brown solid.

Anal. Calcd. for $C_4H_5O_2Br$: Br, 48.5. Found: Br, 21.26.

The analysis shows the presence of one bromine atom for every 3.4 methyl acrylate units.

Reaction of the Brominated Polymer with Potassium Iodide.[6]—A solution of 4.000 g. of the brominated polymer in acetone was made up to exactly 100 cc. This solution was placed in a flask containing 2.0 g. of powdered

potassium iodide and a reflux condenser was attached by a ground joint. The mixture was boiled gently on a steam cone. At intervals 25 cc. of the reaction mixture was removed with a pipet, diluted with 250 cc. of water and titrated with 0.03620 *N* sodium thiosulfate, using starch solution as an indicator. At seventeen, twenty-three and twenty-nine hours, 41.7, 46.3 and 46.0% of bromine, respectively, were removed from the polymer.

A solution of 1.677 g. of the brominated polymer in acetone was made up to exactly 50 cc. The solution was placed in a glass-stoppered Erlenmeyer flask containing 1.0 g. of powdered potassium iodide. The flask, which was allowed to stand at room temperature, was shaken occasionally. At intervals 10-cc. samples were removed, diluted with 125 cc. of water and titrated with 0.03620 *N* sodium thiosulfate.

Under these conditions the percentages of bromine removed from the polymer were 25.9, 26.8, 32.2 and 32.1 after twenty-one, twenty-four, forty-five and seventy-nine hours, respectively.

Attempted Bromination of Polymethacrylyl Chloride.—A sample of polymethacrylyl chloride was obtained through the courtesy of Dr. B. C. Pratt of the du Pont Experimental Station. Four grams of this polymer was dissolved in 50 cc. of phosphorus oxychloride contained in a 100-cc. flask and 3.2 cc. of bromine was added. A reflux condenser protected by a calcium chloride tube was attached to the flask by a ground joint, and the mixture was irradiated for eight days with light from a 100-watt lamp. The product, isolated by the methods employed for the brominated polyacrylyl chloride, was 2.2 g. of brittle, brown solid.

Anal. Found: Br, 0.23.

Summary

Polyacrylyl chloride has been brominated and then esterified to give a polymeric bromoacrylic ester which liberated iodine from potassium iodide solution. This indicates that polyacrylyl chloride has some of its units arranged in a "head to head, tail to tail" fashion.

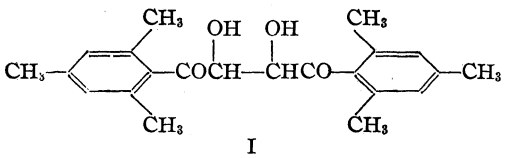
URBANA, ILLINOIS RECEIVED AUGUST 4, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

1,2-Diacylethylene Glycols

BY REYNOLD C. FUSON, C. H. MCBURNEY AND W. E. HOLLAND

Mesitylglyoxal reacts with the binary mixture, Mg + MgI_2,[1] in a very remarkable fashion; the reduction is entirely bimolecular, yielding 1,2-dimesitoylethylene glycol (I).[2] In the present work *t*-butylglyoxal, phenylglyoxal, 3,5-dibromomesitylglyoxal, 2,4,6-triethylphenylglyoxal and isodurylglyoxal have been found to behave in this same manner. In each case the product is the corresponding 1,2-diacylethylene glycol



I

$$2RCOCHO \longrightarrow RCO\underset{|}{\overset{OH}{CH}}—\underset{|}{\overset{OH}{CH}}COR$$

The hindered glyoxals gave only one glycol while phenylglyoxal yielded two—presumably diastereoisomers

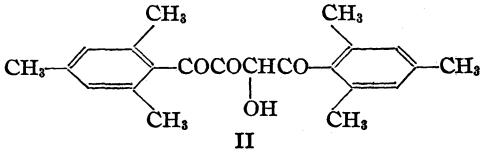
$$C_6H_5CO\underset{|}{\overset{OH}{CH}}—\underset{|}{\overset{OH}{CH}}COC_6H_5$$

Thus it would seem that while steric hindrance is not responsible for the success of the reaction it may influence its course.

Two of the glyoxals, isodurylglyoxal and 3,5-dibromomesitylglyoxal, have not been reported before. They were made from acetoisodurene and 3,5-dibromoacetomesitylene, respectively, by treatment with selenium dioxide. The semicarbazones and the phenylhydrazones of the two glyoxals were prepared. The glyoxals were found to undergo rearrangement to the corresponding glycolic acids when treated with 10% potassium hydroxide solution.

The yield of glycol was found to depend on the time of reaction and on the ether–benzene ratio of the solvent. For example, in one experiment with phenylglyoxal, using an ether–benzene ratio of 1:2, the yield of glycol was only 2% of the theoretical; in another experiment in which an ether–benzene ratio of 2:3 was used the yield was 55%. If too long a reaction time is employed, side reactions occur. When mesitylglyoxal was treated with the binary mixture, Mg + MgI_2, for one hour the resulting glycol was contaminated with 1,2-dimesitoylformoin (II). In view of this fact a standard reaction time of fifteen minutes was used in all of the experiments.

(1) Gomberg and Bachmann, THIS JOURNAL, **49**, 236 (1927).
(2) Gray and Fuson, *ibid.*, **56**, 739 (1934).

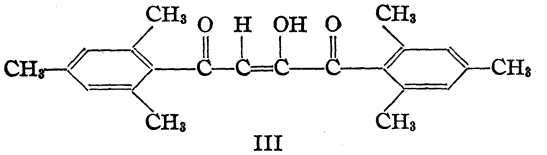


II

To see whether similar glycols might be produced from diketones, mesityl phenyl diketone was subjected to the reduction. The product was 2,4,6-trimethylbenzoin

$$C_9H_{11}COCH(OH)C_6H_5$$

The bimolecular reduction product (I) of mesitylglyoxal underwent dehydration when treated with either oxalic acid or sulfuric acid, producing in both cases the same compound, 1,4-dimesityl-1,3,4-butanetrione enol (III). Likewise, the glycol gave an acetone compound when treated with acetone, magnesium sulfate and sulfuric acid.[3] Oxidation with lead tetraacetate gave mesitylglyoxal.



III

The glycol (I) also underwent oxidation with copper sulfate in pyridine, producing dimesityl diketone; oxidation with selenium dioxide gave dimesityl triketone. Dimesityl tetraketone was probably an intermediate in these reactions, carbon monoxide being lost to give first the triketone and then the diketone

$$C_9H_{11}\underset{\displaystyle OH}{\underset{|}{C}}H-\underset{\displaystyle OH}{\underset{|}{C}}HCOC_9H_{11} \longrightarrow C_9H_{11}COCOCOCOC_9H_{11} \xrightarrow{-CO} C_9H_{11}COCOCOC_9H_{11} \xrightarrow{-CO} C_9H_{11}COCOC_9H_{11}$$

An attempt was made to effect the transposition of a carbonyl group with an α-hydroxyl group by treatment with sodium ethoxide—a procedure which has been used with success by Henze[4] for similar compounds. Instead of the expected rearrangement product there was obtained 1,4-dimesityl-1,3,4-butanetrione enol (III).

The inability of the glycol to pass readily into the enol form was shown by the failure of attempts to prepare a tetraester. Treatment with four moles of ethylmagnesium bromide followed by four moles of acetyl chloride gave the formoin (II) instead of a tetraacetate; heating under reflux with benzoyl chloride according to the method of Lees[5] gave the benzoate of the enol (III) instead of a tetrabenzoate; treatment with sodium acetate and acetic anhydride gave an intractable oil.

(3) Derx, *Rec. trav. chim.*, **41**, 316 (1922).
(4) Henze, *Z. physiol. Chem.*, **232**, 117 (1935).

Experimental

A. Glyoxals

3,5-Dibromomesitylglyoxal.—After 5.1 g. of selenium dioxide had been dissolved by warming in 100 cc. of wet dioxane, 14.5 g. of 3,5-dibromoacetomesitylene was added and the mixture refluxed for four hours. After most of the dioxane had been distilled, 250 cc. of toluene was added and the distillation continued until the distillate was no longer cloudy. The residual toluene was removed under reduced pressure. The glyoxal distilled at 157° (4 mm.); the yield was 41.5% of the theoretical. The **hydrate** melts at 100–102°.

Anal. Calcd. for $C_{11}H_{10}Br_2O_2$: Br, 47.90. Found: Br, 47.89.

The **semicarbazone** after several recrystallizations from alcohol and water melted at 238–241°.

Anal. Calcd. for $C_{12}H_{13}Br_2H_3O_2$: C, 36.83; H, 3.35. Found: C, 37.11; H, 3.71.

The **phenylhydrazone** crystallized from alcohol; m. p. 183–184.5°.

Anal. Calcd. for $C_{17}H_{16}Br_2N_2O$: C, 48.11; H, 3.77. Found: C, 48.44; H, 3.79.

3,5-Dibromomesitylglycolic acid was prepared by heating a suspension of the glyoxal hydrate with 10% sodium hydroxide solution. Acidification produced the white, crystalline acid which, after recrystallization from water, melted at 184–185°.

Anal. Calcd. for $C_{11}H_{12}Br_2O_3$: C, 37.53; H, 3.44. Found: C, 37.64; H, 3.39.

Isodurylglyoxal.—This glyoxal was prepared from acetoisodurene in 72% yield by the method just described; b. p. 123–127° (8 mm.). The hydrate melts at 86–87°.

Anal. Calcd. for $C_{12}H_{14}O_2$: C, 75.79; H, 7.36. Found: C, 75.90; H, 7.42.

The **semicarbazone** after recrystallization from alcohol melted at 207–208°.

Anal. Calcd. for $C_{13}H_{17}N_3O_2$: C, 63.16; H, 6.88. Found: C, 63.19; H, 7.19.

The **phenylhydrazone** crystallized from alcohol; m. p. 118–119°.

Anal. Calcd. for $C_{18}H_{20}N_2O$: C, 77.14; H, 7.14. Found: C, 76.92; H, 7.65.

Isodurylglycolic acid was prepared by heating the glyoxal hydrate with a solution of 10% potassium hydroxide. Acidification produced the white crystalline acid which, after recrystallization from water, melted at 171.5–172°.

Anal. Calcd. for $C_{12}H_{10}O_3$: C, 69.22; H, 7.69. Found: C, 69.48; H, 7.69.

The melting point of this acid is given by Claus and Foecking[6] as 156°. They obtained their product by the

(5) Lees, *J. Chem. Soc.*, **83**, 145 (1903).
(6) Claus and Foecking, *Ber.*, **20**, 3097 (1887).

reduction of isodurylglyoxylic acid. The acetoisodurene from which their glyoxylic acid was prepared may have been contaminated with acetoprehnitene and acetodurene, the isodurene used having been prepared by the action of methyl iodide and aluminum chloride on mesitylene. The isodurene used in the present experiments was made by the action of methyl sulfate upon mesitylmagnesium bromide.[7]

B. Glycols

1,2-Di-(2,4,6-triethylbenzoyl)-ethylene Glycol.—Seven grams of iodine was added in small portions to a warm mixture of 25 cc. of dry benzene, 17 cc. of dry ether and 2.5 g. of magnesium turnings; the additions were made through the condenser at such a rate as to keep the mixture just boiling. After the iodine had all been added and the initial vigorous reaction had subsided, the mixture was refluxed until the iodine color had disappeared. To this mixture, after cooling, was added 8.8 g. of 2,4,6-triethylphenylglyoxal. The flask was stoppered and shaken vigorously, with frequent cooling, for fifteen minutes, then the solution was decanted into 100 cc. of water, shaken and the magnesium hydroxide dissolved with dilute acetic acid. The organic layer was removed, washed with water and sodium thiosulfate solution, and the glycol was isolated by evaporation of the ether and benzene. After recrystallization from ethanol the glycol melted at 104–105° (corr.); yield, 3.7 g., which was 42% of the theoretical.

Anal. Calcd. for $C_{28}H_{38}O_4$: C, 76.66; H, 8.74. Found: C, 76.95; H, 8.81.

1,2-Di-3,5-dibromomesitoylethylene Glycol.—This glycol was obtained by the foregoing procedure in a 27% yield; m. p. 229–232°.

Anal. Calcd. for $C_{22}H_{22}O_4Br_4$: C, 39.42; H, 3.31. Found: C, 39.14; H, 3.64.

1,2-Di-(2,3,4,6-tetramethylbenzoyl)-ethylene Glycol.—Isodurylglyoxal gave a 37% yield of glycol; m. p. 160–161°.

Anal. Calcd. for $C_{24}H_{30}O_4$: C, 75.34; H, 7.92. Found: C, 75.65; H, 7.84.

1,2-Dipivalylethylene Glycol.[8]—*t*-Butylglyoxal was reduced in an atmosphere of nitrogen; otherwise the procedure was the same as that used for the three preceding glycols.

1,2-Dibenzoylethylene Glycol.—Reduction of phenylglyoxal gave two forms of 1,2-dibenzoylethylene glycol. These were separated by digesting the reduction mixture with small portions of ether until the residue had a constant melting point. In this way there was obtained from 19 g. of reaction mixture 3 g. of glycol melting at 125–127°. Although somewhat unstable this high-melting isomer could be recrystallized from ethanol by warming gently and stirring the mixture until solution was accomplished and then chilling the solution, m. p. 126–127.5° (corr.).

Anal. Calcd. for $C_{16}H_{14}O_4$: C, 71.09; H, 5.23. Found: C, 71.03; H, 5.46.

The **diacetate** of this glycol was prepared by refluxing with acetyl chloride for thirty minutes, pouring the reaction mixture into ice water and recrystallizing the solid from ethanol, m. p. 168–169° (corr.).

Anal. Calcd. for $C_{20}H_{18}O_6$: C, 67.75; H, 5.13. Found: C, 68.01; H, 5.21.

When the combined ether filtrates from the digestions were evaporated to one-half their volume and placed in the ice box, a mixture of crystals formed from which several crystals of the known isomer were separated by hand. The rest of the mixture was redissolved in ether and, after seeding with the hand-picked crystals, the solution allowed to evaporate to dryness. In this way 2 g. of the low-melting form of 1,2-dibenzoylethylene glycol was obtained which after recrystallization from ethanol melted at 118–119° (corr.).

Anal. Calcd. for $C_{16}H_{14}O_4$: C, 71.09; H, 5.23. Found: C, 71.28; H, 5.39.

This glycol was also prepared according to the general method of Milas and Sussman[9] using hydrogen peroxide and also by permanganate oxidation by a procedure based on that of Straus and Rohrbacher[10] for Δ'-dihydronaphthalene. Melting points of mixtures showed the products from the three sources to be identical.

2,4,6-Trimethylbenzoin.—The reduction of 5.04 g. of mesityl phenyl diketone with the binary mixture gave 1.5 g. of 2,4,6-trimethylbenzoin.[11]

C. Reactions of 1,2-Dimesitoylethylene Glycol (I)

Dehydration.—(a) Five-tenths gram of the glycol was dissolved in 5 cc. of concentrated sulfuric acid at 0° and allowed to stand at this temperature for thirty minutes. When the deep red solution was poured on ice, the solid enol separated and was isolated by filtration; it was purified by fractional crystallization from benzene, m. p. 112–113° (corr.). A mixture with an authentic sample of 1,4-dimesityl-1,3,4-butanetrione enol (III), prepared according to the method of Lutz,[12] showed no depression of the melting point.

(b) Four grams of the glycol was mixed thoroughly with 20 g. of hydrated oxalic acid and the mixture heated at 160° for four hours. At the end of this time the mixture was cooled and digested with hot water to remove the excess oxalic acid. The yellow enol (III), when recrystallized from ethanol, melted at 112–113° (corr.); yield, 3 g.

(c) A suspension of 3.5 g. of the glycol in 30 cc. of absolute ethanol was cooled to 0° and a solution of 0.23 g. of sodium in 10 cc. of absolute ethanol was added. The flask was closed with a cork and allowed to stand three hours at room temperature, with occasional shaking to prevent the suspension from settling out. The oil obtained by distilling the solvent at 30–40° *in vacuo* was dissolved in 50 cc. of ether and the solution washed with cold, dilute sulfuric acid and then with water. The residual oil obtained by driving off the ether was dissolved in the minimum amount of low-boiling petroleum ether and the solvent allowed to evaporate spontaneously. The residue consisted of yellow crystals covered with a yellow oil, which was removed by pressing the mass on a porous plate. The yellow enol after recrystallization from ethanol melted at 112.5–113° (corr.); yield, 1 g.

(7) Smith, "Organic Syntheses," **11**, 66 (1931).
(8) This compound was made by Dr. H. W. Gray.
(9) Milas and Sussman, THIS JOURNAL, **58**, 1302 (1936).
(10) Straus and Rohrbacher, *Ber.*, **54**, 69 (1921).
(11) Fuson, Weinstock and Ullyot, THIS JOURNAL, **57**, 1803 (1935).
(12) Lutz, *ibid.*, **60**, 705 (1938).

The Acetone Compound.—The glycol when treated with acetone, concentrated sulfuric acid and anhydrous magnesium sulfate according to the method of Derx[3] gave the expected acetone compound, m. p. 117–118° (corr.).

Anal. Calcd. for $C_{25}H_{30}O_4$: C, 76.09; H, 7.67. Found: C, 76.03; H, 7.56.

Oxidation

(a) **Lead Tetraacetate.**—After 3.5 g. of the glycol had been dissolved in 100 cc. of dry chloroform 4.4 g. of lead tetraacetate was added in small portions to the well-stirred solution. At the end of two hours of stirring the insoluble lead acetate was removed by filtration, the solvent distilled and the residual mesitylglyoxal converted to the hydrate. The air-dried hydrate weighed 3.2 g.; yield, 91% of the theoretical. The glyoxal was identified as the phenylhydrazone, m. p. 136.5–137.5° (corr.).[13]

(b) Treatment of the glycol with copper sulfate and pyridine according to the method of Clark and Dreger[14] gave dimesityl diketone, m. p. 120–121°.

(c) After 10 g. of selenium dioxide had been dissolved by warming in 100 cc. of wet dioxane, 10 g. of the glycol was added and the mixture was refluxed for ten hours. One-half the dioxane was removed by distillation and the residue poured into 200 cc. of water. The solid product was dissolved in the minimum amount of low-boiling petroleum ether and the solution allowed to evaporate to dryness. After being freed from unchanged glycol by hand separation, the red dimesityl triketone melted at 110.5–111°; yield, 4.5 g. It was identified by a mixed melting point with an authentic sample.

Reaction with Phenylhydrazine.—After a solution of 2 g. of the glycol, 3 cc. of phenylhydrazine and 40 cc. of ethanol had been heated for forty-eight hours in a sealed tube on the steam cone, it was concentrated to one-half its volume and placed in the ice box overnight. The precipitate amounted to 1 g. of pale yellow crystals which, after three recrystallizations from ethanol, melted at 128–129° (corr.). The compound was not identified.

Anal. Calcd. for $C_{28}H_{28}O_2N_2$: N, 6.59. Found: N, 6.79.

(13) This melting point was erroneously reported as 145–146° by Fuson and Gray, *loc. cit.*

(14) Clark and Dreger, "Organic Syntheses," Coll. Vol. I, 1932, p. 80.

Reaction with Benzoyl Chloride.—After refluxing 2 g. of the glycol with 10 cc. of benzoyl chloride for six hours the solution was cooled to 0° and poured into 10 cc. of cold methanol. The reaction mixture, after standing overnight in the ice box, was freed of the dibenzoate by filtration; the methanol and methyl benzoate were removed by distillation under reduced pressure. After the residue was dissolved in low-boiling petroleum ether and allowed to evaporate spontaneously, the yellow enol benzoate was separated by hand from the white dibenzoate of the glycol. The enol benzoate, after recrystallization from ethanol, melted at 141–142° (corr.) and was identified by a mixed melting point with an authentic sample of the benzoate of 1,4-dimesityl-1,3,4-butanetrione enol.

Anal. Calcd. for $C_{29}H_{28}O_4$: C, 79.05; H, 6.41. Found: C, 79.17; H, 6.73.

Treatment of the Glycol with Ethylmagnesium Bromide and Acetyl Chloride.—To a solution of 1.75 g. of the glycol in 40 cc. of benzene under nitrogen was added slowly with stirring an ether solution of ethylmagnesium bromide (4 moles). After refluxing the mixture for fifteen minutes, 5 cc. of acetyl chloride was added and the refluxing continued for thirty minutes. Removal of the solvents under reduced pressure left a few milligrams of the formoin (II) and an intractable oil. The formoin, after recrystallization from ethanol, melted at 187–188°; the melting point of a mixture with an authentic sample showed no depression.

Treatment of the Glycol with Sodium Acetate and Acetic Anhydride.—Two grams of the glycol was refluxed with 1 g. of anhydrous sodium acetate and 20 cc. of acetic anhydride for six hours. When the reaction mixture was decomposed with water an oil was obtained which could not be distilled or crystallized.

Summary

Five glyoxals have been reduced to the corresponding 1,2-diacylethylene glycols by the action of the binary mixture, Mg + MgI_2.

The properties of the glycol from mesitylglyoxal, 1,2-dimesitoylethylene glycol, have been described in detail.

URBANA, ILLINOIS RECEIVED SEPTEMBER 22, 1939

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, PURDUE UNIVERSITY]

Organic Syntheses with Sulfuryl Chloride[1]

BY W. W. BINKLEY WITH ED. F. DEGERING

The present investigation is a study of sulfuryl chloride in condensation reactions with the lower aliphatic alcohols and the lower dialkylamines.

Esters of Chlorosulfonic Acid.—Since there is some disagreement in the values of the physical constants of the esters of chlorosulfonic acid, we have prepared these substances again and have purified them by careful rectification.[2]

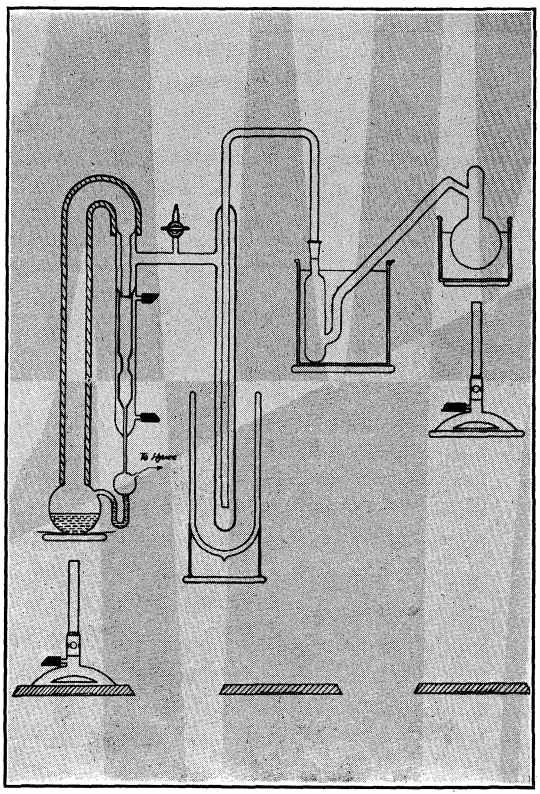


Fig. 1.

Dialkylaminesulfuryl Chlorides.—The lower dialkylaminesulfuryl chlorides may be prepared by the action of sulfuryl chloride on the amine hydrochlorides. However, these chlorides may be obtained in better yields by the careful addition of the amine to a large excess of sulfuryl chloride, followed by gentle refluxing for twenty-four hours.

(1) Abstracted from a portion of a thesis submitted by W. W. Binkley in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Chemistry, June, 1939.

(2) Binkley and Degering, THIS JOURNAL, **60**, 2810 (1938).

Experimental

Sulfuryl chloride (one-third mole) was placed in a three-necked distilling flask equipped with a mechanical stirrer, a reflux condenser, and a small dropping funnel. The flask was surrounded with an ice-bath, and the amine (one-third mole) was added very slowly to the sulfuryl chloride during vigorous agitation. The reaction mixture was warmed and poured into a flask which was connected to a reflux condenser by means of a ground-glass joint. Gentle refluxing was held for twenty-four hours. The dialkylaminesulfuryl chlorides were extracted from the reaction mixture by means of anhydrous ethyl ether and the dimethyl and diethyl compounds purified by rectification under diminished pressure. However, the di-*n*-propyl and di-*n*-butylaminesulfuryl chlorides will not withstand long heating and are better purified by repeated distillations under diminished pressure in the apparatus shown in Fig. 1. The characteristic physical constants and analyses are collected in Table I.

TABLE I

-Aminesulfuryl chloride	d^{25}_4	Ref. index 20°	B. p., °C.	Chlorine, % Calcd.	Found
Dimethyl	1.337	1.4526	66.0/10	24.74	24.7
Diethyl	1.221	1.4564	69.0/5	20.70	20.8
Di-*n*-propyl	1.195	1.4615	83.5/4	17.79	17.9
Di-*n*-butyl	1.142	1.4648	95–6/3	15.60	15.5

All the lower dialkylaminesulfuryl chlorides have an irritating effect on the skin, and the dimethylaminesulfuryl chloride is also a lachrymator. They are colorless liquids insoluble in water but dissolve in the common organic solvents. They react slowly with aqueous solutions of acids and are not attacked readily by aqueous alkali.

Esters of N,N-Dialkylamidosulfonic Acids.—These esters were obtained from the metathesis of diethylaminesulfuryl chloride and the proper sodium alkoxide, and in small yields by the action of the appropriate ester of chlorosulfonic acid on diethylamine.

Experimental

Sodium (0.1 mole), dissolved in 50 ml. of the proper alcohol, was placed in a flask equipped with a mechanical stirrer and a dropping funnel. The dialkylaminesulfuryl chloride (0.1 mole), dissolved in an equal volume of anhydrous ethyl ether, was added dropwise into the sodium alkoxide–alcohol solution during vigorous agitation. After twelve hours of stirring, the insoluble solids were separated with a centrifuge, and the esters purified by rectification under diminished pressure. The average yield was about 6 g. The characteristic physical constants and sulfur contents of only the ethyl, *n*-propyl and *n*-butyl esters are listed in Table II since the methyl ester was not obtained by this procedure.

TABLE II

Diethylamidosulfonate	d^{25}_4	Ref. index 20°	B. p., °C.	Mm.	Sulfur, % Calcd.	Found
Ethyl	1.076	1.4307	86	5	17.68	17.8
n-Propyl	1.068	1.4331	80.5	3	16.41	16.3
n-Butyl	1.046	1.4352	73.5	2.25	15.31	15.3

The alkyl N,N-diethylamidosulfonates are pleasant smelling liquids, only slightly soluble in water but quite soluble in the common organic solvents.

The methyl esters of the N,N-dialkylamidosulfonic acids were prepared by the action of methyl chlorosulfonate on the dialkylamine hydrochlorides and by the alcoholysis of the dialkylaminesulfuryl chlorides with methyl alcohol.

The dialkylamine hydrochloride (0.1 mole) was added in small quantities to methyl chlorosulfonate (0.2 mole) in a small flask. After heating this mixture for one hour on a steam cone, the excess methyl chlorosulfonate was removed with a water pump, and the heating continued for twenty-four hours. The product was purified with methyl alcohol. Yields were 4–6 g.

The dialkylaminesulfuryl chloride (0.1 mole) and 50 ml. of anhydrous methyl alcohol were allowed to reflux for forty-eight hours. The solid ester was crystallized from the reaction mixture and purified further with methyl alcohol. Yields were 2–4 g.

Analytical data and melting points of the methyl N,N-dialkylamidosulfonates are recorded in Table III.

TABLE III

Methyl ester of	M. p., °C.	Sulfur, % Calcd.	Found
N,N-Diethylamidosulfonic acid	80	19.16	19.3
N,N-Di-*n*-propylamidosulfonic acid	135	16.46	16.4
N,N-Di-*n*-butylamidosulfonic acid	117	14.25	14.2

Summary

Sulfuryl chloride has been condensed with lower aliphatic alcohols and/or lower dialkylamines to yield (1) esters of chlorosulfonic acid, (2) dialkylaminesulfuryl chlorides, and (3) N,N-dialkylamidosulfonic acids. Some of the properties of these compounds have been studied and reported.

LAFAYETTE, INDIANA RECEIVED JULY 31, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, NORTH PACIFIC COLLEGE OF OREGON]

The Identification of Organic Acids by the Use of *p*-Chlorobenzyl Pseudothiuronium Chloride

BY BARTLETT T. DEWEY AND ROBERT B. SPERRY

Donleavy,[1] Chambers and Scherer,[2] and Veibel and Lillelund[3] have suggested the use of S-benzylthiuronium chloride as a reagent for the identification of organic acids. The method has the advantages of cheapness and ease of preparation of the reagent, rapidity of the reaction, ease of recovery of the salts, and well-defined crystalline structure of the products. Some of the salts, however, are readily hydrolyzed with subsequent decomposition of the free base into products which have very unpleasant odors, and the salts do not show a satisfactory distribution of melting points.

Thirty-one salts of *p*-chlorobenzyl pseudothiourea have been prepared and their melting points determined in an attempt to find a reagent which retains the desirable features of the above method with a diminution of the undesirable ones.

Experimental.—The reagent was prepared by refluxing a mixture of 161 g. of *p*-chlorobenzyl chloride and 76 g. of thiourea in 200 cc. of ethanol for thirty minutes. The reaction mixture was cooled and the ethanol removed on a suction filter. The *p*-chlorobenzyl pseudothiuronium chloride was recrystallized from a mixture of equal parts of concentrated hydrochloric acid and water. The melting point was 197°. No evidence of polymorphism was observed similar to that recorded by Donleavy[1] and by Veibel and Lillelund[3] for S-benzylthiuronium chloride. Analysis showed 11.68% N; calculated 11.84%.

In the preparation of the salts of organic acids, the acid was carefully neutralized to phenolphthalein with sodium or potassium hydroxide. Care must be exercised that no excess of base is present, for basic solutions cause the formation of the unstable *p*-chlorobenzyl pseudothiuronium hydroxide. To the aqueous solution of the sodium or potassium salt of the acid an equivalent quantity of a cold 10% alcoholic solution of *p*-chlorobenzyl pseudothiuronium chloride was added. If the salt did not precipitate immediately, some of the solvent was removed under diminished pressure and the remaining solution was cooled in ice water. The precipitated salt was removed by filtration.

The precipitated salt was obtained in the pure state in most cases. Ethanol, ether, benzene, ligroin, carbon tetrachloride, and dioxane were tried as solvents when recrystallization was necessary. Some decomposition took place in hot alcoholic solutions. The solubility of the salts in ether, benzene, ligroin, and carbon tetrachloride was too small to make these practicable solvents. The solubility of the salts in dioxane was satisfactory. No decomposition was apparent when the solution was boiled for one hour.

(1) J. J. Donleavy, THIS JOURNAL, **58**, 1004 (1936).

(2) R. F. Chambers and P. C. Scherer, *Ind. Eng. Chem.*, **16**, 1272 (1924).

(3) S. Veibel and H. Lillelund, *Bull. soc. chim.*, (5) **5**, 1153 (1938).

By observing the following precautions, hydrolytic decompositions have been prevented: avoid excess base; keep solutions cool during mixing; avoid long contact of salt with mother liquor; recrystallize from dioxane.

The melting points of twenty-two of the salts prepared lie between 140 and 170°. There is not sufficient diversity to make these salts satisfactory derivatives of general application. Mixtures of salts with identical or nearly identical melting points produce depressions of 5 to 9°. They do offer advantages over S-benzylthiuronium salts in making certain distinctions; formate from butyrate, for example.

Analyses of the salts by the Kjeldahl method show good agreement with the calculated values.

I. ALIPHATIC SALTS

	M. p. cor., °C.		M. p. cor., °C.
Acetate	140	Oxalate	194
Butyrate	139	Palmitate	146
Caproate	143	Propionate	143
Formate	148	Succinate	167
Monochloroacetate	158	Trichloroacetate	148
Oleate	131	Valerate	142

II. AROMATIC SALTS

Benzene sulfonate	184	*m*-Iodobenzoate	154
Benzoate	155	*p*-Iodobenzoate	177
o-Bromobenzoate	165	Phthalate	166
m-Bromobenzoate	161	Salicylate	162
p-Bromobenzoate	172	Sulfosalicylate	181
o-Chlorobenzoate	159	*o*-Toluate	150
m-Chlorobenzoate	157	*m*-Toluate	151
p-Chlorobenzoate	173	*p*-Toluate	161
Cinnamate	167	*p*-Toluenesulfonate	193
o-Iodobenzoate	162		

Summary

p-Chlorobenzyl pseudothiuronium chloride has been prepared and used as the reagent in the preparation of *p*-chlorobenzyl pseudothiuronium salts of organic acids.

The melting points of the salts of thirty-one organic acids have been recorded.

Dioxane has been found to be a satisfactory solvent for the recrystallization of these salts.

PORTLAND, OREGON RECEIVED AUGUST 7, 1939

[CONTRIBUTION FROM THE WILLIAM ALBERT NOYES LABORATORY OF CHEMISTRY OF THE UNIVERSITY OF ILLINOIS]

Infrared Absorption Studies. IX. Bonding of Hydrogen in Nitrogen Compounds

BY A. M. BUSWELL, J. R. DOWNING AND W. H. RODEBUSH

The behavior of hydroxyl hydrogen has been treated at length in previous publications by ourselves and by other authors. In organic molecules the hydrogen of hydroxyl is usually sufficiently active to show bonding (association, chelation or perturbation) with oxygen, hydroxyl or other basic groups. The hydroxyl group is active in the infrared, showing a strong absorption usually in the neighborhood of 2.75 μ. When association or chelation takes place, this absorption is increased markedly and shifted to the neighborhood of 3.0 μ, the extent of the shift and the breadth of the resulting band depending to a considerable extent upon the particular molecules involved. Enolization, for example, is nearly always the result, rather than the cause, of such bonding. With a few exceptions, therefore, the behavior of hydroxyl hydrogen is easily followed by the infrared absorption and definite statements can be made as to whether the hydrogen is bonded or not.

As a matter of fact, little doubt need usually be felt as to the exceptions mentioned above. Certain alcohols show a somewhat lower hydroxyl frequency (longer wave length) than is customary. Examples are given in Figs. 1 and 2. The hydroxyl in benzoin shows an absorption at 2.87 μ under circumstances where there seems to be no question of association or chelation. This displacement must be due to the phenyl group but other factors may be involved.

One peculiar case has been discussed elsewhere. Wulf[1] and his collaborators investigated the *cis* monoxime of benzil and found the second harmonic present contrary to the predictions from the assigned structure. So far as the infrared is concerned the two compounds might be identical and both molecules show evidence of association with increasing concentration. As might have been expected, we have verified the results of Wulf that no chelation occurs.

In a previous publication[2] we have presented results of our investigation of association in the acid amides and oximes. Those compounds in which the hydrogen attached to nitrogen is acidic,

(1) G. E. Hilbert, O. R. Wulf, S. B. Hendricks and U. Liddell, THIS JOURNAL, **58**, 548 (1936).

(2) A. M. Buswell, W. H. Rodebush and M. F. Roy, *ibid.*, **60**, 2444 (1938).

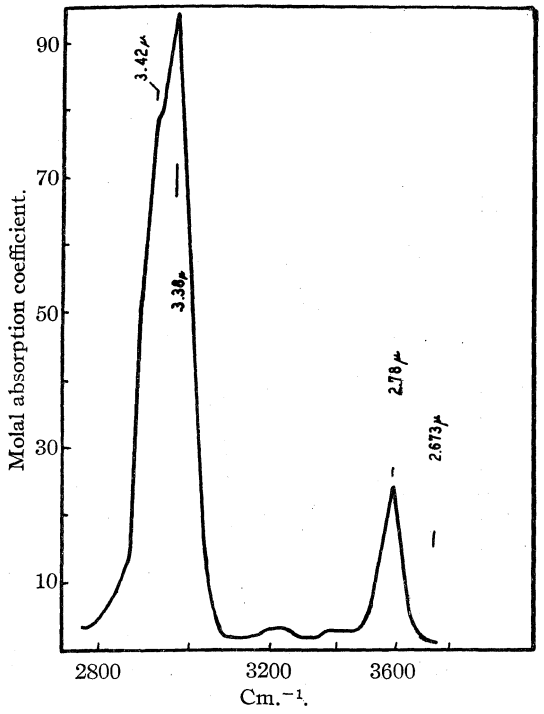


Fig. 1.—Pivaloin in carbon tetrachloride: 0.016 *M* in 1.262-cm. cell.

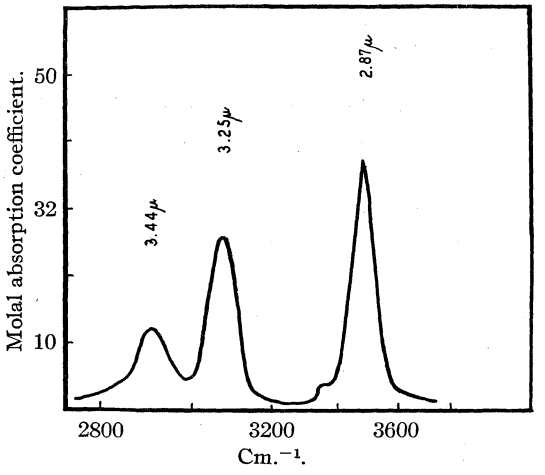


Fig. 2.—Benzoin in CCl_4: 0.016 *M* in 1.262-cm. cell.

as for example the acid amides, show a very strong tendency toward association, greater perhaps even than the alcohols. It was not possible to deduce with certainty in the case of these substances whether the intermolecular association was the result of N–H⟶N or N–H⟶O bonding and in some cases at least there was strong reason to believe that the hydrogen might have shifted to the oxygen in the process of association.

In order to settle the questions suggested above,

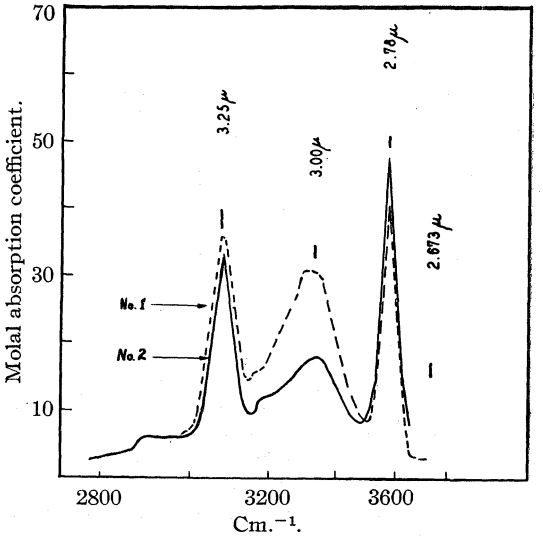


Fig. 3.—*trans* Benzil monoxime in CCl_4: (1) 0.008 *M* in 2.532-cm. cell; (2) 0.002 *M* in 10.180-cm. cell. Identical curves are obtained for the *cis* isomer.

it would be desirable to study nitrogen compounds which do not contain oxygen. Naturally the amines would be the first to be considered. These compounds, however, have proved to be very disappointing as material for infrared study. In the first place the more basic amines show very little absorption due to hydrogen. This low absorption coefficient appears to characterize the N–H bond in the more basic nitrogen compounds. One may assume therefore that the dipole moment of the N–H bond in these molecules is small. The small dipole moment may be taken as an indication that the linkage of hydrogen to nitrogen is largely covalent rather than ionic in character. Since we have assumed elsewhere[3] that the formation of a hydrogen bond involves a transformation of the bond character toward the ionic type, we may therefore anticipate little tendency toward hydrogen bond formation in the more basic types of nitrogen compounds. Even aniline shows no evidence of bonding in the pure liquid (Fig. 4). The absorption at 3.09 μ is apparently present at all concentrations. Liquid aniline has a dielectric constant about the same as liquid acetic acid. The latter substances exist largely in the form of dimers of zero dipole moment but there is no reason to suppose that aniline can form a closed dimer. There is some evidence from other sources[4] of a slight association in aniline but there

(3) W. H. Rodebush and A. M. Buswell, *J. Phys. Chem.*, **43**, 219 (1939).

(4) M. J. Copley, G. T. Zellhoefer and C. S. Marvel, THIS JOURNAL, **60**, 2666 (1938).

is certainly no strong tendency as exists for example in the alcohols.

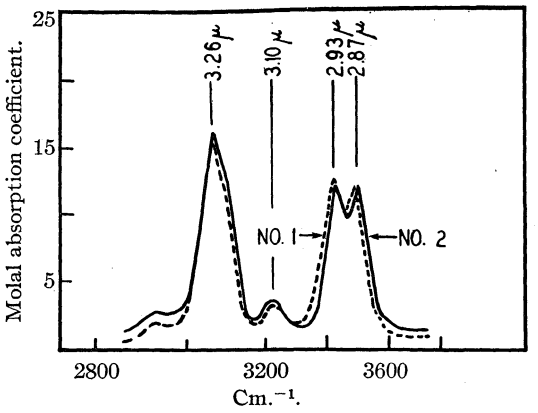


Fig. 4.—Aniline (in CCl_4): (1) 0.64 *M* in 0.158-cm. cell; (2) 0.01 *M* in 10.180-cm. cell.

One must assume that in the case of N–H the tendency toward bonding is small; the shift in frequency when a bond is found likewise small according to the rule of Venkateswaran and the increase in absorption is not comparable to that observed with O–H. Hence for all these reasons we do not expect to find a strong absorption characteristic of N–H ⟶ N or N–H ⟶ O bonding. The foregoing postulates will constitute the basis for some of our significant conclusions later on in this paper.

Since the tendency of aniline toward association appears non-existent it seemed desirable to investigate the tendency of *o*-nitroaniline toward chelation and in particular the acetanilide derivatives where an activation of the hydrogen sufficient to produce bonding might be expected. Acetanilide is itself only slightly soluble in carbon tetrachloride, as might be expected from its similarity to acetamide. *o*-Nitroacetanilide, on the other hand, is fairly soluble and shows no change in absorption with concentration. One must believe, therefore, that its tendency toward association is slight and that this is due perhaps to chelation since the N–H absorption is fairly strong and occurs at 2.96 μ (Fig. 5). One must, of course, consider the question as to whether this is N–H absorption at all. The molecule in question may enolize in two ways. Only one of these could lead to chelation but the 2.96 μ frequency is more nearly what we would expect from an OH ⟶ N bond. On the other hand, we must recognize that the rule of Venkateswaran predicts a small shift and a narrow absorption band for an inactive

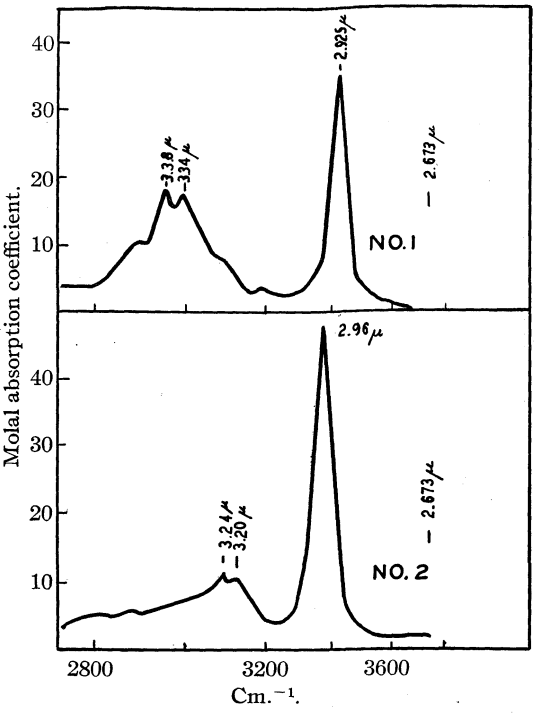


Fig. 5.—(1) 6-Methyl-2-nitroacetanilide (in CCl_4): 0.004 *M* in 5.070-cm. cell; (2) 2-nitroacetanilide (in CCl_4): 0.128 *M* in 0.158-cm. cell.

hydrogen. When the hydrogen of chloroform[5] is bonded, for example, the shift is scarcely observable but a considerable increase in absorption is noted. So here the N–H absorption of acetanilide is about 2.89 μ and the shift to 2.96 μ with increased absorption may well be taken as evidence for chelation. This conclusion seems more necessary when we consider the case of 2-nitro-6-

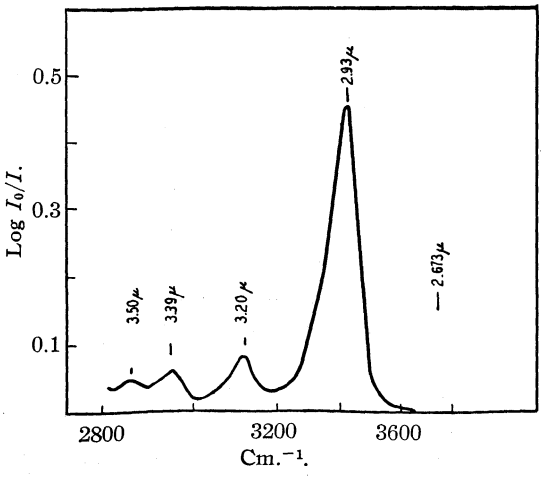


Fig. 6.

(5) A. M. Buswell, W. H. Rodebush and M. F. Roy, THIS JOURNAL, **60**, 2528 (1938).

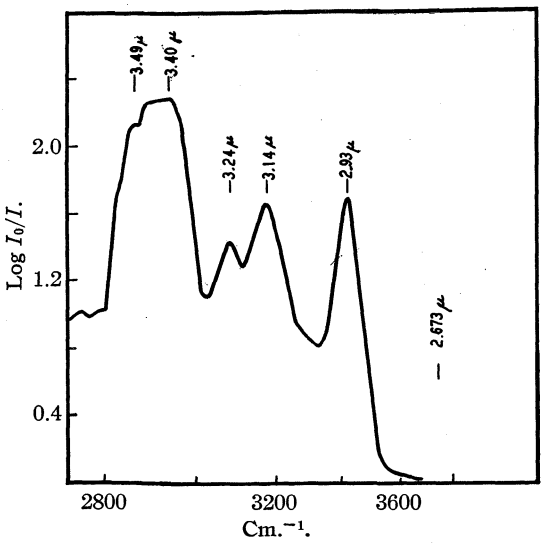


Fig. 7.—50% pyrrole–50% di-*n*-butylamine in ~0.005-cm. cell.

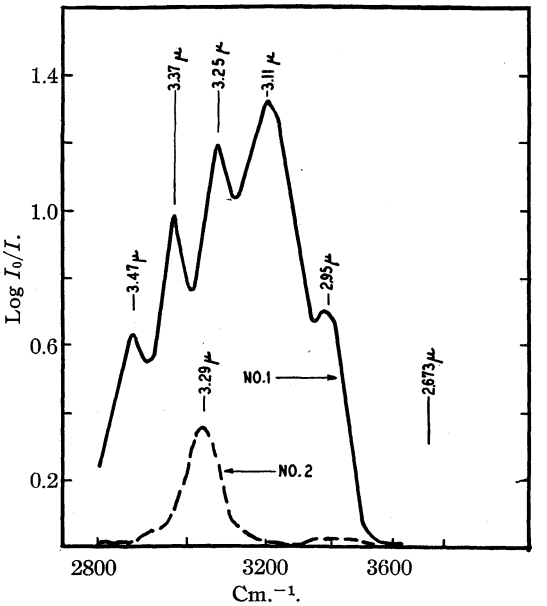


Fig. 8.—(1) 50% pyrrole–50% pyridine in ~0.005-cm. cell; (2) pyridine in ~0.005-cm. cell (half size).

methyl-acetanilide. Chaplin and Hunter[6] have collected a great deal of evidence to show that the methyl derivative is not chelated, presumably because of steric effects between the methyl group and the acetyl group. Certainly the high melting point and low solubility of the methyl derivative argue for association in the solid state into large polymers. The N–H frequency is shifted only a little from that of acetanilide and its absorption is not much stronger so that we assume there is only a slight tendency toward chelation. On the other hand, the obvious absence of association both in the solid state and in solution in the case of *o*-nitroacetanilide seems to have no other explanation than chelation. Acetanilide itself must be strongly associated in the crystalline phase since it is slightly soluble. N-Methylacetanilide shows considerable increase in solubility and in its basic properties presumably because of the disappearance of this association.

Two nitrogen compounds which contain a hydrogen of sufficient activity to form bonds are hydrogen azide and pyrrole.[7] The first of these will be discussed in detail elsewhere. Neither compound shows much tendency toward association. Liquid pyrrole has an absorption at 2.93 μ whereas in dilute solution the absorption is at 2.85 μ. With basic substances such as pyridine or dibutylamine, however, an absorption at 3.11 and 3.14 μ, respectively, can be attributed definitely to N–H ⟶ N bonding between molecules. This is characteristic of pyrrole only, however. Hydrogen azide has its fundamental frequency at 3.03 instead of 2.85 μ and the bonded frequency is shifted by a correspondingly greater amount. Each nitrogen compound therefore appears to be a law unto itself. Bonding takes place only when the hydrogen has somewhat of an acidic character and the shift in frequency is itself a variable quantity.

The Protein Problem.—In a previous publication we showed[2] that certain of the amides on association show an absorption similar to gelatine and that this absorption is characteristic of the linkage R—C(=O)—N(H)—R. If this linkage is continued it becomes identical with the peptide linkage. We suspect that the peculiar absorption noted in this type of molecule will be found characteristic of many of the proteins and will give information as to the cross linkage of the proteins through hydrogen bonding.[8] As a preliminary to this we have worked with various polypeptides, diketopiperazines, etc. The difficulties of solubility make it clear that this problem can be continued only by working with the crystalline material and we are developing the technique of measuring the absorption of thin crystalline films. Meanwhile we have prepared one or two dipeptides of sufficient solubility to obtain absorption curves. In

(6) H. O. Chaplin and L. Hunter, *J. Chem. Soc.*, 375 (1938).
(7) O. R. Wulf and U. Liddell, THIS JOURNAL, **57**, 1464 (1935).
(8) L. Pauling and C. Niemann, *ibid.*, **61**, 1860 (1939).

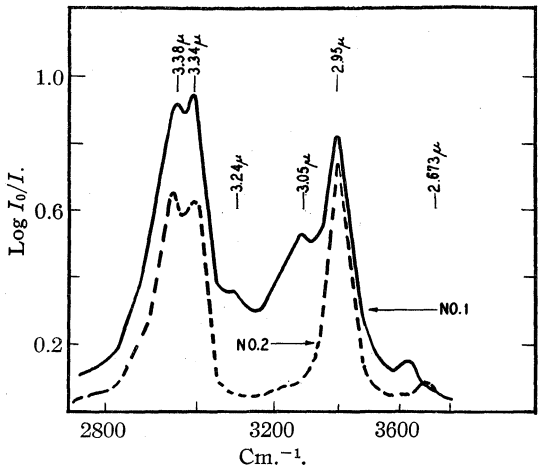
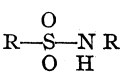
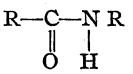


Fig. 9.—Glycylglycine ethyl ester (in CCl_4): (1) satd. soln. (~0.05 *M* in 0.640-cm. cell); (2) 0.008 *M* in 2.532-cm. cell.

Fig. 9 the curves for glycylglycine ethyl ester show, as might of course be expected, a behavior very similar to the monosubstituted amides. The most characteristic thing about this absorption is the appearance at higher concentrations of a strong absorption a little beyond 3.0 μ which by its location and intensity suggests a bonded O–H rather than N–H. Since the possibility of enolization exists in all the compounds studied so far, we were anxious to investigate a compound where enolization could not occur. A promising compound in this respect is a sulfonamide and in Fig. 10 are shown curves obtained upon the benzenesulfonamide of cyclohexylamine. It is obvious at once that this molecule shows the striking behavior on association that is characteristic of the monosubstituted amides. Organic chemists believe that there is no possibility of enolization in the group



and there is of course no indication from infrared data that such enolization occurs in the single molecule. When association occurs, however, there is the same possibility of intermolecular enolization that exists with the group



At first thought it would appear strange that the hydrogen should be transferred to the oxygen but it must be remembered that the nitrogen in this molecule is almost exactly like the nitrogen of sulfamic acid. Sulfamic acid is a strong monobasic acid and in liquid ammonia becomes a dibasic acid. One must therefore assume that the NHR group is very acidic and that the possibility of intermolecular enolization has not been eliminated. It is hoped by further study to determine the exact mechanics of association which produces this type of absorption.

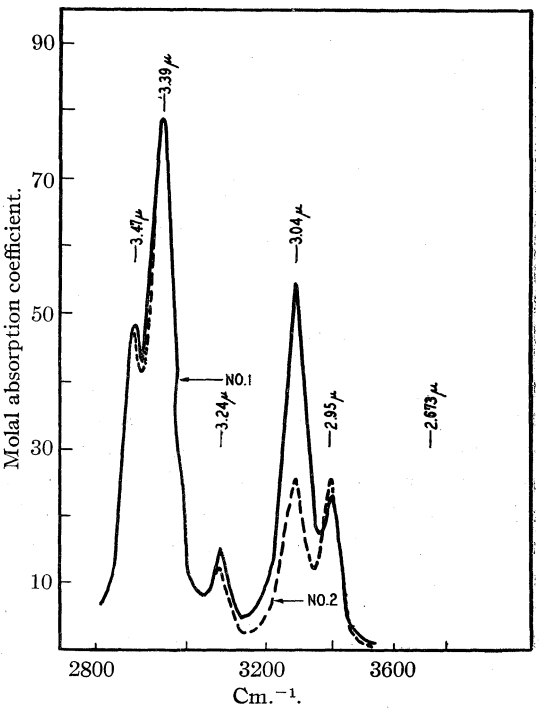


Fig. 10.—Benzenesulfonamide of cyclohexylamine (in CCl_4): (1) 0.008 *M* in 2.532-cm. cell; (2) 0.002 *M* in 10.180-cm. cell.

Summary

An extensive study of nitrogen compounds has been made in the region of the fundamental absorption of the N–H group. It is found that the absorption due to the N–H group is distinctly weaker than for the O–H group and there is a much greater variability in the characteristic frequency. Infrared absorption is a less reliable criterion for bonding of hydrogen attached to nitrogen than for hydrogen attached to oxygen. There is no positive proof of association involving the formation of N–H ⟶ N bonds but there is a strong tendency toward association if the hydrogen is somewhat acidic. The characteristic absorption produced by association of molecules containing the peptide linkage may be due to an enolized hydrogen.

URBANA, ILLINOIS RECEIVED AUGUST 31, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF BROWN UNIVERSITY]

Properties of Electrolytic Solutions. XXI. The Conductance of Tributylammonium Picrate in Ethylene Chloride at 25°

BY DARWIN J. MEAD[1] WITH RAYMOND M. FUOSS[1] AND CHARLES A. KRAUS

I. Introduction

A variety of electrolytes in non-aqueous systems have been studied, but very few examples of very weak electrolytes have been described. Kraus and Fuoss[2] measured tri-*i*-amylammonium picrate in benzene, in ethylene chloride and in a mixture of these two solvents. The purpose of this paper is to present some data of much higher precision than the earlier work, on tributylammonium picrate in ethylene chloride.

II. Apparatus, Materials and Method

The electrical equipment was the same as that described by Cox, Kraus and Fuoss.[3] Conductance cells were of the Erlenmeyer type described by Kraus and Fuoss,[2] having unplatinized electrodes. The cell constants were (I) 0.21299 and (II) 0.015357, as determined by comparison with a cell standardized using Jones and Bradshaw's[4] data on potassium chloride.

Tributylammonium picrate was prepared from tributylamine and picric acid in hot alcoholic solution. The salt was recrystallized from alcohol; m. p. 106.5°.

Ethylene chloride was purified in the usual manner.[5] Solvent conductances ($1.5–3.5 \times 10^{-11}$ mho) were negligible compared to solution conductance even for the most dilute solutions (1×10^{-7} mho).

For the more concentrated solutions the following procedure was used. A quantity (about 4 g.) of salt was weighed into the weighed conductance cell. About 20 cc. (sufficient to fill the electrode chamber) of ethylene chloride was placed in the cell. After dissolving and mixing thoroughly, the cap of the cell was lifted momentarily to release excess pressure. The cell and solution were then weighed and placed in an oil-bath held at 25.000 ± 0.002°. When temperature equilibrium had been established, the resistance of the solution was measured. To make the next solution about 10 cc. of solvent was added. This procedure was repeated until the volume of solution reached about 100 cc., which was the maximum convenient working volume of the cell. In the more dilute region, dilutions were made using a dilution pipet.[5]

Sorption effects in cell II and high resistance values in cell I prevented measurements on solutions more dilute than 10^{-4} *N*.

Polarization, as indicated by change of resistance with frequency, was noticed in the more concentrated solutions. In order to correct for polarization, all solutions were measured at 600, 1000, 2000 and 4000 cycles. Plotting observed resistance against $1/\sqrt{f}$ and extrapolating the resulting straight line gives the resistance corresponding to infinite frequency.[6] This extrapolated resistance was used in calculating the specific conductance of the solution. Figure 1, in which we have plotted the slope of the polarization curves, calculated as $(R_{1000\sim} - R_{\infty})/R_{\infty}$, against *c*, shows that this effect decreases approximately linearly with concentration.

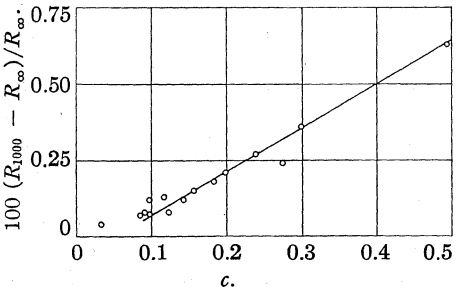


Fig. 1.—Dependence of polarization on concentration.

The solutions used were too concentrated to neglect the difference in density between the solution and the pure solvent in calculating normalities from the experimental weight concentrations. Density measurements were accordingly made at 25° with a Westphal balance. The results are given in Table I. Plotting density against moles of salt per kilogram of solvent gives the following straight line

$$d = 1.2455 - 0.022\,M \qquad (1)$$

where *d* is the density and *M* the molal concentration of the solution.

TABLE I

DENSITY OF SOLUTIONS OF TRI-BUTYLAMMONIUM PICRATE IN ETHYLENE CHLORIDE AT 25°

M	*d*
0.372	1.2373
.235	1.2404
.136	1.2425
.068	1.2442
.067	1.2443

(1) Present address: General Electric Company, Schenectady, N. Y.

(2) Kraus and Fuoss, THIS JOURNAL, **55**, 21 (1933).

(3) Cox, Kraus and Fuoss, *Trans. Faraday Soc.*, **31**, 749 (1935).

(4) Jones and Bradshaw, THIS JOURNAL, **55**, 1780 (1933).

(5) Mead, Fuoss and Kraus, *Trans. Faraday Soc.*, **32**, 594 (1936).

(6) Jones and Christian, THIS JOURNAL, **57**, 272 (1935).

III. Experimental Results and Discussion

The experimental results are summarized in Table II, in which concentration and equivalent conductance are given. Six overlapping runs

TABLE II

CONDUCTANCE OF TRI-BUTYLAMMONIUM PICRATE IN ETHYLENE CHLORIDE AT 25°

c	Λ	c	Λ
0.4945	0.16971	0.031822	0.08582
.4691	.16866	.027174	.08791
.29824	.14140	.024267	.08863
.27426	.13575	.015642	.09752
.23820	.12827	.013818	.09996
.19838	.11875	.012022	.10335
.18214	.11448	.010704	.10805
.15581	.10804	.027921	.11829
.14168	.10441	.027295	.12206
.11582	.09801	.026120	.12985
.11226	.09727	.025354	.13635
.09678	.09352	.024120	.15172
.09508	.09320	.0232326	.16835
.09036	.09236	.0227354	.17964
.06465	.08704	.0215662	.23142
.05251	.08556	.0213743	.24416
.04479	.08519	.036465	.34679
.038162	.08547	.0333864	.4725
.034022	.08603	.0317833	.6425

were made, each with independent initial weighings of salt. The conductance curve is shown in Fig. 2 where log Λ is plotted against log c. In

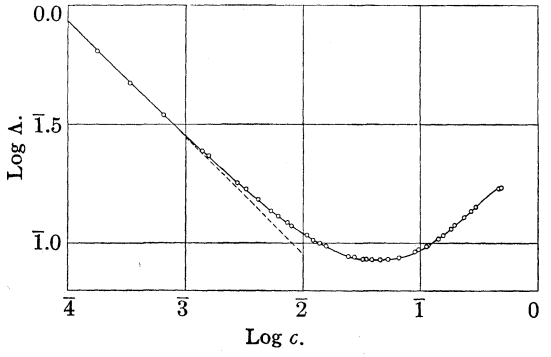


Fig. 2.—Conductance curve for tributylammonium picrate in ethylene dichloride at 25°.

the dilute region we have the usual linear dependence with slope $(-1/2)$, due to mass action.[7] The minimum, produced by triple ions,[8] occurs at $c \approx 4.5 \times 10^{-2} N$, with $\Lambda \approx 8.5 \times 10^{-2}$. In the more concentrated region the curve goes through an inflection point which suggests a maximum at still higher concentrations, due to the increased viscosity.

(7) Fuoss and Kraus, THIS JOURNAL, **55**, 476 (1933).
(8) Fuoss and Kraus, *ibid.*, **55**, 2387 (1933).

In the analysis of conductance data for strong electrolytes, F/Λ is plotted[5] against $c\Lambda f^2/F$. We have plotted the function for the more dilute points on tributylammonium picrate in Fig. 3.

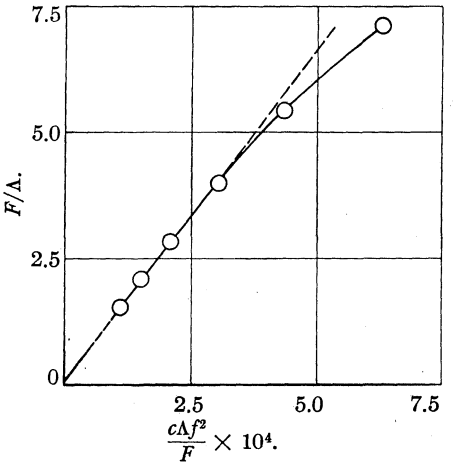


Fig. 3.—Mass action plot.

The intercept is too near zero to allow evaluation of Λ_0, because the salt is so weak. The slope $(1/K\Lambda_0^2)$ can be calculated from values of K and Λ_0 which follow. This calculated slope is shown as a dotted line in Fig. 3. It is obvious that the points approach a straight line with the proper slope as concentration decreases. The critical concentration[9] for ethylene chloride at 25° is 3.4×10^{-4}.

The triple ion function[7] $\Lambda \sqrt{c}\, g(c)$ is plotted against c in Fig. 4; it is linear up to about 0.06 N, where it begins to become concave down. The slope gives a value of 0.045 for the triple ion equilibrium constant. The intercept (8.70×10^{-3}) of the straight line is equal to $\Lambda_0 \sqrt{K}$. If we assume $\Lambda_0 = 60$ (tetrabutylammonium picrate

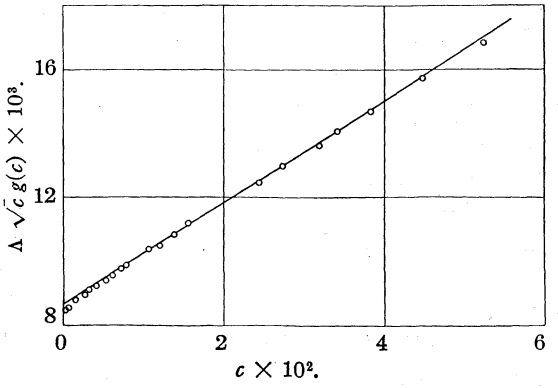


Fig. 4.—Triple ion plot.

(9) Fuoss, *ibid.*, **57**, 488 (1935).

has $\Lambda_0 = 57.40$ in ethylene chloride at 25°[4]) we find 2.10×10^{-8} for the dissociation constant of tributylammonium picrate. This value of K gives a value of 2.4 Å. for the parameter a (effective ion size),[10] which seems unexpectedly small.

(10) Fuoss and Kraus, THIS JOURNAL, **55**, 1019 (1933).

Summary

The conductance of tributylammonium picrate in ethylene chloride has been measured at 25°. The concentration range covered was 1.8×10^{-4} N to 0.5 N.

SCHENECTADY, N. Y. RECEIVED AUGUST 30, 1939

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, No. 734]

The Equilibrium and Kinetics of the Thermal Isomerization of Dichloroethylene Catalyzed by Iodine

BY REUBEN E. WOOD AND ROSCOE G. DICKINSON

The conversion of *cis*- into *trans*-cinnamic acid, catalyzed by iodine in benzene solution, has been found[1] to proceed at rates which can be interpreted in terms of iodine-atom catalysis just as can the photochemical conversion sensitized by iodine.[2] We have found that iodine similarly catalyzes the *cis–trans*-isomerization of dichloroethylene, and have measured reaction rates in the pure liquids and in various solutions. Since the isomerization comes to a measurable equilibrium, we have measured equilibrium constants as well as rates of conversion in both directions.

Materials.—The *cis*- and *trans*-dichloroethylenes were prepared by fractional distillation of mixtures of the isomers obtained from the Eastman Kodak Company. It was found desirable to carry out the distillations under carbon dioxide to avoid oxidation by air; pure *trans*-dichloroethylene was noticeably subject to air oxidation. The distillations were carried out with a five-foot (1.5-meter) column; the final products had boiling-point ranges of less than 0.1° and dielectric-constant ranges of 0.003. The boiling point of the *cis*-dichloroethylene was 59.6° at 745 mm.; the dielectric constant was 9.20 at 25°. The boiling point of the *trans*-dichloroethylene was 47.2° at 745 mm.; the dielectric constant was 2.14 at 25°. After purification the liquids were stored in flasks under an atmosphere of carbon dioxide; liquid for use was forced out by carbon dioxide when desired. The same method of storage was applied to stock solutions of the dichloroethylenes in the various solvents. The liquids thus stored were found to retain their original dielectric constants throughout the duration of the experiments (several months).

Thiophene-free benzene was fractionally crystallized, dried, and distilled.

Cyclohexane (Eastman "Practical") was shaken with fuming sulfuric acid, washed with sodium hydroxide solution, then with water, dried, and distilled. Its dielectric constant was found to be 2.013 at 25°.

Decalin (decahydronaphthalene) (Eastman "Practical") was shaken with anhydrous aluminum chloride and then treated similarly to the cyclohexane. It was found that if the treatment with fuming sulfuric acid was not sufficiently prolonged, the decalin added iodine in the subsequent experiments. The dielectric constant of the purified decalin was 2.150 at 25°.

The iodine was sublimed from potassium iodide–iodine mixture, and resublimed.

Dielectric Constant Measurement.—A method of analysis based on dielectric constant measurement was employed to determine the extent of isomerization. This measurement was made by a substitution method in which the capacitance of a cell containing the solution in question was compared with that of a variable precision condenser. The apparatus involved two oscillating circuits coupled to produce an audible heterodyne beat on a telephone receiver. A quartz crystal oscillating at 1.7 megacycles controlled the frequency of one of these circuits. The frequency-controlling part of the other circuit comprised inductance and capacitance, a part of the latter being furnished either by the cell containing the solution, or by the precision condenser. The essence of the measurement was the rapid substitution, by means of a switch, of the measuring cell for the precision condenser in this circuit; the precision condenser was adjusted so that no perceptible change in pitch of the heterodyne beat occurred when this substitution was made.

The precision condenser was a General Radio instrument; the capacitance range used was from 25 to 110 $\mu\mu$f. A calibration was made which gave corrections of the condenser readings to values linear with the capacitance.

The measuring cell was of glass and substantially of the type described by Doborzynski[3]; it was thermostated at 25°. For analytical purposes only a relation between composition of solution and precision condenser reading was necessary; nevertheless the apparatus was calibrated to give dielectric constants with the aid of a number of liquids of known dielectric constant.

Analytical Method.—The analytical problem was that of determining the fraction of dichloroethylene in the *cis*- or *trans*-form in a solution containing known amounts of solvent, iodine, and total dichloroethylene.

(1) R. G. Dickinson and H. Lotzkar, THIS JOURNAL, **59**, 472 (1937).

(2) A. Berthoud and Ch. Urech, *J. chim. phys.*, **27**, 291 (1930).

(3) D. Doborzynski, *Z. Physik*, **66**, 657 (1930).

Iodine was removed from the solution by inserting a clean, dry, helical coil of copper wire. Blank experiments showed that this method of deiodizing the solution brought about no isomerization of the dichloroethylene. After removal of iodine the solution contained a known ratio of total dichloroethylene to solvent so that a measurement of its dielectric constant enabled the fraction of dichloroethylene in each form to be determined from previous measurements on known solutions containing the same total dichloroethylene. Dielectric constants of some of these solutions are given in Table I.

TABLE I

Dielectric constants at 25° of solutions of *cis*- and *trans*-dichloroethylene undiluted (I), and diluted to ten mole per cent. of total (*cis* and *trans*) dichloroethylene in benzene (II), cyclohexane (III), and decalin (IV). Also shown are the measured dielectric constants of the solvents used.

% *cis* of total $C_2H_2Cl_2$	Dielectric constant I No solvent	II Benzene	III Cyclohexane	IV Decalin
0	2.14	2.256	2.018	2.149
20		2.347		
40	4.52	2.439		
50			2.192	2.274
60	5.93	2.530		
80	7.50	2.620		
100	9.20	2.714	2.375	2.405
Pure solvent		2.269	2.013	2.150

From the precision of the measurements it is estimated that the probable error of a determination of the ratio of *cis*- to total dichloroethylene is about 0.003 in a 10 mole per cent. solution in benzene; the error is, of course, somewhat larger in more dilute solutions.

Experimental Procedure.—Since the isomerizations were often carried out at temperatures considerably above the normal boiling points of the solutions, the reacting solutions were sealed up in thick glass ampoules. A stock solution of dichloroethylene in solvent, which had been made up by weight, was transferred to the ampoule, a weighed amount of iodine in a glass capsule was introduced, and the ampoule was sealed off. All fillings were carried out in such a way that oxygen was largely, although perhaps not completely, absent when the ampoules were sealed off. In the experiments without added solvent, this was accomplished either by filling the ampoule with carbon dioxide initially, or by boiling off considerable liquid after it had been introduced and cooling under carbon dioxide. In the rest, the solution usually was frozen down with solid carbon dioxide, and evacuated and sealed off while frozen. It was shown by blank experiments that no appreciable fractionation resulted from this treatment. In all manipulations care was exercised to keep moisture from the solutions because of the considerable effect of water on the dielectric constants.

After sealing off, the ampoules were placed in a light-tight thermostat. In some experiments this was an electric furnace with thermoregulator and in others a bath of vapor of a boiling liquid. In all rate experiments the average temperature was known to about 0.1°. At the conclusion of the experiment, the ampoule was removed from the thermostat and cooled and kept in the dark until analyzed. The duration of the experiments was sufficiently great so that errors in timing due to the initial heating and final cooling period could be shown to be negligible.

Blank experiments were carried out in which ampoules were made up and treated as usual with, however, the omission of iodine. Such ampoules were made up with the pure dichloroethylenes, and with solutions in each of the solvents. In the absence of iodine, the isomerization was negligible. Similar blanks made with iodine and solvent only gave scarcely appreciable changes in dielectric constant.

Equilibrium Experiments.—In Table II are summarized the results of experiments which were long enough so that equilibrium between the *cis* and *trans* isomers was substantially achieved. Some of these experiments were made with no added solvent; the rest were made with solutions of about ten mole per cent. dichloroethylene in benzene, cyclohexane, or decalin. The dichloroethylene at the start was always all *cis* or all *trans* as shown by the fourth column. The final composition shown in the seventh column is the percentage of the total dichloroethylene which was in the *cis* form at the end of the experiment. The equilibrium constant is given as the ratio of *trans* to *cis* isomer; its value is, of course, independent of whether concentrations or mole fractions are used. Mean values for various solvents and temperatures are given in the last column.

In the solutions studied here the values of the equilibrium constants are seen to depend relatively little either on the temperature or on the solvent. From the equation $-\Delta F^\circ = RT \ln K$, the following values for ΔF° for the conversion of *cis*- into *trans*-dichloroethylene in solution at 150° are obtained: in benzene, 750 cal.; cyclohexane, 630 cal.; decalin, 640 cal. Using the van't Hoff equation, $\frac{d \ln K}{dT} = \frac{\Delta H}{RT^2}$, and values of the equilibrium constant at different temperatures, ΔH may be calculated; the values obtained are, in benzene, 1200 cal.; cyclohexane, 1200 cal.; decalin, 600 cal. Since the probable error of these is at least 200 or 300 calories, it is not certain that the difference between the value for decalin and that for the other solvents is significant.

Values for the equilibrium constant for this reaction in the gaseous state have been given[4,5,6] which are of the same general magnitude as those found here.

The iodine-catalyzed conversion of *cis*- into *trans*-cinnamic acid has been found,[1] in dilute

(4) E. Ebert and R. Büll, *Z. physik. Chem.*, **A152**, 451 (1931).
(5) A. R. Olson and W. Maroney, THIS JOURNAL, **56**, 1322 (1934).
(6) W. Maroney, *ibid.*, **57**, 2397 (1935).

TABLE II

EQUILIBRIUM MEASUREMENTS

Expt.	Solvent	Temp., °C.	Original isomer	Duration, hr.	Mole % iodine in soln.	Mole % *cis* in $C_2H_2Cl_2$ at end	Equil. const., $K = (T)/(C)$	Mean K
7	None	150	*cis*	495	0.32	70.8	0.412	
8	None	150	*cis*	239	.71	71.1	.406	
24	None	150	*trans*	281	.36	70.6	.417	0.412
42	Benzene	150	*cis*	252	.40	71.1	.406	
41	Benzene	150	*trans*	252	.30	70.7	.414	.410
50	Benzene	185	*cis*	21	.43	68.6	.458	
57	Benzene	185	*cis*	5.8	.60	70.0	.447*	
55	Benzene	185	*trans*	7.5	.59	68.1	.453*	
51	Benzene	185	*trans*	21	.43	70.1	.427	
58	Benzene	185	*trans*	21.5	.57	68.5	.460	.455
67	Cyclohexane	150	*cis*	92	1.1	67.6	.479	
60	Cyclohexane	150	*cis*	308	0.67	67.3	.486	
68	Cyclohexane	150	*trans*	92	1.3	68.2	.467	
61	Cyclohexane	150	*trans*	308	0.77	69.0	.449	.470
71	Cyclohexane	185	*cis*	7	.64	66.3	.515*	
72	Cyclohexane	185	*trans*	7	.60	63.9	.531*	.523
96	Decalin	150	*cis*	116	1.33	68.1	.468	
95	Decalin	150	*trans*	100	0.84	68.1	.468	.468
100	Decalin	186	*cis*	10	1.36	66.8	.497	
105	Decalin	186	*cis*	10	1.17	67.3	.486	
101	Decalin	186	*trans*	10	1.31	66.5	.503	.495 ±0.010

* Since the starred experiments were not quite long enough, a small correction of the observed final composition to that at infinite time was made in computing the corresponding K; this required a rough knowledge of the rate constants.

solution in benzene, to proceed at rates which are first order with respect to cinnamic acid and half order with respect to iodine. The assumption of similar kinetics for the dichloroethylenes is found to be in agreement with the data provided that account is taken of the occurrence of reverse reaction. If k_1 and k_2 are specific rate constants for the reactions *cis*-$C_2H_2Cl_2 \underset{2}{\overset{1}{\rightleftarrows}}$ *trans*-$C_2H_2Cl_2$, and if $K = (trans)_{eq}/(cis)_{eq}$ be the equilibrium constant, then $K = k_1/k_2$. The assumption that each reaction is of first order with respect to the reacting isomer and of half order with respect to iodine leads to the integrated expression

$$k_1 = -\frac{K}{t(I_2)^{1/2}(K+1)} \ln \frac{(K+1)\alpha - 1}{K} \qquad (1)$$

for experiments in which the initial dichloroethylene is all *cis*, and to

$$k_1 = -\frac{K}{t(I_2)^{1/2}(K+1)} \ln [1 - (K+1)\alpha] \qquad (2)$$

for experiments in which the initial dichloroethylene is all *trans*. In both of these equations α is the fraction of dichloroethylene in the *cis* form at the time t.

The results of determinations of k_1 are given in Table III. Values of the equilibrium constant needed were taken from the results of Table II calculated to the desired temperature by means of the van't Hoff equation. The numerical values of k_1 in Table III were obtained expressing t in hours and (I_2) as mole fraction of I_2 in the reaction mixture.[7]

Inspection of the values of k_1 shows that these exhibit satisfactorily constant values in a given solvent at a given temperature. In each solvent, the iodine concentration was varied more than 10-fold (22-fold in the case of decalin). In Table III all experiments with added solvent had a total dichloroethylene mole fraction of about 0.1 except experiments 35 and 46. In these the mole fractions were made 0.2 and 0.01, respectively, without producing any significant change in rate constant. Indeed the experiments without added solvent gave values not much different from the others at the same temperature. It may be further noticed that the values found for k_1 are not dependent on which isomer was originally present; this is nearly true even when no added solvent was present so that the medium was largely different in the two cases. In fact the values of k_1 at a given temperature differ by less than 25% in the various media examined.

(7) If the value of K as well as the relation $K = k_1/k_2$ be assumed, it becomes arbitrary whether a given experiment be regarded as a determination of k_1 or of k_2.

TABLE III

RATE MEASUREMENTS

Expt.	Solvent	Temp., °C.	Original isomer	Mole % iodine in soln.	Duration, hr.	Mole % *cis* in $C_2H_2Cl_2$ at end	*K* assumed	k_1 hr.$^{-1}$
9	None	150.0	*cis*	0.1103	31.2	87.6	0.412	0.156
10	None	150.0	*cis*	.2718	30.4	83.3	.412	.157
11	None	150.0	*cis*	.722	18.6	83.3	.412	.158
12	None	150.0	*cis*	1.457	13.0	83.2	.412	.160
19	None	149.7	*trans*	0.686	22.8	44.0	.412	.150
23	None	149.7	*trans*	.2704	24.8	34.3	.412	.150
26	None	149.7	*trans*	.1261	53.2	44.1	.412	.151
35	Benzene	149.6	*cis* 20%	.343	18.0	87.5	.410	.156
47	Benzene	150.0	*cis*	.944	17.5	82.7	.410	.154
48	Benzene	150.0	*cis*	.1104	47.2	83.9	.410	.149
44	Benzene	149.5	*trans*	.1403	40.0	37.6	.410	.148
45	Benzene	149.5	*trans*	1.262	20.8	49.0	.410	.147
46	Benzene	150.0	*trans* 1.09%	0.482	37.5	52	.410	.15
52	Benzene	140.5	*trans*	.2237	91.0	44.4	.396	.0637
56	Benzene	140.5	*trans*	.839	42.6	42.0	.396	.0643
53	Benzene	158.9	*trans*	.801	7.3	35.8	.422	.323
54	Benzene	159.5	*trans*	.0854	28.3	42.8	.423	.339
70	Cyclohexane	150.0	*cis*	.521	22.0	80.5	.470	.191
69	Cyclohexane	150.0	*trans*	.729	21.1	42.9	.470	.177
62	Cyclohexane	150.7	*trans*	1.127	21.0	49.1	.471	.188
63	Cyclohexane	150.7	*trans*	0.2503	21.2	31.4	.471	.187
73	Cyclohexane	159.2	*trans*	.591	8.3	35.8	.486	.389
74	Cyclohexane	159.2	*trans*	1.173	8.3	44.0	.486	.387
99	Decalin	131.1	*trans*	0.812	69.9	31.5	.454	.0303
102	Decalin	131.1	*trans*	1.540	69.9	39.2	.454	.0304
94	Decalin	150.2	*trans*	0.947	18.9	41.5	.468	.163
97	Decalin	150.4	*trans*	.0690	28.8	22.0	.468	.165
104	Decalin	159.9	*cis*	.885	8.6	80.4	.475	.376
98	Decalin	159.4	*trans*	.1427	25.2	43.5	.475	.344
103	Decalin	159.9	*trans*	1.027	8.6	43.5	.475	.378

The variation of the rate constant k_1 with the temperature is shown in Fig. 1 in which ln k_1 is plotted against $1/T \times 10^3$ for each of the solvents. From the slopes of these lines, the values of Q_1 in the Arrhenius equation $\mathrm{d} \ln k_1/\mathrm{d}T = Q_1/RT^2$ can be calculated. The values so obtained are, for benzene solutions 31,200 cal., for cyclohexane solutions 30,800 cal., for decalin solutions 30,200 cal. Values of k_2, the specific rate constant for the *trans* to *cis* reaction, may be obtained from the relation $k_2 = k_1/K$. Values of Q_2 may be obtained from the relation $Q_1 - Q_2 = \Delta H$; those values for Q_2 are 30,000, 29,600, and 29,600 cal., respectively. The probable experimental error is such that it is not certain whether the apparent changes in Q_1 and Q_2 with solvent are real.

In Table IV are given, for different solvents, average values at 150° of the equilibrium constant, and of the rate constants k_1 and k_2 for the *cis* to *trans* reaction and its reverse. It is desirable also to compute rate constants, k_1 and k_2, with (I_2) expressed as a volume concentration instead of a mole fraction. It is easy to show that $k' = kv^{1/2}$ where v is the volume of solution containing a total of one mole of substance. Estimated values of v at 150° for pure dichloroethylene, and for 10 mole per cent. solutions in the various solvents are given in the fifth column. These values were obtained from measurements on the pure substances at lower temperatures on the assumption of additivity of volumes and constancy of thermal expansion coefficient with temperature; their uncertainty probably does

TABLE IV

CONSTANTS IN VARIOUS SOLVENTS AT 150° COMPARING VALUES COMPUTED WITH (I_2) EXPRESSED IN MOLE FRACTIONS WITH THOSE IN VOLUME CONCENTRATIONS

Solvent	*K*	k_1 $\times 10^7$ sec.$^{-1}$	k_2 $\times 10^7$ sec.$^{-1}$	*v*, cc.	k_1' $\times 10^5$ moles$^{-1/2}$ cc.$^{1/2}$ sec.$^{-1}$	k_2' $\times 10^5$ moles$^{-1/2}$ cc.$^{1/2}$ sec.$^{-1}$
None	0.412	430	1044	92	41	100
Benzene	.410	425	1036	104	43	106
Cyclohexane	.470	497	1058	123	55	118
Decalin	.468	445	950	177	59	126

not affect the k's by more than 2%. It is interesting to notice that, in passing from one solvent to another, the k's in which (I_2) is expressed as a mole fraction are much more constant than the k's in which (I_2) is expressed as a volume concentration.

Discussion.—Just as was the case with the isomerization of cinnamic acid, the kinetics of the dichloroethylene isomerization can be accounted for in terms of iodine atom catalysis, and indeed in terms of the same mechanism as discussed in the case of cinnamic acid. In this mechanism atomic iodine is assumed to be in thermal equilibrium with molecular iodine so that proportionality of the rate[1] with the square root of the iodine concentration results.

The same proportionality would exist if the catalyst were iodine ions in equilibrium with molecular iodine, *e. g.*, $I_2 \rightleftarrows I^+ + I^-$. Evidence that an ionic mechanism is, however, not involved here has been obtained somewhat unexpectedly. It was originally planned to measure the dielectric constants of the reacted solutions without first removing iodine. When this was attempted with solutions of iodine in pure *cis*-dichloroethylene the electric oscillations in the dielectric constant apparatus were feeble, and with the more concentrated iodine solutions, entirely absent. On the assumption that this quenching of oscillation resulted from conductance of the solution some approximate conductance measurements were made. It was found that *cis*-dichloroethylene containing 0.02 g. per cc. of iodine had a specific conductance of 3×10^{-6} mho; this was 100 times the conductance of the dichloroethylene alone, and over 1000 times the conductance of a similar solution of iodine in benzene. Since the mobility of iodine ion in dichloroethylene could hardly be of a different order of magnitude from that in benzene, its concentration in benzene must be comparatively low; nevertheless, the specific rate constants are little different in dichloroethylene and benzene. An atomic rather than ionic catalysis accordingly is indicated here.

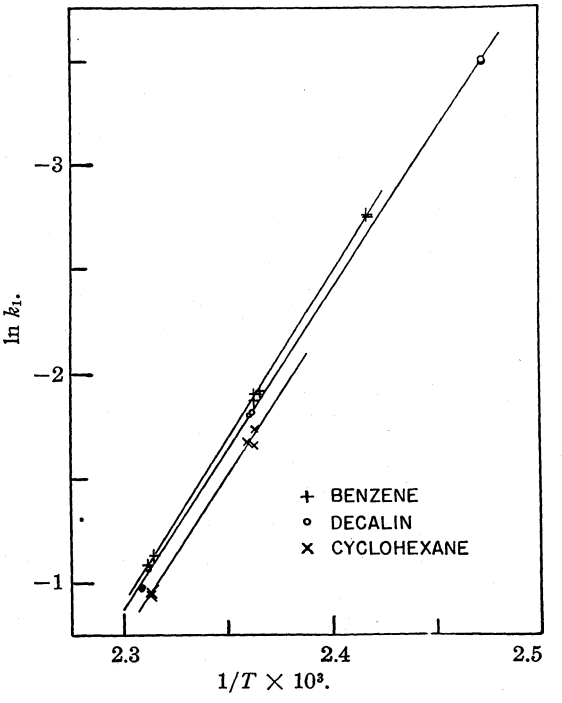


Fig. 1.—Dependence of rate constant on temperature: +, benzene; ○, decalin; ×, cyclohexane.

Summary

Dielectric constants of various liquid mixtures of *cis*- and *trans*-dichloroethylene and of their solutions in benzene, cyclohexane, and decahydronaphthalene have been measured.

Using iodine as a catalyst, equilibria between the *cis* and *trans* isomers have been established and measured in the pure liquids and in the solutions at various temperatures.

Rates of isomerization in the various media have been measured starting with each isomer. Neither the activation energies nor the actual rates vary much from one medium to another of those examined. The rate constants vary somewhat less from solvent to solvent when computed with the iodine expressed as a mole fraction than when computed with it expressed as a volume concentration.

The kinetics are compatible with an iodine-atom catalysis. Evidence against an ionic catalysis is mentioned.

PASADENA, CALIF. RECEIVED SEPTEMBER 18, 1939

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, NO. 736]

The Molecular Structures of Sulfuryl Fluoride and Thiophosphoryl Fluoride

BY D. P. STEVENSON[1] AND HORACE RUSSELL, JR.

The relations between bond length and bond character in molecules containing bonds of the type sometimes called semipolar are not well understood. Among the compounds of phosphorus and sulfur there are a great number of such molecules, some of which have been investigated recently.[2,3,4] In this paper we give the results of an electron diffraction investigation of the structures of two such molecules containing fluorine atoms as well as semipolar double bonds.

Experimental.—The electron diffraction apparatus used in this investigation has been described by Brockway.[5] The camera distance was 10.84 cm., and the wave length of the electrons, determined in the usual fashion,[5] was 0.0611 Å.

Fifty cc. (S. T. P.) of pure thiophosphoryl fluoride was given to us by Professor H. S. Booth and Miss M. C. Cassidy of Western Reserve University, who have described the preparation and purification of the substance.[6] The sample was transferred to a bulb of about 150 cc. capacity which could be attached to the apparatus by means of a ground joint.

The preparation and purity of the sulfuryl fluoride used will be described in a separate paper on the Raman spectrum of this compound.[7] The pressure of the gas in the sample bulb was approximately 200 mm.

Interpretation.—Both the radial distribution method[8] and the correlation method[9] were used in interpreting the electron diffraction photographs. The modified radial distribution formula

$$D(l) = \sum_{n} C_n \frac{\sin s_n l}{s_n l} \quad C_n = f(I_n, s_n) \qquad (1)$$

has been discussed by Schomaker.[10]

It has been remarked in the literature[9,11] that the coefficients Z_iZ_j in the simplified theoretical scattering formula ordinarily used

$$I(s) = \sum\sum Z_iZ_j \frac{\sin l_{ij}s}{l_{ij}s} \qquad (2)$$

are not completely satisfactory when the atoms i and j are members of different rows of the periodic system, and that the more exact expression

$$I(s) = \sum\sum (Z_i - f_i)(Z_j - f_j) \frac{\sin l_{ij}s}{l_{ij}s} \qquad (3)$$

should be used. Since the corresponding coefficients in (2) and (3) differ by as much as 30% when $4 \leqslant s \leqslant 10$ for sulfuryl fluoride and thiophosphoryl fluoride, it was thought that it might be necessary to use (3) rather than (2) in the application of the correlation method to the interpretation of the photographs of these molecules. However, curves calculated according to (2) and (3) were found to be indistinguishable qualitatively and to have differences in the position of their maxima and minima of about 1% within the range of s indicated above. Since for $s \leqslant 12$ the coefficients of (2) and (3) are the same within 2%, it is thus satisfactory to use (2) rather than (3) in interpreting the photographs of sulfuryl fluoride and thiophosphoryl fluoride when $s > 12$. When $s < 12$ the photographs were compared with curves calculated according to (3).

Inasmuch as the two molecules under consideration are rather rigid, it was thought unnecessary to include a temperature factor[5] in the coefficients of the scattering formulas.

Sulfuryl Fluoride.—The photographs of this molecule show seven measurable maxima, six measurable minima, and two shelf-like features. The first shelf, designated a, is a shoulder on the inner side of the first maximum. The second shelf, feature b, is on the outside of the third maximum. The intensities of the maxima decrease uniformly from the first through the seventh. The only irregularity in the decreasing depth of the minima is that the fifth minimum is shallower than either

(1) National Research Fellow.

(2) L. O. Brockway and J. Y. Beach, THIS JOURNAL, **60**, 1836 (1938).

(3) K. J. Palmer, *ibid.*, **60**, 2360 (1938).

(4) J. Y. Beach and D. P. Stevenson, *J. Chem. Phys.*, **6**, 75 (1938).

(5) L. O. Brockway, *Rev. Mod. Phys.*, **8**, 231 (1936).

(6) H. S. Booth and M. C. Cassidy, Boston, A. C. S. meeting, September, 1939.

(7) Horace Russell, Jr., and D. M. Yost, to be published.

(8) L. Pauling and L. O. Brockway, THIS JOURNAL, **57**, 2684 (1935).

(9) L. Pauling and L. O. Brockway, *J. Chem. Phys.*, **2**, 867 (1934).

(10) V. Schomaker, Baltimore, A. C. S. meeting, April, 1939.

(11) M. H. Pirenne, *J. Chem. Phys.*, **7**, 144 (1939).

the fourth or sixth minimum. The visually estimated relative intensities and the measured values of $s\left(s_0 = \frac{4\pi}{\lambda}\sin\frac{\vartheta}{2}\right)$ of the maxima and minima are given in columns 3 and 5 of Table I.

TABLE I

Max.	Min.	I_0	C_n	s_0	s^a	s^a/s_0	s^b	s^b/s_0
a		5	2	3.43	...	....	...	....
1		10	6	5.81	5.54	(0.954)[c]	5.57	(0.959)[c]
	2	−9	−7	7.22	7.24	1.003	7.22	1.000
2		8	8	8.80	8.92	1.014	8.92	1.014
b		4	5	11.21	...	....	...	....
	3	−6	−8	12.26	12.09	0.986	12.03	0.981
3		6	8	13.92	13.89	0.998	13.72	0.986
	4	−4	−6	15.41	15.48	1.005	15.42	1.001
4		4	6	16.77	16.94	1.010	16.91	1.008
	5	−2	−3	17.82	18.12	1.017	18.00	1.010
5		3	5	19.10	19.10	1.000	19.01	0.995
	6	−3	−6	20.51	20.49	0.999	20.50	1.000
6		2	4	22.09	21.89	.991	21.83	0.988
	7	−1	−2	23.25	23.22	.999	23.21	.998
7		1	2	25.02	24.55	(.981)[c]	24.49	(.979)[c]
		Average of 11 features				1.002 ± 0.007		0.998 ± 0.008

[a] From curve for model with S − F/S − O = 1.56/1.43. F − O/S − O = 2.36/1.43. [b] From curve for model with S − F/S − O = 1.56/1.43, F − O/S − O = 2.38/1.43. [c] Omitted from average.

The radial distribution function (1), calculated with the coefficients C_n of column 4, Table I, is shown in Fig. 1, curve B. The first maximum at 1.48 Å. is an unresolved average of the sulfur–oxygen and the sulfur–fluorine distances. If one assumes the sulfur–oxygen distance to be 1.43 Å., the distance found in sulfuryl chloride,[4] one may estimate the sulfur–fluorine distance to be 1.52 Å. Since the term involving the fluorine–oxygen distance is four times as important in the scattering formula as the terms involving the fluorine–fluorine and oxygen–oxygen distances, the second peak at 2.37 Å. probably corresponds closely to the fluorine–oxygen distance.

If one assumes, as has been found to be the case for sulfuryl chloride,[4] that the sulfuryl fluoride molecule is a bisphenoid with symmetry C_{2v}, there are three parameters which determine the form of the intensity curves. These may be conveniently taken as ρ_1, the ratio of the sulfur–fluorine to sulfur–oxygen distance, ρ_2, the ratio of the fluorine–oxygen to sulfur–oxygen distance, and β, the fluorine–sulfur–fluorine angle.

The radial distribution function indicates that the value of ρ_1 is in the vicinity of 1.52/1.43 and the value of ρ_2 is near 2.37/1.43. Eighteen curves were calculated,[2] for models with the parameters ρ_1 and ρ_2 in the ranges $1.48/1.43 \leqslant \rho_1 \leqslant 1.60/1.43$ and $2.32/1.43 \leqslant \rho_2 \leqslant 2.44/1.43$.

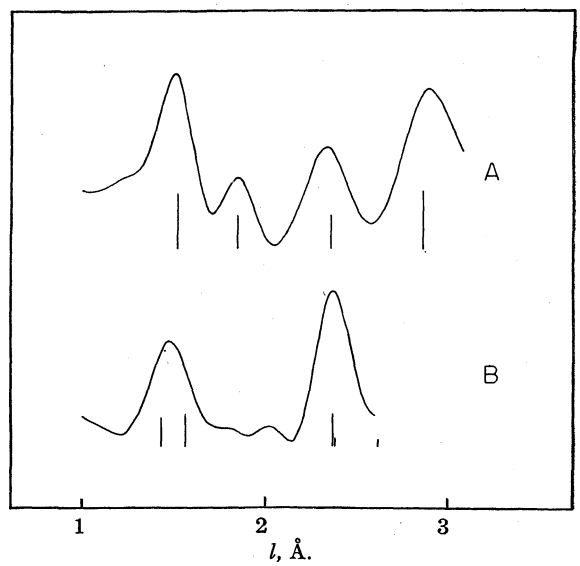


Fig. 1.—Radial distribution function, $D(l)$ *vs.* l: Curve A, thiophosphoryl fluoride; Curve B, sulfuryl fluoride. The vertical lines represent the internuclear distances found.

The parameter β was assumed to be 100° for all these curves. This is roughly the value found for the chlorine–sulfur–chlorine angle in sulfuryl and thionyl chlorides, and the qualitative and quantitative character of the theoretical curves is quite insensitive to variations in the value of this parameter. Some of these curves are shown in Fig. 2. Of these curves only the two with ρ_1 = 1.56/1.43 and ρ_2 = 2.36/1.43 or 2.38/1.43 are in agreement with the appearance of the photographs. Curves were then calculated for models with these values of ρ_1 and ρ_2 with β = 90 and 110°. The curves with β = 90° are unsatisfactory because feature b disappears while for β = 110° the fifth maximum is too low. This is illustrated by curves E_1 and E_2 of Fig. 2.

Quantitative comparison of the photographs with the curves for ρ_1 = 1.56/1.43, β = 100° and ρ_2 = 2.36/1.43 and 2.38/1.43 is made in Table I, columns 7 and 9. The agreement is quite satisfactory. The final results for the structure of sulfuryl fluoride are

S–F = 1.56 ± 0.02 Å.	∠F–S–O = 105 ± 2°
S–O = 1.43 ± 0.02 Å.	∠F–S–F = 100 ± 8°
F–O = 2.37 ± 0.02 Å.	∠O–S–O = 130 ± 10°

Thiophosphoryl Fluoride.—The photographs of thiophosphoryl fluoride were exceptionally clear, showing nine rings. The first and third maxima appear weaker than the second maximum, and the fifth maximum is weaker than the

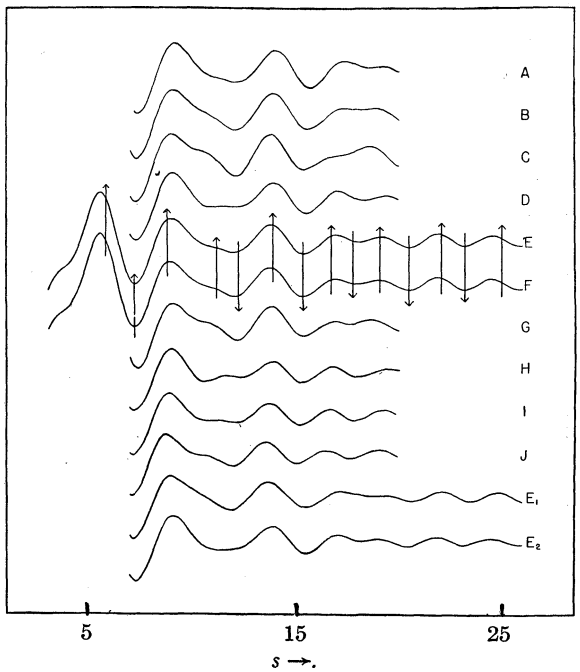


Fig. 2.—Theoretical scattering curves for sulfuryl fluoride:

Curve A, ρ_1 = 1.52/1.43; ρ_2 =	2.32/1.43; and β =	100°
Curve B,	2.36/1.43	100°
Curve C,	2.40/1.43	100°
Curve D, ρ_1 = 1.56/1.43	2.32/1.43	100°
Curve E,	2.36/1.43	100°
Curve F,	2.38/1.43	100°
Curve G,	2.40/1.43	100°
Curve H, ρ_1 = 1.60/1.43	2.32/1.43	100°
Curve I,	2.36/1.43	100°
Curve J,	2.40/1.43	100°
Curve E_1, ρ_1 = 1.56/1.43	2.36/1.43	110°
Curve E_2,	2.36/1.43	90°

fourth and sixth maxima. The fourth minimum is deeper than the third minimum and the sixth minimum is slightly deeper than the fifth minimum. The visually estimated relative intensities are given in Table II along with the values of $s_{obs.}$.

The radial distribution function calculated according to (1), with the coefficients C_n, given in column 4 of Table II, has four maxima (see curve A, Fig. 1) at 1.50, 1.85, 2.33, and 2.90 Å. These correspond to the four distances, phosphorus–fluorine, phosphorus–sulfur, fluorine–fluorine and fluorine–sulfur. The fluorine–phosphorus–fluorine and fluorine–phosphorus–sulfur angles computed from these distances are 100 and 118°, respectively.

If this molecule has the symmetry C_{3v}, two structural parameters determine the shapes of

TABLE II

Max.	Min.	I_0	C_n	s_0	s_c[a]	s_{c/s_0}
1		5	2	2.95	..	..
	2	−9	−5	3.62	..	..
2		10	6	5.06	4.84	(0.957)[b]
	3	−2	−2	5.84	6.28	(1.075)
3		3	3	7.01	6.89	(0.983)
	4	−8	−9	7.67	7.71	1.005
4		8	9	9.17	9.09	0.991
	5	−5	−7	10.15	10.34	1.019
5		4	6	11.46	11.35	0.990
	6	−6	−9	12.36	12.42	1.005
6		6	10	13.89	13.73	0.988
	7	−4	−7	15.57	15.70	1.008
7		4	7	17.67	17.65	0.999
	8	−3	−5	19.36	19.13	0.988
8		3	5	21.73	22.00	1.013
	9	−1	−2	23.25	23.45	1.009
9		1	2	25.19	24.90	0.988

Average of 12 features 1.001 ± 0.010

[a] From model with $\frac{P - F}{P - S} = \frac{1.52}{1.85}$ and ∠F–P–F = 99°.

[b] Values in parentheses omitted from average because of unreliability of measurements.

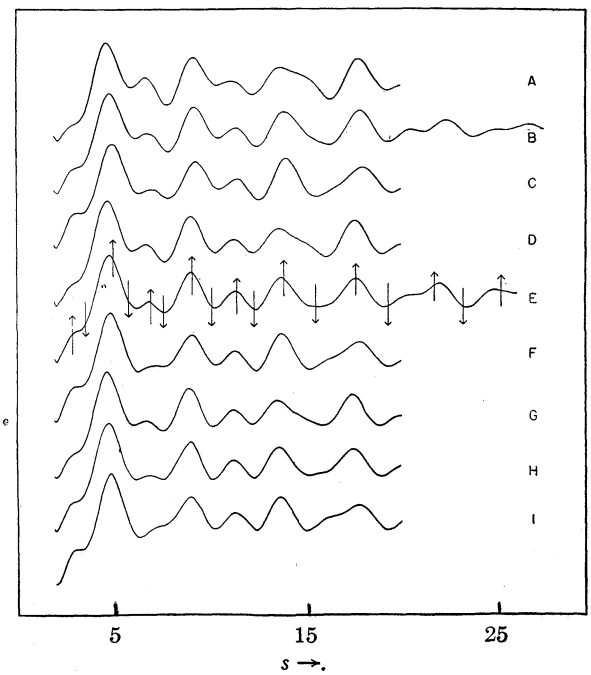


Fig. 3.—Theoretical scattering curves for thiophosphoryl fluoride.

Curve A, ρ = 1.48/1.85 α =	96°
Curve B,	99°
Curve C,	102°
Curve D, ρ = 1.52/1.85	96°
Curve E,	99°
Curve F,	102°
Curve G, ρ = 1.54/1.85	96°
Curve H,	99°
Curve I,	102°

TABLE III

	P–F	P–Cl	P–Y	X–P–X	Reference
PF_3	1.52 ± 0.02 Å.			104 ± 4°	12 and 8
OPF_3	1.52 ± 0.02		1.56 ± 0.02 Å.	107 ± 2°	2
OPF_2Cl	1.51 ± 0.02	2.01 ± 0.02 Å.	1.55 ± 0.03	106 ± 3°	2
$OPFCl_2$	1.50 ± 0.03	2.02 ± 0.02	1.54 ± 0.03	106 ± 3°	2
$OPCl_3$	....	2.02 ± 0.02	(1.58)[a]	106 ± 1°	2
PCl_3	....	2.00 ± 0.02		101 ± 2°	12 and 8
SPF_3	1.51 ± 0.02		1.85 ± 0.02	99.5 ± 2°	This research
$SPCl_3$		2.01 ± 0.02	1.94 ± 0.03	107 ± 3°	4

[a] This distance was assumed.

appropriate models and the form of the theoretical intensity curves. These parameters are conveniently taken as the ratio ρ of the phosphorus–fluorine to the phosphorus–sulfur distance, and α the fluorine–phosphorus–fluorine angle.

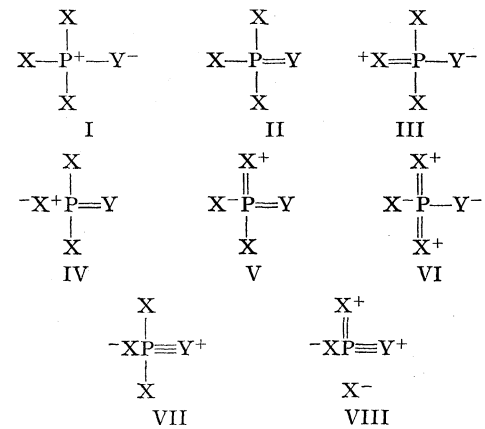
Curves were calculated for eighteen models, in which α was varied from 90–108° and ρ was varied from 1.54/1.85 to 1.46/1.85. A selection of these curves is shown in Fig. 3. All models with $96° \geqslant \alpha \geqslant 102°$ could be eliminated because the appearance of the third maximum on the curves is not that of the photographs and they show an asymmetry on either the outer side of the sixth maximum or the inner side of the seventh maximum while on the photographs these maxima appear quite symmetrical. The model with $\alpha = 99°$ and $\rho = 1.54/1.85$ is unsatisfactory because its fourth minimum is not deeper than its third and the sixth minimum is not deeper than the fifth. The curves for models with $\rho = 1.50/1.85$ and $\alpha = 99°$ show a shelf on the inner side of the ninth maximum and are unsatisfactory for this reason.

The curve calculated for the model $\rho = 1.52/1.85$ and $\alpha = 99°$ is in good qualitative agreement with the photographs. The quantitative comparison of this model with the photographs is shown in Table II. The final results for the structure of thiophosphoryl fluoride are P–F = 1.51 ± 0.02 Å., P–S = 1.85 ± 0.02 Å., ∠ F–P–F = 99.5 ± 2°, and ∠ F–P–S = 118 ± 2°.

Discussion.—Table III presents a summary of the structures found for molecules of the type X_3PY.

The distances predicted by the covalent radius table[13] are P–F (single bond) = 1.74 Å., P–Cl (single bond) = 2.09 Å., P–O (double bond) = 1.57 Å., and P–S (double bond) = 1.95 Å. The structure of thiophosphoryl fluoride presents two interesting differences from the structures of the other molecules in the group that have been studied, a decrease of 0.09 Å. in the phosphorus–sulfur distance and a small fluorine–phosphorus–fluorine angle.

An explanation for the first of these differences may be found from a consideration of the various resonating valence bond structures that may be written for molecules of this type.



The much greater shortening observed for the phosphorus–fluorine distance, 0.22 Å., than for the phosphorus–chlorine distance, 0.08 Å., has been explained by the assumption of a larger contribution of structures IV–VIII to the resultant structure of molecules containing fluorine, made possible by the larger electronegativity[14] of fluorine. Since the electronegativity of oxygen is so much larger than the electronegativity of phosphorus and sulfur, structures VII and VIII are unimportant in the molecules X_3PO. Thus we interpret the extra shortening of the phosphorus–sulfur bond in thiophosphoryl fluoride as due to considerable triple bond character made possible by the large electronegativity of fluorine and the small difference in the electronegativity between phosphorus and sulfur.

Although several explanations for the small fluorine–phosphorus–fluorine angle in thiophos-

(12) L. O. Brockway and F. T. Wall, THIS JOURNAL, **56**, 2373 (1934).

(13) L. Pauling and L. O. Brockway, *ibid.*, **59**, 1223 (1937).

(14) L. O. Brockway, *J. Phys. Chem.*, **41**, 185 (1937).

phoryl fluoride present themselves, a satisfactory one cannot be advanced until more data have been acquired.

The sulfur–fluorine distance in sulfuryl fluoride, 1.56 Å., is 0.12 Å. less than the single bond distance predicted by the covalent radius table.[13] This shortening is not as great as is observed in the fluorine derivatives of phosphorus. A similar situation obtains for the corresponding chlorine compounds of sulfur and phosphorus.

It is of interest to note that, although there is much more shortening in the sulfur–halogen bond in sulfuryl fluoride than in sulfuryl chloride, the sulfur–oxygen distance in sulfuryl fluoride, 1.43 Å., is just that found for this distance in sulfur dioxide,[15] sulfur trioxide,[3] and sulfuryl chloride.[3]

In conclusion it should be remarked that the large uncertainty in the fluorine–sulfur–fluorine angle, ±8°, introduces an uncertainty of less than 0.1 E. U. into the calculation of the rotational entropy from the structure of the molecule.

(15) V. Schomaker and D. P. Stevenson, to be published.

Summary

The structures of sulfuryl fluoride and thiophosphoryl fluoride have been investigated by the electron diffraction technique. The interatomic distances and bond angles are: for sulfuryl fluoride, S–F = 1.56 ± 0.02 Å., S–O = 1.43 ± 0.02 Å., ∠ F–S–O = 105 ± 2°, and ∠ F–S–F = 100 ± 10°; and for thiophosphoryl fluoride, P–F = 1.51 ± 0.02 Å., P–S = 1.85 ± 0.02 Å., ∠ F–P–F = 99.5 ± 2°, and ∠ F–P–S = 118 ± 2°. The relationship between the structures found and the resonating valence bond structures is briefly discussed.

PASADENA, CALIF. RECEIVED SEPTEMBER 25, 1939

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF NEW YORK UNIVERSITY]

Solubility of Barium Iodate Monohydrate in Solutions of Uni-Univalent Electrolytes at 25°, and the Calculation of the Dissociation Constant of Iodic Acid from Solubility Data[1]

BY SOLOMON NAIDICH AND JOHN E. RICCI[2]

Barium iodate was one of the first salts to be used in the testing of theories of solutions of electrolytes through the effect of added electrolytes on the solubility of difficultly soluble salts. Such measurements for barium iodate were made by Harkins and Winninghoff,[3] in barium nitrate, potassium nitrate and potassium iodate solutions; by Polessitskiĭ[4] in potassium nitrate and calcium nitrate solutions up to very high concentrations; and by Macdougall and Davies,[5] in dilute solutions of potassium chloride, nitrate, chlorate and perchlorate, and of calcium chloride.

In the present work, at the expense of repeating some of the measurements already found in the literature, it was decided to attempt to calculate the dissociation constant of iodic acid through the relative effects on the solubility of barium iodate of the simple electrolyte potassium chloride and of the corresponding acid, hydrochloric, and, similarly, through the relative effects of the pair potassium nitrate and nitric acid on the same solubility. Measurements are therefore presented giving the effect of these four uni-univalent electrolytes on the solubility of $Ba(IO_3)_2 \cdot H_2O$ at 25°, calculation of the various Debye–Hückel parameters for the mean activity coefficient of $Ba(IO_3)_2 \cdot H_2O$ in these solutions, and, finally, calculation of the dissociation constant of iodic acid, based on the observed solubility data and certain assumptions to be stated.

(1) Presented before the Division of Physical and Inorganic Chemistry, American Chemical Society, at Boston, September, 1939.

(2) The experimental part of this paper is taken from a thesis submitted by Mr. S. Naidich to the Graduate School of New York University in partial fulfilment of the requirements for the degree of Master of Science, June, 1939.

(3) Harkins and Winninghoff, THIS JOURNAL, **33**, 1827 (1911).

(4) Polessitskiĭ, *Compt. rend. l'acad. sci., U. R. S. S.*, **14**, 193 (1935).

(5) Macdougall and Davies, *J. Chem. Soc.*, 1416 (1935).

Experimental

$Ba(IO_3)_2 \cdot H_2O$, C. P. grade, was washed eight to ten times with distilled water, the smaller particles being removed by a regulated process of sedimentation and decantation. Analysis of the product (dried at about 100°) before use, gave 96.5% $Ba(IO_3)_2$ as compared with the theoretical figure of 96.43% for the monohydrate. The analytical method here and in the solubility determinations themselves was the iodometric titration of the iodate by means of 0.05 *N* sodium thiosulfate solution, previously standardized against pure potassium iodate. The procedure, involving the use of weight burets, was standard; blanks were taken to correct for any iodate in the potassium iodide

used, and for any air oxidation of the excess iodide during the fixed time allowed for the titration.

The electrolyte solutions used as solvents were prepared, in the case of potassium chloride and nitrate, by weight, directly from C. P. recrystallized salts, followed by proper dilution, and by proper aliquoting and dilutions, for the very low concentrations. The hydrochloric acid solvents were made by a series of dilutions from a stock solution standardized gravimetrically; the nitric acid solutions, similarly, from a stock solution standardized volumetrically against pure sodium carbonate, using methyl orange as indicator.

The solubility determinations were carried out in Pyrex glass-stoppered bottles (250 ml. capacity), rotated for several days in a water-bath kept at 25 ± 0.01°. To ensure equilibrium and accuracy, the determinations, for each strength of solvent, were made both from under- and from super-saturation, the analyses moreover being repeated after a day or two in almost every case. Hence in most cases four determinations were made for each point of the reported solubility curves. The saturated solutions were analyzed by withdrawing by means of suction (after allowing some time for settling) a 50 or 100 ml. sample into a calibrated pipet, fitted with quantitative filter paper at the tip, delivering the sample into an Erlenmeyer, and titrating the iodate as described above.

TABLE I

SOLUBILITY OF BARIUM IODATE AT 25°

m	Average $S \times 10^4$	$\sqrt{\mu}$	m	Average $S \times 10^4$	$\sqrt{\mu}$
0	8.177	0.0495	0	8.177	0.0495
	KCl added			KNO_3 added	
0.001	8.357	0.0593	0.001	8.387	0.0593
.005	8.977	.0877	.005	8.937	.0876
.01	9.297	.1131	.01	9.427	.1133
.05012	11.28	.2313	.05012	11.78	.2316
.1002	12.75	.3226	.1002	13.66	.3230
.2454	15.66	.5000	.2454	17.60	.5006
.4908	18.95	.7040	.4908	22.90	.7054
.9817	23.78	.9944	.9817	32.37	.9957
	HCl added			HNO_3 added	
0.0001	8.249	0.0507	0.001101	8.455	0.0603
.0005	8.328	.0548	.005505	9.178	.0909
.001	8.400	.0593	.01101	9.806	.1181
.0025	8.649	.0714	.05505	13.75	.2433
.005	8.986	.0877	.1101	17.53	.3397
.01	9.554	.1135	.2474	25.83	.5050
.05012	12.74	.2323	.4948	39.39	.7117
.1002	15.57	.3239	.9895	68.78	1.005
.2454	22.28	.5021			
.4908	32.39	.7075			
.9817	52.43	.9987			

Results

Table I lists the observed solubilities in the presence of various concentrations of potassium chloride, hydrochloric acid, potassium nitrate and nitric acid. The first column gives the molarity, m, of the solvent electrolyte; the second, the solubility, S, in moles per liter, averaged, in each case, from very closely agreeing results obtained from both under- and super-saturation; the third column lists the square root of the stoichiometric ionic strength, calculated on the assumption of complete dissociation for all electrolytes added.

Log S is plotted against $\sqrt{\mu}$ in Fig. 1. It will be observed that although the chloride curves are distinctly different from the nitrate curves, the relation of the acid to the salt effect is evidently very nearly the same for both cases. The increased solubility of the barium iodate in the presence of acid, as compared to its solubility in the corresponding concentration of potassium salt, evidently is due to the incomplete dissociation of iodic acid formed by double decomposition.

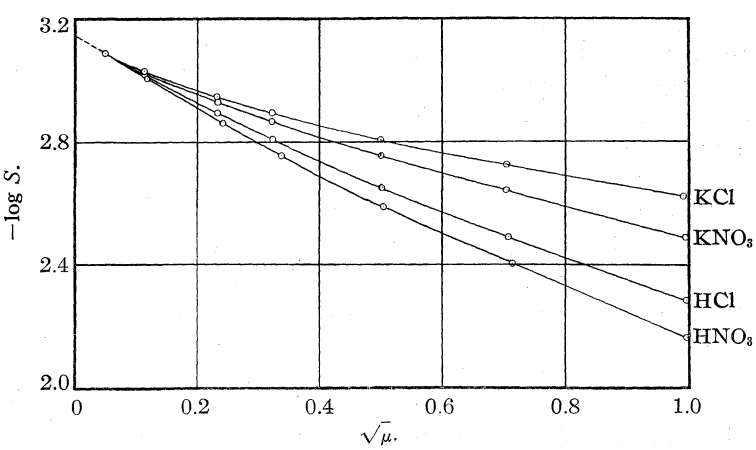


Fig. 1.—Solubility of $Ba(IO_3)_2 \cdot H_2O$ in electrolyte solutions.

Assuming the Debye–Hückel equation in the form

$$\log f_{\pm} = -\frac{B\sqrt{\mu}}{1 + A\sqrt{\mu}} \qquad (1)$$

to hold for the data involving the potassium salts as solvent electrolytes, the results can be used first to calculate, for the chloride and for the nitrate series separately, values of the parameter A, of S_0 (solubility in zero ionic strength) and of $f_{\pm}$, the mean activity coefficient, for the salt in its pure saturated solution. The coefficient $f_{\pm\mu} = S_0/S_\mu$; hence by solving successive sets of simultaneous equations of the form

$$\log S_0 - \log S_{\mu_1} = \frac{-1.01\sqrt{\mu_1}}{1 + A\sqrt{\mu_1}}$$
$$\log S_0 - \log S_{\mu_2} = \frac{-1.01\sqrt{\mu_2}}{1 + A\sqrt{\mu_2}} \qquad (2)$$

in which S_{μ_1} and S_{μ_2} are the observed solubilities in the ionic strengths μ_1 and μ_2, respectively, values of both S_0 and A are obtained. By omitting the determinations in very low concentration of added electrolyte, and combining the solubility in pure water, successively, with the determinations in the strengths shown in column 1 of Table II, the corresponding values of A are calculated.

TABLE II

VALUES OF A, CALCULATED

m	In KCl	In KNO_3
0.05	1.08	0.57
.10	1.10	.64
.25	1.06	.65
.50	1.03	.62
1.0	0.97	.56
Av.	1.05	.61

From these values the mean effective ionic diameter a may be calculated, through the relation $A = 0.328\ a$, yielding $a = 3.20$ Å. for the potassium chloride solutions, and $a = 1.86$ Å. for the potassium nitrate solutions. S_0 can also be calculated, through the solubility in pure water, by the relation

$$\log S_0 = 0.9126\text{–}4 - \frac{1.01(0.0495)}{1 + A(0.0495)}$$

Using $A = 1.05$ (KCl series), $S_0 = 7.33 \times 10^{-4}$ M; with $A = 0.61$ (potassium nitrate series), $S_0 = 7.31 \times 10^{-4}$. These values, averaging 7.32×10^{-4}, agree fairly well with the value obtained by the graphical extrapolation of the curves of Fig. 1 to zero μ; these curves, it is to be noted, give a limiting slope (observed -1.0_1 in each case) in agreement with the theoretical value of -1.01, and a value of S_0 of 7.31 (KCl curve) and 7.36×10^{-4} M (KNO_3 curve). The mean activity coefficient of barium iodate monohydrate in its pure saturated solution at 25° is then calculated to be

$$f_{\pm} = \frac{S_0}{S_w} = \frac{0.000732}{0.000818} = 0.895$$

where S_w is solubility in water; Brönsted and La Mer[6] calculated 0.894 from the data of Harkins and Winninghoff.[3]

Dissociation Constant of Iodic Acid

A.—The numerical results just presented can be used to evaluate the ionization constant of iodic acid, first, on the assumption that the only incompletely dissociated species present is iodic acid. As we shall see later, under B, the final result is changed to a negligible extent only if we correct further for the possible presence of undissociated $BaIO_3^+$ ion.

The assumption underlying the calculations is that the mean activity coefficient of the salt $Ba(IO_3)_2$ remains constant in solutions of the same total ionic strength, regardless of whether the principal electrolyte present is the acid or the potassium salt of a given anion; in other words, that $f_{\pm}$ for $Ba(IO_3)_2$ is the same in solutions of either potassium chloride or hydrochloric acid, at the same μ, and has a different but again a constant value in solutions of either potassium nitrate or nitric acid of the same μ. This amounts to assuming that the parameter A, in the Debye–Hückel expression for $\log f_{\pm}$, is the same, in respect to the effect on $f_{\pm}$ of $Ba(IO_3)_2$, for both the acid and the potassium salt of the same anion. For the particular reaction under consideration, of course, A for the two acids cannot be determined directly without, in fact, assuming a value for the dissociation constant of iodic acid. The equality of A for potassium chloride and for hydrochloric acid solutions therefore remains an assumption here. This assumption seems to be justified to some extent on the basis that the Debye–Hückel parameter A, for potassium chloride, in respect to other reactions, while differing rather regularly from that for potassium nitrate, is apparently the same for the corresponding acid, hydrochloric. Butler,[7] quoting the work of Harned and Åkerlöf[8] (electromotive force measurements), lists a for both potassium chloride and hydrochloric acid as 3.38 Å.

If $f_{\pm}$ is the same in hydrochloric acid and in potassium chloride solutions of the same ionic strength, then it follows that the mean ionic concentration $m_{\pm}$ ($= \sqrt[3]{4\ S^3}$) is also the same in the two solutions, since $f_{\pm}m_{\pm}$ = the mean ionic activity, which is constant. Consequently it follows that we can treat the solubility product likewise as constant in the two corresponding solutions. This last was the assumption made by Pedersen[9] in Bjerrum's laboratory, for the solubility product of calcium oxalate in solutions of either sodium chloride or magnesium chloride, in his recent similar calculation of the dissociation constant of magnesium oxalate; it can be seen of course that the assumption of the constant mean

(6) Brönsted and La Mer, THIS JOURNAL, **46**, 555 (1924).

(7) Butler, "Chemical Thermodynamics," The Macmillan Co., New York, 1934, Vol. II, p. 132.

(8) Harned and Åkerlöf, *Physik. Z.*, **27**, 411 (1926).

(9) Pedersen, *Trans. Faraday Soc.*, **35**, 277 (1939).

TABLE III

CALCULATION OF K_m FOR IODIC ACID WITHOUT CORRECTION FOR THE PRESENCE OF UNDISSOCIATED $BaIO_3^+$

No.	m acid	$S_A \times 10^4$	$S_S \times 10^4$	$m_{IO_3^-} \times 10^4$	$m_{HIO_3} \times 10^4$	m_{H^+}	$\sqrt{\mu}$	$\log K_m + 1$
				In HCl				
1	0.001	8.400	8.357	16.17	0.09	0.000991	0.0593	0.2235
2	.005	8.986	8.974	17.94	.03	.004997	.0877	1.6515
3	.01	9.554	9.297	18.34	.77	.009923	.1131	0.3747
4	.05012	12.78	11.28	21.23	4.25	.04970	.2313	.3949
5	.1002	15.57	12.75	23.08	8.06	.09942	.3226	.4544
6	.2454	22.28	15.66	26.26	18.30	.2436	.5003	.5435
7	.4908	32.39	18.97	29.03	35.75	.4872	.7050	.5973
8	.9817	52.43	23.75	31.97	72.89	.9744	.9951	.6308
				In HNO_3				
1	0.001101	8.455	8.404	16.76	0.15	0.001086	0.0602	0.0840
2	.005505	9.178	8.995	17.81	.55	.005450	.0906	.2467
3	.01101	9.806	9.503	18.72	.89	.01092	.1177	.3611
4	.05505	13.75	12.01	22.45	5.05	.05454	.2422	.3847
5	.1101	17.53	13.97	24.94	10.12	.1091	.3382	.4295
6	.2474	25.83	17.68	29.26	22.40	.2452	.5029	.5055
7	.4947	39.39	23.01	35.18	43.60	.4903	.7087	.5973
8	.9894	68.78	32.34	44.36	93.20	.9801	1.0004	.6688

activity coefficient is implicit in that of the constancy of the solubility product, and that any uncertainty in the values of the various A parameters involved affects the applicability of the solubility product principle which must be used in the calculations.

Setting then the solubility product of barium iodate in solutions of hydrochloric acid equal to its solubility product in the corresponding potassium chloride solution of the same total ionic strength, the various ionic concentrations in the acid solutions can be calculated as follows. If S_S = the observed solubility in salt solution, and S_A that in acid (of the same μ)

$$m_{IO_3^-} = \sqrt{\frac{K_{SP}}{S_A}} = \sqrt{\frac{4S_S^3}{S_A}} \quad (3)$$

$$m_{HIO_3} = 2S_A - m_{IO_3^-} \quad (4)$$

$$m_{H^+} = m_{HCl} - m_{HIO_3} \quad (5)$$

$$\mu = S_A + m_{HCl} + m_{IO_3^-} \quad (6)$$

The value of $m_{IO_3^-}$ thus calculated is a first approximation, based on a value of S_S interpolated on the potassium salt curves to correspond to the uncorrected value of $\sqrt{\mu}$ for the acid solution yielding the observed S_A. On correcting the ionic strength for the undissociated iodic acid, μ now being equal to $m_{HCl} + S_A + m_{IO_3^-}$ (Equation 6), a second approximation was made in the calculation of IO_3^- by re-evaluating S_S to correspond to the corrected value of $\sqrt{\mu}$. The final concentrations thus obtained are given in Table III; the last two columns of this table give the corrected ionic strength (to the half power) and the logarithm of the ionization constant, K_m, of iodic acid in terms of concentrations.

It will be seen that the first two values (lowest concentrations) must be discarded in both the hydrochloric acid and the nitric acid series. This was probably to be expected, since the calculation is based essentially on the difference $S_A - S_S$, which becomes very small in this range and subject to too large a relative error. The thermodynamic constant, K_a, is now calculated from the remaining values of the mass constant, K_m, by an algebraic process similar to the calculation of S_0 from the values of S_μ in the foregoing part. Since, for iodic acid

$$K_a = K_m - \frac{f_{H^+} f_{IO_3^-}}{f_{HIO_3}} \quad (7)$$

we can, by assuming $f_{HIO_3} = 1$, set

$$\log K_a = \log K_m - \frac{1.01\sqrt{\mu}}{1 + A\sqrt{\mu}} \quad (8)$$

K_a can then be calculated by finding a proper value of the parameter A for the data to yield a constant value of K_a through the algebraic solution of successive sets of simultaneous equations of the form

$$\log K_a = \log K_{m_1} - \frac{1.01\sqrt{\mu_1}}{1 + A\sqrt{\mu_1}}$$

$$\log K_a = \log K_{m_2} - \frac{1.01\sqrt{\mu_2}}{1 + A\sqrt{\mu_2}} \quad (9)$$

After averaging the results ($\sqrt{\mu}$ and $\log K_m$) for both the hydrochloric acid and the nitric acid data into one series, combinations of values sufficiently far apart in respect to $\sqrt{\mu}$ were used as simultaneous equations, the calculated A parame-

ter having the values listed in Table IV, which shows also the degree of variability in this "constant."

Table V lists, in the last column, the values of K_a calculated (with $A = 1.25$) from the averaged values of $\sqrt{\mu}$ and of $\log K_m$ taken from Table III.

The average value of K_a thus calculated, without the consideration of the possible presence of undissociated $BaIO_3^+$, is then 0.163.

TABLE IV

VALUES OF A CALCULATED TO FIT EQUATIONS (9)

Combinations used	A
0.01–0.5 N	1.67
.01–1 N	1.66
.05–0.25 N	1.13
.05– .5 N	1.09
.05– .1 N	1.28
.1 – .5 N	1.12
.1 –1 N	1.28
.25–1 N	1.37
Average used	1.25

TABLE V

CALCULATION OF K_a FROM K_m, WITH $A = 1.25$

No.	m_{Acid}	$\sqrt{\mu}$	K_m	K_a
3	0.01	0.1154	0.233	0.185
4	.05	.2368	.245	.161
5	.1	.3304	.277	.161
6	.25	.5016	.335	.162
7	.5	.7069	.396	.166
8	1.0	.9978	.447	.157
	Average			.165
	Average, omitting no. 3			.161

B.—Macdougall and Davies[5] showed that barium iodate cannot be considered to be completely dissociated even in very low concentrations; they calculated the equilibrium constant for the dissociation of the barium mono-iodate ion to be

$$\frac{m_{Ba^{++}} m_{IO_3^-}}{m_{BaIO_3^+}} = 0.08 \qquad (10)$$

As this circumstance would be expected to affect the final result for the dissociation constant of iodic acid to some extent, the calculations were repeated, taking into account therefore the formation of the ion $BaIO_3^+$. The concentration of this ion in the potassium salt solution, (x_s), can be calculated in the potassium chloride and nitrate solutions through the equation

$$\frac{(S_s - x_s)(2S_s - x_s)}{x_s} = K_{BaIO_3^+} \qquad (11)$$

which approximates to

$$x_s = \frac{2S_s^2}{K_{BaIO_3^+} + 3S_s} \qquad (12)$$

since x_s is small compared to S_s.

The value of $K_{BaIO_3^+}$ in terms of concentrations will vary markedly with the ionic strength, according to the expression

$$\log K_{BaIO_3^+} = \log (0.08) + \frac{2.02\sqrt{\mu}}{1 + A\sqrt{\mu}} \qquad (13)$$

(where 2.02 is the Debye–Hückel coefficient for a bivalent ion), and was evaluated accordingly for the various solutions by assuming $A = 1$; the magnitude of the effect here involved, on the final result, is so small that a value of 1 for A, which is reasonable, was taken merely for convenience.

The solubility product in any given salt solution is now given by

$$K_{sp} = (S_s - x_s)(2S_s - x_s)^2 \qquad (14)$$

Before calculating the concentrations in the acid solutions, required for the dissociation constant of iodic acid, it is also necessary to calculate the concentrations, x_A, of the $BaIO_3^+$ in the acid solutions, since, with

$$m_{Ba^{++}} = S_A - x_A \qquad (15)$$

then

$$m_{IO_3^-} = \sqrt{\frac{K_{sp}}{S_A - x_A}} \qquad (16)$$

To calculate x_A, we use

$$\frac{m_{Ba^{++}} m_{IO_3^-}}{m_{BaIO_3^+}} = K_{BaIO_3^+} \qquad (17)$$

or

$$\frac{(S_A - x_A)\sqrt{\frac{K_{sp}}{S_A - x_A}}}{x_A} = K_{BaIO_3^+} \qquad (18)$$

Since x_A is small compared to S_A, this simplifies to

$$x_A = \frac{\sqrt{K_{sp} S_A}}{K_{BaIO_3^+}} \qquad (19)$$

in which $K_{BaIO_3^+}$ is the mass constant calculated according to the earlier equation (13). The remaining quantities are calculated by

$$m_{HIO_3} = 2S_A - m_{BaIO_3^+} - m_{IO_3^-} \qquad (20)$$

$$m_{H^+} = m_{HCl} - m_{HIO_3} \qquad (21)$$

$$\mu = (S_A - x_A) + m_{HCl} + m_{IO_3^-} \qquad (22)$$

The calculations are summarized in Table VI, to which of course the first three columns of Table III should be added, for completeness.

It is interesting to note that the concentration of $BaIO_3^+$ in the salt solutions, x_s, remains constant, irrespective of the actual concentration of $Ba(IO_3)_2$, because of the effect of the ionic strength on $K_{BaIO_3^+}$. Although this sort of constancy was actually assumed as a general case, by Pedersen,[9] for undissociated calcium oxalate, in his calculation of the dissociation constant of magnesium oxalate, it is to be noted that at least in the pres-

ent case the same constancy does not hold as well in the acid solutions.

TABLE VI

CALCULATION OF K_m FOR IODIC ACID, INCLUDING CORRECTION FOR THE PRESENCE OF UNDISSOCIATED $BaIO_3^+$

No.	$x_S \times 10^4$ $m_{BaIO_3^+}$ in K^+ soln.	$x_A \times 10^4$ $m_{BaIO_3^+}$ in acid soln.	$m_{IO_3^-} \times 10^4$	$m_{HIO_3} \times 10^4$	m_{H^+}	$\sqrt{\mu}$	log K_m (+1)
			In HCl				
1	0.13	0.13_2	16.54	0.13	0.000987	0.0590	0.099
2	.13	$.13_6$	17.81	.02	.004998	.0876	1.648
3	.13	$.13_4$	18.20	.79	.00991	.1130	0.3592
4	.13	$.14_0$	21.10	4.24	.04970	.2313	.3932
5	.13	$.14_4$	22.95	8.05	.09942	.3225	.4523
6	.13	$.15_6$	26.14	18.26	.2436	.5001	.5424
7	.13	$.17_3$	28.91	35.70	.4872	.7050	.5960
8	.14	$.20_9$	31.86	72.79	.9744	.9950	.6300
			In HNO_3				
1	0.13	0.13_3	16.62	0.16	0.001085	0.0600	0.0520
2	.13	$.13_6$	17.68	.54	.005451	.0904	.2516
3	.13	$.13_8$	18.56	.92	.01092	.1176	.3429
4	.13	$.15_5$	22.34	5.01	.05455	.2422	.3865
5	.13	$.16_9$	24.84	10.05	.1091	.3381	.4307
6	.13	$.20_0$	29.15	22.31	.2452	.5029	.5058
7	.13	$.25_5$	35.08	43.45	.4904	.7087	.5977
8	.14	$.37_9$	44.29	92.89	.9801	1.0003	.6696

These results, shown in Table VI, are averaged for the two series, in Table VII, which further gives the values of K_a calculated, as above under (**A**), from the mass constant through the equation

$$\log K_a = \log K_m - \frac{1.01\sqrt{\mu}}{1 + 1.25\sqrt{\mu}} \qquad (23)$$

in which the same value of A is used as for the calculations of Table V.

TABLE VII

CALCULATION OF K_a FROM K_m, WITH $A = 1.25$

No.	m_{Acid}	$\sqrt{\mu}$	K_m	K_a
3	0.01	0.1153	0.228	0.178
4	.05	.2368	.245	.160
5	.1	.3303	.276	.160
6	.25	.5015	.334	.163
7	.5	.7069	.395	.165
8	1	.9977	.447	.159
	Average			.164
	Average (omitting no. 3)			.162

It is to be pointed out that the dissociation constants calculated for the data in very low concentrations (perhaps including the concentration 0.01 N in acid) are highly variable and obviously not to be considered for the final value. This low reliability in the results is to be expected for low concentrations because of the nature of the method, which, as already stated, is a differential one, depending primarily on the observed difference between S_A and S_S (a measurement subject to very high relative error at the low acid concentrations) for the determination of the concentration of undissociated iodic acid, on which of course the ionization constant chiefly depends.

Discussion

The final value of K_a therefore, calculated from the solubility data, either with or without the correction for $BaIO_3^+$, is about 0.163. Whether or not the agreement is really to be expected, this value nevertheless agrees fairly well with the best values derived from conductivity work. All the values of the ionization constant of iodic acid in the literature are based on conductivity measurements:

Rothmund and Drucker[10] (1903)	K = 0.18–0.19 at 25°
Onsager[11] (1927)	K = .17 at 25°
Davies[12] (1933)	K = .18(.20?) at 25°
Fuoss and Kraus[13] (1933)	K = .1686 at 25°
Abel, Redlich and Hersch[14] (1934)	K = .26 at 0°
	.19 at 18°,
extrapolating to	.17 at 25°

The best value is accepted to be that of Fuoss and Kraus, 0.1686 at 25°, with which therefore the present value of 0.163 is to be compared. Pedersen,[9] it should be noted, likewise found agreement between values of the ionization constant of magnesium oxalate calculated from solubility data and from conductivity measurements, obtaining 3.8×10^{-4} and 3.9×10^{-4} in the two cases, respectively.

Summary

The solubility of $Ba(IO_3)_2 \cdot H_2O$ was measured at 25° in aqueous solutions of KCl, HCl, KNO_3 and HNO_3, the results being considered from the point of view of the Debye–Hückel equation.

The results are used to evaluate the ionization constant of iodic acid on the assumption of a constant mean activity coefficient for barium iodate in either the acid or the potassium salt solution of the same anion, at the same total ionic strength. Corrections are made for the possible existence of undissociated $BaIO_3^+$ in the solution; this effect however is found to be negligible.

The value of the thermodynamic constant K_a for iodic acid is found to be 0.163, in agreement with the best value (0.1686) derived from conductivity data.

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(10) Rothmund and Drucker, *Z. physik. Chem.*, **46**, 827 (1903).

(11) Onsager, *Physik. Z.*, **28**, 294 (1927), using the data of Kraus and Parker, THIS JOURNAL, **44**, 2429 (1922).

(12) Also based on the data of Kraus and Parker (ref. 11), "Conductivity of Solutions," London, 1933, p. 107.

(13) Fuoss and Kraus, THIS JOURNAL, **55**, 476 (1933).

(14) Abel, Redlich and Hersch, *Z. physik. Chem.*, **170A**, 112 (1934.)

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, NEW YORK UNIVERSITY]

Solubilities of Salts in Dioxane–Water Solvents[1]

BY T. W. DAVIS AND J. E. RICCI WITH C. G. SAUTER

As a study in the problem of the relations between dielectric constant and solubility of electrolytes, we have made measurements of the solubilities of three insoluble compounds, barium iodate, silver acetate and silver sulfate in dioxane–water mixtures at 25° over the complete range of concentrations from 0 to 100% dioxane in intervals of 10% by weight. The measurements extended over a dielectric constant range from 2.10 to 78.55 (the widest variation so far reported in solubility work) and the results have been treated in the light of the interionic attraction theory and of Born's theory of solvent interaction.[2]

I. Materials and Methods

Barium Iodate.—A C. P. grade of barium iodate monohydrate was washed eight to ten times with distilled water, sedimented in tall cylinders to remove smaller sized particles, and dried at 100° before use. Iodometric titration gave 96.5% $Ba(IO_3)_2$ compared with 96.43% theoretical for the monohydrate. The several preparations gave a constant solubility in water.

Silver Acetate.—A C. P. product was used without further treatment. Volumetric analysis for silver gave 64.72% silver compared with a theoretical 64.64%.

Silver Sulfate.—A preparation from Merck was employed without further purification. On the basis of silver content, the salt was 99.9% Ag_2SO_4.

Other Inorganic Salts.—Standard C. P. grade chemicals were used after drying at 100°.

Dioxane.—This solvent came from several sources. The first step in the purification was usually either a refluxing with metallic sodium for several hours or treatment with sodium wire at room temperature for several days. This sodium treatment was then followed by distillation through a 24-inch (61-cm.) packed distilling column. In some cases the dioxane was first treated with alkaline permanganate, distilled, refluxed with lime and then redistilled before being treated with sodium.[3] The density, refractive index and dielectric constant of the preparations checked closely with values to be found in the literature. The freezing points ran between 11.5 and 11.73°, somewhat lower than those reported by several others[3,4] (about 11.8). Such differences have been neglected in the present work since the effect on the calculated dielectric constant of the mixed solvents would be very small. The rapid deterioration of the material is ascribed by Hess and Frahm[4] to oxidation to give an aldehyde, peroxide and other subsequent products. Because of the unstable character of the liquid, it was prepared at frequent intervals during the course of the work.

Solubility Determinations.—The dioxane–water mixtures were made up by weight for each experiment, in glass-stoppered Pyrex solubility bottles of 250 ml. capacity. The liquid was rotated at 25 ± 0.02° with excess solid for one or more days.

Samples for analysis were withdrawn by suction through quantitative filters into calibrated 100-ml. pipets after allowing some time for the undissolved salt to settle. There was no evidence of colloidal character in any of the solutions. The silver-containing samples were titrated, after appropriate dilution in the case of high dioxane ratios, against standard 0.01 *N* potassium thiocyanate solution using weight burets. Some difficulty was encountered in fixing the end-point of this titration in the presence of varying quantities of dioxane; the precipitation of the silver thiocyanate is apparently slow near the equivalence point, and the color is also somewhat abnormal. Very vigorous and prolonged agitation is necessary to overcome the first difficulty, and comparison solutions were used as color standards to fix the final end-point in very high dioxane concentrations.

The iodate solutions were first evaporated to dryness to expel the dioxane which seriously interferes with the observation of the starch–iodine end-point, and which accelerates the liberation of iodine from an acidified potassium iodide solution. The titration of the iodate was performed with a carefully regulated procedure, using frequently standardized thiosulfate solutions delivered from weight burets, appropriate corrections being made for the blanks.

II. Solubilities in Presence of Dioxane

The solubility figures appearing in Tables II, III and IV are in every case the mean of one or more determinations from undersaturation and one or more from supersaturation.

In Table I we have collected the data on the properties of the solvents which are useful in interpreting our solubility figures. The dielectric constants are taken from the report of Åkerlöf and Short[3b]; the densities are interpolated from the measurements of Hovorka, Schaefer and Dreisbach.[5] The coefficients to be used in the Debye-Hückel equation at 25° are listed in the last two columns of the table. Column 5 of the table contains the differences between the reciprocal of the dielectric constants of the several media and the reciprocal of the dielectric constant of water.

(1) Presented at the Baltimore meeting of the American Chemical Society, April, 1939.

(2) M. Born, *Z. Physik*, **1**, 45 (1920).

(3) (a) C. A. Kraus and R. M. Fuoss, THIS JOURNAL, **55**, 21 (1933); C. A. Kraus and R. A. Vingee, *ibid.*, **56**, 511 (1934). (b) G. Åkerlöf and O. A. Short, *ibid.*, **58**, 1241 (1936).

(4) K. Hess and H. Frahm, *Ber.*, **71B**, 2627 (1938).

(5) F. Hovorka, R. A. Schaefer and D. Dreisbach, THIS JOURNAL, **58**, 2264 (1936).

TABLE I

DATA AND CONSTANTS FOR SOLVENTS USED

Wt. % dioxane	Density	Mole % dioxane	Dielec. const. D	$\left(\frac{1}{D}-\frac{1}{D_0}\right)$	$\frac{352.6}{D^{3/2}}$	$\frac{2.914}{D^{1/2}}$
0	0.9970	0	78.55	0.000	0.505	0.3288
10	1.0030	2.223	69.71	.001614	.606	.3490
20	1.0097	4.667	60.81	.003714	.744	.374
30	1.0189	8.063	51.91	.006533	.943	.404
40	1.0263	12.004	43.00	.010525	1.250	.444
50	1.0311	16.987	34.28	.01644	1.757	.498
60	1.0345	23.485	25.86	.02594	2.681	.573
70	1.0372	32.32	17.70	.04377	4.627	.693
80	1.0349	45.01	10.72	.08055	10.04	.890
85	1.0320	53.68	8.16	.1098	15.12	1.020
90	1.0295	64.81	5.61	.1654	26.54	1.230
95	1.0280	79.52	3.69	.2583	49.73	1.517
100	1.0277	100.0	2.101	.4637	115.9	2.011

TABLE II

SOLUBILITY OF SILVER ACETATE IN DIOXANE–WATER MIXTURES AT 25°

Wt. % dioxane	Solubility, S moles/l. $\times 10^4$	$-\log S$	Solubility, X, mole fraction $\times 10^4$	$-\log X$	$\sqrt{\mu}$
0	666.3	1.1763	12.027	2.9198	0.2581
10	503.5	1.2980	9.819	3.0079	.2244
20	363.8	1.4391	7.714	3.1127	.1907
30	245.2	1.6105	5.693	3.2446	.1550
40	151.7	1.8190	3.905	3.4084	.1232
50	85.64	2.0673	2.485	3.6048	.09253
60	42.27	2.3740	1.409	3.8512	.06502
70	17.40	2.7595	0.6818	4.1663	.04171
80	6.11	3.2140	.2925	4.5339	.02472
85	2.85	3.5452	.1552	4.8090	.01688
90	1.54	3.8125	.0949	5.0228	.0124
95	0.21	4.676	.0151	5.8220	.0046
100	.000		.0000		

TABLE III

SOLUBILITY OF SILVER SULFATE IN DIOXANE–WATER MIXTURES AT 25°

Wt. % dioxane	S, moles/l. $\times 10^4$	$-\log S$	X, mole fraction $\times 10^4$	$-\log X$	$\sqrt{\mu}$
0	268.4	1.5712	4.875	3.3121	0.2838
10	155.0	1.8097	3.026	3.5194	.2156
20	83.14	2.0802	1.764	3.7535	.1579
30	40.15	2.3963	0.9326	4.0302	.1098
40	17.03	2.7688	.4387	4.3580	.07157
50	6.02	3.2214	.1747	4.7577	.04245
60	1.80	3.7455	.0600	5.2220	.0232
70	0.63	4.201	.0247	5.6075	.0137
80	.23	4.646	.0110	5.9582	.0082
90	.063	5.201	.00388	6.4110	.0043
100	.0000		.00000		

The experimental figures on the solubilities of the three solutes investigated are presented in Tables II, III and IV both in moles per liter and in mole fractions, assuming normal molecular weights in the liquid. We have included the data in terms of both units because there is question as to which should be used in equilibrium studies. The general practice when dealing with media of different molecular composition is to use mole fractions as the more fundamental units. Scatchard[6] has shown, for example, that the reaction of thiosulfate ion with bromoacetate ion in mixed solvents[7] is in better agreement with prediction when the volume concentrations are corrected to a mole fraction basis. Bell and Gatty,[8] however, have come to the conclusion on theoretical grounds that volume concentrations should be used in calculations of interaction energies in solution. If this is correct, then all the data should appear in volume concentrations. We accordingly have listed the solubilities, in Tables II–IV, in terms of molarities and of mole fractions both, and have in fact carried out most of the subsequent calculations for both sets of units. The same tables also list the figures for the square root of the ionic strength in the several solutions calculated on the basis of 100% dissociation throughout.

Since the barium iodate is a hydrated salt, its activity and solubility must depend on the fugacity of water in the solutions. In every experiment the solid phase at saturation was the monohydrate, as proved by actual analysis, even when the solvent was dioxane, the stability of the solid in the last case being a result of the very low solubility of the salt. In no experiment with barium iodate as saturating phase, or with silver acetate or silver sulfate, was any double compound with dioxane formed. The activity of barium iodate monohydrate in solution being proportional to the activity of the water, we would find the solubility of the hydrate to be greater in solutions of lower water activity, other factors being the same. Accordingly all the solubility figures have been multiplied by the ratio of the aqueous pressure from the solution to that from pure water, using for this purpose the data of Hovorka, Schaefer and Dreisbach.[9] The resulting figure, which is that actually plotted, is the hypothetical solubility of barium iodate monohydrate in pure water of dielectric less than 78.55.

The measurements given in Tables II–IV are plotted in Figs. 1 and 2. The full curves of Fig. 1 show $-\log S$ (molarity) for the three salts studied, as a function of D and of $\left(\frac{1}{D}-\frac{1}{D_0}\right)$,

(6) G. Scatchard, *J. Chem. Phys.*, **7**, 657 (1939).

(7) V. K. La Mer and M. E. Kamner, THIS JOURNAL, **57**, 2669 (1935).

(8) R. P. Bell and O. Gatty, *Phil. Mag.*, **19** [7], 66 (1935).

(9) F. Hovorka, R. A. Schaefer and D. Dreisbach, THIS JOURNAL, **59**, 2753 (1937).

TABLE IV

SOLUBILITY OF $Ba(IO_3)_2 \cdot H_2O$ IN DIOXANE–WATER MIXTURES AT 25°

Wt. % dioxane	S, Moles/l. $\times 10^4$	$-\log S$	$S\frac{P_{H_2O}}{P°_{H_2O}}$	$-\log S\frac{P_{H_2O}}{P°_{H_2O}}$	X mole fraction $\times 10^6$	$X\frac{P_{H_2O}}{P°_{H_2O}}$	$-\log X\frac{P_{H_2O}}{P°_{H_2O}}$	$\sqrt{\mu}$
0	8.145	3.0891	8.145	3.0891	15.273	15.273	4.8161	0.04943
10	4.742	3.3240	4.687	3.3291	9.256	9.147	5.0386	.03772
20	2.526	3.5976	2.463	3.6086	5.361	5.226	5.2818	.02753
30	1.217	3.9147	1.167	3.9329	2.827	2.711	5.5669	.01911
40	0.553	4.2573	0.520	4.2842	1.424	1.3386	5.8733	.01288
50	.278	4.5560	.255	4.5934	0.8067	0.7401	6.1307	.00913
60	.140	4.8539	.124	4.9053	.4665	.4144	6.3826	.00648
70	.110	4.9586	.0933	5.0302	.431	.3655	6.4371	.00574
80	.074	5.1308	.0589	5.2302	.354	.282	6.5501	.00471
90	.0050	6.3010	.0035	6.4548	.0308	.0216	7.6651	.00122
100	.0000		.0000		.0000	.0000		

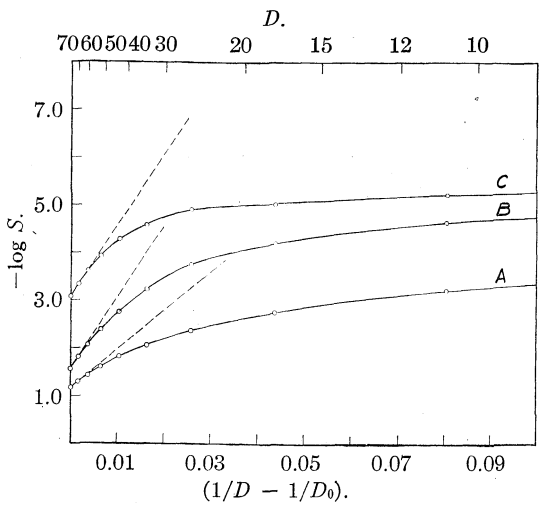


Fig. 1.—Molar solubilities of A (silver acetate), B (silver sulfate) and C (barium iodate hydrate) in water–dioxane mixtures.

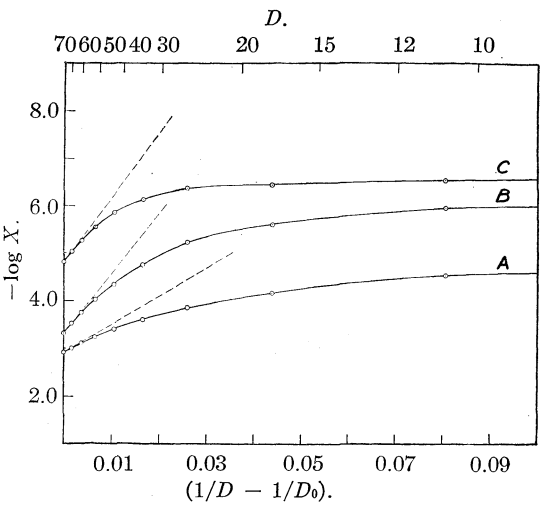


Fig. 2.—Solubilities in mole fractions of A (silver acetate), B (silver sulfate) and C (barium iodate hydrate) in water–dioxane mixtures.

values for which are given in Table I; Fig. 2 shows the corresponding variations of $-\log X$.

Values reported in the literature for the solubility of $Ba(IO_3)_2 \cdot H_2O$ at 25° are

Trautz and Anschütz[10]	5.7×10^{-4} M
Harkins and Winninghoff[11]	7.895×10^{-4} M
Macdougall and Davies[12]	8.10×10^{-4} M
Polessitskii[13]	8.33×10^{-4} M
Present investigation	8.145×10^{-4} M

The numerous determinations of the solubility of silver acetate were reviewed by MacDougall and Bartsch,[14] who themselves found a value of 0.06634 M, as compared with the value here reported of 0.06663 M.

(10) M. Trautz and A. Anschütz, *Z. physik. Chem.*, **56**, 236 (1906).

(11) W. D. Harkins and W. J. Winninghoff, THIS JOURNAL, **33**, 1827 (1911).

(12) G. Macdougall and C. W. Davies, *J. Chem. Soc.*, 1416 (1935).

(13) A. Polessitskii, *Compt. rend. acad. sci., U. R. S. S.*, **14**, 193 (1935).

(14) F. H. MacDougall and C. E. Bartsch, *J. Phys. Chem.*, **40**, 649 (1936).

As for silver sulfate, the only previous determinations at 25° are of rather old date:

	M
Drucker[15] (1901)	0.0257
Rothmund[16] (1909)	.0267
Hill and Simmons[17] (1909)	.02677
Harkins[18] (1911)	.02676
Present investigation	.02684

III. Theory of Solubility

Born[2] has given the following equation for the free energy of charging spheres of radius r_i, in a uniform medium of dielectric constant D, in terms of the charge, $z_i e$, of the spheres, e being the charge of an electron

$$E = \frac{1}{D}\frac{z_i^2 e^2}{2r_i} \qquad (1)$$

(15) K. Drucker, *Z. anorg. Chem.*, **28**, 361 (1901).

(16) V. Rothmund, *Z. physik. Chem.*, **69**, 523 (1909).

(17) A. E. Hill and J. P. Simmons, THIS JOURNAL, **31**, 821 (1909).

(18) W. D. Harkins, *ibid.*, **33**, 1807 (1911).

For a very dilute solution of an electrolyte considered as completely dissociated into spherical ions of radii r_+ and r_-, the energy of interaction of the ions with the medium per mole will be the sum of the individual energies

$$E_+ + E_- = \frac{N\nu_+ z_+^2 e^2}{D\ 2r_+} + \frac{N\nu_- z_-^2 e^2}{D\ 2r_-} = \frac{Ne^2}{D\ 2r}(\nu_+ z_+^2 + \nu_- z_-^2) \qquad (2)$$

independently of the concentrations as long as the solution is so dilute that interionic attractions can be neglected. In (2), r represents an averaged value of the two separate radii, and ν_+ and ν_- are the number of positive and negative ions, respectively, formed in the ionization of one molecule of the electrolyte. N is the Avogadro number.

Combining equation (2) with the ideal relation between free energies, activities and mole fractions, and rearranging the dielectric term, the solubilities in two different media will be related as follows

$$0 = RT \ln \frac{X''}{X'} + \frac{Ne^2}{2r}(\nu_+ z_+^2 + \nu_- z_-^2)\left(\frac{1}{D''} - \frac{1}{D'}\right) \qquad (3)$$

$$0 = RT \ln \frac{(\nu_+ X'')^{\nu_+}(\nu_- X'')^{\nu_-}}{(\nu_+ X')^{\nu_+}(\nu_- X')^{\nu_-}} + \frac{Ne^2}{2r}(\nu_+ z_+^2 + \nu_- z_-^2)\left(\frac{1}{D''} - \frac{1}{D'}\right) \qquad (4)$$

the primes and double primes referring to the two different media and the z's both being taken as positive numbers. On dividing by $RT\ (\nu_+ + \nu_-)$, equation (4) becomes

$$\ln X' = \ln X'' + \frac{Ne^2}{RT2r} z_+ z_- \left(\frac{1}{D''} - \frac{1}{D'}\right) \qquad (5)$$

The solubility of a slightly soluble electrolyte, however, is also dependent on the concentration of ions in the solution, including those from its own dissociation. The effect of the ionic atmosphere is to decrease the activity coefficients of the ions and hence to increase the solubility; and Born's equation should be applied only to solubilities which have been corrected for this ion–ion interaction effect. The magnitude of the correction at 25° is given by the familiar Debye–Hückel expression for the logarithm of the mean activity coefficient of the electrolyte

$$\log f_{\pm} = -\frac{\frac{352.6}{D^{3/2}} z_+ z_- \sqrt{\mu}}{1 + \frac{2.914}{D^{1/2}} a\sqrt{\mu}} \qquad (6)$$

where μ represents the ionic strength and "a" the distance of closest approach of the ions (twice the average radius).

If the solubility of the electrolyte in a solution of ionic strength μ is S_μ, then in a solution of zero ionic strength the solubility S_0 will be given by an expression of the form

$$\log S_0 = \log S_\mu - \frac{B\sqrt{\mu}}{1 + Aa\sqrt{\mu}} \qquad (7)$$

Combining this equation with the Born equation, we find the solubilities in two different media related by the equation

$$\log S' - \frac{B'\sqrt{\mu'}}{1 + A'a\sqrt{\mu'}} = \log S'' - \frac{B''\sqrt{\mu''}}{1 + A''a\sqrt{\mu''}} + \frac{Ne^2 z_+ z_-}{RT\ 2.303a}\left(\frac{1}{D''} - \frac{1}{D'}\right) \qquad (8)$$

Actually the effect of the Debye–Hückel corrections is rather small, as the two terms, being about equal in magnitude, nearly cancel each other. It proves to be empirically true in many cases that the mean activity coefficient of an electrolyte in saturated solution is almost independent of the dielectric constant of the medium. While no especial mention has been made of this fact, several examples may be found in the literature, and data presented later in this report (Table VIII) illustrate approximately the same principle.[14,19,20,21] This regularity and its possible application will be discussed in a later report.

Equations similar to (8) (without the general valence factor) have been used by La Mer and Goldman[19] in connection with their study of thallous iodate in alcoholic solutions, and by Brönsted, Delbanco and Volqvartz.[22] An equivalent valence factor appears in the equation for equilibrium constants in ionic processes, used by MacDougall and Larson,[20] while Dunning and Shutt[23] use a similar equation for solubilities but with a different valence factor. The equation modified for the interionic attraction effects, as given by the Debye–Hückel limiting law only, has been used by Flatt and Jordan.[24]

Brönsted, Delbanco and Volqvartz compared the solubilities of a number of electrolytes in water and in pure organic solvents. The unmodified Born equation was found to be in qualitative agreement with the actual "distribution

(19) V. K. La Mer and F. H. Goldman, THIS JOURNAL, **53**, 473 (1931).

(20) F. H. MacDougall and W. D. Larson, *J. Phys. Chem.*, **41**, 417 (1937).

(21) P. Walden, *Z. physik. Chem.*, **55**, 683 (1906), reported tetraethylammonium iodide to be about 48% dissociated in saturated solution in many solvents.

(22) J. N. Brönsted, A. Delbanco and K. Volqvartz, *Z. physik. Chem.*, **A162**, 128 (1932).

(23) W. J. Dunning and W. J. Shutt, *Trans. Faraday Soc.*, **34**, 1192 (1938).

(24) R. Flatt and A. Jordan, *Helv. Chim. Acta*, **16**, 37 (1937).

ratio of the ions" or the ratio of the solubility in water to that in the organic solvent; but quantitative tests were not made, and intermediate strengths of the mixtures were not used. The data of Flatt and Jordan were extremely limited (the solubility of the perchlorates of potassium, rubidium and cesium in 0, 50 and 75% alcohol, by volume). With only three points for the solubility curve of a given electrolyte, it is no surprise that the theory was found to be in "splendid agreement" with observation. What we are attempting here is a test of the combined Born and Debye–Hückel equations on a whole series of media of varying dielectric constant, using different types of electrolytes, and with a sufficient number of dependable determinations to furnish a drastic test of the mathematical predictions.

IV. Determination of "a" Values

With CARL G. SAUTER

In attempting to test the validity of equation (8), which we may call the "corrected" Born equation, the question immediately presents itself as to the correct values of a to be used in the several terms of the equation.

Ionic diameters for the three solutes examined in this investigation may be calculated from data on the solvent effects of strong electrolytes. Some of the data and computations are to be found in the literature. The values for silver acetate in water, alcohol–water and acetone–water solvents, in the presence of the various electrolytes shown in parentheses, given in Table IX below, are taken from the publications of MacDougall and coworkers.[14,20,25] That given for silver sulfate in the presence of potassium nitrate was calculated from some measurements of Harkins on the effect of potassium nitrate on the solubility of silver sulfate.[18] The value for barium iodate in the presence of potassium nitrate was calculated both from our own measurements and from the data given by MacDougall and Davies[12]; that for barium iodate in the presence of potassium chloride is taken from the measurements and calculations of Naidich.[26]

To supplement to some extent the data already found in the literature, we have made further similar determinations, studying the solubility of barium iodate monohydrate in water at 25° in the presence of varying concentrations of potassium nitrate, barium nitrate, magnesium chloride and potassium bromate; and that of silver acetate in 10% dioxane in the presence of potassium nitrate, sodium nitrate and potassium chlorate, and in 20% dioxane in the presence of potassium chlorate. The results are presented in Tables V, VI and VII; in these tables, $m_\pm$ is the mean ionic concentration of the saturating salt, *i. e.*, $\sqrt[(\nu_+ + \nu_-)]{(\nu_+S)^{\nu_+}(\nu_-S)^{\nu_-}}$, and μ is the ionic strength. S is the solubility in moles per liter of solution. The a values listed in these tables were calculated by the usual methods of applying equation (7).

TABLE V

SOLUBILITY OF BARIUM IODATE MONOHYDRATE IN AQUEOUS SOLUTIONS OF SOME ELECTROLYTES

Molarity of salt	Soly. × 10^4	$-\log m_\pm$	$\sqrt{\mu}$	a calcd., Å.
0	8.145	2.8884	0.04943	
		KNO_3		
0.002	8.513	2.8692	0.06748	1.79
.01	9.383	2.8270	.1132	1.64
.05	11.74	2.7296	.2314	1.82
.2	16.45	2.5831	.4527	2.01
		$Ba(NO_3)_2$		
0.0005	6.955	2.8786	0.0599	3.89
.001	6.206	2.8676	.0697	2.07
.0025	4.963	2.8433	.0948	1.49
.01	3.426	2.7712	.1762	1.49
.025	2.854	2.6947	.2754	1.76
		$MgCl_2$		
0.001023	8.596	2.8650	0.07515	3.53
.005069	9.591	2.8174	.1345	3.53
.02532	11.99	2.7205	.2820	3.53
.1014	16.11	2.5922	.5558	3.50
		$KBrO_3$		
0.000997	8.3			
.002996	8.5			
.005045	9.0			

The figures in Tables VI and VII are summarized in Table VIII, which shows S, the observed solubility, S_0, the solubility calculated at zero ionic strength, and f, the mean activity coefficient ($= S_0/S$). In agreement with the regularity pointed out above, the mean activity coefficient of silver acetate in its pure saturated solution seems to be roughly independent of the dielectric constant of the solvent.

The silver acetate solubilities in presence of salts, in various dioxane–water mixtures, are shown graphically in Fig. 3. The curve for silver acetate in water solvents is taken from the measurements of MacDougall and Rehner.[25] The

(25) F. H. MacDougall and J. Rehner, THIS JOURNAL, **56**, 368 (1934).

(26) S. Naidich and J. E. Ricci, THIS JOURNAL, **61**, 3268 (1939).

TABLE VI

SOLUBILITY OF SILVER ACETATE IN 10% DIOXANE, IN PRESENCE OF ELECTROLYTES

Molarity of salt	Soly., M	$-\log m_{\pm}$	$\sqrt{\mu}$	a calcd., Å.
0	0.05032	1.2980	0.2244	
		KNO_3		
0.009978	0.05099	1.2925	0.2469	(5.47)
.04995	.05377	1.2695	.3221	4.64
.1002	.05619	1.2503	.3954	4.44
.2001	.05929	1.2270	.5093	4.50
.4992	.06476	1.1887	.7510	4.44
.9985	.06959	1.1575	1.033	4.41
		$NaNO_3$		
0.005084	0.05081	1.2941	0.2392	
.009924	.05116	1.2910	.2472	4.01
.04979	.05413	1.2666	.3224	3.93
.09073	.05585	1.2530	.3829	4.21
.09996	.05649	1.2481	.3955	4.01
.1999	.05985	1.2229	.5096	4.07
.4927	.06583	1.1816	.7474	4.04
.9979	.07209	1.1429	1.034	3.90
1.999	.07781	1.1090	1.441	3.93
2.999	.08034	1.0951	1.752	4.01
3.172	.08067	1.0933	1.804	4.04
4.002	.08076	1.0928	2.021	4.21
		$KClO_3$		
0.004987	0.05077	1.2944	0.2361	3.21
.01007	.05127	1.2901	.2477	3.24
.04995	.05429	1.2653	.3228	3.50
.05017	.05429	1.2653	.3232	3.53
.09987	.05695	1.2445	.3960	3.58
.2018	.06093	1.2152	.5126	3.30
.3045	.06453	1.1903	.6075	3.21
.4002	.06637	1.1780	.6831	3.41

TABLE VII

SOLUBILITY OF SILVER ACETATE IN 20% DIOXANE, IN PRESENCE OF POTASSIUM CHLORATE

Molarity $KClO_3$	Soly., M	$-\log m_{\pm}$	$\sqrt{\mu}$	a calcd., Å.
0	0.03613	1.4421	0.1902	
0.009331	.03703	1.4315	.2153	(4.31)
.05005	.04023	1.3955	.3005	3.32
.09988	.04275	1.3691	.3777	3.67
.1506	.04487	1.3480	.4422	3.56
.2000	.04660	1.3313	.4966	3.51
.2996	.04913	1.3087	.5905	3.53

TABLE VIII

MEAN ACTIVITY COEFFICIENT OF SILVER ACETATE IN PURE SATURATED SOLUTION

Solvent	D	S_0	S	f
Water[14]	78.55	0.0531	0.0663	0.800
10% dioxane	69.71	.0396	.0503	.786
20% dioxane	60.81	.0279	.0361	.771

limiting slopes for the different dioxane solvents involved, namely, 0.505 for 0%, 0.606 for 10% and 0.744 for 20% dioxane are shown as dashed lines in the figure for comparison with the experimental curves. In the case of the barium iodate solubilities, in which the measurements extend down to a much lower value of the ionic strength, the observed limiting slope, as has been shown also by Brönsted and La Mer[27] and by Macdougall and Davies,[12] is in actual agreement with the theoretical value of 1.01.

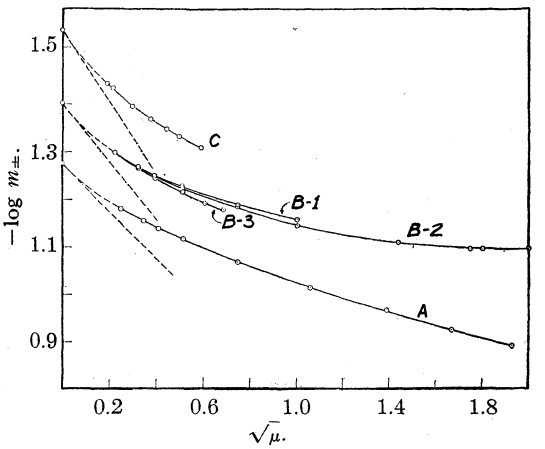


Fig. 3.—Solubility of silver acetate in dioxane–water mixtures in the presence of added salts: A, 0% dioxane, with $NaNO_3$; B, 10% dioxane, with (1) KNO_3, (2) $NaNO_3$, (3) $KClO_3$; C, 20% dioxane, with $KClO_3$.

The various Debye–Hückel values of the a parameter for silver acetate, silver sulfate and barium iodate are summarized in Table IX. Chloupek and Daneš[28] have reported another Debye–Hückel value of a for silver sulfate, determined, however, from studies on the e. m. f.'s of cells. Their values of 1 and 3 Å. for the diameters of the silver and sulfate ions, respectively, may be compared with the figure for this electrolyte given in the table.

TABLE IX

VALUES OF a FROM EFFECT OF SOLVENT SALTS ON SOLUBILITY

Solvent	$AgC_2H_3O_2$	Ag_2SO_4	$Ba(IO_3)_2 \cdot H_2O$
Water	4.35 (KNO_3)	2.43 (KNO_3)	1.80 (KNO_3)
	3.69 ($NaNO_3$)		3.20 (KCl)
			3.52 ($MgCl_2$)
			1.70 ($Ba(NO_3)_2$)
Alcohol (10–30%)	3.99 (KNO_3)		
	3.72 ($NaNO_3$)		
Acetone (10–30%)	3.99 (KNO_3)		
	3.87 ($NaNO_3$)		
Dioxane (10%)	4.48 (KNO_3)		
	4.03 ($NaNO_3$)		
	3.37 ($KClO_3$)		
Dioxane (20%)	3.52 ($KClO_3$)		

It is observed that the values are not and cannot be characteristic of the saturating salt itself

(27) J. N. Brönsted and V. K. La Mer, THIS JOURNAL, **46**, 555 (1924).

(28) J. B. Chloupek and V. Z. Daneš, *Coll. Czech. Chem. Comm.*, **4**, 165 (1932); *B.C.A.*, 572 (1932).

but are averages including the added solvent ions too. It is obvious that we cannot arbitrarily take an average of these parameters in applying Born's equation although we expect the a which should apply to be of the same order of magnitude. We have, therefore, thought it best to calculate a values by applying the "corrected" Born equation (Eq. 8) to solubilities experimentally observed in the several solvents. There may be some question whether the same a should be used in the Debye–Hückel terms as in the Born term, but inasmuch as the latter term far outweighs the others in numerical significance, appreciable variations in a have little effect on the Debye–Hückel corrections, and it seems reasonable to use a single figure for the ion diameters.

We have calculated the a values for the several solutions, combining the solubility in water with the solubility in the several mixed media as indicated in equation 8. The resulting a's are listed in Tables XI, XII and XIII. In each case the values increase with increasing proportion of dioxane. As a result of the mathematical transformations involved in the change of units the a's calculated from molarities are smaller than those based on mole fractions. But whichever units are used, the a values are of about the same magnitude and of the same relative consistency over the entire range; furthermore, they are comparable with a parameters appearing in Table VIII, at least in the water-rich solutions. For the purpose of comparison the various a values for the three separate salts which might possibly be used in testing the Born equation (Eq. 8) are collected in Table X.

The a's so determined and their variations as D changes, test and disprove the validity of the fundamental assumption made in the simple application to solubilities of Born's equation corrected for interionic attraction, namely, that there is a value for a (an effective ionic diameter) which

TABLE X

VALUES OF a FOR POSSIBLE USE IN TESTING EQUATION 8

Source	$AgC_2H_3O_2$	Ag_2SO_4	$Ba(IO_3)_2 \cdot H_2O$
Limiting slope of Fig. 1 (molarities)	3.1	3.1	3.1
Equation 8, 0–10% dioxane (using molarities)	3.05	3.41	3.30
Limiting slope of Fig. 2 (mole fractions)	4.2	3.6	3.2
Equation 8, 0–10% dioxane (using mole fractions)	4.14	3.93	3.57
Equation 8, 0–30% dioxane (using mole fractions)	4.59	4.59	4.28
Average of Debye–Hückel values, Table VIII	3.83	2.43	2.34

TABLE XI

APPLICATION OF EQUATION 8 TO THE SOLUBILITY OF SILVER ACETATE IN DIOXANE–WATER MIXTURES

	Based on molarities			Based on mole fractions				
		Using a = 3.05			Using a = 4.14		Using a = 4.60	
Wt. % dioxane	a calcd., Å.	S calcd. × 10^4	S calcd./S obsd. × 100	a calcd., Å.	X calcd. × 10^4	X calcd./X obsd. × 100	X calcd. × 10^4	X calcd./X obsd. × 100
10	3.05			4.14			10.04	102.2
20	3.26	349.4	96.0	4.36	7.48	96.9	7.99	102.4
30	3.49	206.9	84.3	4.59	5.18	90.9	5.69	99.9
40	3.80	98.6	65.0	4.91	3.03	77.5	3.54	90.6
50	4.29	32.2	37.6	5.48	1.34	53.9	1.71	69.0
60	5.01	5.30	12.5	6.36	0.355	25.2	0.522	37.1
70	6.37	0.186	1.07	7.99	.0293	4.30	.0494	7.24
80	8.98	2.1×10^{-4}	0.0035	11.2	1.9×10^{-4}	0.066	5.9×10^{-4}	0.197
90	14.1	2.5×10^{-10}	2.6×10^{-9}	17.3	2.1×10^{-9}	2.2×10^{-6}	1.9×10^{-8}	2.0×10^{-5}

TABLE XII

APPLICATION OF EQUATION 8 TO THE SOLUBILITY OF SILVER SULFATE IN DIOXANE–WATER MIXTURES

	Based on molarities			Based on mole fractions				
		Using a = 3.41			Using a = 3.93		Using a = 4.60	
Wt. % dioxane	a calcd., Å.	S calcd. × 10^4	S calcd./S obsd. × 100	a calcd., Å.	X calcd. × 10^4	X calcd./X obsd. × 100	X calcd. × 10^4	X calcd./X obsd. × 100
10	3.41			3.93			3.297	109.0
20	3.68	74.36	89.4	4.24	1.601	90.8	1.948	110.4
30	4.00	27.29	67.9	4.59	0.671	72.0	0.940	100.8
40	4.42	6.639	38.9	5.07	.196	44.8	.329	75.1
50	5.00	0.858	14.3	5.72	.0326	18.7	.0703	40.3
60	5.96	.0353	1.96	6.78	.00202	3.38	.00588	9.81
70	8.19	1.01×10^{-4}	0.016	9.36	1.23×10^{-5}	0.050	6.3×10^{-5}	0.262
80	12.6	8.9×10^{-10}	3.9×10^{-7}	14.6	3.6×10^{-10}	3.3×10^{-6}	1.0×10^{-8}	9.3×10^{-5}
90	20.9	5.4×10^{-22}	8.6×10^{-19}	24.3	1.3×10^{-20}	3.3×10^{-16}	1.2×10^{-17}	3.2×10^{-13}

TABLE XIII

APPLICATION OF EQUATION 8 TO THE SOLUBILITY OF BARIUM IODATE MONOHYDRATE IN DIOXANE–WATER MIXTURES

	Based on molarities			Based on mole fractions				
	Using a = 3.30			Using a = 3.57			Using a = 4.30	
Wt. % dioxane	a calcd., Å.	S calcd. × 10^4	S obsd. × $\frac{p_{H_2O}}{p^0_{H_2O}}$ / S calcd. × 100	a calcd., Å.	X calcd. × 10^6	X obsd. × $\frac{p_{H_2O}}{p^0_{H_2O}}$ / X calcd. × 100	X calcd. × 10^6	X obsd. × $\frac{p_{H_2O}}{p^0_{H_2O}}$ / X calcd. × 100
10	3.30			3.57			10.01	109.4
20	3.51	2.274	92.3	3.93	4.684	89.6	5.75	109.8
30	3.80	0.862	73.9	4.28	1.908	70.4	2.735	100.9
40	4.32	.219	42.2	4.89	0.537	40.1	0.955	71.3
50	5.34	.0291	11.4	6.11	.0832	11.2	.201	27.2
60	6.95	.00115	0.93	8.07	.00420	1.01	.0168	4.06
70	11.1	2.8×10^{-6}	.0030	13.3	1.6×10^{-5}	0.0044	1.6×10^{-4}	0.044
80	17.9	1.1×10^{-11}	1.9×10^{-8}	21.9	1.6×10^{-10}	5.8×10^{-8}	1.2×10^{-8}	4.2×10^{-6}
90	23.6	4.5×10^{-24}	1.3×10^{-19}	27.8	5.1×10^{-22}	2.4×10^{-18}	3.2×10^{-18}	1.5×10^{-14}

should remain constant from one medium to another and should be related to the solubility and dielectric by the equations given above.

At this point it may be appropriate to note that deviations from theoretical curves similar to those noted in this communication have been observed and reported by Tomlinson in a study of reaction velocities.[29]

We could proceed, on the other hand, on the more practical basis that the effective a changes as D changes. Then, assuming in the original equation that there is a characteristic value of a ($= a_0$) for the electrolyte in water (this could be taken as the value approached by the composite a when the percentage of dioxane decreases), an appropriate a ($= a_1$) representing the behavior in each successive solvent can be calculated using the modified Born equation

$$\log S' = \log S_0 + z_+z_-\left(\frac{B'\sqrt{\mu'}}{1 + A'a\sqrt{\mu'}} - \frac{B_0\sqrt{\mu_0}}{1 + B_0a\sqrt{\mu_0}} + \frac{242}{a_0D_0} - \frac{242}{a_1D_1}\right)$$

Since the a as already calculated (Tables XI–XIII) is in effect a composite of the diameters for each pair of media, although it is not an arithmetic average, the a values determined in the new way would be even larger than those already calculated. The principle, however, of an effective diameter varying with the medium would offer no possibility of testing the Born equation for the prediction of solubility, inasmuch as we have for the present no independent determination of the change of the diameter, a, for any given electrolyte with respect to change of dielectric. The a would in other words be an adjustable parameter only. We have consequently omitted such additional figures in the preparation of our tables.

(29) H. M. Tomlinson, "Influence of Dielectric Constant upon the Kinetics of the Bromoacetate-Thiosulfate Reaction," Thesis, Columbia, 1939; *cf.* also V. K. La Mer, *J. Franklin Inst.*, **225**, 709 (1939).

V. Solubilities Calculated from Born's Equation

While the variations of the a's cited in the last three tables themselves indicate the failure of Eq. 8 to account for our experimentally determined solubilities, a clearer picture of the extent of this failure may be drawn from a comparison of predicted and determined solubilities. The calculations have been made in terms of mole fractions using first the a values for the 0 and 10% dioxane solutions and again with the a for the 0 and 30% solutions. The calculations have been repeated on a volume–molar basis using the a which fits the 0 and 10% observed solubilities. The calculations, as before, involve successive approximations; first the solubility is computed without correcting for the interionic attraction, then with this preliminary value the interionic attraction terms are added to the equation and a new solubility is computed. Two approximations are all that are needed except for silver sulfate. The calculated solubilities using the a values just noted together with the ratio of the calculated to the experimental figures are given in the three tables. The calculated and observed curves for log S are plotted together in the two sets of concentration units in Figs. 1 and 2. As can be seen from these figures, the calculated values for log S for both molarity and mole fraction units lie in every case on a very nearly straight line with a slight curvature in the first two or three points due to interionic effects where the ionic strength is appreciable, and with a nearly constant slope, given by

$$\text{slope} = 242z_+z_-/a$$

where a has the value used in the given series of calculations. All the predicted values are too small except at a few points where the 30% a is used for the computations since here the straight line of the calculated values cuts through the curve of the observed solubilities at the point for 30% dioxane.

While there is general agreement as to order of magnitude of the solubility down to 40–50% dioxane computed on the basis either of mole fractions or of molarities, even this degree of concordance disappears for solutions containing more than 50% dioxane. This disagreement is a little worse for the two higher valence type electrolytes than for silver acetate. The use of a larger a improves the agreement in the high-dioxane mixtures but makes the figures for the low-dioxane solvents higher than the experimental, as already pointed out.

VI. Discussion

The disagreement between the observed and the calculated solubilities is seen to be substantially the same for either the volume or the mole fraction units of concentration. The question then of the proper concentration units to use would seem to involve factors of minor importance as compared to the larger discrepancies noted between observed and theoretical solubilities.

In seeking some explanation for the wide deviations between prediction and experiment in these solubilities, we observe that three assumptions involved in Eq. 8 may have to be modified in such a way as to bring about better agreement. These assumptions are (1) a constant diameter for the several electrolytes independent of the medium, (2) a homogeneous structureless character for the dielectric medium and (3) the absence of molecular or ionic associations.

While it may seem reasonable to suppose that variable solvation will lead to a changing effective diameter in different media, it is likely that ions in solutions containing even small percentages of water will be fully hydrated or nearly so, so that for practically the whole range of dioxane–water mixtures, a should be nearly constant for a given electrolyte. Moreover, if the extent of solvation is actually smaller in dioxane-rich solutions, smaller diameters should be expected, whereas, as already seen, the observed solubilities require much larger values to bring about agreement with the Born equation. There seems to be no independent method of estimating these ionic diameters in solution, so that our conclusions regarding them must remain speculative.

Scatchard[30] has shown that the e. m. f. of cells made up of hydrogen chloride in aqueous alcoholic solutions may be accounted for by taking a as equal to 4 Å. up to 50% alcohol and decreasing a to about 2 Å. in absolute alcohol. On the other hand, the values for sodium chloride and potassium chloride in aqueous alcohol are not much different from the a's for these salts in water.[27]

The observation also of rather constant values of a over a wide temperature range for cadmium sulfate and zinc sulfate in water[31] and the very small variation of a for hydrogen chloride in several dioxane–water solvent mixtures[32] may be noted as further evidence for the belief that for a given salt the values of a should be characteristic only of the electrolyte and independent of the medium. It would be pointless then to try to bring the Born equation into agreement with our experiments by artificial adjustments of the a's.

The assumption of continuous character of the solvent medium is apt to be a serious source of error in mixed solvents. The question is related to that of the effective diameter of solvated ions. It is to be expected that in a mixed solvent the more polarizable substance, water in the present case, will be preferentially oriented around the ions; with more soluble electrolytes such as sodium nitrate, this phenomenon may lead to the formation of two liquid layers. While this factor has often been mentioned (for example, by Scatchard[30] in 1925), few calculations of its consequences have been made. Using the Debye expression for the distribution of molecules in a dielectric mixture around a univalent ion,[33] in conjunction with Born's equation, Dunning and Shutt[23] report a calculation of the effective radius of silver chloride when dissolved in a one molar aqueous solution of urea, this radius agreeing more closely with crystallographic values than the radius determined from the Born equation alone. The calculation, however, is very tedious, and while the correction introduced will be in the right direction of increasing the solubilities calculated for a

(30) G. Scatchard, THIS JOURNAL, **47**, 2098 (1925).

(31) V. K. La Mer and W. G. Parks, *ibid.*, **53**, 2040 (1931); I. A. Cowperthwaite and V. K. La Mer, *ibid.*, **53**, 4333 (1931).

(32) H. S. Harned, J. O. Morrison, F. Walker, J. G. Donelson and C. Calmon, *ibid.*, **61**, 49 (1939).

(33) P. Debye, *Z. physik. Chem.*, Cohen Festband, 56 (1927).

given ion size, there is still doubt whether a constant a can be determined for the whole series of solvents, especially when ion association becomes important.

The effect of selective dipole concentration around the ions would not enter into solutions of salts in pure organic solvents of low dielectric; but in most of these liquids the solubility of electrolytes having slight solubility in water will be below the limit of quantitative estimation, and no tests can be applied. One may suggest that the small but detectable dissolving in 90% dioxane of such a difficultly soluble substance as barium iodate, while its solubility in a single solvent of the same dielectric capacity would probably be zero,[34] is evidence that the preferential adsorption of water around ions has a tremendous effect in determining solubility in solvents containing water.

Another effect particularly important in solvents of low dielectric constant is ion clustering in the Bjerrum sense.[35] Such clustering will result in an increased solubility over that calculated assuming complete dissociation. A formula for the formation of binary pairs for a uni-univalent electrolyte has been given by Fuoss and Kraus as a function of the diameter of the ions and the dielectric of the medium,[36] in the approximate and simplified form

$$\frac{1}{K} = \frac{4\pi N}{1000} a^4 \frac{DkT}{e^2} \exp.\left(\frac{1}{a}\frac{e^2}{DkT}\right)$$

where K is the dissociation constant and the other letters have their usual significance. Application of this equation gives approximately 3.1×10^{-6} and 1.1×10^{-12} as the values of K for silver acetate in 80 and 90% dioxane, respectively, where our value of a, namely, 3.05, is taken to define the corresponding value of K. Such results would indicate negligible quantities of silver acetate in molecular form when the ion concentrations are of the magnitudes given in column 3 of Table XI. Smaller a values in the Fuoss and Kraus equation will give, it is true, a K sufficiently small to account for observed solubilities. If a is taken as one-half of 3.05 Å., roughly correct solubilities are predicted. The magnitude of K calculated according to this equation is extremely sensitive to small changes in a. Uncertain, therefore, as a itself is, any value of K derived in the Fuoss and Kraus manner must be considerably in doubt. It is unlikely, furthermore, that the mean ionic diameter for silver acetate can be much smaller than 3.05 Å., for it usually has been found that the parameters fitted into the ordinary Debye–Hückel equation are smaller than expected in the sense that sometimes negative values are found, while a more extended treatment such as that of Gronwall, La Mer and Sandved[37] leads always to positive and hence physically plausible values of a. It is possible that the a's we have used, which are in general agreement with Debye–Hückel values, are too small also.

Several authors have declared that in media below about 60 in dielectric capacity, most of the divalent ions will be associated and that below a dielectric of about 30 univalent ions will be largely associated into neutral molecules. If this be the case in our experiments, the solutions should behave like non-electrolytes where the dioxane percentages exceed 50 approximately, and the solubilities should be nearly proportional to the mole fractions of water in the mixtures. This is not observed, as seen from the data in Tables II–IV, so that we may infer that the solutions of the un-ionized salts here studied are not ideal.

A complete prediction of solubilities in the light of modern theories would involve an estimation of the solubility by the corrected Born equation followed by a calculation of solvent segregation around the ions, a redetermination then of the ionic solubility and a determination of the Bjerrum ion association using the Kraus and Fuoss method of calculation. Such a series of calculations has not yet been made, but while laborious it would have some interest as a test of the combined theories.

Summary

The solubilities of silver acetate, silver sulfate and barium iodate have been determined at 25° in a series of dioxane–water solutions extending from 0 to 100% dioxane. The dielectric constants cover the range 2.1 to 78.55.

The solvent effect of potassium nitrate, barium nitrate, magnesium chloride and potassium bromate solutions on barium iodate in water has been examined experimentally. The solvent effects of potassium nitrate, sodium nitrate and potas-

(34) Thallous iodate has negligible solubility in alcohol, of much higher dielectric than 90% dioxane; *cf.* La Mer and Goldman, ref. 19.

(35) *Cf.* evidence from absorption curves reported by H. v. Halban and B. Szigeti, *Helv. Chim. Acta*, **20**, 746 (1937).

(36) R. M. Fuoss and C. A. Kraus, THIS JOURNAL, **55**, 1019 (1933).

(37) T. H. Gronwall, V. K. La Mer and K. Sandved, *Physik. Z.*, **29**, 358 (1928).

sium chlorate on silver acetate in 10% dioxane solutions, and of potassium chlorate on silver acetate in 20% dioxane, have also been investigated. The corresponding Debye–Hückel a parameters have been calculated.

The Born equation even when corrected for interionic effects fails to account for the course of the solubilities as the percentage of dioxane increases, predicting in each case lower solubilities than those observed. The differences increase in media of higher dioxane content, prediction and observation disagreeing even as to order of magnitude in solvents containing more than 50% dioxane by weight. The disagreement is not diminished appreciably by substitution of mole fractions for volume concentrations, showing that this question is of minor importance as a factor in the application of the Born equation.

Modifications to be superimposed on the Born equation to bring it into line with the observations are discussed.

NEW YORK, N. Y. RECEIVED SEPTEMBER 5, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HOWARD UNIVERSITY]

Kinetic Studies on Iodine Derivatives. I. The Thermal Decomposition of Acetyl Iodide[1]

BY J. LESLIE JONES

The thermal[2] and photochemical[3] decomposition of acetaldehyde into methane and carbon monoxide has been investigated by numerous authors. Since the deduction of a possible free radical mechanism for the thermal and photochemical decomposition of acetaldehyde by Rice and Herzfeld,[4] a great deal of controversy has arisen concerning its validity. The opposing theory[2c] assumes that the activation process, thermal or photochemical, is followed by a rearrangement of the acetaldehyde directly into the final products, methane and carbon monoxide.

On the basis of previous investigations[5] it seems probable that the thermal decomposition of alkyl iodides occurs by the breaking of the carbon–iodine bond (temperature range of 250–350°) as the primary process. This reaction is followed by the secondary reactions of the free radicals. By the substitution of an iodine atom for the hydrogen atom of the aldehyde group in acetaldehyde it is possible to study the thermal decomposition of the product, acetyl iodide, in the same temperature range as the alkyl iodides. Such a study casts light upon the mechanism of the thermal decomposition of acetaldehyde, supporting the free radical mechanism. In addition information is gained concerning the secondary reactions of the free radicals involved.

Experimental Section

The rate of decomposition of the acetyl iodide was followed by the pressure change method, employing essentially the apparatus of Jones and Ogg.[5] The quartz spiral manometer prevented the iodine evolved in the reaction from reacting with the mercury in the absolute manometer. A hollow barrel stopcock was employed to close the reaction vessel, employing a plasticizer as lubricant. The compound, di-*o*-xenzyl-monophenyl phosphate,[6] has a vapor pressure of 5 mm. at 285° and a viscosity of 170 centipoises at 60°. The liquid was warmed in a high vacuum system for several hours in order to remove all solvents. All observations indicated that it was unaffected by the iodine generated in the system, as its structure suggested. It was necessary to heat the stopcock closing the reaction vessel to about 110° in order to prevent condensation of iodine.

The acetyl iodide was prepared by the treatment of Eastman Kodak Co. acetyl chloride with an excess of dry hydrogen iodide gas at 0°. The brown crude product (90% yield) was protected from the air and vacuum distilled in an all-glass fractionating system two times, large amounts of the first and third fractions being discarded. A third fractionation was carried out in high vacuum, the product being distilled directly into the reservoir of the system employed for the study of the reaction rates. In

(1) A preliminary report of this paper was presented at the Symposium on the Kinetics of Homogeneous Gas Reactions, University of Wisconsin, June 20–22, 1939.

(2) (a) Fletcher and Rollefson, THIS JOURNAL, **58**, 2135 (1936); (b) Letort, *J. chim. phys.*, **34**, 265 (1937); (c) Staveley and Hinshelwood, *J. Chem. Soc.*, 1568 (1937); (d) Brenschede and Schumacher, *Ber.*, **70B**, 452 (1937); (e) Rollefson and Faull, THIS JOURNAL, **59**, 625 (1937).

(3) (a) See P. A. Leighton, *J. Phys. Chem.*, **42**, 749 (1937), for a complete review to that date; (b) Blacet and Volman, THIS JOURNAL, **60**, 1234 (1938); (c) Gorin, *J. Chem. Phys.*, **7**, 256 (1939); (d) Rollefson and Grahame, paper presented at the "Symposium on the Kinetics of Homogeneous Gas Reactions," University of Wisconsin, June 20–22, 1939.

(4) Rice and Herzfeld, THIS JOURNAL, **56**, 284 (1934).

(5) See Jones, *ibid.*, **60**, 1877 (1938), for complete references to earlier research.

(6) Furnished through the courtesy of the Dow Chemical Company, Midland, Mich.

general about 30–40 g. of acetyl iodide was utilized as a middle fraction from 150–200 g. of crude acetyl iodide. Three different preparations were employed in the experiments and there was no difference in the behavior of each. The product colored brown in the presence of air. Light was excluded from the reservoir. The boiling point of the product was 60° at 145 mm.

Analysis of the gaseous products was done with a modified Bone–Wheeler apparatus handling a maximum of 3 ml. Bromine water was used to measure unsaturates, ammoniacal cuprous chloride for carbon monoxide, cupric oxide combustion for hydrogen and an explosion combustion for saturated hydrocarbons. A 5% sulfuric acid solution was kept in the measuring buret to maintain a constant vapor pressure. The apparatus was not satisfactory, but it was estimated that concentrations could be determined within 5%. Due to the simple products of the reactions, the apparatus was sufficiently accurate to indicate the main reaction involved.

Homogeneity of the Thermal Decomposition.—In order to determine the effect of packing upon the rate of thermal decomposition, a series of experiments were carried out in a 250-ml. spherical Pyrex flask packed with glass tubing to yield a surface–volume ratio of 5.1 cm.$^{-1}$. Experiments were also performed in the same bulb without glass packing, at a surface–volume ratio of 0.72 cm.$^{-1}$. A third series of experiments were carried out in a 1000-ml. flask of surface–volume ratio 0.44 cm.$^{-1}$. The experimental determination of the rate constant directly indicated that the rate of the decomposition was inhibited by packing the reaction vessel.

Further experiments were performed using helium and nitrogen as inert gases. The tank gases were purified by passage over copper screen heated to red heat and then through a liquid-air trap to remove condensable vapors. The gases were purified directly as needed and admitted to the reaction vessel.

Experimental Results

The Stoichiometric Reaction.—The average ratio of the final pressure, P_f, in the reaction to the extrapolated initial gas pressure of pure acetyl iodide, P_i, was 1.45. This value of P_f/P_i was apparently independent of the initial pressure and temperature of the reaction. Such a value indicated that three molecules of gaseous products were formed from two molecules of acetyl iodide. Free iodine was formed quantitatively from the acetyl iodide, as determined by titration of the iodine condensed in a liquid-air trap after an experiment. The residual gas on analysis was shown to consist of equal volumes of carbon monoxide and methane, within an error of ±5%. Observation of the reaction vessel after two or three experiments indicated that a solid product was being deposited on the surface of the vessel. After a half dozen experiments, the surface of the vessel was dark brown in color. The solid product was a closely adherent, non-crystalline substance. All of this evidence indicated that the stoichiometric reaction was probably

$$2CH_3COI = CH_4 + CO + I_2 + CH_2CO \text{ (solid polymer)}$$

The solid product was considered to be polymerized ketene. Because of its adherence to the glass surface, an amount sufficient for analysis could not be obtained. However, a material balance of the reaction products gave its empirical formula. The research of Rice and Greenburg[7a] indicated that the polymerization of ketene was a heterogeneous reaction at room temperature in a Pyrex vessel. Williamson[7b] found that ketene polymerized rapidly at 400–500°. An initial rapid lowering of the gas pressure was followed by a pressure increase. This phenomenon depended upon the initial gas pressure and thus indicated that the polymerization was not a unimolecular reaction.

Kinetics of the Reaction.—The data measuring the rate of decomposition of acetyl iodide fitted most closely the unimolecular expression

$$-d(CH_3COI)/dt = k(CH_3COI)$$

The pressure of acetyl iodide at any time t was given by

$$(CH_3COI) = (1.45P_0 - P_t)/0.45$$

The value of k, the rate constant, was obtained for each experiment by plotting the values of log (CH_3COI) against time. The graphs was straight lines for the experiments performed in unpacked flasks. The linearity of the graphs was maintained up to 65–76% decomposition at the lower temperatures (292–314°), while at 338° the rate constant was maintained up to 90–95% decomposition. The reaction rate constant was definitely a function of the initial pressure of acetyl iodide and, as Table I indicates, increased with the initial pressure. Other data indicated that the reaction was not a simple unimolecular reaction and therefore it was useless to apply the theory of Kassel–Rice–Ramsperger to the falling off of the value of k. If one considered the disappearance of acetyl iodide during the course of our experiment to occur to the extent of 80% before the value of k began to decrease, then the pressure of acetyl iodide fell to about 5–7 mm. before this effect occurred at 338°. Similar limiting pressures were obtained at lower temperatures. In view of the fact that the rate con-

(7) (a) Rice and Greenburg, THIS JOURNAL, **56**, 2132 (1934); (b) Williamson, *ibid.*, **56**, 2216 (1934).

stant for a particular experiment was maintained over a very large change in the concentration of acetyl iodide and yet is a function of the initial acetyl iodide pressure, one must conclude that the products of the decomposition are very efficient in maintaining the proposed chain mechanism over a wide pressure range.

TABLE I

Temp., °K.	P_0,[a] mm.	$k \times 10^3$, sec.$^{-1}$	Temp., °K.	P_0,[a] mm.	$k \times 10^3$ sec.$^{-1}$
565.1	80.8	0.217	599.6	105	2.19
565.3	217	.271	599.3	230	3.24
565.9	275	.341	599.3	280	4.11
566.1	362	.438	597.7	315	3.10
570.3	113	.479	611.5	58.4	2.91
587.7	75	.914	611.3	94.0	3.10
588.7	102	.940	610.6	108	3.96
588.1	186	1.12	611.5	108	3.74
587.9	263	1.61	611.4	111	3.61
588.7	277	1.64	611.2	125	3.89
588.1	282	1.48	611.1	156	4.62
588.3	297	1.66	608.6	167	5.17
602.3	78.0	1.76	611.5	300	6.61
599.5	95.5	1.69	611.3	385	7.78

[a] Initial acetyl iodide pressure.

The study of the effect of packing the vessel cast additional light upon the mechanism of the reaction. The 250-ml. reaction vessel was packed with Pyrex tubing, increasing its surface–volume ratio from 0.72 to 5.1 cm.$^{-1}$. Table II indicates the effect of packing on the rate constants. The values of k are approximately the same in packed and unpacked flasks over the greater portion of the decomposition. At 612°K. in the packed flask, the value of the rate constant began to fall off after about 60% decomposition and in the unpacked flask after about 90% decomposition. This falling off in the value of k is shown graphically in Fig. 1 for experiment number 25. It is evident that the effect of packing is of secondary importance in this reaction for at least 60% of the iodide is decomposed before departure from a first order reaction is noted. Such a departure indicates the existence of secondary chain reactions repressed by the walls of the vessel.

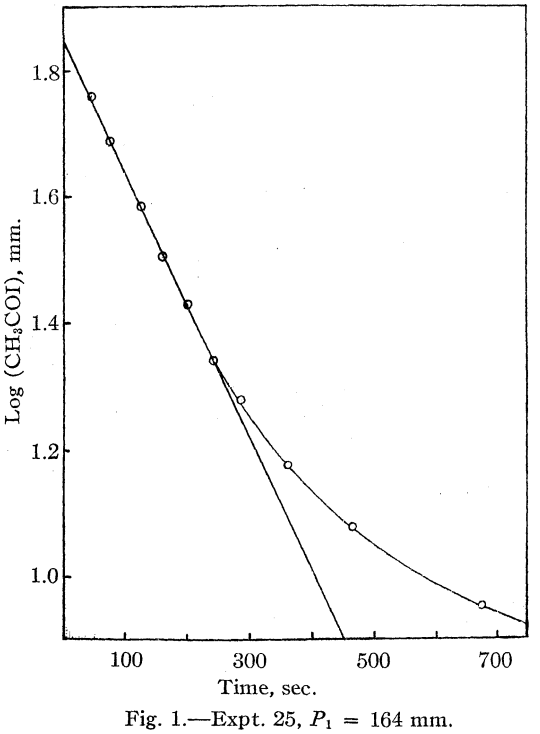


Fig. 1.—Expt. 25, P_1 = 164 mm.

TABLE II

No.	Temp., °K.	P_0, mm.	$k \times 10^3$, sec.$^{-1}$	%[c] decomp.
	PACKED FLASK			
25	612.5	164	4.93	60
26	612.0	208	7.28	70
24	612.5	215	5.52	55
23	611.6	309	6.61	60
27	586.5	145	1.26	75
28	586.3	155	1.22	90
	UNPACKED FLASK			
16[a]	611.2	125	3.89	95
15[a]	611.1	156	4.62	95
22[a]	608.6	167	5.17	85
19[a]	611.5	300	6.61	95
20[a]	611.3	385	7.78	90
33[b]	588.1	186	1.12	80
29[b]	587.9	263	1.61	65
32[b]	588.7	277	1.64	80
30[b]	588.1	282	1.48	80
31[b]	588.3	297	1.66	70

[a] Surface–volume ratio is 0.44 cm.$^{-1}$ (1000 ml.). [b] Surface–volume ratio is 0.72 cm.$^{-1}$ (250 ml.). [c] % decomposition occurring as unimolecular reaction.

Additional experiments were performed to determine the effect of the inert gases nitrogen and helium on the rate of decomposition. It was quite evident, on graphing the rate of change of

TABLE III

No.	P_0, mm.	P_i,[b] mm.	$k \times 10^3$, sec.$^{-1}$	% decomp.
	606.9°K. Nitrogen			
45	134.9	108	3.80	>95
43	194.3	140	5.23	>95
44	196.3	205	5.23	>95
	606.9°K. Helium			
47[a]	128	68	5.18	90
46	145	179	5.52	90

[a] Temperature was 608.1°K. [b] P_i is pressure of inert gas.

acetyl iodide, that the addition of inert gases had little effect on the values of k. Table III gives the values of k in the presence of the inert gases nitrogen and helium, indicating only a slight increase in the value of k on the introduction of an inert gas.

Discussion

All of the above experimental evidence indicates that a chain mechanism is involved in the thermal decomposition of acetyl iodide. The retardation of the decomposition by packing indicates that a chain propagating step is broken by the walls of the vessel. The effect of the products of the reaction in maintaining the rate of pyrolysis during a particular experiment supports the conclusion that the chains are propagated in the gas phase. Addition of the inert gases to acetyl iodide slightly increases the rate constants for the pyrolysis above the value corresponding to the initial pressure of the iodide alone.

In view of the role played by chain reactions, the value of the activation energy obtained by plotting log k vs. t may be of dubious utility unless the activation energies of the elementary chain reactions are known. However, in this particular study the value of the activation energy E has been obtained by plotting the log k against $1/T$ at several initial pressure values for the acetyl iodide (*cf.* Fig. 2). No claim can be made for high accuracy of the activation energy values but their concordance is satisfactory. The average value of E is 43,100 cal./mole.

Previous investigations[4] indicate that the strength of the carbon–iodine bond is approximately 43,000 cal./mole. Admittedly this is an approximation, disregarding the zero point energies of the atoms. However, the present experimental value of E is essentially the same. In view of this fact one can conclude that the primary rate determining step in the decomposition of acetyl iodide is the scission of the carbon–iodine bond. This primary process is then followed by a series of secondary processes best given by the mechanism shown.

		E, kcal./mole	
CH_3COI	$\longrightarrow CH_3CO + I$	43	k_1
CH_3CO	$\longrightarrow CH_3 + CO$	17	k_2
$CH_3 + I_2$	$\longrightarrow CH_3I + I$	12	k_3
CH_3I	$\longrightarrow CH_3 + I$	43	k_4
$CH_3 + CH_3COI$	$\longrightarrow CH_4 + CH_2COI$	8	k_5
CH_2COI	$\longrightarrow CH_2CO + I$	43	k_6
$CH_2=CO$	$\longrightarrow (CH_2CO)_x$(polymer)		k_7
$2I + M$	$\longrightarrow I_2 + M$	0	k_8

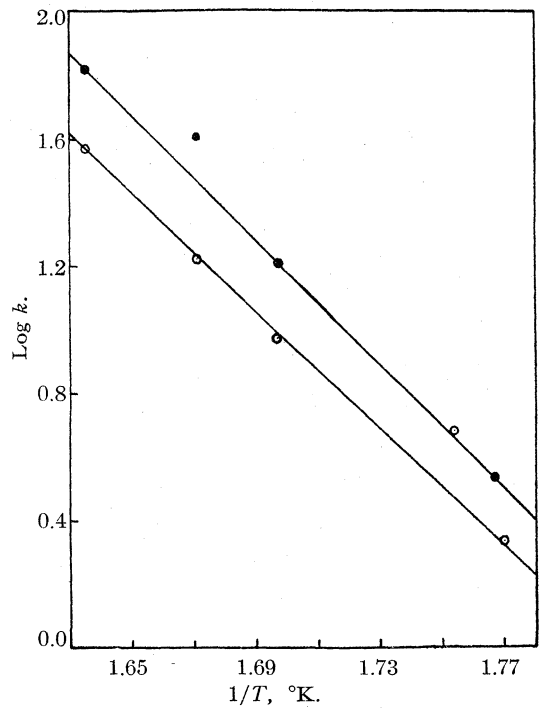


Fig. 2.—●, P_0 approximately 275 mm., E = 44,400 cal./mole; ○, P_0 approximately 100 mm., E = 41,800 cal./mole.

If one sets up in the usual manner equations expressing the stationary state concentrations of methyl and acetyl radicals and methyl iodide, then the rate of disappearance of acetyl iodide is given by the equation

$$-d(CH_3COI)/dt = 2k_1(CH_3COI)$$

The introduction of another possible elementary reaction

$$CH_3CO + I_2 \longrightarrow CH_3COI + I$$

results in a first power term with respect to iodine concentration as a denominator of the above equation. There is no evidence that iodine acts as an inhibitor, except possibly the results obtained in the packed flask and these are of secondary importance.

The evidence is insufficient to justify a statement as to the exact value of the carbon–iodine bond strength, but the value is not markedly affected by the presence of the carbonyl group. The stability of the acetyl radical is in dispute,[8] but the acetyl radical undoubtedly decomposes very rapidly in the temperature region employed in these experiments. Gorin,[8] on the basis of the photolysis of acetone in the presence of iodine,

(8) Gorin, *J. Chem. Phys.*, **7**, 256 (1939); Barak and Style, *Nature* **135**, 307 (1935); Spence and Wild, *J. Chem. Soc.*, 352 (1937).

ascribes a minimum activation energy of 17 kcal. to reaction (2).

The formation and dissociation of methyl iodide, as postulated by reactions (3) and (4), has been established by the work of Ogg[9] on the reduction of methyl iodide by hydrogen iodide. Similar reactions of other lower alkyl iodides have been demonstrated by Jones and Ogg.[10] Rollefson and Faull,[11] in order to account for the iodine-catalyzed decomposition of acetaldehyde, proposed a mechanism involving the above equilibrium. In addition, Etzler and Rollefson[12] in a recent note indicated that a liquid product thought to be methyl iodide had been isolated from the products of the photolysis of acetyl iodide at room temperature.

Rice and Herzfeld in their original paper[3] on the free radical mechanism of acetaldehyde pyrolysis postulated the reaction

$$CH_3CHO + CH_3 \longrightarrow CH_3CO + CH_4$$

ascribing to it an activation energy of 15 kcal. Akeroyd and Norrish[13] have deduced a value of 9.8 kcal. for the above apparent reaction by photochemical methods. However, Burton[14] has calculated a value of 115 kcal. for the strength of the carbon–hydrogen bond in the aldehyde group and thus renders improbable this proposed elementary reaction of Rice and Herzfeld. Taylor and Burton[15] have modified the Rice–Herzfeld mechanism, introducing the radical CH_2CHO as an intermediate instead of the radical CH_3CO. The present research is in agreement with their proposal for here the radical CH_2COI is involved. This radical is able to decompose in this temperature range to yield a stable molecule, ketene, and atomic iodine, in contrast to the inability of the CH_2CHO radical to lose a hydrogen atom. There is existing evidence[6,7] on the polymerization of ketene. Free radicals undoubtedly accelerate this process.

Smith and Taylor,[16] utilizing methyl radicals produced by the photolysis of mercury dimethyl, studied the reactions of hydrocarbons with the methyl radicals. They found a value of 8.3 kcal. for the activation energy of the reaction between ethane and methyl radical to form methane. This evidence supports the probability that the methane is formed essentially in this decomposition by the interaction of methyl radicals and acetyl iodide. Hence, it is also the methyl group of the acetaldehyde which is the principal donor of the hydrogen to form methane, not the aldehyde group.

Further research is in progress on the mechanism of the decomposition of other iodine substituted derivatives with particular reference to iodomethyl ether.

(9) Ogg, THIS JOURNAL, **56**, 526 (1934).
(10) Jones and Ogg, *ibid.*, **59**, 1931 (1937).
(11) Rollefson and Faull, *ibid.*, **59**, 625 (1937).
(12) Etzler and Rollefson, *J. Chem. Phys.*, **6**, 653 (1938).
(13) Akeroyd and Norrish, *J. Chem. Soc.*, 890 (1936).
(14) Burton, *J. Chem. Phys.*, **6**, 818 (1938).
(15) Taylor and Burton, paper presented at the "Symposium on the Kinetics of Homogeneous Gas Reactions," University of Wisconsin, June 20–22, 1939.

Summary

The thermal decomposition of gaseous acetyl iodide was studied in the temperature range 290–340°. The main products of the reaction were identified as carbon monoxide, methane, iodine and polymerized ketene. The decomposition was unimolecular with respect to the acetyl iodide and the rate constants were dependent upon the initial pressure of iodide. The effects of packing the reaction vessel and introducing inert gases were studied. A chain mechanism has been proposed for the decomposition and justified in terms of independent research. The mechanism involves as a primary step the scission of the carbon–iodine bond.

WASHINGTON, D. C. RECEIVED AUGUST 21, 1939

(16) Smith and Taylor, *J. Chem. Phys.*, **7**, 390 (1939).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, IOWA STATE COLLEGE]

Electron Sharing Ability of Organic Radicals. X. Alpha-Substituted Tetrahydroquinolines

BY WILBUR OLDHAM AND I. B. JOHNS

A few measurements are recorded in the literature on the basicity of quinoline[1-5] and quinaldine.[1,3,6] With the exception of the constants found by Goldschmidt for these two heterocyclics, the results are in good agreement. However, the basic strength of the α-substituted tetrahydroquinolines has not been investigated. This manuscript reports the comparison of the ionization constants in absolute methanol of some members of the tetrahydroquinoline series with the constants of the α-substituted pyrrolidine series previously measured in this Laboratory.[7,8]

A most convenient and general method for the preparation of a series of α-substituted quinolines involves the reaction of an organometallic compound, such as $RMgX$[9] or RM,[10] with quinoline. The action of sodamide on quinaldine[11] was employed in the preparation of α-*n*-butylquinoline, this reaction being followed by treatment with *n*-propyl bromide.

Reduction to the tetrahydroquinolines was accomplished by means of metallic sodium in boiling ethyl alcohol,[12,13] since this method besides giving excellent yields is very easily carried out.

Synthesis of Compounds

Tetrahydroquinoline.—Eastman Kodak Co. synthetic practical quinoline, purified by fractionation, was reduced with a seven times excess of metallic sodium in boiling absolute ethyl alcohol. The resulting solution was diluted with water, made acidic with hydrochloric acid and the alcohol removed by heating under a water pump vacuum. The base was freed with solid sodium hydroxide and extracted with ether. Tetrahydroquinoline was recovered in a yield of 85%, b. p. 126° (18 mm.). The hydrochloride melted at 180–181°.

α-Methyltetrahydroquinoline.—Redistilled Eastman quinaldine was reduced exactly as was quinoline. A 70% yield of α-methyltetrahydroquinoline, b. p. 125° (17 mm.), was obtained. The hydrochloride melted at 195–196°.

α-Ethyltetrahydroquinoline.—α-Ethylquinoline was prepared in 20% yield byh eating 0.25 mole of ethylmagnesium bromide for three hours in a sealed bomb at 155° with 0.22 mole of quinoline.[9] The recovered product boiled at 110–112° at 6 mm. The picrate melted at 145–146°.

Reduction with sodium and alcohole gave a 62% yield of α-ethyltetrahydroquinoline, b. p. 110–113° (5 mm.).

Anal. Calcd. for $C_{11}H_{15}N$: N, 8.70; C, 81.90; H, 9.32. Found: N, 8.79, 8.90; C, 81.6, 82.0; H, 9.47, 9.47.

The picrate, prepared in absolute ether, melted at 119–120°. Reher[14] states that the salts of this base are amorphous but the picrate prepared here was not and gave melting point depressions when mixed with the picrate of α-ethylquinoline and with picric acid.

α - *n* - Butyltetrahydroquinoline.—α - *n* - Butylquinoline was prepared by the action of 10 g. of sodamide on 0.105 mole of quinaldine[11] followed by treatment with 0.105 mole of *n*-propyl bromide. The base was isolated in a yield of 42%, b. p. 145–146° (11 mm.). The picrate melted at 163–164°. Reduction with sodium and alcohol gave α-*n*-butyltetrahydroquinoline in 55% yield, b. p. 138° (6 mm.).

Anal. Calcd. for $C_{13}H_{19}N$: N, 7.41; C, 82.54; H, 10.05. Found: N, 7.32, 7.39; C, 82.6, 82.8; H, 9.97, 9.87.

The picrate would not precipitate. The *p*-bromobenzenesulfonamide, recrystallized from petroleum ether, melted at 160–160.5°.

α-Phenyltetrahydroquinoline.—Phenyllithium was prepared in ether according to procedure "C" of Gilman.[15] After filtering off the excess lithium by means of a glass wool plug, an equivalent amount (0.07 mole) of quinoline was added. Hydrolysis with aqueous ammonium chloride, extraction with ether and distillation yielded the 1,2-dihydro compound,[10] which was dehydrogenated to α-phenylquinoline by distillation from zinc dust. The yield was 85%, the base melting at 82.5° after recrystallization from alcohol. The picrate melted at 188.5–189° and the *p*-bromobenzenesulfonamide at 190–191°.

Sodium and alcohol reduction[16] gave α-phenyltetrahydroquinoline in 73% yield, b. p. 196° (8 mm.). The picrate, prepared by evaporating to dryness an ethereal solution of equivalent amounts of the base and picric acid and recrystallizing from alcohol, melted at 129°. The *p*-bromobenzenesulfonamide melted at 201–202°.

(1) Bredig, *Z. physik. Chem.*, **13**, 191 (1894).
(2) Hahn and Klockmann, *ibid.*, **A146**, 373 (1930).
(3) Goldschmidt and Mathiesen, *ibid.*, **119**, 439 (1926).
(4) Kolthoff, *Biochem. Z.*, **162**, 289 (1925).
(5) Walker and Aston, *J. Chem. Soc.*, **67**, 576 (1895).
(6) Felsing and Biggs, THIS JOURNAL, **55**, 3624 (1933).
(7) Goodhue and Hixon, *ibid.*, **56**, 1329 (1934).
(8) Kirchner, "Insecticidal Action of Some Substituted Pyrrolidines," Ph.D. Thesis, Iowa State College, 1939.
(9) Bergstrom and McAllister, THIS JOURNAL, **52**, 2845 (1930).
(10) Ziegler and Zeiser, *Ann.*, **485**, 174 (1931).
(11) Tchitchibabine, *Bull. soc. chim.*, [5] **3**, 1607 (1936); *Rec. trav. chim.*, [6] **57**, 582 (1938).
(12) Kaku, *J. Pharm. Soc. Japan*, **48**, 693 (1928); *C. A.*, **23**, 392 (1929).
(13) Koenigs, *Ber.*, **14**, 100 (1881).
(14) Reher, *Ber.*, **19**, 2996 (1886).
(15) Gilman, Zoellner and Selby, THIS JOURNAL, **55**, 1252 (1933).
(16) Since the completion of this manuscript we have found that platinum on zirconium oxide catalyst, prepared by The American Platinum Works, will reduce α-phenylquinoline to α-phenyltetrahydroquinoline, while the platinum oxide of Adams and Shriner will reduce α-phenylquinoline to α-cyclohexyldecahydroquinoline.

α-*p*-Tolyltetrahydroquinoline.—In exactly the same manner as with α-phenylquinoline, α-*p*-tolylquinoline was prepared from *p*-tolyllithium and 0.13 mole of quinoline. Distillation from zinc dust and fractionation at 190° and 3 mm. pressure gave the base in the theoretical yield. After recrystallization from alcohol, crystals melting at 83° were obtained. The picrate melted at 198.7°.

α-*p*-Tolyltetrahydroquinoline was prepared for the first time by reduction of the corresponding quinoline in 73% yield. It was an almost colorless, viscous liquid, b. p. 210° (14 mm.).

Anal. Calcd. for $C_{16}H_{17}N$: N, 6.28; C, 86.10; H, 7.62. Found: N, 6.41, 6.39; C, 86.20, 86.25; H, 7.81, 7.58.

The picrate after several recrystallizations from alcohol melted at 134–134.5°.

α-*o*-Tolyltetrahydroquinoline.—α-*o*-Tolyllithium, prepared from 0.15 mole of *o*-iodotoluene and an excess of lithium, was treated with 19 g. of quinoline and gave α-*o*-tolylquinoline in 90% yield. Nitrobenzene was used for the dehydrogenation.[10] This base was a heavy oil that solidified on cooling, b. p. 197° (4 mm.). Purification was effected through the picrate. Regeneration with dilute sodium hydroxide yielded crystals that melted at 76–76.2° after being deposited from an ethereal solution.

Anal. Calcd. for $C_{16}H_{13}N$: N, 6.39. Found: N, 6.32, 6.30.

The picrate melted at 176°.

The corresponding tetrahydro compound solidified on cooling, b. p. 200–202° (6 mm.). Recrystallization from 70% alcohol gave α-*o*-tolyltetrahydroquinoline, in 85% yield, melting at 69.5°. A mixed melting point determination with α-*o*-tolylquinoline showed a depression to 45–48°.

Anal. Calcd. for $C_{16}H_{17}N$: N, 6.28; C, 86.10; H, 7.62. Found: N, 6.36, 6.27; C, 85.90, 85.90; H, 7.64, 7.75.

The picrate could not be obtained. The *p*-bromobenzenesulfonamide melted at 193–193.5°.

α-2-Mesityltetrahydroquinoline.—2-Mesityllithium, prepared from 0.166 mole of 2-bromomesitylene and lithium, was treated with 21 g. of quinoline in the way described. After dehydrogenation by means of nitrobenzene, α-2-mesitylquinoline was isolated in a yield of 25%, b. p. 200° (4 mm.). Considerable quantities of bromomesitylene were recovered. The base was recrystallized from petroleum ether and then melted at 69–69.5°.

Anal. Calcd. for $C_{18}H_{17}N$: N, 5.66. Found: N, 5.45, 5.65, 5.64.

The picrate prepared in absolute ether melted at 216.5°.

Reduction gave α-2-mesityltetrahydroquinoline in 83% yield as a heavy, very viscous liquid, b. p. 218° (6 mm.).

Anal. Calcd. for $C_{18}H_{21}N$: N, 5.57; C, 86.06; H, 8.37. Found: N, 8.50, 8.50; C, 86.10, 86.10; H, 8.20, 8.34.

The picrate melted at 164.5–165°.

Measurements of Ionization Constants.—The method used here is the same as that previously used by Goodhue[7] in this Laboratory. The hydrogen-ion concentrations of half-neutralized solutions of the bases in absolute methyl alcohol were determined by means of the normal hydrogen electrode in conjunction with a vacuum tube potentiometer.

The calomel half-cells employed were of the sealed Schollenberger type[17] and were prepared in duplicate using 0.1 *f* sodium chloride in absolute methanol. They were standardized by means of silver–silver chloride electrodes prepared in triplicate both by the method of Harned (type 2)[18] and by that of Rule and La Mer.[19] This latter method, involving the decomposition of a paste mixture of silver oxide and silver chlorate, was found to be more convenient although reproducible results were obtained by both procedures.

Platinum black was deposited on small platinum flags and used as the hydrogen electrodes. These were prepared and used in duplicate.

The purified bases were sealed in glass ampoules for weighing except the α-*o*-tolyltetrahydroquinoline which, being a solid, was weighed in a stoppered weighing bottle. All solutions were made by weight and the concentrations are expressed in molalities.

TABLE I

E. M. F. OF CELLS FOR A SERIES OF ALPHA-SUBSTITUTED TETRAHYDROQUINOLINES IN METHANOL

Pt/H_2 (1 atm.) Amine//NaCl (0.1 *f*), Hg_2Cl_2/Hg salt

α-Substituted radical	Total concn., molal	E. m. f. corr. to 760 mm.	$-\log a_H$	$pK_{B_{CH_3OH}}$
2-Mesityl	0.2710	0.3366	3.78	12.93
	.0385	.3389	3.82	12.89
o-Tolyl	.0378	.3806	4.53	12.18
	.0303	.3802	4.53	12.18
Phenyl	.0407	.3838[a]	4.52	12.19
	.0275	.3859[b]	4.55	12.16
p-Tolyl	.0283	.3981[a]	4.76	11.95
	.0390	.3987[b]	4.77	11.94
H	.0507	.4559	5.81	10.90
	.0370	.4562	5.81	10.90
Methyl	.0240	.4544	5.79	10.92
	.0538	.4607[a]	5.82	10.89
Ethyl	.0410	.4569[a]	5.86	10.85
	.0475	.4565	5.82	10.89
n-Butyl	.0514	.4457	5.63	11.08
	.0450	.4460	5.63	11.08

[a,b] The e. m. f. values were measured using a calomel half-cell of 0.1134 v. except those marked "*a*" in which the value was 0.1174 and those marked "*b*" in which the value was 0.1171 when referred to the normal hydrogen electrode.

The results of the e. m. f. determinations are shown in Table I. The method of calculation is the same as for primary amines in water solutions. The hydrogen-ion activities were calculated from the equation

$$-\log a_H = (E - E_{calomel})/0.059$$

As noted in Table I, the potentials of the calomel cells were 0.1134, 0.1171, and 0.1174 volt.

Since in half-neutralized solutions of amines

(17) Schollenberger, *Ind. Eng. Chem.*, **17**, 649 (1925).
(18) Harned, THIS JOURNAL, **51**, 416 (1929).
(19) Rule and La Mer, *ibid.*, **58**, 2339 (1936).

the degree of hydrolysis becomes equal to the hydrogen-ion activity, then

$$K_{B_{CH_3OH}} = K_{CH_3OH/H \text{ ion activity}}$$

and

$$K_{B_{CH_3OH}} = -\log K_{CH_3OH} - (-\log a_H) = 16.71 - (-\log a_H)$$

The dissociation constant of methyl alcohol was taken as 1.95×10^{-17}.[20]

The ionization constants of the α-substituted quinolines could not be measured by this method because of reduction of the unsaturated bases. Goodhue encountered the same difficulty in attempting to use the hydrogen electrode in measuring the ionization constants of α-substituted pyrrolines in alcohol.[7] Reduction does not occur so readily in aqueous solutions. Felsing and Biggs[6] used the hydrogen electrode to measure the constants for some methylquinolines in water and Starr[21] used this method for some pyrrolines, also in aqueous solution.

Discussion

In Fig. 1 the ionization constants of the α-substituted tetrahydroquinolines have been plotted as functions of the electron sharing ability of the radicals. For purposes of comparison the curves are included for the primary amines measured by Goodhue[7] and for the α-substituted pyrrolidines measured by Goodhue[7] and by Kirchner.[8] The radicals have been placed along the x axis in the way that they were initially arranged by Hixon and Johns[22] from the ionization constants in water of a series of primary amines.

An inspection of these curves shows that the substitution of various groups in the tetrahydroquinoline nucleus affects the ionization constants in exactly the same manner as did substituting the same groups in the primary amines and in the pyrrolidine nucleus. This is to be expected if the substituent radicals affect the polar properties of these amines by means of their valence electrons.

Curve (1) for the pyrrolidines and curve (111) for the tetrahydroquinolines are of the same shape and their difference in slope from the primary amine curve represents the effect of having the substituent radical one carbon removed from the polar group.

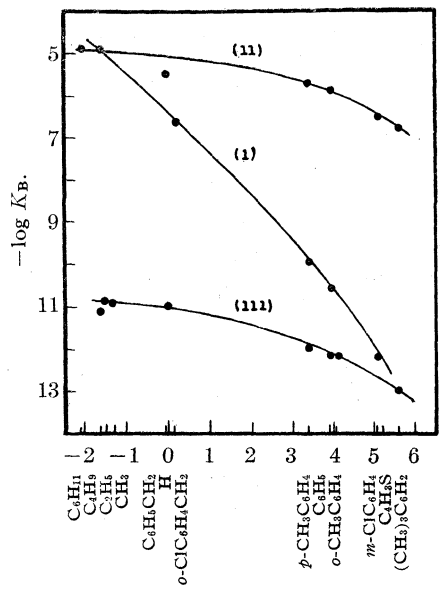


Fig. 1.—The ionization constants of various types of amines in absolute methanol plotted as functions of the electron sharing ability of the organic radicals. Curve (1) is for primary amines, (11) for α-substituted pyrrolidines, and (111) for α-substituted tetrahydroquinolines.

Summary

1. The ionization constants of a series of α-substituted tetrahydroquinolines have been determined in absolute methanol. The substituent radicals were: H, methyl, ethyl, *n*-butyl, phenyl, *o*-tolyl, *p*-tolyl and 2-mesityl.

2. These constants plotted against electron sharing ability functions give a curve similar to that for a series of α-substituted pyrrolidines previously reported.

3. α-Substituted quinolines prepared for the first time were the *o*-tolyl and the 2-mesityl. New α-substituted tetrahydroquinolines include *n*-butyl, *p*-tolyl, *o*-tolyl, and 2-mesityl.

AMES, IOWA RECEIVED AUGUST 23, 1939

(20) Buckley and Hartley, *Phil. Mag.*, [7] **8**, 320 (1929).
(21) Starr, Bulbrook and Hixon, THIS JOURNAL, **54**, 3971 (1932).
(22) Hixon and Johns, *ibid.*, **49**, 1786 (1927).

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE UNIVERSAL OIL PRODUCTS COMPANY]

Hydrogenation of Acetophenone to Cyclohexylmethylcarbinol in the Presence of Solvent

BY V. N. IPATIEFF AND B. B. CORSON

Acetophenone can be selectively hydrogenated in isopentane solution to a 70% yield of cyclohexylmethylcarbinol[1] but the conditions must be controlled carefully.

Experimental

A 3350 cc. bomb was charged with 200 cc. of acetophenone, 400 cc. of isopentane, 40 g. of nickel catalyst,[2] and 100 kg./sq. cm. of hydrogen. The bomb was rotated for six hours at 100°. The product was distilled through a Podbielniak column with a reflux ratio of 10/1. The isopentane was first evaporated. The residue consisted of 20% (by vol.) of ethylbenzene (b. p. 135–137°; $n^{20}D$ 1.4925), 7% of intermediate fraction (b. p. 137–189°; $n^{20}D$ 1.4874), 70% of cyclohexylmethylcarbinol (b. p. 189–190°; $n^{20}D$ 1.4688), and 3% of bottoms ($n^{20}D$ 1.4940).

The ethylbenzene fraction contained about 1% of ethylcyclohexane on the basis of its refractive index and solubility in cold 15% fuming sulfuric acid.

The redistilled cyclohexylmethylcarbinol showed the following constants: b. p. 189.4–189.8° at 761 mm.; $n^{20}D$ 1.4677; d^{20}_4 0.925. *Anal.* Calcd. for $C_8H_{16}O$: C, 74.9; H, 12.6; mol. wt., 128. Found: C, 74.8; H, 12.5; mol. wt., 126.

When an isopentane solution of acetophenone was heated for six hours at 75°, the product was a mixture of 8% of ethylbenzene and 92% of an approximately 50/50 mixture of phenylmethylcarbinol and cyclohexylmethylcarbinol, and when the hydrogenation temperature was 50° the product was mainly unchanged acetophenone.

In the absence of solvent, and using reduced copper as catalyst[3] at 225°, 95% of the product was ethylbenzene. Using cyclohexane as solvent at 100°, the product was a mixture of ethylbenzene, the two alcohols, and acetophenone.

Summary

Acetophenone has been selectively hydrogenated in isopentane solution to cyclohexylmethylcarbinol.

(1) Cyclohexylmethylcarbinol has previously been made through the Grignard reaction (Bouveault, *Bull. soc. chim.*, [3] **29**, 1049 (1903); Sabatier and Mailhe, *Compt. rend.*, **139**, 343 (1904).

(2) The catalyst was a kieselguhr supported nickel (about 70% of nickel) which had been reduced at 430°.

(3) Prepared by reduction in hydrogen at 225° and ordinary pressure of Kahlbaum–Schering granular copper oxide (nickel content, 0.1%).

RIVERSIDE, ILLINOIS RECEIVED SEPTEMBER 1, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF BOTANY, UNIVERSITY OF MINNESOTA]

Pseudo-eleostearic Acid[1]

BY J. P. KASS AND G. O. BURR

Moore[2] has shown that prolonged saponification of linseed oil induces a partial isomerization of its spectroscopically inactive liquid linolenic acid to an absorptive crystalline substance, m. p. 77°, bearing a striking resemblance to the eleostearic acids in the position and intensity of its absorption band and in its failure to form an ether-insoluble hexabromide.

In the course of a spectroscopic study of isomerism in the fatty acids[3] we found it expedient to determine the constitution of this compound, the oxidation products of which, consisting of sebacic, oxalic and butyric acids, establish its structure as 10,12,14-octadecatrienoic acid-1. The shift to a conjugated configuration induced by alcoholic alkalies is thus analogous to the rearrangement of linoleic acid under similar treatment.[4] Like the eleostearic acids (9,11,13-octadecatrienoic acids),[5] the new isomer adds only two molecules of bromine easily, the introduction of the third requiring considerable time or exposure to ultraviolet light. However, its maleic anhydride addition product is not homogeneous and could not be separated into its clearly defined individual components. This points to the geometric configuration of the parent substance as the *trans-trans-trans* or *trans-cis-trans* isomer, either of which may form more than one condensation product.[6]

Since the completion of this investigation, we

(1) This work was supported by grants from the Hormel Foundation, the National Live Stock and Meat Board, and the Graduate School of the University of Minnesota.

(2) Moore, *Biochem. J.*, **31**, 142 (1937).

(3) Kass, Miller, and Burr *Proc. Am. Soc. Biol. Chem.*, **32**, 66 (1938).

(4) Kass, Miller and Burr, THIS JOURNAL, **61**, 482 (1939).

(5) Böeseken, *et al.*, *Rec. trav. chim.*, **46**, 619 (1927).

(6) Morrell and Davis, *Trans. Faraday Soc.*, **32**, 209 (1936).

have been informed[7] that in an independent preliminary study of the oxidation products of the new acid, designated by Moore[7] as "pseudo-eleostearic acid," Prof. T. P. Hilditch obtained sebacic acid and small amounts of monobasic acids having in impure condition an apparent equivalent of about 106. If the latter is assumed to be valeric acid (neutral equiv. 102), an allenic structure is suggested, which is contradicted by the pronounced absorption band at 270 mμ characteristic of the triply conjugated eleostearic acids.[8,9]

Moore[7] considers the spectroscopic activity and the production of sebacic acid indicative of the reorientation of the unsaturated linkages from the 9,12,15 positions of linolenic acid to the 10,12,14 configuration of pseudo-eleostearic acid.

Experimental

Formation of Pseudo-eleostearic Acid.—Moore's uncertain and prolonged saponification procedure, requiring the refluxing of the fatty acids with aqueous alcoholic potash for from seven to twenty-five days,[2] may be advantageously shortened to a matter of hours or minutes by the substitution of anhydrous butanol[4] or ethylene glycol, respectively, as the reaction medium, using approximately equal weights of the fatty acids and the alkali in four volumes of the solvent. The isomerization is completed in from six to twenty-four hours with the former and in from thirty to one hundred and twenty minutes with the latter, the reaction mixture then being acidified and the butanol removed by either steam or vacuum distillation and the glycol by simply washing the acids with water. The usual precautions against oxidation must be observed throughout, and the course of the reaction may be followed spectroscopically, dienometrically, or iodometrically, being considered complete when the absorption bands of the isolated aliquot samples of the mixed fatty acids reach a maximum at 230 and 270 mμ, their diene number exceeds 20, or their iodine number falls to about 150.

Six hundred and twenty-five grams of linseed oil fatty acids from which the solid acids were removed by two crystallizations from ligroin at −18° was refluxed under nitrogen for two hours with an equal weight of potassium hydroxide in 2.5 liters of anhydrous ethylene glycol. The mixture was then cooled, several hundred cc. of water added, and the refluxing resumed for a brief period to saponify the esters. (This step is essential when butanol is used as the solvent, since it shows a pronounced tendency toward esterification in the anhydrous state.) The soap solution was acidified, the fatty acids extracted with 1.5 liters of ligroin, and thoroughly washed with water. The dried ligroin solution was left overnight at −18°, when it deposited 25 g. of practically pure pseudo-eleostearic acid.

Pseudo-eleostearic Acid.—The acid precipitated easily from 85% alcohol as feathery crystals and from hexane as glistening scales. It was relatively insoluble in petroleum ether (30–35°), 1 g. requiring about 175 cc. for solution at 0°. Its m. p. was 77–79° (uncorr.), repeated crystallizations failing to narrow the melting point range, which was rapidly depressed and widened by exposure of the acid to air, so that three trials within two hours showed melting point ranges beginning successively at 75.5, 71.5, and 69° with a final maximum of 75°. The acid showed remarkable susceptibility to oxidation, quickly acquiring an acridly rancid odor and even its ligroin solutions becoming opalescent on boiling.

Anal.[10] Calcd. for $C_{18}H_{30}O_2$: C, 77.70; H, 10.79. Found: C, 77.78; H, 11.02.

The iodine number determinations by the Wijs or Hanus method gave values intermediate between two and three double bonds, rising with time and showing the recurring end-point and precipitation of iodine characteristic of the conjugated fatty acids.[11]

Hydrogenation of Pseudo-eleostearic Acid.—A mixture of the acid and platinum oxide catalyst in acetic acid was shaken for two hours in an atmosphere of hydrogen at room temperature and 40 lb. (3 atm.) pressure. The product was precipitated with water and after one recrystallization from 85% alcohol melted at 69.5–70°, showing no depression with a sample of authentic stearic acid.

Methyl Pseudo-eleostearate.—Ten grams of the acid was dissolved in 100 cc. of 4% methyl alcoholic sulfuric acid and left overnight at room temperature. The solution was then refluxed briefly and finally extracted with ligroin from which 7 g. of the methyl ester, m. p. 41° after recrystallization from methanol or ligroin, precipitated on cooling. The residue was a yellow oil which partially solidified at 0° and yielded an additional 1.5 g. of impure ester. Saponification of the sharply melting ester produced the parent acid, the m. p. of which again was 77–79°. This spread evidently is due to the greater susceptibility of the acid to oxidation.

Disruptive Oxidation of Methyl Pseudo-eleostearate.—A modification of the procedures of Armstrong and Hilditch[12] and of Haworth[13] was used; 5 g. of the ester was dissolved in 130 cc. of purified acetone and 75 g. of powdered potassium permanganate added carefully. The mixture was boiled under reflux and an additional 10 g. of the oxidizing agent added to produce a permanent pink coloration. After three hours, the acetone was evaporated completely, the residue extracted four times with dilute potassium hydroxide solution and the alkaline extract concentrated somewhat. The green extract was decolorized with gaseous sulfur dioxide, acidified with a small quantity of dilute sulfuric acid and distilled to the incipient precipitation of the salts. The residue was thoroughly extracted with ether, which on evaporation left 1.5 g. of a practically white solid contaminated with a yellowish oil, the latter being removed by crystallization from water and charcoal to give an acid with a neutral equivalent of 101.5 and m. p. 131–133°. One recrystallization narrowed the melting

(7) Moore, private communication to G. O. Burr, March 24, 1939.

(8) Dingwall and Thompson, THIS JOURNAL, **56**, 899 (1934).

(9) Hulst, *Rec. trav. chim.*, **54**, 639, 644 (1935).

(10) All micro analyses herein reported were performed by Mr. J. W. Opie of the Department of Organic Chemistry.

(11) Böeseken and Gelber, *Rec. trav. chim.*, **46**, 158 (1927).

(12) Armstrong and Hilditch, *J. Soc. Chem. Ind.*, **44**, 43T (1924).

(13) Haworth, *J. Chem. Soc.*, 1456 (1929).

point to 132–133°, no depression with authentic sebacic acid, m. p. 133°, neut. equiv., 101.07.

The aqueous residue was extracted repeatedly with benzene, then treated with a few drops of bromine, cooled, and the precipitated salts filtered off and discarded. The sulfates were precipitated with barium chloride, the filtrate made alkaline, then acidified with acetic acid and treated with purified calcium nitrate. After several hours the fine precipitate was filtered off, dissolved in hydrochloric acid and reprecipitated with ammonium hydroxide. The white powder, 0.76 g., reduced acid permanganate instantly and left a residue of 36.67% after ignition (calcd. for $CaC_2O_4 \cdot H_2O$, 38.38%).

The distillate, which possessed a pronounced odor of butyric acid, was made alkaline and evaporated to a small volume. It was then acidified, thoroughly extracted with ether, the ether extract washed once with water, and dried overnight with Drierite after preliminary drying over sodium sulfate. Evaporation of the ether left 0.5 g. of a liquid, 0.4 g. of which distilled at 165°. This distillate was miscible with water in all proportions, had a neutral equivalent of 80 and formed a *p*-toluidide, m. p. 69–71° (butyric acid, neut. equiv. 88, *p*-toluidide m. p. 73°).

Bromination of Pseudo-eleostearic Acid.—A solution of 1.5 g. of the acid in 250 cc. of petroleum ether cooled to 0° was brought to a distinct orange color with bromine and left at 0° for three hours. About 0.1 g. of a white powder precipitated, melting at 90–95° from hexane solution. Recrystallization from 1–5 ether–ligroin solution raised the m. p. to 90–100° and further fractionation of the powder from hexane showed its major component to be a crystalline substance, m. p. 104–104.5°.

Anal. Calcd. for $C_{18}H_{30}O_2Br_4$: C, 36.14; H, 5.02. Found: C, 35.73; H, 4.67.

The filtrate from the tetrabromides was treated with an additional portion of bromine and exposed to direct sunlight at room temperature. After twenty-four hours a partially crystalline precipitate appeared. Three successive extractions with boiling hexane yielded a total of 0.25 g. of white powders melting at (I) 125–135°, (II) 140–145°, and (III) 145–151°, respectively. The residue was taken up in ligroin (b. p. 90–95°) and finally recrystallized from ether, in which it is easily soluble, precipitating only in the ice–hydrochloric acid bath as scaly crystals, m. p. 152°. The ether mother liquor was evaporated and the residue combined with the hexane extract III, the mixture being recrystallized from ether to yield an additional crop of solid of m. p. 152°. Both portions were combined and recrystallized again from ether to yield 90 mg. of a crystalline material, m. p. 152–152.5°.

Anal. Calcd. for $C_{18}H_{30}O_2Br_6$: C, 28.50; H, 3.96. Found: C, 28.44; H, 4.17.

The hexane extracts I and II were combined and recrystallized from ligroin (b. p. 90–95°) without much improvement in melting point. However, 15 mg. of a crystalline substance of m. p. 148° was obtained from a 1 : 1 ether–petroleum ether solution. This was evidently the impure hexabromide, the mixed m. p. being 148–152°. Evaporation of the original ligroin mother liquor left only liquid bromides.

The hexabromide is apparently the only solid addition product obtained when pseudo-eleostearic acid is brominated in ultraviolet light; 0.4 g. of the acid in 15 cc. of purified carbon tetrachloride contained in a quartz test-tube was brominated at 0° to an orange color; an excess of one-third of the bromine consumed was added and the solution illuminated with a mercury arc at 50 cm. for one hour. The excess bromine was removed with amylene, the solvent evaporated at the vacuum pump, and the residual oil worked up with hexane. After twelve hours in the icebox, 50 mg. of a crystalline precipitate was obtained, melting at 145–148° after crystallization from ligroin (b. p. 90–95°). One recrystallization from ether raised the melting point to 152.5°. That ultraviolet light induces no isomerization of the parent acid was shown by the unaltered melting point and solubility behavior of a sample of pseudo-eleostearic acid similarly illuminated in a quartz container.

Addition of Maleic Anhydride.—An intimate mixture of equimolar quantities of pseudo-eleostearic acid and maleic anhydride was heated under nitrogen to 145°, when the yellow color of the melt was discharged. The reaction product set to a tacky, plastic mass on cooling. This was subdivided by repeated extraction with boiling hexane into a soluble granular solid and an insoluble sirup. The solid was redissolved several times in hexane, the less soluble sirup being removed each time. The final product was a white, poorly friable powder, sintering at 75° and melting at 77°, the melt becoming clear at 82°.

Anal. Calcd. for $C_{22}H_{32}O_5$: C, 70.21; H, 8.51. Found: C, 69.71; H, 8.21.

The residual sirup set to a brittle solid after complete evacuation of the solvent, and could then be ground to a coarse granular powder similar in melting point and appearance, except for a yellowish tinge, to the hexane extract. Both fractions were extremely soluble in alcohols, ether, acetic acid, and acetone, and were precipitated with ligroin as sirups that became solid on complete removal of the solvent. When the pseudo-eleostearic acid was heated with an excess of maleic anhydride either in the solid state or in a solvent, the reaction mixture remained liquid until the excess of reagent was removed either by distillation or with water, after which the characteristics of the product were those described.

Summary

Linolenic acid is partially converted by alcoholic alkalies into pseudo-eleostearic acid, 10,12,14-octadecatrienoic acid, m. p. 79°, methyl ester, m. p. 41°.

Pseudo-eleostearic acid forms mixed maleic anhydride addition products and mixed bromides, among them a tetrabromide, m. p. 104.5°, and a hexabromide, m. p. 152.5°.

MINNEAPOLIS, MINN. RECEIVED JULY 14, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY, UNIVERSITY OF CALIFORNIA]

The Preparation and Asymmetric Reduction of β-Methylcinnamic Acid

BY DAVID LIPKIN AND T. D. STEWART

H. Erlenmeyer[1] brominated the hydrocinchonine and glucamine salts of cinnamic acid and found that the cinnamic acid dibromide was optically active. The glucamine salt was brominated using only the solid salt, but the hydrocinchonine salt was brominated in chloroform solution as well, under which condition activity of the isolated dibromo acid corresponding to 8% asymmetric synthesis was observed. These experiments have been repeated by us and the results verified.

It is apparent that in chloroform solution the amine and acid are united in such a way as to produce a coupling of the electrical fields of both molecules which extends beyond the three atoms, –N–H–O–, involved in a possible hydrogen bond and includes the asymmetric center of the base and the olefinic bond of the acid. This is not surprising in view of the associated character of such salts in chloroform, but it indicates that the mutual electrical inductions in such salts may be as strong as the intramolecular induction in esters.[2] Vavon and Jakubowicz[3] studied the platinum-catalyzed hydrogenation of six optically active esters of β-methylcinnamic acid. They found that the β-phenylbutyric acid isolated after saponification had a specific rotation in benzene (λ = 5461 Å.) varying from +13.3 to −6.1°, corresponding to as much as 19% asymmetric synthesis.

The present paper describes improved syntheses of β-methylcinnamic and β-(α-naphthyl)-cinnamic acids, and their asymmetric reduction as hydrocinchonine salts.

Preparation of β-Methylcinnamic Acid.—The method of Stoermer, Grimm and Laage[4] has been modified to ensure reproducibility and greater purity of product. Acetophenone (240 g.), 20–30 mesh granulated zinc (196 g.) and sodium-dry benzene (850 ml.) were placed in a 3-liter three-necked flask fitted with a reflux condenser, mercury-sealed stirrer and a dropping funnel. All outlets to the air were closed by drying tubes. The mixture was heated to gentle refluxing on a steam-bath and then the addition of 234 g. of freshly distilled ethyl bromoacetate dissolved in 150 ml. of dry benzene started. This addition was carried out over a period of ten to twelve hours, with continual refluxing and stirring; the heating and stirring were then continued for another six hours. Under these conditions one mole of zinc reacts per mole of the other reagents.

$$C_6H_5COCH_3 + BrCH_2CO_2R \xrightarrow{Zn} C_6H_5C(OZnBr)(CH_3)CH_2CO_2R$$

A competing condensation reaction using one-half this amount of zinc, producing succinic ester, is inhibited by keeping a low concentration of bromoacetic ester and through the use of a large excess of zinc. Similarly reaction of the intermediate zinc derivatives with the ester group likewise is retarded by the slow addition of the ester.

The cooled reaction mixture was decanted from the unused zinc and washed with 400 ml. of 6 *N* hydrochloric acid and 200 ml. of water. Without drying, the mixture was then refluxed by means of an oil-bath in a 3-liter flask fitted with a Dean and Stark[5] tube which was equipped with a stopcock to remove water collected from the reflux. When the water level in the tube had remained constant for half an hour, the water was drawn off and 5 ml. of phosphorus oxychloride added to the flask. Refluxing was then continued until the water collected was again constant (about one-half hour). This portion of water represents the water formed in the catalytic dehydration of the ester and is a good indication of the eventual yield. The benzene was now allowed to distil off, taking care that the oil-bath did not rise above 130° and that prolonged distillation was avoided.

The ester residue was hydrolyzed by adding two liters of 1 *N* methanolic potassium hydroxide and 45 ml. of 40% aqueous potassium hydroxide and refluxing for one and one-half hours. The methanol was then removed by steam distillation and the cooled aqueous residue extracted with ether to remove alkali-insoluble by-products. The latter represented a large portion of the reaction products and contained little acetophenone as such. The aqueous layer was added to one liter of ether and then acidified with 450 ml. of ice-cold 6 *N* sulfuric acid. Two additional ether extracts of 200 ml. each were made and the combined ether extracts dried and the ether distilled off. The crude β-methylcinnamic acid was distilled at 1 mm. pressure, or less, using a 500-ml. Claisen flask with a wide side arm: b. p. (0.6 mm.) 124–127°; b. p. (1 mm.) 135–136° uncorr.; yield 133.6 g. or 41%.

The vacuum distilled product was a slightly yellowish, crystalline solid containing a considerable amount of low-melting material, probably a solid solution of *cis* and *trans* isomers. To remove this, the product was placed in a 500-ml. wide-mouthed flask fitted with a reflux condenser and thermometer whose bulb rested on the bottom of the flask.

(1) H. Erlenmeyer, *Helv. Chim. Acta*, **13**, 731 (1930).

(2) The fact that racemic acids are resolved through fractional crystallization of their salts with active bases gives no evidence as to the molecular forces present in the individual molecules, as no resolution is found unless a crystalline phase separates.

(3) Vavon and Jakubowicz, *Compt. rend.*, **196**, 1614 (1933); *Bull. soc. chim.*, [4] **53**, 1111 (1933).

(4) Stoermer, Grimm and Laage, *Ber.*, **50**, 965 (1917). See also Rupe, *Ann.*, **369**, 321 (1909), and Nieuwland and Daly, THIS JOURNAL, **53**, 1842 (1931).

(5) Dean and Stark, *Ind. Eng. Chem.*, **12**, 486 (1920).

About 35 ml. of pentane was added and refluxed until the boiling point was constant. After cooling, the liquid phase was removed through an immersion filter and the pentane extraction repeated several times until successive extracts had the same boiling point. The remaining solid (the *trans* isomer) was dissolved in ligroin (b. p. 90–100°), using 225 ml. of solvent per 100 g. of acid, charcoal treated, and recrystallized; m. p. 98.4–98.7° corr.; yield, 89 g. or 27%. To remove any possible catalyst poison the product was recrystallized from aqueous methanol, 560 ml. of methanol and 720 ml. of water per 100 g. of acid.

None of the acid fractions gave the lemon-yellow color or intense violet color in concentrated sulfuric acid noted by the above authors and attributed to the stable and labile acids, respectively.

Preparation of β-(α-Naphthyl)-cinnamic Acid.—This acid was prepared by essentially the same procedure as used for the methyl derivative, substituting α-naphthyl phenyl ketone prepared by the method described by Fieser[6] for the acetophenone. The crude yield varied from 55–72%, and it is significant that the alkali-insoluble saponification product was nearly pure α-naphthyl phenyl ketone. The yield of acid was virtually 100% based on the ketone actually consumed. It was purified by crystallization from carbon tetrachloride, acetic acid or absolute ethanol; m. p. 213.1–214.0° corr.

Hydrocinchonine was prepared by catalytic hydrogenation of cinchonine, using palladous chloride as catalyst;[7] crystallization was from dioxane, m. p. 275° corr. (dec.); $[\alpha]^{22}D$ +214° (0.0223 *M* hydrocinchonine in 0.024 *M* aqueous HCl).

Reduction of Hydrocinchonine β-Methylcinnamate by Hydrogen.—The first reduction was carried out in an 0.0434 *M* solution of the salt in absolute ethanol, using 0.076 g. of Adams platinum oxide per each 100 ml. of solution. The catalyst was forty-eight days old. Hydrogen was introduced at a pressure of 41 lb. (3 atm.) per square inch, with vigorous shaking; the reaction was complete in four and one-half hours at room temperature. Special care was used to remove the dextrorotatory hydrocinchonine from the acid. After removing the ethanol by vacuum distillation, the residue was treated with benzene and excess dilute sulfuric acid at room temperature. Three successive acid extracts eventually showed no optical activity nor a test for alkaloid with $KBiI_4$. The optical activity of the benzene solution, assuming a quantitative reduction and recovery, indicated $[\alpha]^{20}_{5461}$ +5°. An alkaline extract of the benzene solution, using 0.1 *N* NaOH, gave an observed rotation of +0.062°, corresponding to $[\alpha]^{20}_{5461}$ +3°. Finally the free acid was recovered in benzene again and the benzene evaporated. The residue at constant weight amounted to 1.07 g. of sirupy liquid; dissolved in benzene at a dilution of 0.065 g./ml., α = +0.629° in a 2-dm. tube or $[\alpha]^{20}_{5461}$ +4.5°. This corresponds to about 8–9% asymmetric synthesis.

A second reduction was made under approximately the same conditions except that the hydrogen pressure was 760 mm., the temperature 25.0°, and using a catalyst twenty-four days old. The recovered β-phenylbutyric acid had an activity of $[\alpha]^{20}_{5461}$ +0.64° in benzene.

(6) Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., New York, N. Y., 1935, pp. 192–196.

(7) Heidelberger and Jacobs, THIS JOURNAL, **41**, 817 (1919).

Reduction of Hydrocinchonine β-(α-Naphthyl)-cinnamate.—The reduction was carried out in 0.05 *M* ethanol solution using 0.106 g. of catalyst in 100 ml. of solution. The temperature was 25.0° and the pressure of hydrogen 760 mm. The recovered reduced acid had an activity corresponding to $[\alpha]^{20}_{5461}$ −0.5° in chloroform solution.

Discussion

The poor and sometimes erratic yields in the Reformatsky reaction employed in these preparations may be attributed to condensations of the bromoacetic ester with itself, producing eventually water-soluble products after saponification. This is clearly indicated in the condensation using α-naphthyl phenyl ketone, in which the unsaponifiable fraction was largely unchanged ketone. The yield of desired condensation product was quantitative on the basis of used ketone, with complete disappearance of the bromoacetic ester and the quantitative consumption of zinc. In the case of acetophenone further side reactions are self-condensation to *sym*-triphenylbenzene (recovered in some experiments) and possibly Claisen-type condensation with the bromoacetic ester to form ketonic products. In this case the alkali-insoluble saponification product was not simply unused ketone, and the yields are uniformly poorer than in the condensation with the purely aromatic ketone. The slow addition of bromoacetic ester to the reaction mixture produces a consistent and apparently nearly maximum yield; the procedure is employable on any scale of operation.

The fact that heterogeneous hydrogenation of these alkaloid salts in alcohol solution leads to partial asymmetric synthesis of the reduced acids indicates that adsorption of these polar substances has not prevented the molecular inductions responsible for the specificity.

The authors wish to acknowledge the careful preparative work done on this problem by Mr. Wilbur Pearlson.

Summary

A procedure for the Reformatsky condensation of aromatic ketones and bromoacetic ester leading to maximum yields and applicable to any scale of operation is given.

The hydrocinchonine salts of β-methylcinnamic acid and β-(α-naphthyl)-cinnamic acid are catalytically reduced in ethanol solution by hydrogen to produce optically active β-phenylbutyric acid and β-(α-naphthyl)-hydrocinnamic acid, respectively.

BERKELEY, CALIF. RECEIVED JULY 17, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

The Asymmetric Reduction of β-Methylcinnamic Acid by *d*-Glucose in the Presence of Raney Nickel

BY T. D. STEWART AND DAVID LIPKIN

The reduction of β-methylcinnamic acid by *d*-glucose in alkaline solution[1] offers the possibility that the β-phenylbutyric acid produced is optically active. Using Raney nickel as a catalyst, and carefully controlled conditions, we have found the specific rotation of the product to be reproducible and to vary from $[\alpha]^{25}_{5461}$ +0.31° to −0.42° (benzene). The highest specific rotation observed for β-phenylbutyric acid is given by H. Rupe for D light, from which we estimate[2] the specific rotation of the pure *levo* form to be $[\alpha]^{20}_{5461}$ −68.5° (benzene). The present paper concerns itself with the factors producing these small but significant changes in the degree of asymmetric synthesis.

A summary of the results obtained and the experimental conditions is given in Table I. The table headings indicate the initial concentrations of the reactants and the order in which they were added. Columns 2, 3, and 4 give, respectively, the amount of Raney nickel used, expressed in grams per liter of reacting solution, and the time and temperature employed in its preparation from the nickel–aluminum alloy. The temperature specified is that of the oil-bath used for the digestion of the alloy with sodium hydroxide; the catalysts are correspondingly called "hot" or "cold," in reference to this temperature. The relative rates of reaction are shown in column 5, and the specific rotation of the product given in column 6.

Reproducibility of the results is shown in Expts 16, 24, and 26. A plot of the alkali consumed *vs.* time in these experiments showed absolute consistency of reaction rate. Polarimeter readings were accurate to 0.01° and the specific rotation is accurate to 0.03–0.04°. Experiments 2 and 17 differed in catalyst preparation, and to a minor extent in reagent concentrations.

Amount of Catalyst.—In Fig. 1 are plotted the data for two series of runs, Expts. 12, 8, 9, and Expts. 18, 24, 13, 21, in each of which the amount of identically prepared catalyst is varied. In the first series the "hot" catalyst was employed; in the second, the "cold" catalyst. It appears anomalous that increased amount of a given surface catalyst should alter the course of the reaction.[3]

TABLE I

EXPERIMENTAL CONDITIONS AND RESULTS

Expt.	Catalyst amt. (g./l.)	Prep. and amt. Time, hr.	Prep. and amt. Temp., °C.	Reaction time for 75% completion	Specific rotation $[\alpha]^{20}_{5461}$
Part A. Concentration and order of mixing: β-methylcinnamate 0.220 *M*; potassium hydroxide 0.330 *M*; *d*-glucose 0.440 *M*; nickel. Temperature of reaction 25°C.					
12	15	2	118	16 hr.	+0.02
8	30	2	118	2.3	− .35
9	60	2	118	0.7	− .39
18	5	72	20	5.0	− .27
16	10	50	20	1.2	− .30
24	10	72	20	1.0	− .25
26	10	72	20	1.0	− .25
13	30	122	20	0.4	− .09
21	60	72	20	.12	− .04
7	30	4	118	2.6	− .23
6	30	7	118	3.0	− .03
Part B. Same as Part A except temperature of reaction 0°; see Expt. 13.					
23	30	72	20	2.3	−0.03
Part C. Concentration same as Part A; order of mixing: salt, alkali, nickel, glucose. See Expts. 8 and 6. Temperature, 25°					
20	30	2	118	1.5	−0.13
22	30	7	118	2.3	− .25
Part D. Concentration and order of mixing: β-methylcinnamate 0.110 *M*; potassium hydroxide 0.137 *M*; *d*-glucose 0.165 *M*; nickel. Temperature 25°					
15	15	2	118	2.4(62%)	−0.19
28	15	4	118	2.8(62%)	− .11
17	15	7	118	4.9(62%)	+ .12
2	15	7	>118	6.5(62%)	+ .31
Part E. Concentrations one-half those of Part A, except that glucose was 0.165 *M* in Expt. 14. Temperature 25°					
14	30	2	118	1.4	−0.32
11	30	2	118	1.1	− .42

(1) Delépine and Horeau, *Compt. rend.*, **204**, 1605 (1937); *Bull. soc. chim.*, [5] **4**, 1524 (1937).

(2) H. Rupe, *Ann.*, **369**, 323 (1909), gives $[\alpha]^{20}_{D}$ −57.23° (benzene) as determined by resolution through the menthyl ester. Levene and Marker, *J. Biol. Chem.*, **93**, 761 (1931); **100**, 685 (1933), obtained $[\alpha]^{25}_{D}$ −46.8° (benzene) from the cinchonidine salt. After laborious crystallization of the quinine salt we have obtained a sample of acid of $[\alpha]^{25}_{D}$ −47.92 and $[\alpha]^{25}_{5461}$ −45.40° (benzene, 0.3280 g./10 ml.).

(3) It is obviously possible as Wieland, *Ber.*, **46**, 3327 (1913), pointed out, that catalytic dehydrogenation of an alcohol may be followed by catalytic hydrogenation of an acceptor of the hydrogen, and in the present case this could result in a symmetric rather than asymmetric reduction. The effects studied here are conceivably concerned with only a small fraction of the total reaction, or may represent the balance between two concurrent stereochemical processes.

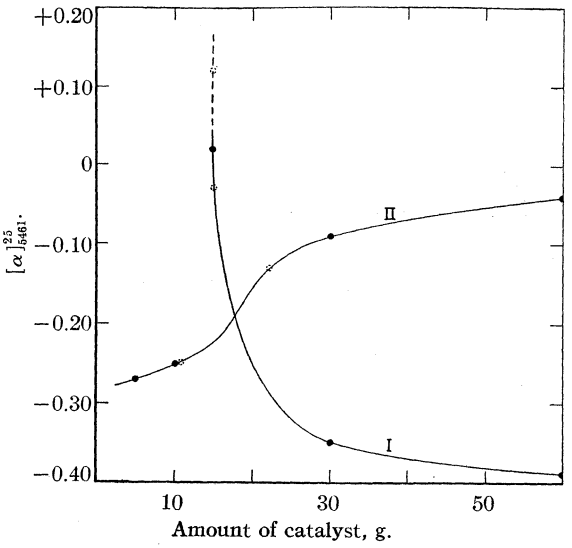


Fig. 1.—Curve I, data from Expts. 12, 8, 9; Curve II, data from Expts. 18, 24, 13, 21. Broken circles plot the specificity only found in Expts. 17, 6 (curve I) and Expts. 20, 22 (curve II), indicative of relative amount of effective catalyst present.

In an attempt to see whether actual concentrations rather than relative concentrations of the reactants were important, all concentrations (and amounts of catalyst) were halved (Expts. 9 and 11) without affecting the specificity appreciably. In all the experiments the ratio of catalyst to reactants increases during the reaction, and the ratio of reactants to each other changes; we are here concerned only with the integrated effect as measured.

A tentative explanation of the effect described in Fig. 1 is as follows. Consider two processes leading to dextro and levo products, P_d and P_l, respectively.

$$\text{Catalyst} + \beta\text{-methylcinnamate} \rightleftarrows C_1 \xrightarrow{\text{glucose}} P_d \quad \text{(A)}$$

$$\text{Catalyst} + \text{glucose} \rightleftarrows C_2 \xrightarrow{\beta\text{-methylcinnamate}} P_l \quad \text{(B)}$$

where C_1 and C_2 are reversibly adsorbed molecules. The ratio of the two products will depend upon the equilibrium or steady state values of C_1 and C_2 and the specific rates of the follow reactions. If the two adsorption processes are of such different rates compared to each other or to the rates of the respective follow reactions that the times required for the achievement of equilibrium or steady state values of C_1 and C_2 differ, then the time required for the over-all reaction becomes important. This is so because if the reaction time is short (large amount of catalyst) the reaction could be complete before the steady states are reached; but if the reaction time is long (small amounts of catalyst) both steady states could be established, leading to a different proportion of the two processes. A seeming independence of the specificity with amount of catalyst at high and low amounts displayed in Fig. 1 could be explained on this basis. The data cannot be used to make a rigid test of this hypothesis, partly because of the factor[3] mentioned above which obscures many effects such as induction periods and absolute rates of reaction, but there are some confirming facts yet to be mentioned. The two curves of Fig. 1, on this basis, suggest that the catalyst will differ in its relative rates of adsorption for the two reactants depending upon the mode of preparation. Thus the "hot" catalyst will be considered provisionally to adsorb glucose the more rapidly (process B) while the "cold" catalyst adsorbs cinnamate the more rapidly. There is no evidence that the "cold" catalyst produces a dextro product (process A) and it may lead only to a levo product when used in small amount and to a racemic product in large amount. On the other hand, the "hot" catalyst apparently participates in both processes.

Time of Catalyst Digestion.—In two series, Expts. 6, 7, 8, and Expts. 17, 28, 15, the nickel alloy was digested for periods of two, four, and seven hours. Concentrations of reactants differed in the two series but were constant within each series. In both cases the negative specific rotations of the products decrease linearly with the digestion time; in the second series this decrease actually results in a positive specific rotation (Expt. 17). This result can be correlated with the facts of the previous section through the simple assumption that continued digestion results in a sintering process that in effect reduces the amount of the catalyst. The destruction of the catalyst may be estimated, for Expts. 6 and 7, from Fig. 1, as amounting to about 50% and 30%, respectively.

Order of Mixing.—In two pairs of identical experiments the order of addition of the glucose and nickel was reversed. In one pair, Expts. 8 and 20, the addition of the sugar last produced a faster reaction and lower specificity in the reaction; in the other pair, Expts. 6 and 22, that order produced a slightly faster reaction but higher specificity (see Fig. 1). In fact, the changes in

specificity were identical in degree, 0.22°, but different in sign.

This behavior may be explained by assuming that the "hot" catalyst, through prior exposure to the β-methylcinnamate, subsequently behaves as would a catalyst which adsorbs that reagent the faster, *i. e.*, a "cold" catalyst. Accordingly in Fig. 1 the specific activities of the products obtained from Expts. 20 and 22 are plotted on Curve II, Fig. 1, and from this the apparent amounts of catalyst present may be read from the plot as 22 g. and 11 g., respectively. As a two-hour "hot" catalyst, the former was 30 g. (Curve I, Fig. 1), or an apparent decrease of 27% effected through change in order of addition of reagents. The latter (Expt. 22) as a seven-hour "hot" catalyst was estimated in the previous section to correspond to only 15.5 g. of two-hour "hot" catalyst, and through the same change in order has decreased 29% (15.5 g. to 11 g.).

Further evidence of the essential identity, aside from effective amount, of the two-hour and seven-hour catalysts, is to be found in the two pairs of experiments, Expts. 8, 15 and 6, 17. In each pair ratios of reactants and catalysts have been similarly changed, in one case with a change in specificity of +0.16° and in the other of +0.15°. This change has been produced by a decrease in the relative glucose concentration and an increase in the dilution (compare the identity of results in Expts. 9, 11), and is in the direction to be expected by a retardation in the rate of adsorption of glucose. A similar effect of decreasing initial glucose concentration is found in Expts. 11, 14.

Effect of Temperature.—Expts. 13 and 23 were identical except for the reaction temperatures, which were 25 and 0°, respectively. The observed decrease in specificity with lower temperature would be expected on the above considerations, because for this catalyst cinnamate is adsorbed the more rapidly, implying that glucose adsorption has a higher activation energy and therefore cinnamate adsorption would be even more highly favored at the lower temperature.

Effect of Platinum Oxide Catalyst.—The use of Adams platinum oxide as catalyst, instead of Raney nickel, results in evolution of some hydrogen gas (dehydrogenation of the sugar) and production of an acid, but virtually no reduction of the cinnamate ion. Different amounts of catalyst were used in two experiments; the order of addition was the same as in Part A, Table I.

Reduction by Means of Monohydric Secondary Alcohols.—*d*-Hexanol-2 and *l*-menthol in the presence of alkali and Raney nickel reduced the unsaturated acid as readily as did glucose, but the reduction product was completely racemic. The catalyst used was digested for seventy-two hours at 20° and was not varied in amount. The reaction time was of the same order as in the case of glucose. With menthol, the solvent used was 65% dioxane in water.

It is possible that any one or all of the alcohol groups in glucose are responsible for the reduction of the β-methylcinnamate ion; in fact, it seems plausible that oxidation of the glucose proceeds first to the osone and then, through an internal Cannizzaro reaction, to gluconate ion. We have ascertained by trial that this last step is rapid compared to the rate of the β-methylcinnamate reduction.

All of the experiments performed under carefully controlled conditions are reported. In addition to these, trials using galactose and lactose were made under conditions which with glucose gave a large negative rotation. These sugars gave products with small positive rotations.

Comparison with Enzyme Reactions.—It should be noted that similar variations in enzyme stereo-specificity have been observed in which the same variables of amount of enzyme, order of mixing, etc., have influenced the optical activity of the product of the enzyme reaction even to an inversion of sign. These studies can only be referred to.[4]

Experimental Part

Materials.—The preparation of β-methylcinnamic acid has been described.[5] The potassium hydroxide solution and water used for dilution were carbonate-free. The *d*-glucose was Baker C. P. analyzed material. For the *d*-hexanol we are indebted to Mr. J. K. Holmes. It was resolved by Pickard and Kenyon's method[6] and had a rotation $[\alpha]^{18}D$ +11.68° (homogeneous). *l*-Menthol from McKesson and Robbins, $[\alpha]^{23}_{5461}$ −58.9° (95% alcohol), was used.

The preparation of Raney nickel was carried out in two ways. The desired amount of 20% sodium hydroxide was

(4) (a) Rosenthaler, *Biochem. Z.*, **14**, 238 (1908); (b) Krieble and Wieland, THIS JOURNAL, **43**, 164 (1921); (c) Krieble, *ibid.*, **35**, 1643 (1913); (d) Dakin and Dudley, *J. Biol. Chem.*, **14**, 155 (1913); **14**, 423 (1913); (e) Neuberg, *Biochem. Z.*, **49**, 502 (1913); **51**, 484 (1913); Neuberg and Simon, *ibid.*, **186**, 331 (1927); **200**, 468 (1928); (f) Mayer, *Biochem. Z.*, **174**, 420 (1926); Gorr and Perlman, *ibid.*, **174**, 433 (1926); Binder-Kotroba, *ibid.*, **174**, 443 (1926); R. Kuhn and Heckscher, *Z. physiol. Chem.*, **160**, 150 (1926); Widmann, *Biochem. Z.*, **216**, 475 (1929).

(5) Lipkin and Stewart, THIS JOURNAL, **61**, 3295 (1939).

(6) Pickard and Kenyon, *J. Chem. Soc.*, **99**, 49 (1911).

placed in a round-bottomed flask and then at room temperature the 50% nickel–50% aluminum alloy was added as rapidly as foaming permitted (one-half to one hour). The alloy was weighed to yield a given amount of nickel upon the assumption of complete removal of the 50% of aluminum. Actually it was found that the aluminum is not completely removed. After completing the addition of the alloy to the alkaline solution, the flask was placed in a glycerol-bath and heated at 115–120° for the desired time interval, after which it was cooled and the nickel washed by decantation an additional five times after the washings first became neutral to litmus. The second procedure differed in that the alloy was added while cooling the alkali in an ice-bath. The flask was then closed with a Bunsen valve and allowed to stand at room temperature for seventy-two hours with occasional shaking. The catalyst was always prepared just prior to use.

Procedure.—The weighed sample of β-methylcinnamic acid was placed in a volumetric flask and known amounts of potassium hydroxide solution added. When the thermostat temperature was reached, the glucose and catalyst, in either order, were added and the flask filled to the mark and shaken. Zero time was taken when the fourth component was added. The reaction mixture was transferred to a specially designed flask to permit vigorous continuous shaking in the thermostat, with provision for sweeping out the air with pure nitrogen and the taking of periodic samples for titration for alkali concentration. The initial alkali concentration was calculated from the amount of acid and base added; completion and rate of the reaction were indicated by the alkali used up.

After completion of the reaction the nickel was filtered off and discarded and the filtrate acidified and extracted with benzene. The benzene layer, after water washing, was filtered through filter paper moistened with benzene, evaporated to constant weight and the residue taken up in 25 ml. of dry benzene for polarimetric observation and titration. To remove any unreduced β-methylcinnamic acid, the benzene solution was extracted by 50 ml. of 0.5 *N* sodium hydroxide and the alkaline extract neutralized to phenolphthalein. Known amounts of 0.020 *M* potassium permanganate were then added until a small addition gave a color persisting for fifteen minutes; 10 ml. of 1 *N* sodium hydroxide was then added and a benzene extraction made to remove any acetophenone; after this the solution was acidified and the reduced acid recovered as before. In all but three experiments the unreduced acid present, as shown by the permanganate reaction, amounted to less than 0.3%. In these cases the following amounts were present: Expt. 12, 28%; Expt. 17, 15%; Expt. 18, 17%. The rotations reported are for the permanganate-treated acid, although in most cases the activity of the treated and untreated samples was identical within experimental error. Vacuum distillation of one sample did not change the rotation; vacuum distillation of 35 g. of accumulated samples resulted in a product which crystallized on standing, b. p. (10 mm.) 150–156°, uncorr.; yield 34 g.

Summary

The reduction of β-methylcinnamate ion by *d*-glucose in alkaline solution, catalyzed by Raney nickel, has been studied with variations in amount of catalyst, temperature, order of mixing, method of preparation of the catalyst, and relative concentrations of solutes. The optical activity in benzene of the resulting β-phenylbutyric acid varied from $[\alpha]_{5461}$ +0.31° to −0.42°, corresponding to about 0.5% asymmetric synthesis. The specificity changed with each variable and a tentative explanation of all of the variations has been presented based upon a simple hypothesis of relative rates of adsorption. Attention is called to the analogous behavior of enzyme catalyzed reactions.

BERKELEY, CALIF. RECEIVED JULY 31, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE ETHYL GASOLINE CORPORATION]

The Redistribution Reaction. IV. Interchange between Triethyllead Chloride and Radioactive Tetraethyllead

BY GEORGE CALINGAERT, HAROLD A. BEATTY AND LEWIS HESS

In the preceding papers of this series[1] it was shown that R_4Pb compounds in general undergo the redistribution reaction in which the intermolecular interchange of R groups leads to the formation of random equilibrium mixtures. Among the effective catalysts for this reaction are the R_3PbX salts, where X is Cl, Br, or I. It is obviously of interest to determine whether these R_3PbX salts also enter directly into this reaction, and whether both the R and X groups are capable of being interchanged with each other. In the first paper of this series it was indicated that such is the case; the present paper gives the experimental details of the study of the simplest possible reaction of this type, that between R_4Pb and R_3PbX, where all the R groups are identical and no new compounds can be formed; a subsequent paper will describe the more general examples wherein compounds containing different R groups are used.

(1) Calingaert and Beatty, THIS JOURNAL, **61**, 2748 (1939); Calingaert, Beatty and Neal, *ibid.*, 2755; Calingaert and Soroos, *ibid.*, 2758.

Study of the present reaction is possible only by the use of some special "tracer" method such as that of radioactive indicators. In the present work, the "tracer" used was lead containing radium D. The β radiation of radium D is so weak that it is desirable to measure instead only the β radiation of its first disintegration product, the bismuth isotope, radium E. The amount of radium E originally present is largely separated from the lead in the course of the chemical reactions used here, but its half-life is short compared with that of radium D. As a result, starting with a preparation containing radium D and no radium E, the concentration of the latter will be within 0.5% of its maximum value after thirty-five days, and will remain so for sixty-five days thereafter.

Procedure.—A solution was made containing equimolecular proportions of radioactive tetraethyllead and inert triethyllead chloride, and was kept at room temperature. Samples were removed at intervals of time from two hours to seven days, and the tetraethyllead and the triethyllead chloride were separated and converted individually to lead sulfate. After the build-up of radium E in each sample was substantially completed, measurements of radioactivity were made.

The data for two duplicate runs given in Table I show that the random distribution of the chlorine atoms between the two lead compounds present takes place rapidly and reaches equilibrium in less than twenty-four hours. Both tetraethyllead and triethyllead chloride are relatively stable compounds under the conditions used, and it is accordingly somewhat surprising to find so rapid an interchange of the chlorine atoms and ethyl radicals.

TABLE I

RADIOACTIVITY OF Et_4Pb AND Et_3PbCl

	Radioactivity, counts per minute			
	Expt. 1		Expt. 2	
Time, hr.	Et_4Pb	Et_3PbCl	Et_4Pb	Et_3PbCl
2	2173	777	2264	953
24	1704	1684	1922	1838
72	1659	1669		
96			1887	1808
168	1673	1679	1887	1703

Experimental.—Lead sulfate which contained about 2×10^{-8} g. of radium D sulfate per g. was reduced to metallic lead by smelting with metallic iron and coke, and this lead was used to prepare the sodium–lead alloy, NaPb, from which radioactive tetraethyllead was synthesized.[2]

To carry out the redistribution reaction, 0.082 mole each of radioactive tetraethyllead and ordinary triethyllead chloride[3] were placed in a small flask under nitrogen, and diluted with sufficient benzene, 77 ml., to dissolve the salt. The solution was maintained at room temperature for one week, with occasional shaking. The reversible side reaction[4] of triethyllead chloride in accordance with the equation $2Et_3PbCl \rightleftarrows Et_2PbCl_2 + Et_4Pb$ was effectively minimized by the low temperature employed, together with the high ratio of ethyl radicals to chlorine. This was evidenced by the very slight precipitation of the nearly insoluble diethyllead dichloride.

Samples were removed for analysis after periods of two hours, and one, three, and seven days, and were treated as follows: most of the benzene was removed by vacuum evaporation at room temperature, 25 ml. of hexane was added to precipitate the triethyllead chloride, the mixture was filtered, and the residue was washed with three 10-ml. portions of hexane, adding the washings to the filtrate. The filtrate and residue were brominated separately with an excess of a solution of bromine in carbon tetrachloride, and the resulting bromides were dissolved in nitric acid and converted to sulfates, which were filtered, washed, dried, and later were measured for radioactivity. The experiment was performed in duplicate.

Measurement of Radioactivity.—The counting system consisted of a scale-of-one counting circuit excited by a Geiger-Müller tube, as described by Duffendack and coworkers.[5] The tube had a background count of less than 20 per minute. Each sample was measured once only, from thirty-two to forty days after its preparation. Each measurement covered a period of twenty minutes, during which the counter was switched off by a time switch for twelve seconds out of each minute, to provide leisure time for recording the count.

The procedure in general was designed to avoid errors from extraneous sources. However, the counts obtained from a considerable number of presumably identical samples showed variations substantially larger than expected, the reason for which was not evident. Such variations also appear in the data in Table I, but do not affect the general conclusions derived from the experiments.

Acknowledgments.—We are indebted to M. Marcel Pochon of Eldorado Gold Mines, Ltd., for a supply of radioactive lead sulfate, to Dr. Oscar E. Harder of the Battelle Memorial Institute for the smelting of this lead sulfate, and to Professor O. S. Duffendack and Dr. Harold Lifschutz of the University of Michigan for advice and assistance in the measurement of radioactivity.

Summary

Using radium D as an indicator, it is shown that an interchange of chlorine atoms and ethyl radicals between tetraethyllead and triethyllead chloride takes place, and reaches equilibrium in less than one day at room temperature.

DETROIT, MICHIGAN RECEIVED SEPTEMBER 22, 1939

(2) Kraus and Callis, U. S. Patent 1,697,245 (1929).

(3) Calingaert, Kurt and Dykstra, to be published.

(4) Krause and von Grosse, "Die Chemie der metall-organischen Verbindungen," Gebrüder Borntraeger, Berlin, 1937, p. 397.

(5) Duffendack, Lifschutz and Slawsky, *Phys. Rev.*, **52**, 1231 1937); Lifschutz and Duffendack, *ibid.*, **54**, 714 (1938).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, OKLAHOMA AGRICULTURAL AND MECHANICAL COLLEGE]

Solubilities of Sodium and Potassium Salts of Nitrophenols and Related Acids[1]

BY O. C. DERMER AND V. H. DERMER

Aqueous solubilities of salts of 2-chloro-3-nitrotoluene-5-sulfonic acid and some similar acids already have been determined in a search for a better precipitant for potassium.[2] The present paper reports results of a like study of salts of a variety of other organic acids, chosen because their potassium salts were either known or hoped to be slightly soluble.

Experimental

Synthesis of Salts.—Picric acid, 2,4,6-trinitro-*m*-cresol (methylpicric acid), picrolonic acid, 5-nitrobarbituric acid, and 2,4-dinitronaphthol-7-sulfonic acid were Eastman Kodak Co. products. Styphnic acid, dipicrylamine, N,2,-4,6-tetranitroaniline, 3-chloro-2,4,6-trinitrophenol (chloropicric acid), 2,3,4,6-tetranitrophenol, and nitranilic acid were made by nitrating resorcinol, 2,4-dinitrodiphenylamine,[3] picramide,[4] *m*-chlorophenol,[5] *m*-nitrophenol,[6] and diacetylhydroquinone,[7] respectively. 1-Phenylbarbituric acid was prepared by condensing malonic acid with phenylurea[8] and was nitrated according to the directions given in "Organic Syntheses" for 5-nitrobarbituric acid.[9] Efforts to prepare pure 1,5-dinitronaphthol-7-sulfonic acid derivatives by nitrating sodium 2-naphthol-7-sulfonate according to the meager directions of Volochneva[10] were abandoned after several failures. 2-Chloro-1,4-dimethyl-3-nitrobenzene-5-sulfonic acid (2-chloro-3-nitro-*p*-xylene-5-sulfonic acid) was prepared from *p*-xylene by the general method described in the first paper of this series;[2] most of the steps were also those employed by Wahl.[11] The successive intermediate stages were 2-chloro-1,4-dimethylbenzene, 2-chloro-1,4-dimethylbenzene-5-sulfonic acid, the corresponding sulfonyl chloride (m. p. 47°, Wahl gave 50°), and 2-chloro-1,4-dimethyl-3-nitrobenzene-5-sulfonyl chloride. 2-Chloro-3-nitrotoluene-5-arsonic acid was synthesized by arsonating *o*-toluidine,[12] introducing a chlorine atom by the Sandmeyer reaction, and nitrating the product.

The salts were made by neutralizing the acid with the calculated amount of the appropriate alkali and recrystallizing the product repeatedly from alcohol or water. The di-metal salts of flavianic acid had to be recrystallized from dilute alkali to prevent hydrolysis, and those containing only one metallic atom per molecule could not be obtained pure. This verifies the statement of Clark and Willits[13] that the dipotassium salt is the one precipitated, but casts some doubt on Volochneva's[10] report that monopotassium 1,5-dinitronaphthol-7-sulfonate is the stable form.

Salts of N,2,4,6-tetranitroaniline, 2,3,4,6-tetranitrophenol, 2-chloro-3-nitrotoluene-5-arsonic acid, and 1-phenyl-5-nitrobarbituric acid were not investigated further after qualitative tests showed their potassium salts to be too soluble to precipitate readily. The others were dried at 105° in a vacuum oven, to reduce the danger of an explosion.[14]

Analysis and Determination of Solubility.—The purity of each salt was tested and the solubility determined by the methods previously used.[2]

Discussion of Results

Table I shows the results of our experimental work. The only reagents in this group useful as potassium precipitants have already been suggested for that purpose: dilituric acid[15] and especially dipicrylamine.[16] Little relation can be traced between structure and solubility of salts; dilituric acid is useful, but the addition of a phenyl group destroys its value. The substitution of a methyl group in the 5-position on the ring in 4-chloro-3-nitrobenzenesulfonic acid makes the potassium salt far less soluble,[2] but addition of another methyl group to the ring yields 2-chloro-1,4-dimethyl-3-nitrobenzene-5-sulfonic acid, which is worthless as a potassium precipitant. The same ruinous effect of a methyl group, or indeed of any group at all in this case, is seen among relatives of picric acid, including also 3,3′-azo-*bis*picric acid (3,3′-dihydroxy-2,4,6,2′,4′,6′-hexanitroazobenzene).[17] It is improbable, therefore, that substituted dipicrylamines would exceed or even equal the parent compound in usefulness.

Summary

The sodium and potassium salts of ten possible potassium precipitants, mostly nitrophenols, have been synthesized and their solubilities at 30°

(1) Most of the material in this paper was presented at the Rochester meeting of the American Chemical Society, September, 1937.

(2) Dermer and Dermer, THIS JOURNAL, **60**, 1 (1938).

(3) Marshall, *J. Ind. Eng. Chem.*, **12**, 336 (1920).

(4) Jones and Willson, *J. Chem. Soc.*, 2277 (1930).

(5) Tijmstra, *Rec. trav. chim.*, **21**, 292 (1902).

(6) Blanksma, *ibid.*, **21**, 256 (1902).

(7) Gutzeit, *Helv. Chim. Acta*, **12**, 726 (1929).

(8) MacBeth, Nunan and Traill, *J. Chem. Soc.*, 1248 (1926).

(9) Hartman and Sheppard, "Organic Syntheses," Vol. XII, John Wiley and Sons, Inc., New York, 1932, p. 58.

(10) Volochneva, *J. Applied Chem. (U. S. S. R.)*, **11**, 369 (1938).

(11) Wahl, *Ann. chim.*, (11) **5**, 5 (1936).

(12) Lewis and Cheetham, "Organic Syntheses," Vol. III, John Wiley and Sons, Inc., New York, 1923, p. 13.

(13) Clark and Willits, *Ind. Eng. Chem., Anal. Ed.*, **8**, 209 (1936).

(14) Berger, *Arbeitsschutz*, No. 3, 73 (1936); *Chimie et Industrie*, **36**, 1140 (1936).

(15) Fredholm, *Z. anal. Chem.*, **104**, 400 (1936).

(16) Kolthoff and Bendix, *Ind. Eng. Chem., Anal. Ed.*, **11**, 94 (1939); see also Sheintzis, *J. Applied Chem. (U. S. S. R.)*, **11**, 1012 (1939); Shapiro, *Zavodskaya Lab.*, **7**, 790 (1938).

(17) Elbs and Schiephake, *J. prakt. Chem.*, **104**, 282 (1922).

TABLE I

ANALYSES AND SOLUBILITIES OF SALTS

Anion	Na salt: % Metal calcd.	Na salt: % Metal found[a]	Na salt: Soly. at 30°, g./100 g. H_2O[b]	Na salt: Soly., millimoles/100 g. H_2O	K salt: % Metal calcd.	K salt: % Metal found[a]	K salt: Soly. at 30°, g./100 g. H_2O[b]	K salt: Soly., millimoles/100 g. H_2O	Soly. Na salt/soly. K salt
2-Chloro-3-nitro-*p*-xylene sulfonate	8.95	8.90	93.4	325	14.32	14.24	9.21	30.4	10.7
Methyl picrate	8.68	8.61	3.15	11.8	13.91	13.93	3.78	13.4	0.88
Chloropicrate	8.06	8.04	31.2	110	12.94	12.94	1.82	6.03	18
Styphnate	8.61	8.72	8.43	31.5	13.81	13.76	1.54	5.42	5.8
Flavianate[c]	12.83	12.91	9.8	27	19.12[d]	19.22	1.03	2.5	10.8
Picrate	8.55[d]	8.62	5.58[e]	20.8	14.61	14.53	0.755[f]	2.84	7.3
Nitranilate	16.79	16.92	0.724	2.64	25.54	25.62	.567	1.85	1.4
Picrolonate	8.01	8.04	0.285	1.00	12.90	12.97	.338	1.12	0.89
Dipicrylamide[g]	4.96	5.05	11.6	25.2	8.20	8.17	.146[h]	0.304	83
Dilituric acid	11.79	11.80	1.034	5.31[i]	18.52	18.69	.086	0.40[j]	13

[a] Average of two values with a mean deviation of 0.3%. [b] Average of two or three values with a mean deviation of 1.4%. [c] Dibasic. [d] Monohydrate. [e] Perhaps the best literature value is given by Fischer, *Z. physik. Chem.*, **92**, 581 (1918), as 4.30 at 25°. [f] Fischer gives 0.645 at 25°. [g] There is disagreement on the names for salts of dipicrylamine; this one is sometimes called "potassium dipicrylaminate." We prefer the name "potassium dipicrylamide" as best indicating the structure of a substituted potassium amide. [h] Kielland, *Ber.*, **71**, 220 (1938), gives the solubility as 0.0025 molar at 25°, which is equivalent to 0.12 g./100 g. H_2O. Kolthoff and Bendix (ref. 16) give the value 0.088 for the same temperature. [i] Fredholm (ref. 15) gives the value as 0.049 molar at 18°. [j] Fredholm gives 0.0022 molar at 18°.

determined. The most sensitive reagents in the group were dipicrylamine and dilituric acid. Introduction of additional groups into the molecules of such potassium reagents as picric acid, dilituric acid, and 2-chloro-3-nitrotoluene-5-sulfonic acid is more likely to decrease than to increase their value.

STILLWATER, OKLAHOMA RECEIVED JULY 20, 1939

[A COMMUNICATION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Hydrogenation of 1,3-Diketones to Ketols

BY PAUL S. STUTSMAN AND HOMER ADKINS

Sprague[1] obtained the ketol $(CH_3)_3CC(O)CH_2CHOHCH_3$ in 68% yield by the hydrogenation of $(CH_3)_3CC(O)CH_2C(O)CH_3$. This rather unexpected result was no doubt due to the relative resistance to hydrogenation of a carbonyl group adjacent to a tertiary butyl group. The study reported herewith was directed toward finding conditions under which other ketols, less resistant to hydrogenation, could be obtained by the partial hydrogenation of the corresponding 1,3-diketones.

Eight diketones, in which R was methyl, ethyl, a propyl or a butyl radical in compounds of the formula $RCOCH_2COCH_3$, were prepared and subjected to hydrogenation over Raney nickel under various conditions in attempting to obtain the optimum yield of the various ketols.

Hydrogenation at 100° over Raney nickel of the diketones dissolved in methanol gave in general the highest yield of ketols. The yields of ketol were where R was methyl 35%, ethyl 51%, *n*-propyl 58%, isopropyl 50%, *n*-butyl 66%, isobutyl 49%, *s*-butyl 64%. Hydrogenation of the diketone dissolved in ether, dioxane or ethanol gave in several cases lower yields, though this difference may have been due more to differences in the losses during isolation rather than to the effect of the solvent upon the rate or course of hydrogenation. The differences between solvents were in most cases negligible, as for example where R was *t*-butyl the yields of the ketol were 66, 68 and 70% in methanol, ether and ethanol, respectively. The 68% yield in ether confirms the yield reported by Sprague referred to above.

The most important consideration, for a given diketone, in determining the yield of ketol is the amount of hydrogen which is absorbed before the reaction is stopped. In order to obtain the yields given above, the shaking of the reaction vessel was stopped after 0.9 to 1.0 mole of hydrogen per

(1) Sprague and Adkins, THIS JOURNAL, **56**, 2669 (1934).

mole of diketone had been absorbed. Since the hydrogenation proceeds rapidly it is not always easy to stop the reaction when the proper amount of hydrogen has been taken up.

Improved yields have been obtained by making use of the technique recently described for the partial hydrogenation of phenanthrene.[2] In this procedure the hydrogenation is carried out under nitrogen with a limited amount of hydrogen. The diketone, methanol and catalyst were placed in the reaction vessel and nitrogen added to a pressure of about 100 atmospheres. One mole of hydrogen per mole of diketone was then added. The mixture was then shaken at 100° until the pressure was constant. The pressure of nitrogen kept the contents of the bomb in the liquid phase even after all the hydrogen had reacted. This procedure enables exactly the proper amount of hydrogen to be added to the diketone and in the three cases in which it was tried raised the yields by 4, 20 and 17%, respectively. The method was tried where R was methyl, *i*-butyl and *s*-butyl. The hydrogenations required about one hundred and ten minutes due to the low pressure of hydrogen, as compared with about twenty minutes under 125 atmospheres of hydrogen.

Hydrogen did not react at the carbonyl next to R until the carbonyl next to the methyl group had been hydrogenated, as the ketols obtained were in each case methylcarbinols, *i. e.*, $RCOCH_2CHOHCH_3$. The structure of the ketols was ascertained by dehydrating each one over oxalic acid[3] to the corresponding unsaturated ketone $RCOCH{=}CHCH_3$, which was then hydrogenated to $RCOCH_2CH_2CH_3$. Solid derivatives of the ketone so prepared were compared by mixed melting points with derivatives of a sample of a ketone of known structure.

The 2,4-dinitrophenylhydrazones of the unsaturated ketones were prepared in six cases. The same derivative was obtained from the ketol as from the unsaturated ketone since the ketol is dehydrated during the process of forming the hydrazone.

The hydrogenation of 1,3-diketones may be continued beyond the ketol stage to give good yields of the glycols of the type $RCHOHCH_2CHOHCH_3$.[1] Glycols where R is ethyl, *n*-propyl, *n*-butyl or *s*-butyl have been prepared for the first time in yields of 92, 94, 94 and 80%, respectively. These hydrogenations were made at 100 to 125° during the course of one and a half to three hours under approximately 100 atm. of hydrogen over 4 g. of Raney nickel. Approximately 25 g. of the diketone was dissolved in 80 ml. of dry methanol and the glycols obtained by fractionation after hydrogenation.

Sprague noted that the hydrogenation of certain 1,3-diketones resulted in the cleavage of the chain with the formation of ketones and aldehydes, *i. e.*

$$t\text{-BuCOCH}_2\cdots\text{COCH}_3 \xrightarrow{H_2} t\text{-BuCOCH}_3 + \text{CH}_3\text{CHO}$$

The splitting was ascribed to cleavage by hydrogen of the carbon to carbon linkage indicated by the dots in the formula. It seemed possible that hydrogenation of the carbonyl group, rather than hydrogenolysis of the carbon to carbon linkage, might have taken place to give a ketol, which might then undergo disproportionation to give the ketone and aldehyde, *i. e.*

$$t\text{-BuCOCH}_2\text{CHOHCH}_3 \longrightarrow t\text{-BuCOCH}_3 + \text{CH}_3\text{CHO}$$

The disproportionation might have occurred in the reaction vessel under the conditions of hydrogenation or during the separation and purification of the products. To test this hypothesis the ketol indicated just above was heated in ether solution at 60° in the bomb in the presence of Raney nickel for twelve hours. No disproportion products were formed and the ketol was recovered unchanged. Since alkali would tend to facilitate disproportionation during the process of working up the reaction products after a hydrogenation, Sprague's procedure was modified in that potassium carbonate was not used for drying the solution of the products before fractionation. Ethylbenzoylacetylmethane, $C_6H_5CO\cdots CH(Et)COCH_3$, was subjected to hydrogenation as by Sprague but the products were isolated without drying them over potassium carbonate. The results showed a 27% cleavage at the linkage indicated by dots in the formula. Ethylbenzoylacetylmethane was used in this experiment in preference to $t\text{-BuCOCH}_2\text{COCH}_3$ because the former undergoes cleavage to a greater extent according to Sprague's results.

There is therefore no evidence that the cleavage observed by Sprague was due to disproportionation of a ketol, but rather it may be regarded as dependent upon hydrogenolysis of the diketone.

The 1,3-diketones were made by condensing ethyl acetate with the proper ketone using sodium

(2) Durland and Adkins, THIS JOURNAL, **60**, 1501 (1938).
(3) Pastreau and Zamenhof, *Compt. rend.*, **182**, 323 (1926).

ethoxide as the condensing agent. The procedure was essentially that previously described and labeled "B."[4] Methyl *i*-propyl[5] and methyl *t*-butyl ketones[6] were made by the methods described in "Organic Syntheses." Methyl ketones containing *n*-propyl, *n*-butyl and *s*-butyl groups were made through the use of acetoacetic ester, the hydrolysis being made as given in "Organic Syntheses."[7] The other monoketones used were commercial products.

Hydrogenations were carried out in various reaction vessels but all those reported herewith were made in a steel bomb having a void of 270 ml. The general procedure was as follows. The diketone (0.15 to 0.35 mole) dissolved in 40 to 80 ml. of dry methanol was placed in the reaction vessel with 3 to 5 g. of Raney nickel. Hydrogenation under a pressure of 100 to 200 atmospheres was allowed to proceed at 100° until one mole of hydrogen per mole of diketone had been absorbed. The time of reaction was in general from five to thirty minutes. The reaction vessel was then cooled to room temperature, the excess hydrogen released, the vessel opened and the reaction mixture and washings filtered. The solvent was then distilled through a fractionating column at atmospheric pressure and the products separated by fractional distillation at a convenient pressure. Both a Widmer and a modified Widmer column were used.[8] The modified Widmer containing a spiral 15 cm. in length with 12 turns of the helix was preferable. Since all the yields reported were isolated by fractionation they represent minimum rather than maximum values. In particular the mechanical losses in the case of the viscous glycols were relatively large.

The ketols (10 to 20 g.) were dehydrated to the unsaturated ketones by slow distillation through the modified Widmer column from a flask containing 0.3 to 0.6 g. of oxalic acid. The water layer in the distillate was discarded, the ketone dried over sodium sulfate and fractionated through the modified Widmer column. The yields were 70 to 90% of the theoretical quantity. The unsaturated ketone (4 to 9 g.) was then hydrogenated over Raney nickel at 30–40° under 100 atm. of hydrogen in a small steel reaction vessel.[9]

The 2,4-dinitrophenylhydrazones of the ketones and ketols were made by the method of Allen[10] or Brady.[11] When R was ethyl, *n*-propyl, *i*-propyl, *n*-butyl, *i*-butyl or *t*-butyl the ketol gave the same derivative as the corresponding unsaturated ketone. The bisphenylurethans of the glycols were prepared as by Tessmer.[12]

The colors of the 2,4-dinitrophenylhydrazones of ketones, after recrystallization from the indicated solvent were as follows: hexene-4-one-3 and heptene-2-one-4, red needles from dry ethanol; 2-methylhexene-4-one-3, orange needles from methanol; octene-2-one-4, orange needles from 95% alcohol; 6-methylheptene-2-one-4, red plates from 95% alcohol; and 2,2-dimethylhexene-4-one-3, yellow needles from a methanol–water mixture. The melting points and analytical data for these and other derivatives are given in Table I.

TABLE I

MELTING POINTS AND ANALYSES OF VARIOUS DERIVATIVES

Compound	M. p., °C.	Nitrogen, % Calcd.	Found
Hexene-4-one-3[a]	164–165	20.14	20.40
Heptene-2-one-4[a]	142–143	19.18	19.29
2-Methylhexene-4-one-3[a]	140–141	19.18	19.28
Octene-2-one-4[a]	108–109	18.30	18.48
6-Methylheptene-2-one-4[a]	101–101.5	18.30	18.56
2,2-Dimethylhexene-4-one-3[a]	135–135.5	18.30	18.51
3-Methylheptanone-4[b]	106–107	22.69	22.78
6-Methylheptanone-4-ol-2[c]	111–113	11.86	11.93
Heptanediol-2,4[d]	101–101.5	7.56	7.67
5-Methylhexanediol-2,4[d]	134–135	7.56	7.60
Octanediol-2,4[d]	126–127	7.29	7.42
6-Methylheptanediol-2,4[d]	143–143.5	7.29	7.30
5-Methylheptanediol-2,4[d]	129–130	7.29	7.45

[a] 2,4-Dinitrophenylhydrazone. [b] Semicarbazone. [c] Phenylhydrazone. [d] Bisphenylurethan.

The saturated ketones, obtained as the result of dehydration of the ketols followed by hydrogenation, all proved to be of the type n-C_3H_7COR where R was a methyl, ethyl, a propyl or a butyl radical. They were identified by solid derivatives as follows: ethyl *n*-propyl ketone, b. p. 123–124°, as a 2,4-dinitrophenylhydrazone, m. p. 136°[10]; dipropyl ketone, b. p. 145–147°, as the semicarbazone, m. p. 131–132°[13]; *i*-propyl *n*-propyl ketone, b. p. 132–134°, as the semicarbazone, m. p. 119–120°[14]; *n*-butyl *n*-propyl ketone,

(4) Sprague, Beckham and Adkins, THIS JOURNAL, **56**, 2665 (1934).
(5) "Organic Syntheses," John Wiley and Sons, New York, N. Y. 1933, Vol. XIII, p. 68.
(6) *Ibid.*, John Wiley and Sons, New York, N. Y. 1932, Coll. Vol. I, p. 451.
(7) "Organic Syntheses," John Wiley and Sons, New York, N. Y. 1932, Coll. Vol. I, p. 343.
(8) Martha E. Smith and Adkins, THIS JOURNAL, **60**, 662 (1938).
(9) Adkins, THIS JOURNAL, **55**, 4272 (1933).
(10) Allen, *ibid.*, **52**, 2955 (1930).
(11) Brady, *J. Chem. Soc.*, 756 (1931).
(12) Tessmer, *Ber.*, **18**, 969 (1885).
(13) Sherrill, THIS JOURNAL, **52**, 1990 (1930).
(14) Michael, *ibid.*, **41**, 418 (1919).

TABLE II

PHYSICAL CONSTANTS AND ANALYTICAL DATA

Compound	B. p., °C.	Mm.	$n^{25}D$	d^{25}_4	MR Calcd.	MR Found	H, % Calcd.	H, % Found	C, % Calcd.	C, % Found
Hexanone-3-ol-5	75–78	12	1.4280	0.950	31.44	31.44	10.42	10.51	62.03	62.04
Pentanone-2-ol-4[19]	93–95	43	1.4238							
Heptanone-4-ol-2	101	24	1.4300	.930	36.06	36.15	10.84	10.91	64.58	64.47
2-Methylhexanone-3-ol-5	72–73	9	1.4278	.929	36.06	36.01	10.84	11.03	64.58	64.43
Octanone-4-ol-2	91	8	1.4333	.920	40.68	40.73	11.19	11.29	66.62	66.41
6-Methylheptanone-4-ol-2	86	9	1.4294	.914	40.68	40.67	11.19	11.30	66.62	66.48
2,2-Dimethylhexanone-3-ol-5[1]	72–74	10	1.4243							
5-Methylheptanone-4-ol-2	113–114	36	1.4318	.921	40.68	40.57	11.19	11.22	66.62	66.69
Hexene-4-one-3[20]	136–139	740	1.4345	.851	29.45	30.04				
2-Methylhexene-4-one-3	147–148.5	739	1.4345	.843	34.07	34.69	10.79	10.96	74.95	74.79
Heptene-2-one-4[20]	156–162	740	1.4383	.852	34.07	34.56				
Octene-2-one-4	178	740	1.4393	.852	38.69	38.96	11.18	11.22	76.14	75.95
6-Methylheptene-2-one-4	168–170	741	1.4388	.841	38.69	39.45	11.18	11.13	76.14	75.97
5-Methylheptene-2-one-4	170	740	1.4400	.848	38.69	39.19	11.18	11.26	76.14	76.04
2,2-Dimethylhexene-4-one-3[1]	153–154	740	1.4380	.843	38.69	39.27				
3-Methylheptanone-4	152–154	740	1.4103	.817	39.16	38.91	12.58	12.68	74.94	74.93
Heptanediol-2,4	107–108	8	1.4386	.926	37.58	37.47	12.20	12.21	63.59	63.54
Octanediol-2,4	117–118	8	1.4422	.918	42.19	42.14	12.41	12.29	65.70	65.74
5-Methylheptanediol-2,4	111–112	8	1.4449	.928	42.19	41.91	12.41	12.46	65.70	65.64

b. p. 168–171°, as the semicarbazone, m. p. 100–101°[15]; *s*-butyl *n*-propyl ketone, b. p. 152–154°, as the semicarbazone, m. p. 106–107°; *i*-butyl *n*-propyl ketone, b. p. 153–155°, as the semicarbazone, m. p. 122–123°[16]; *t*-butyl *n*-propyl ketone, b. p. 143–144°, as the semicarbazone, m. p. 153–154.5°, and oxime, m. p. 77.5–78.5°.[17] The ketol $CH_3CHOHCH_2COCH_3$ was characterized by its phenylhydrazone, m. p. 103–104°.[18]

Summary

Ketols of the type $RCOCH_2CHOHCH_3$ have been prepared in yields averaging above 50% by the hydrogenation over Raney nickel of 1,3-diketones where R is a methyl, ethyl, a propyl or a butyl group. In order to obtain good yields of the ketols it is necessary to interrupt the hydrogenation after the absorption of one mole of hydrogen per mole of ketone. This is most satisfactorily accomplished by having in the reaction vessel no more than the required amount of hydrogen, and adding a sufficient amount of nitrogen to obtain the desired pressure. All of the eight ketols obtained were methylcarbinols, showing that hydrogenation proceeds to completion at the acetyl group before it begins at propionyl, butyryl or valeryl groups.

Evidence is presented that the cleavage of diketones previously reported is really a hydrogenolysis and not a disproportionation of a ketol subsequent to hydrogenation.

MADISON, WISCONSIN RECEIVED SEPTEMBER 28, 1939

(15) Bouveault and Locquin, *Bull. soc. chim.*, [3] **33**, 47 (1905).
(16) Fournier, *ibid.*, [4] **7**, 839 (1910).
(17) Haller and Bauer, *Compt. rend.*, **150**, 568 (1910).
(18) Claisen, *Ann.*, **306**, 325 (1899).
(19) Perkin, *J. Chem. Soc.*, **65**, 825 (1894).
(20) Blaise, *Bull. soc. chim.*, [3] **33**, 47 (1905).

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF MERCK & CO., INC.]

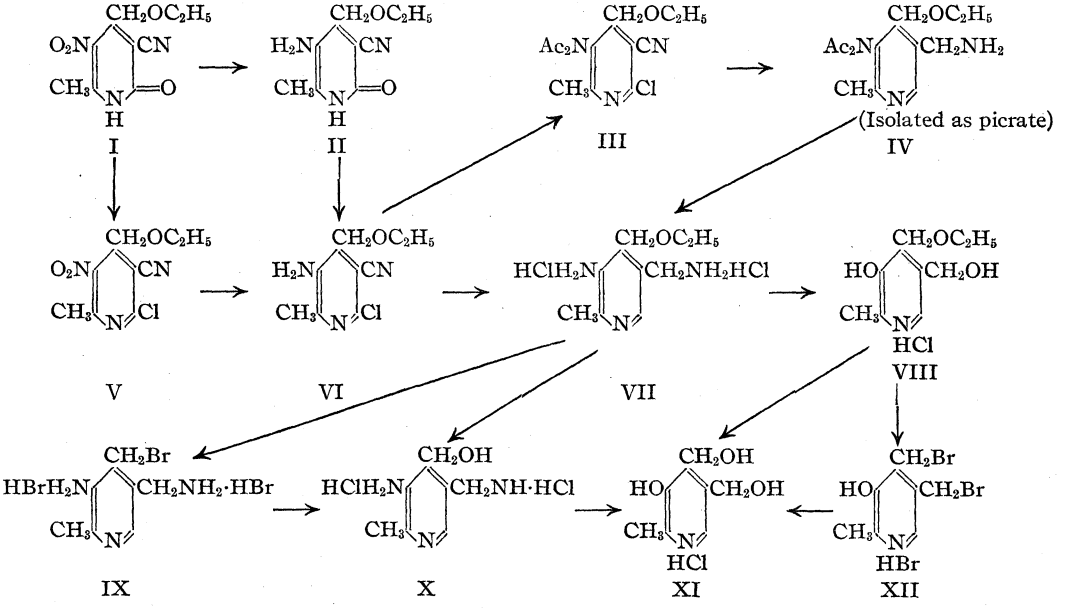
Synthesis of Vitamin B_6. II[1]

BY STANTON A. HARRIS AND KARL FOLKERS

In a previous article[2] a complete synthesis of vitamin B_6 was described. The present paper describes some variations and improvements in this synthesis, along with new derivatives of some of the intermediate compounds. These variations are shown in the set of reactions, I–XII.

The original synthesis is represented by the reactions I → V → VI → VII → VIII → XII → XI. The nitropyridone, I, was prepared by the nitration of 3-cyano-4-ethoxymethyl-6-methyl-2-pyridone, which in turn was prepared by the condensation of ethoxyacetylacetone and cyanacetamide.

The ethoxy-diamine, VII, is the key compound in all these syntheses. This compound was prepared by two new variations of these reactions: I → II → VI → VII and I → II → VI → III → IV → VII. These variations are limited by the low yield in reaction II → VI. Compounds III and IV are not essential to the success of the synthesis of the ethoxy-diamine, VII.



Acetylation of the aminopyridone, II, and the chloroaminopyridine, VI, gave a mono and a diacetate in each case. The question of the position of the second acetyl group in the diacetate of the aminopyridone, II, was settled only by analogy. Since the chloro-aminopyridine, VI, also formed a diacetate and the original pyridone, namely, 3-cyano-4-ethoxymethyl-6-methyl-2-pyridone, did not form an acetate when boiled with acetic anhydride, it was deduced that the diacetate of II had both acetyl radicals attached to the amino group.

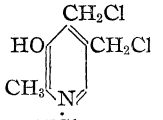
The important variations in the synthesis start with the ethoxy-diamine, VII. The first variation is represented by the reactions VII → VIII → XI. It was found that the ethoxy group of VIII could be split with dilute hydrochloric acid in a bomb tube reaction at 150°. This reaction eliminated the use of constant boiling hydrobromic acid and the necessity for the subsequent hydrolysis of the intermediate dibromide, XII. A second variation is shown by the steps VII → IX → X → XI. These steps also were shortened by another bomb tube reaction to give the third and most practical series of reactions, VII → X → XI. The hydroxy-diamine, X, was more easily isolated and recrystallized than was the 4-ethoxymethyl derivative, VIII, of vitamin B_6.

The 4-ethoxymethyl derivative, VIII, also was deëthylated with concentrated hydrochloric acid

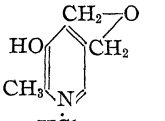
(1) The material in this paper was presented to the Organic Division of the American Chemical Society at Boston, Mass., on September 11, 1939.

(2) Harris and Folkers, THIS JOURNAL, 61, 1245 (1939).

in a bomb tube at 132° to form 2-methyl-3-hydroxy-4,5-*bis*-(chloromethyl)-pyridine hydrochloride, XIII, which was, in turn, hydrolyzed to vitamin B_6 hydrochloride, XI.



XIII



XIV

In the original synthesis,[2] vitamin B_6 hydrochloride, XI, was obtained by hydrolyzing the dibromide, XII, with hot water and removing the bromide ions with silver chloride. On recrystallizing the product from alcohol, a by-product was found in the mother liquors which proved to be an inner ether of the vitamin. This ether, 2-methyl-3-hydroxy-4,5-(epoxydimethyl)-pyridine hydrochloride, XIV, was also obtained by treating both vitamin B_6, XI, and its ethyl ether, VIII, with 50% sulfuric acid. Unlike the ethyl ether, VIII, this new ether was stable toward hydrolysis with dilute hydrochloric acid at 175°. However, it was reconverted to the dibromide, XII, by boiling with 48% hydrobromic acid, which can, in turn, be converted to vitamin B_6 hydrochloride, XI.

Experimental Part

Reduction of 3-Cyano-4-ethoxymethyl-5-nitro-6-methyl-2-pyridone, I.—The reduction was carried out with hydrogen in the presence of Adams catalyst, both in ethyl alcohol and acetic acid. From 22.5 g. of I, the yield of 3-cyano-4-ethoxymethyl-5-amino-6-methyl-2-pyridone, II, was 12.5 g. (63.6%); m. p. 250–255° with decomposition after recrystallization from ethyl alcohol.

Anal. Calcd. for $C_{10}H_{15}N_3O_2$: C, 57.96; H, 6.32; N, 20.28. Found: C, 58.15; H, 6.19; N, 20.67, 20.61.

The reduction of the nitropyridone, I, also was carried out in acetic anhydride and yielded the monoacetate of II. From 23.5 g. of I, dissolved in 200 cc. of acetic anhydride, the yield of 3-cyano-4-ethoxymethyl-5-acetylamino-6-methyl-2-pyridone was 13.3 g. (53.4%); m. p. 260° after recrystallization. An additional 8–9 g. of crude material was obtained from the mother liquor. It was difficultly soluble in acetic anhydride and ethyl alcohol, from which latter it was recrystallized.

Anal. Calcd. for $C_{12}H_{15}O_3N_3$: C, 57.82; H, 6.07; N, 16.85. Found: C, 57.80; H, 6.11; N, 16.99.

The aminopyridone, II, also was acetylated by boiling in an excess of acetic anhydride. In one experiment a small amount of the monoacetate was obtained in addition to a larger quantity of a more soluble product which proved to be a diacetate. After the removal of the acetic anhydride under reduced pressure the residue was oily but, on standing, it gradually crystallized to a solid mass. After three recrystallizations from ethyl alcohol, the diacetate of 3-cyano-4-ethoxymethyl-5-amino-6-methyl-2-pyridone melted at 176°.

Anal. Calcd. for $C_{14}H_{17}O_4N_3$: N, 14.43; CH_3CO, 29.5. Found: N, 14.6; CH_3CO, 28.92, after refluxing in strong alkali for 25.5 hours.

Chlorination of 3-Cyano-4-ethoxymethyl-5-amino-6-methyl-2-pyridone, II.—Two grams of the aminopyridone, II, was treated with 15–20 cc. of phosphorus oxychloride and 4 g. of phosphorus pentachloride and allowed to stand overnight at 30°. The phosphorus oxychloride was removed under reduced pressure and the residue decomposed with ice water. On neutralization with ammonia, a substance crystallized which, after three recrystallizations from alcohol, melted at 146–147° and showed no depression of melting point with a pure sample of 2-methyl-3-amino-4-ethoxymethyl-5-cyano-6-chloropyridine, VI.[2] The yield of crude material was 0.38 g. (16.5%). A large proportion of unchanged starting material was obtained by extracting the aqueous mother liquor with chloroform.

Acetylation of 2-Methyl-3-amino-4-ethoxymethyl-5-cyano-6-chloropyridine, VI.—Two grams of the chloro-aminopyridine, VI, was dissolved in 10 cc. of warm acetic anhydride and then allowed to crystallize. One gram of starting material was recovered. The acetic anhydride solution was decomposed with cold water from which the acetylation product was extracted with chloroform. After washing the solution with sodium bicarbonate and with water and drying over calcium chloride, the chloroform was evaporated. The residue was recrystallized from alcohol and yielded 2-methyl-3-acetylamino-4-ethoxymethyl-5-cyano-6-chloropyridine; m. p. 134–136°.

Anal. Calcd. for $C_{12}H_{14}O_2N_3Cl$: C, 53.83; H, 5.27; N, 15.70. Found: C, 53.65; H, 5.40; N, 15.90.

In a second experiment, 3.8 g. of the chloro-aminopyridine was acetylated by boiling with 25 cc. of acetic anhydride for thirty minutes. The acetic anhydride was removed by distillation under reduced pressure and the residue was treated with 20 cc. of alcohol and 10 cc. of water. After a few minutes, crystallization took place. The crystals were recrystallized by dissolving them in the least possible amount of alcohol and adding water until the solution was slightly cloudy. The yield was 4.3 g. (82.5%) of 2-methyl-3-diacetylamino-4-ethoxymethyl-5-cyano-6-chloropyridine, III; m. p. 90–92°.

Anal. Calcd. for $C_{14}H_{16}O_3N_3Cl$: C, 54.28; H, 5.20; N, 13.57. Found: C, 53.98; H, 4.92; N, 13.34.

Reduction of 2-Methyl-3-diacetylamino-4-ethoxymethyl-5-cyano-6-chloropyridine, III.—A solution of 100 cc. of glacial acetic acid containing 3.09 g. of the chlorodiacetylaminopyridine, III, and 0.82 g. of sodium acetate was shaken with hydrogen in the presence of 10 g. of palladium charcoal and 0.5 g. of Adams catalyst until three moles of hydrogen had been absorbed. The solution was filtered, concentrated, taken up in absolute alcohol, and filtered from the separated sodium chloride. A solution of 2.5 g. of picric acid in hot alcohol was then added and after several minutes crystallization took place. The product was twice recrystallized from alcohol. The yield of the monopicrate of 2-methyl-3-diacetylamino-4-ethoxymethyl-5-aminomethylpyridine, IV, was 1.85 g. (36.4%); m. p. 190–191°.

Anal. Calcd. for $C_{20}H_{24}N_6O_{10}$: C, 47.24; H, 4.75; N, 16.53. Found: C, 47.04; H, 4.72; N, 16.64.

Deacetylation of 2-Methyl-3-diacetylamino-4-ethoxymethyl-5-aminomethylpyridine, IV.—The picrate of IV was decomposed with hydrochloric acid (1:1) and the picric acid was extracted first with nitrobenzene and finally with ether. An attempt was then made to diazotize the free amino group by the addition of one mole of sodium nitrite. The solution was then hydrolyzed by boiling for one and one-half hours with 15% hydrochloric acid, after which it was concentrated to dryness, taken up in absolute alcohol, and treated with acetone. The only product which was isolated was the dihydrochloride of 2-methyl-3-amino-4-ethoxymethyl-5-aminomethylpyridine, VII; m. p. 193–195°.[2] Dr. J. van de Kamp of this Laboratory reported that drying of this compound at 100° under a vacuum from an oil pump raised the m. p. to 204–205°. Recrystallization of the ethoxy-diamine, VII, from 95% alcohol yielded a monohydrate; m. p. 127–129°.

Anal. Calcd. for $C_{10}H_{21}O_2N_2Cl_2$: C, 41.97; H, 7.39; N, 14.68. Found: C, 42.02; H, 7.41; N, 14.93.

Deëthylation of the Dihydrochloride of 2-Methyl-3-amino-4-ethoxymethyl-5-aminomethylpyridine, VII.—The ethoxydiamine, VII (1.55 g.), was treated in a distillation flask with 20 cc. of boiling 48% hydrobromic acid until about one-half of the acid had been distilled. On cooling and scratching the concentrated solution, crystallization took place. The product was recrystallized by dissolving it in a small amount of water and adding 8–10 volumes of alcohol, which yielded the dihydrobromide of 2-methyl-3-amino-4-bromomethyl-5-aminomethylpyridine, IX; m. p. 260–265° with decomposition.

Anal. Calcd. for $C_8H_{14}N_3Br_3$: C, 24.51; H, 3.60; N, 10.72. Found: C, 24.97, 24.90; H, 3.71, 3.62; N, 10.66.

This bromomethyl-diamine, IX, was heated with hot water and then stirred with silver chloride until the bromide ions were completely removed. The solution was concentrated to dryness under reduced pressure and the residue was recrystallized from 95% alcohol. The product was the dihydrochloride of 2-methyl-3-amino-4-hydroxymethyl-5-aminomethylpyridine, X; m. p. 235–237°.

Anal. Calcd. for $C_8H_{15}N_3OCl_2$: C, 40.01; H, 6.30; N, 17.50. Found: C, 39.81; H, 6.14; N, 17.48.

It was found later that the ethoxy-diamine, VII, could be hydrolyzed directly to the hydroxy-diamine, X. A solution of 2.24 g. of VII in 34 cc. of 2.5 *N* hydrochloric acid was heated in a bomb tube for four hours at 175–180°. The slightly colored solution was filtered with charcoal and concentrated to dryness under reduced pressure. The product was recrystallized from water and alcohol. The yield of the hydroxy-diamine, X, was 1.44 g. (76.7%); m. p. 235–237°. There was no depression of mixed melting point with a sample of X obtained above.

Diazotization of the Dihydrochloride of 2-Methyl-3-amino-4-hydroxymethyl-5-aminomethylpyridine, X, to form Vitamin B_6, XI.—A solution of 1.28 g. of the hydroxy-diamine, X, in 22 cc. of water was added simultaneously with a solution of 2.24 g. of sodium nitrite to 45 cc. of hot (90–95°) 2.5 *N* hydrochloric acid. The yellow solution was concentrated to dryness under reduced pressure and the residue washed with acetone, which removed some of the color. The vitamin hydrochloride was extracted from the sodium chloride with hot absolute alcohol. This solution was filtered with charcoal and concentrated to a small volume. On addition of acetone the vitamin B_6 hydrochloride crystallized; m. p. 208°. The yield was 0.5 g. (45.4%).

Anal. Calcd. for $C_8H_{11}NO_3Cl$: C, 46.72; H, 5.88. Found: C, 46.51; H, 5.70.

Conversion of 2-Methyl-3-hydroxy-4-ethoxymethyl-5-hydroxymethylpyridine, VIII, to Vitamin B_6 Hydrochloride.—This ethyl ether of vitamin B_6, VIII, has now been obtained in a purer form with a slightly higher melting point than was reported in a previous paper.[2] It was most easily purified as the free base in acetone solution by the addition of ether and filtration with charcoal. The nearly colorless solution was then treated with dry hydrogen chloride. The precipitated salt was recrystallized from alcohol by the addition of an equal volume of acetone. Washing with acetone gave colorless crystals of 2-methyl-3-hydroxy-4-ethoxymethyl-5-hydroxymethylpyridine hydrochloride, VIII; m. p. 135–136°.

Anal. Calcd. for $C_{10}H_{16}NO_3Cl$: C, 51.38; H, 6.90; N, 6.00. Found: C, 51.20; H, 6.81; N, 6.25, 6.20.

A solution of 4 g. of the ethyl ether, VIII, in 20 cc. of water and 1 cc. of 2.5 *N* hydrochloric acid was heated in a bomb tube at 155–160° for six hours. The slightly colored solution was treated with charcoal, filtered, and concentrated to dryness under reduced pressure. The yield of slightly yellow crystals was 2.92 g. (83%). After recrystallization from absolute alcohol, with the use of charcoal for decolorization, pure white vitamin B_6 hydrochloride was obtained; m. p. and mixed m. p. 208–209°.

The cleavage of the ethoxy group of VIII also was accomplished by dissolving 0.2 g. of this substance in 6 cc. of concentrated hydrochloric acid and heating in a bomb tube at 132° for one hour. On cooling in ice water, crystals separated and were recrystallized from a little concentrated hydrochloric acid. The yield of 2-methyl-3-hydroxy-4,5-*bis*-(chloromethyl)-pyridine hydrochloride, XIII, was 0.09 g. (45%), m. p. 206° with preliminary darkening around 200°.

Anal. Calcd. for $C_8H_{10}NOCl_3$: C, 39.62; H, 4.16; N, 5.78. Found: C, 39.48; H, 3.98; N, 5.94.

This dichloride, XIII (50 mg.), was converted to vitamin B_6 hydrochloride by heating in 10 cc. of water on the steam-bath for one hour. The water was evaporated and the material recrystallized from alcohol and acetone. The first crop of vitamin B_6 hydrochloride (10 mg.) melted at 202–203° and showed no depression of melting point with a pure specimen of the vitamin.

2-Methyl-3-hydroxy-4,5-(epoxydimethyl)-pyridine Hydrochloride, XIV.—In recrystallizing vitamin B_6 prepared by the hydrolysis of 2-methyl-3-hydroxy-4,5-*bis*-(bromomethyl)-pyridine hydrobromide, XII, a by-product was found in the mother liquors. After the pure vitamin hydrochloride crystallized out, a mixture of substances melting at about 195° was obtained. When acetone was added to the final mother liquor a substance melting above 230° was formed. Recrystallization from alcohol yielded 2-methyl-3-hydroxy-4,5-(epoxydimethyl)-pyridine hydrochloride; m. p. 239–240° with decomposition.

Anal. Calcd. for $C_8H_{10}O_2NCl$: C, 51.21; H, 5.37; N, 7.47. Found: C, 51.13; H, 5.21; N, 7.62.

This epoxy compound, XIV, was obtained in small yields when 1-g. quantities of vitamin B_6, XI, and its ethyl ether, VIII, were treated with 15 cc. of 50% sulfuric acid for one hour on the steam-bath. The sulfuric acid was neutralized with sodium hydroxide, the water was evaporated, and the product was extracted with acetone as the free base. The addition of dry hydrogen chloride gave a product which, after crystallization from alcohol, was identical with the by-product described above.

Cleavage of the Epoxydimethyl Group.—2-Methyl-3-hydroxy-4,5-(epoxydimethyl)-pyridine resisted hydrolysis on heating with 2.5 *N* hydrochloric acid at 175° for four hours. However, the ether group was split when 3.7 g. of the epoxydimethyl derivative, XIV, was distilled with 60 cc. of 48% hydrobromic acid until the volume was reduced to 30 cc. After cooling and filtering, the yield of 2-methyl-3-hydroxy-4,5-*bis*-(bromomethyl)-pyridine hydrobromide, XII, was 6.42 g. (86.5%); m. p. 228.5°. This melting point was 5° higher than previously reported.[2]

Anal. Calcd. for $C_8H_{10}NOBr_3$: C, 25.53; H, 2.66; N, 3.72. Found: C, 25.71; H, 2.89; N, 3.73.

Acknowledgment.—The authors are indebted to Messrs. D. F. Hayman and W. Reiss for the microanalyses and to Mr. A. N. Wilson for technical assistance.

Summary

Variations and improvements in the synthesis of vitamin B_6 have been made. The compounds 2-methyl-3-hydroxy-4-ethoxymethyl-5-hydroxymethylpyridine and 2-methyl-3-amino-4-ethoxymethyl-5-aminomethylpyridine have been hydrolyzed directly to the corresponding hydroxy derivatives by heating with dilute hydrochloric acid at 150–175° under pressure. Derivatives of some of the intermediates and a new inner ether of vitamin B_6 have been described.

RAHWAY, N. J. RECEIVED OCTOBER 10, 1939

[CONTRIBUTION FROM THE SANDERS LABORATORY OF CHEMISTRY, VASSAR COLLEGE, AND THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

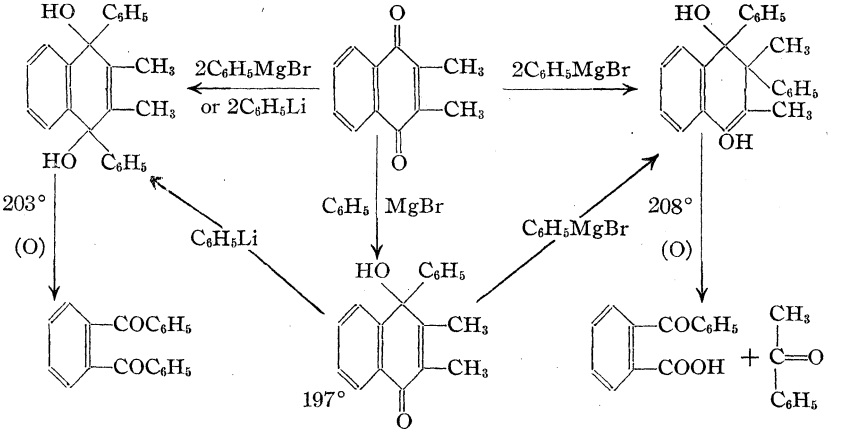
The Reaction between 2,3-Dimethyl-1,4-naphthoquinone and Phenylmagnesium Bromide. II[1]

BY H. MARJORIE CRAWFORD

In an earlier paper[2] it was shown that phenylmagnesium bromide reacts with 2,3-dimethyl-1,4-naphthoquinone to give all of the expected reduction and addition products. These solids accounted for about 30% of the starting material, the other product being a dark, thick oil. No amorphous materials were encountered. Four addition products were described, two resulting from the 1,2- and 1,4-addition of one molecule of phenylmagnesium bromide to one molecule of the quinone, and two resulting from the 1,2-1,2- and 1,2-1,4-addition of two molecules of phenylmagnesium bromide to one molecule of the quinone.

Further reactions of the two di-addition products are described in this paper.

The structures of the two di-addition products were established as shown by the following equations.



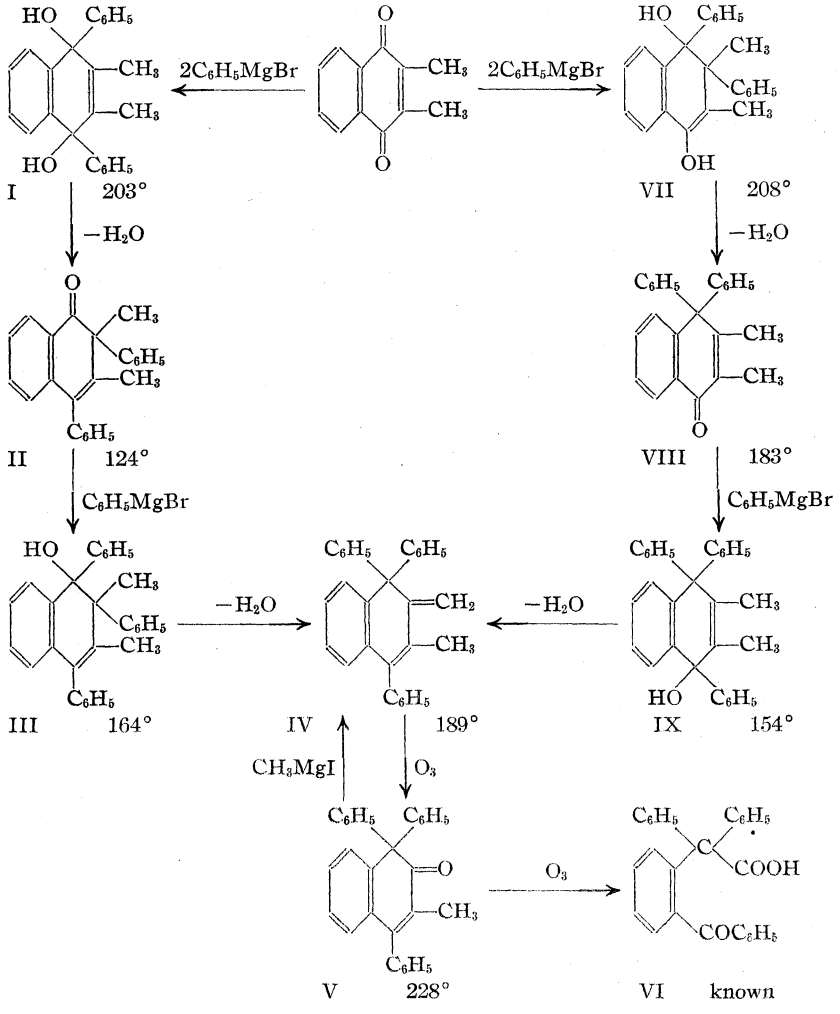
In the Grignard machine, both di-addition compounds showed two active hydrogens. Oxidation of both compounds gave known products which served to locate the phenyl groups. The 203° compound gave *o*-dibenzoylbenzene and the 208° compound gave acetophenone and *o*-benzoyl-

(1) Reported at the fall meeting of the American Chemical Society at Boston, Mass., September, 1939.

(2) Crawford, THIS JOURNAL, **57**, 2000 (1935).

benzoic acid. The 203° compound was also formed by the reaction of phenyllithium on either the 197° mono-addition compound or the original quinone. Phenylmagnesium bromide reacted with the 197° mono-addition compound to give the 208° compound.

Starting with these two di-addition products, parallel series of reactions led to the same product, a hydrocarbon.



The dehydration and rearrangement of I led to the formation of the 124° compound (II). II was oxidized easily to acetophenone and *o*-benzoylbenzoic acid. The formation of these products indicated that the formation of II from I involved the shift of one phenyl group from a carbon next to the ring to a carbon holding a methyl group. Very small amounts of II were available and the only other reactions investigated were those with phenyllithium and with phenylmagnesium bromide. In both of these reactions, decomposition of the metallic product with acid led to the formation of a hydrocarbon (IV). Careful decomposition of the metallic compound with water gave an intermediate carbinol (III) which, in the presence of acid, easily lost a molecule of water and gave the hydrocarbon. This hydrocarbon was difficult to oxidize with ordinary oxidizing agents, but was attacked readily by ozone to give formaldehyde and a ketone (V). When the ketone was treated with methylmagnesium iodide followed by acid, the hydrocarbon was formed again, so no rearrangement occurred during the reaction with ozone. Ozonization of the ketone (V) gave a known keto acid (VI). The structure of this known keto acid located the three phenyl groups in the hydrocarbon (IV) and in the ketone (V).

The same hydrocarbon (IV) was obtained by starting with the other di-addition product (VII) and carrying out the same series of reactions. Dehydration of VII gave the 183° compound (VIII) which was extremely unreactive. VIII was recovered unchanged after attempts at oxidation with potassium dichromate or chromium trioxide in glacial acetic acid, with basic potassium permanganate, with hydrogen peroxide and with ozone. The only reactions which VIII could be made to undergo were reduction with zinc and acetic acid (which gave very small amounts of two reduction products) and the reaction with organo-metallic reagents. When phenylmagnesium bromide or phenyllithium was added to VIII and the metallic compound was decomposed with acid, the hydrocarbon (IV) resulted, but if ammonium chloride was used for the decomposition, an intermediate carbinol (IX) could be isolated. Both ozonization of this carbinol and oxidation with potassium

dichromate in acetic acid gave the same products that would have been obtained from the hydrocarbon, so the first reaction was apparently dehydration and this was followed by oxidation.

Knowing the structures of I, II, IV and VII, the structure proposed for VIII seems the only reasonable one, although all attempts to break it up by oxidation and all attempts to synthesize it have so far proved unsuccessful.

The reactions involved in these dehydrations and rearrangements are all of the pinacol and allylic types. Cases of dehydration accompanied by the migration of a phenyl group are not unusual. The researches of Ramart and Amagat,[3] Bachmann,[4] and Kleinfeller and Eckert[5] showed that, in the cases studied, the phenyl group was the only one to migrate. The tendency of phenyl groups to migrate in preference to methyl groups is shown by the work of McKenzie and Myles[6] and of Orekhov and Tiffeneau.[7]

In most attempts at oxidation of the carbinol (IX) and of the hydrocarbon (IV), either by potassium permanganate, potassium dichromate or ozone, there resulted small amounts of a hydrocarbon, melting at 235°, which was isomeric with the hydrocarbon (IV). An oil was formed when this hydrocarbon was treated with ozone and no structure can be suggested for it at this time.

Experimental

All combustions were carried out using the semi-micro method of Lauer and Dobrovolny.[8] Molecular weight determinations were made by the lowering of the freezing point of benzene or of camphor.

1,4 - Dioxy - 2,3 - dimethyl - 1,4 - diphenyldihydronaphthalene, I, m. p. 203–204°.—Because of its great solubility, this white di-addition product was obtained only occasionally from the mixture of products resulting from the reaction between phenylmagnesium bromide and 2,3-dimethyl-1,4-naphthoquinone. When it was obtained from this mixture, it was in the form of a pale yellow double compound which contained two molecules of the quinone to one molecule of the 203° compound. The quinone could be steam distilled from a solution of the double compound leaving the 203° compound (I). I was obtained in much better yields (20%) by the reaction of 0.2 mole of phenyllithium[9] on 0.1 mole (18.6 g.) of the quinone. The green solid formed in this reaction looked very much like the solid formed during the reaction between phenylmagnesium bromide and the quinone. After standing for two hours, the mixture was decomposed with ice and dilute hydrobromic acid. The organic material was extracted with ether. Evaporation of the ether gave 10 g. of white solid which after recrystallization from 50% alcohol yielded 6.85 g. of I. This compound was also formed, in 50% yield, by the reaction of 0.02 mole of phenyllithium on 0.01 mole of the 197° mono-addition compound.

The Grignard machine showed two active hydrogens. The other analytical data are included in the earlier paper[2] (in which the 203° compound was numbered IX).

Potassium permanganate was not decolorized and heating 1.0 g. of I for one and one-half hours with potassium dichromate gave a small amount of solid melting at 140–143°. Better results were obtained by adding 2.0 g. of I to 2.0 g. of chromium trioxide in 10 cc. of glacial acetic acid and boiling for five minutes. Pouring the mixture immediately into water gave a precipitate which on crystallization from alcohol melted at 145–148° and was identical with a known sample of *o*-dibenzoylbenzene.

Heating I with hydrochloric acid in methyl alcohol or with zinc chloride and hydrochloric acid in benzene caused it to lose a molecule of water and to be transformed almost quantitatively into the 124° compound (II).

1 - Oxo - 2,3 - dimethyl - 2,4 - diphenyldihydronaphthalene, II, m. p. 124°.—This compound was obtained once in the crystallization of the yellow double compound of I and quinone. Later it was easily obtained, in practically quantitative yields, by the dehydration of I.

Oxidation of 1.0 g. of II by boiling for five hours with 3.0 g. of potassium dichromate in glacial acetic acid gave acetophenone and *o*-benzoylbenzoic acid. II decolorized bromine in carbon tetrachloride slowly, but failed to give a semicarbazone. It reacted readily with phenylmagnesium bromide and phenyllithium. When the metallic product was decomposed by acid (after fifteen minutes of standing) there resulted a hydrocarbon (IV). When the metallic product was decomposed carefully with water, a carbinol (III) was obtained.

The analytical data for II are contained in the earlier paper[2] (in which the 124° compound was numbered XI).

1 - Oxy - 2,3 - dimethyl - 1,2,4 - triphenyldihydronaphthalene, III, m. p. 164–174°.—This carbinol was prepared by adding phenylmagnesium bromide in excess to 0.7 g. of II, decomposing the product with water, and extracting with ether. The small amount of solid from the ether solution was crystallized from alcohol, in which it was quite soluble, and melted at 164–174°. Heating in benzene for one hour with a few crystals of zinc chloride and five drops of concd. hydrochloric acid caused 0.2 g. of III to lose water with the formation of the hydrocarbon (IV).

Anal. Calcd. for $C_{30}H_{26}O$: C, 89.51; H, 6.51. Found: C, 88.92, 88.83; H, 6.80, 6.65.

3 - Methyl - 2 - methylene - 1,1,4 - triphenyldihydronaphthalene, IV, m. p. 189–190°.—This hydrocarbon was obtained by the dehydration of either of the carbinols, III or IX. Addition of methylmagnesium iodide to 0.25 g. of the ketone (V) and decomposition of the reaction mixture with hydrochloric acid also gave the hydrocarbon in 76% yield. The best method of preparation, giving practically quantitative yields, was the addition of phenylmagnesium bromide to the 183° compound (VIII) and decomposition

(3) Ramart and Amagat, *Ann. chim.*, **8**, 263 (1927).
(4) Bachmann, THIS JOURNAL, **54**, 1969 (1932).
(5) Kleinfeller and Eckert, *Ber.*, **62**, 1598 (1929).
(6) McKenzie and Myles, *ibid.*, **65**, 209 (1932).
(7) Orekhov and Tiffeneau, *Compt. rend.*, **182**, 67 (1926).
(8) Lauer and Dobrovolny, *Mikrochem.*, Pregl Festschr., 243 (1929).
(9) Gilman, THIS JOURNAL, **54**, 1957 (1932).

of the reaction mixture, after about an hour, with hydrochloric acid. The hydrocarbon was then extracted with ether, the solvent evaporated, and the solid crystallized from a mixture of alcohol and benzene. It was only slightly soluble in isopropyl ether, alcohol and ethyl acetate but was very soluble in benzene. It decolorized bromine in carbon tetrachloride rapidly.

Potassium permanganate in acetone was not decolorized by IV at room temperature. When the hydrocarbon was boiled for four hours with potassium dichromate in glacial acetic acid, a small amount of benzoic acid was isolated along with a neutral oil which could not be crystallized. Ozonization of IV in chloroform or in carbon tetrachloride gave varying results. The solution of the ozonide was poured into water and allowed to stand overnight. The main product from the ether extract was always the ketone (V) with sometimes small amounts of the keto acid (VI) and sometimes small amounts of a hydrocarbon, m. p. 235°. In one case the ozonide was dropped into boiling water containing zinc dust and traces of hydroquinone and silver nitrate. The resulting gases were passed into a solution of methone and there were formed white needles of formaldimethone, identical with synthetic formaldimethone.

Anal. Calcd. for $C_{30}H_{24}$ (384.2): C, 93.71; H, 6.29. Found: C, 93.71, 93.26; H, 6.28, 6.66; mol. wt. (benzene) 360, (camphor) 398, 416.

2 - Oxo - 3 - methyl - 1,1,4 - triphenyldihydronaphthalene, V, m. p. 228°.—This ketone was formed by ozonizing the hydrocarbon (IV) and the carbinol (IX). It is only slightly soluble in alcohol, glacial acetic acid and pyridine, but is fairly soluble in hot benzene. It decolorized bromine in carbon tetrachloride rapidly. Fusion with potassium hydroxide, treatment with semicarbazide and boiling for three hours with potassium dichromate in glacial acetic acid gave only unchanged material. Addition of excess methylmagnesium iodide to 0.25 g. of the ketone and decomposition of the mixture with ice and hydrochloric acid gave 0.19 g. (76%) of the hydrocarbon (IV). Ozonization of 1.0 g. of the ketone in carbon tetrachloride and decomposition of the ozonide with water gave 0.6 g. of a white acid (VI) which decomposed at 218°.

Anal. Calcd. for $C_{29}H_{22}O$: C, 90.11; H, 5.74. Found: C, 90.16; H, 5.95.

Diphenyl-(*o*-benzoylphenyl)-acetic Acid, VI.—This keto acid was obtained by ozonizing the ketone (V). It was recrystallized from benzene and acetone and decomposed at 218°. The acid was transformed into the methyl ester by boiling about 0.3 g. of the acid with 5 cc. of methyl alcohol and two drops of concd. sulfuric acid. A white precipitate formed after forty minutes and the solution was cooled and filtered. The ester melted at 189–190°. This keto acid was then synthesized by the oxidation of 1,1,3-triphenylindene.[10] The methyl ester of this acid had not been reported before and was made by boiling 1.0 g. of the synthetic acid with 20 cc. of methyl alcohol and six drops of concd. sulfuric acid. As in the other case, solid separated after about forty minutes of heating. The solid melted at 188–189° and after recrystallization from methyl alcohol and benzene finally melted at 192–193°. The mixed melting point of this ester with that from the acid resulting from the ozonization of the ketone, was 190.5–192°.

Anal. Calcd. for $C_{28}H_{22}O_3$: C, 82.73; H, 5.45. Found: C, 82.63; H, 5.56.

1,4 - Dioxy - 2,3 - dimethyl - 1,2 - diphenyldihydronaphthalene, VII, m. p. 208–209°.—This compound was the main solid product from the reaction between phenylmagnesium bromide and 2,3-dimethyl-1,4-naphthoquinone.[2] It also resulted from the reaction of phenylmagnesium bromide on the 197° mono-addition compound. It was oxidized easily to acetophenone and *o*-benzoylbenzoic acid by boiling for five hours with potassium dichromate and glacial acetic acid. The Grignard machine showed two active hydrogens. The most interesting reaction of VII was the loss of a molecule of water to give the 183° compound (VIII). This reaction could be brought about by treatment with various reagents. Heating on the steam-bath for two hours with phosphorus tribromide in bromoform, heating for six hours in benzene with about 3 g. of zinc chloride and 3 cc. of concd. hydrochloric acid or heating for one hour with 0.5 g. of iodine in 50 cc. of glacial acetic acid transformed 1.0 g. of VII into VIII in 90% yields. VII was not changed by one-half hour of heating with 20% sulfuric acid nor by warming on the steam-bath with acetic anhydride and sodium acetate.

Other properties and analytical data are included in the earlier paper[2] (in which this compound was numbered VI).

4 - Oxo - 2,3 - dimethyl - 1,1 - diphenyldihydronaphthalene, VIII, m. p. 183°.—This compound was formed in about 90% yields by the loss of a molecule of water from compound VII. It is very soluble in most organic solvents and separates from hot alcohol in glistening white leaflets. Its extreme inertness is its most outstanding characteristic. It was recovered unchanged from boiling for one hour with constant boiling hydrobromic acid, from boiling for seven hours with hydroxylamine, from warming for one hour with semicarbazide, from warming with phenylhydrazine and 2,4-dinitrophenylhydrazine, from warming with aluminum isopropylate, from warming with potassium permanganate and potassium hydroxide, from boiling for five hours with potassium dichromate in glacial acetic acid, from boiling for one hour with chromium trioxide in glacial acetic acid, from warming for six hours with 30% hydrogen peroxide, and from ozonizing for one hour in carbon tetrachloride. It does not decolorize bromine in carbon tetrachloride.

Reduction of 3.2 g. of VIII by boiling for four hours with 5 g. of zinc and 25 cc. of glacial acetic acid gave very small amounts of two neutral products. One melted at 142–143° and analyses corresponded to the addition of two atoms of hydrogen to give the compound $C_{24}H_{22}O$. The other melted at 176–177° and is a hydrocarbon.

The only reactions that took place readily were those with phenylmagnesium bromide and phenyllithium. The Grignard machine showed the addition of one molecule of methylmagnesium iodide and no active hydrogens. When the mixture from the reaction of either phenylmagnesium bromide or phenyllithium on VIII was decomposed with hydrochloric acid, the hydrocarbon (IV) was isolated in 90% yields from the ether extract. If the magnesium compound was carefully decomposed, after about twenty

(10) Kohler, *Am. Chem. J.*, **40**, 231 (1908).

minutes, with ammonium chloride and water, the ether extract gave 90% yields of the carbinol (IX).

Other analytical data on this compound are contained in the earlier paper[2] (in which this compound was numbered VIII).

4 - Oxy - 2,3 - dimethyl - 1,1,4 - triphenyldihydronaphthalene, IX, m. p. 154°.—This carbinol was formed in 90% yields by the addition of phenylmagnesium bromide to VIII. It is very unstable in the presence of acid and when an alcohol solution of the carbinol was treated with hydrochloric acid, a molecule of water was lost with the formation of the hydrocarbon (IV). IX melts at 154° with the loss of a molecule of water and the formation of the hydrocarbon (IV). Warming with zinc chloride and concd. hydrochloric acid in benzene also converted IX to the hydrocarbon (IV). The Grignard machine showed one active hydrogen. Boiling for one hour with potassium permanganate and potassium hydroxide gave 90% of unchanged material. Boiling for one hour with potassium dichromate in glacial acetic acid gave a solid from which, after many recrystallizations from alcohol and ethyl acetate, it was possible to isolate a small amount of the 235° hydrocarbon. Ozonization of IX in chloroform gave the ketone (V), so dehydration to the hydrocarbon (IV) probably occurred before the reaction with ozone.

Anal. Calcd. for $C_{30}H_{26}O$: C, 89.51; H, 6.51. Found: C, 89.31, 88.95; H, 6.80, 6.75.

The 235° Hydrocarbon.—This compound, isomeric with the 189° hydrocarbon (IV), was formed in small amounts in many attempts to oxidize the hydrocarbon (IV) with potassium dichromate or potassium permanganate in glacial acetic acid or with ozone, and to oxidize the carbinol (IX) with potassium dichromate in glacial acetic acid.

Heating the hydrocarbon (IV) with acetic acid alone or with iodine in acetic acid did not convert it into the high melting isomer. Ozone converted 0.4 g. of the 235° compound into an oil from which no solid material could be obtained. The 235° compound was only slightly soluble in alcohol and in ethyl acetate, but could be crystallized from benzene.

Anal. Calcd. for $C_{30}H_{24}$ (384.2): C, 93.71; H, 6.29. Found: C, 93.84, 93.23; H, 6.29, 6.07; mol. wt. (camphor), 360.

The author wishes to thank the University of Minnesota for the courtesy shown her as an Honorary Fellow of the University while on leave from Vassar College in the spring of 1938.

Summary

Starting with the two di-addition products from the reaction between phenylmagnesium bromide and 2,3-dimethyl-1,4-naphthoquinone, parallel series of reactions lead to the same product, a hydrocarbon.

Structures have been assigned to these two di-addition products, to the two compounds resulting from the dehydration and rearrangement of these compounds, and to four new compounds obtained in these series of reactions.

POUGHKEEPSIE, N. Y. RECEIVED AUGUST 24, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. LXXVI. Oxidation and Reduction Products of Equilenin

BY RUSSELL E. MARKER AND EWALD ROHRMANN

In previous work[1] from this Laboratory it was observed that equilenin when reduced with Adams catalyst in acidic ethanol gave approximately a 70% yield of 5,7,9-estratrienol-17. No other reduction products were isolated. Ruzicka, Müller and Mörgeli[2] in a somewhat similar reduction obtained this same product in addition to some α-dihydroequilenin. By modifying the reduction technique these workers were able to obtain a 5,7,9-estratrienediol-3,17 which was identical with one of the diols obtained by the reduction of equilenin with sodium.[2,3,4]

When the hydrogenation of equilenin is carried out in a neutral medium with Adams catalyst, the essential product is α-dihydroequilenin, a product first isolated from the phenolic fraction of mares pregnancy urine by Wintersteiner and co-workers[5] and later prepared by Marker and co-workers[1] by the reduction of equilenin with aluminum isopropylate. The hydrogenation of α-dihydroequilenin in acidic ethanol yields the same 5,7,9-estratrienol-17 as was obtained from equilenin, indicating that the hydroxyl group at C-17 is of the α-configuration.

In a previous comprehensive investigation of the carbinol fraction of mares pregnancy urine[6] we reported the isolation (from the chromic anhy-

(1) Marker, Kamm, Oakwood and Tendick, THIS JOURNAL, **59**, 768 (1937).

(2) Ruzicka, Müller and Mörgeli, *Helv. Chim. Acta.*, **21**, 1394 (1938).

(3) Marker, Rohrmann, Wittle and Tendick, THIS JOURNAL, **60**, 2440 (1938).

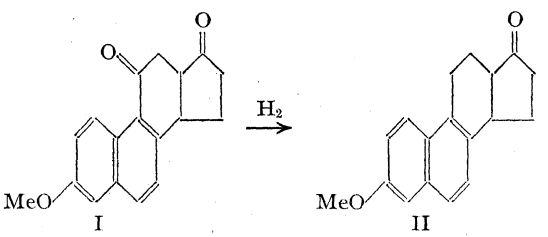
(4) David, *Acta Brevia Neerland Physiol. Pharmacol. Microbiol.*, **8**, 211 (1938).

(5) Wintersteiner, Schwenk, Wirschmann and Whitman, THIS JOURNAL, **58**, 2652 (1936).

(6) Marker and Rohrmann, THIS JOURNAL, **61**, 2537 (1939).

dride oxidation products of a crude carbinol fraction) of a diketone of the composition $C_{18}H_{16}O_2$. This substance formed a mono-semicarbazone, which suggested the presence of a hindered carbonyl group. We now have strong indications that this product is 3-desoxy-11-keto-equilenin. On catalytic hydrogenation in acidic ethanol, it gave a good yield of 5,7,9-estratrienol-17(α) identical with that obtained from equilenin. The fact that the reduction in acidic medium removes the carbonyl group at C-11 is in accordance with the fact that carbonyl groups adjacent to benzenoid ring systems are usually removed on hydrogenation under the proper conditions.

The properties of 3-desoxy-11-ketoequilenin resemble those of the methyl ether of 11-keto-*nor*-equilenin (I) prepared synthetically by Koebner and Robinson.[7] This product (I) formed only a mono-carbonyl derivative and on reduction with a platinum–charcoal catalyst in the presence of palladium chloride yielded the methyl ether of *nor*-equilenin (II).

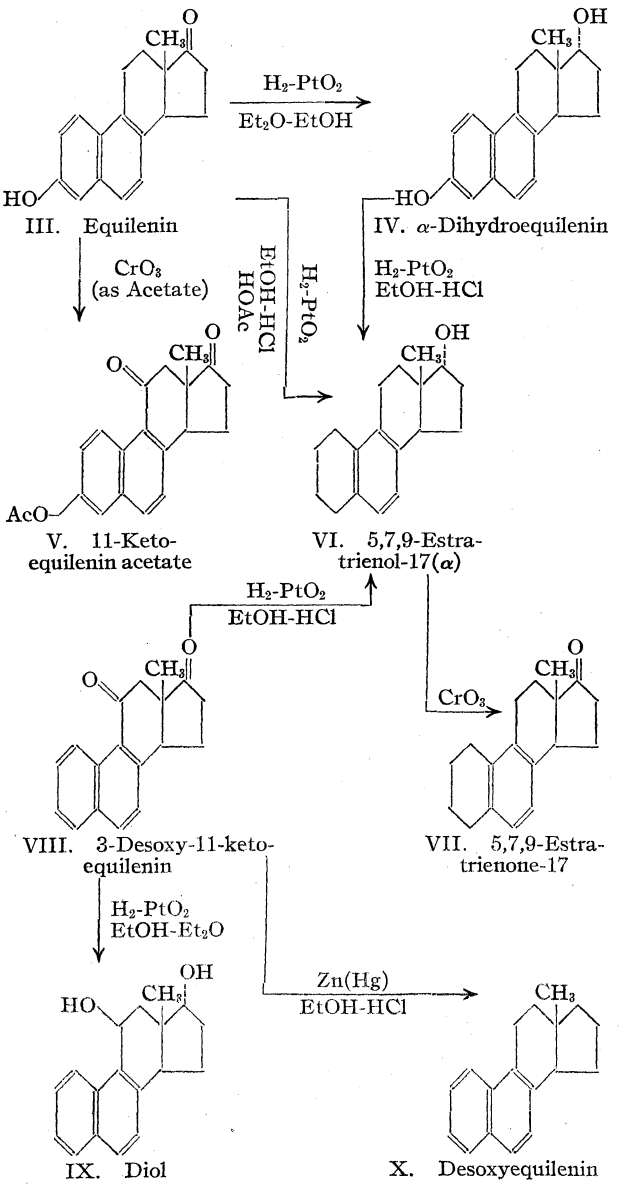


I II

When the hydrogenation of 3-desoxy-11-keto-equilenin was carried out in a neutral medium the product appeared to be a compound in which the two carbonyl groups were reduced to hydroxyl groups. A mild Clemmensen reduction (unamalgamated zinc) of 3-desoxy-11-keto-equilenin yielded a mono-keto derivative while more vigorous reduction (amalgamated zinc) gave desoxyequilenin.

Inasmuch as the 3-desoxy-11-keto-equilenin was obtained from the oxidation of a ketone free (*i. e.*, non-hindered ketones) carbinol fraction, some question might be raised concerning the nature of the compound before oxidation. It now seems highly probable that the carbonyl group at C-11 was introduced during the chromic anhydride oxidation of the carbinol fraction, inasmuch as equilenin acetate upon oxidation with chromic anhydride yields a product which appears to be 11-keto-equilenin acetate. The substance forms only a mono-semicarbazone. The 11-keto-equilenin acetate was obtained in rather poor yields apparently due to the lability of the product to further oxidation under the conditions used.

The introduction of a carbonyl group into the C-11 position by oxidation of equilenin derivatives with chromic anhydride strongly suggests that the 3-desoxy-11-keto-equilenin obtained from the oxidation of the mares urine carbinol fraction was actually formed by the oxidation of 3-desoxy-dihydroequilenin, thus indicating the presence of this substance in mares pregnancy urine.



Equilenin resembles estrone in that it reacts

(7) Koebner and Robinson, *J. Chem. Soc.*, 1994 (1938).

readily with ethyl chloroacetate and sodium ethylate to yield the acetic acid derivative.[8] Catalytic hydrogenation of equilenin-3-oxy-acetic acid in acidic ethanol yielded largely 5,7,9-estratrienol-17(α) and very little acidic material was obtained.

This investigation was supported by a grant from the Committee for Research in Problems of Sex, National Research Council. We also wish to thank Parke, Davis and Company for the supply of urine concentrate and equilenin and for their generous assistance in various phases of this work.

Experimental Part

Hydrogenation of Equilenin and α-Dihydroequilenin.—A mixture of 500 mg. of equilenin, 500 mg. of Adams catalyst, 300 cc. of ether and 10 cc. of absolute ethanol was shaken with hydrogen at three atm. and 25° for fifteen hours. The product was crystallized from 80% ethanol to give compact white crystals, m. p. 245–247°. This gave no depression with an authentic sample of α-dihydroequilenin. It gave a 30° depression with a sample of equilenin of m. p. 257–258°.

Anal. Calcd. for $C_{18}H_{20}O_2$: C, 80.55; H, 7.5. Found: C, 80.8; H, 7.6.

A mixture of 250 mg. of α-dihydroequilenin, 120 cc. of absolute ethanol, 2 cc. of hydrochloric acid and 200 mg. of Adams catalyst was shaken with hydrogen at three atm. for twelve hours at 25°. The product was crystallized from ether–pentane as white needles, m. p. 144–146°. This gave no depression with a sample of 5,7,9-estratrienol-17(α), m. p. 144–146°, obtained from equilenin.

Anal. Calcd. for $C_{18}H_{24}O$: C, 84.3; H, 9.4. Found: C, 84.0; H, 9.5.

5,7,9-Estratrienone-17.—To a solution of 300 mg. of 5,7,9-estratrienol-17(α) in 30 cc. of acetic acid was added a solution of 300 mg. of chromic anhydride in 20 cc. of 80% acetic acid. After standing for one hour at 25°, the mixture was diluted with water and extracted with ether. The ethereal solution was washed with sodium carbonate solution and the ether removed. The residue was crystallized from aqueous methanol as thick white needles, m. p. 107–109°.

Anal. Calcd. for $C_{18}H_{22}O$: C, 85.0; H, 8.7. Found: C, 84.7; H, 8.8.

With hydroxylamine hydrochloride the product yielded an **oxime** which crystallized from acetone as white needles, m. p. 203–205° dec.

Anal. Calcd. for $C_{18}H_{23}ON$: C, 80.25; H, 8.6. Found: C, 80.5; H, 8.3.

Reduction of 3-Desoxy-11-keto-equilenin. (a) By Catalytic Hydrogenation in Acidic Medium.—A mixture of 250 mg. of 3-desoxy-11-keto-equilenin, 120 cc. of absolute ethanol, 200 mg. of Adams catalyst and 2 cc. of concentrated hydrochloric acid was shaken with hydrogen at two atm. for five hours at room temperature. After treatment with Norite the product was crystallized from ether–pentane to give 150 mg. of white needles, m. p. 144–146°. This gave no depression with a sample of 5,7,9-estratrienol-17(α), m. p. 144–146°, prepared by a similar reduction of equilenin.

Anal. Calcd. for $C_{18}H_{24}O$: C, 84.3; H, 9.4. Found: C, 84.2; H, 9.5.

When refluxed for thirty minutes with an excess of acetic anhydride the reduction product yielded an **acetate** which crystallized from methanol as white needles, m. p. 101.5–102.5°. This gave no depression with a sample of the acetate of 5,7,9-estratrienol-17(α), m. p. 102–103°.

Anal. Calcd. for $C_{20}H_{26}O_2$: C, 80.5; H, 8.8. Found: C, 80.5; H, 8.9.

(b) **By Catalytic Hydrogenation in Neutral Medium.**—A mixture of 200 mg. of 3-desoxy-11-keto-equilenin, 60 cc. of ether, 60 cc. of absolute ethanol and 200 mg. of Adams catalyst was shaken with hydrogen at three atm. at room temperature for four and one-half hours. The product was crystallized from ether–acetone as white needles, m. p. 209–212°.

Anal. Calcd. for $C_{18}H_{20}O_2$: C, 80.55; H, 7.5. Found: C, 80.5; H, 7.7.

(c) **By Clemmensen Reduction with Unamalgamated Zinc.**—A mixture of 250 mg. of the 11-keto compound, 40 cc. of 95% ethanol and 10 g. of 20-mesh zinc was refluxed for three and one-half hours during which time 7 cc. of hydrochloric acid was added. The solution was decanted into water and the resulting mixture extracted with ether. The reaction product was sublimed in high vacuum at 130–140° to give a product which crystallized from ether–pentane as needles, m. p. 156–158°.

Anal. Calcd. for $C_{18}H_{18}O$: C, 86.35; H, 7.25. Found: C, 86.3; H, 7.3.

(d) **Clemmensen Reduction with Amalgamated Zinc.**—To a boiling mixture of 100 mg. of the ketone, 25 cc. of ethanol and 5 g. of amalgamated zinc (20-mesh) was added 15 cc. of hydrochloric acid over a period of two hours. The product was sublimed in high vacuum at 60–65° and the sublimate crystallized from methanol and acetone to give white crystals, m. p. 73–75°.

Anal. Calcd. for $C_{18}H_{20}$: C, 91.5; H, 8.5. Found: C, 91.2; H, 8.5.

11-Keto-equilenin Acetate.—To a solution of 2 g. of equilenin acetate (m. p. 158–160°) in 75 cc. of acetic acid was added a solution of 2.5 g. of chromic anhydride in 40 cc. of 80% acetic acid. The mixture was allowed to stand at 25° for five hours, when it was diluted with water and extracted with ether. The ethereal extract was washed well with water and sodium carbonate solution and the ether evaporated. The residual sirup was crystallized first from ether–pentane and then from ether to give compact white crystals, m. p. 195–197°.

Anal. Calcd. for $C_{20}H_{18}O_4$: C, 74.5; H, 5.6. Found: C, 74.7; H, 5.7.

With semicarbazide acetate under the usual conditions the substance yielded a **mono-semicarbazone** which crystallized from aqueous methanol, m. p. 238–241° decomp.

Anal. Calcd. for $C_{21}H_{21}O_4N_3$: C, 66.5; H, 5.6. Found: C, 66.3; H, 5.8.

(8) Marker and Rohrmann, THIS JOURNAL, **61**, 2974 (1939).

Equilenin-3-oxyacetic Acid.—To a mixture of 1 g. of equilenin, 50 cc. of absolute ethanol and 3.5 cc. of ethyl chloroacetate was added a solution of 600 mg. of sodium in 20 cc. of ethanol. The mixture was refluxed for sixteen hours, when 1 g. of potassium hydroxide was added and the mixture refluxed for an additional hour. Upon dilution with water a white precipitate separated which was taken up in ether.

The water layer was acidified with hydrochloric acid and the white solid taken up in a large volume of ether. The ethereal extract was washed twice with sodium carbonate solution. Evaporation of the ether yielded about 200 mg. of unreacted equilenin. The sodium carbonate washings were acidified with hydrochloric acid and the precipitated solid collected and crystallized from acetone–ether as white needles, m. p. 233–236°.

Anal. Calcd. for $C_{20}H_{20}O_4$: C, 74.05; H, 6.2. Found: C, 73.7; H, 6.3.

The neutral fraction which separated upon first dilution of the reaction mixture with water was crystallized from aqueous acetone to give white crystals, m. p. 141.5–143°.

Anal. Calcd. for $C_{22}H_{24}O_4$: C, 75.0; H, 6.8. Found: C, 75.4; H, 7.1.

Hydrolysis of this neutral material with an excess of ethanolic potassium hydroxide yielded an acid which when crystallized from acetone–ether, m. p. 232–235°, gave no depression with equilenin-3-oxyacetic acid. The neutral product was very probably the ethyl ester.

With diazomethane equilenin-3-oxyacetic acid yielded a **methyl ester** which crystallized from acetone–methanol as white plates, m. p. 180–182°.

Anal. Calcd. for $C_{21}H_{22}O_4$: C, 74.5; H, 6.6. Found: C, 74.4; H, 6.5.

Hydrogenation of Equilenin-3-oxyacetic Acid.—A mixture of 800 mg. of equilenin-3-oxyacetic acid, 120 cc. of absolute ethanol, 500 mg. of Adams catalyst and 2 cc. of hydrochloric acid was shaken with hydrogen at two atm. at room temperature for five hours. The reaction products contained no appreciable acidic material. Crystallization from ether–pentane gave white needles, m. p. 144–146°, which gave no depression with a sample of 5,7,9-estratrienol-17(α), m. p. 144–146°.

Anal. Calcd. for $C_{18}H_{24}O$: C, 84.3; H, 9.4. Found: C, 84.0; H, 9.5.

Summary

Equilenin derivatives upon mild oxidation with chromic anhydride yield 11-keto derivatives.

Catalytic hydrogenation of equilenin derivatives in acidic medium gives 5,7,9-estratrienol-17(α).

STATE COLLEGE, PENNA. RECEIVED SEPTEMBER 25, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. LXXVII. The Oxidation of Pregnanetriol-3,4,20(α) and of Coprostanediol-3,4

BY RUSSELL E. MARKER, EUGENE L. WITTLE, LOUIS PLAMBECK, JR., EWALD ROHRMANN, JOHN KRUEGER AND PAUL R. ULSHAFER

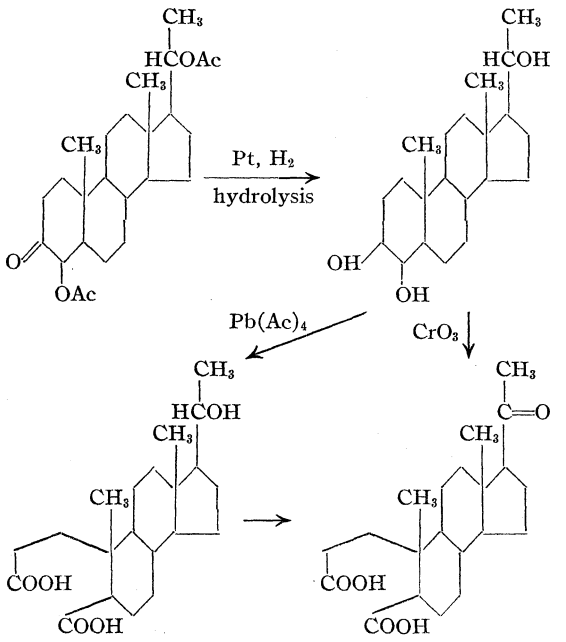
Gardner and Godden[1] oxidized coprosterol and coprostanone with cleavage of the 2,3-bond to a dicarboxylic acid of m. p. 247°. Windaus[2] confirmed Gardner and Godden's work and also oxidized *epi*-coprostanol with chromic oxide to the same acid. Windaus and Riemann[3] oxidized this dibasic acid to isolithobilianic acid which has been proved to have the carboxyl groups in the 2- and 3-positions. We have repeated the oxidation of coprostanone and obtained an acid of m. p. 247°, which appears to be the acid described above. The major oxidation product in the coprostane series, coprostane-2,3-dicarboxylic acid, is therefore formed by cleavage of the 2,3-bond.

On the other hand, oxidative degradations of compounds with the coprostane configuration in the bile acid series result in cleavage of the 3,4-bond as the major reaction. Wieland, Dane and Scholz[4] found that the oxidation of lithocholic acid proceeded with the formation of a 50% yield of lithobilianic acid and a 15% yield of isolithobilianic acid. Thus the oxidative cleavage in this compound took place chiefly at the 3,4-bond, and the substance formed by cleavage of the 2,3-bond was a by-product. Also J. Sawlewicz and T. Reichstein[5] obtained deoxybilianic acid as the major product in the oxidation of α-3-hydroxy-12-keto-cholanic acid. The same is true in the oxidation of other cholic acid derivatives.

Because the major oxidative cleavage in the bile acids of coprostane configuration is at the 3,4-bond, whereas the bile acids of the *allo* series are attacked at the 2,3-bond, it has been generally assumed that all coprostane and cholestane derivatives will behave in the same way. Confusion has resulted in the literature because of this

(1) Gardner and Godden, *Biochem. J.*, **7**, 588–595 (1913).
(2) Windaus, *Ber.*, **49**, 1724–1734 (1916).
(3) Windaus and Riemann, *Z. physiol. Chem.*, **126**, 277 (1923).
(4) Wieland, Dane and Scholz, *Z. physiol. Chem.*, **211**, 261–274 (1932).
(5) Sawlewicz and Reichstein, *Helv. Chim. Acta*, **20**, 992 (1937).

generally accepted but erroneous rule. Sobotka[6] gives the structure of the acid obtained by the oxidation of coprostanone as if a 3,4-cleavage had taken place in spite of the fact that Windaus[3] oxidized the side chain of this acid and obtained isolithobilianic acid, which could only have been formed if the first oxidation had resulted in a 2,3-cleavage in the coprostanone molecule.



Butenandt[7] oxidized pregnanedione with cleavage in ring A and obtained a dibasic acid to which he later assigned the 3,4-dicarboxylic acid structure.[8] We have repeated this oxidation and obtained the acid described by Butenandt. However, when pregnanetriol-3,4,20(α) (prepared by bromination of pregnanedione, followed by potassium acetate treatment, and finally by reduction and hydrolysis of the resulting ketoacetate) was oxidized, the major product was a ketodibasic acid (m. p. 216°), which was different from the acid of m. p. 270° (our melting point 281°) prepared by direct oxidation of pregnanedione with chromic anhydride. The same acid of m. p. 216° was obtained by lead tetraacetate oxidation followed by chromic anhydride treatment. Obviously the oxidation product of pregnanetriol-3,4,20(α) must have been obtained by cleavage of the 3,4-bond which lies between two hydroxyl groups.

(6) Sobotka, "Chemistry of the Sterids," Williams and Wilkins Co., Baltimore, Md., 1938, page 426.

(7) Butenandt, *Ber.*, **63**, 659 (1930).

(8) Butenandt and Schmidt, *ibid.*, **67**, 1893 (1934).

We also carried out an analogous series of reactions on coprostanone. This compound was brominated, and the 4-bromocoprostanone was converted to 4-acetoxycoprostanone by potassium acetate. The resulting compound, by catalytic reduction and hydrolysis, yielded 3,4-dihydroxycoprostane. This diol, on cold oxidation with chromic anhydride in acetic acid, yielded a 3,4-diacid, m. p. 217°, which was different from the 2,3-diacid, m. p. 247°, obtained as the major product of direct cleavage of coprostanone by chromic anhydride in acetic acid. This acid, the 3,4-coprostane-dicarboxylic acid, also gave a large depression in melting point with dihydro-Diels acid of m. p. 251°.

Thus, the point of cleavage of Ring A of the sterols on oxidation is highly dependent on the nature of the group attached to C-17, even though this group is far removed from the point of oxidative attack.

We wish to thank Parke, Davis and Company for their generous support and assistance rendered in the various phases of this work.

Experimental Part

Pregnanetriol-3,4,20(α).—A suspension of 300 mg. of platinum oxide in a solution of 100 cc. of ether, 200 cc. of ethanol, and 1.7 g. of 4,20-diacetoxypregnanone-3, m. p. 250°, was shaken with hydrogen under 3 atm. pressure for four hours. The catalyst was filtered off and the filtrate was evaporated to dryness. The residue was crystallized once from dilute methanol to yield 1.4 g. of unsharply melting product. This diacetoxy-pregnanol gave only a slight precipitate when treated with digitonin in 95% ethanol, and when oxidized with excess chromic anhydride in acetic acid gave nearly a quantitative yield of the starting material, 4,20-diacetoxypregnanone-3, m. p. 250°.

A solution of 900 mg. of 4,20-diacetoxypregnanol-3 in 200 cc. of 95% ethanol was refluxed for two hours with a solution of 1.5 g. of potassium hydroxide in 75 cc. of 75% ethanol. The solution was poured into water and the hydrolyzed product was extracted with ether. The ethereal solution of the triol was washed with water and was then evaporated nearly to dryness. Pregnanetriol-3,4,20(α) crystallized from the concentrated solution in white plates of m. p. 182°. This triol gave no precipitate with digitonin. After recrystallization from ether and acetone it melted at 184°.

Anal. Calcd. for $C_{21}H_{36}O_3$: C, 74.9; H, 10.8. Found: C, 74.8; H, 10.8.

The triacetate was prepared by treatment of 100 mg. of triol with 3 cc. of pyridine and 2 cc. of acetic anhydride for two days. The solution was evaporated *in vacuo*, and the residue was dissolved in ether and dilute hydrochloric acid. The ether layer was washed with water and then with dilute potassium carbonate and finally was evaporated to

dryness. The residue, crystallized from methanol, yielded 75 mg. of triacetate of m. p. 181°.

Anal. Calcd. for $C_{27}H_{42}O_6$: C, 70.1; H, 9.2. Found: C, 70.0; H, 9.3.

Reduction of 4,20-Diacetoxypregnanone-3 with Aluminum Isopropylate.—A solution of 700 mg. of this compound, 1.0 g. of aluminum isopropylate and 100 cc. of dry isopropyl alcohol was refluxed in a fractionating column over a period of six hours while acetone was removed slowly. The solution was then poured into a mixture of ether and dilute hydrochloric acid. The ether was washed with water and then was evaporated to dryness. The residue on standing overnight with an alcoholic solution of digitonin gave no precipitate. It was not readily crystallized and was therefore converted to the triacetate by refluxing with 30 cc. of acetic anhydride for an hour. The solution was evaporated to dryness *in vacuo*, and the residue was crystallized from methanol to yield a product of m. p. 181°. The melting point could not be raised by repeated recrystallizations from alcohol.

Anal. Calcd. for $C_{27}H_{42}O_6$: C, 70.1; H, 9.2. Found: C, 70.0; H, 9.4.

This triacetate gave no depression in melting point with the triacetate of the triol obtained by catalytic reduction.

Oxidation of Pregnanetriol-3,4,20(α).—To a solution of pregnanetriol-3,4,20(α) in 50 cc. of acetic acid at 25° was added a solution of 500 mg. of chromic anhydride in 25 cc. of 90% acetic acid. The solution was allowed to stand for one hour. It was then diluted with water and extracted with ether. The ethereal solution was washed with water and then was extracted with dilute potassium carbonate solution. The ethereal layer yielded a yellow oil which could not be crystallized. The potassium carbonate solution on acidification with dilute hydrochloric acid yielded a white solid of m. p. 212°. It was crystallized from dilute ethanol and dilute acetone to yield 75 mg. of acid of m. p. 216°.

Anal. Calcd. for $C_{21}H_{32}O_5$: C, 69.2; H, 8.9. Found: C, 69.1; H, 8.6.

This acid gave a twenty degree depression in melting point with the 2,3-diacid of *allo*-pregnanone-20[9] of m. p. 218°, and melted at 180–220° when mixed with the 2,3-diacid of pregnanone-20 of m. p. 281° obtained by the direct oxidation of pregnanedione.[7]

The dimethyl ester of the 2,3-diacid of pregnanone-20 was prepared by treatment of the acid in ethereal solution with diazomethane. The solution was evaporated to dryness and the residue was crystallized from methanol to yield a substance of m. p. 87°.

Anal. Calcd. for $C_{23}H_{36}O_5$: C, 70.4; H, 9.3. Found: C, 70.1; H, 9.6.

The oxime was prepared by refluxing a mixture of 50 mg. of this acid, m. p. 216°, 100 mg. of hydroxylamine hydrochloride, 150 mg. of sodium acetate and 25 cc. of ethanol for six hours. The solution was diluted with water, the oxime was filtered off and was crystallized from dilute acetone. The substance melted at 238°.

Anal. Calcd. for $C_{21}H_{33}O_5N$: C, 66.4; H, 8.8. Found: C, 66.2; H, 8.7.

(9) Marker, Kamm and Jones, THIS JOURNAL, **59**, 1596 (1937).

3,4-Diacid of Pregnanol-20(α).—A solution of 100 mg. of pregnanetriol-3,4,20(α), and 200 mg. of lead tetraacetate in 25 cc. of acetic acid was allowed to stand for twenty-four hours at room temperature. The solution was poured into water, extracted with ether, and the ethereal solution was evaporated to dryness. The residue was taken up in 15 cc. of acetic acid and was treated with 10 cc. of 30% hydrogen peroxide for five hours on the steam-bath. The solution was poured into water and was extracted with ether. The ethereal solution was washed with water and was extracted with dilute potassium carbonate solution. The basic solution was then acidified and was extracted with ether. The ethereal solution after being washed with water was evaporated to dryness. The residue melted unsharply at 190–205°. After recrystallizations from dilute acetone and methanol, the substance melted at 231°. This acid (m. p. 231°) with the 3,4-diacid of pregnanone-20, m. p. 216°, melted at 185–200°.

Anal. Calcd. for $C_{21}H_{34}O_5$: C, 68.8; H, 9.4. Found: C, 68.8; H, 9.6.

Oxidation of the 3,4-Diacid of Pregnanol-20.—A solution of 200 mg. of this acid, m. p. 228°, in 50 cc. of glacial acetic acid was shaken at room temperature with 300 mg. of chromic anhydride in 25 cc. of 90% acetic acid for one hour. The solution was poured into 500 cc. of water and the product was extracted with ether. The ethereal solution was washed with water and then was evaporated to dryness. The residue was recrystallized twice from dilute acetone to yield 100 mg. of the 3,4-diacid of pregnanone-20 of m. p. 216°. This acid gave no depression in melting point with the acid of m. p. 216°, prepared by direct chromic anhydride oxidation of pregnanetriol-3,4,20(α).

4-Acetoxycoprostanone.—A solution of 20 g. of 4-bromocoprostanone,[10] in 200 cc. of glacial acetic acid containing 30 g. of fused potassium acetate was refluxed for two hours. The acetic acid was removed *in vacuo* and the organic material was extracted with ether. The ethereal solution was washed with sodium bicarbonate solution, and then was evaporated to dryness. The residue was crystallized from alcohol and yielded 4-acetoxycoprostanone, m. p. 149°.

Anal. Calcd. for $C_{29}H_{50}O_3$: C, 78.3; H, 10.9. Found: C, 78.4; H, 10.9.

Coprostanediol-3,4.—A solution of 5 g. of 4-acetoxycoprostanone in 100 cc. of ether and 100 cc. of ethanol was shaken for three hours with 2.0 g. of platinum oxide catalyst under hydrogen at 3 atmospheres. The catalyst was filtered off and the solvent was removed by evaporation. The residue was hydrolyzed by refluxing for one hour with alcoholic potassium hydroxide. The product had a tendency to form a gel when crystallization was attempted. However, after sublimation in a high vacuum at 200° the diol could be crystallized from alcohol and melted at 185–188°. The product may contain some stereoisomer formed in the reduction.

Anal. Calcd. for $C_{27}H_{48}O_2$: C, 80.1; H, 12.0. Found: C, 80.0; H, 12.0.

Coprostane Diacid-3,4.—To a solution of 4 g. of coprostanediol-3,4 in 100 cc. of glacial acetic acid at room temperature was added a solution of 5 g. of chromic oxide in

(10) Butenandt, *Ber.*, **68**, 2094 (1935).

50 cc. of 90% acetic acid. After standing for fifteen minutes, water was added and the organic material was extracted with ether. The ethereal solution was washed well with water and dilute hydrochloric acid and then with dilute potassium hydroxide. The alkaline solution was acidified and extracted with ether. The ether solution was concentrated and pentane was added. This produced 2.4 g. of crystalline acid, m. p. 207–211°. Coprostane-3,4-dicarboxylic acid crystallized from methanol as large transparent rods, m. p. 217°. It gave a 15–20° depression in melting point with dihydro-Diels acid of m. p. 251°, and also with coprostane-2,3-dicarboxylic acid, m. p. 247°.

Anal. Calcd. for $C_{27}H_{46}O_4$: C, 74.6; H, 10.7. Found: C, 74.8; H, 10.7.

The dimethyl ester was prepared with diazomethane in the usual way. It crystallized from methanol as large white flakes, m. p. 74°.

Anal. Calcd. for $C_{29}H_{50}O_4$: C, 75.3; H, 10.7. Found: C, 75.6; H, 11.0.

Summary

Pregnanetriol-3,4,20(α) was oxidized to the 3,4-dicarboxylic acid of pregnanone-20, which was different from the dicarboxylic acid of pregnanone-20 formed by direct oxidation of pregnanedione. The latter acid must therefore be a 2,3-derivative.

Coprostanediol-3,4 was oxidized to a coprostane-dicarboxylic acid. This acid was different from the dicarboxylic acid obtained by direct oxidation of coprostanone.

The greater part of the oxidative fission of 3-substituted derivatives of the coprostane configuration (except those of the bile acid series) takes place at the 2,3-bond rather than at the 3,4-bond as has been generally assumed.

STATE COLLEGE, PENNA. RECEIVED SEPTEMBER 30, 1939

[CONTRIBUTION FROM THE NICHOLS CHEMICAL LABORATORY OF NEW YORK UNIVERSITY]

The Preparation of Some Py-Amino Quinolines and Derivatives

BY R. R. RENSHAW[1] AND H. L. FRIEDMAN[2]

This paper describes the preparation of several py-amino quinolines and some of their derivatives. The amines were needed for a study of their coupling reactions with benzene diazonium chloride.[3] The 2-aminoquinoline was readily prepared by the sodamide reaction.[4]

Reduction of 3-nitroquinoline[5] gave the 3-aminoquinoline in small over-all yields. For better yields, Wibaut's[6] method was modified by preparing 3-bromoquinoline from quinoline, bromine and sulfur,[7] followed by conversion to the amine with concentrated ammonia and copper sulfate catalyst.[8]

Since it was found that 3-aminoquinoline forms the 4-azo derivative in the coupling reaction with benzenediazonium chloride,[3] an attempt was made to prepare the unknown 4-nitroquinoline. Anhydrous 3-acetylaminoquinoline was nitrated in concentrated sulfuric acid and the acetyl group removed by hydrolysis. A red nitro-amine was formed. An attempt to remove the amino group by diazotization and boiling in alcohol yielded only a nitro-ethoxy derivative. Attempted reduction to the known 3,4-diaminoquinoline[3] failed; the compound could not be reduced. It is tentatively postulated that 4-nitro-3-aminoquinoline was obtained, although the authors have never seen a quinoline compound with a nitro group in the 4 position recorded in the literature.

The 4-aminoquinoline and the 2,4-diaminoquinoline were prepared from the same material, the 2,4-quinoline-dicarboxylic acid.[9] Decarboxylation of the acid in boiling nitrobenzene gave excellent yields of cinchoninic acid which was converted through the acid chloride,[10] methyl ester,[11] and amide[12] to the amine[13] in an over-all yield of 68%. Similarly, it was found that starting with the 2,4-quinolinedicarboxylic acid, the 2,4-diaminoquinoline could be obtained by the same series of reactions in an over-all yield of 50%. The only method of preparation of the

(1) This paper is being published, following the death of Professor Renshaw, by his collaborator.

(2) Present address: Pyridium Corporation, Yonkers, New York.

(3) Renshaw, Friedman and Gajewski, THIS JOURNAL, **61**, 3322 (1939).

(4) Chichibabin, *et al.*, *J. Russ. Phys.-Chem. Soc.*, **46**, 1232 (1914); **50**, 554 (1918); *Ber.*, **58**, 803 (1925).

(5) Bargellini and Settimi, *Gazz. chim. ital.*, **53**, 601 (1923).

(6) Jansen and Wibaut, *Rec. trav. chim.*, **56**, 709 (1937).

(7) Edinger, *J. prakt. Chem.*, **54**, 358 (1896).

(8) Maier-Bode, *Ber.*, **69**, 1536 (1936). Preparation of 3-aminopyridine from 3-bromopyridine.

(9) Pfitzinger, in Houben-Weyl, "Methoden," Vol. IV, 1924, p. 559.

(10) Spaeth and Spitzer, *Ber.*, **59**, 1484 (1926).

(11) Meyer, *Monatsh.*, **22**, 115 (1901).

(12) Wenzel, *ibid.*, **15**, 456 (1894).

(13) Wenzel, *ibid.*, **15**, 457 (1894).

diamine recorded previously in the literature is the reaction of the 2,4-quinolinedisulfonic acid with concentrated ammonia and zinc chloride.[14]

It was found that the 2-carbethoxy group in the 2,4-diethyl ester could be converted readily into the carboxamide group without the 4-carbethoxy group being appreciably affected. Hofmann degradation of the resulting compound gave the hitherto unknown 2-aminocinchoninic acid.[15] The structure was proved by decarboxylation to 2-aminoquinoline and by diazotization to the known 2-hydroxycinchoninic acid.[16]

Experimental Part[17]

3-Aminoquinoline.—*o*-Aminobenzaldehyde[18] and metazonic acid[19] on standing in a weakly acidic solution gave a 22% yield of 3-nitroquinoline,[20] m. p. 129–130°. Ether extraction of the neutral mother liquor gave an approximately equal weight of the oxime of the aldehyde, m. p. 137–37.5°.[21] Reduction of the nitro compound with stannous chloride in concentrated hydrochloric acid,[5] addition of excess sodium hydroxide, and extraction with ether gave a 97% yield of the 3-amine, m. p. 82–83°; acetyl derivative, m. p. 171–172° (anhydrous), 127–128° (hydrate).

Bromination of quinoline with sulfur and bromine according to Edinger[7] gave 3-bromoquinoline in 50% yield, b. p. (24 mm.) 158–162°. Heating with concentrated ammonium hydroxide and copper sulfate catalyst[8] in a rocking autoclave (twelve hours at 160°) and extraction with ether gave the 3-aminoquinoline in 73% yield.

3-Acetylamino-4(?)-nitroquinoline.—Attempted nitration of the acetylamine in glacial acetic acid precipitated the nitrate of the acetylamine, m. p. 195.5° (with decomp. to gas).

3-Acetylaminoquinoline (2 g.) was dissolved in concentrated sulfuric acid (15 cc.), cooled, fuming nitric acid added (1.5 g.), and the solution allowed to stand for one hour at room temperature. The solution was then poured on cracked ice, made basic, and the precipitate crystallized from much water; small golden yellow needles, m. p. 205–206°.

Anal. Calcd. for $C_{11}H_9N_3O_3$: N, 18.2. Found: N, 18.0.

3-Amino-4(?)-nitroquinoline.—The acetylamino-nitroquinoline was hydrolyzed by boiling in 95% alcohol with potassium hydroxide for fifteen minutes. The red solution was then poured into water, boiled to remove the alcohol, cooled, the precipitate filtered and crystallized from water; small lustrous red needles, m. p. 189–189.5°.

Anal. Calcd. for $C_9H_7N_3O_2$: N, 22.2. Found: N, 21.8.

Attempted reduction in hydrochloric acid with stannous chloride failed. The red color did not disappear after heating for one hour. The solution was made basic and extracted with ether. The ether showed a marked blue fluorescence but no diamine was obtained on evaporation. Reductions were also attempted with stannous chloride and hydrogen chloride in alcohol, with iron powder and acetic acid in water, and with zinc dust in alcoholic sodium hydroxide. No color change was found in any case nor could any product resembling a diamine be obtained.

3-Ethoxy-4(?)-nitroquinoline.—Dry sodium nitrite (90 mg.) was added to the nitroaminoquinoline (200 mg.) in cold concentrated sulfuric acid (5 cc.). The solution was allowed to warm to room temperature and stand for fifteen minutes, then poured into 30 cc. of absolute alcohol and boiled. Most of the alcohol was distilled off and a small amount of water added. On further boiling a solid steam distilled and was crystallized from water, approximately 40 mg. of long, slightly tan crystals, m. p. 113–114°. Evaporation of the alcoholic distillate at room temperature left no residue. Ether extraction of the clear liquid remaining in the distilling flask yielded only a little unreacted nitro-aminoquinoline.

Anal. Calcd. for $C_9H_6N_2O_2$ (nitroquinoline): N, 16.1. For $C_{11}H_{10}N_2O_3$ (nitro-ethoxyquinoline): N, 12.8. Found: N, 12.5.

4-Aminoquinoline.—Finely powdered dry quinoline 2,4-dicarboxylic acid (25 g.) was boiled on a hot-plate with nitrobenzene (100 cc.). Decarboxylation was complete in about ten minutes accompanied by solution. On cooling, the cinchoninic acid crystallized out and was recrystallized from water, yield 90%.

The cinchoninic acid (1 part) was boiled with thionyl chloride[10] (3 parts) for ten minutes and the thionyl chloride removed *in vacuo*. The acid chloride–hydrochloride formed gave with methyl alcohol the methyl ester,[9] b. p. (4 mm.) 136–140°, in 83% yield. The ester (10 g.) with ammoniacal methanol (50 cc. saturated with ammonia at 10°) gave the amide[12] in quantitative amount (twelve hours at 50°), rectangular plates, m. p. 179–181°. Hofmann degradation[13] gave the amine in 90% yield, m. p. 69° (hydrate), 154–156° (anhydr.); acetyl derivative, 177–178°.

2,4-Dicarbomethoxyquinoline and 2,4-Dicarbethoxyquinoline.—Quinoline-2,4-dicarboxylic acid (1 part) was refluxed for eight to ten hours on the water-bath with thionyl chloride (10 parts), at which time complete solution was effected. The thionyl chloride was distilled off *in vacuo* and feathery golden-yellow crystals of the dicarbonyl chloride remained. The chloride may be crystallized from ligroin or petroleum ether but this is not necessary for production of the esters.[22]

The dicarbonyl chloride was dissolved in absolute methanol (or ethanol), boiled with bone-black, filtered, water added to turbidity and the solution cooled. The esters formed white needle crystals; dimethyl ester, m. p. 130–131°; diethyl ester, m. p. 74–75.5°; very insoluble in water, soluble in concentrated sulfuric acid (yellow).

Anal. (Dimethyl ester) Calcd. for $C_{13}H_{11}NO_4$: N, 5.71. Found: N, 5.83, 5.60. (Diethyl ester) Calcd. for $C_{15}H_{15}NO_4$: N, 5.13. Found: N, 5.08, 5.18.

(14) German Patent 615,184; *Chem. Abs.*, **29**, 6249 (1935).

(15) This compound has since been prepared by the action of sodamide on cinchoninic acid; Bergstrom, *J. Org. Chem.*, **3**, 233 (1938).

(16) Beilstein, "Handbuch," Vol. 22, p. 233.

(17) All melting points are corrected.

(18) Bamberger, *Ber.*, **34**, 1330 (1901).

(19) Meister, *ibid.*, **40**, 2441 (1907).

(20) German Patent 335,197, *Jahresber. der Chem. Tech.*, **67**, 63 (1921).

(21) Beilstein, Vol. 14, p. 24.

(22) Compare French Patent 806,640 noted after completion of this work.

Quinoline-2,4-dicarboxanilide.—The dicarbonyl chloride was dissolved in an excess of hot aniline. The dianilide crystallized out on cooling. The compound when recrystallized from aniline or nitrobenzene formed small bluish-white needles; very insoluble in hot water, slightly soluble in hot alcohol, m. p. 285–286°. The crystals turn red in cold concentrated sulfuric acid and go into solution (orange) on warming.

Anal. Calcd. for $C_{23}H_{17}N_3O_2$: N, 11.44. Found: N, 11.42, 11.41.

2,4-Dicarbamylquinoline.—The dimethyl ester (10 g.) was heated with ammoniacal methanol (100 cc.) at 85° for twenty hours. The amide, formed in quantitative yield, crystallized from water or alcohol as small white needles, m. p. 277.5–279.5°; soluble in concentrated sulfuric acid (yellow).

Anal. Calcd. for $C_{11}H_9N_3O_2$: N, 19.53. Found: N, 19.33, 19.02.

2,4-Diaminoquinoline.—Fifteen grams of the diamide was added to 725 cc. of a solution containing 50 g. of potassium hydroxide and 23 g. of bromine. The amide dissolved readily in the cold. The solution was heated on the water-bath for one hour, the small amount of dark brown precipitate filtered off, and the solution bone-blacked, filtered and cooled. The diamine slowly crystallized from the solution. More product was obtained by concentrating the solution. The diamine was recrystallized from water (tendency for supersaturation) as lustrous white needles, m. p. 197–198.5°,[23] yield, 85%. The picrate, crystallized from much hot water, melted at approximately 283° (decomp.).

Anal. Calcd. for $C_9H_9N_3$: N, 26.41. Found: N, 26.51. Calcd. for $C_{15}H_{12}N_6O_7$ (monopicrate): N, 21.64. Found: N, 21.84.

(23) The m. p. in German Patent 615,184 is given as 188–190°; the analysis reported was N, 25.3.

2-Carbamylethyl Cinchoninate.—On heating 2,4-dicarbethoxyquinoline with ammoniacal methanol at 50°, the mono amide was formed in 86% yield; slightly soluble in hot alcohol, very insoluble in water, m. p. 226–227.5° (melts to a tan liquid with a green fluorescence).

Anal. Calcd. for $C_{13}H_{13}N_2O_3$: N, 11.41. Found: N, 11.59, 11.56.

2-Aminocinchoninic Acid.—Five grams of 2-carbamylethyl cinchoninate was heated on the steam-bath for one hour with 250 cc. of water containing 10 g. of potassium hydroxide and 4.75 g. of bromine. Solution (red) was effected on warming. The solution, after being cooled, was diluted to dissolve the potassium salt and made weakly acidic with hydrochloric acid. The yellow precipitate of 2-aminocinchoninic acid was crystallized from much water as lustrous tan crystals, m. p. 362° (dec.); soluble in concentrated sulfuric acid (red), concentrated hydrochloric acid (red), and dilute sodium hydroxide; insoluble in alcohol and benzene.

Anal. Calcd. for $C_{10}H_8N_2O_2$: N, 14.9; neut. equiv., 188. Found: N, 14.3; neut. equiv., 187.

Diazotization in concentrated sulfuric acid with dry sodium nitrite and pouring into water gave the known 2-hydroxycinchoninic acid,[16] m. p. 342°. Fusion with soda-lime gave 2-aminoquinoline, white plates from water, m. p. 125–127°.

Summary

Improved preparations of 3- and 4-aminoquinoline, and a new method of preparation of 2,4-diaminoquinoline and of 2-aminocinchoninic acid are described. The attempted preparation of 4-nitroquinoline from 3-aminoquinoline is discussed.

UNIVERSITY HEIGHTS
NEW YORK, N. Y. RECEIVED SEPTEMBER 20, 1939

[CONTRIBUTION FROM THE NICHOLS CHEMICAL LABORATORY OF NEW YORK UNIVERSITY]

Coupling Reactions of Aminoquinolines with Benzenediazonium Chloride. A Study of Orientation in the Quinoline Ring

BY R. R. RENSHAW,[1] H. L. FRIEDMAN[2] AND F. J. GAJEWSKI[3]

Knorr[4] and Marckwald[5] pointed out that the chemical properties of naphthalene and quinoline are best explained by accepting the static bond structure proposed by Erlenmeyer, while the chemical properties of benzene are better explained on the basis of Kekulé's concept of shifting double bonds. More recently Pauling[6] has arrived at the same conclusion from quantum mechanical studies, and Le Fèvre and Le Fèvre,[7] from dipole studies of quinoline, favor the Erlenmeyer structure.

There are several good recent surveys of the naphthalene problem,[8] but quinoline has been given only brief discussions.[7,9] Therefore, a comprehensive study of the coupling reactions of the aminoquinolines was undertaken to char-

(1) This paper is being published, following the death of Professor Renshaw, by his collaborators.

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(3) Present address: General Aniline Works, Inc., Grasselli, N. J.

(4) Knorr, *Ann.*, **279**, 212 (1894).

(5) Marckwald, *Ann.*, **274**, 334 (1893); **279**, 14 (1894).

(6) Pauling in Gilman's "Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., Chap. 22, p. 1876.

(7) Le Fèvre and Le Fèvre, *J. Chem. Soc.*, 1470 (1935).

(8) Fieser in Gilman's "Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., Chap. 2, p. 81; Fieser, THIS JOURNAL, **57**, 1459 (1935); *Ann. Repts. Chem. Soc.*, 281 ff. (1936).

(9) Mills and Smith, *J. Chem. Soc.*, 2724 (1922).

acterize the orientation and the "fixed bond" structure of quinoline, for Fieser[10] has shown that the coupling reaction is indicative of bond structure.

Table I compares the actual results obtained by coupling the different aminoquinolines with benzenediazonium chloride with those to be expected from Erlenmeyer's static formula.

TABLE I

Position of NH_2	Expected coupling	Obsd. coupling
2	2 (diazoamino)	2 (diazoamino
3	4	4
4	3	Failed
2, 4	3	2(?)
5	8 or 6	8 and 6
6	5	5
7	8	(8)
8	5 or 7	5

These results indicate a good agreement with the Erlenmeyer structure. Since both the methods of preparation and of coupling of the mono-bz- and mono-py-aminoquinolines are very different, they are discussed separately below.

Results of Coupling Bz-Aminoquinolines with Benzenediazonium Chloride.—The bz-aminoquinolines were made by the reduction of the corresponding nitro compounds obtained by the appropriate Skraup reactions. The 7-nitroquinoline was also prepared by the lithium nitrate reaction.[11]

The earlier work on the coupling of mono-bz-aminoquinolines was that of Knuepel[12] and of Jacobs and Heidelberger.[13] The former attempted to prepare the azo derivative of 6-aminoquinoline, but obtained the intermediate diazoamino compound, which did not undergo rearrangement. The latter were successful in coupling diazotized aniline with 5-aminoquinoline in dilute acetic acid–sodium acetate solution. The authors have been successful in applying Jacobs and Heidelberger's conditions to all of the mono-bz-aminoquinolines. They have also effected coupling in dilute hydrochloric acid solutions. The former method yielded the purer product.

The structure of each resulting azo compound was determined by the following procedures. (1) Reduction of the azo compound from 8-aminoquinoline gave a diaminoquinoline which melted at 163°. It did not form a phenanthrenequinone condensation product (test for an ortho diamine[14]).

(2) Reduction of the azo compound formed by coupling 5-aminoquinoline in dilute hydrochloric acid gave two diamines. The main product was a diamine of m. p. 163° which gave no melting point depression with the diamine of (1) and gave no phenanthrene-quinone condensation product. The other diamine present could not be purified sufficiently to show a sharp melting point. It gave a condensation product with phenanthrenequinone, m. p. 294–295°, and must, therefore, have been 5,6-diaminoquinoline. Therefore, 8-aminoquinoline coupled mainly in the 8-position and to a slight extent in the 6-position. It was found that coupling of the 5-amine in dilute acetic acid–sodium acetate solution gave only the 8-phenylazo compound.

(3) Reduction of the azo compound from 6-aminoquinoline gave a diamine which yielded a phenanthrenequinone condensation product of m. p. 294–295°. This azine did not depress the melting point of the azine formed in (2), hence, the 6-aminoquinoline coupled in the 5-position.

(4) Reduction of the azo compound from 7-aminoquinoline gave a new diamine which formed a phenanthroquinone azine, showing it to be an ortho diamine. It was not possible to prove the structure of this diamine. It must be either the 7,8- or 6,7-diaminoquinoline. It is tentatively considered the 7,8-diamine.

The hydrochlorides of the phenylazo-aminoquinolines were prepared for bactericidal tests.

Results of Coupling Py-Aminoquinolines with Benzenediazonium Chloride.—The py-aminoquinolines were prepared by various new or improved methods described in a previous report.[15]

Since negative results were obtained in attempting coupling reactions under the same conditions as for the bz-aminoquinolines, various solvents were tried in order to effect coupling. The results of reactions with benzenediazonium chloride are in Table II.

TABLE II

Solvent	$2NH_2$	$3NH_2$	$4NH_2$	$2,4NH_2$
H_2O, HOAc, NaOAc	No	Diazoamino	No	Diazoamino
H_2O, HCl (dil.)	...	No	No	No
H_2O, HCl (excess)	...	No	...	No
H_2O, MeOH	Diazoamino	Diazoamino	No	Diazoamino
HOAc (glacial)	No	Red tar	No	Diazoamino
EtOH (abs.)	Diazoamino	Azo compound	No	No

The coupling of 2-aminoquinoline with benzenediazonium chloride gave a diazoamino compound, an expected result. No attempt was made to rearrange it, since Chichibabin[16] has shown that the analogous diazoamino compound from 2-aminopyridine does not undergo rearrangement, a result confirmed by the authors.

(10) Fieser, THIS JOURNAL, **57**, 1459 (1935).
(11) Bacharah, Haut and Caroline, *Rec. trav. chim.*, **52**, 413 (1933).
(12) Knuepel, *Ann.*, **310**, 87 (1899).
(13) Jacobs and Heidelberger, THIS JOURNAL, **42**, 2284 (1920).
(14) Hinsberg, *Ann.*, **237**, 340 (1887).
(15) R. R. Renshaw and Friedman, THIS JOURNAL, **61**, 3320 (1939).
(16) Chichibabin and Persitz, *Chem. Abs.*, **20**, 2499 (1926).

The 3-aminoquinoline gave in small yield the desired azo compound only by coupling in absolute alcohol. Although the 3-amine is truly aromatic, it gave the diazoamino compound when coupling was effected under the conditions for the bz-aminoquinolines. The 3-diazoaminoquinoline was destroyed readily by boiling in dilute hydrochloric acid. The decomposition is characterized by the appearance of the blue fluorescence of the 3-amine. Reduction of the azo compound 3-aminoquinoline gave a new diamine, m. p. 176–177°,[17] which can be characterized by an intense blue to purple fluorescence in various solvents. This diamine gave a condensation product with phenanthrenequinone, and is, therefore, an ortho diamine. To fix the structure conclusively, 4-aminoquinoline was brominated to yield the 3-bromo derivative[18] and this was converted to the 3,4-diamine with 26% ammonia water.[19] The 3,4-diamine so prepared was identical with that from the reduction of the azo compound. Hence, the 3-aminoquinoline coupling occurred at the 4-position.

The 4-aminoquinoline failed to couple under any conditions tried; the unreacted amine always could be isolated at the end of the reaction. Attempted coupling in absolute alcohol with *p*-nitrobenzenediazonium chloride produced a very interesting phenomenon. A bright red solution was formed which rapidly faded. The fading was accompanied by loss of nitrogen. This effervescence was studied carefully at different temperatures, and was found to occur at as low as −10°. It was not possible to isolate the red compound, since at the temperatures at which it formed, decomposition immediately occurred. Nitrobenzene was isolated from the solution; this is the normal product obtained by the reaction of *p*-nitrobenzenediazonium chloride with hot alcohol.[20] It would appear that an unstable red intermediate was formed and that this immediately decomposed into 4-aminoquinoline, nitrogen, and nitrobenzene. By analogy with 2-aminoquinoline, the formation of a diazoamino compound could be expected. No reason can be given for the instability of the red intermediate without more specific data.

The 2,4-diaminoquinoline was tried in coupling reactions since Morgan and Wootton[21] were able to couple at the position between the two amino groups in substituted meta-phenylenediamines. By analogy it was expected that the 2,4-diamine would couple in the 3-position, no matter which one of the three tautomeric forms might represent the structure. It was found that in glacial acetic acid both benzenediazonium chloride and *p*-nitrobenzenediazonium chloride gave readily yellow-orange compounds which formed yellow hydrochlorides. Without exception it was found that in this series the color of the hydrochlorides of the true azo compounds was red or a deep orange-red, whereas that of the hydrochlorides of the diazoamino compounds was yellow. On this basis it is believed that these compounds are diazoamino. Since 4-aminoquinoline did not undergo coupling reactions under the conditions tried, while 2-aminoquinoline formed a diazoamino compound, it is postulated that 2-diazoamino-4-aminoquinolines are formed.

Experimental Part[22,23]

Bz-Aminoquinolines

6-Amino-5-phenylazoquinoline.—Method I: Benzenediazonium chloride was coupled with 6-aminoquinoline in 0.25 molar hydrochloric acid solution over a period of twelve hours. On salting out the hydrochloride at 60°, it first formed an oil, which on stirring solidified to a light-orange flocculent precipitate. It was purified by dissolving in a minimum amount of water and adding an equal volume of alcohol, whereupon orange needles separated, m. p. 250–255°. These crystals analyzed for the monohydrochloride trihydrate. This product was converted to the monohydrochloride by drying at 120°. The free base was prepared by precipitating it from a solution of the hydrochloride with ammonium hydroxide. It was recrystallized from alcohol, forming light orange needles, m. p. 247–249°.

Method II: Coupling was accomplished in acetic acid–sodium acetate solution in approximately ten minutes. After coupling was complete, the solution was made alkaline with ammonium hydroxide. The precipitated solid was recrystallized from a solution of alcohol and water.

The free base was reduced by means of stannous chloride and concentrated hydrochloric acid. The procedure was the following: after refluxing the reaction mixture for half an hour, it was evaporated to dryness on a water-bath. The residue was dissolved in water and the tin removed by means of hydrogen sulfide. The water solution was evaporated almost to dryness and cooled. The hydrochloride crystallized. It was purified by dissolving in alcohol and

(17) Backeberg and Friedmann, *J. Chem. Soc.*, 976 (1938). These authors did not prepare 3,4-diaminoquinoline.

(18) Claus and Howitz, *J. prakt. Chem.*, [2] **50**, 237 (1894).

(19) Maier-Bode, *Ber.*, **69**, 1536 (1936).

(20) Cameron, *Am. Chem. J.*, **20**, 251 (1898).

(21) Morgan and Wootton, *J. Chem. Soc.*, **87**, 935 (1905).

(22) The experimental work on the bz-aminoquinolines was performed by F. J. Gajewski, that on py-aminoquinolines by H. L. Friedman.

(23) All melting points are corrected.

precipitating with ether. The 5,6-diaminoquinoline was obtained by making a solution of the hydrochloride strongly alkaline with potassium hydroxide. A melting point of 135° was found for this product, whereas that reported is 95[24] and 145°.[25] The phenanthroquinoline azine melted at 294–295°; reported[24] 287–288°.

Anal. Calcd. for $C_{15}H_{12}N_4$: N, 22.57. Found: N, 22.58, 22.48. Calcd. for $C_{15}H_{12}N_4 \cdot HCl$: N, 19.67. Found: N, 19.56, 19.60. Calcd. for $C_{15}H_{12}N_4 \cdot HCl \cdot 3H_2O$: N, 16.54. Found: N, 16.66, 16.57.

5-Amino-8-phenylazoquinoline was first prepared by W. A. Jacobs and M. Heidelberger.[13] It was found, however, that the product after several recrystallizations melted at 191–194°, whereas the reported m. p. is 209–211°. This is to be attributed to the fact that a mixture of two coupling products was obtained as shown below. The hydrochloride, m. p. 225–227°, precipitated as a violet powder when dry hydrogen chloride was passed into a chloroform solution of the free base.

The free base was reduced with stannous chloride and concentrated hydrochloric acid. After refluxing the reaction mixture for one-half hour, the solution became decolorized. Solid potassium hydroxide was added under cooling until a 50% solution was obtained. The yellow solid was filtered and dissolved in ether. By slowly evaporating the ether solution, a crust formed on the side of the evaporating dish, which melted over the range 150–155°. There was present in this crust some 5,6-diaminoquinoline, for a phenanthrenequinone ortho condensation product was obtained. The main diaminoquinoline, obtained in long crystals on the bottom of the evaporating dish, was 5,8-diaminoquinoline, m. p. 163°.

Anal. Calcd. for $C_{15}H_{12}N_4 \cdot HCl$: N, 19.67. Found: N, 19.36, 19.32.

8-Amino-5-phenylazoquinoline was prepared by coupling benzenediazonium chloride with 8-aminoquinoline in acetic acid–sodium acetate solution. The product was recrystallized from alcohol, forming lustrous, deep orange plates, m. p. 133°. No trace of any other coupling product was found. The hydrochloride precipitated as a violet powder, m. p. 221–223°, from a chloroform solution of the free base. The hydrochloride was hydrolyzed readily in water.

The free base was reduced by means of stannous chloride and hydrochloric acid to form 5,8-diaminoquinoline, m. p. 163°. No phenanthrenequinone condensation was obtained even after heating for five hours.

Anal. Calcd. for $C_{15}H_{12}N_4$: N, 22.57. Found: N, 22.66, 22.56. Calcd. for $C_{15}H_{12}N_4 \cdot HCl$: N, 19.67. Found: N, 19.49, 19.30.

7-Amino-8-phenylazoquinoline was prepared by coupling benzenediazonium chloride with 7-aminoquinoline in acetic acid–sodium acetate solution. At first a deep orange oil formed which solidified after one week. Recrystallization from alcohol and water gave light orange needles, m. p. 170–173°. The hydrochloride, m. p. 210–211°, was precipitated by dry hydrogen chloride from a solution of the free base in chloroform. It is easily soluble in water.

Reduction of the free base with stannous chloride and hydrochloric acid, by the same method used for 5-amino-8-phenylazoquinoline, gave a new diaminoquinoline, which crystallized from water as a monohydrate in the form of light yellow needles, m. p. 95–97°. It forms an ortho condensation product with phenanthrenequinone after four hours of heating, m. p. 314°. The structure assigned to this new diamine is the 7,8-diaminoquinoline.

Anal. Calcd. for $C_{15}H_{12}N_4$: N, 22.57. Found: N, 22.65, 22.41. Calcd. for $C_{15}H_{12}N_4 \cdot HCl$: N, 19.67. Found: 19.27, 19.30. Calcd. for $C_9H_9N_3 \cdot H_2O$: N, 23.73. Found: N, 23.65, 23.87. Calcd. for $C_{23}H_{13}N_3$: N, 12.69. Found: N, 12.57, 12.44.

Py-Aminoquinolines

General Directions for Coupling Reactions.—Different methods had to be used in effecting coupling of the py-aminoquinolines and benzenediazonium chloride. Directions are given for 1 g. of amine and an equivalent amount of benzene diazonium chloride. (1) Dilute hydrochloric acid—as for the bz-aminoquinolines. (2) Acetic acid–sodium acetate—as for the bz-aminoquinolines. (3) Excess hydrochloric acid—method according to Ostromisslenski[26] and K. H. Meyer.[27] (4) Aqueous alcohol—the aqueous diazonium solution (15 cc.) was added slowly with stirring to an equal volume of a methanol solution of the amine at a temperature below 5°. (5) Glacial acetic acid—the dry diazonium chloride[28] in 5 cc. of solvent was slowly added with stirring to an equal volume of amine solution keeping the temperature below 10°. (6) Absolute alcohol—the dry diazonium chloride in 15 cc. of solvent was slowly added with stirring to a 5 cc. solution of the amine at a temperature below 10°.

Benzenediazonium chloride was used in all cases except where otherwise specified. Coupling reactions which are recorded in Table II as unsuccessful are not described in detail. In all unsuccessful cases aqueous solutions remained overnight below 5° and non-aqueous solutions were allowed to stand for one week below 10°. These reactions were characterized by a lack of color change and non-appearance of precipitate (in a few cases in excess hydrochloric acid solutions, some amine hydrochloride precipitated). The bulk of the amine was always isolated unreacted from the solutions.

2-Benzenediazoaminoquinoline was formed in both aqueous and absolute alcoholic coupling. The yields were small. From 1 g. of the amine 0.375 g. of product was obtained in absolute alcohol. The product on recrystallization from 95% ethanol formed light tan needles, m. p. 165–166.5°, identical in appearance with that of 2-benzenediazoaminopyridine. It is also stable to hot dilute sodium hydroxide and hydrochloric acid.

Anal. Calcd. for $C_{15}H_{12}N_4$: N, 22.57. Found: N, 22.49, 22.70.

3-Benzenediazoaminoquinoline.—The 3-aminoquinoline was dissolved in a dilute hydrochloric acid solution and the diazonium chloride solution was added. Then a saturated solution of sodium acetate was added until turbidity appeared. After standing overnight below 5°, an orange-tan

(24) Kaufmann, *Ber.*, **50**, 1630 (1917).
(25) Rudy, *ibid.*, **71B**, 847–857 (1938).
(26) Ostromisslenski, THIS JOURNAL, **56**, 1714 (1934).
(27) Meyer, *Ber.*, **54**, 2272 (1921).
(28) Hantzsch and Borghaus, *Ber.*, **30**, 90 (1897); Hantzsch and Jochem, *ibid.*, **34**, 3337 (1901).

precipitate of the diazoamino compound formed. The same compound was obtained from aqueous alcoholic coupling. The compound could be recrystallized from water, m. p. 156–157° (with decomposition). Recrystallization from hot 10% sodium hydroxide gave identical crystals but melting at 177–178° (with decomposition). Undoubtedly different degrees of hydration occurred to account for these discrepancies. It was noted that the melting point of a sample would rise after heating at 80° for several hours. The new melting point was always sharp. Boiling dilute hydrochloric acid destroyed the compound readily with the appearance of the blue fluorescence of 3-aminoquinoline.

Reduction of the compound with stannous chloride and hydrochloric acid resulted in the formation of 3-aminoquinoline.

Anal. Calcd. for $C_{15}H_{12}N_4$: N, 22.57. Found: N, 21.95, 21.46.

4-Phenylazo-3-aminoquinoline was obtained by coupling in absolute ethanol. On mixing the diazonium and amine solutions, a bright red color developed immediately. After standing overnight small dark red crystals formed, m. p. 125–135°. Free chloride ion was present. From 0.5 g. of the amine, 0.45 g. of product was obtained. This product was purified by dissolving in 100 cc. of 0.1 *N* hydrochloric acid, then boiling to decompose any diazoamino compound, filtering to remove a small amount of tar, and precipitating the orange-red free base with ammonia, m. p. 198–201°. This purification yielded 70% of product from the crude. On extracting the basic mother liquor with ether, it was found that 0.015 g. of 3-aminoquinoline per 0.1 g. of crude could be isolated. Hence, the original precipitate was a mixture of the azo compound and the diazoamino or of the azo compound and the amine as hydrochlorides. The azo compound was further purified by recrystallization from hot alcohol and water solution. It formed small, lustrous, light red needles, m. p. 203–204°. Evaporation of a hydrochloric acid solution of the free base gave the dark red hydrochloride, m. p. 228–230°.

Anal. Calcd. for $C_{15}H_{12}N_4$: N, 22.57. Found: N, 22.65, 22.37.

3,4-Diaminoquinoline was obtained by the reduction of the azo compound with stannous chloride and hot dilute hydrochloric acid. After the reaction, excess of base was added and the product extracted with ether. The product was further purified by crystallization from toluene, after bone blacking. White crystals were obtained, m. p. 176–177°.

The same product was obtained by bromination of 4-aminoquinoline[18] and conversion of the 3-bromo-4-aminoquinoline to the diamine by heating with concentrated aqueous ammonia and copper sulfate as a catalyst for twelve hours at 155–160°.[19] The diamine was isolated and purified as above. With hot acetic anhydride the acetyl derivative was obtained, which on crystallization from water formed long, white, cottony needles, m. p. 229–229.5°. The diamine also formed in glacial acetic acid with phenanthrenequinone after heating for one hour, an azine, m. p. 280–281°.

Anal. Calcd. for $C_9H_9N_3$: N, 26.41. Found: N, 26.52.

An attempt to couple 4-aminoquinoline with benzenediazonium chloride failed in all cases tried. The coupling in absolute alcohol as pointed out above was of particular interest. As described above, when the solutions were mixed at −5°, a light red color occurred, but rapidly faded with the evolution of nitrogen. The red color would not develop below −10°. Usually about ten minutes were required for a total loss of color. When *p*-nitrobenzenediazonium chloride was used, unreacted amine and *p*-nitrobenzene were isolated from the solution.

2-Benzenediazoamino-4-aminoquinoline was formed in small yields when coupling was effected in dilute hydrochloric acid solution, and in better yields in aqueous alcohol, and in glacial acetic acid. In excess hydrochloric acid and in absolute alcohol the coupling did not proceed. The product after crystallization from an alcohol–water solution is orange-brown in color, and after drying at 110° for eleven hours melted at 247.5–248.5°. The compound is stable in boiling hydrochloric acid solution.

Anal. Calcd. for $C_{15}H_{13}N_5$: N, 26.61. Found: N, 26.88.

2-*p*-Nitrobenzenediazoamino-4-aminoquinoline precipitated in about ten minutes when coupling was effected in glacial acetic acid. In absolute alcohol a dark red solution was first formed. This color disappeared in about fifteen minutes at −5° accompanied by slow evolution of nitrogen. After this time the yellow hydrochloride precipitated, m. p. 323–325°. It was identical with the product from the former coupling. It is only slightly soluble in hot water and on cooling forms gels. Neutralization of the aqueous solution gave a highly water insoluble, orange free base, m. p. 315.5–316.5°.

Anal. Calcd. for $C_{15}H_{12}N_6O_2$: N, 27.27. Found: N, 27.05, 27.78.

Summary

The orientation in the quinoline ring has been determined by a study of the coupling reactions of all the mono-aminoquinolines. Proofs for the structures of the resulting compounds are given. The results are those to be expected from the application of the Erlenmeyer structure for quinoline.

UNIVERSITY HEIGHTS
NEW YORK, N. Y. RECEIVED SEPTEMBER 20, 1939

[CONTRIBUTION FROM THE PATHOLOGICAL DIVISION, BUREAU OF ANIMAL INDUSTRY]

Lupine Studies. XIV.[1] The Isolation of Anagyrine from *Lupinus laxiflorus* var. *silvicola* C. P. Smith

BY JAMES FITTON COUCH

The leguminous plant *Lupinus laxiflorus* var. *silvicola* C. P. Smith ranges from Mariposa County, Calif., northward to southern Oregon. It has long been of interest among the poisonous lupines because of the atypical symptoms which it produces in livestock. Instead of showing the ordinary and characteristic symptoms of lupine poisoning, animals affected by this species exhibit symptoms closely resembling those caused by the larkspurs, notably *Delphinium barbeyi* Huth.[2] This had resulted in some confusion in diagnosing spontaneous range poisoning.

It has now been found that *Lupinus laxiflorus* var. *silvicola* contains anagyrine, not hitherto known to exist in the genus *Lupinus*. The close relationship of anagyrine to the lupine alkaloids has been shown by Ing.[3] Its occurrence in the genus *Lupinus* is further evidence of the close chemical similarity between the papilionaceous genera.

Anagyrine isolated from this lupine is indistinguishable from the alkaloid isolated from *Anagyris foetida*. It constitutes the major portion if not the whole of the alkaloidal material present. The related alkaloids often associated with anagyrine, cytisine, methylcytisine and sparteine, were not found in *L. laxiflorus* var. *silvicola*.

Anagyrine hydrochloride apparently crystallizes with varying quantities of water. Ing[3] prepared it with one molecule, and Hardy and Galois[4] reported a salt with four molecules. In this paper there are reported preparations with one-half and with three molecules of water.

Anagyrine behaves characteristically in the modified Grant's test for sparteine. When a strip of filter paper is moistened with a chloroform solution of anagyrine, dried and exposed to bromine vapor, the usual orange-yellow color develops. If the strip be now suspended in ammonia vapor, instead of bleaching it develops a pale blue color. On heating the strip the color changes to brown instead of scarlet as in the case of sparteine. This behavior appears to be unique with anagyrine.

The alkaloid and its salts have been compared with monolupine previously reported from *Lupinus caudatus*[5] and have been found to be different. Monolupine is not anagyrine. It differs in optical activity, does not form a very insoluble perchlorate, and mixed melting points of similar salts are markedly depressed and indefinite.

Experimental

Material.—Two lots of plant were examined. The first lot was collected by W. W. Eggleston in the Plumas National Forest, California, in July of 1926 and 1927. The second lot was collected by Forest Ranger Ben Beard at the same place in June and July, 1931. The species was identified by Mr. Eggleston.[6] No chemical differences were found between the two lots. They contained 11.94 and 10.62% of moisture, respectively.

Extraction of the Alkaloids.—The coarsely-powdered dried plants were extracted by alcohol and the alkaloids were recovered by the process already described.[7] The first lot, 3.96 kg., yielded 33.6 g. or 0.97% of crude alkaloid; the second, 14.76 kg., yielded 94.5 g. or 0.71% calculated to moisture-free plant.

Anagyrine Hydrochloride.—The crude alkaloid (10 g.) was dissolved in water, filtered and acidified with hydrochloric acid. The solution was concentrated and allowed to crystallize. The crystals were recrystallized from a mixture of hot alcohol and ethyl acetate. White needles, melting at 235–236° (uncor.) after desiccator-drying, were obtained.

Anal. Calcd. for $C_{15}H_{20}ON_2 \cdot HCl \cdot 3H_2O$ (334.7): H_2O, 16.14; Cl, 10.61; N, 8.37. Found: H_2O, 15.62, 15.48; Cl, 10.84; N, 8.34, 8.35.

To 35.5 g. of crude alkaloid in 100 cc. of acetone was added a mixture of 20 cc. of hydrochloric acid and 20 cc. of alcohol and then enough alcohol, 10 cc., to redissolve the oily precipitate. On cooling, anagyrine hydrochloride crystallized out. The salt was recrystallized from a mixture of 2 parts alcohol and 1 part acetone. After several recrystallizations and drying in a desiccator the salt melted at 284.5–285.5°[8] and did not depress the melting point of authentic anagyrine hydrochloride from *Anagyris foetida*.

Anal. Calcd. for $C_{15}H_{20}ON_2 \cdot HCl \cdot 0.5H_2O$ (289.7): H_2O, 3.11; Cl, 12.25. Found: H_2O, 3.31; Cl, 12.43, 12.42. In water $[\alpha]^{25}D$ −124.2°, l = 2, c = 1.7316, a = 4.3°.

(1) Previous paper, THIS JOURNAL, **61**, 1523 (1939).
(2) A. B. Clawson, *The Official Record*, Feb. 26, 1931, p. 31.
(3) H. R. Ing, *J. Chem. Soc.*, 504–510 (1933).
(4) Hardy and Galois, *Compt. rend.*, **107**, 247 (1888).
(5) J. F. Couch, THIS JOURNAL, **58**, 686–687 (1936).
(6) This species was described as *Lupinus silvicola* by Heller *Muhlenbergia*, **6**, 81 (1910).
(7) J. F. Couch, THIS JOURNAL, **56**, 2434 (1934).
(8) Melting points are corrected unless otherwise indicated.

The anhydrous hydrochloride melted at 295–297°.

Anagyrine perchlorate was prepared according to Ing as long needles soluble in hot water and crystallizing readily from cold, decomposing without melting at a high temperature.

Anal. Calcd. for $C_{15}H_{20}ON_2 \cdot HClO_4$ (344.7): C, 52.22; H, 6.15; N, 8.12. Found[9]: C, 52.13, 52.30; H, 6.37, 6.31; N, 8.10, 8.13.

Anagyrine Gold Chloride.—An aqueous solution of the hydrochloride was treated with excess of gold chloride and the resulting precipitate was recrystallized from boiling dilute hydrochloric acid after filtering from the gold precipitated by reduction. The double salt crystallized in long golden needles melting at 167–168° (uncor.) after desiccator-drying. Analysis indicated somewhat more than the theoretical gold content, possibly due to reduced gold.

Anal. Calcd. for $C_{15}H_{20}ON_2 \cdot HAuCl_4$ (584.2): Au, 33.75. Found: Au, 34.04, 34.09.

Anagyrine Picrate.—The hydrochloride in water treated with alcoholic picric acid gave a bright yellow crystalline precipitate which was collected and dried. It melted at 169.5° and did not depress the melting point of authentic anagyrine picrate. Attempts to recrystallize these picrates from water resulted only in crystals of picric acid.

Anagyrine Base.—Ten grams of the hydrochloride was alkalized with sodium hydroxide and the free alkaloid shaken out with ether. After removal of the solvent the base was distilled under reduced pressure. At 12 mm. the major portion distilled between 260 and 270°. The distillate was a light yellow oil that solidified to a yellow glass. In water solution it gave a red color with ferric chloride and in acid solution readily reduced potassium permanganate. It was levorotatory in alcohol, $[\alpha]^{25}D$ −168°, l = 1, c = 1.0596, a = 1.78°.

Anagyrine Methiodide.—The base, 2 g., in 15 cc. of acetone and 2 cc. of methyl iodide evolved heat and began to deposit crystals within thirty minutes. The crystals were recrystallized from methanol and dried at 110°. They melted at 262–263°.

Anal. Calcd. for $C_{15}H_{20}ON_2 \cdot CH_3I$: I, 32.86. Found: I, 32.77.

Other Bases.—The mother liquors from the hydrochloride were alkalized with sodium hydroxide in water and the liberated bases were shaken out with chloroform. A portion of the residue was shown to be anagyrine. No other base could be identified in the remainder. Cytisine, methylcytisine and sparteine were proved absent by appropriate tests.

(9) The analyses were made by the Arlington Laboratories, V. A. Conard, Director.

Summary

Dry *Lupinus laxiflorus* var. *silvicola* C. P. Smith contains 0.7 to 1% of alkaloids, principally anagyrine. Cytisine, methylcytisine, and sparteine were not found in the plant. Anagyrine gives a characteristic blue color in the modified Grant test for sparteine.

WASHINGTON, D. C. RECEIVED SEPTEMBER 22, 1939

[CONTRIBUTION NO. 389 FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF PITTSBURGH]

A Method for the Preparation of α,β-Diglycerides of Fatty Acids

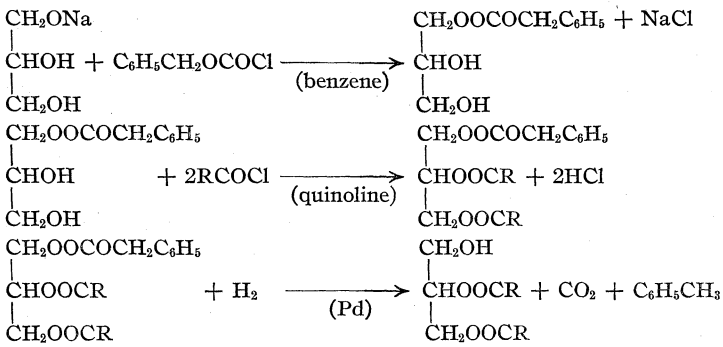
BY B. F. DAUBERT AND C. G. KING

The preparation and identification of α,β-diglycerides of the fatty acids has been difficult, due principally to the migration of acyl groups from the β- to the α′-position, as shown by Fischer.[1] Fairbourne and associates[2,3,4] have shown that the unsymmetrical diglycerides reported by earlier investigators[5,6,7,8,9] were probably the symmetrical isomers or mixtures in every case. The methods reported by Humnicki and Lunkiewicz,[10] Weizman and Haskelberg[11] and Delaby and Dubois[12] also involved reaction conditions that would almost certainly yield products containing little if any of the α,β-diglycerides.

The methods of Abderhalden and Eichwald[13] and Bergmann and associates,[14] using propylamine, and the trityl ether method of Helferich and Sieber,[15] have proved to be satisfactory for the preparation of aromatic α,β-diglycerides, but in no case have α,β-diglycerides of the fatty acids been prepared and characterized as pure compounds. Recently Verkade and associates[16] have outlined a general method for the preparation of α,β-diglycerides that should be satisfactory, involving the catalytic detritylation of α,β-diacyl-α′-trityl glycerol, but their work has not been reported in detail.

(1) Fischer, *Be.*, **53**, 1621 (1920).
(2) Fairbourne and Cowdrey, *J. Chem. Soc.*, 129 (1929).
(3) Fairbourne, *ibid.*, 369, 372 (1930).
(4) Fairbourne, Gibson and Stephens, *ibid.*, 445 (1931).
(5) Guth, *Z. Biol.*, **44**, 78 (1903).
(6) Grun and Theimer, *Ber.*, **40**, 1792 (1907).
(7) Renshaw, THIS JOURNAL, **36**, 537 (1914).
(8) Thomson, *Trans. Roy. Soc. Canada*, **20**, 445 (1926).
(9) Heiduschka and Schuster, *J. prakt. Chem.*, **120**, 145 (1928).
(10) Humnicki and Lunkiewicz, *Bull. soc. chim.*, **40**, 422 (1929).
(11) Weizman and Haskelberg, *Compt. rend.*, **189**, 104 (1929).
(12) Delaby and Dubois, *ibid.*, **187**, 767, 949 (1928).
(13) Abderhalden and Eichwald, *Ber.*, **49**, 2095 (1916).
(14) Bergmann, *et al.*, *ibid.*, **54**, 936 (1921); *Z. physiol. Chem.*, **137**, 27, 47 (1924).
(15) Helferich and Sieber, *ibid.*, **170**, 31 (1927); **175**, 311 (1928).
(16) Verkade, van der Lee, de Quant and Zuydewijn, *Proc. Acad. Sci. Amsterdam*, **40**, 580 (1937).

In the present investigation a new method of synthesis has been established, based upon the reaction between α-monosodium glyceroxide and benzyl chloroformate (carbobenzyloxy chloride), followed by esterification and catalytic reduction, as indicated in the following series of reactions



A brief study was also made of the solubilities and relative migration tendencies of aromatic and aliphatic unsymmetrical diglycerides.

Experimental

Preparation of 3-Carbobenzyloxyglycerol.—3-Monosodium glyceroxide was prepared by the method of Fairbourne and Toms.[17] To 5 g. of the oxide dissolved in 75 ml. of dry benzene there was added, in divided portions, 7.5 g. of benzyl chloroformate, previously prepared by the method of Bergmann and Zervas.[18] During the addition of the benzyl chloroformate the reaction mixture became warm. It was then allowed to stand twenty-four hours at room temperature, heated gently, filtered and the precipitate identified as sodium chloride. The filtrate was boneblacked, filtered and evaporated under reduced pressure. The residue consisted of a pale-yellow, oily liquid. Attempts to crystallize it were not successful. The yield was 8.2 g. (83%).

Anal. Calcd. for $C_{11}H_{14}O_5$: C, 58.40; H, 6.24. Found: C, 58.21, 58.16; H, 6.09, 6.16.

Preparation of 3-Carbobenzyloxy-1,2-dipalmitin.—To 5 g. of 3-carbobenzyloxyglycerol dissolved in 20 ml. of benzene and 5 ml. of quinoline there was added slowly a mixture of 5 g. of palmityl chloride and 5 ml. of quinoline. The mixture was shaken continuously for two hours and set aside at room temperature for four days. The product was then taken up in ether and the solution washed successively with cold 0.5 *N* H_2SO_4, saturated sodium bicarbonate, water and finally dried over anhydrous sodium sulfate. After evaporation *in vacuo* to dryness, the residue was redissolved in ether. Small white crystals separated after twenty-four hours at 5°, m. p. after recrystallization, 71°, yield 5 g. (80%).

Anal. Calcd. for $C_{43}H_{74}O_7$: C, 73.46; H, 10.61. Found: C, 73.09, 73.22; H, 10.73, 10.52.

Preparation of 1,2-Dipalmitin.—3-Carbobenzyloxy-1,2-dipalmitin (2 g.) was suspended in 75 ml. of absolute alcohol and transferred to a hydrogenation bottle together with 0.5 g. of palladium black. Reduction was complete after approximately two hours at room temperature and 30 lb. (2 atm.) pressure. The solution was filtered twice to remove the catalyst, then concentrated by evaporation and cooled for twenty-four hours. The 1,2-dipalmitin separated as flaky, white crystals, m. p. 64° after being recrystallized several times from absolute alcohol, yield 1.2 g. (76%).

Anal. Calcd. for $C_{35}H_{68}O_5$: C, 73.80; H, 12.05. Found: C, 73.89, 73.95; H, 11.67, 11.88.

Golendeev[19] reported a m. p. of 70–73° for 1,2-dipalmitin, but his method of esterifying the corresponding allyl halide (heating with the potassium salt of the fatty acid) would almost certainly cause a rearrangement of the structure to produce the 1,3-dipalmitin, m. p. 69.5°.

A second preparation of 1,2-dipalmitin, identical with the above product, was made by the method proposed by Verkade.[16] It was necessary to carry out the reduction at 45 lb. (3 atm.) pressure, 45–50°. For additional identification the triglyceride, 1-*p*-bromobenzoyl-2,3-dipalmitin, m. p. 68.8°, previously made by an independent method[20] was prepared from 1,2-dipalmitin by direct esterification.

Using the same procedure as outlined above for dipalmitin, 1,2-dimyristin was prepared, m. p. 59°, yield 80%.

Anal. Calcd. for $C_{31}H_{60}O_5$: C, 72.59; H, 11.79. Found: C, 72.25, 72.31; H, 11.56, 11.62.

The m. p. of the intermediate carbobenzyloxy-1,2-dimyristin was 67–68°.

Anal. Calcd. for $C_{39}H_{66}O_7$: C, 72.39; H, 10.28. Found: C, 72.11, 72.20; H, 10.06, 10.13.

Preparation of 3-Carbobenzyloxy-1,2-glyceroldibenzoate.—Essentially the same method as outlined above for 3-carbobenzyloxy-1,2-dipalmitin was followed for the preparation of the analogous dibenzoate.

Anal. Calcd. for $C_{25}H_{22}O_7$: C, 69.11; H, 5.10. Found: C, 68.86, 68.92; H, 5.17, 5.21.

Preparation of 1,2-Dibenzoate of Glycerol.—The 1,2-dibenzoate was prepared from the carbonate as described for 1,2-dipalmitin, but considerable difficulty was encountered in crystallizing the sirupy liquid remaining after evaporation of the solvent. Crystallization was accomplished after the product had been held two weeks in a vacuum desiccator, m. p. 58°, yield 70% (Helferich and Sieber[15] 58″–59°).

The 1,2-dibenzoate of glycerol thus obtained was used to prepare 1,2-dibenzoyl-3-trityl glycerol, m. p. 91°.

For further identification, the 1-*p*-bromobenzoyl-2,3-dibenzoate of glycerol, m. p. 107°, was prepared from the above 1,2-dibenzoate and also from 1-*p*-bromobenzoyl glycerol and benzoyl chloride.

Anal. Calcd. for $C_{24}H_{19}O_6Br$: Br, 16.54. Found: Br, 16.38, 16.45.

Migration of Acyl Groups.—When 1,2-dipalmitin was allowed to stand for twenty-four hours in solution in 0.1,

(17) Fairbourne and Toms, *J. Chem. Soc.*, **119**, 1035 (1921).
(18) Bergmann and Zervas, *Ber.*, **65**, 1194 (1932).
(19) Golendeev, *J. Gen. Chem. U. S. S. R.*, **6**, 1841 (1936).
(20) Daubert and King, THIS JOURNAL, **60**, 3003 (1938).

0.05 and 0.025 *N* alcoholic hydrochloric acid or ammonia (prepared by passing the gases into alcohol), there was a marked drop in melting point of the recovered product. There was no change in the melting point of 1,2-dibenzoyl glycerol, however, when identical tests were made, giving further evidence of the greater stability of the β-type aromatic esters compared to the β-glycerides of fatty acids.

Solubilities.—In an earlier publication[19] it was noted that the solubility ratios of the α- and β-aromatic and aliphatic monoglycerides in ether were reversed, the aromatic α-esters being more soluble than the β-isomers, but in the aliphatic series, the α-esters were less soluble than the β-isomers. A similar reversal of solubility in alcohol will be noted from the data in Table I.

TABLE I

SOLUBILITIES

Compound	Solvent	Temp., °C. (±0.01°)	Soly. g. per 100 ml.
α-Monopalmitin	Alcohol	25	4.09
β-Monopalmitin	Alcohol	25	4.61
α-*p*-Bromobenzoate	Alcohol	26	16.05[a]
β-*p*-Bromobenzoate	Alcohol	26	4.41[a]
β-*p*-Bromobenzoyl-α,α′-benzylidene glycerol	Alcohol	26	0.50
	Ether	26	1.15
β-Palmityl-α,α′-benzylidene glycerol	Alcohol	26	1.75
	Ether	26	17.40

[a] Repeated from an earlier paper for comparison.[20]

Summary

A new method for the synthesis of α,β- or 1,2-diglycerides has been described, in which sodium glyceroxide and benzyl chloroformate served as intermediates. Good yields were obtained and the reaction conditions made it possible to avoid the common β- to α-shift in structure.

1,2-Dipalmitin, m. p. 64°, 1,2-dimyristin, m. p. 59° and 1,2-dibenzoate of glycerol, m. p. 59°, were prepared and their structures were verified by making derivatives of known constitution.

A solution of 1,2-dipalmitin in 0.1 to 0.025 *N* alcoholic hydrochloric acid and ammonia underwent a rapid change in structure, but the analogous 1,2-dibenzoate was stable under the same conditions of exposure.

PITTSBURGH, PENNA. RECEIVED AUGUST 4, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

On the Effect of Acids in the General Meaning of the Term on the Activity of Invertase

BY WALTER ABBOTT WISANSKY

That the value of the *p*H of a solution in which an enzyme is acting, is a most important factor in controlling the activity of the enzyme, is well known. For example, the enzyme invertase has its maximum power for inverting sucrose in a range of *p*H values surrounding *p*H 4.5. If the *p*H value is raised or lowered sufficiently away from *p*H 4.5, the activity of invertase diminishes.

The explanation of the *p*H effect on enzymatic activity has been sought for a long time. The ionization hypothesis of Michaelis[1] has been a much favored suggestion in spite of certain shortcomings.[2] On the basis of this hypothesis invertase is supposed to be active only in the un-ionized condition.

In considering the effect of *p*H changes, workers have only been concerned with the effect produced on enzymatic activity by changes in the thermodynamic activity of one acid, oxonium ion. Since Brönsted[3] and others have demonstrated the generality of the term "acid," it became of interest to determine whether or not any acid, in the general meaning of the term, could alter the activity of enzymes. It was thought that if neutral acids could exert some effect on the activity of the enzyme invertase under conditions which purported to keep the degree of ionization of the enzyme constant (conditions such as constant ionic strength, and constant *p*H value), then one might impute to oxonium ion a role similar to that played by neutral acids in controlling the enzymatic activity of invertase, beyond oxonium ion's assured role of controlling the degree of ionization of the protein enzyme.

Since in practically all enzyme work, buffers are employed to regulate the *p*H, and since buffer solutions contain acids in the general meaning of the term, here is a very convenient source of acids whose effects on the activity of invertase it is proposed to consider.

The effects of neutral buffer acids on the activity of invertase have been studied.

In brief, the plan pursued in studying the effects of buffer acids on the activity of invertase

(1) L. Michaelis and H. Davidsohn, *Biochem. Z.*, **35**, 386 (1911).
(2) J. M. Nelson, *Chem. Rev.*, **12**, 1 (1933).
(3) J. N. Brönsted, *ibid.*, **5**, 231 (1928).

was to determine the enzymatic activity in solutions of different buffer concentration, at various *p*H values, keeping the ionic strength of all the buffer solutions constant.

If the total buffer concentration of a solution is varied, the *p*H will remain practically the same and, if the ionic strength is kept constant, the degree of ionization of an enzyme (invertase in this case) in the solution should be unchanged.

Any observed loss in enzymatic activity obtained by increasing the buffer concentration in solution would then be due either to the increase in the concentration of neutral buffer acid or to the greater specific action of the potassium buffer salt as compared to potassium chloride. (The potassium chloride is added to the more dilute buffer solutions to build up the ionic strength to a given value.)

A salt like potassium acetate might well be expected to diminish the activity of invertase after the fashion of potassium chloride.[4] The effect of potassium acetate might be greater or less than that of potassium chloride. It was therefore necessary to determine whether or not any observed change in invertase activity with variations in total buffer concentration is due to buffer salt or buffer acid. One could distinguish between the two possibilities, as will be seen shortly, by studies of the influence of varying buffer concentrations on the activity of invertase at different *p*H values and at constant salt concentration.

As is evident from Fig. 1,[5] *p*H–activity curves for invertase obtained in the presence of different concentrations of acetate ion appear to spread fanlike from an origin near the *p*H optimum, as one passes to more acid *p*H values.

The results of other experiments not reported here indicate a similar effect when one substitutes a formate buffer in place of the acetate buffer Also this effect appears to be independent of the degree of purification of the invertase preparation used, being the same for preparations of very low time value[6] (*i. e.*, pure preparations of time values as low as 0.14 and 0.17 min.) as for a cruder commercial preparation known as Convertite.

In order to find out from Fig. 1 whether it is the difference in concentration of acetate ion or acetic acid which causes the difference between the two *p*H activity curves, consider the following.

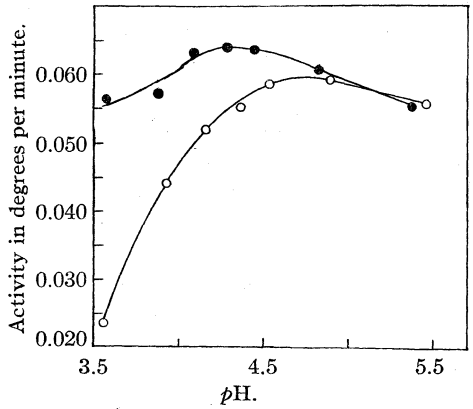


Fig. 1.—*p*H–activity curves based on data obtained in the presence of different concentrations of acetate ion; 10% sucrose; invertase preparation R(0.17); ionic strength, 0.2; ●, 0.02 molar total acetate; ○, 0.2 molar acetate ion.

Suppose the activity of invertase in a solution 0.02 molar in acetate ion is compared with that in a solution 0.05 molar in acetate ion, both solutions at *p*H 4.6. The mole fraction of acetate ion is 0.5. Therefore there is in each solution, respectively, 0.02 and 0.05 molar acetic acid. The activity of invertase is next examined at a more acid *p*H where the mole fraction of acetate ion is now 0.1. There is, in the dilute acetate solution 0.02 molar acetate ion and 0.18 molar acetic acid, and in the more concentrated buffer solution there is 0.05 molar acetate ion and 0.45 molar acetic acid. The difference in concentration of neutral acid has gone up from 0.03 molar at *p*H 4.6 to 0.27 molar at the more acid *p*H.

In Fig. 1, just as in the above example, parallel to the increase in the activity difference between the two *p*H–activity curves, there is a simultaneous increase in the difference of the acetic acid concentration as the *p*H is lowered. This points to the neutral acid as the cause of the loss in activity of invertase, as the buffer concentration is increased.

As further evidence that it is the neutral acid which causes the activity loss rather than the greater inhibitory effect of acetate ion over chloride ion, at *p*H values acid to 4.5, it is seen that on the alkaline side of the *p*H optimum practically no difference in the activity as measured in solutions of different buffer concentrations

(4) M. Washburn, Dissertation, Columbia University (1932).

(5) The numerical data are not given for brevity's sake. An idea of the accuracy of the measurements may be had from Table I in the experimental section. The activities upon which the figures in this paper are based were usually about the order of magnitude of 0.0500 degree per minute, it having been found that such a magnitude is conducive to greatest accuracy.

(6) C. O'Sullivan and F. W. Thompson, *J. Chem. Soc.*, **57**, 834 (1890).

is present. If acetate ion were a more effective retardant of invertase activity than chloride ion, then on the alkaline side of the *p*H optimum this effect should again be in evidence since the enzyme is quite sensitive to salt on the alkaline side as on the acid side of the *p*H optimum. There is, however, little difference between the "potassium acetate" curve (concentrated buffer), and "potassium chloride" curve (dilute buffer) in this region of *p*H.

As a final check, *p*H–activity curves were obtained in the presence of constant concentrations of acetic acid. From Fig. 2 it is evident that, to a first approximation, a given increase in acetic acid concentration causes a certain loss in activity independent of *p*H when this is in the optimum zone.

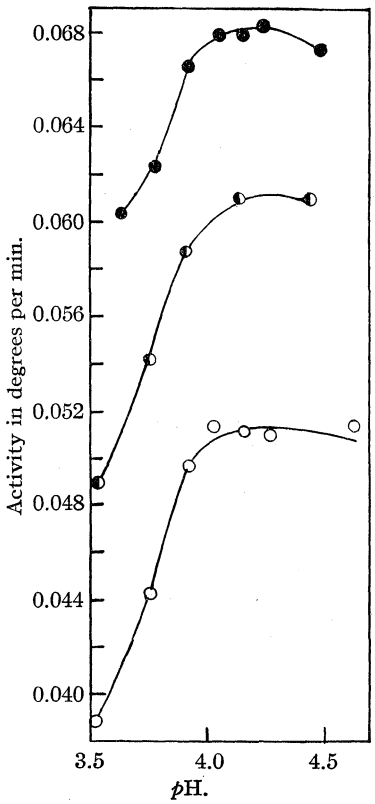


Fig. 2.—*p*H–activity curves based on data obtained in the presence of constant concentrations of acetic acid; 5% sucrose; invertase preparation, commercial Convertite; ionic strength 0.5; ●, 0.01 molar acetic acid; ◐, 0.2 molar acetic acid; ○, 0.5 molar acetic acid.

It is again plain that neutral acetic acid can decrease the activity of invertase.

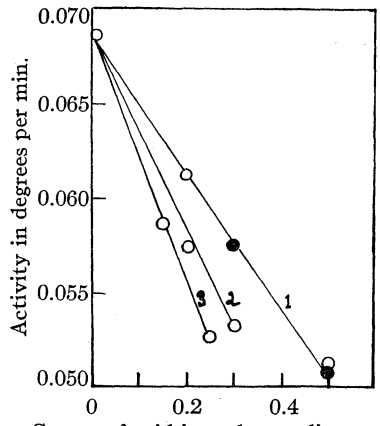


Fig. 3.—Data showing the variation of invertase activity with concentration of acid; 5% sucrose; open points refer to Convertite preparation; closed points refer to preparation R(0.14); curve 1, acetic acid, ionic strength 0.5; curve 2, formic acid, ionic strength 1.7; curve 3, acid phthalate ion, ionic strength 0.5.

In Fig. 3 data are plotted showing the effects of formic acid and acid phthalate ion (a charge type acid) on the activity of invertase as compared to the data on the retardation produced by acetic acid. The activities at zero buffer concentration have been equated. The *p*H values all lie in the optimum zone. The formic acid buffer experiments were performed at an ionic strength of 1.7 since at *p*H values close to the optimum *p*H 4.5 the buffer is practically neutralized and since a fairly large formic acid concentration was required. Because of the larger salt concentration present, a comparison of the effect of formic acid on the activity of invertase with that of acetic acid and acid phthalate ion may not be justified. The effect of these two latter acids on the activity of invertase was studied in 0.5 molar salt solutions.

There is a linear relation between the concentration of acid and the drop in invertase activity. This may be more apparent than real, however, since no correction was applied to correct for the loss in activity that accompanied the displacement of water by acids and salts.[7]

While acetic acid is a stronger acid than acid phthalate ion, as evidenced by their dissociation constants, the latter is the more effective retardant.

(7) It was shown by Nelson and Schubert[8] that decreasing the water concentration even in an essentially aqueous solution produces a loss in the activity of invertase.

(8) J. M. Nelson and M. Schubert, THIS JOURNAL, **50**, 2188 (1928).

Discussion

It is evident from the above that acids in the general meaning of the term can diminish the activity of invertase. It is probable that the effect can be extended to other enzymes. It is therefore suggestive to postulate something as to the meaning of the acid effect.

Mirsky and Pauling[9] hypothesize that proteins are held in their particular configurations through the medium of hydrogen bonds. In the light of this idea, it is suggested that in the case of the retardation of invertase activity by acids, these latter form intermolecular hydrogen bonds with certain electronegative groups in the enzyme protein, which groups are bound by intramolecular hydrogen bonds to other similar groups in the protein. There is a sort of competition in this respect. The result is a breaking of some of the weaker bonds in the protein with the further result that the enzyme passes into some more unspecified form of less enzymatic activity.

Since oxonium ion is an acid, it too might be expected to exert its effect upon the enzyme in a manner similar to that of neutral acids. The first step in the attack of oxonium ion would be the formation of an intermolecular hydrogen bond with the concurrent breaking of an intramolecular hydrogen in the protein enzyme. This would again result in the formation of a more unspecified configuration possessing less activity as an enzyme. The fact that water might subsequently be dissociated from the newly formed hydrogen bond complex, yielding a protein with an extra proton (*i. e.*, a change in the degree of dissociation of the enzyme) may be of secondary importance. In short it is suggested that changes in oxonium ion concentration in altering the activity of invertase do so by bringing about changes in the enzyme protein of a deeper sort than mere ionization changes.

Experimental

(1) The salts and acids used in this investigation were C. P. grade. They were used without further purification. The sucrose used was obtained in a grocery store.

(2) In the experiments on buffer acids it was necessary to know accurately the amount of buffer acid, the concentration of salt (buffer salt and potassium chloride) and that of sucrose in the reaction mixture.

Buffer solutions of known acid and salt concentrations were prepared by standardizing the acid constituent against potassium hydroxide. The alkali was standardized against potassium acid phthalate; 4 molar solutions of the acids were kept in resistance glass bottles; 1 and 2 molar solutions of potassium hydroxide were kept in paraffin lined bottles protected from carbon dioxide. In preparing the buffer a known volume of buffer acid of accurately known concentration was titrated with standard alkali until a given fraction was neutralized. From a knowledge of the total volume of solution, the buffer salt and acid concentration was calculated. A definite volume of the solution so prepared was pipetted into a 250-cc. volumetric flask, keeping in mind the concentration of buffer required to exist in the final reaction mixture. To the volumetric flask was added sucrose and potassium chloride (in sufficient amount to give the required ionic strength in the reaction mixture); 25.00 ± 0.05 cc. of invertase solution was pipetted in six seconds into 200 cc. of solution prepared as above. At recorded time intervals 25.00 cc. of reaction mixture was pipetted into bottles containing sufficient alkali to stop the reaction (*p*H alkaline to phenolphthalein). After allowing five to fifteen minutes for mutarotation, the rotations of the samples were determined. The activity was expressed as the average change in rotation in degrees per min. Usually four constants were used in calculating the average activity.

In calculating the ionic strength, the contribution due to the ionization of the acid constituent of the buffer was neglected, its contribution being too small to affect the activity of invertase when the ionic strength is high (see Table I).

TABLE I

Ionic strength	Enzymatic activity and a. d.	*p*H
0.20	0.380 ± 0.001	3.94
.22	.375 ± .001	3.96
.23	.375 ± .003	3.96

(3) *p*H measurements were made using both the glass and hydrogen electrodes.

(4) **Invertase Preparations.**—The author is grateful to Mr. Stanley Lewis of these laboratories for the preparation of the following highly purified yeast invertase preparations, RaDKDADSDAD[10] time value 0.14 min. known in this paper as R(.14), RaDAceSKSAD time value 0.17 min. known in paper as R(.17). A commercial invertase preparation known as Convertite also was used.

(5) Hydrolyses were conducted at 25.00 ± 0.02°.

Acknowledgment.—The author wishes to express his appreciation to Professor J. M. Nelson for his friendly advice and constructive criticism throughout the course of this investigation.

Summary

1. It has been demonstrated that acids in the general meaning of the term can retard the enzymatic activity of invertase under conditions which purport to hold the degree of ionization of the enzyme constant (*i. e.*, conditions such as constant ionic strength and constant *p*H).

2. It has been suggested that oxonium ion and

(9) A. E. Mirsky and L. Pauling, *Proc. Nat. Acad. Sci. U. S.*, **22**, 439 (1936).

(10) For the meaning of the letters which refer to steps in the purification see Lutz and Nelson, *J. Biol. Chem.*, **107**, 169 (1934).

acids in general may alter the activity of an enzyme by causing the rupture of intramolecular hydrogen bonds in the enzyme protein. The results of such bond breaking may be the arising of modified forms of the enzyme with more internal degrees of freedom, possessing less catalytic activity.

NEW YORK, N. Y. RECEIVED SEPTEMBER 27, 1939

[CONTRIBUTION FROM THE BASIC SCIENCE RESEARCH LABORATORY OF THE UNIVERSITY OF CINCINNATI]

Kinetics of Polyesterification: A Study of the Effects of Molecular Weight and Viscosity on Reaction Rate[1]

BY PAUL J. FLORY

Introduction

Investigators in the field of macromolecular chemistry have been prone to attribute the apparent sluggishness of some polymer reactions either to an inherent diminished reactivity of large molecules, or to the high viscosity of the reaction medium. Various arguments have been advanced in an effort to show theoretically that increase in size of the molecule and increase in viscosity should decrease reactivity.[2,3] However, no direct experimental evidence has been advanced to prove even the existence of an effect of either molecular weight or viscosity on reactivity of polymer molecules.

The problem of the effect of viscosity on reaction rate of liquid phase reactions in general has been the subject of frequent discussion,[4] but again conclusive experimental evidence does not seem to be available. Moelwyn-Hughes[5] has concluded that the rate of collision between solute and solvent molecules should increase proportionally with viscosity and, hence, the rate of a reaction between solute and solvent should be proportional to viscosity also. More recently Rabinowitch and Wood[6] have shown with exceptional clarity that one should expect no effect of viscosity on reaction rate, except at very high viscosities (very low rates of diffusion) or when a large fraction of collisions leads to reaction.

The study of the kinetics of a condensation polymerization offers a splendid opportunity to observe the effects of molecular weight and viscosity on reaction rate. Both molecular weight and viscosity increase continuously as such reactions proceed. It should be possible, therefore, to observe the effects of molecular weight and viscosity on reaction rate, if such effects exist.

The present investigation has been primarily concerned with the kinetics of polyesterification reactions between glycols and dibasic acids. The kinetics of several esterifications involving monofunctional reactants have been investigated also, in order that the polyesterification reactions could be compared with similar reactions in which neither molecular weight nor viscosity underwent appreciable change. All of these reactions have been followed by titration of the total free carboxyl in samples removed from the reaction mixture at suitable intervals.

In contrast to monofunctional esterification where there are only two species of reactants, many species of molecules are present during polyesterification. Any one of these species bearing an hydroxyl group may react with any other bearing a carboxyl; the product of this reaction may react with another molecule, etc. Many reactions are occurring simultaneously: *i. e.*, monomers react with monomers, dimers, trimers, etc., dimers react with monomers, dimers, trimers, etc., trimers react with monomers, etc., etc. A complete kinetic analysis, treating each of these reactions individually, is obviously hopeless. All of these reactions, however, are chemically identical, and their rates may differ only in so far as reactivity is affected by molecular weight. Instead of attempting to unravel the maze of individual reactions, one may consider merely the reaction of all functional groups, disregarding the size of the molecule to which each group is attached. If, as usually has been supposed, reac-

(1) A portion of this work was included in a paper presented before the Organic Plastics Section, Paint and Varnish Division of the American Chemical Society at the Boston Meeting, September 14, 1939.

(2) C. E. H. Bawn, *Trans. Faraday Soc.*, **32**, 178 (1936).

(3) H. Dostal, *Monatsh.*, **67**, 63 (1935); **70**, 409 (1937); H. Mark, *Nature*, **140**, 8 (1937).

(4) See E. A. Moelwyn-Hughes, "Kinetics of Reactions in Solution," Oxford Univ. Press., New York, N. Y., 1933, p. 51.

(5) Reference 4, pp. 19, 159 *et. seq.*

(6) E. Rabinowitch and W. C. Wood, *Trans. Faraday Soc.*, **32**, 1381 (1936).

tivity decreases with increase in size of the molecule, then the ratio of the rate of polyesterification to the rate of a simple esterification at the same degree of reaction should decrease as the reactions progress. The results presented below show that polyesterification and esterification reactions follow identical courses.

Experimental

Materials.—Diethylene glycol, lauryl alcohol, adipic acid, lauric acid, and caproic acid were obtained from the Eastman Kodak Company. Decamethylene glycol, which had been prepared by hydrogenation of diethyl sebacate, was obtained from the University of Illinois. The diethylene glycol was carefully fractionated through a carborundum packed column. The boiling point was practically constant throughout almost the entire distillation, 129.5 to 130.0° at 10.5 mm. A center cut was retained for use. Decamethylene glycol was treated with boiling 5% aqueous caustic to remove unreduced ester, then recrystallized three times from ethylene dichloride. The final product had a freezing point of 71.9 (±0.1)°. Lauryl alcohol, freezing at 21.9 (±0.1)°, was used without further purification.

Adipic acid was recrystallized from conductivity water; m. p. 151.5°; neutral equivalent 72.9, 73.0; calcd. 73.07. Caproic acid, neutral equivalent 117.6, calcd. 116.2, and lauric acid, neutral equivalent 200.6, 200.9, calcd. 200.3, were used with no further purification.

Apparatus and Procedure.—The apparatus consisted of a Pyrex reaction bulb of about 50 cc. capacity sealed to the bottom of a 15-mm. tube about 25 cm. long. Through a stopper at the top of this tube a pipet was inserted. The pipet was used to remove samples, and also for admitting a slow stream of nitrogen through the reaction mixture in order to facilitate removal of water. The effluent stream of nitrogen and water vapor passed through a 12-mm. tube sealed to the vertical tube just below its upper end. This side tube sloped upward at about 45° from horizontal for about 30 cm., and then led downward to a dry-ice trap. With the apparatus designed in this way loss of glycol was minimized by condensation in the side arm, followed by its return to the reaction mixture. Glycol is lost more readily during the early stages of the reaction; later on nearly all glycol molecules have reacted at one end or the other (or both) and hence are no longer volatile.

The reaction bulb and adjacent tubing were carefully cleaned before each experiment. This is especially important since esterification is an acid catalyzed reaction, and hence is sensitive to traces of acids or bases.

Equivalent quantities of glycol (or alcohol) and acid were placed in the reaction bulb which was then sealed onto the vertical tube. The reaction bulb and several cm. of the vertical tube above were heated with a vapor-bath, which remained within 0.2° of constant temperature throughout any one experiment. Liquids used in the vapor-bath were toluene boiling at 109°, phenetole at 166°, and *m*-cresol, 202°. From time to time samples were removed, weighed and titrated (at 20–25°) with 0.1 *N* alcoholic potassium hydroxide, using phenolphthalein indicator. High molecular weight samples, which tended to dissolve slowly, were dissolved in hot chloroform, cooled and then titrated. The end-point was very sharp.

Reactions catalyzed with *p*-toluenesulfonic acid were carried out in the same manner except that, due to the lower temperature, 109°, it was necessary to reduce the pressure to about 200 mm. in order to ensure rapid removal of water.

Experimental Results

From the neutral equivalent determined by titration one can calculate both the extent of reaction p, *i. e.*, the ratio of the number of ester groups to the number of ester plus free carboxyl groups, and the degree of polymerization DP, which is defined as the average number of glycol and dibasic acid residues per molecule. The number of free carboxyl groups will equal the number of molecules, provided that equivalent amounts of glycol and dibasic acid are used and that the only reaction occurring is intermolecular esterification. When these conditions are fulfilled the neutral equivalent must be equal, therefore, to the average molecular weight, and

$$DP = \frac{\text{neut. equiv.} - 18}{\text{mean segment weight}} = 1/(1 - p) \qquad (1)$$

where the mean segment weight is half the molecular weight of the structural unit —ORO—COR'CO— of the polymer.

As Goldschmidt[7] has shown, esterification reactions are hydrogen ion catalyzed. In the absence of a strong acid catalyst a second molecule of the carboxylic acid undergoing esterification must function as catalyst. Therefore, the reaction rate is proportional to the hydroxyl concentration and to the square of the carboxyl concentration. When hydroxyl and carboxyl groups are present in equal numbers, the process becomes a third order reaction,[8] for which

$$2kt = 1/C^2 - 1/C_0^2 \qquad (2)$$

where k is the velocity constant, C is the concentration of unreacted groups at time t, and C_0 is the initial concentration. If one neglects the effect on concentration of the decrease in volume due to loss of water, this equation may be replaced by

$$2C_0^2kt = 1/(1 - p)^2 - 1 \qquad (3)$$

with which the data presented below will be compared. The error arising from the use of (3) rather than (2) is appreciable only during the

(7) H. Goldschmidt and co-workers, *Z. physik. Chem.*, **60**, 728 (1907); **70**, 627 (1910); **81**, 30 (1913); *Ber.*, **29**, 2208 (1896). See also Hinshelwood and co-workers, *Trans. Faraday Soc.*, **30**, 935, 1145 (1934); *J. Chem. Soc.*, 593 (1939).

(8) P. J. Flory, THIS JOURNAL, **59**, 466 (1937).

first part of the polymerization, which is of minor interest here.

TABLE I

DIETHYLENE GLYCOL–ADIPIC ACID AT 166°

t in min.	Neutral equiv.	p	DP	$1/(1-p)^2$
6	143.3	0.1379	1.160	1.346
12	161.5	.2470	1.328	1.761
23	189.0	.3675	1.581	2.50
37	233.0	.4975	1.990	3.96
59	293.0	.6080	2.55	6.47
88	363.5	.6865	3.19	10.18
129	451	.7513	4.02	16.16
170	532	.7894	4.75	22.6
203	606	.8161	5.44	29.6
235	673	.8349	6.06	36.7
270	738	.8500	6.67	44.4
321	832	.8672	7.53	56.7
397	947	.8837	8.60	73.8
488	1072	.8974	9.75	95.0
596	1198	.9084	10.92	119.0
690	1309	.9163	11.94	142.5
793	1404	.9220	12.82	164.0
900	1507	.9273	13.77	189.5
1008	1569	.9303	14.33	206
1147	1691	.9354	15.48	239
1370	1835	.9405	16.81	283
1606	1973	.9447	18.08	327

Data from two typical experiments are given in Tables I and II. Extents of reaction and DP's have been calculated using (1). In Figs. 1 and 2, $1/(1-p)^2$ is plotted against t for the reaction of

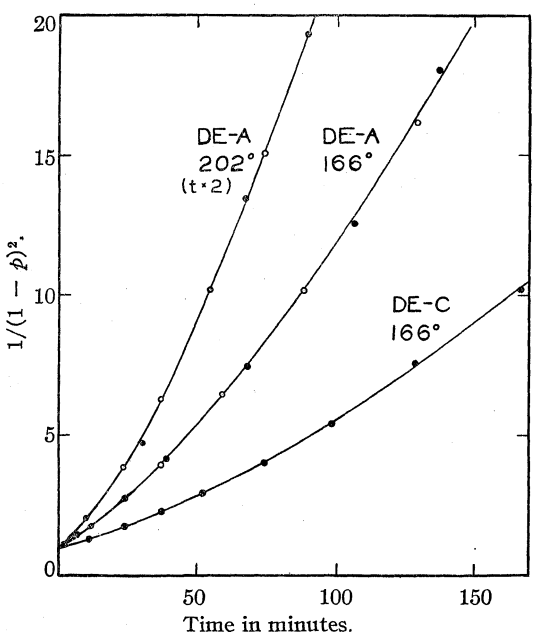


Fig. 1.—Diethylene glycol–adipic acid (DE-A) and diethylene glycol–caproic acid (DE-C) reactions during initial stages. Time values at 202° have been multiplied by two.

TABLE II

LAURYL ALCOHOL–ADIPIC ACID REACTION AT 202°

t in min.	Neutral equiv.	p	$1/(1-p)^2$
4	344.5	0.2609	1.83
15	532	.5307	4.53
28	742	.6669	9.01
43	955	.7425	15.08
65	1227	.8004	25.1
91	1525	.8400	39.0
116	1772	.8624	52.7
148	2050	.8812	70.9
183	2330	.8957	91.8
226	2581	.9059	112.9
267	2840	.9145	136.9
322	3105	.9219	163.8
378	3365	.9279	192.3

diethylene glycol with adipic acid at 166 and 202°, and of the same glycol with caproic acid at 166°. It has been necessary to use two graphs having different scales in order to show effectively the entire course of the reaction. Dots and circles are used to distinguish data obtained in different experiments. The agreement between two such sets of points indicates the reproducibility. Data from the reactions of decamethylene glycol with adipic acid, lauryl alcohol with adipic acid, and lauryl alcohol with lauric acid are shown in Fig. 3.

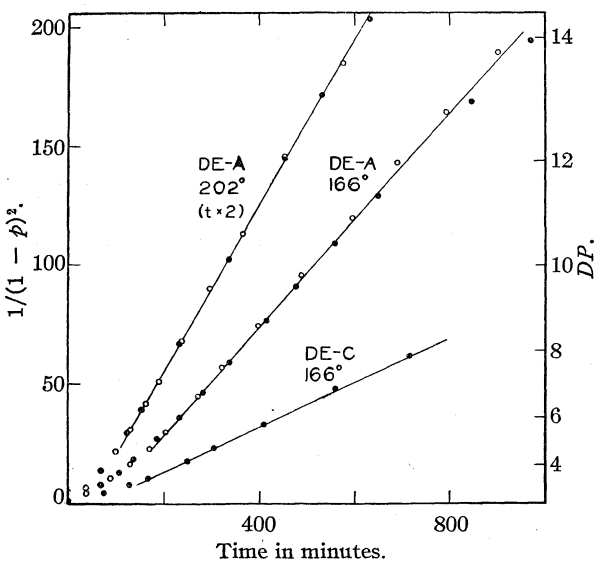


Fig. 2.—Diethylene glycol–adipic acid (DE-A) and diethylene glycol–caproic acid (DE-C) reaction including later stages of the reactions. Time values at 202° have been multiplied by two.

During the portion of the reaction shown in Fig. 1 the relationship between $1/(1-p)^2$ and t is definitely not linear, in disagreement with the

third order equation (3). However, at the larger extents of reaction included in Figs. 2 and 3 the data do approach this linear relationship. Straight lines have been drawn through the points in these two figures in order to show clearly the range over which $1/(1 - p)^2$ is approximately linear with t. Attempts to fit the data to an equation for a reaction of lower order have not been successful; although such equations offer somewhat better agreement within a limited range during the early portion of the reaction, they fail completely at higher extents of reaction.

In the case of the diethylene glycol–caproic acid reaction, reliable data could not be obtained beyond the range given in Fig. 2, due to excessive loss of the comparatively volatile caproic acid. With diethylene glycol and adipic acid at extents of reaction somewhat beyond those covered in Fig. 2 the points fell consistently below the extrapolation of the straight lines shown in the figure. This is attributed to the effect of the inevitable slight loss of the glycol by volatilization. Small losses of one reactant are of no consequence except at large extents of reaction where the concentration of unreacted functional groups is so low that a small deficiency of one functional group produces an appreciable reduction in rate. This deviation sets in at a much later stage in the reaction of decamethylene glycol with adipic acid, since this glycol is less volatile.

Careful examination of the data presented in the figures fails to reveal any significant dissimilarities between polyesterification and esterification. The courses which they follow are so similar that their points may be made to follow approximately the same curve by merely multiplying all time values for one of them by a suitable factor.

Velocity constants for the esterifications and polyesterifications included in this investigation are given in Table III. These have been evaluated, using (3), from the slopes of the straight lines in Figs. 2 and 3.[9] The velocity constants fall into two groups, those for reactions of diethylene glycol and ethylene glycol being lower than those for decamethylene glycol and lauryl alcohol. Between polyesterifications and esterifications within each group there are no important differences in the values of the velocity constants. The lower rates of the esterifications compared with polyesterification (see Fig. 3) are due merely to the diluting effect of the larger proportion of hydrocarbon chain in the esterification reactions which have been studied.

These velocity constants are some ten to twenty times larger than those calculated from Fairclough and Hinshelwood's[10] data for esterification of dilute solutions of various aliphatic acids in ethanol. The energy of activation, 13 kcal., calculated from rates of the diethylene glycol–adipic acid reaction at 166 and at 202°, is slightly less than the value, 15.0 kcal., obtained by these authors for esterifications in ethanol.

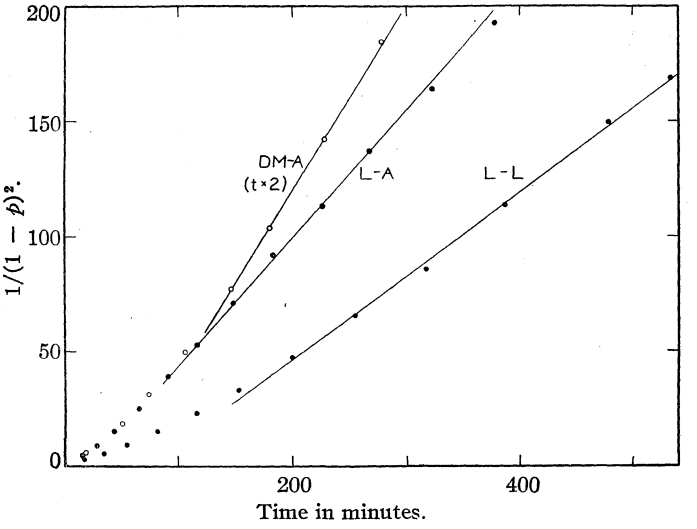


Fig. 3.—Decamethylene glycol–adipic acid (DM-A), lauryl alcohol–adipic acid (L-A), and lauryl alcohol–lauric acid (L-L) reactions at 202°.

TABLE III

VELOCITY CONSTANTS FOR POLYESTERIFICATION AND ESTERIFICATION

Reaction	$k \times 10^{-2}$ at 202° in (equiv./1000 g.)$^{-2}$ min.$^{-1}$
HO—$(CH_2)_2$—O—$(CH_2)_2$—OH + HOOC—$(CH_2)_4$—COOH	0.41
HO—$(CH_2)_2$—O—$(CH_2)_2$—OH + H—$(CH_2)_5$—COOH	0.35
HO—$(CH_2)_2$—OH + HOOC—$(CH_2)_4$—COOH	~0.5
HO—$(CH_2)_{10}$—OH + HOOC—$(CH_2)_4$—COOH	1.63
H—$(CH_2)_{12}$—OH + HOOC—$(CH_2)_4$—COOH	1.57
H—$(CH_2)_{12}$—OH + H—$(CH_2)_{11}$—COOH	2.5

Over the portions of the polyesterifications shown in Figs. 2 and 3 the molecular weight increases about fourteen-fold. In this range the viscosity increased from about 0.015 to 0.30 poise,

(9) The velocity constant for the ethylene glycol–adipic acid reaction could not be determined accurately due to the volatility of this glycol. The experimental data have not been included here.

(10) R. A. Fairclough and C. N. Hinshelwood, *J. Chem. Soc.*, 593 (1939).

in the diethylene glycol–adipic acid reaction. In the esterification reactions the viscosity remains practically constant, at about 0.01 poise, except for a probable slight decrease. The polyesterification reaction is unaffected, therefore, by increase in viscosity, as well as by increase in molecular weight, within the range investigated.

Several experiments on the reaction of diethylene glycol with adipic acid catalyzed by a small amount of *p*-toluenesulfonic acid (0.004 mole per mole of glycol) have been carried out at 109°. These should be second order, according to the results of numerous researches[7] on acid catalyzed esterifications. For a second order reaction, $1/(1 - p)$ increases linearly with time. In striking similarity to the reaction in the absence of added catalyst, the slope of $1/(1 - p)$ plotted against t (see Fig. 4) increases at first, but becomes constant later on. Even as far as DP 90 no tendency of the slope to decrease, as would occur if reactivity decreased as the average molecular weight increases, has been observed. The viscosity increase accompanying this increase in molecular weight is over two thousand-fold.

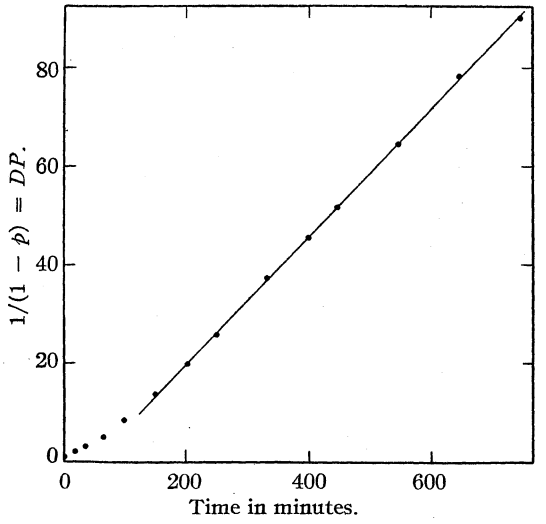


Fig. 4.—Diethylene glycol–adipic acid reaction at 109° catalyzed by 0.4 mole per cent. of *p*-toluenesulfonic acid.

It has been suggested in the past that the rate of polyester formation is governed by the rate at which moisture formed in the reaction escapes from the molten polymer.[11] Recently Schulz[12] has offered a detailed analysis of polyesterification based on the assumption that this is the rate controlling process. In order to test this assumption, diethylene glycol and adipic acid were heated (without catalyst) at 166° under reduced pressure (about 200 mm.), instead of at atmospheric pressure as in other experiments. More efficient removal of moisture resulting from this reduction in pressure should have brought about an increase in the rate of reaction, if the escape of water were the rate determining step. The data obtained in this experiment are given in Table IV.

TABLE IV

REACTION OF DIETHYLENE GLYCOL WITH ADIPIC ACID UNDER REDUCED PRESSURE AT 166°

t in min.	p	t interpolated from expts. at 1 atm.
6.5	0.1535	6
23.5	.3947	23
55	.5927	55
84	.6793	84
135	.7633	137
176	.7983	176

That the reaction velocity is not affected by the reduction in pressure is shown in the table by a comparison of time values with those for the same extent of reaction interpolated from the curve in Fig. 1.[13] The rate must be controlled by factors inherent in the mechanism of the reaction, and not by escape of moisture as Schulz has assumed.

Obviously it is necessary to provide adequate means for escape of water formed in the reaction; otherwise the occurrence of the reverse reaction, hydrolysis, would set up an equilibrium and further polymerization would cease. According to the usual practice, which was followed essentially here, a stream of gas bubbled through the polyester is used to provide for escape of water. Only a very gentle gas stream is required to maintain the normal rate, which cannot be exceeded by increasing the rate of bubbling.

The slow rate of advancement of polyesterification when the average molecular weight becomes large, sometimes attributed in the past to a low reactivity of large molecules or to the difficulty of removing moisture, is a consequence of the kinetic order (third) of the reaction. The rate, being proportional to the third power of the concentration of unreacted functional groups, decreases rapidly as the extent of reaction increases.

(11) See, for example, W. H. Carothers, *Chem. Rev.*, **8**, 367 (1931).
(12) G. V. Schulz, *Z. physik. Chem.*, **A182**, 127 (1938).

(13) The experiment at reduced pressure from which the data in Table IV were taken was not extended to large extents of reaction. The excessive loss of glycol under these conditions might have vitiated results at larger extents of reaction.

Although initially the reaction is rapid, a very long time is required for close approach to complete reaction, which is essential for attainment of high molecular weight.

Discussion

The failure of the reaction to adhere to the third order equation (3) during the first stages of the reaction is difficult to explain. A part of this deviation can be attributed to the decrease in volume due to loss of water (*i. e.*, to the error arising from the use of (3) rather than (2)). This will not account for the entire deviation, however.

Inasmuch as esterification is catalyzed by hydrogen ions (or hydrogen donors, *i. e.*, acids), it probably is sensitive to the nature of the reaction medium. For example, the change in dielectric constant which occurs as hydroxyl and carboxyl groups are converted to ester may influence the reaction rate. In dilute solutions, which have been used almost exclusively in previous work on esterification, the change in properties of the reaction medium as the esterification progresses is inappreciable. If the process is sensitive to changes in the reaction medium, then in the present experiments deviation from third order may be expected, except at large extents of reaction where one is dealing with a dilute solution of functional groups.

The above discussion has been presented merely as a possible explanation for the peculiar course of the reaction. Whatever the cause of this behavior may be, it is typical of both polyesterification and esterification. The fact of primary importance to this investigation is their similarity, in spite of the high molecular weight and viscosity attained in the former.

Bawn[2,14] has attempted to show, on the basis of the transition state method developed by Eyring[15] for the treatment of reaction velocity from a statistical mechanical point of view, that reactivity should decrease continually as size of the molecule increases. According to the transition state method[15]

$$k = K^* (k'T/h) \qquad (4)$$

where k is the velocity constant, k' is Boltzmann's constant, T is the absolute temperature, h is Planck's constant and K^* is the constant for the equilibrium between normal molecules and activated complexes.

$$K^* = (F_{ab}^*/F_aF_b) \exp(-E_0/k'T) \qquad (5)$$

where (F_{ab}^*/F_aF_b) is the ratio of the partition function for the activated complex to the product of the partition functions for the reactants, and E_0 is the activation energy at the absolute zero. Evans and Polanyi[16] have shown that the partition function factor F_{ab}^*/F_aF_b must be smaller for the recombination of radicals (*e. g.*, CH_3) than for the recombination of atoms (*e. g.*, H). Bawn considers that this decrease in "steric factor" will continue indefinitely as the complexity of the molecule increases. Thus, in the vinyl type of polymerizations, in which a polymer molecule bearing a free radical adds on monomers consecutively, he concludes that the rate should decrease with each successive addition of monomer, the rate finally approaching zero when the polymer molecule becomes very large.

An increase in complexity of one of the reacting molecules modifies both F_{ab}^* and the product F_aF_b. Unless the increase in complexity involves modification at a point in the molecule very close to the functional group, both F_{ab}^* and F_aF_b will be altered by virtually identical factors for the added degrees of freedom. The structure in the immediate vicinity of the functional group of a polymer molecule is independent of its degree of polymerization. Hence, contrary to Bawn's conclusion, no decrease in rate of polymerization due to a decrease in the partition function factor with increasing length of the molecule should be expected.

Rabinowitch and Wood[6] have shown convincingly that the actual collision rate in the liquid phase is not affected appreciably by changes in viscosity, although the rate of diffusion is materially decreased. Even if the frequency of collision is decreased by low mobility of large polymer molecules, the duration of collisions must be proportionately increased. Hence, the concentration of molecules in the collided state cannot be affected by either molecular size or viscosity. Consequently, the rate of reaction should be independent of these factors.

The same conclusion follows directly from the transition state method, since the activated complex is in thermodynamic equilibrium with the reactants; the concentration of activated complexes will not be affected by changes in mobility, unless the mobility is too low to maintain their equilibrium concentration.

(14) See also reference 3.

(15) H. Eyring, *J. Chem. Phys.*, **3**, 107, 492 (1935).

(16) M. G. Evans and M. Polanyi, *Trans. Faraday Soc.*, **31**, 875 (1935). See also C. E. H. Bawn, *ibid.*, **31**, 1536 (1935).

Rabinowitch and Wood[6,17] have pointed out that at sufficiently high viscosities the rate of diffusion will become too slow to maintain the "equilibrium" number of pairs of reactants adjacent to each other in the liquid (*i. e.*, within colliding distance of each other). Diffusion, rather than the passage of molecules through the activated state, becomes the rate controlling step when such viscosities are reached, and the rate will no longer be independent of molecular size and viscosity. For most reactions (those with very low values of E_0 excepted) extremely high viscosities would be required to effect a perceptible decrease in rate.

Some time ago the author published equations[18] for calculating the numbers of molecules of various sizes in a linear condensation polymer. The validity of these equations rested entirely on the postulate, presented at that time without experimental proof, that the functional groups of all molecules, regardless of size, are equally reactive. Dostal[19] objected to the size distribution equations on the grounds that this postulate could not possibly be valid. The present investigation furnishes proof that this postulate is correct. The quantities of molecules of various sizes in a linear condensation polymer can be determined reliably, therefore, by simple calculation using the distribution equations referred to above.

(17) See also E. Rabinowitch, *Trans. Faraday Soc.*, **33**, 1225 (1937).

(18) P. J. Flory, THIS JOURNAL, **58**, 1877 (1936).

(19) H. Dostal, *Monatsh.*, **70**, 324 (1937).

Summary

1. The kinetics of two polyesterifications, diethylene glycol–adipic acid, and decamethylene glycol–adipic acid, have been compared with several non-polymer forming esterifications, diethylene glycol–caproic acid, lauryl alcohol–adipic acid, and lauryl alcohol–lauric acid. Preliminary experimental data on the reaction of diethylene glycol with adipic acid catalyzed by *p*-toluenesulfonic acid have been presented also.

2. As the reactions proceed (in the absence of catalyst) the course followed corresponds to a continuous increase in kinetic order, becoming approximately third order at large extents of reaction.

3. Polyesterification and esterification follow similar courses, from which it has been concluded that reaction rate is not affected by either increase in molecular weight or the concurrent increase in viscosity.

4. This conclusion has been shown to be in agreement with theory, contrary to previous theoretical deductions.

5. The slow rate of polyesterification when the average molecular weight is large is due to the third order character of esterification.

CINCINNATI, OHIO RECEIVED SEPTEMBER 30, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE CITY COLLEGE OF THE COLLEGE OF THE CITY OF NEW YORK]

Acetometallates. II. Acetozincate

BY ALEXANDER LEHRMAN AND PHILIP SKELL

It has been shown[2a] that the solubility of metal hydroxides in aqueous solutions of alkali metal hydroxides can best be explained as the formation of hydroxyl complex ions. $M(OH)_2$, for example, may dissolve to give $M(OH)_4^{=}$. In the case of zinc, Goudriaan[1] isolated as a solid phase the compound $Na_2O{\cdot}ZnO{\cdot}4H_2O$ which was formerly thought to be $Na_2ZnO_2{\cdot}4H_2O$, but which according to the complex ion hypothesis could also be written as $Na_2Zn(OH)_4{\cdot}2H_2O$. More recently, Scholder and co-workers[2] have isolated a monoand a disodium zincate in both the anhydrous and hydrated condition. On the basis of the ease of removal of water from these compounds it was concluded by Scholder that they were $NaZn(OH)_3$ and $Na_2Zn(OH)_4$, respectively, and their hydrates, rather than the various hydrates of $NaHZnO_2$ and Na_2ZnO_2. Subsequently Brintzinger and Wallach[3] showed from the rate of diffusion of zincate ions through a cellophane membrane that their ionic weight is consistent with the formula $Zn_2(OH)_8^{==}$. More light could be thrown on the question if the system $NaOH–Zn(OH)_2$ could be shown to be a simple binary system with com-

(1) Goudriaan, *Rec. trav. chim.*, **39**, 505 (1920).

(2) (a) R. Scholder, *Z. angew. Chem.*, **46**, 509 (1933); (b) R. Scholder and H. Weber, *Z. anorg. allgem. Chem.*, **215**, 355 (1933); (c) R. Scholder and G. Hendrich, *ibid.*, **241**, 76 (1939).

(3) H. Brintzinger and J. Wallach, *Z. angew. Chem.*, **47**, 61 (1934).

pound formation. Such an investigation has not been carried out because zinc hydroxide readily decomposes to the oxide on heating.

For further elucidation it was necessary to resort to the results obtained in analogous systems where the possibility of a phenomenon similar to dehydration is not present. Davidson and co-workers[4] have demonstrated a very close similarity between the water and the acetic acid systems. Davidson and McAllister[4c,d] have carried this analogy into the field of amphoterism. Whereas Goudriaan and Scholder have shown the existence of two solvated compounds of zinc hydroxide and sodium hydroxide in which the ratios of $Zn(OH)_2$ to NaOH were 1:1 and 1:2, Davidson and McAllister were able to obtain from glacial acetic acid solution a solvated compound in which the ratio of zinc acetate to sodium acetate was 1:2, namely, $Na_2Zn(C_2H_3O_2)_4 \cdot 4HC_2H_3O_2$ which has been named sodium acetozincate solvate. Unlike zinc hydroxide the analogous zinc acetate cannot undergo "dehydration" reaction but instead undergoes pyrolytic decompositions on continued heating of the melt. It was thus found feasible to determine the liquidus curve of the unsolvated system zinc acetate–sodium acetate and in this way cast some light on the analogous zinc hydroxide–sodium hydroxide system.

Experimental

Materials.—Zinc acetate and sodium acetate were recrystallized from dilute acetic acid and then dehydrated by the methods of Davidson and McAllister.[4c]

Apparatus.—The temperature measuring device was a single copper–constantan thermocouple and potentiometer. A description of the wire, apparatus, and standardization appear in the literature.[5]

The bath was about 300 ml. of the eutectic mixture of lithium, potassium and calcium nitrates contained in a wide-mouthed Pyrex Erlenmeyer flask.[6]

Method.—The salts were weighed (to the nearest centigram) into 2.5 × 20 cm. Pyrex tubes, the zinc acetate being placed below the sodium acetate. The total weight of each sample was 12 g. The tube was placed in the bath whose temperature was controlled by inserting a thermometer enclosed in a Pyrex shield. The salts were stirred with the thin Pyrex tube containing the thermocouple.

To prevent pyrolytic decomposition of the zinc acetate, five drops of glacial acetic acid were added when the salts were partially melted. All except very small quantities of the acid distilled out of the mixtures since the temperatures of the mixtures were usually raised to about 250°. This small amount of acetic acid enabled us to obtain and maintain a clear melt for a time sufficient to determine the melting point. If this aid is omitted it is almost impossible to get clear melts and maintain them so during the determination of the melting point.

After the mixtures had been melted the temperature of the bath was lowered and the mixtures stirred constantly. Considerable supercooling usually preceded initial crystallization. It was necessary to determine the temperature of disappearance of the last crystal as the mixture was heated. The bath was heated slowly until a large part of the crystals had dissolved and then very slowly to obtain the melting point. The disappearance of the last crystal was observed easily by placing the source of a sharp beam of light behind the bath so that the beam passed through the melt before reaching the eye. The temperature was noted when a clear sharp image of the light source could be seen through the melt. This obviated the possibility of too low a reading because of the presence of very fine crystals. This method was found to be very convenient and to give consistent and reproducible values.

All melting points recorded are the result of at least three determinations coming within a range of one degree.

Results and Discussion

Temperatures of the disappearance of the last crystal are given in the table and plotted in Fig. 1.

TABLE I

THE SYSTEM ZINC ACETATE–SODIUM ACETATE

Compn., mole fraction of zinc acetate	M. p., °C.	Eutectic temp., °C.
0.000	328.3	
.101	313.4	
.200	277.5	
.226	261.4	
.265	233.2	218.0
.280	223.3	220.0
.300	225.7	
.333	227.2	
.333	227.1	
.333	227.1	
.350	226.4	
.400	220.2	
.460	203.9	
.480	198.0	
.490	194.6	
.500	192.5	
.510	189.1	
.520	183.0	178.6
.550	180.9	175.3
.600	197.8	
.667	212.5	
.700	221.8	
.800	236.5	
1.000	242.4	

The eutectic between the sodium acetate and compound regions was found by means of time–temperature cooling curves on mixtures up to

(4) (a) A. W. Davidson, THIS JOURNAL, **50**, 1890 (1928); (b) A. W. Davidson and W. McAllister, *ibid.*, **52**, 507 (1930); (c) A. W. Davidson and W. McAllister, *ibid.*, **52**, 519 (1930); (d) A. W. Davidson and E. Griswold, *ibid.*, **57**, 423 (1935).

(5) (a) Lehrman, Selditch and Skell, THIS JOURNAL, **58**, 1612 (1936); (b) Lehrman and Leifer, *ibid.*, **60**, 142 (1938).

(6) Lehrman, *et al.*, *ibid.*, **59**, 179 (1937).

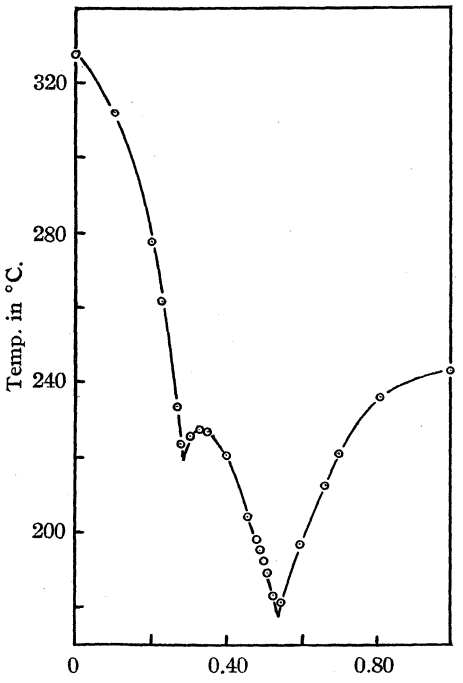


Fig. 1.—Mole fraction of $Zn(C_2H_3O_2)_2$.

0.26 mole fraction zinc acetate to lie between 218 and 220°.

At temperatures below 210° the melts were extremely viscous so that great difficulty was experienced in obtaining crystallization and reproducible melting points. If cooling was rapid stable glasses resulted.

An attempt was made to obtain evidence for the existence of the compound 1 sodium acetate: 1 zinc acetate (0.5 mole fraction of zinc acetate). A number of melting point determinations were made in this region. These freezing points alone, however, did not disprove the existence of this compound, for a slight rise in the curve to a maximum at 50 mole per cent. would not have been detected. However, the point of incipient melting seen on a mixture of 0.49 mole fraction of zinc acetate was 183°. This is wholly inconsistent with the supposition that a maximum in the curve exists at 0.5 mole fraction of zinc acetate. Further, the mixture of mole fraction 0.500 did not behave like a pure compound in that it did not solidify at anything that might reasonably be considered a constant temperature. We found no evidence for the existence of a one to one compound. An attempt was made to check this conclusion by optical and X-ray examination of the mixtures. Neither proved feasible.

The curve definitely points to the existence of the compound $2NaC_2H_3O_2 \cdot ZnC_2H_3O_2$ or $Na_2Zn(C_2H_3O_2)_4$—sodium acetozincate in the unsolvated system. This suggests the existence of the analogous sodium zincate as $Na_2Zn(OH)_4$.

Summary

1. The liquidus curve of the binary system zinc acetate–sodium acetate has been determined.

2. The compound $2NaC_2H_3O_2 \cdot Zn(C_2H_3O_2)_2$ or $Na_2Zn(C_2H_3O_2)_4$ was shown to exist.

3. The analogy between this compound and the hydroxyl zincates was discussed.

NEW YORK, N. Y. RECEIVED SEPTEMBER 9, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF SAN FRANCISCO]

Hydrolysis of Stannous Ion in Stannous Perchlorate Solutions

BY MEL GORMAN

The hydrolysis of stannous ion in stannous perchlorate solutions containing free perchloric acid has been investigated by adding sodium hydroxide solution and measuring the *p*H during the titration with a hydrogen electrode.[1] The purpose of the present investigation is to determine the extent of hydrolysis of stannous ion by a method involving the potentiometric measurement of the mean ion activity of total free perchloric acid and an analysis of total stannous ion concentration.

Method and Apparatus

The stannous perchlorate solutions containing free perchloric acid were prepared by the method of Noyes and Toabe,[2] and the concentration of free acid was determined by their method. A fresh stannous perchlorate solution was prepared for each experiment and stored in contact with metallic tin under nitrogen for at least one day before being used. The concentration of total stannous ion was obtained by titration in an atmosphere of nitrogen with 0.1 *N* iodine using starch indicator.

The mean activity of the hydrogen and perchlorate ions in the solutions of stannous perchlorate and perchloric acid was obtained with the aid of a hydrogen electrode and a

(1) Prytz, *Z. anorg. allgem. Chem.*, **174**, 355 (1928).

(2) Noyes and Toabe, THIS JOURNAL, **39**, 1539 (1917).

normal calomel electrode using cells of the following type

Pt, H_2, $Sn(ClO_4)_2$, $HClO_4$ | saturated NH_4NO_3 | KCl (1 *N*), Hg_2Cl_2, Hg (1)

at 25.0°. The commercial hydrogen used was passed through alkaline pyrogallate solution and then through water at 25° before passing into the stannous perchlorate solution. The partial pressure of the hydrogen was obtained by subtracting the vapor pressure of water from the barometric pressure. The platinum electrodes were strips of approximately one square centimeter. They were cleaned and freshly platinized for each experiment.

The constancy of the reference electrode was checked from time to time during the investigation by connecting it through a bridge of saturated potassium chloride to a solution of 0.05 *M* potassium acid phthalate into which dipped a hydrogen electrode, and noting the electromotive forced developed. The observed and calculated voltages agreed to within 0.5 millivolt.[3]

Experimental Results and Calculations

The calculation of the composition of each solution based on the equation

$$Sn^{++} + H_2O \longrightarrow SnOH^+ + H^+ \qquad (1)$$

was performed as follows. The activity of the total perchloric acid was computed from the voltage of the cell. The activity of the total hydrogen ion was assumed equal to the mean ion activity of the total perchloric acid, and in turn the activity of the total hydrogen ion was assumed equal to its concentration. The concentration of free acid subtracted from the concentration of total hydrogen ion gives the concentration of $SnOH^+$ and of hydrogen ion due to hydrolysis. By subtraction of $SnOH^+$ from total stannous ion the concentration of unhydrolyzed stannous ion can be found. The values of the equilibrium quotient, K_1, were computed from the relation

$$K_1 = c_{SnOH^+} a_{H^+} / c_{Sn^{++}} \qquad (1)$$

in which c is concentration in moles per liter and a is activity. The experimental results and values of K_1 are listed in Table I. μ is the ionic strength.

In Fig. 1, curve I represents log K_1 against $\mu^{1/2}$. The shape of the curve demonstrates that the equilibrium quotient is varying with ionic strength in accord with the theory of Debye and Hückel. However, extrapolation of this curve to zero ionic strength does not give the true equilibrium constant for the reaction because of

(3) When the saturated potassium chloride bridge was replaced by a bridge of saturated ammonium nitrate the electromotive force was five millivolts lower. An attempt to use this difference as a correction factor to the observed voltages of cells of type (1) in calculating the mean ion activity of perchloric acid was unsuccessful.

TABLE I

E. m. f. H_2 = 1 atm.	Total H^+ activity	Free $HClO_4$ moles/l.	Total Sn^{++} moles/l.	$\mu^{1/2}$	$K_1 \times 10^2$
0.3199	0.2520	0.2390	0.0935	0.71	4.06
.3363	.1330	.1173	.1189	.68	2.02
.3341	.1450	.1356	.0939	.64	1.61
.3323	.1552	.1520	.0565	.56	0.92
.3674	.0403	.0342	.0449	.42	.63
.3671	.0404	.0346	.0455	.42	.59
.3817	.0227	.0151	.0389	.35	.55
.3914	.0157	.0109	.0184	.24	.56
.3955	.0132	.0104	.00936	.18	.56
.4009	.0108	.00846	.00672	.16	.59
.4078	.00822	.00651	.00396	.12	.62

the uncertainty introduced by the assumption that the activity of total hydrogen ion equals the concentration of total hydrogen ion in making the calculation for $SnOH^+$ by difference between total acid and acid from hydrolysis. Actually this difference term is the subtraction of a concentration from an activity and hence the result is neither of these quantities. In order to obtain the actual concentration of $SnOH^+$ the hydrogen ion concentration must be known. By retaining

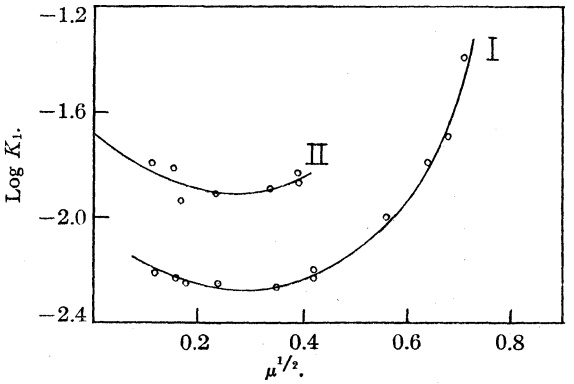


Fig. 1.—Plot of log K_1 against square root of ionic strength.

the assumption that the mean ion activity of the perchloric acid is equal to the activity of the hydrogen ion, the concentration of the latter can be obtained by dividing its activity by its activity coefficient. The activity coefficient of hydrogen ion in a solution of given ionic strength can be calculated from the values of the mean ion activity of perchloric acid and of sodium perchlorate at the stated ionic strength, if in the latter we consider that the activity coefficients of the sodium ion and perchlorate ion are equal.[4]

(4) The activity coefficients of perchloric acid and sodium perchlorate were obtained from Landolt-Börnstein, "Physikalisch-chemische Tabellen," Erg. III, pp. 2144 and 2153 (1936), respectively.

In the range of concentration up to an ionic strength of 0.2 the sodium ion and perchlorate ion activity coefficients are no doubt equal to within two or three per cent. Therefore the activity coefficients of hydrogen ion were computed and used in conjunction with the hydrogen ion activities in solutions of this investigation up to an ionic strength of 0.2 in the calculation of the concentrations of total hydrogen ion. With the aid of these latter values corrected concentrations of $SnOH^+$ and stannous ion were calculated. Using these figures new equilibrium quotients were calculated according to equation 1 and their logarithms plotted against $\mu^{1/2}$ as in Fig. 1, Curve II. The extrapolation to zero ionic strength was accomplished by the method of Randall and Vietti,[5] and the value of the equilibrium constant, K_1^0, is estimated to be 0.02.

According to Prytz[1] the hydrolysis of stannous ion is represented by the equation

$$2Sn^{++} + H_2O = Sn_2O^{++} + 2H^+ \qquad (2a)$$

or

$$2Sn^{++} + 2H_2O = Sn_2O_2H_2^{++} + 2H^+ \qquad (2b)$$

The analytical data of Table I were used to calculate the composition of each stannous perchlorate solution and the equilibrium quotients based on equation 2. The logarithms of these equilibrium quotients when plotted against $\mu^{1/2}$ give a U-shaped curve which does not permit extrapolation to zero ionic strength according to the limiting law of Debye and Hückel. Since Randall and Vietti have shown that in such a plot the curve will resemble one of the family of logarithm of activity coefficient *vs.* $\mu^{1/2}$ for single electrolytes, it is obvious that equation 1, and not equation 2, represents the hydrolysis of stannous ion.

(5) (a) Randall and Vietti, THIS JOURNAL, **50**, 1526 (1928); (b) Randall, *J. Chem. Ed.*, **8**, 1062 (1931); (c) see also Bray and Hershey, THIS JOURNAL, **56**, 1889 (1934).

Summary

Solutions of stannous perchlorate containing free perchloric acid have been analyzed. The variation of the equilibrium quotient, K_1, with ionic strength proves that the hydrolysis follows the equation $Sn^{++} + H_2O = SnOH^+ + H^+$. The value of the equilibrium constant, K_1^0, at 25° is 0.02.

SAN FRANCISCO, CALIF. RECEIVED SEPTEMBER 25, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE INSTITUTE OF TECHNOLOGY, UNIVERSITY OF MINNESOTA]

A Study of Diffusion Processes by Electrolysis with Microelectrodes[1]

BY H. A. LAITINEN AND I. M. KOLTHOFF

Introduction

The diffusion of an electro oxidizable or reducible substance in solution can be studied by measuring the current obtained using suitable electrodes in an electrolysis cell if the supply of electro reducible or oxidizable material is determined only by the rate of diffusion of the material to one of the electrodes, and if well-defined boundary conditions of concentration can be maintained at the electrode surface. The latter condition is fulfilled if the concentration of diffusing material is maintained at a value of practically zero at the electrode surface by maintaining a potential at the electrode such that the diffusing material is immediately oxidized or reduced upon reaching the electrode surface.

The theory of the diffusion process in the vicinity of an electrode depends upon the geometric characteristics of the electrode and surrounding solution. Two extreme geometric cases are represented by a flat electrode, to which diffusion can occur from only one direction (linear diffusion), and a spherical electrode, to which diffusion can occur from all directions (spherically symmetrical diffusion). The equations for the current as a function of time, for linear and spherically symmetrical diffusion, are given below, as well as experimental results on the determination of current–time curves with microelectrodes of various types to determine the conditions under which theoretical diffusion conditions in electrolysis can be fulfilled.

The theoretical relation between current and time for linear diffusion has been derived by Cottrell[2] and MacGillavry and Rideal[3] and is

$$i = -A\sqrt{\frac{D}{\pi t}}\,nFC \qquad (1)$$

(1) This paper is based on a thesis to be submitted by H. A. Laitinen to the Graduate Faculty of the University of Minnesota in partial fulfilment of the requirements for the degree of Doctor of Philosophy, June, 1940.

(2) F. G. Cottrell, *Z. physik. Chem.*, **42**, 385 (1902).

(3) D. MacGillavry and E. K. Rideal, *Rec. trav. chim.*, **56**, 1013 (1937).

where A is the area of the electrode, D and C are the diffusion coefficient and concentration of the diffusing material in the bulk of the solution, respectively, n is the number of electrons involved in the electrode reaction, and F is the faraday.

It is seen that in a given case, $i\sqrt{t}$ is a constant, and that the value of this constant can be calculated if the concentration C, and the diffusion coefficient of the electroactive substance, and the area of the electrode are known.

The corresponding theoretical current–time equation for spherical diffusion is[2]

$$i = -4\pi RnFDC - A\sqrt{\frac{D}{\pi t}}nFC \qquad (2)$$

where R is the radius of the spherical electrode. By comparing equations (1) and (2) it is apparent that for spherical and linear diffusion to electrodes of equal area, the theoretical currents at any time differ by a constant amount, namely, the steady state current with spherical diffusion given by the first term of equation (2).

Experimental

Platinum microelectrodes of various shapes as shown in Fig. 1 were constructed. The various flat electrodes, types A, C, D, F and G, were of very nearly equal area. Electrodes A, C and D permit only linear diffusion in horizontal, upward and downward directions, respectively, while electrodes B, E, F and G approach spherical diffusion to varying degrees of approximation. The linear diffusion electrodes were specially constructed to be as uniform as possible in cross-section by finely grinding the ends of two pieces of glass tubing and cementing a platinum plate between the two pieces of tubing with de Khotinsky cement using a larger piece of glass tubing as a mold. The details of construction are shown in Fig. 1, H. Electrode E most closely approached spherical diffusion, and consisted of a spherical ball of platinum of approximately the same area as the flat electrodes, on the end of a fine platinum wire coated with sealing wax, so that only the spherical surface acted as an electrode. Electrode B consisted of a platinum wire about 4 mm. in length and 0.5 mm. in diameter.

In general, the experiments were run by applying a constant potential to the microelectrode, this potential corresponding to a point near the middle of the diffusion current region of the electrolysis process as determined from a current–voltage curve obtained with the platinum wire microelectrode (type B, Fig. 1). At such a potential, the diffusing material undergoes an immediate electrode reaction upon reaching the electrode, so that its concentration is maintained at a value practically equal to zero at the electrode surface. A large silver–silver chloride electrode in 0.1 N potassium chloride was used as the second electrode. The electrolysis cell was of the type previously described,[4] employing a sintered glass diaphragm to separate the two electrodes. Hereafter, all potentials of the platinum micro-electrodes are referred to the 0.1 N silver–silver chloride electrode.

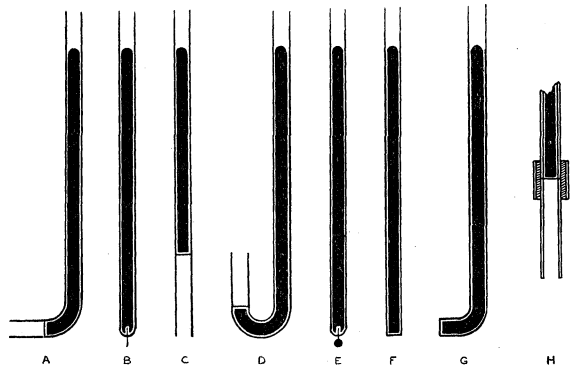


Fig. 1.—Various shapes of platinum electrodes.

The current was measured at various time intervals after beginning electrolysis by noting the deflection of a calibrated wall-type galvanometer in series with the electrolysis cell, and provided with a suitable shunt arrangement to change the galvanometer sensitivity during each run. The electrical circuit was the same as that described by Lingane and Kolthoff[5] except that the standard 10,000-ohm resistance used to calibrate the galvanometer was not left in series with the galvanometer and cell during the experiments, in order that the changing iR drop across this resistance during the experiments would not change the applied e. m. f. across the terminals of the cell. The small change in iR across the galvanometer itself, resulting in a slight shift of the potential of the micro electrode during an experiment, did not affect the current measurement since the same current was obtained over a range of potentials corresponding to the diffusion current region of the electrolysis process.

In the case of electroreductions, dissolved air was removed by bubbling nitrogen through the solution for about thirty minutes. In the case of electro-oxidations, it was found to be unnecessary to remove the dissolved oxygen because no reduction of oxygen occurred at the positive potential used.

The residual current in the absence of electroactive material was determined separately for each value of the time and was subtracted from the measured current. The current thus corrected was used in the calculation of $i\sqrt{t}$.

All measurements were made with the electrolysis cell in a water thermostat regulated to $\pm 0.02°$, with the stirrer mounted on wall brackets so that mechanical vibrations were eliminated.

The Oxidation of Ferrocyanide Ions.—A solution 1.00×10^{-3} M in potassium ferrocyanide and 0.1 N in potassium chloride was electrolyzed at 25°, applying a constant potential of +0.700 volt, and measuring the current at various times after beginning electrolysis. The current–time curves obtained with electrodes A, B, C, E, F and G (Fig. 1) are shown plotted in Fig. 2, together

(4) J. J. Lingane and H. A. Laitinen, *Ind. Eng. Chem., Anal. Ed.*, **11**, 504 (1939).

(5) J. J. Lingane and I. M. Kolthoff, THIS JOURNAL, **61**, 825 (1939).

with the theoretical curves for linear and spherical diffusion calculated from equations (1) and (2). The areas of the various flat electrodes were all equal to 0.0707 sq. cm. The diffusion coefficient D was calculated using the equation given by Lingane and Kolthoff,[5] and found to be equal to 0.74×10^{-5} cm.^{2} sec.$^{-1}$. Introducing the values of D and C in equations (1) and (2) yields the theoretical equations

$$i\sqrt{t} = 10.4 \quad \text{(linear diffusion)} \qquad (3)$$

$$i = 0.674 + 10.4t^{-1/2} \quad \text{(spherical diffusion)} \qquad (4)$$

where the current is expressed in microamperes and the time in seconds.

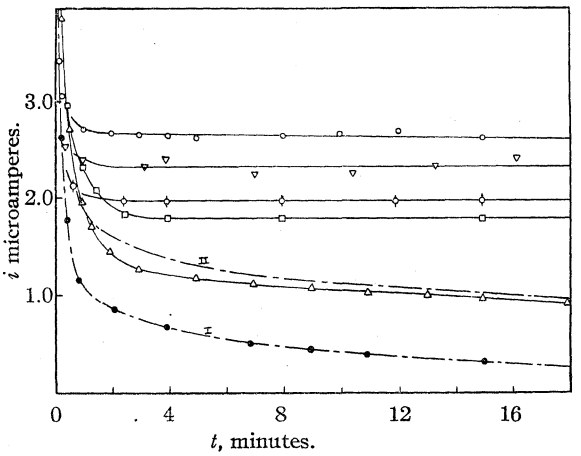


Fig. 2.—Current–time curves for electrolysis of 0.001 M $K_4Fe(CN)_6$ in 0.1 N KCl with various shapes of platinum microelectrodes: ●, electrode C; △, electrode A; □, electrode F; ◌, electrode B; ▽, electrode E; ○, electrode G. Dashed curves: theoretical curves for (I) linear diffusion, (II) spherically symmetrical diffusion.

From Fig. 2 it is evident that the theoretical results are obtained in this case only when the diffusion is linear and in an upward direction. With downward linear diffusion (electrode D) abnormally large currents were obtained which did not give a smooth current–time curve and were therefore not included in Fig. 2. After six to seven minutes, the current was about twice as large as calculated from equation (4), and after this length of time the current fluctuated irregularly, even increasing periodically.

Curve I, Fig. 2, which yielded results in close agreement with theory, was repeated several times using larger concentrations of potassium ferrocyanide so that better accuracy in current readings could be obtained. A typical set of data is given in Table I for the oxidation of 4.88×10^{-3} M potassium ferrocyanide in 0.1 N potassium chloride. The electrode area in this case was 0.1016 sq. cm., and the theoretical equation was $i\sqrt{t} = 73.4$ microamp. sec.$^{1/2}$. The average value of $i\sqrt{t}$ from the 26 points in Table I is 72.3 microamp. sec.$^{1/2}$, in excellent agreement with the theoretical value. Duplicate experiments gave results deviating only ±0.5 to ±1.0% in the value of $i\sqrt{t}$.

TABLE I

VARIATION OF CURRENT WITH TIME IN THE ELECTROLYSIS OF 0.00488 M POTASSIUM FERROCYANIDE IN 0.1 N POTASSIUM CHLORIDE

Solution saturated with air; E_{Pt} = +0.700 volt *vs.* 0.1 N AgCl; temp., 25°; area of electrode, 0.1016 sq. cm.

t, sec.	i μ amp.	i(corr.) μ amp.	$i\sqrt{t}$ μ amp. sec.$^{1/2}$	t, sec.	i μ amp.	i(corr.) μ amp.	$i\sqrt{t}$ μ amp. sec.$^{1/2}$
110	6.90	6.85	71.8	540	3.125	3.107	72.2
120	6.62	6.57	71.9	600	2.975	2.958	72.4
150	5.92	5.88	71.7	630	2.895	2.878	72.7
180	5.41	5.37	72.1	660	2.830	2.814	72.3
210	5.02	4.99	72.3	720	2.715	2.099	72.4
240	4.70	4.67	72.3	780	2.605	2.590	72.3
270	4.40	4.37	71.8	840	2.515	2.500	72.5
300	4.19	4.16	72.1	900	2.433	2.419	72.6
330	4.00	3.98	72.3	960	2.355	2.342	72.6
360	3.82	3.80	72.1	1020	2.285	2.272	72.6
390	3.685	3.663	72.3	1080	2.215	2.203	72.4
420	3.540	3.519	72.1	1140	2.160	2.148	72.5
480	3.325	3.306	72.4	1200	2.102	2.091	72.4

The reason for the deviating results obtained if the diffusion did not proceed in an upward direction becomes apparent when the relative densities of 0.001 M potassium ferrocyanide (the diffusing material) and 0.001 M potassium ferricyanide (the oxidation product near the electrode surface) are considered. Although the difference in density is only of the order of one unit in the fifth decimal place, 0.001 M potassium ferricyanide is less dense than 0.001 M potassium ferrocyanide.[6] Unless the direction of diffusion is such that the less dense solution (either the diffusing material or the electrode reaction product) lies above the denser solution, convection currents due to density gradients cause a greater supply of diffusing material to reach the electrode than by diffusion alone, and consequently the measured current is abnormally large.

A simple experimental check of this explanation was made as follows: a solution of 0.001 M potassium ferrocyanide in 0.1 M potassium chloride and 1% in cane sugar was prepared, thus a solution of the same electrolyte concentrations as the original ferrocyanide solution but somewhat more dense due to the presence of the sugar. A thin layer (1 or 2 mm.) of this solution was carefully placed near the platinum surface of elec-

(6) A. Heydweiller, *Z. anorg. allgem. Chem.*, **116**, 42 (1921).

trode D under the original solution by means of a capillary pipet and allowed to diffuse upward for about an hour, so that a sufficient downward density gradient should exist near the electrode surface to overcome any small density gradient in the opposite direction due to the electrode reaction. A current–time curve was then run and found to be identical with the curve obtained previously using electrode C (upward diffusion). This experiment gave conclusive proof that density gradients in the downward direction are necessary to stabilize concentration gradients and lead to theoretical diffusion conditions.

It is therefore to be expected that the theoretical current–time curve for spherical diffusion could never be obtained in aqueous solution, since, in general, spherically symmetrical concentration gradients result in spherically symmetrical density gradients, and convection currents around the electrode inevitably result. From Fig. 2 it is apparent that with various shapes of platinum electrodes approaching spherically symmetrical diffusion conditions, the current tends to approach a "steady state" value, *i. e.*, becomes practically constant after a few minutes. The steady state current, however, is a function not only of the electrode area, but also of the shape of the electrode, and in the case of the flat electrodes depends also on the position of the electrode with regard to the solution. Thus with two flat plates of platinum sealed on the ends of pieces of glass tubing (electrodes G and G), but arranged vertically and horizontally, respectively, a smaller steady state current was obtained with the surface of the electrode horizontal than with a vertical surface, because the horizontal surface acted to stabilize to a certain extent the concentration gradient of ferrocyanide ions.

In general, the steady state current was found to be least subject to irregular periodic fluctuations in the case of the platinum wire electrode (type B) than in any other case investigated including flat surfaces in various orientations and a spherical platinum surface. Apparently the most uniform and reproducible state of convection is obtained with the platinum wire electrode. Since the current reaches a steady value after two to four minutes and remains very nearly constant for relatively long intervals of time, this electrode has been used by us for determining current–voltage curves similar to those obtained with the dropping mercury electrode.

The Diffusion of Ferrocyanide Ions in Gelatin and Agar Gels.—In order to check the theoretical current–time equation for spherically symmetrical diffusion, experiments were performed by allowing the diffusion process to occur in a stiff gel surrounding the electrode, instead of in less viscous aqueous media in which disturbing convection currents occurred.

The absence of convection currents due to density gradients in the vicinity of the electrode was shown by electrolyzing 0.0200 *M* potassium ferrocyanide in 0.5 *N* potassium chloride in a 3% agar gel and in a 4% gelatin gel using electrodes C and D, in which linear diffusion occurred in upward and downward directions, respectively. Identical current–time curves were obtained with the two electrodes, in contrast to the results obtained in aqueous medium.

From the values of $i\sqrt{t}$ thus obtained, which remained constant to $\pm 0.5\%$ for a period of twenty minutes, the diffusion coefficient of the ferrocyanide ion was calculated to be 0.65×10^{-5} cm.^{2} sec.$^{-1}$ for the 3% agar gel and 0.61×10^{-5} cm.^{2} sec.$^{-1}$ for the 4% gelatin gel, as compared with the value 0.74×10^{-5} cm.^{2} sec.$^{-1}$ for an aqueous solution at infinite dilution.

The theoretical current–time curve for spherical diffusion to electrode E for the electrolysis of 0.0200 *M* potassium ferrocyanide in 0.5 *N* potassium chloride in a 3% agar gel becomes

$$i = 15.45 + 322\, t^{-1/2} \text{ microamperes} \qquad (5)$$

when t is expressed in seconds.

Equation (5) and the experimental curve obtained with electrode E in the 3% agar gel are shown plotted in Fig. 3.

It is evident from Fig. 3 that the theoretical and experimental curves are almost identical in shape from a period of five minutes to 110 minutes, although the experimental points in general lie about 5 to 7% below the corresponding theoretical points. The gelatin gel showed a similar behavior, both curves being lower than for the agar gel because of the lower diffusion coefficient in the gelatin gel.

The low observed current and the increasing percentage deviation with time may be explained by the fact that a truly spherical diffusion field does not exist, due to the presence of the coated platinum wire and glass tube above the spherical electrode. The theoretical diffusion layer extends a distance of several millimeters from the electrode surface after a time of two hours, so that a hindering effect becomes quite possible.

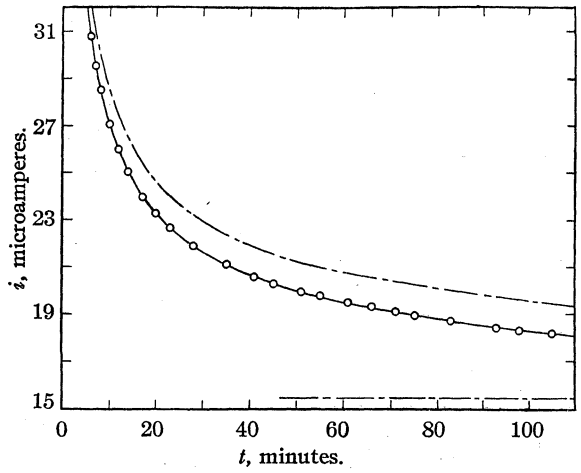


Fig. 3.—Current–time curves for electrolysis of 0.0200 M $K_4Fe(CN)_6$ in 0.5 N KCl in 3% agar gel. Spherical platinum electrode, R = 0.0950 cm. Full curve, experimental; dashed curve, theoretical; lower dashed line, theoretical steady state current.

The Reduction of Ferricyanide Ions.—An air-free solution of 5.01 × 10^{-3} M potassium ferricyanide in 0.1 N potassium chloride was electrolyzed at 25° using electrodes C and D by applying a constant potential of −0.50 volt and determining the current–time curves.

A constant value of $i\sqrt{t}$ was obtained with electrode D (downward diffusion). The experimental value of $i\sqrt{t}$ is compared with the calculated value in Table II.

With electrode C (upward diffusion) abnormally large currents were obtained and irregular fluctuations occurred after about eight minutes of electrolysis.

It is evident that exactly the opposite results (with respect to direction of diffusion) were obtained with the reduction of ferricyanide ions as compared with the oxidation of ferrocyanide ions. Since the electrode reaction is opposite in the two cases, opposite changes in density near the electrode occur, and the results obtained are exactly those predicted on the basis of the direction of the density gradients.

TABLE II

ELECTROLYSIS OF $K_4Fe(CN)_6$, $K_3Fe(CN)_6$ AND $AgNO_3$ IN EXCESS OF INDIFFERENT ELECTROLYTE

Area of electrode 0.1016 cm.², temp. = 25°.

Ion	Concn. mmol./liter	D^0 cm.² sec.$^{-1}$ × 10^{-5}	$i\sqrt{t}$ microamp. sec.$^{1/2}$ Calcd.	Obsd.	Diff., %
$Fe(CN)_6^{----}$	4.88	0.74	73.4	72.3	−1.5
$Fe(CN)_6^{---}$	5.01	.89	82.8	80.4	−2.9
Ag^+	5.00	1.69	113.7	115.4	+1.5

The Deposition of Silver Ions.—Current–time curves were obtained using electrode C in an air-free solution of 5.00 × 10^{-3} M silver nitrate in 0.1 N potassium nitrate at 25°, with an applied potential of −0.10 volt on the microelectrode. The average value of $i\sqrt{t}$ obtained in several such experiments is compared with the calculated value in Table II.

The Temperature Coefficient of the Quantity $i\sqrt{t}$.—For a given linear diffusion electrode and solution, equation (1) may be written in terms of ionic equivalent conductance and temperature[4] to give

$$i\sqrt{t} = k(\lambda^0 T)^{1/2} \qquad (6)$$

where T is the absolute temperature. Differentiating equation (6) with respect to the temperature, we have

$$\frac{d(i\sqrt{t})}{dT} = \frac{k}{2}(\lambda^0 T)^{-1/2}\left(\lambda^0 + T\frac{d\lambda^0}{dT}\right) \qquad (7)$$

Equation (7) may be expressed in terms of the fractional changes of $i\sqrt{t}$ and λ^0 per degree by dividing by the value of $i\sqrt{t}$ at the temperature T, as given by equation (6). The temperature coefficient of $i\sqrt{t}$ becomes

$$\frac{1}{i\sqrt{t}}\frac{d(i\sqrt{t})}{dT} = \frac{1}{2}\left(\frac{1}{T} + \frac{1}{\lambda^0}\frac{d\lambda^0}{dT}\right) \qquad (8)$$

The values of $i\sqrt{t}$ have been measured for temperatures of 25 to 35° for the ferrocyanide, ferricyanide and silver ions. The measured values of the temperature coefficient and the values calculated from equation (8) are given in Table III.

TABLE III

TEMPERATURE COEFFICIENT OF THE QUANTITY $i\sqrt{t}$ IN LINEAR DIFFUSION

Ion	$\frac{1}{\lambda^0}\frac{d\lambda^0}{dT}$ deg.$^{-1}$	$\frac{1}{i\sqrt{t}}\frac{d(i\sqrt{t})}{dT}$ deg.$^{-1}$ Calcd.	Obsd.
$Fe(CN)_6^{----}$	0.0195	0.0114	0.0101
$Fe(CN)_6^{---}$	.0185	.0109	.0118
Ag^+	.0200	.0116	.0116

The calculated and measured values are average temperature coefficients over the temperature range 25 to 35°, expressed in terms of the fraction of the 30° value of $i\sqrt{t}$ and λ^0. For th esilver and ferrocyanide ions, the conductance data of Johnston[7] and Swift[8] were used; for the ferricyanide ion the value of λ^0 of Hartley and Donaldson[9] was used, and the temperature coefficient

(7) J. Johnston, THIS JOURNAL, **31**, 1010 (1909).
(8) E. Swift, Jr., *ibid.*, **60**, 728 (1938).
(9) G. S. Hartley and G. W. Donaldson, *Trans. Faraday Soc.*, **33** 457 (1937).

of λ was calculated from the data of Watkins and Jones[10] on the equivalent conductance of potassium ferricyanide at various temperatures, and the values given by Johnston[7] for the equivalent ionic conductance of the potassium ion at various temperatures.

Discussion

Cottrell[2] has shown in a linear diffusion experiment on zinc sulfate that the quantity $i\sqrt{t}$ remained constant to $\pm 5\%$ for a period of over two days, but made no theoretical calculation of the value of the constant obtained.

It is evident from the data given in Table I that in our experiments the extreme limits of fluctuation in $i\sqrt{t}$ were only $\pm 0.5\%$ from the average value, in 26 readings over a period of twenty minutes. In other experiments a constancy was obtained over a period of several hours, but in general a slight drift toward higher values with very long periods of time was observed, due to unavoidable vibrations.

The data given in Table II show that the observed values for the quantity $i\sqrt{t}$ show a deviation from those calculated from the equivalent ionic conductances at infinite dilution of -1.5, -2.9 and $+1.5\%$ for the ferrocyanide, ferricyanide, and silver ions, respectively. These data are in essential agreement with those of Lingane and Kolthoff[5] on diffusion currents with the dropping mercury electrode.

The observed values of the temperature coefficient of $i\sqrt{t}$ are in good agreement with the calculated values over the same temperature range, as is evident from the data given in Table III. The agreement is probably within the experimental error, since the measurements were made only over a temperature range of ten degrees.

Summary

1. Current–time curves with various shapes of electrodes and diffusion fields in the electro oxidation of ferrocyanide ions were determined, and the condition under which theoretical diffusion conditions can be obtained are discussed. Theoretical conditions were not obtained with spherically symmetrical diffusion in aqueous solution, but were approached in 3% agar and in 4% gelatin gels.

2. With linear diffusion in such a direction as to produce a density gradient in the downward direction, the quantity of $i\sqrt{t}$ was found to be constant to $\pm 0.5\%$ over a period of twenty minutes.

3. The temperature coefficient of the quantity $i\sqrt{t}$ was found to be in agreement with the calculated value.

(10) C. Watkins and H. C. Jones, THIS JOURNAL, **37**, 2626 (1915).

MINNEAPOLIS, MINN. RECEIVED AUGUST 22, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE JOHNS HOPKINS UNIVERSITY]

The Specific Heat of Some Ethylene Halides[1]

BY WILFORD E. RAILING[2]

The problem whether there is free or restricted rotation about the carbon–carbon bond in ethane and its derivatives has led to considerable research upon the 1,2-disubstituted ethanes. Of these, the chloro and bromo derivatives have received the greatest attention. Time–temperature heating curves made by White and Morgan[3] revealed a transition or hump in the specific heat curve in 1,2-dibromoethane at $-23°$. Since the dielectric constant is only minutely affected by the transition, it is likely that the change of state does not affect the polarity of the molecule. Since these transitions are most effectively studied by means of heat capacity measurements, the heat capacities of 1,2-dibromoethane (ethylene bromide), 1,2-dichloroethane (ethylene chloride), and 1,2-bromochloroethane (ethylene chlorobromide) have been determined in the range 90–320°K.

Apparatus and Procedure

The calorimeter employed was the same calibrated conduction calorimeter and the procedure was the same as employed by Stull.[4]

Materials

Benzene.—J. T. Baker C. P. thiophene-free material was distilled through a five-foot (1.5 m.) column packed with glass helices similar to those described by Young and Jasaitis.[5] The middle fraction was then fractionally

(1) Part of a dissertation presented to the Faculty of Philosophy of the Johns Hopkins University in partial fulfilment of the requirements for the degree of Master of Arts.

(2) Present address: E. I. du Pont de Nemours and Co., Box 389, Wilmington, Del.

(3) White and Morgan, *J. Chem. Phys.*, **5**, 655 (1937).

(4) Stull, THIS JOURNAL, **59**, 2729 (1937).

(5) Young and Jasaitis, *ibid.*, **58**, 377 (1936).

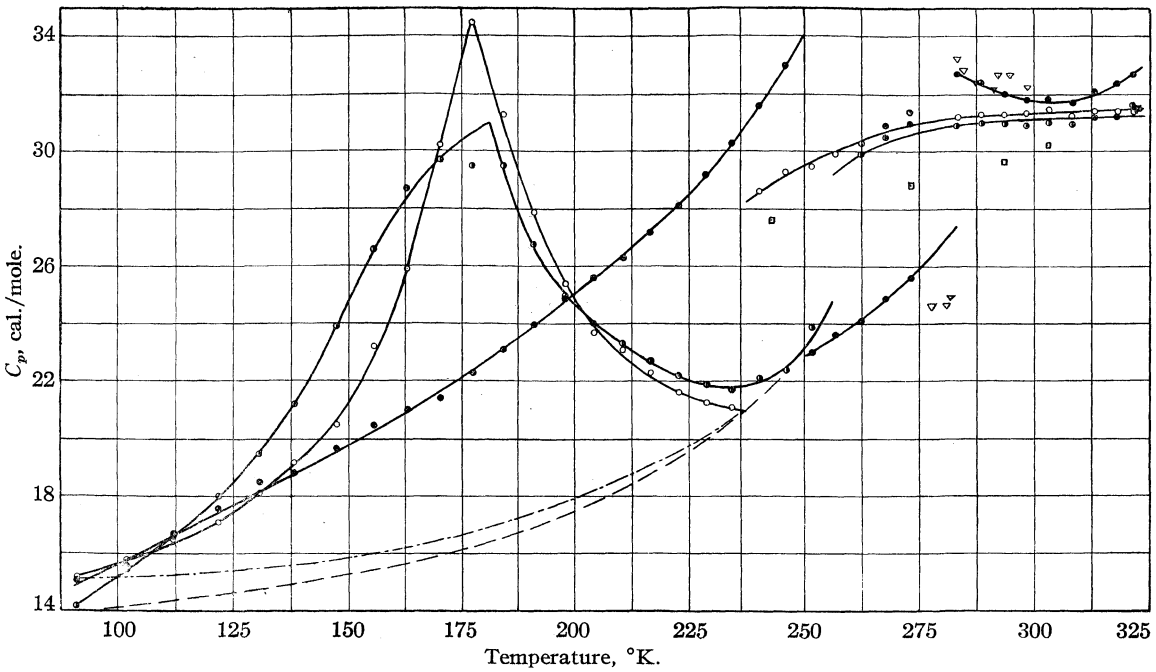


Fig. 1.—Molal heat capacities: ○, 1,2-dichloroethane, mol. wt., 98.97; moles in sample, 0.0358; ●, 1,2-dibromoethane, mol. wt., 187.88; moles in sample, 0.0328; ◐, 1,2-bromochloroethane, mol. wt., 143.42; moles in sample, 0.0343. — - —, extrapolated "Normal" heat capacity for dichloroethane. — —, extrapolated "Normal" heat capacity for bromochloroethane. △, Previously published values for dibromoethane. □, Previously published values for dichloroethane. 0°C. = 273.10°K.; 1 calorie = 4.1850 abs. joules.

crystallized six times, about one-fifth of the material being discarded each time. This was again distilled through the column and a fraction boiling over a 0.02° range was obtained. This material was used in all the calibration runs. The amount of premelting indicated a purity of 99.997 mole per cent.

Ethylene Chloride.—Eastman Kodak Co. material was distilled twice through a five-foot column, a fraction with a boiling range of 0.02° being obtained. This fraction was fractionally crystallized twice and given a final distillation before using; b. p. 83.8°, m. p. −35.5°. The amount of premelting indicated a purity of 99.96 mole per cent.

Ethylene Chlorobromide.—Eastman Kodak Co. material was distilled twice through a 40-cm. Vigreux column, and a 0.2° fraction was obtained. This fraction was recrystallized six times, and given a final distillation before using; m. p. −16.7°. The amount of premelting indicated a purity of 99.8 mole per cent.

Ethylene Bromide.—Eastman Kodak Co. material was given the same treatment that was given the chlorobromide; m. p. 9.93°. The amount of premelting indicated a purity of 99.92 mole per cent.

Experimental Results

The accuracy of averaged determinations obtained with this calorimeter has been placed within 0.75–1.25% of the true values by Stull.[4] It is the author's opinion that a better value for the accuracy would be 1–2%. The heats of fusion are probably accurate to 1% or better, instead of Stull's estimate of 3–4%.

The thermocouples used in this work had been calibrated by Stull,[4] and were used about a year after his research. Comparison of the melting and transition points of several materials with the literature values showed that the calibration had not changed appreciably.

The experimental specific heat values were plotted against the temperature, and a smooth curve drawn through the points. These smooth curves together with the experimental values are sketched in Fig. 1. The values of the experimental points may be read off the figure within the limit of the accuracy (1–2%).

It will be seen that the chlorobromide and chloride exhibit humps of considerable magnitude in the specific heat curve for the solid. To calculate the increase in heat content represented by these humps, the course of the "normal" heat capacity curve was charted as shown by the broken lines in the diagrams. The values of the special increments of heat content estimated in this manner are probably within 10% of the correct values. These values, together with the other transition and heats of fusion data, are presented in Table I,

TABLE I

HEATS OF TRANSITION AND FUSION DATA IN CALORIES PER MOLE AND °C.

	Fusion, This Research	Transition, This Research	Fusion, Demerliac	Fusion, Petersson
1,2-Dichloroethane	2090 at −35.5°	680	....	...
1,2-Dibromochloroethane	2300 at −16.7°	740	....	...
1,2-Dibromoethane	2590 at 9.93°	450 at −22.5°	2540 at 9.55°	2440 at 8.0°

together with the results obtained by other observers. The error in the heat of transition of the bromide is probably less than 2%. The heats of fusion have been corrected for premelting, and represent the heat of fusion for a 100% pure compound. The specific heat values for the solids just below the melting point have also been corrected for premelting.

The previously published data of the specific heats of these compounds[6] disagree somewhat with the values presented here, as can be ascertained from Fig. 1. It should be noted, however, that except for one set (Leblanc and Mobius),[6] the data are from forty to seventy-five years old. The values of Leblanc and Mobius for the bromide agree well with our results in the liquid state, but their values for the solid are about 3% lower than those presented here. No heat capacity data could be found in the literature for ethylene chlorobromide.

The heat of fusion of the bromide is about 2% higher than any previously observed values.[7] This may be due to the fact that a correction for premelting has been included in the data presented here. The melting point of Demerliac's sample (9.55°) is almost 0.4° lower than our value (9.93°). Premelting may have influenced Demerliac's determination. The other reported value,[8] was measured on a sample whose melting point (8°) indicated such an impure material that its heat of fusion is undoubtedly too low. These results will be found in Table I.

Early in this experimental investigation it was found that series of heat capacity determinations made successively on the same sample of ethylene chloride displayed systematic disagreements which could not be attributed to the functioning of the calorimeter. The disagreement was most noticeable in the liquid state. Calibration runs made with benzene checked with their usual accuracy, proving that the fault was not with the calorimeter. It became apparent that the observed heat capacity depended upon the thermal history of the sample. Determinations were then made in the liquid state upon an "annealed" sample, *i. e.*, a sample which had been liquid for a considerable time. Care was taken not to freeze any of this sample when it was cooled down. Determinations carried out upon these annealed samples agreed very well. Determinations made on solid samples that were frozen more slowly than they were melted during the run agreed well; but the measurements upon the liquid made immediately after melting did not agree with those made upon the annealed liquid. The type of results obtained can be seen from Fig. 2, where it can be seen that there are humps in the curves obtained from the recently thawed samples. The magnitude of this hump varied somewhat from run to run. The heat capacity values all approached the values of the annealed liquid at higher temperatures.

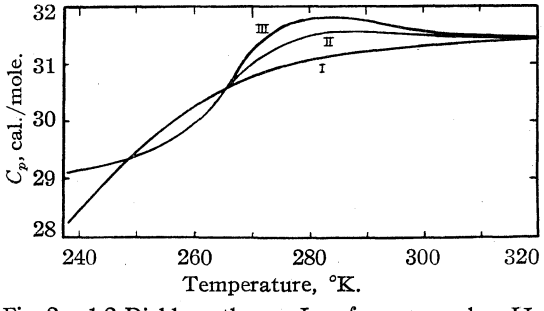


Fig. 2.—1,2-Dichloroethane: I, unfrozen sample; II, rapidly frozen sample; III, slowly frozen sample.

It was also observed that the more rapidly the sample was frozen, the smaller were the specific heat values of the solid in the region of the transition. The greatest variance was about 1 cal./mole/°C.

Effects similar to these were observed in the chlorobromide, though of a lesser magnitude. The heat capacity values in Table I for these two compounds were obtained upon the annealed liquid and the slowly frozen solid. No such effects were noticed in the case of the bromide. However, a slight, constant deviation, not exceeding the limits of experimental error, was noticed in the case of the liquid, depending upon whether the sample had been frozen rapidly or slowly.

(6) Demerliac, *J. Phys. Radium*, **7**, 591 (1898); "International Critical Tables," Vol. V; Landolt–Börnstein–Roth–Scheel, "Physikalische-chemische Tabellen," J. Springer, Berlin, 1927; Leblanc and Mobius, *Ber. Sachs. Akad. Wiss. Leipzig, Math. Phys. Klasse*, **85**, 75 (1933); Regnault, *Mem. Ak. Roy. Inst. (France)*, **26**, 262 (1862).

(7) Demerliac, *loc. cit.*

(8) Petersson, *Ber.*, **27**, 6 (1894).

Discussion

It is now widely believed that rotation about the carbon–carbon bond in ethane and its derivatives is not free but restricted by an energy barrier of appreciable magnitude. This amounts to more than 5 kg. cal./mole in the case of the halogen derivatives studied here, according to Beach and co-workers.[9] Dielectric constant, dipole moment and Raman spectra measurements indicate that while the solid is almost entirely in the *trans* configuration, considerable rotatory oscillation about the carbon–carbon bond takes place in the liquid state or in solvents. These measurements indicate that the motion is much more pronounced in ethylene chloride and chlorobromide than in the bromide.

Kohlrausch[10] interpreted his Raman spectral studies as indicating the existence of *cis–trans* isomers. Stuart[11] considers that the mutual repulsion of the chlorine atoms would prevent a stable *cis* form. Mizushima and Morino[12] suggest that there may be a potential minimum other than the *trans* configuration. Beach and co-workers,[9] however, interpret their electron diffraction patterns as indicating no other such potential minimum. Their measurements were carried out upon the gaseous phase. In the liquid phase the molecules, due to their greater proximity, may influence each other in such a manner as to render stable such a position of potential minimum.

If it is assumed that a configuration of minimum energy exists other than the *trans* configuration, the data and observations reported above may be explained in the following manner:[13]

1. There exists a dynamic equilibrium between the *cis* and *trans* configurations of the material. In the liquid state, there is a considerable amount of the *cis* form present, while the solid contains very little, if any. This is supported by the Raman spectra measurements of Mizushima and Morino[14] on the solid ethylene halides, in which the line attributed by them to the *cis* form is absent. It is further assumed that it takes an appreciable time for a quantity of one isomer to change into the other.

2. When a sample of an ethylene halide is frozen rapidly, insufficient time is allowed for all of the molecules to assume the *trans* form, and an appreciable amount of the *cis* configuration is frozen in.

White and Morgan[3] suggest that the transition in ethylene bromide might mark the onset of a rotation about the zigzag Br–C–C–Br axis. Probably only the *trans* configuration could undergo this transition, as too much space would be necessary for the *cis* form to rotate. The transitions in ethylene chloride and chlorobromide may be of the same type, in which only the *trans* configuration might be expected to take part.

If an ethylene chloride sample is frozen so rapidly that some of the *cis* form is frozen into the solid, then the heat capacity values in the region of the transition might be smaller than if only *trans* molecules were present, since the *cis* form would not be expected to undergo this zigzag rotation. This was observed experimentally in the case of the chloride and the chlorobromide.

3. A sample that was frozen slowly, upon melting, would consist almost entirely of *trans* molecules, since the normal crystal lattice accommodates only *trans* molecules. But if a rapidly melted sample of the normal solid were heated, *trans* molecules would have to isomerize to the *cis* modification, in order to establish the equilibrium state stable at a temperature just above the melting point. Since the *cis* form would be expected to have a higher energy content than the *trans* form, due to dipole interaction, etc., this isomerization might be expected to absorb heat, thereby increasing the apparent heat capacity of the sample. As the isomerization proceeds and equilibrium is approached, the heat capacities should approach the normal values. As Fig. 2 shows, this is what was observed experimentally. The peak is not so high for a rapidly frozen sample, since some *cis* is already present in the solid state, and therefore less isomerization occurs.

As has already been mentioned, the difference in heat capacity in the liquid state of ethylene bromide between a recently frozen sample and an annealed sample was noticeable, but very slight, being within the limits of experimental error. Mizushima and Morino,[15] as a result of their dipole moment and Raman spectra measurements,

(9) Beach and co-workers, *J. Chem. Phys.*, **6**, 639 (1938); THIS JOURNAL, **61**, 303 (1939).

(10) Kohlrausch, *Z. phys. Chem.*, **B18**, 61 (1932).

(11) Stuart, *Physik. Z.*, **32**, 793 (1931).

(12) Mizushima and Morino, *Sci. Papers Inst. Phys. Chem. Research* (Tokyo), **29**, 188 (1936).

(13) For convenience, the other minimum energy configuration will be called the *cis* configuration to differentiate it from the *trans* form, but this is not intended to imply that this other stable position necessarily involves rotation of 180° from the *trans* form.

(14) Mizushima and Morino, *Sci. Papers Inst. Phys. Chem. Research* (Tokyo), **26**, 1 (1934).

(15) Mizushima and Morino, *ibid.*, **25**, 159 (1934).

concluded that less deviation from the *trans* position occurs in the bromide than in the chloride and chlorobromide. Therefore, to obtain equilibrium in the liquid state of the recently thawed bromide, fewer of the *trans* molecules need isomerize and the effect upon the heat capacity would be considerably less.

The transition in the bromide has been observed by White and Morgan.[3] They explain it as being due to the setting in of rotation about the zigzag Br–C–C–Br axis rather than a rotation about the carbon–carbon bond, since the dielectric constant through the transition was only minutely affected. Raman spectra measurements show that upon solidification, rotation of one halogen with respect to the other is greatly restricted. Since the heat of transition is small, compared to the heat of fusion, this is a plausible explanation of the transition.

However, the transition is of the sharp or fusion type, rather than the gradual or rotational type, and may be just a phase transition. The transitions in the chloride and the chlorobromide are of the hump or rotational type, and may well be attributed to zigzag rotation about the X–C–C–X axis, since the dielectric constant of the chloride was unaffected in the region of the hump. Further information upon these transitions is necessary to establish this point.

While heating through the transition in the bromide, it was noticed that the sample superheated, sometimes as much as 0.35°. The same effect was noticed by White and Morgan.[3]

Acknowledgment.—The author is greatly indebted to Drs. W. T. Ziegler and E. R. Blanchard, whose assistance in carrying out this work and writing this paper was invaluable.

Summary

1. The heat capacities of 1,2-dibromoethane, 1,2-dichloroethane, and 1,2-bromochloroethane have been measured over the range 90–320°K.

2. Heats of fusion and transition have been measured for these compounds.

3. Certain phenomena in connection with the thermal history of these compounds and its effect upon the specific heat have been interpreted in the light of restricted intramolecular rotation in these compounds.

BALTIMORE, MD. RECEIVED AUGUST 26, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DICKINSON COLLEGE]

The Viscosity of Solutions of Sulfur Dioxide in Organic Liquids

BY S. B. CUPP AND H. E. ROGERS

This paper is a continuation of the work begun by Lewis[1] and Adams and Rogers[2] on the viscosity of solutions of sulfur dioxide in organic liquids. The present paper includes data concerning the effect of dissolved sulfur dioxide on the viscosity of *n*-propyl bromide, *i*-propyl bromide and *n*-butyl bromide.

Experimental Part

n-Propyl bromide, *i*-propyl bromide and *n*-butyl bromide were each washed four to six times with concentrated sulfuric acid, followed by a solution of sodium carbonate, dried over calcium chloride and distilled.

	B. p., °C.	d^{25}_4	$n^{25}D$
n-Propyl bromide	70.9	1.3430	1.4313
i-Propyl bromide	59.6	1.3060	1.4220
n-Butyl bromide	101.6	1.2689	1.4373

The apparatus and procedure were the same as described in the earlier paper.[2]

(1) J. R. Lewis, THIS JOURNAL, **47**, 626 (1925).
(2) H. E. Adams and H. E. Rogers, *ibid.*, **61**, 112 (1939).

Discussion

Density data for solutions of sulfur dioxide in *n*-propyl bromide, *i*-propyl bromide, and *n*-butyl bromide are found in Table I. Each liquid shows an expansion, in volume, when sulfur dioxide is dissolved in it. In the case of the *n*-propyl bromide solutions, mixtures from 0 to 60% sulfur dioxide have almost the same density as the pure *n*-propyl bromide.

In Fig. 1, the viscosity data in Table II are plotted. The viscosity is plotted against weight % and each curve is concave upward. Similar curves are obtained when the viscosity is plotted against volume %. The viscosity curves in Fig. 1 appear to be typical. The *n*-butyl bromide shows the greatest sag, as is to be expected. The difference between the viscosities of the pure sulfur dioxide and the pure *n*-butyl bromide is greater than it is for the other two liquids; consequently

TABLE I

DENSITY DATA AT 25°

n-Propyl bromide Wt. % of SO_2	D. of soln.	*i*-Propyl bromide Wt. % of SO_2	D. of soln.	*n*-Butyl bromide Wt. % of SO_2	D. of soln.
0.00	1.3430	0.00	1.3060	0.00	1.2689
18.50	1.3430	11.71	1.3083	13.98	1.2780
35.61	1.3436	19.46	1.3107	23.37	1.2843
47.90	1.3436	33.33	1.3163	33.01	1.2906
62.83	1.3470	53.77	1.3266	43.00	1.2986
77.27	1.3513	63.29	1.3338	52.87	1.3076
93.51	1.3587	83.16	1.3491	60.44	1.3155
100.00	1.3680	91.75	1.3599	76.73	1.3342
		100.00	1.3680	86.38	1.3483
				100.00	1.3680

VISCOSITY DATA AT 25°

n-Propyl bromide Wt. % of SO_2	Viscosity in centipoises	*i*-Propyl bromide Wt. % of SO_2	Viscosity in centipoises	*n*-Butyl bromide Wt. % of SO_2	Viscosity in centipoises
0.00	0.4797	0.00	0.4438	0.00	0.5914
9.46	.4311	13.79	.3789	12.44	.4942
28.00	.3527	21.72	.3499	33.24	.3877
47.13	.3076	36.13	.3133	53.14	.3237
73.97	.2679	50.18	.2870	76.06	.2786
85.75	.2569	65.24	.2664	89.53	.2592
100.00	.2472	82.68	.2555	100.00	.2472
		100.00	.2472		

the sag is not so great for the *i*-propyl bromide and *n*-propyl bromide curves.

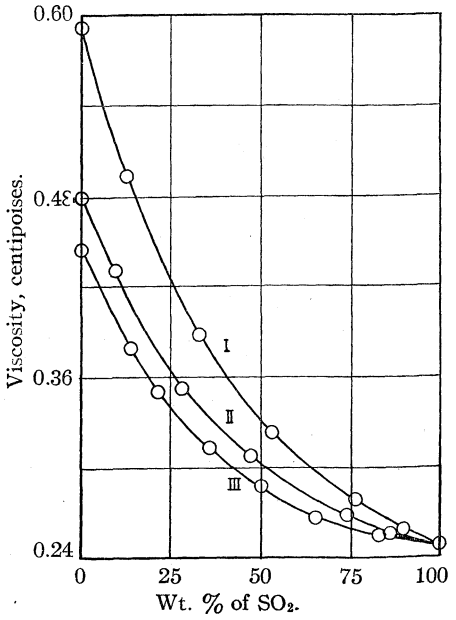


Fig. 1.—I, *n*-Butyl bromide; II, *n*-propyl bromide; III, *i*-propyl bromide.

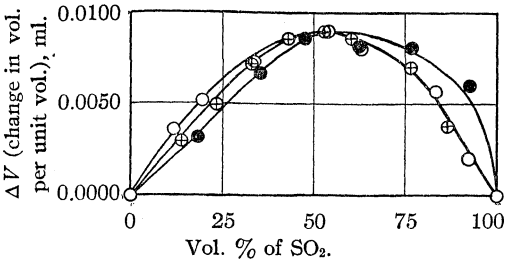


Fig. 2.—⊕, *n*-Butyl bromide; ●, *n*-propyl bromide; ○, *i*-propyl bromide.

Change in volume per unit volume (ΔV) has been plotted against volume per cent. in Fig. 2. ΔV was calculated using the expression in the earlier paper.[2] An expansion, on mixing, was found for each liquid. In the earlier work,[2] it was observed that ΔV was greatest for carbon tetrachloride, chloroform being next and bromoform the least. This was the same order as observed for the density-volume % curves for these three liquids. In this work, the maximum value for ΔV is practically the same for *n*-propyl bromide, *i*-propyl bromide, and *n*-butyl bromide. However, Fig. 1 and Fig. 2 give further evidence for the well-known fact that when liquids show an expansion in volume, on mixing, the fluidity of the mixture is greater than the fluidity calculated from the fluidities of the pure liquids. It is difficult to obtain an exact order for the fluidity and ΔV curves as was done in the earlier paper[2] because the expansion, on mixing, in each case, is almost identical.

Summary

1. The viscosities and densities of many solutions of sulfur dioxide in *n*-propyl bromide, *i*-propyl bromide, and *n*-butyl bromide were measured at 25°.

2. Expansion in volume, on mixing, was found in each case.

3. The results support the well-known fact that when liquids show an expansion, on mixing, the fluidity of the solution is greater than the fluidity calculated from the fluidities of the pure liquids.

CARLISLE, PENNA. RECEIVED SEPTEMBER 13, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

Ketene and its Dimer

BY CHARLES D. HURD AND ARTHUR S. ROE

Toward some hydroxyl-containing compounds ketene behaves as an efficient acetylating agent but toward others it is either non-reactive or sluggish. In the latter category are phenols and tertiary alcohols. Van Alphen[1] reported no reaction at room temperature between ketene and phenol, but Rice and co-workers[2] showed that the acetylation proceeded quantitatively at the boiling point. With *t*-butyl alcohol, there was no acetylation at room temperature[3] and the reaction was very slow at its boiling point.[2]

In view of the established catalytic effect[4] of a trace of sulfuric acid or *p*-toluenesulfonic acid on the analogous acetylation of carbohydrates, it was decided to try these catalysts on the reaction between ketene and phenol or tertiary alcohols. The results were striking. With only a trace of either acid it was found possible to effect complete conversion at room temperature of phenol to phenyl acetate, *t*-butyl alcohol to *t*-butyl acetate,[5] and *t*-pentyl alcohol to *t*-pentyl acetate.

Ketene and Aldehydes.—Ketene, in the presence of potassium acetate, is known to react with aldehydes like benzaldehyde[6] and cinnamic aldehyde[3] to yield anhydrides of unsaturated acids. Benzaldehyde yields cinnamic acetic anhydride, as follows

$$C_6H_5CHO + 2CH_2CO \longrightarrow C_6H_5CH{=}CHCOOCOCH_3$$

No such reaction occurs, however, between ketene and butyraldehyde.

Benzaldehyde differs from butyraldehyde in that it has no hydrogen on the α-carbon. Cinnamaldehyde differs in that it is unsaturated on the α-carbon. Acrolein and crotonaldehyde resemble cinnamaldehyde in this respect. Formaldehyde, like benzaldehyde, has no α-hydrogen. If methyl formate may be regarded as an aldehyde because of its CHO group, it also falls in the group of compounds with no α-hydrogen. These four aliphatic compounds—formaldehyde, acrolein, crotonaldehyde and methyl formate—were tested for their reactivity toward ketene. Reaction occurred in all instances, but the substances obtained were unsaturated red oils of high molecular weight (1500–2000).

If the reaction had proceeded like the reaction with benzaldehyde, acrolein would have produced β-vinylacrylic acetic anhydride (I), formaldehyde would have yielded acrylic acetic anhydride (II), and methyl formate would have given rise to methoxyacrylic acetic anhydride (III).

(I) $CH_2{=}CH{-}CH{=}CH{-}CO{-}OCOCH_3$
(II) $CH_2{=}CH{-}CO{-}OCOCH_3$
(III) $CH_3OCH{=}CH{-}CO{-}OCOCH_3$

The course of the reaction was affected little by temperature, for the polymeric products were formed when the reaction was performed at 20° or −80°.

Ketene and Formic Acid.—The general reaction of ketene with acids yielding mixed acetic anhydrides[6,7] was applied to formic acid: $HCOOH + CH_2{=}CO \longrightarrow HCOOCOCH_3$. Formic acetic anhydride, thus produced, was pure by analysis and possessed the boiling point reported by Béhal[8] who prepared it from acetic anhydride and formic acid.

Graves' patent,[9] which appeared since completion of our work, should be mentioned. He states: "Ketene-containing gases from the pyrolysis of acetone were passed into 101.5 grams of 99% formic acid until the gain in weight was 90 grams. The product was acetoformic anhydride." Presumably acetic formic anhydride was in mind rather than "acetoformic anhydride," which would be $(CH_2COCO)_2O$, the anhydride of acetoformic acid. The substance was not purified by distillation nor characterized by reactions and no claim for it was made in the patent. The only claims were for acetic pyruvic anhydride, made from pyruvic acid and ketene.

Formic acetic anhydride proved to be an excellent formylating agent toward aniline

$$C_6H_5NH_2 + HCOOCOCH_3 \longrightarrow C_6H_5NHCHO + CH_3COOH$$

No acetanilide was produced. Since aniline reacts with acetic benzoic anhydride[7] to yield acetanilide and benzoic acid, this places the phenyl,

(1) Van Alphen, *Rec. trav. chim.*, **43**, 760 (1924); **44**, 838 (1925).
(2) Rice, Greenberg, Waters and Vollrath, THIS JOURNAL, **56**, 1760 (1934).
(3) Hurd and Williams, *ibid.*, **58**, 962 (1936).
(4) Hurd, Cantor and Roe, *ibid.*, **61**, 426 (1939).
(5) Morey, *Ind. Eng. Chem.*, **31**, 1129 (1939).
(6) Hurd and Thomas, THIS JOURNAL, **55**, 275 (1933).
(7) Hurd and Dull, *ibid.*, **54**, 3427 (1932).
(8) Béhal, *Compt. rend.*, **128**, 1460 (1899).
(9) Graves, U. S. Patent 2,135,709, Nov. 8, 1938.

methyl and hydrogen radicals in this decreasing order of electron attraction: $C_6H_5 > CH_3 > H$. This follows because the splitting of the symmetrical —C(=O)—O—C(=O)— group in the mixed anhydrides must be governed by the terminal groups (R or R′ in R—CO—O—CO—R′).

Non-reaction of Ketene and Tetraethyllead.—Ketene was found to be indifferent toward tetraethyllead. After passing 0.3 mole of ketene into 0.11 mole of tetraethyllead, the latter was poured slowly into concd. hydrochloric acid. The ethane evolved measured 2.38 liters (S. T. P.), compared with the calculated 2.4 liters. This non-reaction with ketene is in contrast to its violent behavior toward diethylmagnesium,[3] and its smooth reaction with diethylzinc.

The Dimer of Ketene

The dimer is known to be either acetylketene (IV) or β-crotonolactone (V) or, more probably, an equilibrium mixture of them, because on ozonolysis[3] it yielded pyruvic aldehyde. Since electron

IV V

readjustment is all that is necessary to maintain the equilibrium between IV and V, they are resonance isomers. This should cause lessened chemical reactivity and it is well known that acetylketene is more sluggish than ketene.

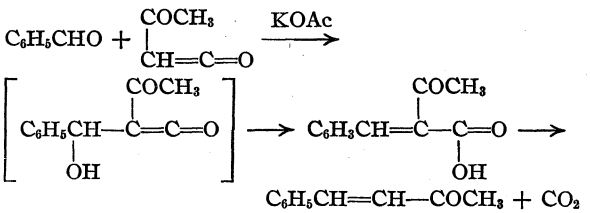
Parachor.—In the earlier work[3] the parachor of acetylketene was reported to be 182. This value was redetermined on material of greater purity and was found to be 188.0. Since that part of the calculated parachor which is contributed by the atoms alone is 127.6, the structural correction factor for the functional group involved (IV ⇄ V) is 60.4.

Enolization.—Acetylketene is a ketone as well as a ketene, so it is capable of enolization. Grignard and Blanchon[10] showed that enolization could be induced by branched-chain Grignard reagents, the amount of enolization being registered by the quantity of hydrocarbon evolved. Kohler and Thompson[11] showed that in some instances one might mistake reduction by the Grignard reagent for enolization, in which case propylene would be formed. The reaction of *i*-propylmagnesium bromide and acetylketene yielded propane, in an amount pointing to 23% enolization. A trace of propylene was present but the gas was chiefly propane.

Pyrolysis.—The pyrolysis of acetylketene at 550° yielded[3] methane, carbon monoxide, carbon, and dehydroacetic acid, but no ketene. It was thought that ketene might be formed at higher temperatures. At 650° over half of the dimer was depolymerized to ketene. As would be expected much gas was formed concurrently.

$$CH_3COCH{=}C{=}O \longrightarrow 2CH_2{=}C{=}O$$

Acetylketene and Benzaldehyde.—By analogy with the synthesis of cinnamic acid from ketene, benzaldehyde and potassium acetate, one would anticipate the synthesis of benzalacetone from acetylketene. This reaction was found to occur.



Carbon dioxide was evolved copiously and a 31% yield of benzalacetone was obtained.

A similar experiment was performed with carbon suboxide, O=C=C=C=O, which is a diketene,[12] but no reaction occurred. This non-reaction with benzaldehyde in the presence of potassium acetate must be associated with the absence of the —CH=C=O group in C_3O_2.

In view of the fact that ketene and diethylzinc react[3] to produce 2-butanone, it was hoped that acetylketene and diethylzinc might react smoothly. An immediate yellow precipitate formed when diethylzinc was added to acetylketene but in a few minutes this material congealed exothermically to a black tar, too stiff to stir. It was possible to keep the yellow precipitate, however, if toluene or benzene were used as diluents; but no products could be obtained from it by hydrolysis with steam, or with sulfuric acid solution, or with benzoyl chloride. Only tars resulted.

Experimental Part

Ketene was prepared in a ketene lamp[3] which delivered 0.1 mole per hour. A liberal supply of acetylketene ("Diketene") was donated by the Carbide and Carbon Chemicals Corporation through the courtesy of Dr. R. W. Mc-

(10) Grignard and Blanchon, *Bull. soc. chim.*, **49**, 27 (1931).

(11) Kohler and Thompson, THIS JOURNAL, **55**, 3822 (1933).

(12) This term is not to be confused with the trivial name "Diketene" which is used sometimes for acetylketene. The latter is a monoketene, not a diketene, and in its resonance modification it is not a ketene at all.

Namee. For it, we are deeply grateful. Part of the acetylketene was stored for a year in a glass-stoppered bottle in a refrigerator. It gradually became quite dark in color, but the greater part of the acetylketene was still present as such at the end of the year. Pure acetylketene will leave a residue of dehydroacetic acid if distilled at atmospheric pressure but no such residue occurs on vacuum distillation. The acetylketene was always distilled prior to use, b. p. 43° (28 mm.).

Ketene and Tertiary Alcohols.—To 0.1 mole of *t*-butyl or *t*-pentyl alcohol was added either 1 drop of concd. sulfuric acid or 0.01 g. of *p*-toluenesulfonic acid. Then the stream of ketene was passed in for seventy minutes. Heat developed at once so the reaction was cooled in an ice-bath. The solutions became slightly yellow in color, less color being apparent in the solution containing the toluenesulfonic acid.

The solutions were treated with 10 cc. of 6 *N* sodium hydroxide and washed with 10 cc. of water. Both of these aqueous solutions were extracted with ether, the ether solution being added to the ester layer. The ether solution was dried with potassium carbonate, the ether carefully removed on a water-bath, and the residue distilled. The *t*-butyl acetate was collected at 94–95° and no liquid came over at 82°, indicating that all the alcohol had been esterified. Similarly, the *t*-pentyl acetate was collected at 123–124°, with no distillate at 100°. The yields of esters in all four experiments were uniformly high at 86–89%.

Ketene and Phenol.—To a solution of 9.4 g. (0.1 mole) of phenol in 40 cc. of dry ether was added a drop of concd. sulfuric acid (A) or 0.01 g. of *p*-toluenesulfonic acid (B). Ketene was bubbled through for an hour and a half. It was necessary to cool the reaction to prevent volatilization of the solvent. The solution was yellow at the end of the reaction, more so with A than with B. It was washed with 20 cc. of 6 *N* sodium hydroxide and then with 20 cc. of water. The aqueous solutions were washed with ether, which was added to the ester layer. The ether solution was dried with potassium carbonate. The ether was removed on a water-bath and the product distilled. In both runs, the yield of phenyl acetate, b. p. 190–191°, was 12.1 g. or 89%.

Ketene and Acrolein.—The acrolein used in these experiments contained the trace of hydroquinone (1:1000) which was added as a preservative. Ten grams (0.18 mole) of it with 1.5 g. of anhydrous potassium acetate were placed in a flask fitted with inlet and exit tubes and a mercury-sealed stirrer. Then 0.2–0.3 mole of ketene was passed into the flask. Heat was evolved so an ice-bath was used after the first hour of reaction. The reaction product was a viscous red oil which decomposed to a black tar on attempted distillation at 19 mm. The red oil was soluble in dioxane and in dilute sodium hydroxide. From the alkaline solution acids precipitated an amorphous brown solid which melted between 75–150°.

The red oil was dried for a week in a vacuum desiccator over sulfuric acid. Pure dioxane, kindly furnished by Dr. R. Umhoefer of this Laboratory, was used as a cryoscopic solvent. The apparent molecular weight of the polymer was 1987, since the freezing point lowering caused by dissolving 0.7014 g. in 18.4906 g. of dioxane was 0.089°.

The course of the reaction with ketene was similar at −80°. The reaction mixture changed slowly to a dark red, viscous liquid, then solidified after two hours. This solid melted at room temperature, then decomposed with evolution of gas, and congealed to a red glass. An intractable oily product was formed by addition of the red solid to a solution of aniline in ether.

In two subsequent experiments of the same size at −80°, the red reaction product was treated in one case with ice water, and in the other with 50 cc. of ethyl alcohol.

From the former, 15.5 g. of brown tar separated and from the latter 11 g. of similar product. The material was soluble in acetone, but could not be crystallized from it. Extraction of the tar with ether yielded 1 cc. of oil on evaporation but it contained no β-vinylacrylic acid for none of the tetrabromide (m. p. 160°) was obtained on treatment with bromine.

Ketone and Monomeric Formaldehyde at −80°.—Liquid formaldehyde was prepared[13] by condensing formaldehyde gas in a trap at −80°. To 4 cc. of this liquid was added 0.05 g. of fused potassium acetate, then ketene was passed into the tube for one hour at −80°. The mixture turned yellow at once and became red before the reaction was over. A small portion of the reaction product was removed and allowed to come to room temperature. It turned a darker red and became viscous after a few minutes. Part of the polymer was dried *in vacuo* over sulfuric acid for a week. The freezing point lowering caused by dissolving 0.6140 g. in 17.1042 g. of dioxane was 0.097°. This indicates a molecular weight of 1740.

The remainder of the mixture was kept at −80° and 30 cc. of a solution of bromine in carbon tetrachloride was added. The solution was left at room temperature overnight. The solvent was removed under diminished pressure, leaving a small amount of a red oil which gave a positive halogen test. Three cc. of water was added to the oil without apparent reaction. The water was removed on the steam-bath and the residue extracted with hot benzene. Any dibromopropionic acid would dissolve in this solvent, but only a trace of red tar remained after evaporation of the benzene. No dibromopropionic acid was isolated, which proved that no acrylic acid, as such, was in the reaction mixture.

Ketene and Methyl Formate.—Ketene was passed for seven hours into a stirred mixture of 28.7 g. of methyl formate and 1.5 g. of fused potassuim acetate, the temperature being maintained at −15° by an ice–salt bath. The color change was from yellow to deep red. The final red sirup weighed 55.2 g. On distillation there was obtained 16.8 g. of a mixture of methyl formate and acetone at 42–45°, and 4.1 g. of acetic anhydride at 39° (30 mm.). The latter, with *p*-toluidine, yielded aceto-*p*-toluidide, m. p. 146–147°. There appeared to be considerable decomposition during the distillation.

To perform the reaction at a lower temperature, 8.4 g. (0.2 mole) of ketene was liquefied and distilled slowly into 12 g. (0.2 mole) of methyl formate and 1 g. of fused potassium acetate at −80°. The yellow color appeared at once but the color did not become red as in the other experiment. When all the ketene was introduced the reaction product was an orange solid. When a little of it was brought to

(13) Spence and Wild, *J. Chem. Soc.*, 338 (1935).

room temperature it melted to a yellow liquid which changed rapidly to the thick red oil mentioned before.

Half of the orange solid was transferred to a flask containing 30 cc. of aniline. The product was a red oil which could not be crystallized or identified.

One-quarter of the orange reaction product from another identical run at −80° was added to water, another quarter to methanol, another to ethanol, and the remainder to 1-butanol. The solutions were kept at 0° for six hours. Orange-brown solids separated in all instances. They were soluble in acetone or dioxane. For purification they were dissolved in acetone and precipitated by petroleum ether. Then the yellow solids were dissolved in dioxane and precipitated by methanol. The melting points of the material from the reactions with water (A), methanol (B), ethanol (C) and butanol (D), respectively, were 71–73°, 67–69°, 66–68°, 64–66°.

Saponification equivalents were determined in the usual manner by heating with standard alcoholic potash. These values were obtained for A–D: 44.5, 48.5, 49.7, 51.5.

Molecular weights were taken cryoscopically in dioxane as before. The values for A, B and C were 1498, 1524, 1533.

Ketene and Crotonaldehyde.—Twenty grams of crotonaldehyde (b. p. 103–104°) and 0.2 g. of potassium acetate were taken. When ketene was introduced heat and a slight coloration developed immediately, so the reaction was cooled in an ice-bath. After three hours the reaction had stopped. The brown reaction mixture was poured into 50 g. of ice. About 22 cc. of a brown liquid separated. It was soluble in acetone or dioxane but was insoluble in benzene, alcohol, ethyl acetate and petroleum ether. The apparent molecular weight of the tar, taken cryoscopically in dioxane as before, was 1761.

Ketene and Formic Acid.—Anhydrous formic acid (13.8 g., 0.3 mole), prepared from the 85% acid by refluxing with phthalic anhydride,[14] was treated with a stream of ketene gas (0.3 mole) freed from acetone vapors. The reaction product was distilled at 19 mm. and 15 cc. of formic acetic anhydride was collected at 33–33.5°: $n^{20}D$ 1.3940; d^{20}_4 1.1458.

Anal. Subs. 0.7216, 0.9094. Cc. of 0.0854 *N* base, 190.31, 240.32. Cc. calcd. for $HCOOCOCH_3$, 192.04, 242.01. Per cent. purity, 99.1, 99.3.

Aniline was added to 8 g. of ice-cold formic acetic anhydride. Distillation of the products at 29 mm. yielded 4 g. of acetic acid up to 50°, 2.5 g. of an intermediate fraction, and 9.2 g. of formanilide at 178–179°. The small amount of residue contained no acetanilide, crystallizable from hot water. The formanilide melted at 46°.

Acetylketene

Surface Tension and Parachor.—The capillary rise method of determining the surface tension was used. The radius of the capillary was found to be 0.0219 cm. by using pure thiophene-free benzene as a standard for calibration. Pure water served as a check on this result. Then pure acetylketene was taken. The latter was freshly distilled (b. p. 43.0–43.1° at 28 mm.). The density of this acetylketene was found to be 1.0817 at 25° since 0.8956 cc. weighed 0.9688 g. The data on surface tension are:

Substance	Water	Acetylketene
Temperature, °C.	25	25
Density	0.9971	1.0817
Av. capillary rise, cm.	6.73	2.92
Surf. tension, dynes/cm., found	71.98	33.89
Value in "Int. Crit. Tables"	71.97	...

From this, the parachor, $M\gamma^{1/4}/D - d$, is calculated to be 188.0 for acetylketene.

Enolization.[15]—*i*-Propylmagnesium bromide was prepared in 75 cc. of dry *n*-butyl ether from 12.3 g. of *i*-propyl bromide and 2.5 g. of magnesium. Then 4.561 g. of pure acetylketene (in 50 cc. butyl ether) was placed in a 250-cc. three-necked flask fitted with a mercury-sealed stirrer. The exit tube led from the flask through a small vertical condenser to an inverted, brine-filled bottle. The apparatus was swept out with nitrogen, placed in an ice-bath, and 36 cc. of Grignard solution was added slowly until no more gas was evolved. An excess of 4 cc. was then added and the reaction was allowed to come to room temperature while it was stirred for three hours.

The volume of the gas evolved at S. T. P., also corrected for the 40 cc. of Grignard solution, was 286.2 cc. This was 0.0128 mole. Since 0.0543 mole of acetylketene was used, there was 23.6% enolization, assuming that only one carbonyl enolized.

Analysis of the gas revealed only propane, propylene and nitrogen (no CO_2, H_2, O_2, CO). The propylene was 1.8% by volume, as determined by absorption in 83% sulfuric acid. The propane was 21.8% by volume. In duplicate analyses, the ratio of contraction (after combustion of the C_nH_{2n+2}) to absorption (of CO_2 after combustion) was 1.03 and 0.97. For propane this ratio should be 1.

Pyrolysis at 650°.—Acetylketene was introduced slowly by mercury displacement into the top of a vertical Pyrex tube maintained at 650° by automatic control. The effective volume of the tube was 156 cc. The exit gas flowed through two ice-cooled traps, vertically through a water-cooled condenser, and then through two aniline traps. The acetylketene taken was 51.4 g. and that recovered in the trap was 12.6 g. (chiefly acetylketene, but it contained a little dehydroacetic acid). The duration of the experiment was seventy-eight minutes, hence, the contact time was about ten seconds.

There was an indication of 19.8 g. of ketene because 63.5 g. of acetanilide, m. p. 114–115°, was obtained.

Reaction with Benzaldehyde.—A 200-cc. three-necked flask was fitted with a dropping funnel, mercury-sealed stirrer and condenser. Into it was placed 19.8 g. (0.18 mole) of freshly distilled benzaldehyde and 2 g. of fused potassium acetate.

During ninety minutes, 15.7 g. (0.187 mole) of acetylketene was added. Heat was applied to start the reaction, after which the heat generated sufficed to sustain it. A light yellow color soon developed which changed to a dark red. Between 1–1.5 liters of carbon dioxide (proved by lime-water test) was evolved.

The reaction mixture was poured into 50 cc. of dilute

(14) Pryanishnikov and Shakhova, *J. Gen. Chem.* (U. S. S. R.), **2**, 84 (1932); *C. A.*, **27**, 2672 (1933).

(15) Preliminary work on this was performed by Jonathan W. Williams.

hydrochloric acid. No visible reaction occurred though a heavy oil separated. The aqueous layer was washed with 25 cc. of benzene, which was added to the oil. The solution was placed on a water-bath to remove the solvent, then distilled at 13 mm.

Fraction	Temp., °C.	Wt., g.	Remark
1	to 60	0.52	.....
2	60–63	8.31	Benzaldehyde
3	63–125	0.84	.....
4	125–128	1.94	Benzalacetone
5	128–130	6.44	Benzalacetone
Residue		7.07	

Fraction 2 was identified as benzaldehyde by preparation of the phenylhydrazone, m. p. 154–155° (literature value 156°). Fractions 4 and 5 were identified as benzalacetone. They solidified in the icebox to crystals which melted at 37–38° (literature, 42°); 0.1 g. gave 0.17 g. of benzalacetone phenylhydrazone, m. p. 154–155° (literature, 156–157°). The total yield of benzalacetone was 8.38 g., or 0.0574 mole. Mixed melting point of phenylhydrazones of fractions 2 and 4 was 125–130°.

Summary

Ketene, in the presence of a trace of sulfuric acid or *p*-toluenesulfonic acid, causes complete acetylation of phenol, *t*-butyl alcohol, or *t*-pentyl alcohol at room temperature.

Ketene, in the presence of potassium acetate, reacts with acrolein, crotonaldehyde, formaldehyde (monomer), or methyl formate to yield in all cases complex reaction products of high molecular weight. These reactions proceeded even at −80°.

Formic acid and ketene give rise to formic acetic anhydride which, in turn, reacts with aniline to yield formanilide, not acetanilide.

Ketene does not react with tetraethyllead.

Pyrolysis of acetylketene at 650° brings about depolymerization to ketene.

Toward *i*-propylmagnesium bromide, acetylketene displays 23% enolization.

The parachor of acetylketene was found to be 188 instead of 182 as previously reported.

Acetylketene, in the presence of potassium acetate, reacts with benzaldehyde with the production of benzalacetone and carbon dioxide. No such reaction occurs between carbon suboxide and benzaldehyde.

The product of reaction of acetylketene and diethylzinc is a yellow solid which yielded nothing but tars on hydrolysis or on reaction with benzoyl chloride.

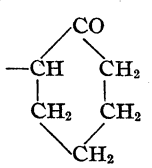
EVANSTON, ILLINOIS RECEIVED SEPTEMBER 16, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY, NORTHWESTERN UNIVERSITY]

Preparation and Pyrolysis of Cyclohexanone

BY CHARLES D. HURD, HARRY GREENGARD AND ARTHUR S. ROE

Ordinarily, ketene is prepared by pyrolysis of acetone. A chain mechanism involving radicals has been proposed[1] to explain it. One would predict analogously that cyclohexanone should give rise to ketene because of the three possible radicals (I–III) formed by dehydrogenation of cyclohexanone, ketene and ethylene appear to be



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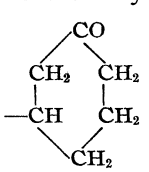

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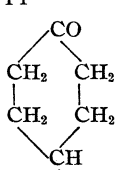


III

plausible products from each. No ketene was observed, however, when cyclohexanone was pyrolyzed in a tube at 700° or in a ketene lamp.

The observed products were water, cyclohexadiene, ethylene, carbon monoxide, and small amounts of hydrogen and methane.

When cyclohexanone was refluxed for five days, five-sixths of it was still intact but the remainder condensed to cyclohexylidenecyclohexanone.

An interesting development of the present work was the synthesis of cyclohexane in 60% yield by dehydrogenation of cyclohexanol over copper chromite.

Experimental

Cyclohexanone.—A horizontal Pyrex tube (25 × 2 cm.) was filled with pumice coated with the Adkins copper chromite catalyst, prepared as directed by Dunbar and Cooper.[2] It was heated electrically to 290–310°. The vapor of 150 g. of cyclohexanol was forced through the hot tube during eight hours by dropping the liquid slowly into an attached flask at 220°. The reaction products were condensed, dried with potassium carbonate, and distilled. Twelve grams of cyclohexene was collected at 75–85°

(1) Rice and co-workers, THIS JOURNAL, **53**, 1959 (1931); **56**, 1761 (1934).

(2) Dunbar and Cooper, *ibid.*, **58**, 1053 (1936).

There was 8 g. of an intermediate fraction between 85–155°, then 91 g. of cyclohexanone was collected at 155–156.5°. The residue weighed 30 g. The yield was 60% of the theoretical. The cyclohexanone was identified as the semicarbazone, m. p. 165°.

Pyrolysis

By Refluxing.—Twenty-four grams of cyclohexanone was refluxed for one hundred and fifteen hours. The solution became orange-colored. On vacuum distillation, 20 g. of the ketone was recovered at 60–64° (30 mm.), and 2.5 g. of cyclohexylidenecyclohexanone was collected at 158–162° (30 mm.). The oxime of the latter melted at 147–152°.

Through Hot Tube.—During one hour, 24 g. of cyclohexanone was passed through a Pyrex combustion tube heated to 700–725°. The tube was 120 × 2 cm. and was filled with pieces of porcelain. Condensables were removed from the gas stream by a coil condenser, then the gas was passed through aniline. The condensate, on distillation at 85–100°, yielded 1 g. of a mixture of water (droplets visible) and cyclohexadiene. At 150–160° there was collected 2.5 g. of cyclohexanone (oxime, m. p. 87°). The cyclohexadiene was converted into 1,2,3,4-tetrabromocyclohexane, m. p. 140°, on treatment with bromine in carbon tetrachloride.

No acetanilide was found in the aniline trap; hence, no ketene was formed.

With Ketene Lamp.—Ninety grams of cyclohexanone was placed in the ketene lamp[3] and decomposed during one hour. The effluent gas was conducted through aniline. The volume of unabsorbed gas (S. T. P.) was 6.8 liters. No acetanilide was obtained from the aniline trap.

Summary

Cyclohexanone is formed in good yields by dehydrogenation of cyclohexanol. The cyclohexanone yielded no ketene on pyrolysis at 700° but some cyclohexadiene was identified. Prolonged refluxing gave rise to small amounts of cyclohexylidenecyclohexanone.

(3) Hurd and Williams, THIS JOURNAL, **58**, 962 (1936).

EVANSTON, ILLINOIS RECEIVED SEPTEMBER 26, 1939

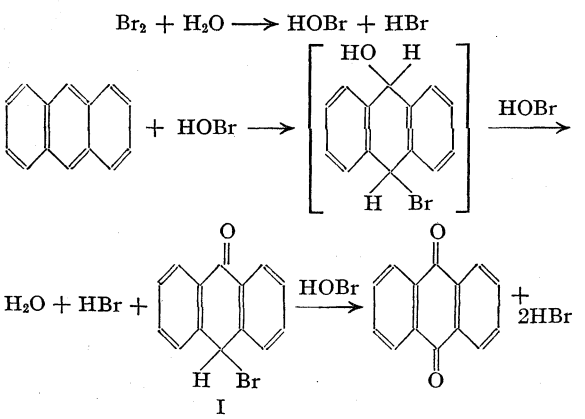
[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

The Reaction of Bromine with Anthracene in Dioxane

BY CHARLES C. PRICE AND CLAY WEAVER

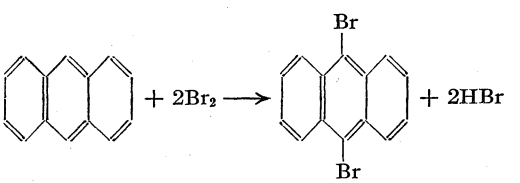
In experiments on the reaction of anthracene with bromine using dioxane as a solvent,[1] it was noted that more hydrogen bromide was evolved than could be accounted for on the basis of bromination of the hydrocarbon, since two-thirds to three-fourths of the bromine consumed appeared as hydrobromic acid after addition of water to the reaction mixture.

As a tentative explanation, it was assumed that the bromination of a mole of anthracene induced the bromination of one or two moles of dioxane by an ionic mechanism. It has been discovered,



I

however, that the anomalous formation of hydrobromic acid in dioxane, even with material which had been distilled from sodium, was due to the presence of traces of water. In the presence of the basic solvent, the water and bromine react with the anthracene as hypobromous acid, leading to the formation of 9-bromoanthrone (I) and anthraquinone, thus accounting for the high percentage of acid formed. When precautions were taken to exclude atmospheric moisture from freshly dried dioxane, the normal reaction took place.



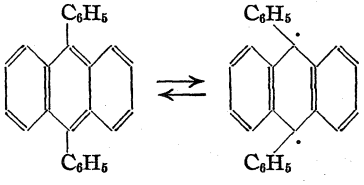
Since this eliminates the evidence for the ionic mechanism suggested by Price and Thorpe[2] for the *cis–trans* isomerization of diethylmaleate in the presence of bromine and anthracene, the alternative atomic-free radical mechanism they suggested is therefore to be preferred, not only from analogy with the photochemical reaction,[3]

(1) Price, THIS JOURNAL, **58**, 1834 (1936).

(2) Price and Thorpe, *ibid.*, **60**, 2839 (1938).

(3) Wachholtz, *Z. physik. Chem.*, **125**, 1 (1929); Schmidt, *ibid.*, **B1**, 205 (1930).

but on the basis of the structure of anthracene (particularly its *meso*-diaryl derivatives). Dufraisse[4] has recently suggested that the reactivity of these compounds, especially their ability to form peroxides on exposure to oxygen, is analogous to the behavior of triarylmethyl radicals, and that these molecules actually exist to some extent as di-radicals.



Experimental

Reagents.—Anthrone, prepared from anthraquinone,[5] was reduced to anthracene according to Martin's directions.[6] The anthracene crystallized as plates which melted at 216–216.5° (corr.) and which showed a deep purple fluorescence. Commercial dioxane was purified according to the directions of Scatchard and Benedict,[7] b. p. 100.5–101° (corr.). Bromine was purified as before.[1] The purified dioxane did not react with this bromine, even up to 75°.

Procedure.—Standard bromine and anthracene solutions (*ca.* 1%) in dry dioxane (protected from atmospheric moisture) were mixed. Canary yellow needles separated in one minute. At the end of fifteen minutes the reaction mixture was poured into water containing potassium iodide. The bromine consumed by one sample was 0.0496 mole and the hydrogen bromide evolved 0.0494 mole, by another 0.0472 and 0.0463 mole, respectively, the required values for the equation of the formation of 9,10-dibromoanthracene. This substance was isolated by filtration after the titrations. It formed canary yellow needles from acetic acid, m. p. 221° (corr.). From a 0.50-g. sample, 0.93 g. (99%) was obtained.

If precautions to exclude atmospheric moisture were not observed, 9-bromoanthrone and anthraquinone were isolated as well. In a particular experiment, 5 cc. of water and 1.2 g. each of bromine and anthracene were added to 95 cc. of dioxane. A sample of this mixture showed a ratio of 0.0566 mole of bromine consumed to 0.0996 mole of hydrogen bromide evolved. After thirty minutes the reaction mixture was poured into 100 cc. of water. The precipitate (0.6 g.) was recrystallized from benzene–petroleum ether to give thick square plates of 9-bromoanthrone (I), m. p. 142–144° (corr.), with decomposition.[8]

Anal. Calcd. for $C_{14}H_9OBr$: Br, 29.30. Found: Br, 29.35.

Extraction of the aqueous filtrate with ether, followed by evaporation of the solvent, yielded 0.6 g. of pale yellow needles of anthraquinone, m. p. 280–282° (corr.).

When a higher percentage of water was added, all the bromine consumed appeared as hydrogen bromide and the sole product was anthraquinone.

Summary

Unless moisture is excluded rigorously, the reaction of bromine with anthracene in dioxane leads to the formation of 9-bromoanthrone and anthraquinone, as well as the normal product, 9,10-dibromoanthracene.

(4) Dufraisse, *Bull. soc. chim.*, [5] **6**, 422 (1939).

(5) "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1931, p. 52.

(6) Martin, THIS JOURNAL, **58**, 1438 (1936).

(7) Scatchard and Benedict, *ibid.*, **58**, 837 (1936).

(8) Goldman (*Ber.*, **20**, 2437 (1887)) and Meyer (*Ann.*, **379**, 62 (1911)) each report a melting point of 148°.

URBANA, ILLINOIS RECEIVED OCTOBER 14, 1939

[A COMMUNICATION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Chlorination of Butyl Trichloroacetates

BY HOWARD M. WADDLE AND HOMER ADKINS

The direct chlorination of *n*-butyl, *i*-butyl and *s*-butyl trichloroacetates seemed to offer a method for the preparation of chlorobutanols and of ascertaining the relative reactivity toward chlorine of hydrogens on primary, secondary and tertiary carbon atoms.[1]

Buffet found that *n*-butyl trichloroacetate could be rather rapidly chlorinated at 110–120° under the light from a 150-watt tungsten electric light bulb. Various monochlorobutyl trichloroacetates were formed which could be methanolyzed to the corresponding chlorobutanols.

(1) Geo. M. Buffet, Ph.D. Thesis, University of Wisconsin, Madison, 1933.

$$CCl_3CO_2C_4H_9 + Cl_2 \longrightarrow CCl_3CO_2C_4H_8Cl + HCl$$
$$CCl_3C_4H_8Cl + CH_3OH \longrightarrow CCl_3CO_2CH_3 + ClC_4H_8OH$$

Later experience showed that it was preferable to separate carefully the chloro-esters by fractional distillation and to saponify the pure esters, rather than to attempt to separate the alcohols obtained by methanolysis or hydrolysis of a mixture of esters.

n-Butyl, *i*-butyl and *s*-butyl trichloroacetates were prepared in 82 to 89% yields by refluxing two moles of trichloroacetic acid and four moles of the alcohol for six to eight hours. The excess alcohol and water were removed by distillation through a Vigreux column, 35 cm. in length. Emulsions are likely to be formed if the alcohol is not rather completely removed before the crude esters are

washed with 10% sodium carbonate solution. The esters were then washed with water, dried over calcium chloride and distilled under reduced pressure at temperatures no higher than 100°. An automatic separator proved useful in the preparation of *s*-butyl trichloroacetate.

The chlorinations were carried out in a liter, round-bottomed, Pyrex flask provided with three side arms. A stirring device, operating through a mercury seal, was placed in the neck of the flask. A thermometer well, an inlet tube for chlorine and a water-cooled reflux condenser were connected through the side arms of the flask. The chlorine passed through a wash bottle[2] containing sulfuric acid into a liter flask and then through a flowmeter and capillary tube into the bottom of the reaction mixture. The exit gases from the reaction mixtures passed up through a coil condenser.

The procedure for chlorination was as follows. Two moles of the ester (440 g.) was placed in the reaction flask and heated to 120° in an electrically heated and controlled oil-bath.[3] A 200-watt clear glass, tungsten light bulb was placed 5 cm. from the surface of the reaction flask which was immersed in the oil-bath to the top of the liquid in the flask. Chlorine was then passed in at the rate of 15 to 20 g. per hour, the reaction mixture being kept at 120 ± 2°. Chlorination was continued (seven to ten hours) until the increase in weight of the reaction flask corresponded to two moles of chlorine (69.9 g.). The product was water white.

The reaction mixtures after chlorination were separated into their components by the use of a packed column of the total reflux–partial take off variety. The packed section of the column was 18 mm. in diameter and 100 cm. in length surrounded by an evacuated jacket. The packing consisted of helices containing 1 to 2 turns, 7 mm. in diameter and made from glass rod 1 mm. in diameter. The air space about the evacuated jacket was electrically heated and maintained at a constant temperature by controlling the current passing through a heating unit of nichrome wire. The pressure within the column during fractionation was held constant by means of a manostat.[4]

The esters were distilled from a flask, immersed in an electrically heated and controlled oil-bath, and connected to the column by a ground glass joint. The procedure used in operating the column is well outlined by Morton.[5] The first distillation of a reaction mixture (510 g.) was carried out rather rapidly during thirty-six hours divided into three intervals. The second fractionation required sixty hours divided into 6 intervals, the reflux ratio being about 20 to 1. Ebullition tubes were not used.

Each of the three butyl trichloroacetates gave four fractions: A, unchanged ester, B and C, two different monochlorobutyl trichloroacetates, and D, a dichlorobutyl trichloroacetate. The weights of the fractions from chlorinated *n*-butyl trichloroacetate (510 g.) were A, 78 g., B, 158 to 175 g., C 93 g. and D, 50 g. From the chlorinated *i*-butyl ester (510 g.) the corresponding weights were A, 81 g., B, 118 to 122 g., C, 139 g. and D, 41 to 56 g., while from the chlorinated *s*-butyl ester (508 g.) the weights were for A, 83 to 84 g., B, 137 to 144 g., C, 122 to 130 g. and D, 21 to 37 g.

The fractions containing the mono- and dichlorobutyl trichloroacetates were washed with 2% sodium carbonate solution and with water, dried over calcium chloride and refractionated. The monochloro esters were rather rapidly distilled, with ebullition tubes, through a Vigreux column 7 cm. in length, while for the dichloro esters a modified Widmer with a spiral 12 cm. in length was used. Data on the physical properties of the various esters are given in Table I.

The ester was saponified at temperatures below 35° during the course of five to seven hours. The ester was rapidly stirred while an equivalent molecular amount of sodium hydroxide in a 10% solution in water was added over a period of several hours. After saponification was complete the solution was extracted continuously with ether for twelve hours. After removal of the ether the chloro-alcohol was distilled under reduced pressure through a modified Widmer column having a spiral 20 cm. in length. A capillary ebullition tube for the inlet of air was used in the distillation.

Chlorobutanols were obtained from five of the nine chloro esters which were isolated. Certain physical properties and the analyses of the alcohols, and the melting point and analyses of their phenyl urethans are given in Table I.

The lower boiling monochloro esters (the fractions labeled B) from the *i*-butyl and *s*-butyl esters reacted with sodium hydroxide much more slowly than in the case of the five esters referred to just above. Approximately one-half of the ester was recovered unchanged after reaction for several hours with a molecular equivalent of sodium hydroxide. *i*-Butyraldehyde was detected among the products from the saponification of the monochloro-*i*-butyl ester. The saponification of this latter ester (32 g.) was then attempted, using two molecular equivalents of sodium hydroxide at 75° for three hours. A stream of nitrogen was passed through the reaction mixture to remove *i*-butyraldehyde as rapidly as it was produced. The aldehyde (5 g.) was condensed in a trap surrounded with solid carbon dioxide. It was identified by boiling point and the formation of a 2,4-dinitrophenylhydrazone, m. p. 185°. There was also obtained 4 g. of a compound, b. p. 69–70° (7 mm.), which was halogen-free and appeared to be a glycol. It was not identified.

The saponification of the lower boiling monochloroester from *s*-butyl trichloroacetate gave no products boiling above 56° and only a small amount of that compound. No other liquid product was obtained by saponification with two moles of sodium hydroxide at 40°. Sufficient quantities of the fractions containing the dichloro esters from *i*-butyl and *s*-butyl trichloroacetates were not available for saponification studies.

The data given above may be summarized as follows. There remains after the reaction of one mole of chlorine with one mole of *n*-, *i*- or *s*-butyl trichloroacetate at 120° approximately 0.2 mole of unchanged ester, a little over 0.5 mole of monochloroesters and a few hundredths of a mole of

(2) McKenney, *Ind. Eng. Chem., Anal. Ed.*, **6**, 258 (1934).

(3) Waddle and Imhoff, *J. Chem. Ed.*, **15**, 191–192 (1938).

(4) Hershberg and Huntress, *Ind. Eng. Chem., Anal. Ed.*, **5**, 144 (1933).

(5) Morton, "Laboratory Technique in Organic Chemistry," McGraw-Hill Book Co., New York, N. Y., p. 83.

TABLE I

PHYSICAL PROPERTIES AND ANALYTICAL DATA

Compound	B. p. °C.	Mm.	$n^{25}D$	d^{25}_4	M_D Calcd.	M_D Found	Chlorine, % Calcd.	Chlorine, % Found
n-Butyl alcohol[a]	100–101	24	1.4495	1.266				
i-Butyl alcohol[a]	93–94	24	1.4456	1.255				
s-Butyl alcohol[a]	88–89	19	1.4440	1.252				
2-Chlorobutanol-1[a]	94–96	5	1.4728	1.390	51.03	51.24	55.8	55.3
4-Chlorobutanol-1[a]	113–116	5	1.4800	1.417	51.03	50.92	55.8	56.0
Dichlorobutanol-1[a]	127–131	5	1.4930	1.497	55.98	55.89	61.5	60.7
2-Chloro-2-Me-propanol-1[a]	80–81	5	1.4658	1.369	51.03	51.35	55.8	55.6
3-Chloro-2-Me-propanol-1[a]	98–99	5	1.4742	1.397	51.03	51.22	55.8	55.7
Dichloro-2-Me-propanol-1	101–105	5	1.4862	1.477	55.98	56.04	61.5	60.2
3-Chlorobutanol-2[a]	83–84	5	1.4671	1.373	51.03	51.34	55.8	55.8
1(?)-Chlorobutanol-2[a]	91–93	5	1.4713	1.395	51.03	50.89	55.8	55.8
Dichlorobutanol-2[a]	108–110	5	1.4850	1.475	55.98	55.06	61.5	61.7
2-Chlorobutanol-1	74–76	25	1.4410	1.062	27.06	26.99	32.7	33.3
4-Chlorobutanol-1	72–75	10	1.4551	1.125	27.06	26.18	32.7	36.0
Dichlorobutanol-1	87–93	6	1.4786	1.273	31.93	31.73	49.6	50.3
3-Chloro-2-Me-propanol-1	76–78	21	1.4460	1.083	27.06	26.74	32.7	33.2
1(?)-Chlorobutanol-2	56	12						
	68–70	27	1.4410	1.068	27.06	26.86	32.7	32.6

	M. p.	Carbon, %		Hydrogen, %	
2-Chlorobutanol-1[b]	52.5–53.5	58.02	58.10	6.20	6.37
4-Chlorobutanol-1[b]	54–55	58.02	58.16	6.20	6.44
3-Chloro-2-Me-propanol-1[b]	63.5–64	58.02	58.07	6.20	6.52
1(?)-Chlorobutanol-2[b]	78.5–79	58.02	58.03	6.20	6.42

[a] Trichloroacetate. [b] Phenyl urethan.

dichloroesters. About 25% of the original ester has not been accounted for except in intermediate fractions and the residue after distillation.

From each of the three butyl trichloroacetates two different monochlorobutyl esters have been produced and separated by fractionation. The structures tentatively assigned to these six alcohols, separated as trichloroacetates, are given below. The figures given after each formula represent the moles of ester isolated from the reaction of one mole of a butyl ester and one mole of chlorine.

I	$CH_3CH_2CHClCH_2OH$	0.33
II	$ClCH_2CH_2CH_2CH_2OH$	.19
III	$(CH_3)_2CClCH_2OH$	.24
IV	$ClCH_2CHCH_2OH$ (with CH_3 branch)	.27
V	$CH_3CHClCHOHCH_3$	.28
VI	$CH_3CH_2CHOHCH_2Cl$ or $ClCH_2CH_2CHOHCH_3$	.25

Four of the alcohols, I, II, IV and VI, have been obtained in a pure state in yields of 83, 86, 76 and 44%, respectively, from the saponification of the esters. The esters of the other two alcohols, III and V, underwent other reactions as well as saponification when attempts were made to prepare the alcohols.

The evidence for the structures suggested for the alcohols is as follows. The chlorobutanol believed to have the structure I was converted into the dichloride through the use of thionyl chloride and pyridine.[6] The dichlorobutane so obtained has a b. p. of 127°, $n^{25}D$ 1.4420, $n^{15}D$ 1.4468, which agrees with the values of b. p. 124° and $n^{15}D$ 1.4474 reported by Navez.[7] The 1,3-dichlorobutane is reported to boil somewhat higher.[8] It is quite possible that both the 2- and 3-chlorobutyl esters were produced by chlorination.

4-Chlorobutanol-1 was prepared from tetrahydrofuran[9] and its phenyl urethan compared with the phenyl urethan of the alcohol, II, believed to have that structure. The boiling points and refractive indices of the two samples of the alcohol and the melting points and mixed melting points of the phenyl urethans, 54–55°, showed them to be identical.

Formulas III and IV represent the only possible chloro-*i*-butanols. An ester of the alcohol IV would boil higher than an ester of the alcohol III, so that formula III is assigned to the alcohol

(6) Clark and Streight, *Proc. Roy. Soc. Canada*, **23**, III, 77 (1929).
(7) Navez, *Bull. soc. chim. Belg.*, **39**, 435 (1930).
(8) Fargher and Perkin, *J. Chem. Soc.*, **105**, 1356 (1914).
(9) Starr and Hixon, THIS JOURNAL, **56**, 1595 (1934).

of the lower boiling ester. The attempted saponification of this lower boiling ester gave *i*-butyraldehyde as the only definitely characterized product. The rearrangement of a chloro alcohol of the type of III to an aldehyde is an orthodox reaction.

All three of the possible chloro-*s*-butyl alcohols have been reported, but solid derivatives have not been prepared nor the physical properties of the alcohols carefully defined. 3-Chlorobutanol-2, b. p. 138–139° (753 mm.), was prepared by the addition of hypochlorous acid to butene-2.[10] 4-Chlorobutanol-2, b. p. 70° (13 mm.), has been prepared from methylmagnesium iodide and β-chloropropionaldehyde.[11] 1-Chlorobutanol-2, b. p. 52° (15 mm.), has been prepared by the reaction of chloroacetaldehyde and ethylmagnesium bromide.[12]

The 3-chloro alcohol would be the lowest boiling of the isomers, and would be the more unstable. It therefore seems probable that the lower boiling of the monochloro esters derived from *s*-butyl ester would be an ester of the 3-chloro isomer. All attempts to saponify this ester gave products such as would correspond to *sym*-dimethylethylene oxide. This is a not unexpected result for the ester of such an alcohol. It should be noted that the ester of similar structure from *i*-butyl trichloroacetate also failed to give a chloro alcohol upon saponification.

There is no adequate basis for deciding whether the chlorobutanol-2 isolated was the 1- or 4-chloro compound. The boiling point is close to that reported for the 1-chloro compound. It would appear that the 4-chloro compound boils somewhat higher.[10] The low yield of alcohol obtained by saponification also suggests the 1-chloro isomer since the 4-chloro alcohol would have a structure similar to 3-chloro-2-methylpropanol-1, which was obtained in excellent yield from its trichloroacetate.

(10) Henry, *Compt. rend.*, **145**, 499 (1907).
(11) Krassuski, *ibid.*, **145**, 763 (1905).
(12) Fourneau and Ramart-Lucas, *Bull. soc. chim.*, [4] **25**, 367 (1919).

Summary

The *n*-, *i*- and *s*-butyl trichloroacetates have been chlorinated and in each case two monochlorobutyl trichloroacetates have been separated as the major products of chlorination. The corresponding monochlorobutyl alcohols have been obtained in four cases by saponification of the esters while in two cases attempts at saponification failed to yield the alcohols.

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Relative Oxidation Potentials of Ketones

BY FRED W. COX[1] AND HOMER ADKINS

Ketones may be arranged in a series according to their strength as oxidizing agents, *i. e.*, of their oxidation potentials. A ketone high in the series will oxidize rather completely the alcohol corresponding to a ketone low in the series. In such a comparison the quinones will be at the top and the dialkyl ketones at the bottom of the series. For example, diphenoquinone is probably one of the most powerful oxidizing agents among the ketones while di-*i*-propyl ketone is one of the weakest. The quinones have been compared with each other by virtue of the fact that the reduction of a quinone to a hydroquinone is a strictly reversible process, and that an aqueous solution containing appreciable quantities of these two substances, and having a fixed hydrogen-ion concentration, establishes a definite and accurately determinable potential on a platinum electrode. A comparison of the oxidation potential may be expressed in volts, as for example 0.95 for diphenoquinone, 0.71 for *p*-benzoquinone, 0.48 for α-naphthoquinone and 0.15 for 9,10-anthraquinone.[2]

The present paper is concerned with the comparison of several ketones which are much weaker as oxidizing agents than the quinones referred to above. It is not possible as yet to express quantitatively their oxidation potentials. It must suffice to state their strength as oxidizing agents in terms of a standard ketone. However, it is hoped that the gap in the series of ketones between the quinones and benzophenone may be bridged by the study of ketones of intermediate oxidation po-

(1) Procter and Gamble Fellow, 1938–1939.
(2) Fieser in Gilman, "Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1938, p. 96.

tentials. It will then be possible to express the oxidation potentials of all members of the series in the same units.

The comparisons here reported are based upon the fact that a ketone and a secondary alcohol may be equilibrated, in the presence of aluminum *t*-butoxide, against the alcohol corresponding to the ketone and the ketone corresponding to the alcohol[3]

$$R_2CO + R'_2CHOH \rightleftharpoons R_2CHOH + R'_2CO$$

The general procedure for equilibration was as follows. Equimolecular amounts (0.01 mole) of a ketone and an alcohol were weighed into a test tube with a constricted neck. Fifteen ml. of toluene containing 2.5 g. of aluminum *t*-butoxide (0.01 mole) was added, the tube sealed off and suspended in a thermostat held at 100°. After a period of twenty to 620 hours a sample from the reaction mixture was analyzed by means of a polarograph.

In order to utilize the polarographic method of analysis at least one of the two ketones in the mixture must be unsaturated since saturated ketones do not show a depolarization potential. In the majority of cases benzophenone was the ketone upon which the analysis was based, while in other instances phenyl ketones carrying an ethyl, *n*-propyl, *i*-propyl, *n*-butyl or *n*-amyl group were used. Equilibrium in the reaction mixtures was always attained from both directions.

In the majority of cases approximately the same concentration of ketones was present after 150 to 200 hours no matter from which direction the reaction was run. For example, in the equilibration of benzophenone against phenyl *i*-propyl ketone, the concentration of benzophenone present after 150 hours was about 47.7 mole per cent. (the maximum deviation from the average being 1.8%) no matter whether the original reaction mixture contained Ph_2CO and *i*-PrCHOHPh or Ph_2CHOH and *i*-PrCOPh. However, in some cases equilibrium was not attained after 150 to 200 hours so that the period of reaction was prolonged to over 600 hours. For example, the concentration of benzophenone present in a reaction mixture varied as much as 7.6% after 200 to 250 hours, depending upon whether the reaction mixture originally contained Ph_2CO and *i*-BuCHOHPh or Ph_2CHOH and *i*-BuCOPh. However, after 600 hours the maximum deviation was 1.4%. After many comparisons had been made, it was found that while the concentration of a ketone was independent, after a suitable interval, of the direction from which the reaction proceeded, it was not independent of the time of reaction. For instance, in the comparison of benzophenone and phenyl *i*-propyl ketone there were variations from a value of 47.6% after 150 to 200 hours, to values of 53.3% after 200 to 250 hours, and 39.3% after 380 to 430 hours. It should be emphasized that each of these values could be duplicated within 1 or 2% from either direction, if the time interval was constant.

It is apparent that a side reaction was occurring which modified the concentration of ketones. This side reaction could not be a condensation for it will be shown in another paper that the ketones under consideration do not undergo such a reaction with aluminum *t*-butoxide. It is probable that the side reaction was of the type

$$3Ph_2CHOH + Al(OC_4H_9)_3 \longrightarrow 3Ph_2CO + 3C_4H_{10} + Al(OH)_3$$

The formation of aluminum hydroxide and butane was indicated by the fact that reaction mixtures in some cases became gelatinous and considerable pressure was developed within the tubes after a few hundred hours.

In order to test the oxidation of alcohols by aluminum *t*-butoxide a few experiments were made in which various phenyl carbinols (0.01 mole) were allowed to react with an equimolecular amount of aluminum *t*-butoxide in 15 ml. of toluene at 100° in a sealed tube for 132 hours. Ketones were produced to the following extent, based upon polarographic analysis, Ph_2CO 4%, EtCOPh 5.5%, *n*-PrCOPh 1%, *i*-PrCOPh 2.4%, *n*-BuCOPh 1.2%, *n*-AmCOPh 4.3%. None of the polarographical non-reducible ketones were studied from this standpoint because of the lack of a convenient method of analysis for the ketones, but it must be assumed that any of the alcohols might undergo oxidation to the extent of a few per cent. within one hundred hours.

In order to minimize the effect of the side reaction upon the concentration of ketones in the reaction mixture, the procedure was modified so that equilibrium would be reached in a shorter time. The reaction mixtures were made up containing *both* ketones and *both* alcohols under comparison, the concentrations in one set of reaction mixtures being somewhat to the "right" of the probable equilibrium concentrations, while the

(3) Adkins and Cox, THIS JOURNAL, **60**, 1151 (1938).

other set was somewhat to the "left." For example, the earlier work suggested that the concentration of benzophenone in equilibrium with diethyl ketone would be about 33 to 34% if it were not modified by a side reaction. Reaction mixtures were therefore made up which contained in one case 0.0025 mole of Ph_2CO, 0.0075 Ph_2CHOH, 0.0075 Et_2CO and 0.0025 of Et_2CHOH, and in the second case 0.0040 Ph_2CO, 0.0060 Ph_2CHOH, 0.0060 Et_2CO and 0.0040 Et_2CHOH, respectively. The first set of mixtures after ninety-six hours gave 32.3, 31.7 and 30.6% benzophenone, while the second set gave values of 30.7 and 32.2.

In only three cases in these later studies did the average of the values from reaction in one direction differ by more than about 1% from the average of the values attained from the other. Thus, equilibrium approximately was attained after a maximum of ninety-six hours and in many cases in much shorter lengths of time. In three mixtures containing di-*i*-propyl or di-*i*-butyl ketones reaction was so slow that even after ninety-six hours the values were from 2.5 to 6% apart. In calculating the relative reactivity of the ketones the average of the values from one direction with that from the other was taken as the true concentration of the ketones at equilibrium.

There is presented in Table I a summary of the experimental data upon which the relative reactivities given in Table II are based. For purposes of comparison the value of 1.00 is assigned to di-*i*-propyl ketone. All the other ketones studied, with possibly one exception, are stronger oxidizing agents than is the standard ketone. That is to say, in an equilibrium mixture there would be a higher concentration of the di-*i*-propyl ketone than of any of the other twelve ketones. Stated in another way, it may be said that di-*i*-propylcarbinol has the greatest tendency to be oxidized as compared with the various carbinols investigated, while cyclohexanol has the least tendency to be oxidized. It may be said that cyclohexanone has the highest oxidation potential, *i. e.*, it is endowed with more power as an oxidation agent than any of the other ketones investigated.

The first four columns of figures in Table II give the relative reactivity values as calculated from the experimental comparisons. The "relative reactivity" values are obtained, for example, by dividing the mole per cent. of benzophenone (24.1%) at equilibrium by the mole per cent. of di-*i*-propyl ketone (75.9%) to give a value of 0.32 for benzophenone.

In the case of the dialkyl ketones, which could not be equilibrated against di-*i*-propyl ketone because of the lack of a convenient and accurate method of analysis, the relative reactivities were calculated indirectly; *i. e.*, for diethyl ketone against benzophenone the ratio of diethyl ketone to benzophenone in the equilibrium mixture is 68.5/31.5, which when multiplied by the ratio of benzophenone to di-*i*-propyl ketone, 24.1/75.9, gives a value of 0.69 for the relative reactivity of diethyl ketone on the basis of di-*i*-propyl ketone being 1.00.

For ten of the ketones experimental comparisons have been made against two different ketones while diethyl ketone was equilibrated against four different ketones. In general it would appear that the oxidizing power of a ketone, relative to the standard ketone, is independent of the particular ketone with which it is compared in experiment. One exception is that the value for diethyl ketone against phenyl *n*-amyl ketone is 0.63, while the other three values for diethyl ketone are 0.69, 0.68 and 0.70. However, if the value for diethyl ketone is calculated through the benzophenone equilibria with diethyl ketone and with phenyl *n*-amyl ketone, then the value is 0.67, which is in excellent agreement with the other values. In a similar manner the value for dibutyl ketone may be raised from 0.92 to 0.96, which is in agreement with that expected for a dialkyl ketone.

The values given in the last column of Table II may thus be taken as fairly accurately depicting the relative tendency of a given ketone to oxidize an alcohol corresponding to one of the other ketones. The values for cyclohexanone and di-*i*-butyl ketone have been enclosed in parentheses to indicate that they are less certain than for the other ketones. The difficulty with di-*i*-butyl ketone is that it is reduced so slowly and di-*i*-butylcarbinol is oxidized so slowly that equilibrium was not obtained within the time limits used in the case of the other ketones and alcohols. The amount of di-*i*-butyl ketone present was 78% when equilibrium was approached from one direction and 72% when approached from the other. The average of these values, 75%, was assumed to be the concentration of the ketone at equilibrium.

TABLE I

COMPOSITION OF REACTION MIXTURES

Ketone A	Ketone B	Time, hrs.	(From B side) % Ketone A	(From B side) Av.	(From A side) % Ketone A	(From A side) Av.	Av. % A	Max. dev., %	Av. dev., %
Ph_2CO	PrCOPh	48	33.1	33.7	33.7	33.7	33.7	0.6	0.4
		96	34.3						1.2
Ph_2CO	*i*-PrCOPh	48	43.8	44.3	46.1	45.6	45.0	2.2	0.9
		96	44.7		45.0				2.0
Ph_2CO	EtCOPh	61	38.0	38.5	37.9	39.0	38.8	1.3	0.8
		94	38.9		40.1				2.1
Ph_2CO	*n*-BuCOPh	62		34.9	36.1	36.4	35.7	1.1	0.8
		91			36.8				2.2
		92	35.2		36.6				
		92	34.6		36.2				
Ph_2CO	*n*-AmCOPh	61	36.7	36.9	38.0	37.9	37.4	0.7	0.5
		94	37.0		37.8				1.3
Ph_2CO	Et_2CO	91		31.5	30.7	31.5	31.5	0.9	0.7
		96	32.3		32.3				2.2
		96	31.7						
		96	30.6						
Ph_2CO	*n*-Pr_2CO	38	24.6	24.9	25.0	25.1	25.0	1.8	0.8
		92	25.1		23.2				3.2
		92			26.5				
		92			25.7				
Ph_2CO	*i*-Pr_2CO	38	21.2	21.9	27.7	26.2	24.1	3.6	2.2
		62	22.9		26.3				9.1
		91	21.5		23.9				
		91	22.1		26.9				
Ph_2CO	*n*-Bu_2CO	38	23.7	24.3	23.5	23.7	24.0	0.9	0.5
		62	24.9		23.9				2.1
EtCOPh	*i*-Pr_2CO	91	33.2	32.2	35.0	33.9	33.1	1.9	1.1
		91	31.2		32.7				3.3
n-PrCOPh	Et_2CO	91	48.7	47.2	47.8	46.7	47.0	1.7	1.3
		91	45.6		45.6				2.8
n-PrCOPh	*n*-Pr_2CO	91	39.9	39.8	36.2	38.2	39.0	2.8	1.4
		91	39.6		40.2				3.6
n-PrCOPh	*i*-Pr_2CO	60	36.0	36.4		38.5	37.5	1.5	1.1
		60	36.8		38.5				2.9
		107			38.5				
n-PrCOPh	*n*-Bu_2CO	91	40.3	39.6	39.6	39.3	39.5	0.8	0.5
		91	38.9		38.9				1.3
i-PrCOPh	Et_2CO	48	33.9	35.6	34.5	36.3	36.0	3.1	2.0
		48	37.3		38.0				5.6
i-PrCOPh	*i*-Pr_2CO	60	27.8	27.6		28.5	28.1	0.9	0.5
		60	27.3		28.0				1.8
		107			29.0				
i-PrCOPh	*t*-BuCOMe	91	38.3	37.8		38.0	37.9	0.6	0.4
		91	37.3		38.0				1.1
n-BuCOPh	*i*-Pr_2CO	91	33.8	33.3	36.1	35.8	34.6	1.8	1.2
		91	32.8		35.4				3.5
n-AmCOPh	*i*-Pr_2CO	91		33.6	32.4	33.3	33.5	1.1	0.7
		96	34.1		34.1				2.1
		96	33.0						
n-AmCOPh	Et_2CO	96	44.0	44.1	44.4	44.6	44.4	0.4	0.3
		96	44.1		44.8				0.7
Ph_2CO	*t*-BuCOMe	62	35.3	33.8		35.2	34.5	2.2	1.3
		91	32.4						
		96	34.3		36.7				3.8
		96	33.1		33.6				

TABLE I (*Concluded*)

Ketone A	Ketone B	Time, hrs.	(From B side) % Ketone A	Av.	(From A side) % Ketone A	Av.	Av. % A	Max. dev., %	Av. dev., %
Ph_2CO	*i*-Bu_2CO	24	23.0		29.0		26.5		
		24	23.1	23.1	30.8	29.9			
		72	21.2	22.1	27.0	26.9	24.5		
		72	22.9		26.8				
i-PrCOPh	*i*-Bu_2CO	24	23.2		36.3		29.8		
		48	21.4	22.0	27.7	27.9	25.0		
		110	21.5		28.1				
		110	23.0						
Ph_2CO	Cyclohexanone	24	58.9		65.6		62.3		
		48	63.0		58.4		60.7		
		92	56.8	56.3	55.6	56.4	56.4		
		92	55.7		57.2				
i-PrCOPh	Cyclohexanone	21	65.8		70.4		68.1		
		48	57.2		59.2		58.7		

TABLE II

RELATIVE REACTIVITIES OF VARIOUS KETONES

Ketone	Other ketone in equilibrium mixture: *i*-Pr_2	Ph_2	*n*-PrPh	*i*-PrPh	*n*-AmPh	Av. Value
Cyclohexanone		(0.19)		(0.18)		(0.19)
Ph_2CO	0.32					.32
i-PrCOPh	.39	.39				.39
EtCOPh	.50	.51				.51
n-AmCOPh	.50	.53				.52
n-BuCOPh	.53	.57				.55
n-PrCOPh	.60	.63				.62
t-BuCOPh		.63		.64		.64
Et_2CO		.69	0.68	.70	0.63	.68
i-Bu_2CO		(.93)		(.92)		(.93)
n-Pr_2CO		.95	.94			.95
n-Bu_2CO		1.01	.92			.97
i-Pr_2CO	1.00	1.00	1.00	1.00	1.00	1.00

The difficulty with cyclohexanone is that it so readily undergoes condensation

$$2C_6H_{10} \rightleftharpoons HOC_6H_{10}C_6H_9O \rightleftharpoons C_6H_9C_6H_9O + H_2O$$

Cyclohexylidene–cyclohexanone, the final condensation product, apparently was not formed, since this compound would show up on a polarographic analysis, but it is possible that the hydroxy ketone first formed would modify the oxidation reduction equilibrium. Possibly the value 0.19 assigned in the table to cyclohexanone is a little too low, but it certainly is not higher than 0.24.

An examination of the data in the last column of Table II reveals several general tendencies rather clearly. The diaryl ketones are better oxidizing agents than the alkyl aryl ketones and they in turn are better oxidizing agents than the majority of the dialkyl ketones. However, there are marked differences among the aliphatic ketones. The *t*-butyl group has an effect markedly similar to an aryl group, for pinacolone and butyrophenone have the same value when they are compared against benzophenone. Diethyl ketone is a stronger oxidizing agent than are dipropyl and dibutyl ketones. The difference between alkyl groups is also shown by the fact that *i*-propyl phenyl ketone has a value of 0.39, while the corresponding *n*-propyl phenyl ketone has a relative reactivity of 0.60 or more.

Most striking of all is the fact that the saturated ketone, cyclohexanone, has an oxidation potential higher than any other ketone, even than the highly unsaturated ketone, benzophenone.

In general there is a parallelism between the depolarization potential or "reduction potential" as measured on a polarograph and the strength of a ketone as an oxidizing agent as determined by equilibration. That is, the aliphatic ketones have a high depolarization potential and a low oxidation potential while the quinones have a very low depolarization potential and a high oxidation potential.[2] However, the depolarization potential cannot be safely used as a guide in predicting the strength of a ketone as an oxidizing agent. For example, the propyl phenyl ketones give practically identical values for depolarization potentials (1.60 to 1.61 volts) while they are quite different as oxidizing agents as noted in a preceding paragraph. An even greater discrepancy is found in the case of cyclohexanone, whose depolarization potential is so high that it cannot be measured, yet it is a stronger oxidizing agent than any of the alkyl aryl ketones, all of which show depolarization potentials.

It must be kept clearly in mind that the oxidation potential of a ketone cannot be considered apart from the reducing power of the alcohol corresponding to it. In this paper for the sake of simplicity reference has been made particularly

to the oxidation potential of a ketone rather than to the reduction potential of the alcohol, but in reality one cannot measure the one tendency without the other. In the systems under investigation the alcohols are present at least in part as aluminum alkoxides and the ketones as addition products with aluminum alkoxides. Tendencies to form these compounds probably vary among the alcohols and ketones under consideration so that the relative reactivities of the ketones as oxidizing agents may be thus modified.

Preparation of Ketones and Alcohols.—The various alkyl phenyl ketones were made by the Friedel and Crafts synthesis, using the proper acid chloride (100 to 150 g.) in excess benzene (130 to 340 ml.) with aluminum chloride (122 to 312 g.). The yields were of the order of 80% of the theoretical amount. Di-*n*-butyl ketone was made as by Breise and McElvain.[4] Benzophenone and pinacolone were made as described in "Organic Syntheses."[5]

All of the six phenyl carbinols as well as methyl-*t*-butylcarbinol, di-*i*-butylcarbinol and di-*n*-butylcarbinol were made by hydrogenation of the corresponding ketones dissolved in ethanol, over Raney nickel or copper chromite. The reaction was stopped after one mole of hydrogen per mole of ketone had been absorbed in the case of the phenyl ketones, otherwise hydrogenolysis of the hydroxy group will occur. The hydrogenations were made under 200 to 300 atm. at temperatures between 95 and 150°. From one-half to three hours were required, using 1 to 2 g. of catalyst per 0.5 mole of ketone. The yield of alcohols averaged 87% of the theoretical amount.

i-Propylphenylcarbinol was also made by reduction of the ketone with aluminum *i*-propoxide, but the yield was only 60%. Both of the propyl phenyl carbinols were also made by the Grignard reaction, the yields being about 88% of the theoretical amount.

The ketones and alcohols not referred to above were obtained from the Eastman Kodak Company.

The reaction mixtures were analyzed as follows. A sample (0.7 ml.) from the reaction mixture was pipetted into a weighed 25-ml. Erlenmeyer flask and weighed. The sample was diluted to approximately 25 ml. with 92.5% isopropyl alcohol and again weighed. The mixture was shaken thoroughly and allowed to stand for several hours during which time it was repeatedly shaken. A sample (1 ml.) of the clear, supernatant liquid was withdrawn and added to a polarographic cell containing 3 ml. of 92.5% isopropyl alcohol and 1 ml. of a 0.84 *N* solution of tetramethylammonium hydroxide.

Three polarographic curves were then made for the solution, and the average wave height computed by the Borcherdt "b" method.[6] Comparing the wave heights so obtained to a graph giving the relationship of wave height to concentration (from Table III) gave the moles, *C*, of the reducible ketone in the polarographic cell. From *C* was calculated the percentage, *K*, of the polarographically reducible ketone in the equilibrium mixture by means of the following relationship

$$K = \frac{C \times 5}{1000} \cdot \frac{V}{d} \cdot \frac{W}{S} \cdot \frac{100}{B}$$

where *V* is the weight of the sample plus the weight of the isopropyl alcohol added; *W* is the total weight of the materials placed in the sealed tube; *S*, the weight of the 0.7-ml. sample; *B*, the moles of the ketone possible of existing in the reaction mixture (0.01 mole in the experiment as carried out above); and *d*, the density of the isopropyl alcohol solution of the sample. The constant "5" represents the volume of liquid in the polarographic cell, "1000," the number of ml. in a liter, and "100" is the factor for converting to percentage. For all practical purposes the value of *d* may be considered to be the same as that for the density of the isopropyl alcohol solution used in the dilution.

In the cases where there were two polarographically reducible ketones in the reaction mixture, the older "ratio of wave heights" method was employed in the analysis,[6] the single ketone method being useful as an alternate method for verifying the value obtained by the ratio method.

The reaction mixtures always contained one of the six phenyl ketones listed in Table III. There are given in Table III the measured wave heights for two or three polarograms for each of three concentrations for each of the six ketones. The data show very clearly the reproducibility of the polarograms and the constancy of the relationship of wave height to concentration of any of the

TABLE III

RELATIONSHIP OF WAVE HEIGHTS TO CONCENTRATION OF VARIOUS KETONES

Concn. of ketone	3.2×10^{-3}	2.0×10^{-3}	0.8×10^{-3}
	Wave heights in cm.		
Ph_2CO	15.78	9.96	3.97
	15.80	9.88	3.98
	15.75	9.90	3.94
EtCOPh	15.76	10.12	3.97
	15.89	10.18	3.98
n-PrCOPh	15.78	9.86	3.84
	15.66	9.70	3.84
	15.60	9.72	3.96
i-PrCOPh	15.80	9.95	3.92
	15.91	9.95	3.92
	15.80	9.82	3.97
n-BuCOPh	15.78	9.98	4.00
	16.03	9.98	3.97
	15.78	9.98	3.98
n-AmCOPh	15.69	9.70	4.00
	15.62	9.70	4.03
			4.00
Av. value for six ketones	15.79	9.92	3.96
Max. dev. in cm.	0.24	0.22	0.12
Av. dev. in cm.	.09	.11	.04
Av. dev. in %	.6	1.1	.9
Ratio of wave heights	3.99	2.50	1.00
Ratio of concns.	4.00	2.50	1.00

(4) Breise and McElvain, THIS JOURNAL, **55**, 1697 (1933).

(5) "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1932, pp. 89 and 451.

(6) Borcherdt, Meloche and Adkins, THIS JOURNAL, **59**, 2173 (1937).

six ketones. As noted in the earlier paper, acetophenone shows an anomalous behavior.

The relationship of wave height to concentration of ketone was found to be independent of the presence of toluene, *t*-butyl alcohol, aluminum hydroxide, and another ketone, or alcohol such as was known to be present in the reaction mixtures. However, the relationship is not independent of the concentration of water or tetramethylammonium hydroxide in the polarographic cell. The relationship is not independent of the characteristics of the particular capillary electrode.

Summary

Thirteen representative ketones have been compared with each other as oxidizing agents. A numerical statement of the result of the comparison is given in the last column of Table II. The comparisons were made by equilibrating two ketones against each other in the presence of aluminum *t*-butoxide and the alcohols corresponding to the ketones. The concentration of the ketones at equilibrium was determined by means of a polarograph.

MADISON, WISCONSIN RECEIVED SEPTEMBER 28, 1939

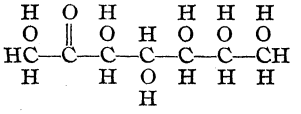
[CONTRIBUTION FROM THE LABORATORY OF BIOLOGICAL CHEMISTRY, LOYOLA UNIVERSITY SCHOOL OF MEDICINE]

The Reduction Products of *d*-Glucoheptulose[1]

BY FRED L. HUMOLLER, STANLY J. KUMAN AND FRED H. SNYDER

In 1928 Bertrand and Nitzberg[2] prepared *l*-glucoheptulose (designated by them as α-glucoheptulose) by the action of *Bact. xylinium* on α-glucoheptitol. In their studies on the structure of this ketoheptose they subjected it to the action of sodium amalgam. From the reaction products they isolated α-glucoheptitol and a substance which they named α-glucoheptulitol. This new substance melted at 144° and showed a specific rotation of −2.24°.[3] Later Khouvine and Nitzberg[4] repeated the work of Bertrand and Nitzberg and also obtained α-glucoheptulitol as one of the reduction products of *l*-glucoheptulose. They assumed, though not without reservations, that α-glucoheptulitol was either β-*d*-glucoheptitol or β-*l*-glucoheptitol.

In 1930 Austin[5] prepared *d*-glucoheptulose by the rearrangement of α-*d*-glucoheptose in lime water. Because of its method of preparation and because of the identity of its osazone with that obtained from α-*d*-glucoheptose, Austin assigned to *d*-glucoheptulose the formula



From its formula it can be seen that *d*-glucoheptulose should yield upon reduction of its ketone group α-glucoheptitol or β-*d*-glucoheptitol, or both, provided the structure which Austin assigned to this ketose is correct.

However, when Khouvine and Nitzberg[6] reduced *d*-glucoheptulose with sodium amalgam, they obtained α-glucoheptitol and the enantiomorph of α-glucoheptulitol but not β-*d*-glucoheptitol as predicted by Austin's formula. This new substance, which they called α-*d*-glucoheptulitol, melted at 143–143.5° and showed a specific rotation of +2.10°. From their studies on the structure of this substance they came to the conclusion that it was not identical with either β-*d*-glucoheptitol or β-*l*-glucoheptitol, but that it might be a heptitol of unknown structure. They suggested that the glucoheptulitols might be formed by the local concentration of alkali during the reduction with sodium amalgam. This view was strengthened by the fact that when they reduced *d*-glucoheptulose catalytically no α-*d*-glucoheptulitol was obtained but only the two glucoheptitols predicted by Austin's formula.[7]

In view of the findings of the French workers it seemed desirable to us to extend their studies on the structure of the glucoheptulitols. For that purpose *d*-glucoheptulose was prepared by the rearrangement of α-*d*-glucoheptose, using Austin's method[5] with some modifications. These modifications were introduced in the separation of the

(1) These studies, a portion of which was reported on the program of the meeting of the American Chemical Society in Milwaukee, September, 1938, were abstracted in part from a dissertation submitted by Mr. Kuman to the Graduate School of Loyola University in partial fulfilment of the requirements for the degree of Master of Science.

(2) Bertrand and Nitzberg, *Compt. rend.*, **186**, 925 (1928).

(3) Bertrand and Nitzberg, *ibid.*, **186**, 1172 (1928).

(4) Khouvine and Nitzberg, *ibid.*, **196**, 218 (1933).

(5) Austin, THIS JOURNAL, **52**, 2106 (1930).

(6) Khouvine and Nitzberg, *Compt. rend.*, **198**, 985 (1934).

(7) Khouvine, *ibid.*, **204**, 983 (1937).

ketoheptose from the unchanged aldoheptose. Whereas Austin had carried out this separation by oxidizing the unchanged aldoheptose with bromine and separating the salt of the aldonic acid from the ketoheptose by alcohol, advantage was taken of the fact that diphenylmethane-dimethyldihydrazine reacts very readily with certain aldoses at room temperature but does not react with ketoses.[8] By means of this reagent it was easily possible to separate the ketose nearly quantitatively from the aldose.

d-Glucoheptulose, prepared in this manner, proved to be identical with a sample left by the late Dr. Austin. The reduction of this ketose was carried out with sodium amalgam at room temperature in a medium kept faintly acid to litmus by frequent additions of sulfuric acid. Several reductions were carried out and in all but one case α-*d*-glucoheptulitol was one of the products of the reaction, the only other crystalline product which could be isolated being β-*d*-glucoheptitol. In one case both α-glucoheptitol and β-*d*-glucoheptitol were obtained along with α-*d*-glucoheptulitol. Both glucoheptitols were identified by comparing their physical constants with those of the respective glucoheptitols prepared by the reduction of the crystalline aldoheptoses and with the constants given in the literature.

The α-*d*-glucoheptulitol obtained, after having been recrystallized three times from absolute ethanol, melted at 141°[9] and showed a specific rotation of +2.04° in water. Further recrystallizations from ethanol failed to change these constants. The molecular weight of α-*d*-glucoheptulitol, as determined by the cryoscopic method, was found to be 192. An elementary analysis of this substance for carbon and hydrogen gave values which differed from those calculated for a heptitol by amounts greater than could be accounted for by experimental errors (Table I). Attempts to determine the number of hydroxyl groups in α-*d*-glucoheptulitol were unsuccessful, for in every attempt to prepare the acetate of glucoheptulitol only the heptaacetate of α-glucoheptitol was obtained. The identity of this heptaacetate was proved by elementary analysis, melting point, absence of optical rotation and melting point when mixed with a sample of pure heptaacetate of α-glucoheptitol. In the same manner every attempt to prepare a trityl derivative of α-*d*-glucoheptulitol yielded as the only crystalline product a substance which was proved to be identical, according to the standards mentioned in the case of the acetate, with the ditrityl derivative of α-glucoheptitol.

TABLE I

ELEMENTARY ANALYSIS OF α-*d*-GLUCOHEPTULITOL

% C	% H	Remarks
39.37	7.80	Bertrand and Nitzberg, *Compt. rend.*, **186**, 1773 (1928)
40.54	7.51	Humoller, Kuman and Snyder, av. of 11 macro-analyses
40.50	7.40	Schoeller, Berlin, Germany (com. analyst), av. of 2 micro-analyses
39.61	7.60	Values calcd. for a heptitol

(8) Von Braun, *Ber.*, **43**, 1495 (1910); **50**, 42 (1917).

(9) All melting points obtained by the authors were determined in a capillary glass tube suspended in a bath of sulfuric acid and are not corrected for stem exposure. The French workers used the bloc Maquenne for their melting point determinations.

In further studies to elucidate the structure of α-*d*-glucoheptulitol it was subjected to the action of acid and alkali. Boiling α-*d*-glucoheptulitol with 0.1 *N* sulfuric acid for thirty minutes left it totally unchanged. Similarly, boiling it with 10% barium hydroxide for ninety minutes did not produce any change, since the unchanged glucoheptulitol could be isolated from the solution. However, when α-*d*-glucoheptulitol was boiled with 10% sulfuric acid for seventy-five minutes, some reaction did take place, for the only crystalline substance which could be isolated from the solution was α-glucoheptitol besides a small quantity of unchanged glucoheptulitol.

Considering all the properties of glucoheptulitol thus far mentioned, one might be tempted to assume that this substance is an anhydride of α-glucoheptitol, crystallizing as four molecules of anhydride with three molecules of water. It would be necessary to assume three molecules of water of crystallization in order to satisfy the values obtained for carbon and hydrogen in the elementary analysis of α-*d*-glucoheptulitol.[1] It is, however, difficult to visualize a substance containing water of crystallization which can be recrystallized repeatedly from anhydrous solvents and which can be heated in a high vacuum at 100° without any loss of this water of crystallization.

The conclusion, therefore, seems justifiable that α-*d*-glucoheptulitol is not a pure chemical substance but consists of mixed crystals, made up very largely of α-glucoheptitol plus a small amount of an optically active impurity. This latter substance is probably a decomposition product of *d*-glucoheptulose formed during the reduction of the ketose. This conclusion has been reached in

spite of three statements appearing in the literature: (a) The French workers in their several papers on the properties and structure of the glucoheptulitols state that they are pure substance and probably are heptitols of unknown structure; (b) Elsner in Tollens' "Handbook on Carbohydrates"[10] assumes that α-glucoheptulitol is identical with β-*d*-glucoheptitol; (c) and the Armstrongs in their monograph on carbohydrates[11] state that α-glucoheptulitol is a heptitol not identical with the β-glucoheptitols.

Proof of the validity of the conclusion that α-*d*-glucoheptulitol consists of mixed crystals of α-glucoheptitol with a small amount of an optically active impurity is furnished by the solubility studies shown in Table II. As can be seen from this table, when α-glucoheptitol and β-*d*-glucoheptitol or α-*d*-glucoheptulitol and β-*d*-glucoheptitol are dissolved together in methanol their solubilities are additive or nearly so. However, quite different results were obtained when the solubility of α-glucoheptitol and of α-*d*-glucoheptulitol as well as that of a mixture of these two substances was determined. A saturated solution of α-*d*-glucoheptulitol contained 63.5 mg. of substance per 10 ml. and a saturated solution of α-glucoheptitol in the same solvent contained 69.9 mg. of substance. If now a solution of methanol was saturated with respect to both α-glucoheptitol and α-*d*-glucoheptulitol, it contained 71.3 mg. of solids, or the same amount, within limits of experimental error, as a saturated solution of α-glucoheptitol alone in methanol. In other words, a solution saturated with respect to α-glucoheptitol is also saturated with respect to α-*d*-glucoheptulitol.

Experimental

Preparation of *d*-Glucoheptulose.—α-*d*-Glucoheptose was rearranged in lime water according to the method of Austin,[5] and from the rearrangement a mixture of *d*-glucoheptulose and α-*d*-glucoheptose was obtained. An aqueous solution of 278 g. of this material in 1500 ml. of solution was prepared. Iodimetrically it was found that the solution contained 67.5 g. of aldoheptose. To this solution was added 58 g. of diphenylmethane-dimethyldihydrazine dissolved in 1500 ml. of 95% ethanol, and the solution allowed to stand overnight. The precipitate of the dihydrazone of α-*d*-glucoheptose was filtered off and washed with 100-ml. portions of ethanol: yield 52 g.; m. p. 167°.

To the combined filtrate and washings obtained, an excess of formaldehyde was added in order to remove the uncombined diphenylmethane-dimethyldihydrazine. After standing at room temperature overnight, the dihydrazone of formaldehyde was filtered off and discarded. The filtrate was concentrated to a small volume under reduced pressure. It was then rediluted and redistilled several times to remove all traces of formaldehyde. The formaldehyde-free sirup was then taken up in 300 ml. of a 7:3 mixture of methanol and ethanol. Upon seeding and cooling the system soon solidified to a crystalline mass. In this way 212 g. of crude *d*-glucoheptulose, m. p. 163°, was obtained and recrystallized to melt at 169°.

Reduction of *d*-Glucoheptulose.—Twenty grams of *d*-glucoheptulose was reduced with sodium amalgam at room temperature in the usual manner. After removing the sodium sulfate with ethanol, the system was concentrated to a thin sirup which was taken up in 100 ml. of boiling anhydrous ethanol. Upon cooling, a precipitate consisting of fine needles aggregating in rosets began to form. After standing in the refrigerator overnight, the crystals were filtered off, washed with cold ethanol and dried *in vacuo* to give 10 g. of Crop I, melting at 139°. The mother liquors were concentrated to a sirup and taken up in 50 ml. of boiling anhydrous ethanol. Upon standing in the refrigerator overnight the solution yielded 4 g. of crystalline material as Crop II, m. p. 116°, consisting of small rectangles and fine needles.

Crop I was dissolved in 20 ml. of water, filtered through hardened filter paper, concentrated to a thin sirup under reduced pressure and taken up in 100 ml. of boiling absolute ethanol. After chilling the solution for several hours 9 g. of crystalline material was obtained which melted at 141°. Three subsequent recrystallizations from ethanol as well as recrystallizations from anhydrous methanol and from aqueous dioxane failed to alter the melting point of this substance. It was optically active, $[\alpha]^{28}D$ +2.04° (*c*, 0.760; *l*, 2; H_2O). This substance is therefore α-*d*-glucoheptulitol.

Crop II was dissolved in a small quantity of boiling methanol, filtered and allowed to crystallize. Its melting point after this treatment was 119°. Another recrystallization from the same solvent brought the melting point up to 125°, but under the microscope two types of crystals still could be seen. Through fractional crystallization from hot methanol four different crops were obtained: Crop IIa, m. p. 129°, Crop IIb, m. p. 128°, Crop IIc, m. p. 126°, Crop IId, m. p. 126°. Crops IIa and IIb were combined and recrystallized from methanol to yield a product which crystallized in small rectangular plates melting at 129°. Crop IIc was recrystallized twice from methanol to yield a substance melting at 129°. All three crops were combined and recrystallized from methanol to yield 1 g. of small rectangular plates, m. p. 129°. They showed a slight optical activity, $[\alpha]^{25}D$ +0.62° (*c*, 1.004; *l*, 2; H_2O). When mixed with a sample of β-*d*-glucoheptitol, obtained by the reduction of crystalline β-*d*-glucoheptose, it melted at 129°. The substance therefore is β-*d*-glucoheptitol.

Crystals of Crop IId when mixed with crystals of β-*d*-glucoheptitol melted at 115°; when mixed with crystals of α-glucoheptitol (m. p. 129°) they melted at 127°. No op-

(10) Tollens-Elsner, "Kurzes Handbuch der Kohlenhydrate," 4th ed., Verlag Johann Ambrosius Barth, Leipzig, Germany, 1935, p. 407.

(11) E. F. Armstrong and K. F. Armstrong, "The Carbohydrates," 5th ed., Longmans, Green and Co., London, 1934, p. 148.

tical rotation was observed. Presumably Crop IId consisted of impure α-glucoheptitol.

Effect of Acid upon α-*d*-Glucoheptulitol.—Six grams of α-*d*-glucoheptulitol was dissolved in 30 ml. of 10% sulfuric acid and boiled under the reflux for seventy-five minutes. The solution was decolorized with charcoal and its specific rotation was found to be $[\alpha]^{25}D$ −1.83°. The filtrate, obtained after removal of the sulfate ions as barium sulfate, was concentrated to a thin sirup. This sirup was taken up in 85 ml. of hot absolute ethanol. After the solution was cooled, copious crystallization occurred. The crystals were filtered off and after having been dried *in vacuo* at room temperature they weighed 3 g. After three recrystallizations the substance melted at 129° and was found to be optically inactive. A mixture of some of these crystals with pure α-glucoheptitol melted at 129°. Hence this substance is α-glucoheptitol. The mother liquors from the first crystallization of this crop were concentrated to a thin sirup and taken up in absolute ethanol. On cooling a second crop, weighing 0.5 g., was obtained. This crop showed a melting point of 138° and a specific rotation of $[\alpha]^{25}D$ +2.4° (*c*, 0.480; *l*, 1; H_2O), hence it consisted of impure α-*d*-glucoheptulitol. The mother liquors of this crop were strongly levorotatory. They were not investigated any further.

Treatment of α-*d*-glucoheptulitol with 0.1 *N* sulfuric acid at boiling temperature had no effect upon the substance, for it could be recovered unchanged nearly quantitatively.

Effect of Barium Hydroxide upon α-*d*-Glucoheptulitol.—Four grams of α-*d*-glucoheptulitol was dissolved in 30 ml. of 10% barium hydroxide solution and boiled for ninety minutes. After removing the barium as the sulfate the solution was concentrated to a thin sirup under reduced pressure. The sirup was taken up in 50 ml. of boiling ethanol and allowed to crystallize. After drying *in vacuo* at room temperature the crystals weighed 3.1 g. They showed a melting point of 139° and when mixed with a sample of the starting material the melting point remained unchanged.

Reaction of α-*d*-Glucoheptulitol with Acetic Anhydride.—Four grams of α-*d*-glucoheptulitol was heated with acetic anhydride and fused zinc chloride in the usual manner.[12] The product obtained crystallized in rhombic plates, and after one recrystallization from ethanol the crystals melted at 115°. The yield of acetate, starting with 4 g. of α-*d*-glucoheptulitol, was 6 g. The acetate was optically inactive. A mixture of this acetate with the heptaacetate prepared from crystalline α-glucoheptitol did not show any depression of the melting point.

Anal. Calcd. for $C_{21}H_{30}O_{14}$: C, 49.79; H, 5.97. Found: C, 49.65; H, 6.08.

Similar results were obtained when the milder pyridine method of acetylation[13] was used. Again the only crystalline product obtained was found to be identical with α-glucoheptitol heptaacetate.

Reaction of α-*d*-Glucoheptulitol with Trityl Chloride.—The trityl derivative of α-*d*-glucoheptulitol was prepared in the usual manner.[14] When 2 g. of α-*d*-glucoheptulitol was allowed to react with 6 g. of trityl chloride in 25 ml. of anhydrous pyridine according to this procedure, there was isolated a crystalline substance. After three recrystallizations from a 2:1 mixture of methanol and ethanol, it weighed 3.1 g. and showed a melting point of 142–143°. The substance was optically inactive. Mixed with a sample of the dityrityl derivative prepared from α-glucoheptitol (m. p. 142–143°), it showed no depression of the melting point.

Anal. Calcd. for $C_{45}H_{44}O_7$: C, 77.57; H, 6.37. Found: C, 77.82; H, 6.47.

Solubility Studies.—The solubility of α-*d*-glucoheptulitol alone or when mixed with one of the glucoheptitols was determined by suspending an excess of the substances listed in Table II in 30 ml. of anhydrous methanol. The suspensions, contained in tightly stoppered 1 × 8″ (2.5 × 20 cm.) test-tubes, were placed into a shaking machine which operated within an incubator set at 37 ± 1°. The suspensions were shaken for two days and then filtered as quickly as possible. Then 10-ml. portions of the filtrate were pipetted into weighed evaporating dishes and the solvent driven off by heating the dishes on a steam-bath. The dishes were then dried to constant weight in a vacuum desiccator. The results of this study are listed in Table II.

TABLE II

SOLUBILITY STUDIES ON α-*d*-GLUCOHEPTULITOL[a]

Substance	Mg. in 10 ml. of methanol		Av.	Calcd.[b]
β-*d*-Glucoheptitol	47.8	48.0	48.0	
	48.2	48.0		
α-*d*-Glucoheptulitol	63.2	63.5	63.5	
	63.7			
α-Glucoheptitol	69.7	70.0	69.9	
	69.6	70.2		
α-Glucoheptitol + α-*d*-Glucoheptulitol	70.3	71.4	71.3	133.4
	72.0	71.6		
β-*d*-Glucoheptitol + α-*d*-Glucoheptulitol	110.0	109.4	109.8	111.5
	110.2	109.7		
β-*d*-Glucoheptitol + α-Glucoheptitol	112.7	112.3	112.6	117.9
	112.8	112.5		

[a] These studies were carried out in an incubator kept at 37.0 ± 1°. [b] These values were obtained by adding the average solubility of each constituent of the mixture.

Molecular Weight of α-*d*-Glucoheptulitol.—The molecular weight of α-*d*-glucoheptulitol was determined by the cryoscopic method. When 1.0009 g. of the substance was dissolved in 24.95 g. of water, the following lowering of the freezing point of the solution was observed: 0.388°; 0.383°; 0.389°; 0.389°; average, 0.387°. Substituting the average value, 0.387°, in the formula Molecular Weight = kw/dW, where w is the number of grams of solute dissolved in W g. of solvent, thereby causing a lowering of its freezing point of d degrees, and using 1860 as the value for k, the molecular weight of α-*d*-glucoheptulitol was found to be 192.3.

Summary

1. It has been shown that diphenylmethanedimethyldihydrazine is a convenient reagent to

(12) Fischer, *Ann.*, **270**, 64 (1892).
(13) Behrend and Roth, *Ann.*, **331**, 359 (1904).
(14) Helferich, Moog and Juenger, *Ber.*, **58**, 872 (1925).

separate mixtures of *d*-glucoheptulose and α-*d*-glucoheptose.

2. When *d*-glucoheptulose was reduced with sodium amalgam β-*d*-glucoheptitol and a substance which Khouvine and Nitzberg have called α-*d*-glucoheptulitol were obtained.

3. Evidence has been presented to show that the substance called α-*d*-glucoheptulitol is not a pure chemical entity but consists of mixed crystals of α-glucoheptitol plus a small amount of an optically active impurity. This evidence is, briefly:

From the values obtained in elementary analyses and in molecular weight determinations it is not possible to write a formula which is consistent with the chemical behavior of the substance.

The substance when heated in a 10% solution of sulfuric acid goes over into α-glucoheptitol.

The substance when treated with acetic anhydride and a catalyst forms the heptaacetate of α-glucoheptitol.

The substance when treated with trityl chloride in the presence of pyridine forms the ditrityl derivative of α-glucoheptitol.

A saturated solution of α-glucoheptitol in methanol is also saturated with respect to this substance.

CHICAGO, ILLINOIS RECEIVED AUGUST 26, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE UNIVERSAL OIL PRODUCTS COMPANY]

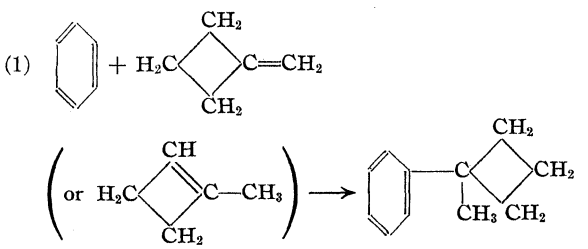
Reaction of Benzene with Methylcyclobutene and Methylenecyclobutane in the Presence of Sulfuric Acid[1]

BY V. N. IPATIEFF AND HERMAN PINES

The reaction between alkenes and aromatic hydrocarbons proceeds readily in the presence of various condensing agents.[2] Of the cycloalkenes only those containing five- and six-membered rings have been studied.

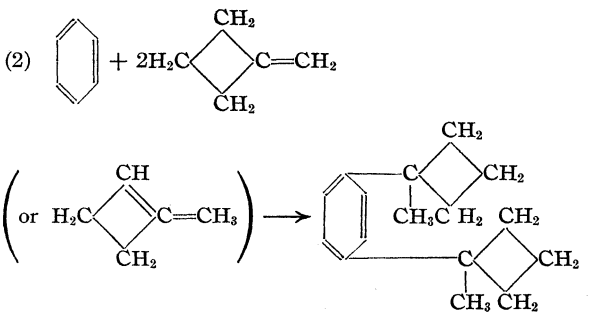
We were interested in studying the reaction of benzene with a cycloalkene containing a four-membered ring, in order to determine whether methylcyclobutylbenzene would be formed and whether a cyclobutyl group attached to a phenyl group is more stable than an unarylated cyclobutane. It was found that a mixture composed of methylcyclobutene and methylenecyclobutane reacts readily with benzene in the presence of 96% sulfuric acid at 0–10° to yield a product consisting of mono-, di- and trimethylcyclobutylbenzenes.

The reaction proceeds according to the equation



(1) Presented before the Division of Organic Chemistry of the American Chemical Society at Boston, Mass., Sept. 11–15, 1939.

(2) Ipatieff, Pines and Schmerling, paper presented before the Organic Division at the American Chemical Society meeting, Milwaukee, Wisconsin, September, 1938.



The monosubstituted benzene, which is probably 1-methyl-1-phenylcyclobutane,[3] contains a cyclobutyl ring which is stable toward nitrating mixture consisting of 1 vol. concentrated nitric and 2 vol. of concentrated sulfuric acid. A nitro compound was obtained from which a solid monoacetamino derivative was prepared. The cyclobutyl ring in methylcyclobutane decomposes when subjected to similar treatment.

The di-substituted benzene consists mainly of *p*-di-(1[1]-methylcyclobutyl)-benzene which melts at 33–34°. The higher-boiling fractions consist of tri-(1[1]-methylcyclobutyl)-benzene.

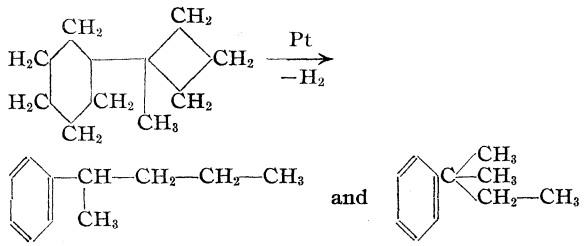
The cyclobutyl ring in the di-substituted benzene is stable toward 2% potassium permanganate at 100° and toward dilute nitric acid at a

(3) The position of the methyl group was not established, but on the basis of reaction of alkenes with benzene[2] one would expect the phenyl group to attach itself to the carbon atom of cyclobutyl containing the methyl group.

temperature of 135°. At 160° oxidation takes place yielding terephthalic acid.

The effect of hydrogen on the cyclobutyl ring was studied with 1-methyl-1-phenylcyclobutane, which undergoes hydrogenation at 65° in the presence of a solvent and a nickel catalyst to yield 1-methyl-1-cyclohexylcyclobutane; if the hydrogenation is carried out at 125° the cyclobutyl ring decomposes and amylcyclohexane is obtained.

The cyclobutyl ring in 1-methyl-1-cyclohexylcyclobutane decomposes when passed over platinized alumina at 250°; a mixture of *t*-amylbenzene and 2-phenylpentane was obtained. This proceeds according to the equation



The percentage of the two amylbenzenes present in the mixture was determined by comparing the melting point of its diacetamino derivative with the melting points of known mixtures of the diacetamino derivatives of *t*-amylbenzene and 2-phenylpentane (Curve 1).

Experimental Part

Preparation of Methylcyclobutane.—This compound was prepared by debrominating[4] pentaerythrityl bromide[5] with zinc dust. A mixture of methylcyclobutene and methylenecyclobutane[6] was obtained having a boiling point of 40–42.5° at 736 mm. The yield was 65%.

Reaction of Methylcyclobutene and Methylenecyclobutane with Benzene.—The apparatus consisted of a 200-cc. three-necked flask, equipped with a mercury-sealed stirrer, a water-jacketed dropping funnel, and a reflux condenser. The flask was immersed in ice water. Thirty grams of 96% sulfuric acid and 35 g. (0.45 mole) of benzene were placed in the flask and cooled to 4°. A mixture consisting of 25 g. (0.37 mole) of methylenecyclobutane and methylcyclobutene and 35 g. (0.45 mole) of benzene was added during one hour. Two layers were formed: acid layer, 31.3 g., and hydrocarbon layer, 93.5 g. The latter was washed and dried. It was stable toward a 2% potassium permanganate solution, which indicates the absence of olefins. The combined product of three experiments was distilled over metallic sodium.

The benzene was distilled at atmospheric pressure and the methylcyclobutylated benzene under 8 mm. pressure. The following fractions were separated: (1) b. p. 69° at 8 mm., 40 wt. %; (2) 125–143° at 8 mm., 49%; (3) 155–182° at 8 mm., 11%.

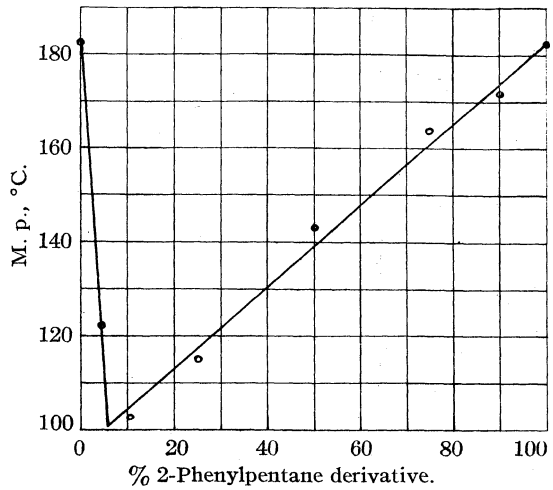


Fig. 1.—Melting point curve for mixtures of the diacetamino derivatives of 2-phenylpentane and *t*-amylbenzene.

On the basis of the distillation it was computed that the reaction mixture consists of

50 Moles mono-methylcyclobutylbenzene
45 Moles di-methylcyclobutylbenzene
5 Moles tri-methylcyclobutylbenzene

The following products were isolated and analyzed.

Fraction 1 consists of 1-methyl-1-phenylcyclobutane, b. p. 69° at 8 mm.; boiling point determined by Cottrell method;[7] 208.6° at 760 mm., dt/dp (760–740 mm.) = 0.05°/mm.; $d^{20}_{vac.}$ 0.9192; $d^{40}_{vac.}$ 0.9044; $-dD/dt$ = 0.00074; $n^{20}D$ 1.5132.

Anal. Calcd. for $C_{11}H_{14}$: C, 90.18; H, 9.82. Found: C, 89.94; H, 9.83.

Monoacetamino derivative[8] (1[1]-methyl-1-cyclobutyl-4-acetaminobenzene), melting point 144°.

Anal. Calcd. for $C_{13}H_{17}O$: C, 76.79; H, 8.43; N, 6.89. Found: C, 76.75; H, 8.32; N, 6.62.

Diacetamino derivative (1[1]-methyl-1-cyclobutyl-2,4-diacetaminobenzene).—Melting point 202°.

Anal. Calcd. for $C_{15}H_{20}O_2N_2$: N, 10.77. Found: N, 10.97.

Fraction 2 was redistilled under 6 mm. pressure. The major part of the product boiled at 124–128° and had $n^{20}D$ 1.5194–1.5245, corresponding to di-(1[1]-methylcyclobutyl)-benzene. Cut b. p. 123–125° at 6 mm., $n^{20}D$ 1.5203, $d^{20}_{vac.}$ 0.9344, $d^{40}_{vac.}$ 0.9198.

Anal. Calcd. for $C_{16}H_{22}$: C, 89.35; H, 10.63. Found: C, 89.48; H, 10.43.

This product crystallizes in ice. A solid was separated which after repeated crystallizations had m. p. 34° and by oxidation was proved to correspond to 1,4-di-(1[1]-methylcyclobutyl)-benzene.

(4) Rave and Tollens, *Ann.*, **276**, 61 (1893); Gustavson, *J. prakt. Chem.*, [2] **54**, 98 (1896).

(5) H. B. Schurink, "Organic Syntheses," Vol. 17, p. 73.

(6) Philipov, *J. prakt. Chem.*, **93**, 102 (1916).

(7) Cottrell, THIS JOURNAL, **41**, 721 (1919); Bruun and Hicks-Bruun, *Bur. Standards J. Research*, **6**, 871 (1931).

(8) Ipatieff and Schmerling, THIS JOURNAL, **59**, 1056 (1937); **60**, 1476 (1938).

Anal. Calcd. for $C_{16}H_{22}$: C, 89.35; H, 10.65. Found: C, 89.51; H, 10.52.

Oxidation.—Seven-tenths gram of the product of b. p. 124–128° at 6 mm. was heated at 160° for two hours in a 60-cc. sealed tube with 12 cc. of 77% nitric acid and 24 cc. of water, according to the procedure recently described.[9] Terephthalic acid was obtained (40% yield). The dimethyl ester of the acid had a melting point of 140° and showed no depression in melting point when mixed with an authentic sample.

Anal. Calcd. for $C_{10}H_{10}O_4$: C, 61.83; H, 5.19. Found: C, 61.60; H, 5.13.

Fraction 3.—B. p. 155–182° under 8 mm., $n^{20}D$ 1.5342.

Anal. Calcd. for $C_{21}H_{30}$: C, 89.29; H, 10.71. Found: C, 89.31; H, 10.42.

Preparation of 1-Methyl-1-cyclohexylcyclobutane.—Nine grams of 1-methyl-1-phenylcyclobutane was dissolved in 10 cc. of *n*-pentane and hydrogenated in a 125-cc. autoclave in the presence of nickel–kieselguhr catalyst[10] at 65° and under the initial hydrogen pressure of 100 atmospheres. The hydrogenated product did not react with nitrating mixture, which indicates the absence of an aromatic ring. The hydrogenated product distilled at 72–73° at 9 mm., 201.5° at 760 mm. dt/dp (752–739 mm.) = 0.08°/mm.; $n^{20}D$ 1.4662; d^{20}_4 0.8595.

Anal. Calcd. for $C_{11}H_{20}$ (1-methyl-1-cyclohexylcyclobutane): C, 86.75; H, 13.25. Found: C, 86.56; H, 13.45.

Dehydrogenation.—1-Methyl-1-cyclohexylcyclobutane was passed over platinized aluminum oxide at 250°. Details have been given in another paper.[11] Aromatic hydrocarbons were obtained distilling at 187 to 192° at 741 mm. and having $n^{20}D$ 1.4861.

A diacetamino derivative[8] was prepared which melted at 144–145°. It consisted of equimolal proportions of *t*-amylbenzene and 2-phenylpentane. This was proved by preparing a melting point curve of the two amylbenzenes and by taking a mixed melting point of the unknown with a mixture of the authentic diacetamino derivatives of the amylbenzenes.

Acknowledgment.—The authors wish to express their thanks to Mr. M. Savoyias for the assistance which he rendered in the laboratory operations.

Summary

A mixture consisting of methylcyclobutene and methylenecyclobutane reacts with benzene in the presence of sulfuric acid to yield: (a) 1-methyl-1-phenylcyclobutane, characterized by solid mono- and diacetamino derivatives; (b) *p*-di-(1¹-methylcyclobutyl)-benzene, isolated as a crystalline compound; and (c) tri-(1¹-methylcyclobutyl)-benzene.

Hydrogenation of 1-methyl-1-phenylcyclobutane yielded 1-methyl-1-cyclohexylcyclobutane. The latter on dehydrogenation decomposed into *t*-amylbenzene and 2-phenylpentane.

The cyclobutyl ring becomes very stable toward sulfuric acid or nitrating mixture when a phenyl group is attached to it.

RIVERSIDE, ILLINOIS RECEIVED OCTOBER 5, 1939

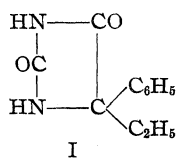
(9) Pines, Grosse and Ipatieff, THIS JOURNAL, **61**, 641 (1939).
(10) Ipatieff and Corson, *Ind. Eng. Chem.*, **30**, 1039 (1938).
(11) Pines and Ipatieff, THIS JOURNAL, **61**, 1077 (1939).

[CONTRIBUTION NO. 169 FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, THE UNIVERSITY OF TEXAS]

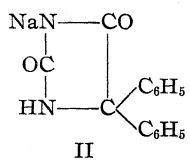
5-[α-(*s*-Butoxy)]-ethyl-5-alkyl Hydantoins

BY ROBERT J. SPEER AND HENRY R. HENZE

During the past few years in this Laboratory considerable attention has been given to the synthesis of hydantoins, a few of which have been shown to possess sufficient physiological activity to warrant continued research in this field. Previous papers of this series have reported extended use of Bucherer's[1] method for the production of substituted hydantoins by interaction of an aqueous alcoholic solution of potassium cyanide and ammonium carbonate with appropriate ketones. The latter have included examples of alkoxymethyl alkyl (or aryl) ketones, phenoxymethyl alkyl (or aryl) ketones, 1,3-dichloroisopropoxyethyl alkyl (or aryl) ketones, dialkylaminoacetones, alkyl nitroaryl ketones, and β-chloroethoxyalkyl alkyl ketones.[2] Although, as yet, but two 5,5-disubstituted hydantoins, namely, Nirvanol (I)[3] and Dilantin (II),[4] have found actual clinical use,



I



II

the hydantoin nucleus offers potentiality as an innocuous heterocycle to which may be attached

(1) Bucherer and Lieb, *J. prakt. Chem.*, [2] **141**, 5 (1934).
(2) Preceding paper in this series, Lingo with Henze, THIS JOURNAL, **61**, 1574 (1939).
(3) Swiss Patent 72,561 (1916).
(4) Putnam and Meritt, *Science*, **85**, 526 (1937).

groupings appropriate to produce additional derivatives of importance as soporifics or anticonvulsants. Since it is known that the ethyl and *s*-butyl groups are of special physiological potency, it seemed of interest to prepare a series of hydantoins containing these groups connected in an alkoxyalkyl linkage, namely, as the *s*-butoxyethyl grouping. While the preparation of analogous and in a few cases isomeric hydantoins has been accomplished previously, the procedure of Bucherer[1] has not been utilized for the synthesis of 5-(*s*-butoxyethyl)-5-alkyl (or aryl) hydantoins.

Experimental

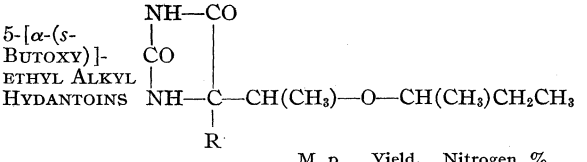
Preparation of α-(*s*-Butoxy)-ethyl Alkyl Ketones.—The nine ketones used as intermediates in the production of the butoxyethyl hydantoins were prepared by the interaction of the appropriate Grignard reagents and *s*-butyl α-cyanoethyl ether as described previously.[5]

Synthesis of 5-[α-(*s*-Butoxy)]-ethyl-5-Alkyl Hydantoins.—The production of nine members of this series of compounds was accomplished by the interaction of an aqueous alcoholic solution of potassium cyanide and ammonium carbonate with the appropriate butoxyethyl alkyl ketones. One part (0.05 mole) of a ketone was mixed with a suspension of 1.25 parts of potassium cyanide and 3.0 parts of ammonium carbonate in 7–8 volumes of 50% alcohol. Upon warming the mixture to 55–60° for five to six hours, the solids gradually dissolved with evolution of gas, followed in most cases with the separation of the solid reaction product from the warm solution. At the termination of this period of warming the mixture was cooled and the product removed by filtration. Concentration of the filtrate with subsequent acidification yielded additional crystalline material, although in the cases of the *s*-propyl and *s*-butyl derivatives there was considerable tendency toward the formation of oily material. However, in these instances, after solidification of the oil no trouble was experienced in purification by further crystallization.

All of the hydantoins of this series are white crystalline solids soluble in alcohol, acetone, benzene, and chloroform but insoluble in water and petroleum ether. Purification was effected by recrystallization from 50–60% ethyl alcohol or from a benzene–petroleum ether mixture. In some instances treatment with Norite was necessary for complete removal of color. These compounds, in general, possess sharp melting points, fusing to form light straw colored liquids without decomposition. Data for melting points, percentage yields, and the analyses for nitrogen content of these hydantoins are presented in Table I.

TABLE I

5-[α-(*s*-BUTOXY)]-ETHYL ALKYL HYDANTOINS



	—R	M. p., °C. (corr.)	Yield, %	Nitrogen, % Calcd.	Found
1	—CH_3[a]	203–204	36	13.08	13.14
2	—CH_2CH_3	190	41	12.27	12.19
3	—$CH_2CH_2CH_3$	205–206	24	11.56	11.70
4	—$CH(CH_3)_2$	196–197	22	11.56	11.70
5	—$CH_2CH_2CH_2CH_3$	204–205	36	10.93	11.01
6	—$CH_2CH(CH_3)_2$	192	44	10.93	11.00
7	—$CH(CH_3)CH_2CH_3$	189–190	30	10.93	10.89
8	—$CH_2CH_2CH_2CH_2CH_3$	178	31	10.36	10.36
9	—$CH_2CH_2CH(CH_3)_2$	177	40	10.36	10.58

[a] Calcd. for $C_{10}H_{18}N_2O_3$: C, 56.05; H, 8.47. Found: C, 56.13; H, 8.65.

Summary

The series of 5,5-disubstituted hydantoins, potentially important as soporifics or anti-convulsants, has been extended to include nine new *s*-butoxyethyl alkyl hydantoins.

AUSTIN, TEXAS RECEIVED OCTOBER 16, 1939

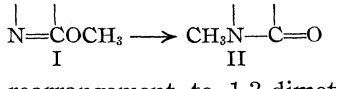
(5) Speer with Henze, THIS JOURNAL, **61**, 1226 (1939).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, KWANGSI UNIVERSITY, CHINA]

Researches on Pyrimidines. The Molecular Rearrangement of 4-Methyl-5-*n*-propyl-2,6-dimethoxypyrimidine[1]

BY YUOH-FONG CHI, SHAO-SENG WEI AND MEI-SENG LIANG[2]

Previous publications by Hilbert and Johnson from the Yale laboratories,[3] and later by Chi, Wei and Pan[4] have shown that pyrimidine lactim-ethers of configuration I undergo rearrangement to their isomeric and stable lactam forms II. For example, 2,6-dimethoxypyrimidine and 2-oxy-3-methyl-6-methoxypyrimidine on heating both



underwent rearrangement to 1,3-dimethyluracil. Under similar conditions 4-methyl-5-*n*-butyl-2,6-dimethoxypyrimidine and 2-oxy-3,4-dimethyl-5-*n*-butyl-6-methoxypyrimidine are converted to 1,3,4-trimethyl-5-*n*-butyluracil.

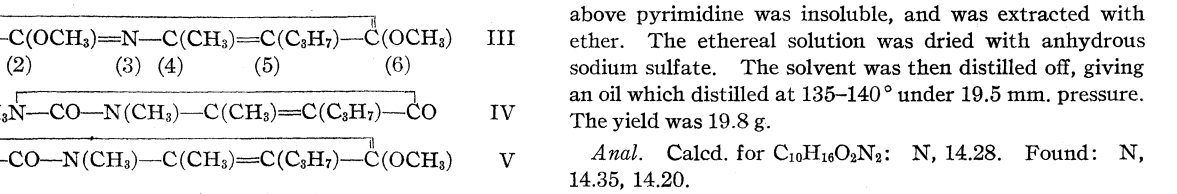
(1) This paper is constructed from a dissertation presented by Shao-Seng Wei and Mei-Seng Liang to the Faculty of Kwangsi University as partial fulfilment of the requirements for the degree of Bachelor of Science in June, 1938.

(2) The authors desire to express their appreciation to Professor Treat B. Johnson of Yale University for his assistance in preparing this paper for publication.

(3) Hilbert and Johnson, THIS JOURNAL, **52**, 2001 (1930).

(4) Chi, Wei and Pan, *ibid.*, **60**, 1719 (1938).

In this paper the authors describe the conditions under which 4-methyl-5-*n*-propyl-2,6-dimethoxy-pyrimidine (III) rearranges into (a) 1,3,4-trimethyl-5-*n*-propyluracil (IV) and (b) 2-oxy-3,4-dimethyl-5-*n*-propyl-6-methoxy-pyrimidine (V).



The authors have made the observation that the pyrimidine (III) is rearranged smoothly to the lactam modification (IV) by heating at 260–280°. On the other hand, when heated at 50–60° under the catalytic influence of methyl iodide, the partially rearranged pyrimidine (V) is formed. This latter pyrimidine is stable only at low temperatures and undergoes rearrangement at 260–280° to the *lactam* form (IV).

Experimental Part

VI, NHCONHC(CH$_3$)=C(C$_3$H$_7$)CO, 4-Methyl-5-*n*-propyl-uracil.—This pyrimidine was prepared by digesting 4-methyl-5-*n*-propyl-2-thiouracil[5] with chloroacetic acid. Thirty grams of the thiouracil was digested with a solution containing 60 g. of ClCH$_2$COOH in 150 cc. of water for two hours, whereupon 26 g. of the desulfurized pyrimidine separated as needles, melting at 247–249°. The same pyrimidine also is formed by digesting 2-ethylmercapto-4-methyl-5-*n*-propyl-uracil[5] with strong hydrochloric acid. Twenty-five grams of this mercaptopyrimidine yielded 20 g. of the uracil compound melting at 246–247°.

4-Methyl-5-*n*-propyl-2,6-dichloropyrimidine, VII.—Sixteen and eight-tenths grams of VI was refluxed with 100 cc. of phosphorus oxychloride in an oil-bath at 120–130° until hydrogen chloride gas ceased to be evolved. This took twelve hours. The excess of phosphorus oxychloride was removed by heating the reaction mixture on a water-bath under a vacuum. There was obtained a brown viscous residue which did not solidify. The residue was treated with cracked ice to decompose phosphorus compounds, and then extracted with ether. The ethereal solution was washed with water, dried with calcium chloride and filtered. After distilling the solvent from the ethereal solution, an oil was obtained which was purified by distillation under a vacuum. The pyrimidine VII boils at 163° under 35 mm. pressure, at 149° under 20.8 mm. pressure or at 145–146° under 19.5 mm. pressure, and melts at 31–33°. The yield is 16.4 g. or 80%.

Anal. Calcd. for C$_8$H$_{10}$N$_2$Cl$_2$: N, 13.66. Found: N, 13.9, 13.86.

4-Methyl-5-*n*-propyl-2,6-dimethoxypyrimidine, III.—Four and six-tenths grams of metallic sodium was dissolved in 50 cc. of absolute methyl alcohol. To the cold methyl alcohol solution of sodium methylate, there was slowly added a solution of 20.5 g. of VII in 50 cc. of absolute methyl alcohol. This gave an immediate precipitation of sodium chloride. After the separation of sodium chloride by filtration, the excess of methyl alcohol was distilled off on a water-bath. There remained an oil, which was shaken with 30 cc. of 30% sodium hydroxide solution in which the above pyrimidine was insoluble, and was extracted with ether. The ethereal solution was dried with anhydrous sodium sulfate. The solvent was then distilled off, giving an oil which distilled at 135–140° under 19.5 mm. pressure. The yield was 19.8 g.

Anal. Calcd. for C$_{10}$H$_{16}$O$_2$N$_2$: N, 14.28. Found: N, 14.35, 14.20.

4-Methyl-5-*n*-propyl-2,6-diethoxy-pyrimidine, VIII.—This pyrimidine was prepared by a procedure similar to that used for synthesizing the corresponding dimethoxy-pyrimidine described above. This distilled as a colorless oil, boiling at 145–148° under 18 mm. pressure. The yield was 8.9 g. from 10.2 g. of the corresponding dichloro-pyrimidine.

Anal. Calcd. for C$_{12}$H$_{20}$O$_2$N$_2$: N, 12.49. Found: N, 12.79, 12.88.

Methylation of VI.—(A) Four and two-tenths grams of VI was dissolved in sodium hydroxide solution, containing 2.2 g. of NaOH in 150 cc. of water. To this ice-cooled solution, 5.5 cc. of dimethyl sulfate was added drop by drop while the solution was shaken vigorously. It was then boiled for ten minutes. On cooling, 1,4-dimethyl-5-*n*-propyl-uracil (IX) separated. After recrystallization from benzene and petroleum ether, it melted at 193.5–194°. The yield was 2 g. On mixing with 3,4-dimethyl-5-*n*-propyl-uracil (X), described below, its melting point was strongly depressed.

Anal. Calcd. for C$_9$H$_{14}$O$_2$N$_2$: N, 15.38. Found: N, 15.76.

(B) Six-tenths gram of sodium was dissolved in 100 cc. of absolute alcohol, and then 2.1 g. of VI was dissolved in the alcoholate solution. To this cold solution, 2.5 cc. of dimethyl sulfate was then added slowly with frequent shaking. The mixture now was heated for two hours. After distilling off the excess alcohol, the residue was treated with water and extracted with benzene. The benzene solution was dried and solvent removed as usual, whereupon a solid residue was obtained. After crystallizing from benzene and petroleum ether, it melted at 193–194°. On mixing with IX described above, there was no lowering of the melting point.

The Molecular Rearrangement of 4-Methyl-5-*n*-propyl-2,6-dimethoxy-pyrimidine (III). (A) Rearrangement of (III) to (IV).—Two grams of III was heated in an oil-bath at 260–280° for three hours. At first, there was vigorous ebullition which gradually subsided and finally ceased as the proportion of the rearranged compound increased. On cooling, the brown colored reaction product completely solidified. It was dissolved in hot benzene, to which petroleum ether was added just to turbidity. On cooling, the rearranged product separated in needles. After recrystallization from a benzene–petroleum ether mixture, it melted at 74–75°. The yield was 1.8 g. or 90%.

Anal. Calcd. for C$_{10}$H$_{16}$O$_2$N$_2$: N, 14.28. Found: N, 14.21, 14.30.

(5) Chi and Chang, THIS JOURNAL, **60**, 1721 (1938).

(B) **Rearrangement of (III) to (V).**—Nine and eight-tenths grams of III was treated with 14.1 g. of freshly distilled methyl iodide. The mixture was then heated in a sealed tube at 50–60° for eight hours. After the tube was opened, the excess of methyl iodide was removed by a blast of air and the residue distilled under a vacuum. Compound V when pure boils at 180–182° under 4.5 mm. pressure and solidifies on slow cooling. The yield was quantitative. For analysis, it was recrystallized from petroleum ether, separating in needles.

Anal. Calcd. for $C_{10}H_{16}O_2N_2$: N, 14.28. Found: N, 14.16.

The structure of the compound was established by its behavior on hydrolysis, giving X.

Formation of X.—Compound V was heated with dilute hydrochloric acid for one hour. The solution was evaporated to dryness on a water-bath and the residue dissolved in hot water, whereupon X crystallized on cooling in colorless needles, melting at 148–150°.

Anal. Calcd. for $C_9H_{14}O_2N_2$: N, 15.38. Found: N, 15.50, 15.47.

(C) **Rearrangement of the Partially Rearranged Pyrimidine (V) into the Completely Rearranged Pyrimidine (IV).**—Five grams of V was heated at 330–350° for six to eight hours. The reaction mixture solidified on cooling. It dissolved in a little hot benzene, to which petroleum ether was added just to turbidity, whereupon (IV) separated in needles, melting at 74–75°. It proved to be identical with 1,3,4-trimethyl-5-*n*-propyluracil (IV) obtained by heating pyrimidine (III).

Anal. Calcd. for $C_{10}H_{16}O_2N_2$: N, 14.28. Found: N, 14.41, 14.55.

Summary

1. The action of phosphorus oxychloride on 4-methyl-5-*n*-propyluracil produces 4-methyl-5-*n*-propyl-2,6-dichloropyrimidine.

2. This 2,6-dichloropyrimidine reacts with sodium methylate and with sodium ethylate in a characteristic manner, giving the corresponding 2,6-dimethoxy-pyrimidine, and 2,6-diethoxy-pyrimidine derivatives, respectively.

3. 4-Methyl-5-*n*-propyl-2,6-dimethoxy-pyrimidine and 2-oxy-3,4-dimethyl-5-*n*-propyl-6-methoxy-pyrimidine can be rearranged to their isomeric and stable *lactam* modification, 1,3,4-trimethyl-5-*n*-propyluracil, on heating at an elevated temperature. On the other hand, 4-methyl-5-*n*-propyl-2,6-dimethoxy-pyrimidine rearranges only partially on heating with methyl iodide at 50–60° to 2-oxy-3,4-dimethyl-5-*n*-propyl-6-methoxy-pyrimidine.

WUCHOW, CHINA RECEIVED JULY 5, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, BANTING INSTITUTE, UNIVERSITY OF TORONTO]

Oxidation of Glycosides by Means of Lead Tetraacetate in Aqueous Solution

BY J. M. GROSHEINTZ

In a previous paper[1] there was described a new technique for the application of lead tetraacetate as an oxidizing agent. It was shown that the cleavage of the carbon chain in compounds containing two and three adjacent hydroxyl groups could be carried out in aqueous solution as well as in non-aqueous solution. Lead tetraacetate therefore can replace periodic acid in most instances in which aqueous solvents are required.

E. L. Jackson and C. S. Hudson,[2] in their determination of ring structure and alpha- and beta-configuration of glycosides, thoroughly investigated the cleavage of the carbon chain of a number of glycosides by oxidation with periodic acid. In the present paper parallel experiments with lead tetraacetate are reported in order to show the similar action of this reagent on glycosides in aqueous solution.[3] Starting with the optical antipodes of two glycosides used by E. L. Jackson and C. S. Hudson[2] the oxidation products and their derivatives were compared with the products already known.

The oxidation of alpha- (I) and beta-methyl-*l*-arabinopyranosides with lead tetraacetate in water was shown to remove carbon atom 3 and form carbonyl groups at carbon atom 2 and 4, producing the two enantiomorphic forms of methoxy-diglycolic aldehyde[4] (II).

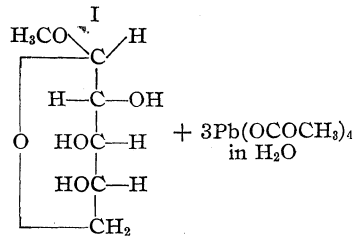
Contrary to previous experience,[1] *three* molecules of lead tetraacetate, instead of two, were required to complete this reaction. In seeking for

(1) Erich Baer, J. M. Grosheintz and H. O. L. Fischer, THIS JOURNAL, **61**, 2607 (1939).

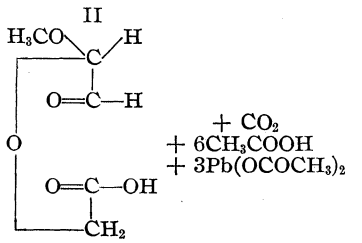
(2) E. L. Jackson and C. S. Hudson, *ibid.*, **59**, 994 (1937).

(3) Compare also W. S. McClenahan and R. C. Hockett, *ibid.*, **60**, 2061 (1938).

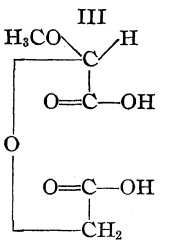
(4) The oxidation products are named in accordance with E. L. Jackson and C. S. Hudson, *ibid.*, **59**, 994 (1937), as derivatives of diglycolic aldehyde. Prefixes D′ and L′ distinguish the configuration of carbon atom 1 in the products from the alpha- and beta-methyl-glycosides, L′ signifying the configuration of carbon atom 1 as in alpha-methyl-*l*-arabinopyranoside.



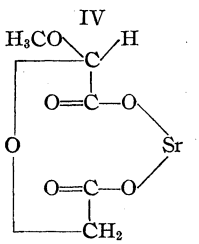
α-Methyl-*l*-arabinopyranoside



L′-Methoxy diglycolic aldehyde



L′-Methoxy-diglycolic acid



Strontium-L′-methoxy-diglycolate

an explanation for this utilization of a third molecule of lead tetraacetate, it was found that one molecule of formic acid in aqueous solution is oxidized by one molecule of lead tetraacetate, yielding one molecule of carbon dioxide.[5] This observation shows that in cases where the velocity of cleavage of the carbon chain between the three adjacent hydroxyl groups is low compared to the rate of oxidation of the formic acid, one must allow for an excess of one mole of lead tetraacetate being used up by the formic acid formed during the reaction.

Further oxidation of the D′- and L′-methoxy-diglycolic aldehydes with bromine water in the presence of strontium carbonate produced the D′- and L′-methoxy-diglycolic acids, the latter being isolated as the crystalline strontium salts. The optical rotations of the starting materials in aqueous solution were $[\alpha]^{20}D$ +17.3° for the alpha-methyl-*l*-arabinopyranoside (m. p. 131°) and $[\alpha]^{21}D$ +246° for the beta-methyl-*l*-arabinopyranoside (m. p. 169–170°). The following rotations for the oxidation products were observed: $[\alpha]^{20}D$ +123.2° and $[\alpha]^{23}D$ −122.5° for the D′- and L′-methoxy-diglycolic aldehydes (II), $[\alpha]^{20}D$ −12.8° and $[\alpha]^{21}D$ +12.7° for the D′- and L′-methoxy-diglycolic acids (III); $[\alpha]^{20}D$ −56.4° and $[\alpha]^{20}D$ +56.4° for the strontium salts of D′- and L′-methoxy-diglycolic acids (IV). The L′-compounds are derived from the alpha-methyl-*l*-arabinopyranoside, the D′-compounds from the beta-methyl-*l*-arabinopyranoside. The optical rotation of each of these compounds checks closely with those obtained by the oxidation of alpha- and beta-methyl-*d*-arabinopyranosides, as recorded by E. L. Jackson and C. S. Hudson.

Experimental

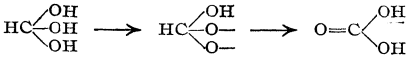
Oxidation of alpha-Methyl-*l*-arabinopyranoside.—A solution of 2.00 g. of alpha-methyl-*l*-arabinoside in 20 cc. of distilled water was poured into 50 cc. of glacial acetic acid[6] containing 13.0 g. of lead tetraacetate, partially undissolved. Within the next six hours 4.0 g. of lead tetraacetate was added in small portions, until the solution turned slightly brown and turbid (=3.2 mole of lead tetraacetate). The solution was then made up to 500.00 cc. with 80 cc. of *N* sulfuric acid and distilled water. The precipitate of lead sulfate was removed by centrifuging and the content of aldehyde determined according to the method of Willstätter and Schudel. The calcd. yield of L′-methoxy-diglycolic aldehyde is 1.61 g.; found, 1.58 g. = 98% yield. The optical rotation of the solution was $\alpha^{23}D$ −0.39, c = 0.316.

The solution was then freed from the slight excess of sulfuric acid with the exact amount of barium acetate and the water and the acetic acid were removed from the dialdehyde by distillation *in vacuo* (bath 35–40°). In order to remove the last traces of acetic acid, the residue was dissolved in 30 cc. of benzene and the solvent evaporated *in vacuo* (bath 35–40°). This operation was repeated twice and the remaining dialdehyde was dried for one hour in high vacuum (40°).

The dialdehyde was then dissolved in 300 cc. of distilled water; 18 g. of strontium carbonate and 8 g. of bromine were added and the mixture was shaken for one hour. After standing at room temperature for an additional sixteen hours, the excess bromine was removed by aeration and the strontium carbonate by filtration. The solution was concentrated and made up to 250.00 cc. The rotation of the strontium L′-methoxy-diglycolate in the solution containing strontium bromide was $[\alpha]^{25}D$ +55.1°.

The bromide ions in the solution were removed by shaking with 25 g. of silver carbonate, and the silver ions precipitated by hydrogen sulfide. The solution was concentrated *in vacuo* (45–50°) to about 100 cc., then filtered

(5) It can be assumed that the formic acid is present in its *ortho* form and that the following steps are involved



This reaction does not take place in dry organic solvents, or in aqueous solution by means of periodic acid.

(6) The amount of water and glacial acetic acid can be chosen freely according to the solubility and amount of substance used. Lead tetraacetate can also be added to the aqueous solution of the glycoside in finely powdered form.

and concentrated again to about 10 cc. This liquid was left to evaporate over phosphorus pentoxide for two days and yielded 2.1 g. of crystalline strontium L'-methoxy-diglycolate. After drying the strontium salt over phosphorus pentoxide for six hours at 100° in high vacuum, it showed the optical rotation $[\alpha]^{20}D$ +56.4°.

Anal. Calcd. for $C_5H_6O_6Sr$: C, 24.03; H, 2.40; Sr, 35.01. Found: C, 23.90; H, 2.53; Sr, 34.98.

Oxidation of beta-Methyl-*l*-arabinopyranoside.—The procedure was the same as reported for alpha-methyl-*l*-arabinopyranoside. The optical rotation of the D'-methoxy-diglycolic aldehyde was $[\alpha]^{20}D$ +123.2° ($\alpha^{20}D$ +1.98°; c = 1.61, H_2O; tube 1 dm.) and the yield determined by titration according to the method of Willstätter and Schudel was 1.53 g. = 95%. The yield of strontium salt was 71%; $[\alpha]^{20}D$ −56.4° ($\alpha^{20}D$ −1.36°; c = 2.41, H_2O; tube 1 dm.) for the anhydrous substance.

Anal. Calcd. for $C_5H_6O_6Sr$: C, 24.03; H, 2.40; Sr, 35.01. Found: C, 23.95; H, 2.55; Sr, 34.96.

Oxidation of Formic Acid.—A roughly 5% aqueous solution of formic acid was prepared and its exact amount of acid determined by titration; 10 cc. of this solution, containing 0.5253 g. of formic acid, was added to 25 cc. of glacial acetic acid and 6 g. of lead tetraacetate in an apparatus suitable for the quantitative determination of carbon dioxide. The mixture was shaken gently and kept at 35°, raising the temperature to 45° within the next half hour, after which time the reaction was completed. In three such experiments 0.4952 g., 0.4843 g., 0.4978 g. of CO_2 were found; yields were 98.8, 96.4 and 99.3%.

Summary

It has been shown that the oxidative cleavage of alpha- and beta-methyl-*l*-arabinopyranosides can be carried out quantitatively in aqueous solution with lead tetraacetate. Three moles of the oxidizing agent, instead of two, are required to complete this reaction. The reason for this excess consumption of reagent is that in aqueous solution the one mole of formic acid formed during the first reaction is oxidized by one mole of lead tetraacetate to one mole of carbon dioxide.[6]

TORONTO, CANADA RECEIVED OCTOBER 2, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF THE GENERAL ELECTRIC CO.]

Mechanism of the Reaction between Phthalic Anhydride and an Aminodiol[1]

BY MURRAY M. SPRUNG

Much attention has been devoted recently to the mechanism of polycondensation reactions.[2] Aside from the interesting theoretical deductions to which this work has led, the important practical result is that it is now usually possible to predict whether a condensation reaction will lead to the formation of low molecular weight substances, linear polymers or cross-linked types of resins. The last named are formed, in general, when the initial reactants have higher combined functionalities than 2:2.[2b]

Esterification and amidation reactions conform to these general schemes. Bi-bi-functional esterifications lead to cyclic monomers when rings of five or six members can result; otherwise linear polymers usually are formed. Bi-tri-functional esterifications practically always lead to net-like, cross-linked polymers. As for amidations, Carothers and Berchet[3] found that five and six ring monomers are formed exclusively, that a seven ring monomer and the corresponding linear polymer appeared simultaneously, and that reactions which might lead to cyclic monomers having eight or more ring atoms led, instead, exclusively to polymers.

Hydroxy amines would be expected to react with dibasic acids in accord with these now well-established principles. An amino-alcohol should give a linear polymeric ester-amide; whereas an aminodiol should give a product having a three dimensional, network structure analogous to that of glyceryl phthalate. This product, furthermore, should show the property of passing suddenly through the sol–gel transformation at a definite, critical stage in the polycondensation reaction.

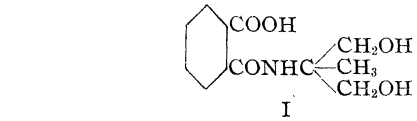
Preliminary Results.—The reactions of 2-amino-2-methyl-1-propanol with adipic acid, and of 2-amino-2-methyl-1,3-propanediol with succinic, maleic, adipic and sebacic acids gave the results anticipated on the basis of these considerations. In the first case, the product was a thermoplastic resin and apparently a linear polymer. In the latter cases, cross-linked resins were formed which were converted to insoluble, infusible materials when the combined esterification and amidation

(1) Presented at the Boston meeting of the American Chemical Society, September 11–16, 1939.

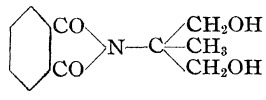
(2) See, for example, (a) Carothers, THIS JOURNAL, **51**, 2548 (1929); (b) *Trans. Faraday Soc.*, **32**, 39 (1936); (c) Dostal and Raff, *Monatsh.*, **68**, 188 (1936); (d) Flory, THIS JOURNAL, **58**, 1877 (1936); **59**, 466 (1937); (e) Dreher, *Kunststoffe*, **28**, 35 (1938); (f) Stoll and Bouvé, *Helv. Chim. Acta*, **18**, 1087 (1935).

(3) Carothers and Berchet, THIS JOURNAL, **52**, 5289 (1930); see also Carothers, U. S. Patents 2,071,253, 2,130,523, 2,130,947 and 2,130,948 (1937 and 1938).

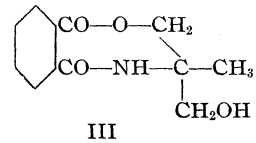
reactions had proceeded to the extent of about 65–75% of that theoretically possible. However, when the aminodiol was caused to react with phthalic acid (or its anhydride), it was found possible to carry the reaction to completion (*i. e.*, to collect 100% of the theoretically available water of reaction) without observing the formation of a gel structure. The product obtained under these conditions was a colophony-like, brittle, amorphous solid, which appeared to be a mixture of several ingredients. In order to obtain an explanation of this rather unexpected result, attempts were made to break down the reaction into distinct stages and to isolate the low molecular weight intermediates involved.



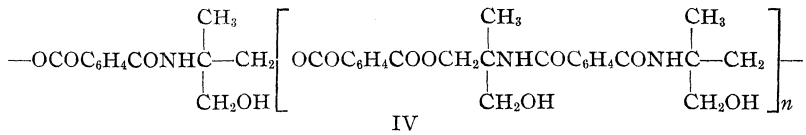
I



II



III



IV

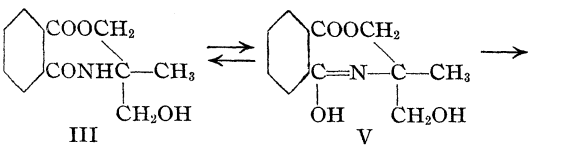
First Stage: Opening of the Anhydride Ring.—Phthalic anhydride and 2-amino-2-methyl-1,3-propanediol, heated to a temperature of 135–145° for two and one-half hours, gave a soft, stringy, sticky, resinous-appearing material which could not be purified by crystallization or solvent extraction (and which naturally could not be distilled without further reaction occurring). However, analysis of the crude reaction product for acidity, saponification equivalent, and hydroxyl indicated that it consisted mainly of the substituted phthalamic acid, namely, N-(1,1-dimethylol)-ethylphthalamic acid (I). The first step in the reaction therefore consists essentially in addition of the *amino group* of the aminodiol to the anhydride linkage of phthalic anhydride.

Second Stage: Ring Closure.—When the reactants were mixed in equimolar proportions and heated at 150–200° for two hours, almost exactly one mole of water was collected. The product was very similar in appearance to that described above, and could not be separated into crystalline fractions by solvent treatment. However, in this case over 50% of the crude reaction product was distillable. The main portion of the distillate consisted of a sluggish, pale yellow liquid boiling at 207–220° at 6 mm., and at 172–177° at about 50 microns. The undistillable portion was a dark colored, hard, brittle, fusible and soluble resin.

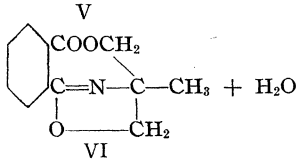
A priori, three substances might be formed under these conditions: the dimethylol phthalimide (II), the cyclic ester-amide (III), or a linear polymeric structure of which (IV) represents one possibility.

Analyses of the main fraction of the distillate gave results reasonably well in accord with those demanded by structures (II) or (III). However, the hydroxyl analyses (using the acetic anhydride–pyridine method) failed to give consistent results, indicating structure (II) in some cases, and something intermediate between (II) and (III) in others. This main fraction, when exhaustively purified by crystallization, gave a well-defined solid, analyzing as expected for $C_{12}H_{13}NO_4$. The formation of a *dibenzoyl derivative* (with benzoyl chloride in pyridine) favors the dimethylol phthalimide structure (II), but leaves unanswered the question as to why the pyridine–acetic anhydride method does not give results consonant with this structure.

Third Stage: Effect of Excess Phthalic Anhydride.—The colophony-like resin obtained when the reactants were used in the ratio 3 phthalic:2 aminodiol, was subjected to vacuum distillation. Over 50% of it distilled over as a thick, viscous, pale reddish liquid. Redistillation under very low pressure yielded two crystalline fractions which, on further purification, gave colorless solids of the composition $C_{12}H_{11}NO_3$ and $C_{19}H_{17}NO_5$, respectively. The latter substance has not been identified as yet. The substance $C_{12}H_{11}NO_3$ is obviously a dehydration product of the substance $C_{12}H_{13}NO_4$. The only reasonable structure which can be assigned to it is one that could result from



III V



VI

the ester amide (III), by enolization to the isoamide (V) and subsequent dehydration to an oxazoline derivative (VI).

On the other hand, it is difficult to see how a substance of the composition $C_{12}H_{11}NO_3$ could be formed from the dimethylol phthalimide structure (II). The structure (VI) represents the very rare case of a five, a six and an eight ring, fused conjointly.[4]

Attempts to reduce the compound $C_{12}H_{11}NO_3$ to a derivative of phthalaldehydic acid ethylene imino acetal failed. Nevertheless, the presence of a basic nitrogen atom was established by the formation of a picrate (m. p. 146–147°). In absolute alcoholic solution an abnormal picrate (m. p. 225–226°, composed of two moles of the "oxazoline" and one of picric acid) was obtained, even in the presence of excess picric acid. This peculiar observation has no obvious explanation.

It is now possible to interpret the observations made during acylation of the compound $C_{12}H_{13}NO_4$. This substance probably has the 8 ring ester-amide structure (III), but is capable of forming a diacyl derivative of the isoamide form (V). Acetic anhydride (in pyridine) does not acylate the "enol" hydroxyl completely, thus giving analytical results between those expected for the normal and iso structures. On the other hand, benzoyl chloride, a more vigorous acylating agent, forces the enol hydroxyl to react completely.

The oxazoline (VI) might be formed from the esteramide (III) during distillation. However, there was no evidence of its presence in the distillate from the 1:1 reaction product. When, however, this product was heated to 200° with an equivalent amount of phthalic anhydride (but without allowing water to distil out), it was possible to isolate the "oxazoline," by means of solvent extraction and fractional crystallization, and without distillation.

Review of Pertinent Literature

The mechanism outlined above is amply supported by existing literature. A substance very closely related to the structure (III) was obtained as early as 1905 by Gabriel[5] by treating N-β-bromoethyl phthalimide with dilute aqueous potassium hydroxide. The corresponding eight-ring thioamide was formed when N-β-thioethyl phthalamic acid was treated with concentrated hydrobromic acid,[6] and a homologous substance was similarly obtained from N-β-methyl-β-carbethoxythiophthalimide by Mylius.[7] Richard Meyer as early as 1903[8] prepared cyclic diamides having 7, 8 and 14 ring atoms by condensing *o*-phenylenediamines with malonic, succinic, isosuccinic, adipic and phthalic acids, their anhydrides or esters. Very little attention seems to have been devoted to these interesting results of Meyer, or to the equally significant observations of Gabriel and co-workers.[5,6,7]

The assumption that the ester-amide reacts in the isoamide form is also in accord with previous observations. Hantzsch has demonstrated,[9] on the basis of spectroscopic measurements, that trichloroacetamide and benzamide exist in solution largely in the isoamide form. Further, it has long been known that N-β-bromoethyl benzamides are converted to 2-aryloxazolines by boiling with hot water or dilute alkali.[10] Closely related to the present case are the formation of 2-phenylbenzoxazoline by heating *o*-benzaminophenol above its melting point[11]; of *o*-benzoylphenylurethan from urethan, benzoyl chloride and sodium[12]; and of phenylalkyloxazolones from benzoylglycine and its homologs.[13] Similarly, intramolecular acylations, leading to the formation of benzoxazones, occur when anthranilic acid or its derivatives are treated with dehydrating agents such as acetic anhydride.[14]

Conclusions

The mechanism of the reaction of 2-amino-2-methyl-1,3-propanediol on phthalic anhydride is accordingly believed to involve the following steps (1) opening of the anhydride ring to give a dimethylol phthalamic acid; (2) intramolecular esterification to give an 8 ring esteramide; (3) dehydration, through the isoamide form of the esteramide, to yield an oxazoline; (4) simultaneous occurrence of intermolecular condensation reac-

(4) The only analogous structure known to the writer is that of an oxy-lactam recently reported as formed from a diketo cholanic acid monoxime by reductive amidation (Barnett and Reichstein, *Helv. Chim. Acta*, **21**, 926 (1938)).

(5) Gabriel, *Ber.*, **38**, 2389 (1905).

(6) Gabriel and Colman, *ibid.*, **45**, 1643 (1912).

(7) Mylius, *ibid.*, **49**, 1091 (1916).

(8) Richard Meyer, *Ann.*, **327**, 1 (1903).

(9) Hantzsch, *Ber.*, **64**, 661 (1931); *cf.* Ramart-Lucas and Wohl *Compt. rend.*, **196**, 120 (1933).

(10) Elfelat, *Ber.*, **24**, 3222 (1891); Gabriel and Neumann, *ibid.*, **25**, 2385 (1892); Soloman, *ibid.*, **26**, 1322 (1893); Saulmann, *ibid.*, **33**, 2639 (1900).

(11) Hübner, *Ann.*, **210**, 385 (1882).

(12) Hantzsch, *Ber.*, **26**, 928 (1893).

(13) Mohr and Stroschein, *ibid.*, **42**, 2521 (1909).

(14) Anschütz, Schmidt and Greiffenberg, *ibid.*, **35**, 3474, 3480 (1902); Mohr and Köhler, *ibid.*, **40**, 997 (1907); Erlenmeyer, *Ann.*, **337**, 265 (1904); Heller and Fiesselmann, *ibid.*, **324**, 134 (1902); Angeli and Angelico, *Gazz. chim. ital.*, **30**, II, 278 (1900); Bogert and Seil, THIS JOURNAL, **29**, 529 (1907).

TABLE I

REACTIONS OF 2-AMINO-2-METHYL-1-PROPANOL AND 2-AMINO-2-METHYL-1,3-PROPANEDIOL WITH VARIOUS ACIDS (OR DERIVATIVES)

Reactants		Molar ratio	Time, hr.	Temp., °C.	Water formed, cc.			Nature of product
Amine component	Acid component				Obsd.	Calcd.	% of Calcd.	
Amino alcohol	Diethyl adipate	2/1	7	170–190	111[a]	110	99[b]	Thick sirup
Amino alcohol	Adipic acid	2/2	4	160–190	73	72	(100)	Thick balsam, thermoplastic
Amino diol	Adipic acid	1.1/1.5	2	125–195	42	54	77	Stiff balsam, thermosetting[c]
Amino diol	Adipic acid	1.1/1.5	4	154–195	46	54	85	Gelled resin
Amino diol	Sebacic acid	3.2/4.5	4	142–184	127	162	77	Stiff, hard balsam, thermosetting
Amino diol	Maleic anhyd.	1.1/1.5	1/4	110–160	4.5	27	66.5[d]	Gelled resin
Amino diol	Succinic anhyd.	1.1/1.5	1/4	.....	2.5	27	59.5[d]	Soft balsam, thermosetting[e]
Amino diol	Phthalic anhyd.	2.2/3.0	3	150–220	55	54	(100)[d]	Hard, brittle, amorphous, thermoplastic
1,1,1-Trimethylol propane[f]	Phthalic anhyd.	0.55/0.75	1 1/2	195–250	7.7	13.5	78.5	Gelled resin

[a] Alcohol. [b] On the basis of amine titrations, this reaction is virtually completely amidolysis, with only a small amount of alcoholysis. [c] Acid value, 152. [d] These calculations take into account the opening of the anhydride ring. [e] Acid number, 258. [f] Run for comparison with amino diol, since it has a similar structure.

tions, giving rise to the formation of resinous by-products of the soluble, fusible (non-cross-linked) type.

Experimental

General Procedure for Preparation of Resins.—The aminoalcohol or aminodiol and the appropriate acid or acid derivative were mixed in a three-necked flask fitted with a thermometer, stirrer and short column to which a condenser was attached. The mixture was heated by means of a free flame and maintained at such temperature that even distillation occurred. The course of the reaction was followed roughly by the volume of water (or alcohol) collected; and was checked qualitatively by the rapidity with which the sol–gel transformation was observed to occur when a small sample was spread on a metal surface at 200°. Table I summarizes these experiments.

First Stage of the Reaction between 2-Amino-2-methyl-1,3-propanediol and Phthalic Anhydride.—One mole each of the aminodiol (105 g.) and phthalic anhydride (148 g.) were heated in a 3-necked flask at a temperature of 135–145° for two and one-half hours, with stirring. Practically no water was formed. The acid value decreased from an initial value of 444 to a final value of 223 (calcd. 222), indicating that virtually complete addition to the anhydride linkage had been accomplished. The product was a soft, stringy, reddish resin, which became brittle at about −10°. Numerous attempts to purify this material by crystallization failed, as did attempts to obtain acyl derivatives. Acyl halides reversed the reaction by which it is formed, giving phthalic anhydride and the aminodiol as the sole recognizable products. The crude product, on analysis, gave results reasonably well in accord with those required by the dimethylol phthalamic acid (I).

Calcd. for $C_{12}H_{15}NO_5$: neutral equivalent, 253; saponification value, 0; hydroxyl equivalent, 126.5. Found: neutral equivalent, 251; saponification value, 24[15]; hydroxyl equivalent, 133.

Second Stage of the Reaction between 2-Amino-2-methyl-1,3-propanediol and Phthalic Anhydride.—One mole of phthalic anhydride (148 g.) and 1.1 mole of the aminodiol (115.5 g.) were heated and stirred for two hours at a temperature of 150–200° (thermometer in the liquid). Twenty cubic centimeters of water was collected (calcd., 18 cc.). The product was a sticky, thermoplastic, resinous-appearing substance. A sample was subjected to vacuum distillation. Around 50% of it distilled over as a sluggish, pale reddish liquid (b. p. 207–220° (6 mm.)) which solidified to a stiff balsam-like material.

Anal. Found: sap. equiv., 226, 232; hydroxyl equiv., 234, 218; N (Kjeldahl), 6.15. Calcd.: sapon. equiv., 235; hydroxyl equiv., 235 (structure III), 117.5 (structure II); N, 5.95.

A second sample was distilled under high vacuum. About fifty per cent. of it (boiling point, 172–178° at about 50 microns) was thus obtained as a pale yellow, sluggish liquid which slowly solidified on standing several weeks at room temperature. (A small amount of a higher boiling fraction (b. p. 200–220° at 0.3–0.7 mm.) was also obtained.)

Anal. Found: hydroxyl equiv., 143; N (Kjeldahl), 5.72; mol. wt. (camphor), 247. Calcd.: hydroxyl equiv., 235 or 117.5; N, 5.95, mol. wt., 235.

A sample was further purified by crystallization as follows: from benzene, from ethyl acetate and carbon tetrachloride, from carbon tetrachloride, from ethyl acetate and petroleum ether. Fine, silky, colorless needles were obtained; m. p. 90.5–91.0°.

Anal. Calcd. for $C_{12}H_{13}NO_4$: C, 61.25; H, 5.57; N, 5.95; mol. wt., 235. Found: C, 60.80, 61.50, 61.09, 60.98; H, 5.55, 5.84, 5.72, 5.68; N, 5.93, 6.26; mol. wt., 256, 247.

This compound did not form a picrate nor a nitroso derivative. A benzoyl derivative was formed (in good yield) with benzoyl chloride in pyridine. It melted at 121.5°, after crystallization, once from 95% alcohol and twice from benzene.

Anal. Calcd. for $C_{26}H_{21}O_6N$: C, 70.43; H, 4.74; N, 3.16; mol. wt., 443. Found: C, 70.59, 70.59; H, 4.88, 4.96; N, 3.36, 3.38; mol. wt., 461, 426.

Third Stage of the Reaction between 2-Amino-2-methyl-1,3-propanediol and Phthalic Anhydride.—The reaction

(15) Saponification value, calcd. for the alternate ester structure, i. e., mono-(β-methyl-β-amino-γ-hydroxy)-propyl phthalate, 223.

was carried out as indicated in Table I. A hard, brittle, amber-colored, easily friable, amorphous solid was obtained. The crude product was analyzed. *Anal.* Found: sapon. equiv., 200, 197; N (Kjeldahl), 4.98.

One hundred grams of this crude product, on vacuum distillation in a stream of nitrogen, gave *ca.* 50 g. of a hard, granular, semi-crystalline material, boiling at 195–205° at 2 mm. A portion of it was crystallized from ethyl acetate and then four times from ethylene chloride. A small amount of a colorless, micro-crystalline powder was thus obtained, having a sharp melting point of 165°. A second sample of the crude, colophony-like product was distilled at 2–6 mm. pressure (b. p. 140–219°, mainly 213–219°) and the main fraction redistilled under high vacuum. Three crystalline fractions were thus obtained: (1) b. p. 110–140° (0.07–0.10 mm.); (2) b. p., 145–160° (0.05 mm.); (3) b. p. 165–180° (0.05–0.2 mm.). Fraction (1) was crystallized four times from ethylene chloride. Beautiful, glistening crystals were obtained, melting at 160.5°. A microscopic examination showed large, nearly square, flat plates, some of them elongated to laths.

Anal. Calcd. for $C_{12}H_{11}NO_3$: C, 66.34; H, 5.11; N, 6.45; mol. wt., 217. Found: C, 66.14, 65.78; H, 5.10, 5.14; N, 6.39, 6.42; mol. wt., 235, 227.

The purified material gave a picrate, with 30% excess picric acid in absolute alcohol; melting point, 225–226° (decompn.). Analysis indicated that it contained two moles of the compound $C_{12}H_{11}NO_3$ combined with one of picric acid.

Anal. Calcd. for $2C_{12}H_{11}NO_3 \cdot C_6H_3N_3O_{10}$: N, 10.57. Found: N, 10.48, 10.55. The same substance was formed when picric acid was used in 100% excess. Found: N, 10.57, 10.34.

A little warm water was added to the filtrate from which the 2:1 picrate separated and the solution was again cooled. A second crystalline picrate was thus obtained which melted sharply at 146–147°, and analyzed for the 1:1 compound.

Anal. Calcd. for $C_{12}H_{11}NO_3 \cdot C_6H_3N_3O_{10}$: N, 12.54. Found: N, 12.45, 12.17.

An attempted reduction of the compound $C_{12}H_{11}NO_3$ with zinc and acetic acid failed. Treatment with sodium in absolute alcohol resulted in hydrolysis to 2-amino-2-methyl-1,3-propanediol and sodium phthalate (identified by analysis of the sodium salt, and conversion to phthalic acid, m. p. 187.5°; mixed m. p. 189°; positive fluorescein test).

Anal. Calcd. for $C_8H_4O_4Na_2 \cdot 2H_2O$: Na, 18.9. Found: Na, 19.1, 19.2.

The second fraction obtained on distillation was crystallized as follows: twice from ethyl acetate, once from ethylene chloride and once from benzene and ethyl acetate. Fine, dense, colorless, powdery crystals resulted; m. p. 165–165.2°; mixed m. p. with the compound $C_{12}H_{11}NO_3$, 160–160.5°. Under the microscope it appeared as small clusters of laths, arranged radially, having an extinction coefficient of 38° (sample a). A small amount was purified further by twice crystallizing it from absolute alcohol. The melting point was unchanged (sample b). *Anal.* Calcd. for $C_{19}H_{17}NO_5$: C, 67.32; H, 5.02; N, 4.13; mol. wt., 339. Found: (a) C, 66.90, 66.77; H, 5.33, 5.33; N, 4.20, 4.18; mol. wt., 280, 302. (b) C, 67.15, 67.09; H, 5.33, 5.25; N, 4.22, 4.14; mol. wt., 281, 294.

This substance does not form a picrate. Treatment with sodium and alcohol, followed by acidification, gave some phthalic acid and a small amount of a substance of m. p. 227–228° (decomp.) which has not been identified. Benzoic acid could not be detected, although the analytical composition points to this substance as a possible component of the compound.

Reaction of the Second Stage Product with Excess Phthalic Anhydride.—Forty-five grams of the 1:1 reaction product was heated in a long-necked flask with 50 g. of phthalic anhydride for twenty minutes at 170–200°. The resinous product which resulted was extracted successively with hot ethylene chloride and hot ethyl acetate, and each solution was shaken with sodium carbonate solution to remove phthalic acid and unreacted phthalic anhydride. The ethylene chloride solution was evaporated and treated with warm heptane. Five grams of a colorless powder was obtained which was crystallized several times from a mixture of ethylene chloride and carbon tetrachloride. The small amount of purified material obtained was identified as the oxazoline derivative, $C_{12}H_{11}NO_3$, by melting point and mixed melting point. From the ethyl acetate solution, a substance was obtained (by concentration and precipitation with heptane) which melted unsharply at 155–165° after crystallization from carbon tetrachloride, and which was not identical with any of the substances previously described.

Anal. Found: N, 3.70, 3.71.

This may possibly be a substance derived from two moles of phthalic anhydride and one mole of the aminodiol. Such a compound would have the composition $C_{20}H_{15}NO_6$ (calcd.: N, 3.83).

Summary

1. Succinic, maleic, adipic and sebacic acids react with 2-amino-2-methyl-1,3-propanediol to give "heat convertible" resins.

2. Phthalic anhydride, under the same conditions, gives a mixture of crystalline compounds and, as by-products, resins which are probably linear polymers.

3. This reaction has been shown to involve the following stages: (a) addition to form a dimethylol phthalamic acid (I); (b) intramolecular esterification to an 8-ring ester-amide (III); (c) dehydration, through the isoamide form, to give an oxazoline derivative (VI) which contains a five, a six and an eight ring fused together.

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α-Alkylsulfonylamides[1]

BY AUSTIN POMERANTZ[2] AND RALPH CONNOR

In the previous study[3] of α-sulfonylamides the most effective hypnotic was α-*n*-butylsulfonyl-*n*-butyramide. Since this was the only purely aliphatic derivative investigated, the synthesis of a series of α-alkylsulfonylamides was undertaken. From the results described in the preceding paper[4] it seemed advisable to avoid the alkylation reaction previously employed and attention was therefore directed toward the reaction of mercaptides with α-bromoamides, followed by oxidation.

$$RSNa + R'_2CBrCONH_2 \longrightarrow RSCR'_2CONH_2 \xrightarrow{H_2O_2} RSO_2CR'_2CONH_2$$

$$R' = -H \text{ or } -C_nH_{2n+1}$$

Using conditions somewhat similar to those previously described,[3] the reactions of ethyl, *n*-propyl and *n*-butyl mercaptans with chloroacetamide, α-bromopropionamide, α-bromo-*n*-butyramide, α-bromoisobutyramide, α-bromo-*n*-valeramide, α-bromoisovaleramide and α-bromo-*n*-caproamide were carried out and the α-(alkylthio)-amides oxidized to the corresponding α-alkylsulfonylamides.[5] This synthesis proved to be satisfactory; the results are given in the experimental part. The sulfides were readily purified by crystallization but in several cases developed a slight odor of mercaptan on long standing. The oxidations were generally satisfactory but in a few cases the sulfones were rather difficult to purify.

The method of synthesis makes the structures of the products fairly certain. Furthermore, α-*n*-butylsulfonyl-*n*-butyramide and α-*n*-butylsulfonyl-*n*-caproamide were identical with the compounds previously prepared by the alkylation method.[4] The only reactions about which there seemed to be any uncertainty were those of α-bromoisobutyramide. Considering the behavior of the corresponding ester with the sodium derivatives of active methylene compounds,[6] it seemed possible that a mercaptide might cause the elimination of hydrogen bromide from α-bromoisobutyramide with the formation of α-methylacrylamide; addition of mercaptan to the conjugated system would give a β-(alkylthio)-amide isomeric with the desired product. However, β-(*n*-butylthio)-isobutyramide was prepared by the reaction of *n*-butyl mercaptan with α-methylacrylamide.[7]

$$n\text{-}C_4H_9SH + CH_2{=}C(CH_3)CONH_2 \xrightarrow{\text{piperidine}} n\text{-}C_4H_9SCH_2CH(CH_3)CONH_2$$

The product differed from that obtained by metathesis; this establishes the fact that the α-bromoamides react normally with mercaptides to give α-alkylthio derivatives.

Experimental Part

Melting points are uncorrected unless otherwise specified. The acids and mercaptans were products of the Eastman Kodak Company. The ligroin used was the fraction boiling at 70–90°. Pure α-bromopropionamide was obtained in 70% yields from methyl α-bromopropionate[8] but the ethyl ester gave unsatisfactory results. Some of the other α-bromoamides were prepared from the α-bromo acid chlorides by the method of Bischoff.[9] The most satisfactory general method was the bromination of the fatty acids and isolation of the pure α-bromo acids by the method described for α-bromo-*n*-caproic acid.[10] The α-bromo acid chlorides were prepared by the method described for *n*-butyryl chloride[11] and were satisfactory for use without distillation. They were converted to the amides by the use of ammonium hydroxide as described below. All but two of the α-bromoamides had been prepared previously.[9]

α-Bromoamides.—The middle neck of a 1-liter, three-necked, round-bottomed flask was fitted with a mechanical stirrer and gas outlet tube. A gas inlet tube long enough to extend below the surface of the reaction mixture and a dropping funnel were inserted in the other necks. The flask was immersed in an ice–salt-bath, 235 ml. of concentrated ammonium hydroxide added and ammonia gas bubbled into the cold solution over a period of about one hour. The crude acid chloride from one mole of α-bromo acid was then added dropwise over a period of about three hours. During this time the temperature of the ammoniacal solution was maintained at about 0° and ammonia gas passed into the mixture continuously. The in-

(1) This communication is constructed from a thesis submitted by Austin Pomerantz in partial fulfilment of the requirements for the degree of Doctor of Philosophy at the University of Pennsylvania in June, 1939.

(2) Harrison Fellow in Chemistry, 1938–1939; Harrison Scholar in Chemistry, 1937–1938.

(3) d'Ouville and Connor, THIS JOURNAL, **60**, 33 (1938).

(4) Pomerantz and Connor, *ibid.*, **61**, 3139 (1939).

(5) The pharmacological examination of these compounds is being carried out under the direction of Dr. Robert S. Shelton of the Wm. S. Merrell Company and will be reported elsewhere.

(6) Rydon, *J. Chem. Soc.*, 1444 (1936).

(7) The authors are grateful to the Rohm and Haas Company for a generous supply of α-methylacrylamide.

(8) Jacobs and Heidelberger, "Org. Syntheses," Coll. Vol. I, p. 147.

(9) Bischoff, *Ber.*, **30**, 2312 (1897).

(10) Clarke and Taylor, "Org. Syntheses," Coll. Vol. I, p. 108.

(11) Helferich and Schaefer, "Org. Syntheses," Coll. Vol. I, p. 142.

TABLE I

α-(ALKYLTHIO)-AMIDES

Compound	M. p. (corr.), °C.	Nitrogen, %[a] Calcd.	Found	Sulfur, %[b] Calcd.	Found
$C_2H_5SCH_2CONH_2$	50.5–51[c]	11.8	11.9	26.90	26.90
$C_2H_5SCH(CH_3)CONH_2$	65–65.5	10.5	10.5	24.07	24.24
n-$C_3H_7SCH(CH_3)CONH_2$	56.5–57	9.52	9.45	21.78	21.86
n-$C_4H_9SCH(CH_3)CONH_2$	60.5–61.5	8.69	8.66	19.88	19.66
$C_2H_5SCH(C_2H_5)CONH_2$	100.5–101	9.52	9.47	21.78	21.80
n-$C_3H_7SCH(C_2H_5)CONH_2$	78–78.5	8.69	8.64	19.88	20.02
n-$C_4H_9SCH(C_2H_5)CONH_2$	65–65.5	7.99	7.94	18.29	18.22
$C_2H_5SC(CH_3)_2CONH_2$	93.5–94	9.52	9.46	21.78	21.84
n-$C_3H_7SC(CH_3)_2CONH_2$	95–95.5	8.69	8.66	19.88	19.83
n-$C_4H_9SC(CH_3)_2CONH_2$	107.5–108	7.99	7.95	18.29	18.37
$C_2H_5SCH(n$-$C_3H_7)CONH_2$	101.5–102	8.69	8.72	19.88	19.92
n-$C_3H_7SCH(n$-$C_3H_7)CONH_2$	98.5–99	7.99	7.95	18.29	18.36
n-$C_4H_9SCH(n$-$C_3H_7)CONH_2$	64.5–65	7.40	7.38	16.94	16.85
$C_2H_5SCH(i$-$C_3H_7)CONH_2$	111–111.5	8.69	8.65	19.88	19.62
n-$C_3H_7SCH(i$-$C_3H_7)CONH_2$	98.5–99	7.99	7.97	18.29	18.54
n-$C_4H_9SCH(i$-$C_3H_7)CONH_2$	75–75.5	7.40	7.32	16.94	17.07
$C_2H_5SCH(n$-$C_4H_9)CONH_2$	84.5–85	7.99	7.90	18.29	18.25
n-$C_3H_7SCH(n$-$C_4H_9)CONH_2$	100.5–101	7.40	7.44	16.94	17.06
n-$C_4H_9SCH(n$-$C_4H_9)CONH_2$	86.5–87	6.89	6.87	15.77	15.99

[a] Nitrogen analyses were made by the semi-micro Kjeldahl method. The values reported are the average of two determinations which did not differ more than 0.07% from the mean. [b] Sulfur analyses were made by the macro Parr bomb procedure. [c] This compound is included because the melting point had previously been reported[14] as 44°. The values for α-(n-propylthio)-acetamide and α-(n-butylthio)-acetamide agreed with those previously observed.[3,15]

soluble product was separated by filtration, washed with a small amount of cold water, dried and recrystallized from benzene or a mixture of benzene and ligroin. The yield of recrystallized material was 50–70% based on the α-bromo acid.

α-Bromo-n-valeramide.—The purified material melted at 78.5–79° (corr.).

Anal. Calcd. for $C_5H_{10}ONBr$: N, 7.78. Found: N, 7.77, 7.87.

α-Bromo-n-caproamide.—The purified material melted at 58.5–59° (corr.).

Anal. Calcd. for $C_6H_{12}ONBr$: N, 7.22. Found: N, 7.27, 7.28.

α-(Alkylthio)-amides.—To a sodium ethoxide solution prepared by dissolving sodium in absolute alcohol (approximately 50 ml. of alcohol per 0.1 gram atom of sodium) was added an equivalent amount of the mercaptan. The mixture was cooled in an ice–salt-bath[12] to 0° and the α-haloamide added in portions with shaking. The mixture was kept in the ice-bath during the mixing, since the reaction was noticeably exothermic. The mixture was shaken frequently and allowed to come to room temperature as the bath melted. After standing at room temperature for two to five days the reactions were complete, except those involving α-bromoisobutyramide; in these cases the reactions were carried out for two weeks at room temperature. The insolubility of the amide and the decreased reactivity of the tertiary halogen probably combined to retard the reaction of α-bromoisobutyramide.

After the reaction was complete most of the alcohol was removed from the mixture under reduced pressure. In most cases the amides were fairly insoluble in water and were isolated by pouring the distillation residue on chipped ice and collecting the solid product on a filter. The aqueous filtrates contained small amounts of the α-(alkylthio)-amides which were readily removed by ether extraction. The solvent was removed on the steam-bath, the residues dissolved in hot dilute alcohol, decolorized with charcoal and crystallized by the addition of more water. The amount of material so obtained was usually small, especially with the higher homologs.

The α-(alkylthio)-acetamides and α-(ethylthio)-propionamide were too soluble in water to be isolated in good yields by the above method. In these cases the residues remaining after the removal of the solvent were diluted with water (one to two times the original volume of the reaction mixtures) and extracted with four 100-ml. portions of ether. The extracts were dried over sodium sulfate and the ether removed on the steam-bath. The residues were oils but were readily crystallized from ligroin; in a few cases a little benzene was added to increase the solubility. The properties and analyses of the products are given in Table I.

Using 0.15 to 0.30 mole of reactants, the amount of α-(alkylthio)-amides averaged 88%. α-(Ethylthio)-propionamide (64% yield) was the only product obtained in less than 80% yield.

β-(n-Butylthio)-isobutyramide.[13]—A mixture of 14.0 ml. (11.7 g., 0.13 mole) of n-butyl mercaptan, 11.1 g. (0.13 mole) of α-methylacrylamide[7] (m. p. 107.5–110°) and 0.5 ml. of piperidine in 50 ml. of absolute alcohol was

(12) The effect of temperature upon this reaction has already been described.[3]

(13) The procedure is that used by Nicolet, THIS JOURNAL, **57**, 1098 (1935), for α,β-unsaturated esters and ketones.

(14) Claesson, *Bull. soc. chim.*, [2] **23**, 444 (1875).

(15) Uyeda, *J. Chem. Soc. Jap.*, **50**, 687 (1929).

TABLE II

α-ALKYLSULFONYLAMIDES[a]

Compound	M. p. (corr.), °C.	Nitrogen, %[b] Calcd.	Found	Sulfur, %[b] Calcd.	Found
$C_2H_5SO_2CH_2CONH_2$	98.5–99[c]	9.27	9.17	21.21	21.11
n-$C_3H_7SO_2CH_2CONH_2$	104–104.5[d]	8.48	8.37	19.40	19.44
$C_2H_5SO_2CH(CH_3)CONH_2$	126–126.5[e]	8.48	8.47	19.40	19.47
n-$C_3H_7SO_2CH(CH_3)CONH_2$	122–122.5	7.82	7.82	17.89	17.91
n-$C_4H_9SO_2CH(CH_3)CONH_2$	114–114.5	7.25	7.19	16.59	16.54
$C_2H_5SO_2CH(C_2H_5)CONH_2$	168–168.5	7.82	7.81	17.89	17.74
n-$C_3H_7SO_2CH(C_2H_5)CONH_2$	137–137.5	7.25	7.28	16.59	16.70
$C_2H_5SO_2C(CH_3)_2CONH_2$	92.5–93[f]	7.82	7.78	17.89	17.79
n-$C_3H_7SO_2C(CH_3)_2CONH_2$	99.5–100.5[f]	7.25	7.56[h]	16.59	...[h]
n-$C_4H_9SO_2C(CH_3)_2CONH_2$	77.5–78[f]	6.76	6.68	15.47	15.27
$C_2H_5SO_2CH(n\text{-}C_3H_7)CONH_2$	117.5–118	7.25	7.27	16.59	16.39
n-$C_3H_7SO_2CH(n\text{-}C_3H_7)CONH_2$	125–125.5	6.76	6.74	15.47	15.48
n-$C_4H_9SO_2CH(n\text{-}C_3H_7)CONH_2$	125–125.5[g]	6.33	6.34	14.49	14.39
$C_2H_5SO_2CH(i\text{-}C_3H_7)CONH_2$	122–123.5	7.25	7.15	16.59	16.50
n-$C_3H_7SO_2CH(i\text{-}C_3H_7)CONH_2$	116–117	6.76	6.79	15.47	15.49
n-$C_4H_9SO_2CH(i\text{-}C_3H_7)CONH_2$	126.5–127[g]	6.33	6.33	14.49	14.51
$C_2H_5SO_2CH(n\text{-}C_4H_9)CONH_2$	112–112.5[g]	6.76	6.76	15.47	15.46
n-$C_3H_7SO_2CH(n\text{-}C_4H_9)CONH_2$	119–119.5[g]	6.33	6.29	14.49	14.24

[a] Unless otherwise noted, the sulfones were recrystallized from water. The properties of α-n-butylsulfonylacetamide, α-n-butylsulfonyl-n-butyramide and α-n-butylsulfonyl-n-caproamide agreed with those previously reported.[3,4] [b] See Table I, footnotes [a] and [b]. [c] Recrystallized from alcohol. [d] Recrystallized from benzene–alcohol. [e] Recrystallized from benzene–methanol. [f] Recrystallized from benzene–ligroin. [g] Recrystallized from dilute alcohol. [h] See the remarks about the impure nature of this compound in the discussion of the preparation of α-alkylsulfonylamides.

heated on the steam-bath for six and one-half hours. Most of the alcohol was then removed by distillation and the solution poured on chipped ice. The crude material weighed 12.3 g. (54%), m. p. 52–53°. Recrystallization from ligroin gave a pure product, m. p. 54.5–55° (corr.).

Anal. Calcd. for $C_8H_{17}ONS$: N, 7.99; S, 18.29. Found: N, 8.01, 8.09; S, 18.35.

α-Alkylsulfonylamides.—The sulfide was dissolved in a mixture of equal parts by volume of glacial acetic acid and acetic anhydride, using about 100 ml. of this solvent per 0.1 mole of sulfide. The solution was cooled in an ice–salt-bath and maintained at approximately 0° while 30% hydrogen peroxide was added slowly. Approximately 27 ml. of peroxide (30–35% excess) was used per 0.1 mole of sulfide. The mixture was allowed to come slowly to room temperature as the ice-bath melted and to stand at room temperature for at least three days. A small amount of manganese dioxide was added carefully to decompose the excess peroxide, the solution transferred to a Claisen flask and the solvent entirely removed under a pressure of not more than 30 mm. The solid residue was dissolved in a proper solvent, in most cases water, decolorized with charcoal and allowed to crystallize. In many cases a pure product was obtained from the first crystallization but the caproamides and α-n-ethylsulfonyl-n-valeramide were difficult to purify and required several recrystallizations. The oxidation of α-(n-propylthio)-isobutyramide was quite unsatisfactory (28%) and its abnormality verified by check runs. In this case the product gave a cloudy melt, the analytical data were unsatisfactory and numerous recrystallizations from benzene–ligroin and from acetone (using dry-ice) did not improve the product. The yields of α-alkylsulfonylamides averaged 72%, using 0.1 to 0.2 mole of sulfide. The products are described in Table II.

Summary

The reactions of the sodium mercaptides from ethyl, n-propyl and n-butyl mercaptans with seven α-haloamides have been carried out and the twenty-one α-(alkylthio)-amides oxidized to the corresponding sulfones, which are under examination as hypnotics. The metathesis reaction of the α-bromoamides was shown to be normal by the synthesis of the β-isomer from the reaction of n-butyl mercaptan with α-methylacrylamide. The preparation of α-bromoamides, including two not previously reported, has been described.

PHILADELPHIA, PENNA. RECEIVED AUGUST 30, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

The Preparation of Sulfamic Acid by the Hydroxylamine–Sulfur Dioxide Reaction

BY H. H. SISLER AND L. F. AUDRIETH

The reaction of hydroxylamine with sulfur dioxide (or sulfurous acid) is one of the few reactions in which the hydroxylamine molecule plays the role of an augmenting agent,[1] for in this reaction the sulfur dioxide is nitridized to sulfamic acid.

(a) $NH_2OH + SO_2 \longrightarrow NH_2SO_3H$

It is not surprising, however, that hydroxylamine should behave in this manner in certain of its reactions, for it is an aquo ammono analog of hydrogen peroxide,[2] just as the sulfamic acid which is formed is an aquo ammono sulfuric acid.

In addition to its interest from a theoretical point of view, the nitridation of sulfur dioxide by hydroxylamine salts represents one of the best known laboratory methods for the preparation of sulfamic acid.[3] An analogous reaction of acetoxime with aqueous solutions of sulfur dioxide also has been recorded.[4] It is interesting to note

(b) $(CH_3)_2C{=}NOH + H_2O + SO_2 \longrightarrow (CH_3)_2C{=}O + NH_2SO_3H$

that normal sulfites do not react with hydroxylamine derivatives in this way.[5]

Hitherto, these nitridation reactions always have been carried out either by saturating an aqueous solution of the hydroxylamine derivative with sulfur dioxide and allowing it to stand in the cold for an extended period of time, or by bubbling sulfur dioxide through the solution for about forty-eight hours. These procedures have two disadvantages: (1) low yields are obtained, and (2) a relatively long period of time is required to carry out such preparations.

A study of the hydroxylamine–sulfur dioxide reaction was undertaken primarily in an effort to obtain experimental facts which would permit an elucidation of the mechanism of the reaction. The procedure for preparation also was improved and modified by carrying out the reaction under pressure. The experimental portion of this paper deals with the effects of such variables as the concentrations of the hydroxylamine salt, and of hydronium ion, and time upon the yield of sulfamic acid. The reaction between acetoxime, as an example of a hydroxylamine-yielding compound, and sulfur dioxide was also subjected to investigation.

(1) Franklin, "The Nitrogen System of Compounds," Reinhold Publishing Corporation, New York, N. Y., p. 212.

(2) Sisler and Audrieth, *Proc. Ill. Acad. Sci.*, **31**, 145 (1938).

(3) Raschig, *Ann.*, **241**, 161 (1887).

(4) Schmidt, *J. prakt. Chem.*, **44**, 513 (1891).

(5) Raschig, "Schwefel und Stickstoff Studien," Verlag Chemie, G. m. b. H., Berlin, p. 225.

Experimental

Reaction of Hydroxylamine Sulfate with Sulfur Dioxide.—An aqueous solution of hydroxylamine sulfate was cooled to approximately −80° in a dry-ice–acetone mixture. An excess of sulfur dioxide was then condensed in the container. The container was transferred to an autoclave and allowed to warm to room temperature. Under these conditions, the reaction mixture was subject to a pressure of 3.5–4 atmospheres, approximately equal to the vapor pressure of sulfur dioxide at room temperature. After a certain time interval, the pressure was released, and the excess sulfur dioxide allowed to escape. The sulfamic acid which had crystallized was removed by filtration, and the adhering liquid removed as completely as possible by suction on a Buchner funnel. The product was dried by washing with alcohol and ether, and was found to contain only a small trace of sulfate. To recover the sulfamic acid remaining in the solution, the filtrate was treated with concentrated sulfuric acid and cooled in an ice–salt mixture. In typical experiments such as are recorded in Table I, two factors were varied: (1) the reaction time, and (2) the concentration of hydroxylamine sulfate solution.

TABLE I

REACTION OF HYDROXYLAMINE SULFATE WITH SULFUR DIOXIDE UNDER PRESSURE

$(NH_3OH)_2 \cdot H_2SO_4$, g.	H_2O, g.	Concn., equivs. $(NH_2OH)_2 \cdot H_2SO_4$ per 1000 g. H_2O	Time, hr.	Temp., °C.	NH_2SO_3H obtained, g.	Yield, %
1 41	50	10.0	18.3	0	15.5	32
2 16.5	50	4.0	23	25	14	72
3 17	50	4.1	6	25	13	65
4 16.5	20	10.1	15	25	3	15
5 16.5	35	5.7	15	25	11	56
6 16.5	50	4.0	15	25	13	67

Examination of the data listed in Table I shows that the reaction of sulfur dioxide with highly concentrated solutions of hydroxylamine sulfate goes much more slowly than with more dilute solutions. It was thought that this phenomenon might be due to the high concentration of hydronium ions which would be built up under these circumstances as illustrated by the equation

(c) $NH_3OH^+ + SO_2 + 2H_2O \longrightarrow NH_2SO_3^- + 2H_3O^+$

This hypothesis was substantiated by means of the following experiments. A mixture of 16.8 g. of hydroxylamine sulfate, 25 g. of water, and 75 g. of 98% sulfuric acid was sealed in the autoclave with a large excess of sulfur dioxide and allowed to remain at room temperature for sixty-six

hours. No sulfamic acid was obtained. A similar result was obtained when a solution of 16.8 g. of hydroxylamine sulfate in 50 g. of 98% sulfuric acid and 50 ml. of water was treated with sulfur dioxide under pressure for forty-six hours. Sulfamic acid was obtained in both cases by subsequent neutralization and further treatment with sulfur dioxide.

Reaction of Acetoxime with Sulfur Dioxide.—A solution of 11 g. acetoxime in 10 ml. of water and 30 ml. of ethyl alcohol was saturated at 0° with sulfur dioxide gas, and was kept in a stoppered flask at that temperature for a total of three days. The solid sulfamic acid which formed was removed from time to time by filtration and more sulfur dioxide added as needed to keep the solution saturated. The product was washed with alcohol and ether, and dried in air. A total yield of 11.1 g. of sulfamic acid (corresponding to 76% of the theoretical yield) containing neither sulfate nor oxime was obtained.

In carrying out the reactions of acetoxime with sulfur dioxide under pressure at 0°, an aqueous solution of acetoxime in a glass pressure bottle was cooled to approximately −80° in a dry-ice–acetone mixture. An excess of sulfur dioxide was condensed on the frozen mass, and the bottle sealed. The temperature was allowed to come to 0°, and kept at that point by placing the bottle in an ice-bath. After a certain time had elapsed the bottle was again cooled, opened, and the excess sulfur dioxide allowed to escape. The sulfamic acid which had crystallized from the solution was removed by filtration, and dried by washing with alcohol and ether. The results of a number of typical experiments are listed in Table II. A similar series of experiments was carried out at approximately 25° (in an autoclave). The results of these experiments are also listed in Table II.

TABLE II

REACTION OF ACETOXIME WITH SULFUR DIOXIDE UNDER PRESSURE

$(CH_3)_2CNOH$, g.	H_2O, g.	Temp., °C.	Time, hr.	NH_2SO_3H obtained, g.	Yield, %
10	20	0	1.5	9.3	70
20	20	0	3	18.0	68
10	10	0	5.5	10.2	77
14.5	14.5	25	2	14.5	75
10	10	25	5	12.0	90
10	10	25	11.75	12.0	90

Discussion

It is evident from the data in Table I that the yield of sulfamic acid from the reaction of hydroxylamine salts with sulfur dioxide is greatly increased and the time required for the reaction decreased by operating under pressure. This is also true of the acetoxime reaction. The results of these experiments also show that the reaction is inhibited by excessive concentrations of hydronium ions. This fact was demonstrated by the failure of hydroxylamine salts to nitridize sulfur dioxide in the presence of concentrated sulfuric acid, and is further supported by the data from experiments four, five and six in Table I, which show that much lower yields of sulfamic acid are obtained from concentrated solutions of hydroxylamine salts than from more dilute solutions. As may be seen from equation (c), two moles of hydronium ion are released for each mole of hydroxylamine sulfate that reacts. Hence, with concentrated solutions of hydroxylamine sulfate high concentrations of hydronium ions are quickly built up, inhibiting the reaction.

Examination of the data from experiments two, three and six in Table I indicates that the formation of sulfamic acid becomes much slower as the reaction proceeds. Thus, the yield after a six hour reaction time was only 7% less than that after a twenty-three hour period, other conditions being comparable in the two experiments. This effect may be attributed to the formation of hydronium ions as the reaction proceeds, and to the decrease in the amount of hydroxylamine sulfate present.

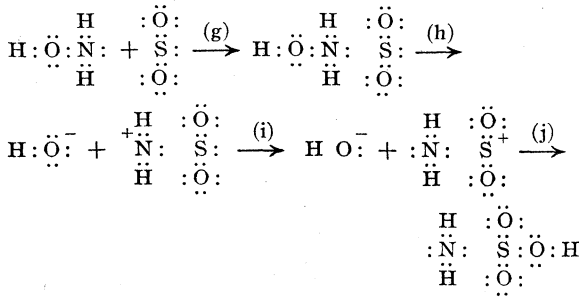
A comparison of the data presented in Table II with those given in Table I shows that much better yields of sulfamic acid are obtained in a shorter length of time by the reaction of sulfur dioxide with acetoxime than by the corresponding reaction with hydroxylamine sulfate. This is not an altogether unexpected result when considered in the light of the effect of high concentrations of hydronium ions on the reaction. As is shown in equation (b), sulfamic acid is the only product contributing hydronium ions in the acetoxime reaction, and the hydronium ion concentration which can be built up from this source is limited by the relatively low solubility of sulfamic acid. This would seem to explain why, under similar conditions, acetoxime gives 90% yields of sulfamic acid after five hours, whereas hydroxylamine sulfate gives only 72% yields after twenty-three hours.

The nitridation of sulfur dioxide to sulfamic acid by hydroxylamine may be explained by the mechanism

(d) $SO_2 + H_2O \underset{}{\overset{+H_2O}{\rightleftharpoons}} H_2SO_3 \overset{+H_2O}{\rightleftharpoons} H_3O^+ + HSO_3^- \overset{+H_2O}{\rightleftharpoons} 2H_3O^+ + SO_3^=$

(e) $:\ddot{O}::\ddot{S}:\ddot{O}: \rightleftharpoons :\ddot{O}:\ddot{S}:\ddot{O}: \rightleftharpoons :\ddot{O}:\ddot{S}::\ddot{O}:$

(f) $H:\ddot{N}:\ddot{O}:H^+ + H_2O \rightleftharpoons H_3O^+ + :\ddot{N}:\ddot{O}:H$ (H on N)



The sulfur dioxide molecule is generally assumed to exist in the resonance forms indicated in (e). The hydroxylammonium ion exists in equilibrium with the hydroxylamine molecule (f). The middle resonance form of the sulfur dioxide molecule, having only six electrons in the outer shell of the sulfur atom, may unite with the hydroxylamine molecule by accepting the free pair of electrons on the nitrogen atom (g). As in Whitmore's electronic mechanism for rearrangements of the Beckmann type,[6] the hydroxyl group may form an ionic bond leaving the nitrogen with a positive charge (h). However, since the nitrogen atom has a much greater affinity for the electron pair than does the sulfur atom, the free pair of electrons on the sulfur atom shifts immediately to the nitrogen atom (i). The negatively charged hydroxyl group can then unite with the positively charged sulfur atom, forming the sulfamic acid molecule (j).

It is probable that steps (h), (i), and (j) take place almost simultaneously. That is certainly the case with steps (h) and (i) due to the greater mobility of the electron pair than of the hydroxyl group. The fact that step (i) can take place probably makes possible step (h). The removal of the electron pair by the oxygen from the nitrogen atom in step (h) does not necessarily mean that the hydroxyl group ever exists as a free ion, but merely that it forms an ionic bond. In fact, it is likely that the hydroxyl group is never out of the sphere of influence of the rest of the molecule during the rearrangement.

This mechanism satisfactorily accounts for the fact that the reaction is inhibited by a large hydronium ion concentration, for the excess of hydronium ions should drive the equilibrium in (f) far to the left so that the free pair of electrons furnished by the nitrogen on the hydroxylamine molecule would be covered up by protons. It also explains why, in the presence of enough alkali to change all the sulfur dioxide, sulfurous acid, and bisulfite to normal sulfite, and to neutralize the acid attached to the hydroxylamine, no reaction takes place, for, as shown in (d), two moles of hydroxide ion would completely convert all the sulfur dioxide to normal sulfite, leaving no free sulfur dioxide to react with the hydroxylamine. Thus, an excess of acid renders the hydroxylamine incapable of coördination, while an excess of alkali makes the existence of sulfur dioxide or of sulfurous acid impossible.

(6) Whitmore, THIS JOURNAL, **54**, 3274 (1932).

Summary

1. The procedure for the preparation of sulfamic acid by the interaction of hydroxylamine salts and hydroxylamine-yielding compounds with sulfur dioxide has been improved by operation under pressure.

2. A mechanism for the reaction has been proposed involving coördination between the hydroxylamine molecule and sulfur dioxide with subsequent rearrangement to sulfamic acid.

URBANA, ILLINOIS RECEIVED JULY 10, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

The Action of Liquid Ammonia upon Sulfur Trioxide Addition Compounds

BY H. H. SISLER AND L. F. AUDRIETH

Theoretically, interaction of ammonia with sulfur trioxide should lead to ammonium sulfamate; actually, ammonium imidodisulfonate is obtained almost exclusively. However, when aqueous ammonia acts upon various sulfur trioxide–tertiary amine addition compounds[1] appreciable quantities of ammonium sulfamate are formed. In order to gain a clearer insight into the mechanism of these reactions, and also to prevent the simultaneous action of water (present in aqueous ammonia), the behavior of these sulfur trioxide addition compounds in liquid ammonia was investigated. The addition compounds studied were those with pyridine,[2] dimethylaniline,[3] dioxane,[4] hydrogen chloride (chlorosulfonic acid), and sodium chloride (sodium chlorosulfonate). The reaction products were analyzed for sulfamate, imidodisulfonate, and sulfate.

Recorded observations that ammonium imidodisulfonate is the sole product of the reaction of sulfur trioxide with liquid ammonia were verified.

Experimental

Method of Analysis.—The reaction products were analyzed by the following procedure. Sulfate and imidodisulfonate were precipitated as the respective barium salts by the addition of barium chloride to an ammoniacal, aqueous solution of the reaction product. The filtrate was next acidified with dilute hydrochloric acid, then treated with potassium nitrite solution for the purpose of converting the sulfamate ion into sulfate, which was then precipitated as barium sulfate.

$$NH_2SO_3^- + NO_2^- \longrightarrow N_2 + SO_4^= + H_2O$$

The joint precipitate of basic barium imidodisulfonate and barium sulfate was extracted with dilute hydrochloric acid, leaving the barium sulfate in the filtering crucible. The imidodisulfonate was estimated as barium sulfate after treatment of the acidified filtrate with nitrite and barium chloride. This procedure gives results which are fairly reproducible, but is not satisfactory for exact work due to the facts, (1) that the precipitate of basic barium imidodisulfonate is slightly soluble in water, and (2) that complete precipitation of sulfate as barium sulfate is difficult in the presence of large amounts of sulfamate ion.[5]

Experimental Results.—Pyridine–sulfur trioxide and dimethylaniline–sulfur trioxide were added directly to liquid ammonia at −33°. These reactions, while vigorous, could be controlled without difficulty. However, both dioxane–sulfur trioxide and liquid ammonia had to be precooled to the temperature of a solid carbon dioxide–ether bath to moderate the reaction. The chlorosulfonic acid was dissolved in a large excess of chloroform (20 g. in 140 ml. of $CHCl_3$) and then added slowly to liquid ammonia. Even under these conditions the reaction was found to be a very vigorous one, as was the reaction between sodium chlorosulfonate and ammonia. In every case, the excess of ammonia was allowed to evaporate and the residual product, after treatment to remove amine or solvent, was washed with ether and dried to constant weight. Samples were analyzed by the procedure given above.

Quantities of sulfur trioxide addition compounds used varied from 15 to 40 g. Large excesses of liquid ammonia (between 200 and 400 ml.) were used in all experiments. Typical experimental results are reproduced in Table I. The percentage composition of the reaction products, also the ratio of the percentages of ammonium sulfamate to triammonium imidodisulfonate, are given in each case.

TABLE I

Addn. cpd.	$(NH_4)_2SO_4$, %	$NH_4N(SO_3NH_4)_2$, %	$NH_2SO_3NH_4$, %	$\frac{\%NH_2SO_3NH_4}{\%NH_4N(SO_3NH_4)_2}$
$C_5H_5N \cdot SO_3$	13.5	2.1	83.5	39.8
	15.5	3.4	80.5	23.7
$C_6H_5N(CH_3)_2 \cdot SO_3$	13.5	8.6	72.3	8.4
	30.2	9.8	56.5	5.8
	36.8	6.4	55.0	8.6
$O(CH_2CH_2)_2O \cdot SO_3$	34.9	15.7	51.5	3.3
	30.1	15.2	56.8	3.7
$HCl \cdot SO_3$[a]	7.7	7.5	53.0	7.1
	11.5	8.1	51.0	6.3
$NaCl \cdot SO_3$[a]	13.2	4.3	41.5	9.7
	14.5	4.2	39.0	9.3

[a] NH_4Cl and NaCl, respectively, make up the rest of the reaction product.

Discussion

The reactions of ammonia with chlorosulfonic acid and sodium chlorosulfonate obviously are ammonolytic in character, involving replacement of a negative constituent by the amido group and leading to the formation of the sulfamate. The same mechanism also characterizes the reaction of ammonia with sulfur trioxide addition compounds. In fact, the tertiary amine complexes have been shown to be esters of N,N-disubstituted sulfamic acids, existing in the betaine form.[2]

If the three addition compounds of sulfur trioxide with pyridine, dimethylaniline, and dioxane are arranged in the order of the relative predominance of the sulfamate over the imidodisul-

(1) Baumgarten, *Ber.*, **59**, 1976 (1926).
(2) Baumgarten, *Ber.*, **59**, 1166 (1926).
(3) Willcox, *Am. Chem. J.*, **32**, 446 (1904).
(4) Suter, Evans and Kiefer, THIS JOURNAL, **60**, 538 (1938).
(5) Divers and Haga, *J. Chem. Soc.*, **69**, 1634 (1896).

fonate in their respective ammonolytic products, the following series is obtained

$C_5H_5N \cdot SO_3 > C_6H_5N(CH_3)_2 \cdot SO_3 > O(CH_2CH_2)_2O \cdot SO_3$

This is also the order of their decreasing stability toward water.[1,4] In view of the fact that imidodisulfonate only is formed when ammonia and sulfur trioxide react, it is logical to conclude that the presence of this product is due to the ammonation of sulfur trioxide held but loosely by the donor molecule. Consequently, the less stable the sulfur trioxide complex, that is, the weaker the coordinate bond holding the sulfur trioxide molecule, the greater will be the proportion of imidodisulfonate in the ammonolytic product.

Summary

Reactions of liquid ammonia with sulfur trioxide addition compounds result primarily in the formation of ammonium sulfamate. These reactions are considered to be ammonolytic in character.

URBANA, ILLINOIS RECEIVED JULY 26, 1939

[CONTRIBUTION FROM THE DANIEL SIEFF RESEARCH INSTITUTE]

The Photochemical Decomposition of Solid Hydrogen Compounds at Low Temperatures

BY L. FARKAS, Y. HIRSHBERG AND L. SANDLER

Very little has been known previously of the photochemical decomposition of solids at low temperatures.[1,2] It seemed, therefore, worth while to investigate reactions involving the liberation of hydrogen, since the ortho–para concentration of the hydrogen may reveal interesting features of the decomposition mechanism. It is well known that below 200°K. the ortho–para ratio of equilibrium hydrogen is dependent on the temperature and thus this ratio may indicate at which effective temperature the photochemical formation of the hydrogen has taken place.

In the following some experiments on the photochemical decomposition of hydrogen iodide, formaldehyde and methyl alcohol at temperatures between 65° and 85°K. are reported. All these substances give off hydrogen (besides other reaction products) when decomposed photochemically.[1,3,4]

Experimental

Hydrogen iodide was prepared in the usual way by catalytic combination of hydrogen with iodine and repeated fractional distillation at low temperatures.[5] It was kept in a glass bulb and was perfectly white in the solid state. Apiezon grease was used for the taps, which was only slowly attacked by hydrogen iodide.

The methyl alcohol was the purest obtainable product. As a source of formaldehyde, the vapor of 40% aqueous solution was used.

The experimental arrangement is shown in Fig. 1. The hydrogen iodide, formaldehyde or methyl alcohol was condensed on spot S of tube V, which contained liquid air. The glass tube was specially thin at S, in order to improve the heat exchange between the condensed substance and the liquid air. The amount of substance on S was adjusted by a lock system between the tap T and the storage bulb so as to form a white circle of about 5 mm. diameter and of about 10,000–100,000 molecular layers. A mercury arc served as a light source and the ultraviolet light entered through the quartz window Q opposite the spot S.

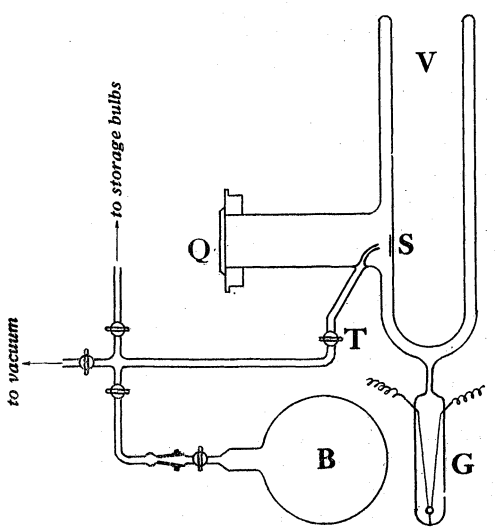


Fig. 1.

Occasionally the temperature of the tube was lowered to 65° K. by pumping off the liquid air. After the substance was condensed into the reaction vessel, the tap T was closed and the evolution of hydrogen during the illumination followed up by the Pirani gage (G). The illumination was continued until 30–40 cu. mm. of gas at S. T. P. was

(1) Bonhoeffer and L. Farkas, *Z. physik. Chem.*, **132**, 235 (1928).
(2) Hilsch and Pohl, *Ann. Physik*, [5] **32**, 155 (1938).
(3) *Cf.* Loecker and Patat, *Z. physik. Chem.*, **B27**, 431 (1934).
(4) Patat, *Z. Elektrochem.*, **41**, 494 (1935).
(5) *Cf.* Farkas and Melville, "Experimental Methods in Gas Reactions," The Macmillan Co., New York, 1939, p. 160.

evolved. The lamp was then switched off and the gas collected in a large bulb (B). The analysis of the ortho–para composition of the hydrogen was carried out by the micro-conductivity method.[6]

Experiments with Hydrogen Iodide.—During the illumination only a small amount of gas was given off by the hydrogen iodide crystals; the greater part of the photochemically formed hydrogen remained trapped in the solid. All the gas was given off immediately when the liquid air level in the tube V was lowered below the spot (S), as then the substance sublimed to the lower part of the tube.

TABLE I

No.	Time of illumination, min.	Temp., °K.	% p-H_2	Equilibration %
1	70	85	34.3	46
2	30	~70	38.6	~44
3	35	65	40.8	45
4	36	85	34.5	47
5	30	85	33.8	44
6	195	85	37.6	63
7	45	85	35.8	54

Experiments 1 and 4 (Table I) show that at 85°K. the evolved hydrogen contained 34% para-hydrogen corresponding to an ortho–para ratio in equilibrium at 115°K.[7]

In order to test the possibility of a secondary ortho–para conversion taking place after the illumination, normal hydrogen was introduced into the reaction vessel. It was found, however, that no conversion to para-hydrogen occurred in the presence of the hydrogen iodide crystals. When the hydrogen trapped inside the crystals was left in them for one hundred and fifty minutes at 85°K. after the illumination had been switched off (expt. 5), no change in the para-hydrogen concentration was observed, showing the absence of any secondary para–ortho conversion within the solid in the "dark." All these experiments show definitely that the formation of the para-hydrogen takes place during the illumination and the para–ortho concentration is in some way determined by the temperature of the solid hydrogen iodide.

By lowering the temperature of the liquid air to 70–65°K. (expt. 2 and expt. 3), para-hydrogen of higher concentration than in expts. 1 and 4 was obtained, the percentage of "equilibration," however, was the same as before. These experiments prove that the para-hydrogen is formed inside the solid during the illumination and not at the time when it is given off by the solid. The temperature at which the sublimation took place was the same in all experiments.

The simplest explanation for the fact that the apparent "equilibration" is not complete is that the actual temperature of the solid during the illumination is higher than that of the liquid air in the tube V. Experiments 6 and 7 show indeed that there is a marked increase in the para-hydrogen concentration of the evolved hydrogen if the amount of heat transferred from the outside or from the source to the illuminated substance is diminished. This was obtained (1) by reducing the light intensity of the mercury lamp through intensive cooling and through increasing the distance between reaction vessel and light source (in expt. 6), (2) by cutting off the infrared radiation by a water filter, (3) by shielding the reaction vessel with tin foil against temperature radiation from outside and (4) by removing continually the gas evolved during the illumination (in expt. 7). These experiments indicate that the para-hydrogen content of the gas formed during the decomposition corresponds nearly or completely to the temperature of the solid hydrogen iodide.

Experiments with Formaldehyde and Methyl Alcohol.—In the photochemical decomposition of formaldehyde hydrogen and carbon monoxide are formed.[3] There is also a possibility of carbon monoxide formation in the photolysis of methyl alcohol by secondary decomposition of the formaldehyde primarily formed.[4] The carbon monoxide was removed from the evolved gas by a cuprous chloride–ammonia solution.[8]

It was found that in all cases normal hydrogen was evolved (see Table II).

TABLE II

No.	Substance	Time of illumination, min.	Temp., °K.	% p-H_2
1	H_2CO	150	85	25
2	CH_3OH	110	85	25
3	CH_3OH	300	85	25
4	CH_3OH	300	75	25

Discussion of the Experiments with Hydrogen Iodide.—The photochemical decomposition of gaseous hydrogen iodide takes place according to the mechanism[1,9]

$$HI + h\nu \longrightarrow H + I \quad (1)$$
$$H + HI \longrightarrow H_2 + I \quad (2)$$
$$I + I \longrightarrow I_2 \quad (3)$$

The same decomposition takes place also in the liquid[10] and the solid state.[1]

The present experiments have shown that the para–ortho ratio of the hydrogen formed corresponds to the temperature of the solid.

There are two different processes which may bring about the equilibration of the photochemically formed hydrogen. One is the catalytic conversion of hydrogen under the influence of the inhomogeneous magnetic field of the iodine atom[11] and the other the reaction (2).

The iodine atom has a paramagnetic ground level $^2P_{3/2}$ and it was shown by Rosenbaum and Hogness[12] that the conversion of para-hydrogen in the reaction $H_2 + I_2 \rightleftarrows 2HI$ is caused by the

(6) A. Farkas, *Z. physik. Chem.*, **B22**, 344 (1933).

(7) *Cf.* A. Farkas, "Orthohydrogen, Parahydrogen and Heavy Hydrogen," Cambridge University Press, 1935, p. 14.

(8) The standard solution of cuprous chloride–ammonia, as used in gas analysis, removes carbon monoxide quantitatively from an $H_2 + CO$ mixture also at low pressures ($\sim 10^{-2}$ mm.) without converting para-hydrogen at an appreciable rate (see forthcoming publication).

(9) Warburg, *Ber. Berl. Akad.*, 314 (1916); 300 (1918).

(10) Bodenstein and Lieneweg, *Z. physik. Chem.*, **119**, 123 (1926).

(11) L. Farkas and Sachsse, *Z. physik. Chem.*, **B23**, 1 (1933).

(12) Rosenbaum and Hogness, *J. Chem. Phys.*, **2**, 267 (1934).

paramagnetic action of the iodine atoms present in thermodynamic equilibrium concentration.

A very rough calculation shows that an equilibration by the reaction

$$I + o\text{-}H_2 \rightleftarrows I + p\text{-}H_2 \qquad (4)$$

is only possible if the relevant conditions for the conversion in the solid are very favorable. The lower limit for the theoretical half-life time is given by

$$\tau_{theor.} = 0.69/W_{solid}Z_{solid}[I] \qquad (5)$$

(W_{solid} the transition probability $p \rightleftarrows o$ per collision, Z_{solid} the collision frequency between H_2 and I in the solid, [I] the stationary concentration of the iodine atoms), if for W_s, Z_s, [I] the upper limits are used.[13]

W_{solid} is, as a first approximation, equal to $W_{gas} = 4 \times 10^{-12}$. For the calculation of Z_{solid}, the approximation of Rabinowitch[14] is used according to which $Z_{solid} = Z_{coörd.}\ \nu$, $Z_{coörd.}$ denoting the number of coördinations of the pair $H_2 + I$ per second and ν the number of vibrations during a coördination. In this formula it is assumed that each vibration during the coördination is equivalent to a collision in the gas. The order of magnitude of Z is 3×10^{12} sec.$^{-1}$mole^{-1}l.[15]

The upper limit for [I] will be obtained by considering their production and recombination by diffusion. The time necessary for a particular iodine atom to diffuse the mean distance $\bar{x} = 1/[I]^{1/3}$ between two iodine atoms is given by the expression $t = \bar{x}^2/2D = 1/2D[I]^{2/3}$. Then the iodine atom under consideration will be somewhere on the surface of a sphere with a radius $\bar{x}$. It will collide with another iodine atom with the probability $\sim 4a_I^2/\bar{x}^2$ (coördination number = 8, $\pi a_I^2 = 10^{-15}$ cm.^{2} is the cross section of the iodine atom).

If n iodine atoms are formed per sec., and cm.^{3}, and $[I] = nt_0$, t_0 being the mean life time of an iodine atom, t_0 will be given by the expression

$$(nt_0)^{-2/3} = 8Dt_0a_I^2(nt_0)^{2/3}$$

Using the values $D = 10^{-11}$ cm.^{2} sec.$^{-1}$ and $n = 3 \times 10^{17}$ sec.$^{-1}$ cm.$^{-3}$ (calcd. from the rate of decomposition) one obtains $t_0 = 6$ min. and $[I] = 1.8 \times 10^{18}$ cm.$^{-3}$ $= 3 \times 10^{-3}$ mole/l. On the basis of these figures the half-life time in the solid is $\tau_{theor.} = 20$ min.

Since expts. 1, 3 and 4 have shown that the equilibration of hydrogen is (nearly) completed during the illumination, it is obvious that the half-life time of the conversion must be small compared with the time of illumination. Putting $\tau_{exptl.}$ at least one-sixth of the time of illumination, *i. e.*, 300 min., $\tau_{theor.}$ seems compatible with the experimental result. The margin between these figures, however, is not very large and owing to the nature of simplifications made in the calculation of $\tau_{theor.}$, the value obtained seems far too small. The authors believe that the conversion by the action of iodine atoms is not likely to be the decisive process for the equilibration.

The other possibility for the equilibration is reaction (2). In this reaction about 30,000 cal. are evolved. This circumstance makes it difficult to understand that in this process equilibrium hydrogen of low temperature should be formed, as the heat evolved in the reaction should raise the effective temperature of the particles concerned. Hydrogen corresponding to a low temperature equilibrium could only be formed if the heat of reaction is completely dissipated during the collision $H + HI_{solid}$ and is taken up by the whole hydrogen iodide lattice. Although at present we have no information of the energy exchange in this type of reaction, the present experiments seem to indicate that such dissipation of energy actually occurs.

Discussion of the Experiments with Formaldehyde and Methyl Alcohol.—The photochemical decomposition of formaldehyde takes place according to

$$HCHO + h\nu \longrightarrow CO + H_2 \qquad (6)[3]$$

Two different mechanisms have been suggested for the primary process involved in the photolysis of formaldehyde

$$H_2CO + h\nu \longrightarrow H_2 + CO \qquad (7)[3]$$
$$H_2CO + h\nu \longrightarrow 2H + CO \qquad (8)[16,17]$$

The photolysis of methyl alcohol takes place according to

$$CH_3OH + h\nu \longrightarrow CH_2O + H_2 \qquad (9)$$

and equations analogous to (7) and (8) can be considered as primary processes of this reaction.

If the hydrogen atoms formed in reaction (8) would react with another formaldehyde molecule according to

(13) In the following it is assumed that the hydrogen is dissolved in the solid in molecular form. If microscopic bubbles are formed inside the crystals, the rate of conversion would appear diminished.

(14) Rabinowitch, *Trans. Faraday Soc.*, **33**, 1225 (1937).

(15) According to L. Farkas and U. Garbatski [*Trans. Faraday Soc.*, **35**, 263 (1939)], the rate of conversion of para-hydrogen in presence of nitric oxide in aqueous solution is much slower than the rate corresponding to $Z_{liquid} = Z_{coörd.} \times \nu$.

(16) Norrish, *Nature*, **141**, 1138 (1938).

(17) Bergmann and Samuel, *ibid.*, **141**, 832 (1938).

$$H + H_2CO \longrightarrow H_2 + \dot{H}CO \qquad (10)$$

one might expect the formation of para-hydrogen as found in the decomposition of hydrogen iodide. Thus the absence of para-hydrogen formation can be regarded as excluding the step (10). Consequently the conclusion offers itself that, whichever the actual primary process may be, (7) or (8), the two atoms forming a hydrogen molecule must come from the same parent formaldehyde molecule. The state of affairs in the photolysis of methyl alcohol is exactly analogous.

As no detailed knowledge about the energy exchange during collisions in solids is yet available, one cannot decide between the primary reactions (7) and (8) on the basis of the present experiments. The suggestion that a dissipation of energy takes place at collisions within a solid, as proposed for the reaction $H + HI_{solid}$, would favor mechanism (7) according to which no such dissipation of energy can occur.

Summary

It is found that para-hydrogen is formed when irradiating solid hydrogen iodide at low temperatures. Two explanations are given and discussed: (a) the hydrogen primarily formed can be converted by the paramagnetic action of free iodine atoms; (b) the heat formed in the reaction $H + HI_{solid} = H_2 + I$ is dissipated in the solid. In the photolysis of formaldehyde and methyl alcohol under the same conditions normal hydrogen is formed. This seems to indicate that the two hydrogen atoms forming a molecule are coming from the same formaldehyde or methyl alcohol molecule.

REHOVOTH, PALESTINE RECEIVED AUGUST 1, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF PHYSICAL CHEMISTRY, THE HEBREW UNIVERSITY]

The Catalytic Interaction of Acetylene and Hydrogen on Platinum

BY A. FARKAS AND L. FARKAS

In a series of communications the catalytic hydrogenation of ethylene,[1] benzene[2] and acetone[3] on platinum was investigated. In the first two examples, the hydrogenation consists of the addition of hydrogen to a double bond. In the case of acetone the reduction reaction can be envisaged as a similar type of process. In the present communication the hydrogenation of acetylene was investigated under similar conditions, this reaction being chosen as representative of hydrogen addition to triple bonds.

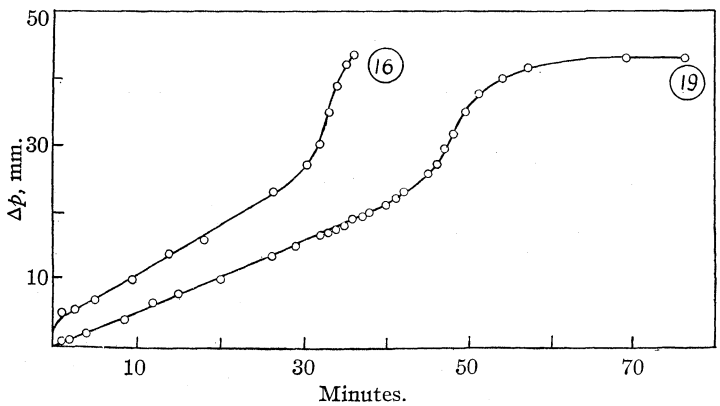


Fig. 1.—Hydrogenation of acetylene: expt. 16, 25 mm. C_2H_2 + 60 mm. H_2 at 101°; expt. 19, 21 mm. C_2H_2 + 49 mm. H_2 at 97°.

Experimental

The general experimental technique was similar to that previously described.[1] A platinized platinum foil (10 × 10 mm.) was used as the catalyst in a reaction vessel of 75 cc. volume. Hydrogen and acetylene were admitted to the reaction vessel through a U-tube kept at −80°. Acetylene was prepared from calcium carbide and purified according to the usual method.[4]

Dependence of the Hydrogenation on Pressure.—In some experiments, first acetylene was admitted to a given pressure and then condensed in a thin side-tube. Subsequently hydrogen was introduced and then acetylene quickly evaporated, the reaction time being calculated from this moment. The progress of the reaction under these conditions is shown in Fig. 1 (expt. 16). The reasons for the sudden drop in the pressure in the first half minute

(1) Farkas and Farkas, THIS JOURNAL, **60**, 22 (1938).
(2) Farkas and Farkas, *Trans. Faraday Soc.*, **33**, 827 (1937).
(3) Farkas and Farkas, THIS JOURNAL, **61**, 1336 (1939).
(4) Farkas and Melville, "Experimental Methods in Gas Reactions," Macmillan and Co., Ltd., London, 1939, p. 167.

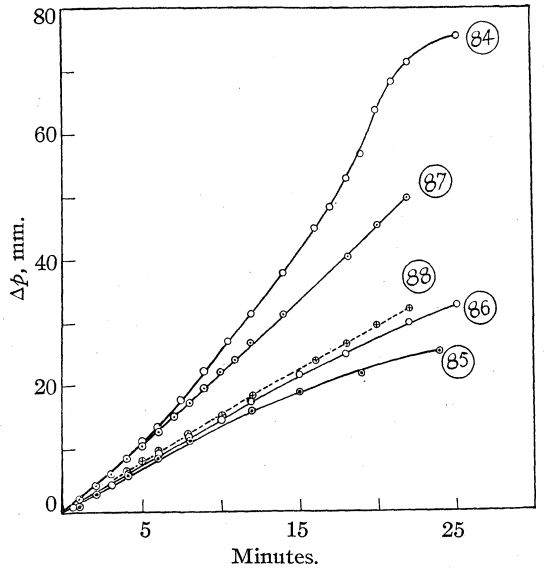


Fig. 2.—Hydrogenation of acetylene at 25°. Dependence on the hydrogen pressure: expt. 84, 40 mm. C_2H_2 + 114 mm. H_2; expt. 87, 39.5 mm. C_2H_2 + 94.5 mm. H_2; expt. 88, 41 mm. C_2H_2 + 92 mm. D_2; expt. 86, 40 mm. C_2H_2 + 70 mm. H_2; expt. 85, 40 mm. C_2H_2 + 51.5 mm. H_2.

were that the pressure of the acetylene was rather low at the beginning of the evaporation, and that the reaction is strongly inhibited by the acetylene. If, however, the hydrogen was added to the acetylene directly without the latter being condensed, as in expt. 19, Fig. 1, the initial pressure drop is absent and the pressure decreases regularly. The sudden pressure drop in the thirtieth and fortieth minutes, respectively, will be referred to below.

The dependence of the hydrogenation on the hydrogen pressure is given in Fig. 2, and that of the acetylene pressure in Fig. 3. These results show that with increasing pressure of acetylene the rate of hydrogenation decreases, while it increases with the hydrogen pressure. The inhibition of the hydrogenation by acetylene is similar to, but more pronounced than, the inhibition of the hydrogenation of ethylene by ethylene.

In the course of the hydrogenation it has been observed repeatedly that at a certain stage the rate of hydrogenation increases rapidly. Examples of this behavior were given in Figs. 1, 2 and 3, expts. 16, 19, 84, 79 and 82. The rate of the hydrogenation in expts. 79 and 84, and in expts. 21 and 22 in which the catalyst was somewhat less active, is shown in dependence of time in Fig. 4. This acceleration is due to two causes: first, the reaction rate increases on account of the acetylene pressure being reduced, and, second, the hydrogenation of the ethylene, which occurs in the second half of the reaction, is much faster than the formation of ethylene. The moment when all acetylene is used up is marked by an arrow in Fig. 4. It will be noted that the sudden increase in the rate of hydrogenation coincides with this moment.

Para-conversion and Hydrogenation.—In order to gain some information on the relative adsorbabilities of hydrogen and acetylene, the rate of hydrogenation and the rate of the para-hydrogen conversion were measured simultaneously. It is interesting to note that from a few experiments with para-hydrogen the same conclusions could be drawn with regard to the composition of the adsorption layer as from the whole series of experiments in which the pressure of the reactants was varied systematically.

The rate of the para-hydrogen conversion in the

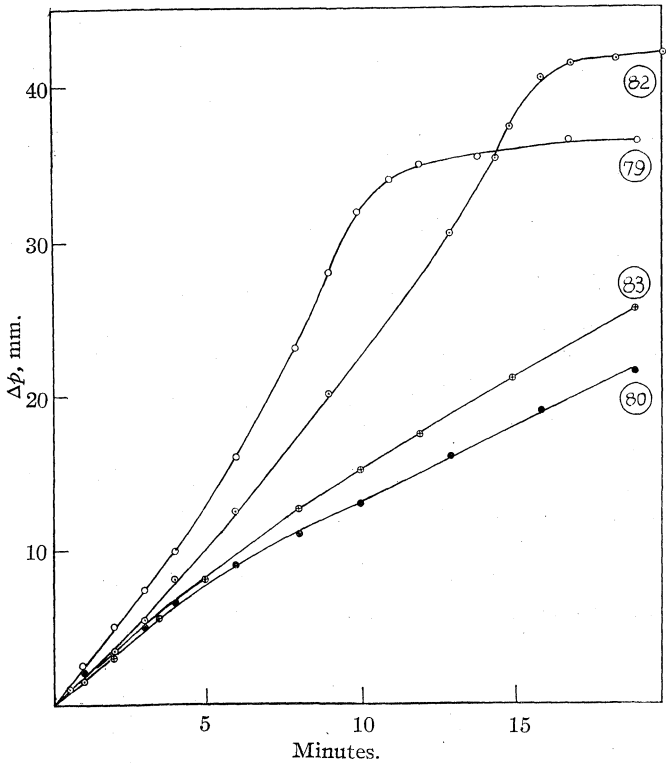


Fig. 3.—Hydrogenation of acetylene at 24°, dependence on the acetylene pressure. Expt. 79, 17.5 mm. C_2H_2 + 72.5 mm. H_2; expt. 82, 23.5 mm. C_2H_2 + 72.5 mm. H_2; expt. 83, 56 mm. C_2H_2 + 72 mm. H_2; expt. 80, 76 mm. C_2H_2 + 71 mm. H_2.

TABLE I

No.	°C.	Reaction mixture	Rate of conversion, mm./min.	Rate of hydrogenation, mm./min.	Ratio $\frac{\text{Conversion}}{\text{Hydrogenation}}$
54	20	74 mm. p-H_2	18.5	..	..
52	20	76 mm. p-H_2 + 19 mm. C_2H_4	6.7	0.83	8.1
53	20	73 mm. p-H_2 + 19 mm. C_2H_2	1.15	.21	5.5
9	22	27 mm. p-H_2 + 36 mm. C_2H_2	0.24	.084	2.8
27	88	27.5 mm. p-H_2 + 16.5 mm. C_2H_2	.089	.0065	7.3
33	20	88 mm. p-H_2 + 17 mm. C_2H_2	1.18	.22	5.4

absence and presenc e of acetylene or ethylene is shown in Fig. 5. As will be recognized from this figure, by the addition of 19 mm. of acetylene to 73 mm. of para-hydrogen, the rate of conversion was reduced by a factor of 15, whereas the same amount of ethylene reduced the rate of para-conversion only by a factor 3. These results show that acetylene replaces the hydrogen to a great extent in the adsorption layer and is much more strongly adsorbed than ethylene.

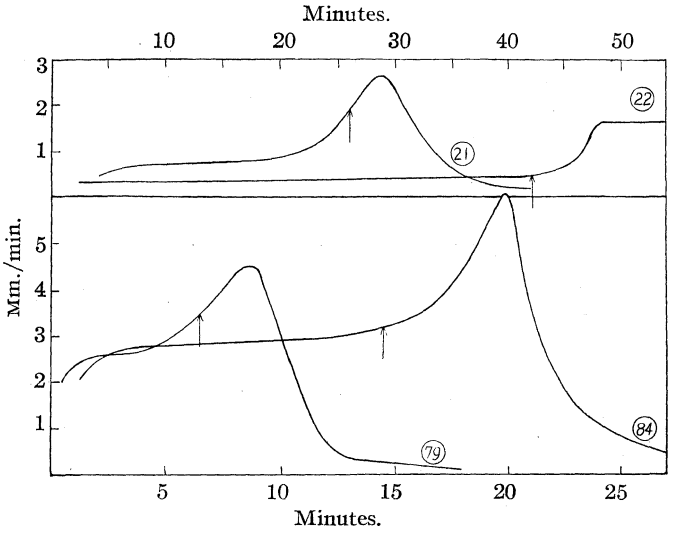


Fig. 4.—Rate of hydrogenation of acetylene—Expt. 21, 18 mm. C_2H_2 + 102 mm. H_2 at 89°; expt. 22, 15 mm. C_2H_2 + 55 mm. H_2 at 92°; expt. 79, 17.5 mm. C_2H_2 + 72.5 mm. H_2 at 24°; expt. 84, 40 mm. C_2H_2 + 114 mm. H_2 at 25°.

The rates of the conversion and hydrogenation reactions and their ratio are given in Table I for catalysts in different states of activity.

The dependence of the hydrogenation on temperature could not be determined with great accuracy on account of a gradual deactivation of the catalyst, especially at higher temperatures. In Table II the first group of figures refers to the catalyst in a more active state, and the second group to a less active catalyst.

TABLE II

No.	°C.	C_2H_2, mm.	H_2, mm.	Rate, mm./min.
55	15	30	72	0.29
58	47	31	78	2.0
57	57	31	76	3.9
64	72	30.5	78.5	0.13
63	98	30.5	78.5	.68
65	147	30.0	79.0	15.0

From these results an energy of activation of 12–17 kcal. can be calculated for the hydrogenation of acetylene. These figures are somewhat higher than the energy of activation for the hydrogenation of ethylene, which was found to be between 7 and 10 kcal. on the same catalyst and in the same temperature range.

Hydrogenation with Deuterium.—In Fig. 2, expts. 87 and 88 show the comparison of two hydrogenation experiments performed by hydrogen and deuterium. It will be recognized that the rate of hydrogenation by deuterium is about 1.5 smaller than that by hydrogen.

In hydrogenation experiments with deuterium the progress of the exchange reaction

$$C_2H_2 + HD \rightleftarrows C_2HD + H_2$$

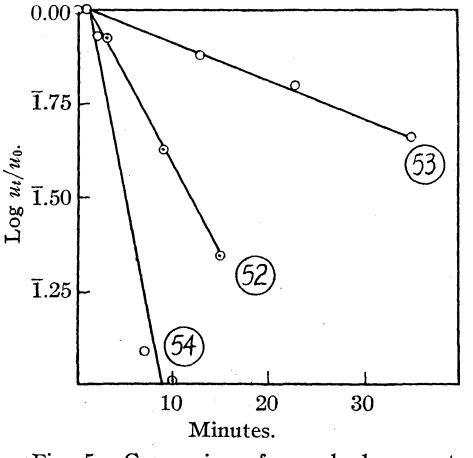


Fig. 5.—Conversion of para-hydrogen at 20°. u_0 and u_t denote the excess concentration of parahydrogen relative to normal hydrogen at the time $t = 0$ and t. Expt. 54, 74 mm. p-H_2; expt. 52, 76 mm. p-H_2 + 19 mm. C_2H_4; expt. 53, 73 mm. p-H_2 + 19 mm. C_2H_2.

also was investigated and compared with the exchange of ethylene. The results indicate that the exchange of acetylene is very much slower than that of ethylene. For example (expts. 24 and 25), at 90° the D-content of 88 mm. of deuterium (initial D-content 99%) in a mixture with 38 mm. of acetylene decreased only by 1%, while all of the acetylene was hydrogenated to ethylene. On the other hand, in a mixture of 47 mm. of ethylene and 62 mm. of deuterium the D-content decreased by 34% when the hydrogenation was completed. Qualitatively the same results were obtained when the exchanges of acetylene and ethylene were compared in the same run. In these experiments a relatively rapid exchange was observed as soon as most of the acetylene was converted into ethylene.

Discussion

The most striking feature of the hydrogenation of acetylene is the fact that the addition of two molecules of hydrogen occurs in two distinct steps. The acetylene is first converted to ethylene and the ethylene is only reduced further to ethane after all (or nearly all) of the hydrogen has been used up. This phenomenon, which is usually referred to as "selective hydrogenation" in organic chemistry, becomes manifest through the sudden change in the rate of hydrogenation as soon as all acetylene is used up.

The explanation for the selective hydrogenation is quite clear and already has been given.[5] It is due to the different absorbabilities of acetylene and of ethylene, but not to different rates of hydrogenation, though in the present case its occurrence can be ascertained kinetically by the sudden change of the reaction rate.

The strong adsorption of acetylene offers a ready explanation for the dependence of the rate of hydrogenation on the acetylene and hydrogen pressures also.

It is suggested that in the catalytic hydrogenation of ethylene the activation consists essentially of the dissociation of hydrogen.[1] This implies that the addition of hydrogen atoms to ethylene occurs with very little energy of activation. The experiments on the hydrogenation of acetylene by deuterium indicate that the same holds true for the hydrogenation of acetylene. The rates of hydrogenation by hydrogen and by deuterium differ by the same factor as was found for ethylene and for the rate of dissociation of hydrogen and deuterium on a similar catalyst.

The relatively higher energy of activation can be accounted for as caused by the extensive displacement of hydrogen by acetylene in consequence of the latter being very strongly adsorbed.

Concerning the mechanism of the catalytic hydrogenation, complete accord has not yet been reached. These authors[6] have the opinion that hydrogenation consists of the simultaneous addition of two hydrogen atoms to unsaturated bonds while Horiuti and Polanyi[7] envisage the hydrogenation as the consecutive and independent addition of hydrogen atoms. Recently Twigg and Rideal[8] came to the same conclusion with regard to hydrogenation as the present authors, while they retain the mechanism suggested by Horiuti and Polanyi for explaining exchange reactions (see below).

If one considers the complete hydrogenation of acetylene under the assumption that one hydrogen atom is added after the other, the following steps are involved

$$C_2H_2 + H \longrightarrow C_2H_3 \quad (1)$$
$$C_2H_3 + H \longrightarrow C_2H_4 \quad (2)$$
$$C_2H_4 + H \longrightarrow C_2H_5 \quad (3)$$
$$C_2H_5 + H \longrightarrow C_2H_6 \quad (4)$$

Steps (1) and (3) represent the addition of hydrogen atoms to adsorbed molecules, while steps (2) and (4) involve the recombination of radicals with hydrogen atoms. This is an essential difference, as one would expect reactions (2) and (4) to proceed with less inertia than reactions (1) and (2), respectively. In other words, the *a priori* probability for a hydrogen atom to be added to the radicals C_2H_3 or C_2H_5 is larger than the probability of being added to the molecules C_2H_2 or C_2H_4, respectively. This means that the addition of the second hydrogen atom to acetylene will follow very quickly the addition of the first, since through the addition of the first atom the inertia inherent in the hydrogenation reaction has been removed. The same holds *mutatis mutandis* for the addition of hydrogen atoms to ethylene also.

Thus it will be recognized that even if in the hydrogenation of acetylene or ethylene the hydrogen atoms are added in consecutive steps, in each case the second atom will be added at a larger speed than the first. Therefore, the addi-

(5) Farkas, *Trans. Faraday Soc.*, **35**, 906 (1939).

(6) Farkas and Farkas, *ibid.*, **33**, 837 (1937).

(7) Horiuti and Polanyi, *ibid.*, **30**, 1164 (1934).

(8) Twigg and Rideal, *Proc. Roy. Soc.* (London), **171A**, 55 (1939).

tion of the two hydrogen atoms can be regarded for practical purposes as occurring simultaneously.

The second kind of reaction which occurs in the interaction of acetylene and hydrogen is the exchange reaction of the type

$$C_2H_2 + HD \rightleftarrows C_2HD + H_2$$

Though this exchange reaction is not much in evidence in the interaction of hydrogen and acetylene, it will be recognized that its consideration will lead to some important conclusions with regard to the mechanism of the exchange reactions in general.

Two different mechansims for the exchange reaction between unsaturated hydrocarbons and deuterium have been suggested. The so-called "dissociative" mechanism suggested by the present authors[1,2,5,9] consists of the detachment of hydrogen atoms from the hydrocarbon molecules followed by the recombination of the hydrocarbon radicals with deuterium atoms which in turn have been formed by the dissociation of deuterium molecules on the surface of the catalyst. The "associative" mechanism originally suggested by Horiuti and Polanyi[7] is closely connected with the atomic mechanism of hydrogenation and is based on a secondary decomposition of the half hydrogenated form. This mechanism is advocated also by Twigg and Rideal.[8]

As support for the associative mechanism usually the ease is referred to by which the unsaturated hydrocarbons exchange as compared with saturated compounds. This is true in the case of ethylene and ethane but by no means can be generalized. This is best seen in the example of the three compounds, acetylene, ethylene and ethane. In this system a sharp distinction between the rate of exchange of saturated and unsaturated compounds cannot be made since the rate of exchange of ethylene is much larger than either that of ethane or of acetylene.

While the small rate of exchange of ethane compared with that of ethylene is explained readily by the associative mechanism as being due to the saturated character of ethane, the difference in the rate of exchange of acetylene and of ethylene cannot be traced to the same reason as both compounds are unsaturated.

Therefore, in general it cannot be maintained that saturated and unsaturated hydrocarbons undergo exchange reactions with essentially different rates, the more so since ready exchange of saturated compounds also has been observed.[10] Consequently, there is no reason to assume different mechanisms for the exchange reactions of saturated and unsaturated hydrocarbons and it appears that the dissociative mechanism is applicable to both types of exchange reactions.

According to the dissociative mechanism, the rate of exchange depends on the adsorbability of the hydrocarbons, and on the ease with which hydrogen atoms are detached from the hydrocarbon molecule. Thus qualitatively one might suppose that while acetylene is adsorbed strongly when compared with ethane, the hydrogen atoms are detached so much less readily that the effect of the adsorbability is compensated. On the other hand, both adsorbability and dissociation rate are apparently in a favorable relation in the case of ethylene to induce a relatively rapid exchange.

In fact the state of affairs is more complicated, as the rate of exchange depends not only on the absolute concentration of the hydrocarbon, but also on its relation to the concentration of hydrogen on the surface of the catalyst. It seems, however, that a detailed discussion of the kinetics of exchange reactions from this point of view is premature.

Summary

1. The catalytic hydrogenation of acetylene was investigated at pressures of 70–150 mm. and in the temperature range of 20–140° on a platinum catalyst. The rate of hydrogenation increases with increasing hydrogen pressure but is strongly reduced with increased acetylene pressure.

2. If the hydrogenation is carried out by parahydrogen, the ortho–para conversion proceeds very much more slowly than in the absence of acetylene. The ratio of the rate of hydrogenation by hydrogen to that by deuterium is 1.5 at 20°.

3. The hydrogenation of acetylene proceeds in two distinct stages: first, all acetylene is reduced to ethylene and only then is ethylene hydrogenated to ethane. The start of the second step is indicated by a sudden increase in the rate of hydrogenation.

4. The catalytic exchange of hydrogen atoms between acetylene and molecular deuterium is very much slower than that between ethylene and deuterium under similar conditions.

5. The results indicate that acetylene is

(9) Farkas, Farkas and Rideal, *Proc. Roy. Soc.* (London), **146A**, 630 (1934).

(10) Farkas and Farkas, *Nature*, **143**, 244 (1939); *Trans. Faraday Soc.*, **35**, 917 (1939).

strongly adsorbed on the surface of the catalyst and that acetylene can displace both hydrogen and ethylene in the adsorption layer. The mechanisms of hydrogenation and exchange reactions are discussed.

JERUSALEM, PALESTINE RECEIVED AUGUST 1, 1939

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY (NO. 713), AND FROM THE DEPARTMENT OF CHEMISTRY AT THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

Evidence for Existence of a Selenium Iodide

BY JAMES D. MCCULLOUGH[1]

Various attempts[2] have been made in an effort to detect compound formation between selenium and iodine, but in no case have these led to positive conclusions. During a recent study of the various crystalline forms of elementary selenium made by the author, it was observed that a color change occured when selenium was added to a solution of iodine in carbon tetrachloride. Since selenium is not measurably soluble in carbon tetrachloride in any form, this change seemed significant. Accordingly the following experiments were carried out using carefully purified materials throughout.

Absorption Spectrum Studies.—Light from an incandescent bulb was passed through two similar glass absorption cells placed in series, one of which was filled with a solution containing 0.885 g. of iodine per 1000 g. of carbon bisulfide and the other with a solution containing 0.195 g. of crystalline α-monoclinic selenium per 1000 g. of the solvent. After preparing photographs with this arrangement, the solutions were mixed, the two cells filled with the resulting solution and a second set of absorption spectra prepared.

In Fig. 1, curve A is a reproduction of a microphotometer tracing of the absorption spectrum of the unmixed solutions while curve B is a similar record for the mixed solutions. Since the ordinates represent relative transmission, there is a new region of absorption from 4200 to 4500 Å. on mixing. Because of the care taken in purifying the selenium and iodine used, this must mean that a compound is formed which is responsible for the increased absorption.

The Selenium–Iodine Equilibrium.—Weighed quantities of iodine and carbon tetrachloride were placed in glass-stoppered bottles with an excess of hexagonal selenium and shaken for twenty-four hours or longer in a thermostat at 25°. The solutions were then allowed to settle for at least ten minutes, after which samples of about 200 g. were removed by slowly forcing the solution in a closed system through a sintered glass filter into a weighed, glass-stoppered flask. After weighing

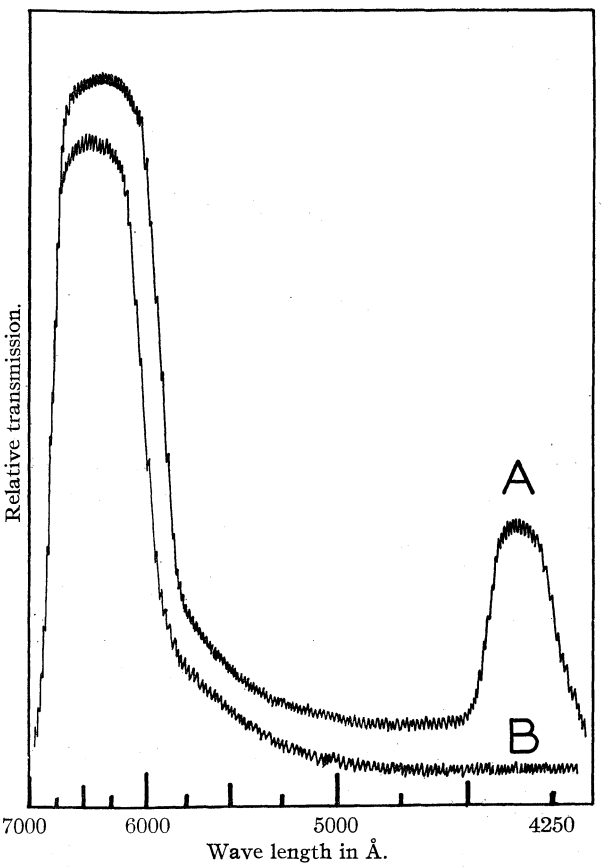


Fig. 1.—Reproduction of microphotometer records of absorption spectra of solutions of selenium and iodine in carbon bisulfide. Curve A is for the superimposed solutions before mixing, while curve B is for the solutions after mixing. Curve A has been displaced upward to reduce overlapping.

(1) Present address: Department of Chemistry, University of California at Los Angeles.

(2) (a) F. Olivari, *Chem. Zentr.*, **100, I,** 83 (1910); (b) Beckmann and Hanslian, *Z. anorg. Chem.*, **80,** 221 (1913); (c) Beckmann and Faust, *ibid.*, **84,** 103 (1914); (d) Beckmann and Grünthal, *ibid.*, **84,** 97 (1914); (e) Pellini and Pedrina, "International Critical Tables," Vol. IV, p. 24; (f) R. Wright, *J. Chem. Soc.*, **107,** 1527 (1915); and (g) Beckmann and Platzmann, *Z. anorg. Chem.*, **102,** 215 (1918).

the sample, 100 ml. of 3 *N* sodium hydroxide solution was added, the mixture shaken and then transferred to a separatory funnel, where the shaking was continued for several minutes. By this process the selenium and iodine are both quite completely transferred to the aqueous layer, the selenium being oxidized mainly to selenite, with perhaps some selenate. After separating the two layers, the aqueous phase was saturated with sulfur dioxide and an equal volume of concentrated hydrochloric acid was added. More sulfur dioxide was then passed in and the solution was boiled to coagulate the elementary selenium, a process which required several hours. Near the end of the precipitation process a small quantity of hydrazine hydrochloride was added to precipitate any of the element left in the form of selenate. The selenium was collected in a sintered glass crucible, washed with water, then with alcohol, dried for several hours at 105° and then weighed.

The results of these experiments are shown in Table I. It is seen that there is a linear relationship between the quantity of selenium dissolved and the concentration of iodine. This is what would be expected for an equilibrium of the type:

$$n\text{Se(solid)} + I_2 = Se_nI_2$$

This is evidence that the compound has two atoms of iodine per molecule but leaves the number of selenium atoms undetermined.

TABLE I

SELENIUM–IODINE EQUILIBRIUM IN CARBON TETRACHLORIDE

Moles I_2 per 1000 g. solvent	Gram atoms Se per 1000 g. solvent	Moles I_2 / G atoms Se
0.04236	0.00106	40.0
.05622	.00140	40.1
.07620	.00191	39.9

The author wishes to acknowledge his indebtedness to Dr. Arnold O. Beckman, in whose laboratory this work was done, for suggesting the study of selenium and for his interest in the problem.

Summary

1. Absorption spectra give strong evidence in favor of compound formation between selenium and iodine in carbon bisulfide.

2. Quantitative measurements of the equilibrium between selenium and iodine in carbon tetrachloride show the presence of a compound having the formula Se_nI_2 with n undetermined.

LOS ANGELES, CALIF. RECEIVED JUNE 13, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE INSTITUTE OF TECHNOLOGY OF THE UNIVERSITY OF MINNESOTA]

Amperometric (Polarometric) Titrations. I. The Amperometric Titration of Lead with Dichromate or Chromate

BY I. M. KOLTHOFF AND YU-DJAI PAN

The classical methods of electrometric titrations are the potentiometric and conductometric titrations. In potentiometric titrations the potential of a suitable indicator electrode is measured during the titration and the end-point is characterized by a more or less pronounced change of the potential upon addition of a small amount of reagent. In conductometric titrations the electrical conductance of the titration mixture is measured during the titration and the end-point is found graphically as the point of intersection of the lines giving the changes of conductance before and after the equivalence point. To these two methods may be added another which we propose to call "*amperometric titrations.*" In amperometric titrations the current which passes between two suitable electrodes at a constant applied e. m. f. is measured. Depending upon the conditions one or both electrodes are placed in the titration medium. Quite generally, the end-point is found as the point of intersection of two lines giving the change of the current before and after the equivalence point.

The principle underlying amperometric titrations was mentioned as early as 1897 by Salomon[1] and later by Nernst and Merriam.[2] It is peculiar that these papers have escaped the attention of analytical chemists. It was shown by the above authors that the so-called "diffusion current"[3] is proportional to the concentration of the electro-reduced substance. In a paper entitled "On a Galvanometric Titration Method"

(1) E. Salomon, *Z. physik. Chem.*, (a) **24**, 55 (1897); (b) **25**, 366 (1898); (c) *Z. Elektrochem.*, **4**, 71 (1897).

(2) W. Nernst and E. S. Merriam, *Z. physik. Chem.*, **53**, 235 (1905).

(3) For terminology compare I. M. Kolthoff and J. J. Lingane, *Chem. Rev.*, **24**, 1 (1939).

Salomon[1c] described the amperometric titration of chloride with silver nitrate. He placed two silver electrodes in dilute potassium chloride, applied an e. m. f. of 0.1 v. and titrated with silver nitrate. Until the equivalence point the "residual current" was very small, but after the equivalence point both electrodes became depolarized, resulting in a sudden, large deflection of the galvanometer which was placed in the circuit. Nernst and Merriam[2] placed two palladium electrodes, saturated with hydrogen, in solutions of various acidities and alkalinities and determined the current which passed through upon application of a small e. m. f. Both electrodes adopted the hydrogen potential and the e. m. f. of the cell was zero. The current passing through upon application of a small e. m. f. was determined approximately by Ohm's law ($E = i R$). When the solution contained an excess of acid, the hydrogen ion concentration at the cathode decreased and at the anode increased during the electrolysis. This caused concentration polarization which remained small as long as the current which passed through was small and the excess of acid was great. Similarly, the concentration polarization was found to be small in alkaline medium. However, in neutral medium, when the hydrogen ion concentration is only of the order of 10^{-7}, a slight electrolysis gives rise to a considerable concentration polarization and the setting up of an appreciable back e. m. f. Under ideal conditions the current should quickly drop to zero. Thus, the current passing between two hydrogen electrodes at a small applied e. m. f. during the titration of an acid with a base, or *vice versa*, decreases continuously until the equivalence point is reached and then increases again. Fresenius[4] has investigated the possibility of the determination of small hydrogen ion concentrations by making use of the above principle, but in this particular instance the method is of little importance.

The method proposed by Salomon[1] in 1897 resembles very closely the so-called "dead stop end-point method" of Foulk and Bawden.[5] In their application of this method to various oxidation–reduction titrations, Guzman and Rancano[6] proposed the name "depolarimetry," as the end-point usually is characterized by a sudden depolarization or polarization of one or of both of the electrodes. Heyrovsky and Berezicky[7] used a depolarized anode and the dropping mercury electrode as indicator electrode in the titration of barium with sulfate and suggested the name "polarographic titration." Majer,[8] discussing the titration of lead with sulfate and the fundamentals of the method, coined the term "*polarometric titrations*." As it is the current which is measured during the titration, we prefer to call this type of titration "*amperometric* (or galvanometric, [Salomon]) titration," corresponding to the use of the words potentiometric and conductometric titrations.

So far, no systematic studies have been made of the possibilities and limitations of amperometric titration methods. At present, we are engaged with such studies, using the dropping mercury electrode or a platinum wire microelectrode as the indicator electrode. It is expected that this type of titration will find at least as extensive an application as potentiometric titrations experience now. We find the amperometric method especially useful in the titration of very dilute solutions. For the sake of brevity we will not discuss the general characteristics of amperometric titrations, their possibilities and limitations, but will postpone such a discussion until more experimental data have been made available.

In the present paper the amperometric titration of lead with chromate or dichromate is discussed, using the dropping mercury electrode as indicator electrode.

Experimental

Apparatus.—The set-up used is given in Fig. 1. A is a battery composed of three dry cells with a total voltage of 4.5 v. R is a potential divider composed of two rheostats, one with 1000 and the other with 10 ohms resistance. R_s is a four dial standard resistance box of 9999 ohms, connected in series with the cell. The potential drop across the resistance box is measured with a student's potentiometer P, using a portable galvanometer as a null point instrument. The magnitude of the current which passes through is calculated with the aid of Ohm's law.[9] S. C is a standard cell of known e. m. f. G. S. is a gang switch which makes the various connections with the potentiometer. By the proper adjustment of the potential divider a known e. m. f. E_c is applied between the dropping cathode

(4) L. R. Fresenius, *Z. physik. Chem.*, **80**, 481 (1912).

(5) C. W. Foulk and A. T. Bawden, THIS JOURNAL, **48**, 2045 (1926).

(6) J. Guzman and A. Rancano, *Anales soc. españ. fis. quím.*, **32**, 590 (1934); Guzman, *ibid.*, **33**, 109 (1935); see also *Z. anal. Chem.*, **103**, 445 (1935).

(7) J. Heyrovsky and S. Berezicky, *Coll. Czech. Chem. Commun.*, **1** 19 (1929).

(8) V. Majer, *Z. Elektrochem.*, **42**, 120, 122 (1936).

(9) For details and also for the use of a shunted d'Arsonval galvanometer see J. J. Lingane and I. M. Kolthoff, THIS JOURNAL, **61** 825 (1939).

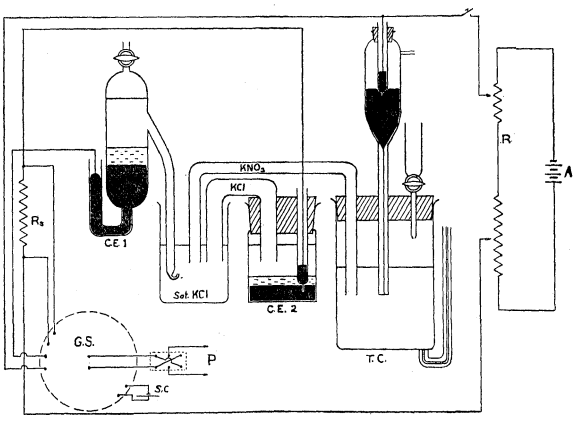


Fig. 1.—Diagram of the set-up.

and a standard saturated calomel electrode (C. E. 1). Another saturated calomel electrode (C. E. 2) was used as a practically depolarizable anode in the electrolysis cell, electrolytic contact with the catholyte in the titration cell being made by two salt bridges. One siphon filled with a 3% agar gel saturated with potassium chloride made electrolytic contact between the anode and a saturated solution of potassium chloride in a beaker, and a second siphon filled with a gel saturated with potassium nitrate made electrolytic contact between the saturated potassium chloride solution and the catholyte in the titration cell. In ordinary work the use of two calomel electrodes is not necessary, as a slight polarization of the anode does not affect the results. In the present work it was preferred to use the C. E. 1 as a reference electrode in order to measure or adjust at any desired time the potential of the dropping electrode against an unpolarized electrode. The use of the outside anode (C. E. 2) can also be dispensed with, as a large layer of pure mercury on the bottom of the titration cell can serve as an internal anode. This involves the practical disadvantage of the use of much mercury, as the cell has to be cleaned after each titration, and a new layer of pure mercury must be added for the next titration. In many titrations a large silver–silver chloride electrode can serve as an internal anode. However, since the use of the external anode does not involve any difficulties and such a saturated calomel electrode can be used for a long period of time, we have not made a special study of the use of suitable unpolarizable internal anodes.

The titration cell T. C. of the model given in Fig. 1 had a capacity of about 100 ml. It was provided with an inlet tube for nitrogen (or hydrogen for the removal of dissolved oxygen before and during the titration. Since oxygen is reducible at the dropping mercury electrode, giving one wave due to reduction to hydrogen peroxide at a relatively small applied e. m. f., and a second drawn out wave due to reduction to hydroxyl ions at higher voltages, the removal of oxygen is recommended, especially in the titration of very dilute solutions. The titration cell was closed with a four-hole rubber stopper; one hole served for the introduction of the salt bridge, the second for the introduction of the buret, the third for the introduction of the mercury capillary and the fourth for the outlet of the gas (not shown in the figure). In most cases the reagent was added from a calibrated semi-microburet of 5 or 10 ml. capacity and with scale divisions of 0.01 ml. The concentration of the reagent was at least 10 times greater than the solution to be titrated. The drop time of the capillary was of the order of three seconds. As in the following work the temperature of the solution remained sensibly constant during the titration, the titration cell was not placed in a thermostat.

Performance of the Titration.—When the characteristics of the substance to be titrated and of the reagent are not known, it is always necessary to determine the current voltage curve of both in the medium in which the titration is being carried out. In order to eliminate the migration current[10] and to reduce the resistance, it is always advisable to have a sufficient excess of indifferent electrolyte present. When the current–voltage curves of the substance to be titrated and of the reagent have been determined, the potential of the dropping electrode is adjusted at the beginning of the titration to such a value that the diffusion current of one or of both of them is obtained. In the case of the titration of dilute lead solutions in the presence of an excess of indifferent electrolyte the diffusion current of lead (after suppression of the maximum with methyl red) was obtained at cathode potentials (against the satd. calomel electrode) between −0.7 and −1.4 v. The shape of the current–voltage curves of potassium chromate and dichromate depend greatly upon the *p*H of the solution When the *p*H of the solution is smaller than 6, the reduction begins immediately upon short circuiting without an applied e. m. f. The reduction proceeds from the hexavalent to the trivalent state. With increasing applied e. m. f., another wave occurs corresponding to the reduction of the trivalent to the divalent chromium and at still greater negative potential a third wave occurs corresponding to the reduction to metallic chromium. The interpretation of the polarograms of chromate is involved and will be discussed in a subsequent paper with Dr. J. J. Lingane. In the present work the cathode potential as a rule was adjusted to a value at which the diffusion currents of lead and of chromate (to Cr^{+++}) were obtained. When at the proper cathode potential, E_c, lead is titrated with chromate or dichromate, the diffusion current of the lead decreases during the titration and becomes equal to the residual current of the medium at the cathode potential at the equivalence point. If the solubility of the precipitate at the equivalence point is negligible and the medium does not contain electroreducible substances at the applied cathode potential, the residual current at the equivalence point is almost equal to zero. Upon addition of an excess of reagent, the diffusion current of chromate is obtained which increases with increasing excess added. When the values of the current (corrected for volume change) are plotted against the amounts of reagent added, two straight lines are obtained which intersect at the end-point (see Fig. 2). In order to obtain straight lines it is necessary to correct for the volume changes during the titration. When the original volume of the solution to be titrated is V ml., the amount of reagent added is X ml. and the current measured is i, then

$$i_{corr.} = \frac{V + X}{V} i$$

(10) *Cf.* J. J. Lingane and I. M. Kolthoff, THIS JOURNAL, **61**, 1045 (1939); see also Ref. 3.

In all of the figures $i_{corr.}$ is plotted against the volume of reagent added. In all of the titrations of lead with chromate or dichromate it was necessary to make only a few (three or four) readings before and after the end-point. However, in order to obtain a greater accuracy a large number of measurements has been made.

The titrations were performed in the following way. A measured volume (usually 50 ml.) of the lead solution was introduced with the aid of a calibrated pipet into the titration cell, and the latter covered with the rubber stopper. Nitrogen (or hydrogen) was passed through for about ten minutes. In the meantime the potentiometer system was adjusted against the Weston standard cell. After passage of the nitrogen the dropping electrode and the reference electrode (Fig. 1) were connected and the desired value of E_c was applied. The dropping electrode was then connected with the saturated calomel electrode which served as anode and by a change of the switch the current measuring device was introduced in the circuit. A measured volume of the reagent was added from the microburet, nitrogen was passed through for one minute to remove any oxygen and to effect a good mixing and the current was measured again. If necessary, the cathode potential was readjusted to its original value. This process was repeated after successive additions of reagent. If necessary, the constancy of the current was checked before a new addition of reagent. If no other reducible substances are present in the solution, the approach of the end-point is indicated by the current, which becomes smaller and smaller. When the solubility of the precipitate is negligibly small it is desirable to make a greater number of measurements in the vicinity of the end-point in order to find the location of the minimum with a greater degree of accuracy. On the other hand, if the solubility is appreciable, there is no practical advantage in making many readings near the end-point. In such a case the minimum current does not necessarily correspond to the location of the equivalence point (*e. g.*, in the titration of lead with dichromate, see Fig. 2). In such cases points are required only at that distance from the end-point where the (corrected) current–reagent line has become straight.

At the end of the titration the values of the current are corrected for the volume effect and plotted against the volume of reagent added. The point of intersection of the two straight lines marks the end-point.

Materials Used.—All chemicals used were of reagent quality. The lead nitrate was recrystallized twice from water and dried at 120°. A standard solution was prepared and the concentration determined by precipitation as chromate and iodometric titration of the precipitate. The potassium dichromate was a standard substance. The C. P. potassium chromate was recrystallized from water and dried at 120°. Its stock solution was standardized iodometrically and compared with a standard dichromate solution.

Experimental Results

In Fig. 2 are represented the results obtained in the titration of 50 ml. of 0.01 *M* lead nitrate which was 0.1 *N* in potassium nitrate with 0.05 *M* potassium dichromate at a cathode potential E_c of

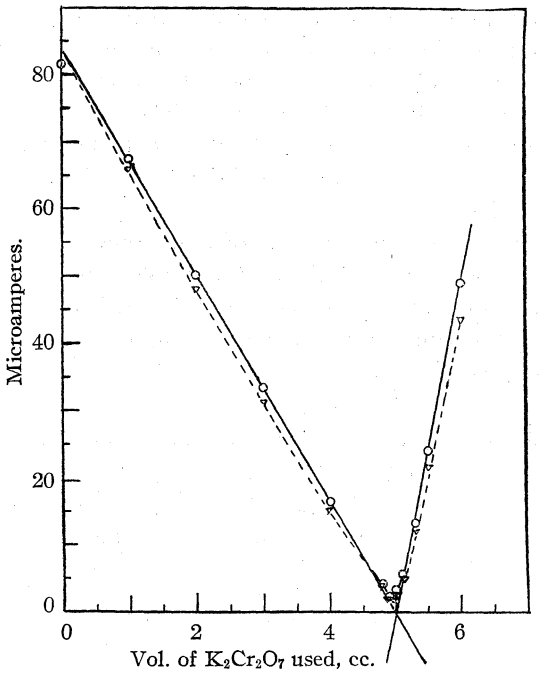


Fig. 2.—Titration of 50 cc. of 0.01 *M* $Pb(NO_3)_2$ in 0.1 *N* KNO_3 with 0.05 *M* $K_2Cr_2O_7$ at $E_c = -1.0$ v.

−1.0 v. *vs.* S. C. E. The dotted lines give the values of the current as actually determined; the drawn lines give the values after volume correction. It is seen that after correction two straight lines were obtained which intersected exactly at the equivalence point. The reproducibility and accuracy were excellent; the end-point was found in four different titrations after addition of 5.00 ± 0.01 ml. of dichromate. From Fig. 2 it is seen that the residual current at the equivalence point was relatively great, and that both the precipitation and the reagent lines were curved in the neighborhood of the end-point. The large residual current at the end-point is to be attributed to dissolved lead chromate while the straight lines intersect at a point where the residual current is smaller than 1 microampere. The relatively large solubility of the lead chromate under the above experimental conditions is due to the free acid which is formed during the titration

$$Cr_2O_7^{=} + 2Pb^{++} + H_2O \longrightarrow 2PbCrO_4 + 2H^+$$

When neutral lead nitrate solutions were titrated with potassium chromate solutions in 0.1 to 1 *N* potassium nitrate the residual current at the point of intersection of the two lines was always found to be less than 1 microampere. However, under the latter conditions the end-point was always found 0.8 to 1% before the equivalence

point, the deviation undoubtedly being due to coprecipitation of basic lead chromate with the neutral lead chromate. For this reason we prefer to carry out the titration with potassium dichromate in neutral or slightly acid medium or with potassium chromate in a buffered or acid solution.

As experimental details of amperometric titrations are not described in the literature, some values of the current measured during a titration and the same data corrected for the volume effect are given in Table I.

TABLE I

TITRATION OF 50 ML. 0.01 *M* $Pb(NO_3)_2$ (IN 0.1 *M* KNO_3) WITH 0.05 *M* $K_2Cr_2O_7$: $E_c = -1.0$ v.

Ml. of $K_2Cr_2O_7$ added	*i* determined, microamp.	$i_{corr.}$ for dilution, microamp.
0	81.56	81.56
1.0	66.22	67.50
2.0	48.34	50.20
3.0	31.66	33.60
4.0	15.25	16.45
4.8	3.79	4.15
4.9	2.09	2.30
5.0	2.9	3.19
5.1	5.1	5.62
5.3	12.03	13.3
5.5	21.86	24.0
6.0	43.86	49.1

As the slope of the reagent line is steeper than that of the lead (precipitation) line, the actual minimum is not found at but before the equivalence point (Fig. 2).

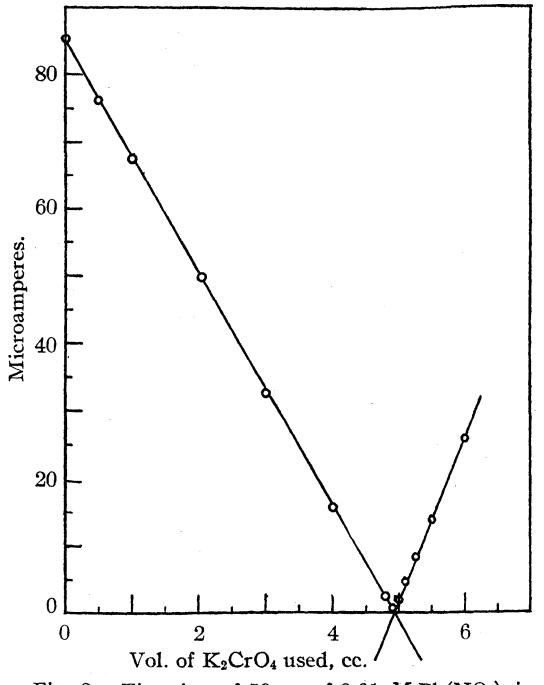


Fig. 3.—Titration of 50 cc. of 0.01 *M* $Pb(NO_3)_2$ in 0.1 *N* KNO_3 with 0.1 *M* K_2CrO_4 at $E_c = -1.2$ v.

The amount of potassium nitrate present in the lead solution was found to be without effect upon the results, if enough was added to eliminate the migration current. Titrations were carried out in 1 *M* potassium nitrate instead of in 0.1 *M* nitrate, the end-point being found again after addition of 5.00 ml. of dichromate.

A straight precipitation line was not obtained in the absence of potassium nitrate. The current at the beginning of the titration is much greater than the diffusion current of lead, as the initial current is the sum of the diffusion current and the migration current. During the titration the amount of dissolved lead decreases, while the concentration of the soluble reaction products potassium nitrate and nitric acid increases. Consequently, the contribution of the migration current becomes less and less the nearer the end-point is approached and during the precipitation of the last 20% of the lead the currents practically correspond to the diffusion current of the dissolved lead. An example of the titration of 0.01 *M* lead nitrate with 0.05 *M* dichromate in the absence of added salt is given in Fig. 4.

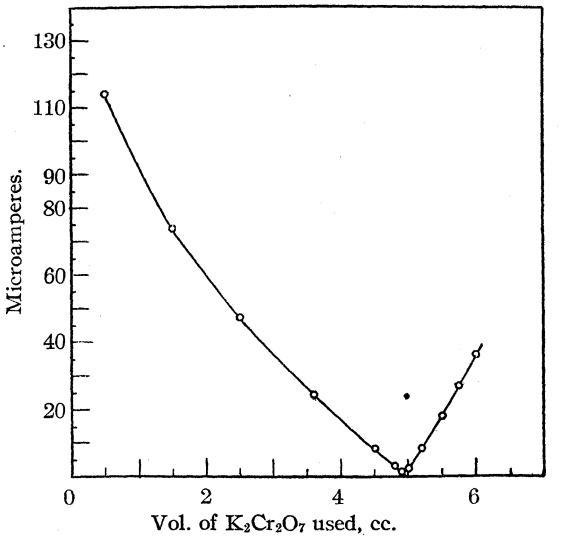


Fig. 4.—Titration of 50 cc. of 0.01 *M* $Pb(NO_3)_2$ with 0.05 *M* $K_2Cr_2O_7$ at $E_c = -1.0$ v.

As the solubility of lead chromate in dilute nitric or perchloric acids is small, titrations of lead could be carried out at relatively high acidities. Three titrations of 50 ml. of 0.01 *M* lead nitrate in 0.01 *N* perchloric acid and 0.1 *N* potassium nitrate and three titrations in 0.1 *N* per-

chloric acid were carried out. Again, the results were perfectly reproducible and accurate within 0.2%. Results obtained in 0.01 and 0.1 *N* acid are given graphically in Fig. 5 in which only the corrected values of the current are plotted. The solubility of the lead chromate and therefore the residual current near and at the equivalence point increase with increasing acidity. In the titration in 0.01 *N* perchloric acid the residual current at the equivalence point was found to be 7.0 microamperes, and in 0.1 *N* perchloric acid 10.1 microamperes. In all these titrations the cathode potential need not be adjusted very accurately; it may vary between −0.8 and −1.2 v., and in neutral solutions it even may be −1.5 v.

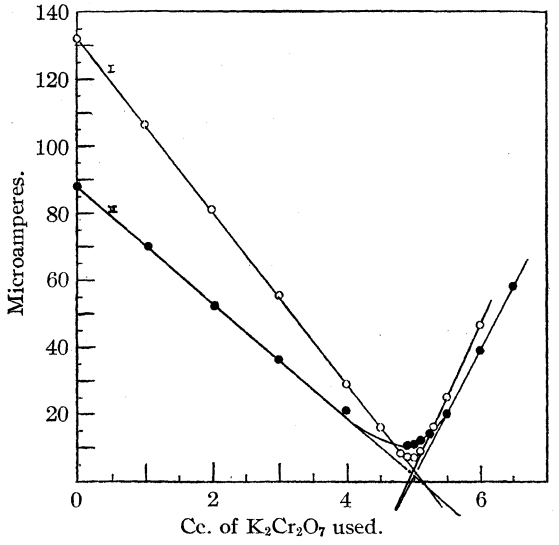


Fig. 5.—Titration of 50 cc. of 0.01 *M* $Pb(NO_3)_2$ in 0.1 *N* KNO_3: (I) in 0.01 *N* $HClO_4$, at E_c = −1.2 v.; (II) in 0.1 *N* $HClO_4$, at E_c = −1.15 v.; with 0.05 *M* $K_2Cr_2O_7$.

Titrations also have been carried out with dichromate and chromate in an acetate buffer with a *p*H of 4.2 at cathode potentials varying between −0.8 and −1.4 v. and accurate results again were obtained. Acetate increases the solubility of the lead chromate and also the residual current at the equivalence point.

The polarogram of 0.001 *M* potassium dichromate in the acetate buffer of *p*H of 4.2 is given in Fig. 6. Evidently the dichromate is already reduced without applying any external e. m. f. The same, of course, is true when the solution is more acidic. Thus, it is possible to carry out the titration without application of an external e. m. f. Under such conditions, which are very

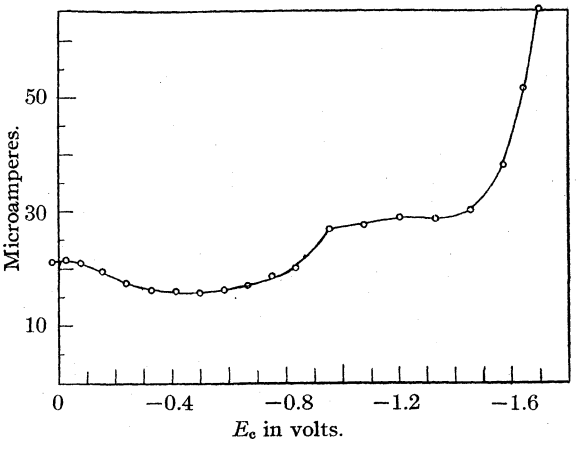


Fig. 6.—Current–voltage curve of 0.001 *M* $K_2Cr_2O_7$ in an acetate buffer of *p*H 4.2.

simple from the practical point of view, the lead is not electro reduced and does not yield a diffusion current. The current remains practically zero until the equivalence point is reached and increases very rapidly (diffusion current of chromate) upon addition of an excess of reagent. An example of such a titration is given in Fig. 7, in which 0.01 *M* lead nitrate in the acetate buffer of *p*H of 4.2 was titrated with 0.05 *M* dichromate without the application of an external e. m. f. Similar results were obtained in more acid media. The performance of the lead titration without application of an external e. m. f. is of particular advantage in cases in which the solution contains constituents which are electro-reduced at potentials at which lead yields a diffusion current. Such a titration can be carried out simply by short circuiting the dropping electrode and the anode and

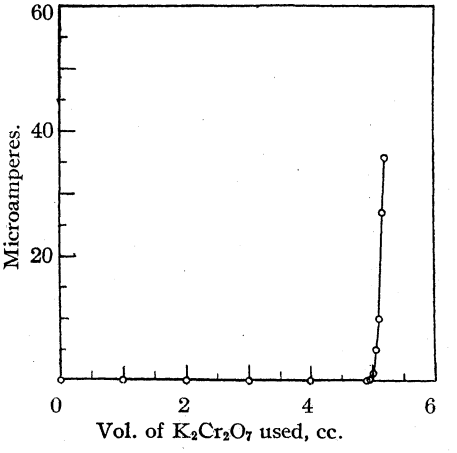


Fig. 7.—Titration of 50 cc. of 0.01 *M* $Pb(NO_3)_2$ in acetate buffer of *p*H 4.2 with 0.05 *M* $K_2Cr_2O_7$ at E_c = 0.

measuring the current in one of the ways described before. It is also possible to use a microammeter for the measurement of the current. We have used a Weston microammeter with 150 scale divisions, each division corresponding to 0.2 microamp. The disadvantage of the instrument is the relatively large fluctuations of the needle during the formation of a drop of mercury, making the determination of the average value of the current relatively difficult.

In the above we have discussed the titration of 0.01 *M* lead solutions under varying conditions. The titration of 0.001 *M* solutions can also be carried out quickly and accurately. In Fig. 8 the data are listed which were obtained in the titration of 50 ml. of 0.001 *M* lead nitrate in 0.01 *M* potassium nitrate with 0.005 *M* dichromate at $E_c = -1.0$ v.

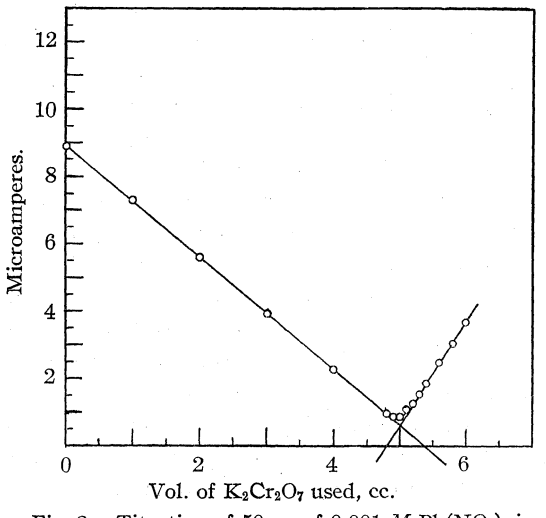


Fig. 8.—Titration of 50 cc. of 0.001 *M* $Pb(NO_3)_2$ in 0.01 *N* KNO_3 with 0.005 *M* $K_2Cr_2O_7$ at $E_c = -1.2$ v.

In three titrations the amount of dichromate used at the point of intersection corresponded within 0.3% with the theoretical amount. When the titration was carried out with potassium chromate instead of dichromate solution the error was even greater than in the titration of more concentrated lead solutions with chromate. The point of intersection with 0.001 *M* lead solutions at E_c values of from -1 to -1.4 v. occurred 3–5% before the equivalence point (coprecipitation of basic salt). The error was eliminated or at least reduced to less than 0.5% by performing the titrations in an acetate buffer with a *p*H of about 4.0.

Titration of Lead in the Presence of Barium.—Although both lead and barium chromate are slightly soluble, the latter differs from the forme in that it is freely soluble in dilute acid. Severa titrations with 0.05 *M* dichromate were carriec out with 50 ml. of a mixture which was 0.01 *M* in lead, 0.01 *M* in barium and 0.01 *M* in perchloric acid. The point of intersection was found 0.1 tc 0.3% before the lead equivalence point. The concentration of the barium even could be increased to 0.1 *M* without affecting the results. In three titrations with a mixture in which the ratio of lead to barium was 1 to 10 and the perchloric acid concentration was 0.01 *N*, the end-point was found within 0.3% of the theoretical value. No irregularities were noticed during the titration (see Fig. 9).

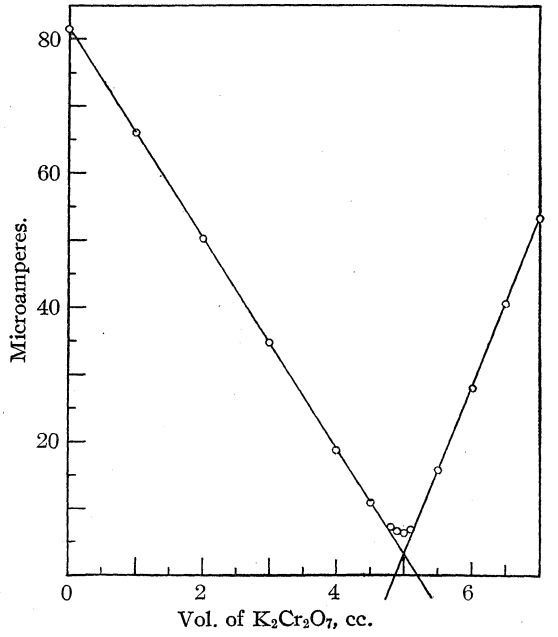


Fig. 9.—Titration of 50 cc. of 0.01 *M* $Pb(NO_3)_2$ in 0.1 *M* $Ba(NO_3)_2$ and 0.01 *N* $HClO_4$ with 0.05 *M* $K_2Cr_2O_7$, at $E_c = -1.0$ v.

In acid medium the lead also can be titrated in the presence of barium without applying an external e. m. f. The titration curves were identical with that given in Fig. 7.

Since the lead chromate is much less soluble than barium chromate an attempt has been made to determine both lead and barium in one titration by fractional precipitation with potassium chromate at cathode potentials (-0.8 to -1.4 v.) at which the lead yields a diffusion current and the barium is not electro-reduced. If all of the lead would precipitate before the precipitation of barium the current would decrease to practically

zero at the point where all of the lead is precipitated, it would then remain very small until all of the barium is precipitated, and it would increase in the usual way with an excess of chromate. It is evident from Fig. 10 that a marked coprecipitation of barium chromate occurs during the precipitation of lead. In the titration of 50 ml. of a mixture which was 0.01 *M* in lead and 0.01 *M* in barium nitrate with 0.2 *M* potassium chromate at $E_c = -1.0$ v., the first end-point (precipitation of lead) was found about 20% after the equivalence point. The second end-point corresponding to quantitative precipitation of lead and barium was found at the correct location. In a subsequent paper the amperometric titration of barium will be discussed more in detail.

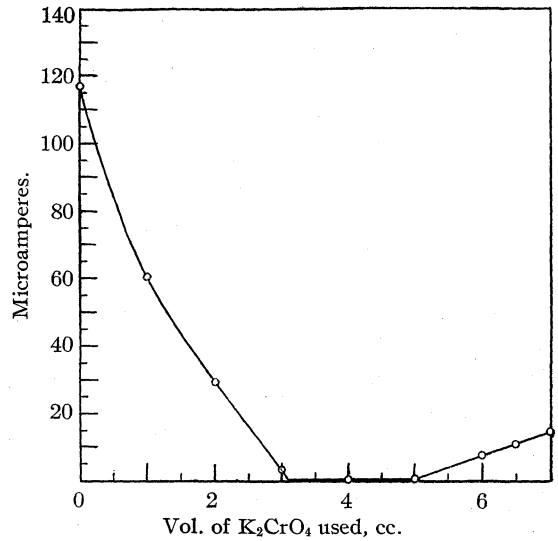


Fig. 10.—Titration of 50 cc. of 0.01 *M* $Pb(NO_3)_2$ in 0.01 *M* $Ba(NO_3)_2$ with 0.2 *M* K_2CrO_4 at $E_c = -1.0$ v.

Summary

1. The word "amperometric titration" is coined and the historical development of this type of titration is discussed.

2. Lead can be titrated accurately, precisely and rapidly by amperometric titration with dichromate or chromate, using the dropping mercury electrode as an indicator electrode. The titration can be carried out without applying an external e. m. f.

3. Even 0.001 *M* lead solutions can be titrated with a high degree of accuracy.

4. Lead can be titrated amperometrically in the presence of large amounts of barium when the solution is slightly acid with perchloric acid. The fractional precipitation of lead and barium in neutral medium with potassium chromate does not yield good results due to coprecipitation of barium chromate with lead chromate.

MINNEAPOLIS, MINN. RECEIVED AUGUST 14, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE INSTITUTE OF TECHNOLOGY OF THE UNIVERSITY OF MINNESOTA]

Studies on Aging and Formation of Precipitates. XXX. The Determination of the Specific Surface of Silver Bromide by the Radioactive and Dye Methods

BY I. M. KOLTHOFF AND A. S. O'BRIEN[1]

In studies on aging of silver bromide it was of interest to determine the specific surface of various products. Dyes, such as orthochrom T,[2] methylene blue,[3] or pinacyanol[4] have been used for this purpose. In this Laboratory wool violet has proved to be of great value in the determination of the specific surface of various precipitates. For this reason, the adsorption of this dye on silver bromide was studied under varying conditions and compared with the adsorption of methylene blue. In order to know the density of occupation of the adsorbed dye on the saturated surface it was necessary to have available the magnitude of the specific surface of the various products used. Particularly when dealing with freshly prepared, heterodisperse precipitates of silver bromide, consisting of extremely fine particles, it was hardly possible to determine the surface microscopically or ultra-microscopically, as the precipitates could not be peptized completely. For this reason, we have made a study of the radioactive method for the determination of the specific surface, the principles of which originated with Paneth[5] and have been successfully applied in this Laboratory. In the present study it was attempted to determine the kinetic equilibrium i

(1) From a doctor's thesis submitted by Albert S. O'Brien to the Graduate School of the University of Minnesota, June, 1938.

(2) Sheppard and Crouch, *J. Phys. Chem.*, **32**, 751 (1928).

(3) Wulff and Seidl, *Z. wiss. Phot.*, **28**, 239 (1930).

(4) Sheppard, Lambert and Keenan, *J. Phys. Chem.*, **36**, 174 (1932).

(5) F. Paneth, *Physik. Z.*, **15**, 924 (1915); *Z. Elektrochem.*, **28**, 11 (1922); Paneth and W. Vorwerk, *Z. physik. Chem.*, **101**, 445, 48 (1922).

the exchange between a radioactive bromide solution and inactive bromide in the surface of the silver bromide. When equilibrium is established, the following relation holds

$$\frac{Br^*_{surf.}}{Br^*_{sol.}} = \frac{Br_{surf.}}{Br_{sol.}} \quad (1)$$

or

$$Br_{surf.} = \frac{Br^*_{surf.}}{Br^*_{sol.}} Br_{sol.} = R.\ Br_{sol.} \quad (2)$$

in which the asterisk denotes the radioactive bromine. The application of equation (1) or (2) requires the limitation of the exchange to the surface layer only.

Experimental

Preparation of Radioactive Bromide.—Ethyl bromide (C. P.) was dehydrated over anhydrous calcium chloride, filtered and stored in glass-stoppered bottles. One ml. of an approximately 0.08 molar bromine solution in carbon tetrachloride was added to 1 liter of ethyl bromide. After thorough mixing, the flask was suspended at the center of a ten-gallon (40-liter) crock of water. The water was used to reflect the neutrons back into the flask. Soft glass bulbs, about 5 mm. in diameter, containing approximately 100 mg. of beryllium and from 100 to 140 millicuries of radon were secured through the courtesy of Dr. D. Hull of the Division of Physical Chemistry in this University. After radiating from sixteen to twenty hours the bulb was removed and the bromine reduced and extracted by shaking the ethyl bromide in a separatory funnel with 40 ml. of 0.1 molar sodium acid sulfite solution. The ethyl bromide left was dehydrated again and used in subsequent experiments. The aqueous layer containing the radioactive bromide was transferred to a 250-ml. Erlenmeyer flask and the dissolved ethyl bromide boiled off at reduced pressure. The solution was about 0.0013 molar in bromide. Water or solutions of inactive potassium bromide were added to it until the desired volume and bromide concentration were obtained. The four and one-half hour isotope was used in the present experiments, as the thirty-four hour isotope does not have much opportunity to build up and the isotopes of shorter life have almost decayed before the readings are started. In our work no readings were made before three hours had elapsed from the time of the removal of the beryllium–radon bulb.

Measurement of Radioactivity.—A great number of copper dishes of uniform dimensions was prepared and a measured volume of the radioactive solution was evaporated on a steam-bath in a copper dish; if the solution was acid it was neutralized before evaporation. The radioactivity of the residue was measured by placing the dish in the holder under the aluminum window of an ionization chamber. The amplifying circuit, constructed with the valuable aid of Dr. C. S. Copeland, was essentially the one recommended by DuBridge and Brown,[6] details of which are given in the thesis of the junior author.[1]

In all the experiments, the "rate of drift" method was used in measuring the activity of the residue, by determining the rate of the drift of the galvanometer light across an arbitrary number of cm. on a scale.

Materials Used.—Most of the chemicals were of C. P. quality and recrystallized if desirable. A product of wool violet 5BN, purified in the laboratories of the National Aniline Company, was used without further purification. The sample of methylene blue used satisfied the requirements of the "U. S. Pharmacopoeia X."

Analytical.—The dye concentration was determined colorimetrically using a photoelectric colorimeter. Solutions containing small amounts of suspended silver bromide were made entirely clear by addition of sodium thiosulfate. The latter salt did not affect the absorption spectrum of wool violet. In some cases the wool violet concentration was also determined by the chemical method using ceric sulfate or permanganate as oxidizing agents.

The concentration of (inactive) bromide in solution ($Br^-_{sol.}$ in equation 2) was determined by the hypochlorite procedure following the directions of Kolthoff and Yutzy.[7]

Products of Silver Bromide

Well Aged "Product E."—A 200-g. portion of silver bromide was precipitated by adding 0.4 *M* potassium bromide to a slight excess of 0.4 *M* silver nitrate. After washing the precipitate thoroughly with large quantities of water, it was suspended in 0.5 *M* potassium bromide and drastically aged for three days in a stoppered bottle at 95°. The product was then collected on a sintered glass filter, washed thoroughly with water, then with ethanol and finally with ether. It was air-dried until the odor of ether was no longer perceptible. It was then heated at 90° for two hours, ground in an agate mortar and kept in a brown bottle in a desiccator over anhydrous calcium chloride.

Fresh Silver Bromide from 0.1 *M* Solutions (Product B).—Separate samples weighing 0.094 g. were prepared by adding 5 ml. of 0.102 *M* potassium bromide to 5 ml. 0.1 *M* silver nitrate. The samples were not made air-dry, but kept in suspension and investigated immediately after preparation.

Fresh Silver Bromide from 0.43 *M* Solutions (Product A).—Separate samples weighing 2 g. were prepared by adding 25 ml. of 0.423 *M* potassium bromide to 25.5 ml. of 0.423 *M* silver nitrate. Further treatment will be described below.

Determination of Surface by Radioactive Method

Aged Silver Bromide (Product E).—The speed of exchange of radioactive bromide in solution with inactive bromide in the precipitate was determined by shaking at 25° 2-g. samples of product E with a mixture of 4 ml. of 0.001 *N* potassium bromide and 10 ml. of 0.00104 *N* radioactive bromide.

The results are plotted in Fig. 1, in which the amount of exchanged bromide is expressed in equivalents per gram of silver bromide. When the exchange is limited to the surface only this amount of exchanged bromide corresponds to the specific surface ($Br_{surf.}$ in equation 2). From the figure it is seen that the amount of bromide exchanged increases continuously and fairly rapidly with the time of shaking. From the relatively large amount of bromide exchanged it

(6) DuBridge and Brown, *Rev. Sci. Instr.*, **4**, 532 (1933).

(7) Kolthoff and Yutzy, *Ind. Eng. Chem., Anal. Ed.*, **9**, 75 (1937).

is evident that during the shaking much of the radioactive bromide is being incorporated into the solid. This must be due to recrystallization.

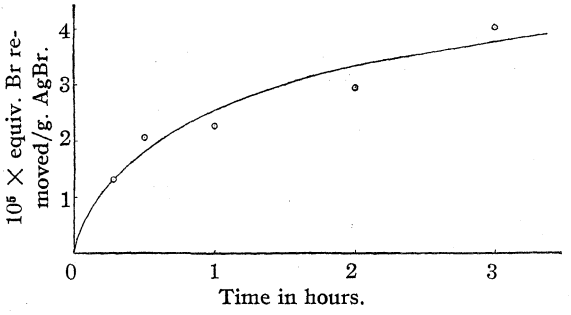


Fig. 1.—Penetration of radioactive bromide ions into aged AgBr.

The speed of recrystallization of this well-aged silver bromide decreases with decreasing temperature. The slope of the exchange curve was found to be much less at 0° than at 25°, but even at this lower temperature most of the radioactive bromide removed from the solution was being incorporated in the precipitate and only a small fraction was present on the surface.

In previous work carried out in this Laboratory and elsewhere[8] it was found that recrystallization and perfection, even of fresh and highly imperfect precipitates, can be prevented by coating the surface of the particles with a layer of a suitable dye. Therefore, experiments were carried out in which the speed of exchange was determined with aged and fresh silver bromide after the particles had been covered with a layer of wool violet or methylene blue or gelatin.

In the following experiments 2 or 4 g. samples of product E were shaken with 4 ml. of a 0.1% solution of wool violet or of methylene blue in 0.001 *M* bromide. After shaking for thirty minutes, 10 ml. of a radioactive solution which was 0.00107 *M* in bromide was added and the mixture shaken for a given period of time, after which the activity of the supernatant liquid was determined. The results are given in Table I and plotted in Fig. 2 (lines 1 and 2).

TABLE I

SPEED OF EXCHANGE OF Br* WITH AgBr (PRODUCT E) IN THE PRESENCE OF WOOL VIOLET OR METHYLENE BLUE

AgBr in g.	Time of shaking with Br*, hr.	Wool violet adsorbed R	Wool violet adsorbed Br^- exchanged $\times 10^5$ in equiv. per 1 g. AgBr	Methylene blue adsorbed R	Methylene blue adsorbed Br^- exchanged $\times 10^5$ in equiv. per 1 g. AgBr
2	1	0.354	0.248		
2	2	.374	.262	0.318	0.223
2	3	.380	.266	.332	.232
2	4	.403	.282	.346	.242
2	5	.41	.287		
4	1	.735	.257	.602	.211
4	2	.769	.268	.624	.218
4	3	.784	.274	.638	.226
4	4	.800	.280	.677	.237
4	5	.834	.292		

(8) Compare also Mare, *Z. physik. Chem.*, **61**, 385 (1908); **67**, 470 (1909); **68**, 104 (1909); **73**, 685 (1910); **75**, 710 (1911); also, Stevenson, *Kolloid Z.*, **10**, 249 (1912).

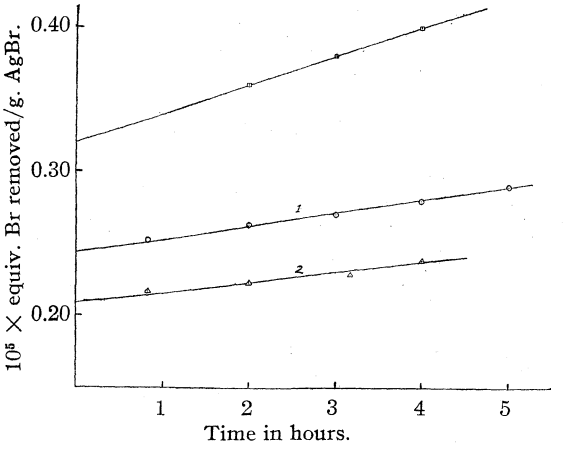


Fig. 2.—Specific surface of aged silver bromide: ⊙, wool violet coated AgBr; ⧋, methylene blue coated AgBr; ⊡, gelatin coated AgBr.

The results of experiments carried out in the presence of gelatin are given in Table II and also in Fig. 2.

TABLE II

SPEED OF EXCHANGE OF Br* WITH AgBr (E) IN THE PRESENCE OF GELATIN (FIRST SHAKEN 16 HRS. BEFORE ADDN. OF r.a.Br^-)

Time of shaking with Br*, hr.	Presence of gelatin (First shaken 16 hrs. before addn. of r.a.Br^-) With 10 mg. of gelatin R	With 10 mg. of gelatin Br exchanged $\times 10^5$ in eq. p.g. AgBr	With 1 mg. of gelatin R	With 1 mg. of gelatin Br exchanged $\times 10^5$ in eq. p.g. AgBr
1	0.584	0.409		
2	.664	.464	0.516	0.361
3	.736	.515	.549	.384
4	.756	.530	.572	.400

A comparison of the data in Figs. 1 and 2 reveals that adsorbed wool violet, methylene blue and gelatin almost completely prevent the further recrystallization of the aged silver bromide. Extrapolation to a time of shaking of zero should, in the presence of an inhibitor, yield the number of equivalents of bromide in the surface of 1 g. of silver bromide (E). In this way a specific surface of 0.24×10^{-5} equivalent of bromide per gram was found in the presence of wool violet and of 0.21×10^{-5} equivalent per gram in the presence of methylene blue. The values found in the presence of gelatin were somewhat greater, 0.33×10^{-5} in the presence of 1 mg., and 0.37×10^{-5} in the presence of 10 mg. of gelatin. These higher values may be attributed to the fact that the samples had been shaken for sixteen hours with the gelatin solution, and only for half an hour with the dye solutions; more peptization may have occurred after the longer period of shaking with gelatin. It is of interest to note that the slope of the line in the presence of 1 mg. of gelatin is much less than in the presence of 10 mg.

From the agreement of the values of the specific surface found in the presence of the acid dye wool violet and the basic dye methylene blue and from the fact that the specific surface was found to be independent of the amount of silver bromide shaken, it may be concluded that the "dye radioactive method" yields good results in the determination of the specific surface of aged silver bromide.

Fresh Silver Bromide (Product B).—The speed of penetration of radioactive bromide into fresh precipitates of silver bromide is extremely great. Consequently, the radioactive method cannot be used in the determination of the specific surface of fresh silver bromide unless the recrystallization is prevented by the addition of dyestuffs. In the following experiments 2 ml. of a 0.1% solution of wool violet in 0.001 *M* bromide was added to 10 ml. of the freshly prepared suspension of product B which contained 0.094 g. of silver bromide. After shaking for ten to fifteen minutes 10 ml. of about 0.008 *M* radioactive bromide solution was added and the suspensions further shaken for various periods of time, after which the activity was determined in an aliquot part of the supernatant liquid. Similar experiments were performed in which 2 ml. of 0.1% solution of methylene blue in 0.001 *M* bromide was added to the fresh suspension instead of wool violet. In all these experiments the concentration of bromide in the radioactive suspension was 0.004 *M*. In order to increase the percentage of activity removed, the experiments were repeated at a smaller final bromide concentration of 0.00175 *M* (with wool violet) and of 0.00166 *M* (methylene blue). All of the results are reported in Table III and those at the smaller bromide concentration are given graphically in Fig. 3.

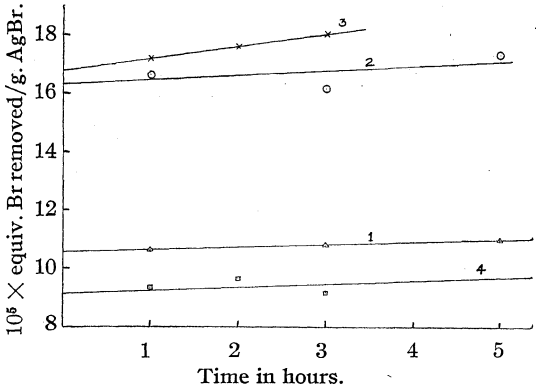


Fig. 3.—Specific surface of fresh silver bromide: ×, AgBr from 0.1 *N* reagents, wool violet–gelatin; △, AgBr from 0.1 *N* reagents, wool violet coating; ⊙, AgBr from 0.1 *N* reagents, methylene blue coating; ⊡, AgBr by method A, wool violet coating.

Experiments were also carried out in the presence of a mixture of gelatin and wool violet. Gelatin alone does not prevent entirely the recrystallization of fresh silver bromide. As wool violet is effective in preventing further recrystallization, the method could be used in the determination of the specific surface of silver bromide aged in the presence of gelatin.

In the experiments reported in Table IV, 2 mg. of wool violet was added to the fresh suspension of product B, and after ten minutes of shaking 10 mg. of gelatin dissolved in 2 ml. of 0.001 *M* bromide. After further shaking for one hour the radioactive bromide solution was added. In other experiments the suspension was first shaken with 10 mg. of gelatin and subsequently for one hour in the presence of wool violet–radioactive bromide solution. The results are given in Table IV and on curve 3 in Fig. 3.

TABLE III

SPEED OF EXCHANGE OF Br* WITH FRESH SILVER BROMIDE (B) IN THE PRESENCE OF 2 MG. OF WOOL VIOLET OR MG. OF METHYLENE BLUE

Time of shaking with Br*, hr.	Dye used	(Br⁻) in final suspension 0.004 *M* Br⁻ exchanged × 10^5 in equiv. R	per g. of AgBr	(1) in final suspension 0.0017 to 0.00166 *M* Br⁻ exchange × 10^5 in equi R	per g. of AgB
1	W.V.	0.123	11.6	0.260	10.7
2	W.V.	.134	12.7		
3	W.V.	(.119)	(11.2)	.264	10.8
4	W.V.	.141	13.3		
5	W.V.			.268	11.0
1	M.B.	.189	17.4	.428	16.7
2	M.B.	.189	17.4		
3	M.B.	.208	19.2	.416	16.2
4	M.B.	.212	19.6		
5	M.B.			.445	17.3

TABLE IV

SPEED OF EXCHANGE OF Br* WITH FRESH SILVER BROMIDE (B) IN THE PRESENCE OF 2 MG. OF WOOL VIOLET AND 10 MG. OF GELATIN

Time of shaking with Br*, hr.	First shaken 10 min. with W. V., then gelatin added Br⁻ exchanged × 10^5 in equiv. R	per 1 g. of AgBr	First shaken 1 min. with gelatin, then W. V. added Br⁻ exchanged × 10^5 in equiv. R	per 1 g. of AgBr
1	0.254	17.0	0.260	17.4
2	.306	20.5	.263	17.6
3	(.259)	(17.3)	.286	19.1

In a similar way fresh product A yielded an exchange of 9.0×10^{-5} equivalent of bromide per gram (see line 4 in Fig. 3).

Determination of Specific Surface by the Dye Method.—The adsorption of wool violet on fresh and old products of silver bromide was determined from solutions being either 0.001 *M* in silver or 0.001 *M* in bromide. Independent of the age of the silver bromide, it was found that the amount of dye adsorbed on the saturated surface is twice as great from the silver as from the bromide solutions. Fresh silver bromide coated with dye did not age on further shaking, the amount of dye adsorbed remaining constant with time. In this respect the silver bromide behaves like other fresh precipitates. A summary of the results obtained with the various products is given in Table V. In all of the experiments it was ascertained that the final dye concentration was large enough to have the surface saturated with the dye. In the experiments with methylene blue paraffin lined bottles were used.

Discussion of Results

1. The radioactive method applied in the presence of wool violet or methylene blue yields identical results with well-aged silver bromide. It was found that 0.046 and 0.039%, respectively, of the bromide was present in the surface of silver bromide E. Fresh product B yielded by the "wool violet–r.a." method a specific surface of 10.5×10^{-5} equiv. of bromide per gram, corresponding to the presence of 2.0% of all the bromide in the

TABLE V

ADSORPTION OF WOOL VIOLET (W.V.) AND METHYLENE BLUE (M.B.) ON FRESH AND AGED SILVER BROMIDE (SHAKEN FOR THIRTY MINUTES)

Product AgBr	Amt. taken, g.	Medium	Dye	Final concn. of dye mg. per l.	Dye removed in %	Dye absorbed in mg. per g. AgBr	Dye absorbed in moles per g.
E	10	0.001 *N* Ag	W.V.	54	79	0.158	2.08×10^{-7}
E	10	.001 *N* Ag	W.V.	160	36	.150	
E	10	.001 *N* Br	W.V.	150	48	.090	
E	10	.001 *N* Br	W.V.	150		.085[a]	1.17×10^{-7}
E	5	.001 *N* Br	M.B.	210	19	0.070–0.076	1.95×10^{-7}
B	0.19	.001 *N* Ag	W.V.	110	45	12.1	1.59×10^{-5}
B	.19	.001 *N* Br	W.V	160	21	5.4	0.71×10^{-5}
B	.094	.001 *N* Br	M.B.	107	35	7.6	2.0×10^{-5}
A	2	.0005 *N* Ag	W.V.	326	52	10.85	1.43×10^{-5}
A	2	.0005 *N* Br	W.V.	256	49	4.90	0.65×10^{-5}

[a] After centrifuging, most of the supernatant liquid was decanted and the dye concentration was determined in the mother liquor. The weight of the remaining precipitate and mother liquor was determined and the total amount of dye in this mixture measured after dissolving it in sodium thiosulfate. From the known weight of the precipitate and the dye concentration of the mother liquor and of the total amount of dye in the mixture, the amount of dye adsorbed on the precipitate was calculated.

surface. With the slightly aged product A the values were 9.1×10^{-5} equiv. per g. corresponding to 1.7% surface.

The "methylene blue–r.a." method with the fresh product B yielded a value of the specific surface which was 60% greater than that obtained with the "w.v.–r.a." method, although both methods gave identical results with the aged product E. The difference found with the fresh product undoubtedly is to be attributed to an adsorption of bromide in the form of methylene blue bromide on the active surface of the fresh product. In agreement with this interpretation it is found that the ratio of adsorbed wool violet (from excess of silver) to methylene blue on the saturated surface of aged product E is equal to 0.158/0.073 = 2.16, while this ratio on fresh product B is 12.1/7.6 = 1.6, showing that the adsorption of methylene blue as compared with wool violet is greater on the fresh than on the aged product. The specific surface of product B determined by the "r.a. method" in presence of a mixture of wool violet and gelatin is found equal to that found with the "r.a. methylene blue" method. The radioactive bromide solution used was slightly acid; at the positive side of the isoelectric point, positively charged gelatin particles are adsorbed and also an equivalent amount of bromide, explaining the difference between the "r.a. w.v. gelatin" and the "r.a. w.v." methods on the one hand and the similarity between the former and the "r.a. methylene blue" method on the other.

2. Taking the value of the specific surface determined by the "r.a. w.v." method as a standard, it is possible to calculate the number of bromide ions on the surface per molecule of adsorbed wool violet or methylene blue. A summary of the data is given in Table VI.

TABLE VI

DENSITY OF OCCUPATION OF WOOL VIOLET AND METHYLENE BLUE ON SATURATED SURFACE OF FRESH AND AGED SILVER BROMIDE

Dye	Medium	No. of bromide ions in surface per 1 molecule adsorbed dye: Product E	B	A
W.V.	0.001 *N* Ag	10.9	6.6	6.4
W.V.	.001 *N* Br	20.2	14.8	14.2
M.B.	.001 *N* Br	11.6	5.2	

The density of occupation of adsorbed wool violet on the aged product E, even in the presence of an excess of silver, is very small as compared to that found with other precipitates such as lead sulfate, barium sulfate, and lead chromate. In the latter cases the dye probably is oriented with its polar groups perpendicular to the surface of the polar adsorbents, whereas with the less polar silver bromide the adsorbed dye may be in a more flat position on the surface.[9] The fact that the density of occupation in an excess of silver is twice as great as in an excess of bromide suggests that in the latter case the dye is held in a monomolecular layer and that an extra layer is adsorbed as silver salt when the solution contains an excess of silver. On fresh precipitates the density of occupation of adsorbed wool violet is

(9) Compare Rabinovich and Natanson, *J. Phys. Chem. U. S. S. R.*, **11**, 434 (1930); and espec. Leermakers, Carroll and Staud, *J. Chem. Phys.*, **5**, 873 (1937); Sheppard, Lambert and Walker, *ibid.*, **7**, 265 (1939).

about 1.7 (excess silver) to 1.4 (excess bromide) times as great as on the aged products. It is not possible to say whether this is due to a changed orientation of the adsorbed dye or to other causes.

On the aged product 1 molecule of methylene blue was found to be adsorbed per 11.6 bromide ions on the surface. This value is in fair agreement with that reported by Wulff and Seidl[3] of 7.6 for a well-aged product the surface of which was measured microscopically and found to be about 2.5 times as great as that of our product E. The increased density of occupation of methylene blue on the fresh products has been explained above.

3. From a practical point of view the wool violet method either in an excess of silver or in an excess of bromide seems satisfactory for the determination of the specific surface of silver bromide of varying ages. The values found by the wool violet method are in satisfactory agreement with those found by the "w.v. r.a." method. In Table VII is given the ratio of the specific surfaces of the products determined by different methods.

TABLE VII

COMPARISON OF VARIOUS METHODS FOR DETERMINATION OF SPECIFIC SURFACE

	"r.a. W.V."	W.V. (Ag^+)	W.V. (Br^-)	"r.a. M.B."	M.B.
Surface B/ Surface E	47	77	64	73	104
Surface B/ Surface A	1.16	1.12	1.10		

Summary

1. A rapid incorporation of radioactive bromide into well-aged silver bromide occurs when a solution of the former is shaken with the solid.

2. Adsorbed wool violet and methylene blue limit the exchange between solution and solid to the surface layer only. Use of this is made in the radioactive determination of the specific surface of fresh and aged products of silver bromide. Adsorbed gelatin inhibits the recrystallization of aged silver bromide.

3. Wool violet is found suitable for the determination of the specific surface of silver bromide. From a solution containing an excess of silver the amount of dye adsorbed is twice as great as that from a solution containing an excess of bromide.

4. The saturated surface of an aged product of silver bromide contained per 10.9 bromide ions 1 molecule of wool violet (excess Ag^+) or per 20.2 bromide ions 1 molecule of wool violet (excess Br^-), and per 11.6 bromide ions 1 molecule of methylene blue (excess Br^-). With a fresh product the following figures were found: 6.5, 14.5, and 5.2, respectively.

MINNEAPOLIS, MINN. RECEIVED MAY 15, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE INSTITUTE OF TECHNOLOGY OF THE UNIVERSITY OF MINNESOTA

Studies on Aging and Formation of Precipitates. XXXI. The Aging of Silver Bromide

BY I. M. KOLTHOFF AND A. S. O'BRIEN[1]

In previous studies it has been found that fresh imperfect precipitates perfect themselves as a result of repeated recrystallizations which take place mainly in liquid films around the primary particles. Consequently, lattice material may deposit in interstices of an agglomerate of primary particles, thus cementing the latter together and causing a marked decrease of the specific surface of the precipitate.[2] The speed of this kind of aging was found to be determined by the solubility of the precipitate in the aging medium or more exactly in the liquid film around the particles. Ostwald ripening involving the growth of large particles at the cost of small ones was found to be of secondary significance with regard to the type of aging discussed above.

In the present paper studies on the aging of freshly prepared silver bromide are reported. It was found again that the speed of aging increased with increasing solubility of the precipitate. However, when the solubility had reached a certain minimum value, further decrease of the solubility did not affect the still fairly large speed of aging. Evidence is given in this paper that this relatively rapid aging is due to a thermal aging of silver bromide which also occurs in the dry state even at room temperature.

In general the aging was followed by two methods: (a) by determining the decrease of the

(1) From a doctor's thesis submitted by Albert S. O'Brien to the Graduate School of the University of Minnesota, June, 1938.

(2) Compare S. E. Sheppard and R. H. Lambert, *Colloid Symposium Monograph*, **6**, 276 (1928).

specific surface of the precipitate as indicated by the decrease of the amount of wool violet adsorbed on a saturated surface; (b) by determining the speed of exchange between radioactive bromide in solution and inactive bromide in the aging solid. This speed is governed by two factors: the specific surface and the degree of perfection of the precipitate. For this reason more comprehensive conclusions can be arrived at from the dye experiments.

For details regarding the radioactive experiments and the measurement of the wool violet adsorption reference is made to a previous paper.[3]

Experimental

Preparation of Silver Bromide and Study of Aging by the Dye Method.—The specific surface and other characteristics of the precipitate were found to depend upon the method of precipitation. By adopting a definite technique it was possible to obtain reproducible results. To weighed 120-ml. bottles each containing 25 ml. of 0.426 *M* silver nitrate and 0.5 ml. 0.1 *M* silver was added from a pipet in twenty-five seconds 25 ml. of 0.426 *M* potassium bromide. The bottles were swirled in a uniform manner during the precipitation of the 2.0 g. of silver bromide. The bottles were stoppered quickly, shaken vigorously by hand for fifteen seconds and the mother liquor which was 0.001 *N* in silver nitrate was decanted carefully. If the products were to be suspended in dilute silver nitrate solutions for aging, the precipitates were washed three times by decantation with 0.001 *M* silver nitrate. After completion of the washing the bottle was inverted carefully and allowed to drain, after which a convenient volume of aging solution was added. If the aging was to occur in dilute bromide solution, the precipitate was washed three times with water and once with 0.001 *M* bromide, and then it was treated as above. It was impossible to wash the fresh precipitate more than once with 0.001 *M* potassium bromide, as part of it would become peptized. After addition of the aging solution the bottles usually were placed on a mechanical shaker (200 phases per minute). After aging, a sufficient volume of a 0.1% wool violet solution was added to ensure a final dye concentration of 0.01 to 0.02% (saturated surface), and if necessary silver nitrate to give a final silver concentration of 0.001 *M*. The bottles were then replaced on the shaker for about one-half hour, weighed, and centrifuged until the supernatant liquids were perfectly clear. In an aliquot part of the latter, the dye concentration was determined with the aid of a photoelectric colorimeter and the amount of wool violet adsorbed per 1 g. of silver bromide calculated.

General Observations Regarding the Dye Adsorption.—Systematic investigations were carried out to determine the conditions under which the surface became saturated with wool violet. The results are given in a detailed and tabulated form in the thesis of the junior author[1]; they indicate that the surface was saturated when the silver concentration was greater than 0.0005 *M* and the final dye concentration greater than 0.030 g. per liter. The amount of dye adsorbed did not change upon shaking for longer than fifteen to thirty minutes, indicating that adsorption equilibrium was obtained quickly and that no further aging occurred after the precipitate was covered with the dye. In all of the experiments the dye adsorption was determined from a solution which was 0.001 *M* in silver nitrate. Independent of the age of the precipitate it was found that the amount of dye on the saturated surface from a dye solution which contained an excess of bromide was one-half of that from a dye solution containing silver.

Air-dried samples were prepared and kept at room temperature in the dark for a week. Five grams of such a product was exposed for fifteen minutes to direct sunlight, the product being stirred repeatedly during the exposure. The product was dark gray after fifteen minutes, but adsorbed the same amount of wool violet (excess of silver) as the pure yellow unexposed sample. A sample of the gray product was exposed to bromine vapor, the excess of which was removed by a current of air. The product became completely yellow again and adsorbed the same amount of wool violet as before. These experiments show that a photochemical decomposition of the silver bromide does not affect the dye adsorption on the surface.

Aging of Silver Bromide. Wool Violet Method

Aging in Excess of Silver.—Experiments were carried out in which the fresh precipitate after washing was aged by shaking in 0.001 *M* silver nitrate for various periods of time. The results are given in Table I and also on curve 1 in Fig. 1. Even the fresh precipitate settles rapidly in an excess of silver nitrate. Sets of experiments comparable to those in Table I were carried out in which the precipitate was centrifugally packed before the aging, or in which the aging was carried out in 0.01 *M* silver nitrate or in a mixture which was 0.001 *M* in silver and 0.2 *M* in potassium nitrate. The results were the same as given in Table I.

TABLE I

AGING OF SILVER BROMIDE IN 0.001 *N* SILVER NITRATE

	Aged in 0.001 *M* $AgNO_3$ (shaken)		Centrifuged in 0.001 *M* $AgNO_3$ and allowed to stand
Time of aging	Wool violet adsorbed in mg. per g.	Br × 10^5 in equiv. on surface of 1 g. AgBr	Wool violet adsorbed in mg. per g.
5 min.	10.15	8.85	
15 min.			5.4
1 hr.	6.6	5.75	5.1
6 hrs.	3.3–3.6	2.9–3.1	
24 hrs.	3.05	2.65	2.9
2 days	2.2	1.9	1.9
1 week	1.4	1.2	
2 weeks	1.3	1.1	

Several experiments were made in which dye was added immediately after precipitation without removing the mother liquor. In this way it was found that the fresh precipitate adsorbed 15.9–16.0 mg. wool violet per gram, corresponding to 13.9–14.0 × 10^{-5} equivalent of bromide in the surface of 1 g. This tremendous surface development corresponds to 2.6% of all the bromide in the surface.

Aging in Excess of Bromide (0.001 *M*).—The results of experiments carried out under different conditions are

(3) I. M. Kolthoff and A. S. O'Brien, THIS JOURNAL, **61**, 3409 (1939).

TABLE II

SPEED OF AGING OF SILVER BROMIDE IN 0.001 *M* POTASSIUM BROMIDE UNDER VARYING CONDITIONS

Wool Violet in mg. adsorbed per 1 g. of silver bromide (satd. surface)

Time of aging, hr.	Shaken	Not shaken	Centrifuged, not shaken[a]	Centrifuged and shaken[b]	Aged in 0.2 *M* KNO_3 shaken[c]	Aged in 0.2 *M* KNO_3, not shaken	Centrifuged, aged in 0.2 *M* KNO_3, not shaken	Centrifuged, aged in 0.2 *M* KNO_3, shaken
1/4	3.5–3.6	2.8–3.1	2.7					
1/2	2.8–2.9		2.1–2.3		1.5; 1.5			
1	2.05–2.15		1.8	1.7–1.8	1.3–1.35	1.7–1.8	1.6; 1.6	1.3–1.4
6	1.35–1.40	1.65–1.75	1.30–1.40		0.80; 0.80	1.0–1.1	1.05; 1.05	0.8–0.9
24	0.8–0.9	1.25	1.1–1.25	0.4–0.5		0.60–0.70	0.8; 0.8	0.5; 0.5

[a] The precipitates after washing with water and 0.001 *M* bromide were shaken with the latter solution for two minutes, centrifuged for ten minutes at 2000 r. p. m. After centrifuging the samples were allowed to stand in a dark room for a given period of time. Then silver nitrate and wool violet were added, etc. [b] After centrifuging the samples were shaken during the aging. [c] After washing of the precipitates as above, they were suspended in a solution which was 0.001 *M* in bromide and 0.2 *M* in potassium nitrate and shaken during the aging.

TABLE III

EFFECT OF EXCESS OF Ag^+ OR Br^- ON FURTHER AGING OF SILVER BROMIDE

15-Min. old product			6-Hr. old product		
Further aging in	Time of additional aging in min.	Wool violet adsorbed in mg. per g.	Further aging in	Time of additional aging in min.	Wool violet adsorbed in mg. per g.
		6.5–6.6			3.4–3.7
0.002 *M* Ag^+	15	6.05–6.05	0.005 *M* Ag^+	15	3.5–3.6
.002 *M* Br^-	15	4.0–4.2	.005 *M* Br^-	15	2.4–2.7

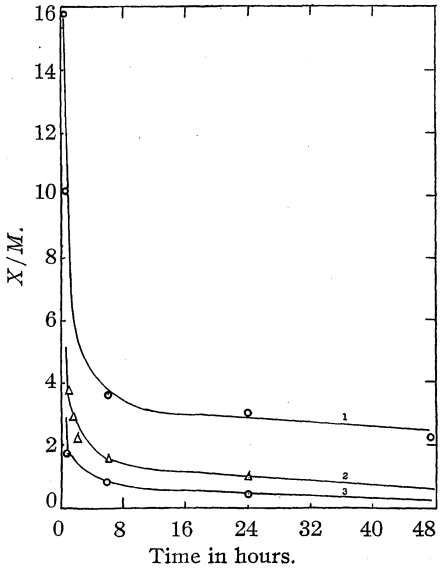


Fig. 1.—The aging of AgBr. Aging media: 1, 0.001 *M* $AgNO_3$; 2, 0.001 *M* KBr; 3, 0.001 *M* KBr, 0.2 *M* in KNO_3.

given in Table II; and some of them in Fig. 1. Comparison of Tables I and II (see also Fig. 1) shows that especially the initial speed of aging is much greater in 0.001 *M* bromide than in 0.001 *M* silver. It was of interest to study the effect of the silver and bromide concentration more systematically. In the first place experiments were carried out in which the fresh precipitate was aged in 0.1 *M* potassium bromide instead of 0.001 *M* solution. The fresh precipitate gave almost complete sol formation; after five minutes of shaking most of the precipitate had flocculated, while after fifteen minutes all of the precipitate settled rapidly. After this period of aging the precipitate was washed rapidly and the dye adsorption was determined in 0.001 *M* silver under standard conditions. The precipitate adsorbed 1.18 to 1.26 mg. of wool violet per gram, while after aging for the same period in 0.001 *M* bromide the dye adsorption amounted to 3.5 to 3.6 mg. per g. If we realize that the fresh precipitate adsorbs 16.0 mg. wool violet per gram the tremendously rapid aging in excess of bromide becomes very striking.

Experiments were performed using 2-g. portions of carefully prepared fifteen-minute old, and six-hour old precipitates of silver bromide prepared from 0.3 *M* solutions which were further aged at varying silver or bromide concentrations. The results are given in Table III.

Finally, a set of experiments was performed in the following manner. Silver bromide was precipitated from 0.426 *M* solutions as described previously. Immediately after precipitation the *p*Ag was adjusted to definite values (silver electrode in suspension) and kept as constant as possible. After aging for fifteen minutes silver nitrate was added to give a *p*Ag of 3 and the adsorption of wool violet determined. The results are given in Table IV.

TABLE IV

AGING OF FRESH PRECIPITATE FOR FIFTEEN MINUTES AT VARYING *p*Ag(*p*Br)

*p*Ag during aging	2	3	4	5	6	7	8	9
Wool violet adsorbed in mg. per g.	11.7	11.7	8.8	5.9	5.0	3.9	3.0–3.1	2.5

At a *p*Ag smaller than 3 the speed of aging did not further decrease, but with increasing *p*Ag the rate of aging increased rapidly. The isoelectric point of fresh silver bromide was found to be located close to a *p*Ag of 5, while the equivalence point is located close to a *p*Ag of 6. At

values of pAg smaller than about 5 the precipitate contains adsorbed bromide.

Aging in Other Media.—In order to investigate the effect of the solubility of silver bromide in the aging medium, studies were made in which the fresh precipitate was kept suspended in various solvents. The results are given in Table V and graphically in Fig. 2. From the curves,

TABLE V

AGING OF SILVER BROMIDE IN VARIOUS MEDIA

Aging medium	Time of aging, hr.	Wool violet removed, %	Wool violet adsorbed in mg. per g.
0.001 M $AgNO_3$ in 1 M NH_3	1	1	<0.1
.001 M $AgNO_3$ in 1 M NH_3	6	0	< .1
.001 M $AgNO_3$ in 99%	1	47	7.0
ethanol	6	27	4.1
Benzene	20	25	2.5

it is seen that the speed of aging is of the same order in 0.001 M silver nitrate in water as in benzene. This made us suspect that under certain conditions the nature of the solvent did not play a part and that we were dealing with a thermal aging of the solid. In order to substantiate this conclusion, fresh samples of the precipitate were washed with water, ethanol and ether, after which air was drawn through until the odor of ether was no longer perceptible. Samples were then allowed to stand in dry bottles in a desiccator protected from light for given periods of time, after which the wool violet adsorption was determined. A comparison of the figures in Tables I and VI (see also curves 1 and 4 in Fig. 2) reveals that the surface decreases at about the same speed when the precipitate is kept in the dry state as when it is suspended in 0.001 M silver nitrate. It is to be expected that the speed of thermal aging will increase greatly with increasing temperature. Experiments were carried out, therefore, in which the precipitate was aged in dry bottles containing a trace of bromine vapor at 100°. The bromine was added to prevent the auto-decomposition of the fresh precipitate at 100°. When the latter was heated to 100°, in the dark a trace of bromine was developed and the surface became dark. When heated in the presence of a trace of bromine vapor the color of the precipitate did not change. After the heating, the samples were cooled and the trace of bromine was removed with a current of air before determining the adsorption of wool violet.

TABLE VI

AGING OF SILVER BROMIDE IN THE DRY STATE

Time of aging	Aged at 25°		Aged at 100°	
	Wool violet removed, %	Wool violet adsorbed in mg. per g.	Wool violet removed, %	Wool violet adsorbed in mg. per g.
1/4 hour	66	6.6		
1/3 hour			41.5	2.3
1 hour			64.5	1.6
1.5 hours	58	4.4		
3.5 hours	68	3.4	68	1.3
17 hours	48	2.4	87	0.9
50 hours			26	.65
3 days	67–70	1.7–1.8		
7 days	53–55	1.05–1.1	0	.1
85 days	51	0.74		

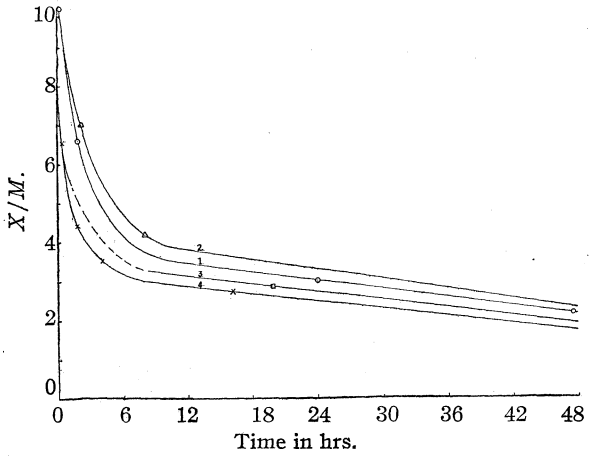


Fig. 2.—Aging of silver bromide. Aging media: 1, 0.001 N $AgNO_3$ water; 2, 0.001 N $AgNO_3$ ethanol; 3, benzene; 4, air dried.

Qualitatively, the coarsening and perfection of the particles when aged in the dry state at room temperature can be shown by a decrease of the peptizability. When a 0.7-g. portion of the fresh air-dried product was shaken with 100 ml. of 0.01 M potassium bromide in a glass-stoppered graduated cylinder, about 80 to 90% of the solid settled out immediately; nevertheless the supernatant liquid consisted of an opaque yellow sol. When the solid was aged for twenty hours at room temperature the supernatant liquid obtained on shaking was only slightly turbid, while after aging for three months in the dry state none of the precipitate could be peptized in 0.01 M bromide.

Aging Studied by the Radioactive Method.—The speed of penetration of radioactive bromide when a solution of the latter was shaken with the solid was determined. Details regarding the experimental technique are given in a previous paper[3] and the thesis of the junior author.[1] Several 0.094-g. samples of silver bromide were prepared by adding 5 ml. of 0.102 M potassium bromide to 5 ml. of 0.1 M silver nitrate. Immediately after precipitation 10 ml. of a radioactive bromide solution of known composition was added and the mixture shaken for a given period of time. From the known activity and the bromide concentration of the mixture (0.0015 M) the number of equivalents of bromide ions exchanged per gram of silver bromide was calculated. The results are given in Table VII and in curve 1 of Fig. 3.

TABLE VII

SPEED OF PENETRATION OF RADIOACTIVE BROMIDE INTO FRESH SILVER BROMIDE

Time of shaking with Br,*[a] hr.	0.094-g. sample in 0.0015 M KBr		0.47 g. sample in 0.1 M KBr	
	Activity removed, %	Equiv. Br^- × 10^5 exchanged per g. AgBr[b]	Activity removed, %	Equiv. Br^- × 10^5 exchanged per g. AgBr
1/4	80.5	219	54.4	506
1/2	86.6	345	58.4	598
1	92.5	653	60.4	659
2	92.7	675	62.0	691
4	93.0	696	63.0	725

[a] The asterisk denotes radioactive bromide.

[b] 1 g. AgBr contains 5.33 milliequivalents of bromide.

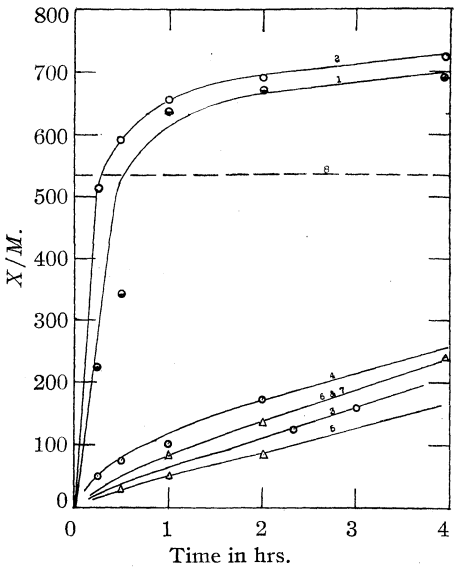


Fig. 3.—The rate of penetration of radioactive bromide ions in various AgBr precipitates: 1 and 2, fresh AgBr; 3, AgBr aged 2 hours in 0.001 *M* $AgNO_3$; 4, AgBr aged 2 hours in 0.001 *M* KBr; 5, AgBr aged 2 hours in 0.001 *M* KBr, 0.2 *M* in KNO_3; 6 and 7, fresh AgBr, with gelatin coating; 8, equilibrium value.

Another set of experiments was carried out with 0.47-g. samples which were washed quickly and shaken with 20 ml. of a radioactive solution which was 0.1 *M* in bromide (curve 2, Fig. 3). One gram of silver bromide contains 533 $\times 10^{-5}$ equivalent of bromide per gram, indicated by the dotted line in Fig. 3. Both fresh precipitates apparently are subject to very rapid recrystallizations. Within an hour of shaking the apparent amount of exchanged bromide is found greater than 100%, indicating the heterogeneous distribution of the active bromide through the precipitate during the early stages of aging. It is to be expected that the curves would show a maximum value after a longer time of shaking and then slowly would approach the point corresponding to homogeneous distribution of the radioactive bromide. The speed of penetration decreases very rapidly upon aging of the precipitate. Curve 3 of Fig. 3 (see also Table VIII) gives the time–penetration curve after aging of the precipitate represented by curve one for two hours in 0.001 *M* silver nitrate. Curve 4 of Fig. 3 refers to a precipitate (prepared as that of curve 1) which had been aged by shaking for two hours in 10 ml. of 0.0C *M* potassium bromide. At the end of this period 0.2 g potassium nitrate and 10 ml. of a radioactive bromid solution were added and the speed of penetration was deter mined.

TABLE VIII

SPEED OF PENETRATION OF RADIOACTIVE BROMIDE INTO SILVER BROMIDE AGED FOR 2 HOURS

Time of shaking with Br,* hr.	Aged in 0.001 *M* $AgNO_3$	Aged in 0.001 *M* KBr	Aged in 0.001 *M* KBr + 0.2 g. of KNO_3
1/4		46	19
1/3	33		
1/2		61	38
1		101	56
2	121 (2 1/3 hrs.)	178	88
3	165		

A similar experiment was carried out in which the agin occurred in 0.001 *M* potassium bromide containing th potassium nitrate (curve 5, Fig. 3). The aging is found t be more pronounced in the presence of potassium nitrate a result in agreement with that obtained from the experi ments with wool violet.

Speed of Penetration in the Presence of Gelatin.—In a previous paper[3] it was shown that adsorbed gelatin pre vented or at least inhibited the penetration of radioactive bromide into aged silver bromide and that, practically speaking, only exchange with bromide ions in the surface layer occurred. The following experiments show that gelatin inhibits but does not prevent the penetration of radioactive bromide into fresh silver bromide when the latter is shaken with a solution of the former. Samples of precipitates (0.094 g.) were prepared from 0.1 *M* solution (excess of Br 0.001 *M*). Immediately after precipitation 10 mg. of gelatin dissolved in 4 ml. 0.001 *M* bromide was added and the bottle shaken for ten minutes. Ten ml. of r. a. bromide solution (0.0039 *M* in bromide) was added and the mixture shaken. Similar experiments were carried out with 1 mg. instead of 10 mg. of gelatin. The number of equivalents of Br exchanged $\times 10^5$ in the presence of 10 mg. of gelatin were 85, 135, and 244 after one, two, and four hours of shaking, and in the presence of 1 mg. of gelatin 98 and 164 after one and three hours of shaking. From these results and the curves 6 and 7 in Fig. 3 it is evident that adsorbed gelatin does not prevent the recrystallization and perfection of fresh silver bromide. It is of interest to mention that the effect of 10 mg. of gelatin was found to be the same as that of 1 mg.

Discussion

1. The speed of aging in 0.001 *M* bromide was found to be much greater than in 0.001 *M* silver nitrate, it increased with increasing bromide concentrations, but increasing concentration of silver was of no further consequence. The great effect of an excess of bromide is attributed to an adsorption of this ion which gives rise to the formation of argento bromide ions in the liquid film around the particles, resulting in an increased solubility and speed of recrystallization of silver bromide in the liquid jackets.[4] The rate of aging in an excess of silver was not found to be affected by the presence of potassium nitrate by shaking and by other factors. On the other hand, shaking and the presence of salt had a distinct effect upon the aging in an excess of bromide (see Table II and Fig. 1). This is attributed by us to a colloidal solution. Upon longer periods of aging, the suspensions which had been shaken had aged

(4) Compare I. M. Kolthoff and H. C. Yutzy, THIS JOURNAL, **59**, 1634 (1937).

more than those which had been allowed to stand. This effect is easily explained by an Ostwald ripening which will be much more rapid in the shaken than in the unshaken suspension. The aging in excess of bromide was strongly promoted by the presence of potassium nitrate in a concentration of 0.2 *M*. The salt flocculates the sol, the number of particles in an agglomerate being dependent upon the concentration and kind of flocculating electrolyte. It seems to us that another factor, namely, the distance of approach of the particles in the agglomerate may be of primary importance in connection with the aging. When the particles are close together less recrystallization is necessary to cause cementing than when the particles are farther apart. We have indication that the distance of approach becomes smaller with increasing concentration of flocculating electrolyte and with increasing flocculating power. In order to test this point, experiments were carried out in which to the fresh suspension of silver bromide in 0.001 *M* potassium bromide, aluminum nitrate was added in a concentration of 0.0004 *M* and 0.001 *M*, respectively. After half an hour of shaking followed by removal of the aluminum the amount of wool violet adsorbed per gram was 1.9 mg. (0.0004 *M* Al) and 1.5 mg. (0.001 *M*), respectively, while in the absence of aluminum this amount was 2.8 to 2.9 mg.

2. An increase of the solubility of the precipitate by the addition of ammonia increases the rate of aging. The most striking result of this study is that, when the solubility has reached a minimum value, the rate of aging no longer depends upon the solubility of the precipitate in the aging medium. Then, it was found that the rate of aging was practically equal in aqueous and ethanolic 0.001 *M* silver nitrate, in pure benzene, and in the air-dried state. Apparently, under the latter conditions the aging cannot occur by recrystallization by way of solution but in the solid itself. Fresh products of silver bromide are extremely imperfect and have a tremendous surface development (2–3% is surface), and, consequently, they have a very large active surface. Silver bromide molecules located on the latter are much richer in energy than those on normal surface which in turn are richer in energy than those within the lattice. The thermal mobility of well-aged silver bromide is very small but that of our fresh products is quite pronounced. This is substantiated by the following experiments.[5] When fresh air-dried silver bromide is shaken with a solution of radioactive bromine in ethyl bromide or with anhydrous vapors of r. a. bromine, a rapid exchange between the radioactive bromine and the inactive bromide in the silver bromide occurs, resulting in a heterogeneous distribution of the active constituent through the solid. The speed of exchange decreased rapidly with increasing age of the precipitate.

Moreover, we found that fresh silver bromide has a relatively large electrical conductivity which, partly at least, is ionic. The properties of fresh bromide seem to be quite abnormal and it is planned to study the physical and also the chemical properties of such products in greater detail in the near future.

Summary

1. The rate of aging of silver bromide is much greater in a medium containing an excess of bromide than of silver, and it increases with the bromide concentration of the solution.

2. The colloidal state of the precipitate in an excess of bromide is of importance with regard to the speed of aging.

3. The effect of shaking upon aging indicates that upon longer periods of aging in a liquid medium of suitable solving power a slight Ostwald ripening occurs.

4. Adsorbed gelatin does not prevent the penetration of radioactive bromide into fresh silver bromide.

5. When the solubility of the silver bromide in the aging medium has reached a minimum value, recrystallization by way of solution becomes of no consequence. It is shown that fresh silver bromide is subject to a rapid thermal aging in the dry state, even at room temperature.

MINNEAPOLIS, MINN. RECEIVED MAY 15, 1939

(5) I. M. Kolthoff and A. S. O'Brien, *J. Chem. Phys.*, **7**, 401 (1939).

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, No. 721]

Ionization Constants and Hydrolytic Degradations of Cyameluric and Hydromelonic Acids

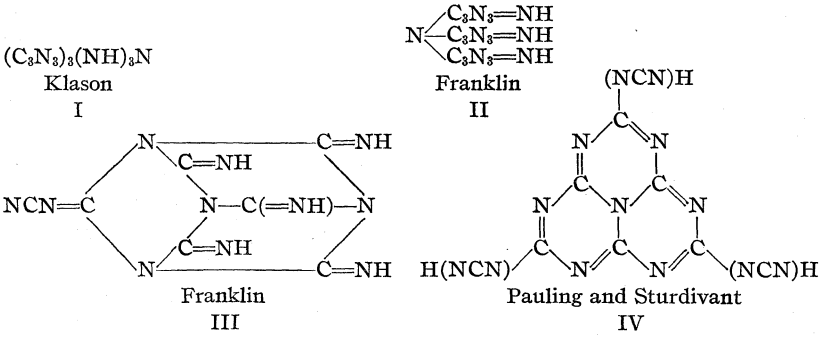
BY C. E. REDEMANN AND H. J. LUCAS

Recently the question of the structure of cyameluric and hydromelonic acids has been reopened by Pauling and Sturdivant.[1] It is rather surprising that cyameluric acid and related compounds, for example melon, melam, melem, and hydromelonic acid, should have received so little attention at the hands of organic chemists. With the exception of a limited amount of work by E. C. Franklin[2] and students, the problems in this field have been neglected for many years. Since most of these compounds are insoluble both in organic solvents and in water, show neither melting nor boiling points, are inert chemically with the exception that they undergo hydrolytic cleavage, and do not yield derivatives which are readily identified, it is probable that the reasons for this neglect bear some relation to their physical and chemical properties.

Tripotassium melonate, the potassium salt of hydromelonic acid, first described by Gmelin[3] as an undesirable by-product when too high a temperature was used in the preparation of potassium thiocyanate by the fusion of sulfur, potassium ferrocyanide and potassium carbonate, was obtained also by Liebig, who dissolved melon in fused potassium thiocyanate.[4,5] Potassium melonate is formed also by heating antimony or bismuth trichloride with potassium thiocyanate. As the result of numerous careful analyses of potassium and silver melonate, Liebig[6] proposed the empirical formula $C_9H_3N_{13}$[7] for hydromelonic[8] acid. Attempts to prepare the pure acid have not been entirely successful due to the great tendency of the acid to polymerize in concentrated aqueous solution.

Cyameluric acid is probably the most important of the compounds discussed in this paper since its nucleus appears to be common to most members of the series. Potassium cyamelurate is formed by the alkaline hydrolysis of melon, or of potassium melonate.[5] When the potassium salt is acidified with a strong acid, sparingly soluble cyameluric acid separates. Henneberg named the acid and assigned to it the formula $H_3C_6O_3N_7$ on the basis of analyses of the salts and of the acid. It seems probable that Liebig[6] was the first to prepare this acid, but he was unable to obtain constant analyses for his product, probably because he recrystallized the acid from a hot hydrochloric acid solution, a procedure now known to cause rapid hydrolysis.

Structures of Hydromelonic Acid.—Only four structures have been proposed



Structure I was proposed by Klason[8] in 1886, and II by Franklin[2a] in 1922. The latter appears to be nothing more than an interpretation of the former. His second structure,[9] III, proposed in 1935, is essentially the structure of hexamethylenetetramine in which three of the six pairs of hydrogen atoms are replaced by the cyanimino group, (=NCN), and the other three by the imino group, (=NH). Structure IV, proposed by Pauling and Sturdivant[1] in 1937, is based upon their belief that hydromelonic acid, $C_6N_7(NCNH)_3$, bears to cyameluric acid, $C_6N_7(OH)_3$, the same relation that

(1) Pauling and Sturdivant, *Proc. Natl. Acad. Sci.*, **23**, 615 (1937).

(2) (a) Franklin, THIS JOURNAL, **44**, 507 (1922); (b) Burdick, *ibid.*, **47**, 1485 (1925).

(3) Gmelin, *Ann.*, **15**, 252 (1835). This salt is also called potassium hydromelonate in the older literature.

(4) (a) Liebig, *Ann.*, **50**, 337 (1844); (b) **61**, 262 (1847).

(5) Henneberg, *ibid.*, **73**, 228 (1855).

(6) Liebig, *Ann.*, **95**, 257 (1855).

(7) Actually $C_{18}H_3N_{18}$ on the basis of the atomic weights of that time.

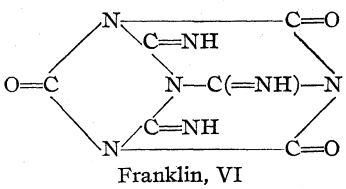
(8) The name was assigned by Gmelin on the basis that the polymer was converted to melon by loss of water when heated, hence the acid was thought to be a hydrate of melon. Klason, *J. prakt. Chem.*, [2] **33**, 289 (1886), called this compound cyamelon, under which name some of the literature appears.

(9) E. C. Franklin, "The Nitrogen System of Compounds," The Reinhold Publishing Corp., New York, 1935, p. 107.

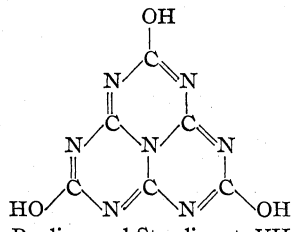
cyanuric tricyanamide, $C_3N_3(NCNH)_3$, bears to cyanuric acid, $C_3N_3(OH)_3$. The planar cyameluric nucleus is shown to have, according to quantum mechanical calculations, a high degree of stability. The stabilization due to resonance is approximately 150 kcal. per mole.

Structures of Cyameluric Acid.—Only three structures have been proposed for cyameluric acid

$(CN)_6O(NH)(OH)_2$
Klason, V



Franklin, VI



Pauling and Sturdivant, VII

Structure V, proposed by Klason,[8] was thought by him to represent the anhydride of an acid having the formula $(HO)_2(CN)_3NH(CN)_3(OH)_2$ (VIII). In structure VI, proposed by Franklin, the central group of atoms has the hexamethylene arrangement as in the hydromelonic acid structure proposed by him, III, and in structure VII, proposed by Pauling and Sturdivant, this group has the planar cyameluric arrangement, as in their structure for hydromelonic acid, IV.

Hydrolytic Degradations

If hydromelonic acid is correctly represented by Structure I or II, then on hydrolysis to cyameluric acid of structure V (the anhydride of VIII), one mole of I or II should yield approximately one mole of cyanuric acid, one mole of cyameluric acid, three moles of ammonia and no carbon dioxide on the assumption that the C_3N_3 groups represent cyanuric acid nuclei and that the cyanuric and cyameluric acids undergo no further hydrolysis. Cyameluric acid of structure V on further hydrolysis should be capable of yielding two moles of cyanuric acid, since in the acid VIII, of which V is the anhydride, there are two C_3N_3 nuclei.

On the other hand, if hydromelonic acid is either III or IV, on hydrolysis to cyameluric acid of structure VI or VII, respectively, one mole should yield not more than one mole of cyameluric acid and at the same time, six equivalents each of ammonia and carbon dioxide. Further hydrolysis of cyameluric acid should yield not more than one mole of cyanuric acid and, at the same time, four equivalents of ammonia and six equivalents of carbon dioxide if converted to cyanuric acid. Actually Liebig[6] isolated from the alkaline hydrolysis of cyameluric acid ammeline, ammelide, and cyanuric acid by progressively increasing the duration of hydrolysis.

Hydromelonic Acid.—When potassium melonate was hydrolyzed in 6 *N* nitric acid, 0.72 mole of cyanuric acid per mole of potassium melonate in the form of the insoluble cupric ammonium salt was obtained. Some hydrolysis of cyanuric acid took place at the same time. When hydrolyzed under alkaline conditions, the ratio of equivalents of carbon dioxide to those of ammonia varied from 1.25 to 1.11 (Table I). Even when hydrolysis was only a fraction of that possible, the $CO_2/2NH_3$ ratio was greater than unity. If hydromelonic acid had structure I or II, this ratio presumably would be below unity at the beginning of the hydrolysis, because carbon dioxide could come only from the breakdown of a C_3N_3 nucleus which is quite stable to further hydrolysis. Since

TABLE I

ALKALINE HYDROLYSIS OF POTASSIUM MELONATE

Sample, g.	KOH, *N*	Time, hrs.	NH_3 equiv.	CO_2 equiv.	Ratio $CO_2/2NH_3$	Extent of hydrolysis,[a] %
0.6531	5.45	1	0.00151	0.00188	1.25	15.7
1.6319	6.0	2	.01796	.02091	1.17	74.7
2.0526	3.5	2	.01464	.01628	1.11	59.3
2.5338	3.7	4	.0328	.0376	1.14	107

[a] Expressed as percentage of theoretical amount of ammonia, on the basis of structure III or IV, if the hydrolysis stopped at cyameluric acid.

potassium cyamelurate, under these conditions, was found to yield carbon dioxide and ammonia in the ratio of 2.24 (equivalents), the deviation from unity in the case of potassium melonate can be ascribed to the partial hydrolysis of the cyamelurate formed. The deviation from the ratio $^6/_4$ in the case of the latter compound probably is due to the formation of ammeline and ammelide, giving theoretical ratios of 3 and 2, respectively. Thus, the data from both acid and alkaline hydrolysis of hydromelonic acid favor structures III and IV over I and II. The hydrolysis is probably best represented by the equation

$$K_3C_9N_{13} + 6KOH + 6H_2O \longrightarrow K_3C_6O_3N_7 + 6NH_3 + 3K_2CO_3$$

Henneberg[5] attempted to write an equation expressing this hydrolysis involving ammelide as one of the products and omitting carbonate.

Cyameluric Acid.—Hydrolysis at 100° in concentrated nitric acid, conditions under which cyanuric acid is attacked but slowly, yielded 0.935 mole of cyanuric acid per mole of cyameluric acid. These results show that cyameluric acid may be represented by either structure VI or structure VII, for only one mole of cyanuric acid would result, but not by structure V, for two moles of cyanuric acid should result if the acid has the last structure.

Ionization Constants of the Acids

On the basis of the Franklin structures III and VI, the two respective acids, hydromelonic and cyameluric, should resemble each other closely as regards their acid strengths, because the atomic groupings responsible for acidity are identical in the two cases, and the groups responsible for the difference in structure, *i. e.*, C=NCN and C=O, respectively, are somewhat remote from the acid groups. Since the inductive effect of each of these two groups, before it can have an influence upon the acidic imino group, must pass through a tertiary nitrogen atom and a double bond, each of which alone has a pronounced damping effect upon induction, the acid strengths of III and VI would be expected to be similar. On the other hand, on the basis of the Pauling and Sturdivant structures, hydromelonic acid IV would be expected to be a much stronger acid than cyameluric acid VII. The hydromelonate ion, $C_9N_{13}^{\equiv}$, should have a much higher stability with respect to hydromelonic acid, $H_3C_9N_{13}$, than cyamelurate ion, $C_6O_3N_7^{\equiv}$, has with respect to cyameluric acid, $H_3C_6O_3N_7$. This is due to the fact that in the former case there are additional structures among which resonance can take place, for in the group of atoms IX, $(CNCN)^-$, the negative charge may be on either of the two nitrogen atoms as shown by X $\left(C—\ddot{\bar{N}}—C\equiv N:\right)$ and XI $\left(C—\ddot{N}=C=\bar{N}:\right)$. Since there are three such groups in the hydromelonate ion, the multiplicity of forms is markedly enhanced in comparison to the forms of the free acid, in which this additional type of resonance is not so important. Thus, from structural considerations, one would expect hydromelonic acid to be much stronger than cyameluric acid on the basis of the Pauling and Sturdivant structures, and to be little if any stronger on the basis of the Franklin structures.

Moreover, as Pauling and Sturdivant have pointed out, hydromelonic acid (IV) would bear the same relationship to cyameluric acid, VII that tricyanomelamine bears to cyanuric acid Tricyanomelamine is such a strong acid that the constant cannot be determined by conductimetric methods,[10] thus approaching the strong mineral acids in strength, whereas cyanuric acid is a weak acid.

The apparent ionization constants of hydromelonic, cyameluric and cyanuric acids were determined by titration of the potassium salts with standard hydrochloric acid, using a glass electrode to measure the *p*H. The solubility of the acids is too low to permit of their use for making titration curves and, in addition, hydromelonic acid polymerizes irreversibly. The cyanuric acid curve was made for the purpose of comparison. From the titration curves, apparent ionization constants were estimated for the acids by taking the *p*H at the "half-neutralization" points. These approximate values for the apparent ionization constants were then adjusted until the calculated titration curves fitted the observed curves very accurately. In this way a value of 1.66×10^{-7} was found for the first ionization constant of cyanuric acid, a value which is in fairly good agreement with that of 1.8×10^{-7} found by Hantzsch[11] but in poor agreement with that of 3.8×10^{-7}, found by Bader.[12]

The curves for the titrations are shown in Fig. 1 and the values for the ionization constants of hydromelonic and cyameluric acids are listed in Table II. Those for the second ionization constant of hydromelonic and the first ionization constant of cyameluric acid are approximations only, because of the separation of a solid phase in the titration shortly before the respective "half-neutralization" points were reached. On this account the assumed values of these two constants, which have been adjusted so as to fit the remainder of the respective curves, are subject to some error.

TABLE II

IONIZATION CONSTANTS

	Hydromelonic acid	Cyameluric acid	Cyanuric acid
K_1	Large	*Ca.* 1.0×10^{-3}	1.66×10^{-7}
K_2	*Ca.* 3.16×10^{-3}	6.30×10^{-7}	
K_3	1.26×10^{-5}	1.12×10^{-9}	

Hydromelonic acid is a much stronger acid than cyameluric, as the curves and table show. These results favor structures IV and VII of Pauling and

(10) Madelung and Kern, *Ann.*, **427**, 26 (1922).
(11) Hantzsch, *Ber.*, **39**, 139 (1906).
(12) Bader, *Z. physik. Chem.*, **6**, 289 (1890).

Sturdivant for these acids. That the cyameluric nucleus is strongly electronegative is shown by the comparison of ionization constants in Table III.

TABLE III

COMPARISON OF IONIZATION CONSTANTS

	K_A		K_A
Hydromelonic acid	Large	Cyameluric acid	1×10^{-3}
Benzoylcyanamide[12]	1.86×10^{-2}	Benzoic acid	6×10^{-5}
Acetylcyanamide[12]	1.54×10^{-4}	Acetic acid	1.6×10^{-5}

In the first column, the common radical is the substituted cyanamino group, H(NCN)[13] and in the second, the OH group.

In a subsequent communication the results of attempts to prepare derivatives of cyameluric acid will be presented. The authors gratefully acknowledge the inspiration of Professor Linus Pauling, who suggested the investigation of cyameluric and hydromelonic acids.

Experimental

Melon.—The following procedure based upon that of Henneberg[5] was most satisfactory. Chlorine gas was passed into a vigorously stirred solution of 1 kg. (12.3 moles) of pure[14] sodium thiocyanate in 2.5 liters of water. The temperature was maintained below 70–80° by external cooling. When the mixture became so thick that stirring was no longer effective, it was cooled to room temperature, the sludge of "pseudothiocyanogen"[15] was filtered off and the filtrate was treated again with additional chlorine. This process was repeated until no further pseudothiocyanogen was formed. The combined precipitate of pseudothiocyanogen was well washed with boiling water to remove all soluble salts, then dried at 120°, giving 512 g. of product.

The 512 g. of pseudothiocyanogen, divided into two batches, was converted into melon by heating in 25-cm. porcelain evaporating dishes with a large brush flame from a Meker type burner until all volatile products were expelled. The light yellow residue of crude melon weighed 240 g.

Other methods of preparing melon were less satisfactory on a laboratory scale. The slow heating of ammonium thiocyanate is reported to give good yields[16] but requires special equipment and much time.

Potassium Melonate.—The following modification of Liebig's[4b] method was most satisfactory. Eighty grams of pure potassium thiocyanate was slowly melted in a 10-cm. porcelain casserole and held at a moderate temperature until all moisture was expelled and a quiet melt was obtained. The temperature was then increased to a dull red heat and 40 g. of melon was added in portions of 5 to 10 g., each portion being allowed to dissolve before another was added. The carbon disulfide which is evolved was allowed to burn. When all the melon had dissolved the mixture was heated more strongly until only very little more carbon disulfide was produced. At this point a few drops of the melt were removed on the end of a Pyrex rod and its solubility[17] in hot water tested. Heating was continued until a 0.1 to 0.2 g. portion of the salt was completely soluble in 5 ml. of hot water. The entire operation required approximately one-half hour. After cooling, the salt was ground into coarse particles, dissolved in hot water, decolorized with carbon, filtered and allowed to cool. The fine felted needles, when air dried, weighed 38.8 g. Repeated crystallization gave a snow-white product.

Liebig's method using potassium thiocyanate and antimony trichloride gave a product which was hard to free from antimony salts.

Sodium Melonate.—Burdick[2b] prepared this salt by heating sodium thiocyanate with antimony trichloride. By dissolving 26 g. of melon in 50 g. of fused sodium thiocyanate, 11 g. of pure white fine needle crystals of sodium melonate was obtained. The sodium salt is very similar in appearance to and less soluble than the potassium salt.

Potassium Cyamelurate.—Two methods, both suggested by Henneberg,[5] were used.

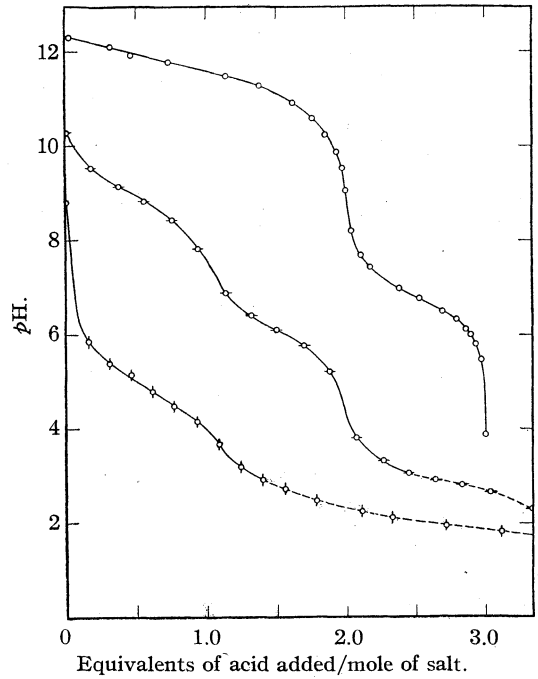


Fig. 1.—○, Cyanuric acid; -○-, cyameluric acid; ◌, hydromelonic acid; – – –, solid separating out.

(13) Madelung and Kern[10] believe that the group present in tricyanomelamine is —NH—C≡N, and not —N=C=NH. However, resonance between these two structures would be expected, and Dr. E. W. Hughes has verified this for the group in the molecule of dicyandiamide (private communication).

(14) A crude grade of sodium thiocyanate prepared by dissolving sulfur in fused sodium cyanide gave only slightly smaller yields.

(15) The name "pseudothiocyanogen" is here applied to the crude mixture composed of isoperthiocyanic acid, kanarin, and various polymers of isoperthiocyanic acid obtained by this procedure instead of to the part insoluble in alkali.

(16) Gludd, Keller and Klempt, *Z. angew. Chem.*, **39**, 1071 (1926).

(17) The test for solubility is very essential, for if heating has been for too short a time or at too low a temperature an insoluble product is formed.

A.—A solution of 20 g. (0.04 mole) of hydrated potassium melonate in 80 ml. of 4 *N* potassium hydroxide solution was boiled under reflux for two hours. A crop of slightly colored crystals of potassium cyamelurate was filtered off after cooling, and a second crop after concentrating the filtrate to one-third its initial volume. The two crops of crystals were washed with alcohol and air-dried; weight 11 g. or 70%. Crystallization from a hot moderately dilute solution with generous use of decolorizing carbon yielded pure white stout needles.

B.—A suspension of 30 g. of crude melon was boiled with 300 ml. of 3 *N* potassium hydroxide for forty-five minutes and the undissolved solid was filtered out. The crystals which separated from the filtrate were filtered off, washed with alcohol and air-dried. Boiling the original undissolved solid with the last filtrate and proceeding as above gave an additional amount. The total weight of potassium cyamelurate was 23 g.

Sodium Cyamelurate.—This salt, which was mentioned casually by Henneberg, is easily prepared in the same manner as the potassium salt by substituting 4 *N* sodium hydroxide for the potassium hydroxide in method (A) above. The yield is 50 to 60% of the theoretical assuming structure (IV) for hydromelonic acid and (VII) for cyameluric acid.

Anal. Calcd. for $Na_3O_3C_6N_7 \cdot 5^1/_2H_2O$: Na, 17.8; H_2O, 25.6. Found: Na, 17.7, 17.8; H_2O, 25.3, 25.4.

Cyameluric Acid.—Acidification of a moderately dilute aqueous solution of the sodium or potassium salt with 6 *N* hydrochloric acid added very slowly from a buret with effective stirring, followed by chilling in an ice-bath, gave a white crystalline powder. This was filtered off, washed well with cold water and air-dried.

Anal. Calcd. for $C_6H_3O_3N_7 \cdot 3H_2O$: C, 26.17; H, 3.27. Found: C, 25.88; H, 3.24.

Precipitation from a hot solution yields an impure product due to the rapid hydrolysis of cyameluric acid to ammelide and ammeline in acid solution. Crystallization from boiling water causes considerable decomposition due to the low *p*H of the solution of this comparatively strong acid.

The acid does not reduce alkaline permanganate either in the cold or upon prolonged boiling; it gives no enol reaction with ferric chloride. Most of its metallic salts are very sparingly soluble.

Acid Hydrolysis of Hydromelonic Acid.—A solution of 2.231 g. of potassium melonate in an excess of 6 *N* nitric acid was gently boiled for one and one-half hours. The solution was made alkaline with a slight excess of 15 *N* ammonium hydroxide, then sufficient cupric ammonium sulfate solution was added to color the solution a dark blue. The amethyst-red precipitate which gradually separated was filtered off, dried and weighed; weight 0.454 g. (72.5% of theoretical, assuming one mole of cyanuric acid per mole of hydromelonic acid).

The Alkaline Hydrolysis of Potassium Melonate.—A series of quantitative determinations of the amount of ammonia and carbon dioxide produced in the hydrolysis of potassium melonate to potassium cyamelurate was made as follows. The ammonia was carried over into standard hydrochloric acid by a current of purified air. The excess acid was then titrated with a standard sodium hydroxide solution using the mixed indicator, *p*-nitrophenol—methyl red. The amount of carbonate formed was determined by the method of Winkler as follows. The alkaline solution in the boiler was diluted to 250 ml., then an aliquot portion was taken. An excess of barium chloride solution was added to the aliquot, then the sodium hydroxide was carefully titrated with a standard hydrochloric acid solution using phenolphthalein as indicator. The data thus obtained are given in Table I.

As a check on the method, potassium melonate was replaced by urea. In this case the ratio of equiv. CO_2/equiv. NH_3 was 1.03. The difference between 1.03 and 1.00 represents about the accuracy to be expected from this method of analysis.

When potassium cyamelurate replaced potassium melonate, 2.24 was the ratio of equiv. CO_2/equiv. NH_3. This would indicate that the cause of a ratio greater than unity in the case of the hydrolysis of potassium melonate is a further hydrolysis of the potassium cyamelurate.

Acid Hydrolysis of Cyameluric Acid.—Two grams of cyameluric acid, purified through the copper ammonium salt, was digested with 10 ml. of concd. nitric acid on a steam-bath for four hours. The solution was diluted to 20 ml., cooled to 0°, saturated with the oxides of nitrogen obtained from the action of concd. nitric acid on metallic copper in order to destroy ammonium ions and make sure that all —NH_2 groups were converted into —OH groups, and evaporated to dryness on a water-bath. The residue was washed onto a weighed Gooch crucible, using 18 ml. of water, dried and weighed; weight 0.975 g. This represents 93.5% of that theoretically obtainable assuming one mole of cyanuric acid per mole of cyameluric acid. The residue gave the characteristic insoluble amethyst-colored copper ammonium salt of cyanuric acid.[18]

Electrometric Titrations of Hydromelonic and Cyameluric Acids.—Potassium melonate, 0.3707 g. (7.45×10^{-4} mole) crystallized four times from water, was dissolved in 50 ml. of water. Potassium cyamelurate, 0.2576 g. (6.62×10^{-4} mole) thrice crystallized from water, was dissolved in 50 ml. of water. In each solution was placed a glass electrode, a standard calomel electrode, and a mechanical stirrer. The former was titrated with 0.2899 *N*, the latter with 0.2493 *N* hydrochloric acid. The e. m. f. measurements were made with a student type potentiometer and a high sensitivity galvanometer in the former case, and with a Beckman *p*H meter in the latter case. Conversion to *p*H values in the former case was made by comparison with standard buffer solutions. The results are shown as the curves in Fig. 1.

Summary

Improved methods have been described for the preparation of melon, potassium and sodium melonate, potassium and sodium cyamelurate, and cyameluric acid. Titration of potassium melonate and cyamelurate, using the glass electrode, shows that hydromelonic acid is much stronger than cyameluric acid.

The titration data and results of hydrolysis

(18) S. P. Mulliken, "Identification of Pure Organic Compounds," Vol. II, John Wiley and Sons, Inc., New York, 1916, p. 84.

indicate that the molecules of these two acids contain the planar cyameluric nucleus of Pauling and Sturdivant.

PASADENA, CALIFORNIA RECEIVED AUGUST 10, 1939

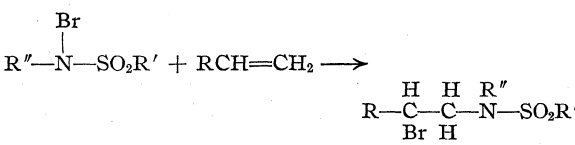
[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY, THE UNIVERSITY OF CHICAGO]

The Addition of N-Haloamides to Olefins

BY M. S. KHARASCH AND HILL M. PRIESTLEY

An unsuccessful attempt to add N-haloamides to olefins is recorded by Seliwanoff.[1] Foldi,[2] however, showed that 1-phenylpropene and N-bromo-N-methylbenzenesulfonamide ($C_6H_5SO_2NBrCH_3$) react to give at least two addition isomers. The reaction was considered by Földi to be of limited applicability, since all the purely aliphatic olefins tried by him yielded the dibromo derivatives when treated with the N-bromo-N-methylbenzenesulfonamide.

We have succeeded in extending this interesting reaction to include aliphatic olefins such as propene, 2-methylpropene, and vinyl chloride, as well as styrene. We have also demonstrated that in the reaction



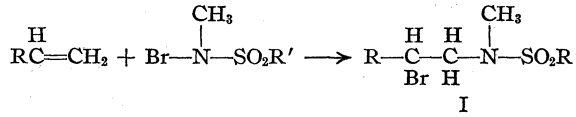
the radicals R, R′ and R″ play only a minor part, since we have employed in these reactions with equal success the phenyl-, *p*-tolyl-, and benzylsulfonyl derivatives of methylamine, benzylamine, phenethylamine, and β-bromo-α-phenylethylamine.

The addition of the bromo derivatives of the sulfonamides to olefins appears to be a unique reaction. We have been unable to obtain addition products of olefins with the following N-bromo-compounds: N-bromobenzamide, N-bromo-N-methylbenzamide, N-bromo-N-methyl-N-carbobenzoxamine, N-bromo-triphenylmethylamine, N-bromosaccharine, N-bromophthalimide, and N-bromosuccinimide.

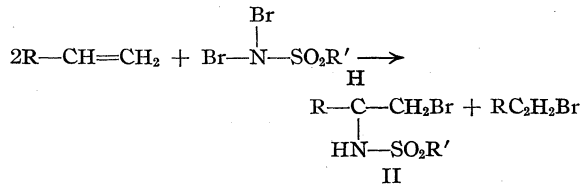
In addition to standardizing the conditions of addition of N-bromosulfonamides to olefins, we have succeeded in effecting the addition of N,N-dibromo derivatives of aromatic sulfonamides, *e. g.*, N,N-dibromo-*p*-toluenesulfonamide, to styrene, anethole, and isosafrole.

(1) Seliwanoff, *Ber.*, **26**, 426 (1893).
(2) Földi, *ibid.*, **63**, 2257 (1930).

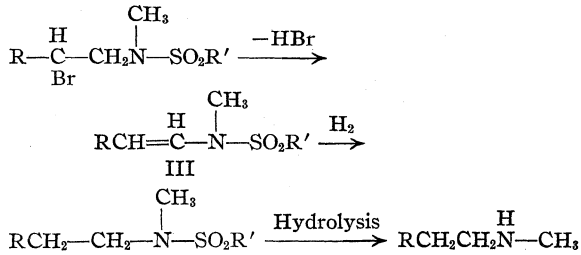
The positions taken by the nitrogen and bromine atoms of the N-bromo- and N,N-dibromosulfonamides is of considerable theoretical interest. The N-bromo-N-methyl aromatic sulfonamides add to propene, 2-methylpropene, vinyl chloride, and styrene to yield products in which the bromine atom takes the same position as the bromine atom in the "normal" addition[3] of hydrogen bromide to these olefins



The N,N-dibromosulfonamides, on the other hand, add to olefins to yield products in which the bromine takes the same position as in the "abnormal" addition of hydrogen bromide. A brominated olefin is formed at the same time.



The structure of the products of reaction I was proved by conversion into known compounds by the following series of reactions. The intermediates cited were all isolated and characterized.



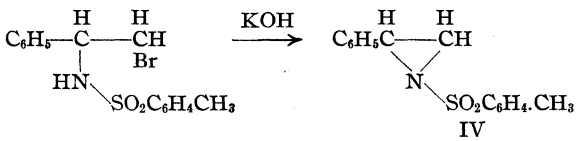
The elimination of hydrogen bromide from I usually was effected by heating the addition product with quinoline or with sodium ethoxide in al-

(3) For definition of "normal" and "abnormal" additions of hydrogen bromide consult the paper by Kharasch, Englemann, and Mayo, *J. Org. Chem.*, **2**, 288 (1937); Kharasch, Kleiger and Mayo, *ibid.*, **4**, 428 (1939).

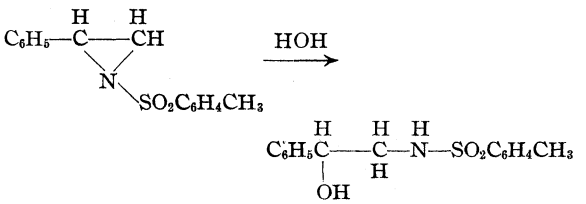
cohol. Palladium, on barium sulfate, usually served as the catalyst in the hydrogenation reactions, and the hydrolysis was effected with the aid of hydrogen chloride at 150°. The same end-product, namely, R–CH_2–CH_2–NH–CH_3, also was obtained in one step if sodium was added to an amyl alcohol solution of the addition product.

In the course of study of the structure of the products formed by the addition of aromatic N,N-dibromosulfonamides to styrene, anethole, and isosafrole, a number of extremely interesting intermediates were isolated.

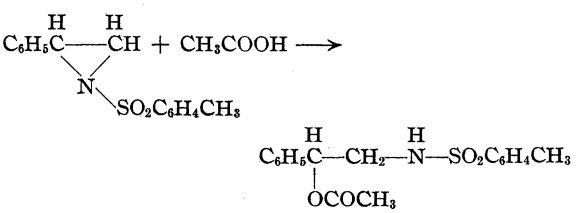
Thus, when the addition product of styrene and N,N-dibromo-*p*-toluenesulfonamide was treated with aqueous or alcoholic alkali, the N-*p*-tolylsulfonyl derivative of phenylethylenimine (styrenimine) was obtained.



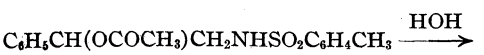
The imine derivative was easily cloven by many reagents. When boiled with water it was easily transformed into the expected *p*-toluenesulfonyl derivative of 2-phenyl-2-hydroxyethylamine.

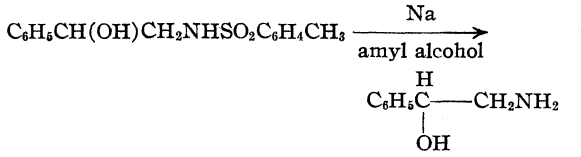


From cold glacial acetic acid the imine derivatives could be recovered unchanged, but heating the mixture for a short time caused the following reaction to take place

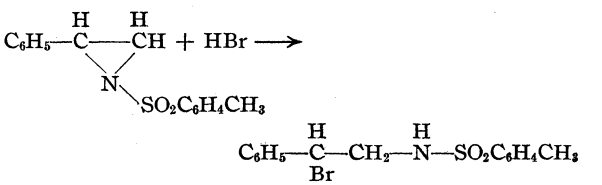


The structure of this compound was proved by saponification of the acetate group and treatment of the resulting compound, dissolved in boiling amyl alcohol, with sodium, to yield 2-phenyl-2-hydroxyethylamine.



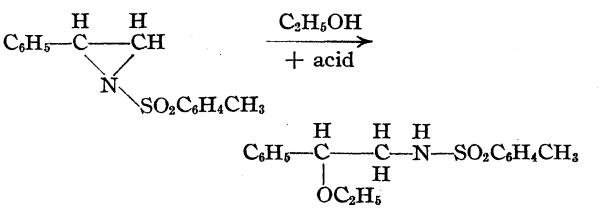


The N-substituted imines combined, at room temperatures, very readily with hydrogen chloride, hydrogen bromide, and hydrogen iodide, but with trichloroacetic and crotonic acids only upon warming. The nature of the products formed is best illustrated by a study of the addition of hydrogen bromide to the substituted imine. When the N-substituted imine, derived from styrene, is treated with hydrogen bromide at room temperatures, a compound of melting point 111° (VI) is obtained.

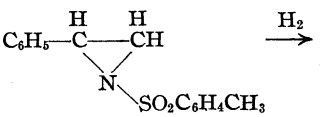


This substance is isomeric with the compound II (m. p. 167°) from which the imine is prepared. Furthermore, treatment of VI with sodium acetate yielded the same product as was obtained by direct action of acetic acid on the substituted imine IV.

Ethyl alcohol, even at the boiling point, does not cause the cleavage of the substituted imine. However, boiling an ethyl alcohol solution of it in the presence of a small amount of trichloroacetic acid, or the addition of a little cold 50% solution of sulfuric acid in alcohol to an alcoholic solution of the imine, causes the following reaction to take place



Catalytic reduction of IV, N-(*p*-toluenesulfonyl)-styreneimine gave N-phenethyl-*p*-toluenesulfonamide, which upon hydrolysis yielded phenethylamine.

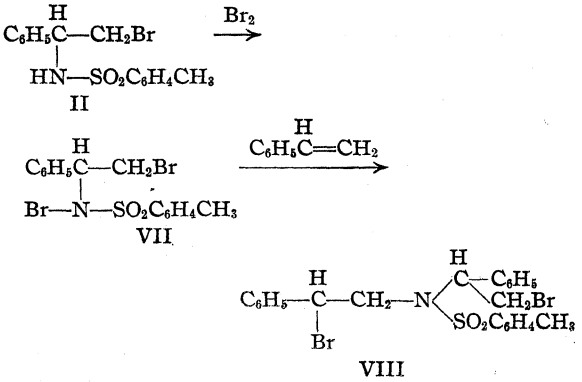


$$C_6H_5CH_2CH_2\overset{H}{N}—SO_2C_6H_4CH_3 \xrightarrow{\text{Hydrolysis}} C_6H_5CH_2CH_2NH_2$$

The same end-product was obtained by treating a solution of IV in amyl alcohol with sodium.

Compounds III and IV, obtained by elimination of hydrogen bromide from I and II, respectively, can be differentiated by their reactions with a neutral solution of potassium permanganate. The unsaturated compound III decolorizes the solution instantly, while the substituted imine IV is not affected by it.

It is of interest to note here that compound II, since it is a N-substituted *p*-toluenesulfonamide, reacts with bromine to give the N-bromo derivative of the substituted *p*-toluenesulfonamide VII which reacts smoothly with styrene to give an addition product VIII



Experimental

The sulfonamides and the corresponding N-bromosulfonamides were prepared by well-known methods or suitable modifications thereof.

1-Phenyl-1-bromo-2-(N-methylbenzenesulfonamido)-ethane (IX).—To 10 g. of N-bromo-N-methylbenzenesulfonamide was added 8 cc. of styrene. The mixture was warmed by the hand, until a reaction set in, after which it was cooled immediately in running water. After reaction was complete (disappearance of yellow color), the excess styrene was removed under reduced pressure. The residue was a thick sirup, which on cooling became a hard, glassy mass, but did not crystallize. For analysis, it was purified by dissolving in 25 cc. of warm absolute alcohol, and chilling the solution. A sirup separated. The alcoholic solution was decanted, and the sirup was washed with 10 cc. of cold alcohol. The substance was freed from alcohol by drying *in vacuo* for two hours at 70°, and then overnight in a vacuum desiccator over sodium hydroxide.

1-Phenyl-1-bromo-2-(N-methyl-*p*-toluenesulfonamido)-ethane (X).—To 16 cc. of styrene was added, in 5 g. portions, at first with cooling, a total of 32 g. of N-bromo-N-methyl-*p*-toluenesulfonamide. After the reaction, the warm mixture was dissolved in 60 cc. of absolute alcohol and seeded with a crystal from a previous preparation. The solid mass was collected on a filter, washed with a little alcohol, and finally crystallized from 120 cc. of alcohol. The yield was 32 g.

1-Phenyl-1-acetoxy-2-(N-methyl-*p*-toluenesulfonamido)-ethane (XI).—Ten grams of (X) was refluxed with 100 cc. of glacial acetic acid and 6 g. of sodium acetate for four hours. The cooled solution was decanted from the sodium bromide, concentrated to about one-third volume, and poured into 300 cc. of ice-cold water. On standing the material crystallized. Crystallization may be hastened by rubbing a part of the semi-solid mass with a little alcohol, and introducing the crystals into the main portion. The material was recrystallized from 30 cc. of 95% alcohol, and the crystals were washed with 10 cc. of ice-cold alcohol; yield, 3.5 g. A second crop of 5 g. of less pure material was obtained by working up the mother liquor.

1-Phenyl-1-hydroxy-2-(N-methyl-*p*-toluenesulfonamido)-ethane (XII).—The 3.5 g. of (XI) was dissolved in 25 cc. of absolute alcohol, and was treated with a solution of 0.6 g. of sodium hydroxide in 3 cc. of water. The resulting solution was heated on the water-bath for half an hour under reflux. The alcohol was then removed by evaporation, and to the residue water was added. The resultant oil was dissolved in benzene, washed with a little water, and the benzene solution was concentrated under reduced pressure. A pale-yellowish, thick oil remained. It was dried in the vacuum desiccator over sulfuric acid, but did not crystallize.

Methyl-(2-phenyl-2-hydroxyethyl)-amine.—A solution of 2 g. of (XII) in 60 cc. of amyl alcohol was brought to boiling, and 3.6 g. of sodium was added in small pieces. After the sodium had all dissolved, the amyl alcohol solution was shaken with 25 cc. of water to decompose the sodium amylate. The alcohol solution was separated and extracted several times with 5% hydrochloric acid. The combined hydrochloric acid extracts were evaporated on the water-bath to a small volume, extracted twice with ether to remove amyl alcohol, and made alkaline with solid potassium hydroxide. On cooling of the solution, the base separated in crystalline form. It was extracted with ether, the ether was distilled, and the solid residue was dried *in vacuo* over sulfuric acid. The yield was 0.8 g. (80% of the calculated).

1-Phenyl-2-(N-methyl-*p*-toluenesulfonamido)-ethylene (XIII).—A solution of 2.5 g. of (X) in 2.5 cc. of anhydrous quinoline was boiled for ten seconds. To the cooled solution was added dilute hydrochloric acid, and the crystalline precipitate was thoroughly washed with water. The material was crystallized from 25 cc. of alcohol; yield, 1.4 g., m. p. 106–107°. The alcoholic filtrate was examined for any possible isomers, but was found to contain the same compound in less pure form (m. p. 105°). The same compound was also prepared by treating a solution of 2.5 g. of (X) in 10 cc. of absolute alcohol, and refluxing for ten minutes with 15 cc. of a 3% solution of sodium ethoxide. Eight ml. of water was added to the hot solution; on cooling, 1.5 g. of white plates, m. p. 107°, was obtained.

Catalytic Reduction and Subsequent Hydrolysis to Methylphenethylamine.—A solution of 2.5 g. of (XIII) in 5 cc. of methyl alcohol was hydrogenated, with the aid of 0.8 g. of a 5% palladium–barium sulfate catalyst. In 10

minutes, 98 cc. of hydrogen (1 mole) was taken up, and absorption ceased. The alcohol was allowed to evaporate spontaneously. The residue was a sirup, which could not be brought to crystallization. It was heated with 6 cc. of concentrated hydrochloric acid at 150° for two hours. The contents of the tube were diluted with a little water, 0.5 g. of charcoal was added, and the mixture was filtered. Steam was passed into the filtrate until 50 cc. of distillate (which was discarded) had collected. The solution in the distilling flask was concentrated to a small volume on the water-bath, made alkaline, and steam-distilled until no more amine passed over (litmus). The volume of the distillate was about 50 cc. It was extracted with an equal volume of ether, the ethereal solution was washed with a little water, and dried over solid sodium hydroxide for two days. On passage of dry hydrogen chloride into the clear ethereal solution, the amine hydrochloride separated in the form of white plates. The precipitate was collected by filtration, washed with ether, and dried *in vacuo* over solid sodium hydroxide. The substance melted at 162°. It was not hygroscopic. The melting point of methylphenethylamine hydrochloride is reported by Johnson and Guest[4] as 152–154°, and by Decker and Becker[4] as 156–157°. Methyl-(1-phenylethyl)-amine hydrochloride is reported[5] to melt at 173°. To remove all doubt, the mercuric chloride double salt, the oxalate, and the urea derivative were prepared, the melting points of which were, respectively, 174, 186, and 143°. The corresponding melting points recorded in the literature[6] are 173, 184, and 141°.

Reduction of 1-Phenyl-1-bromo-2-(N-methyl-*p*-toluenesulfonamido)-ethane (X) with Sodium in Amyl Alcohol Solution.—The reduction was carried out in the manner described for the preparation of methyl-2-phenyl-2-hydroxyethylamine, excepting that the acid extract was not concentrated prior to the addition of alkali. Pure methyl-1-phenylethylamine hydrochloride, m. p. 162°, was obtained.

Reduction of 1-Phenyl-1-bromo-2-(N-methylbenzenesulfonamido)-ethane (IX) with Acid and Iron Filings.—In absolute alcoholic hydrogen chloride IX was reduced to the corresponding ethane with iron filings. The gummy product was then hydrolyzed with concentrated hydrochloric acid (two hours, 150°). The resultant methylphenethylamine hydrochloride was purified by solution in alcohol and precipitation with ether; m. p. 152–154°.

1-Phenyl-1-bromo-2-(N-benzylbenzenesulfonamido)-ethane (XIV).—To a solution of 5.0 g. of N-benzylbenzenesulfonamide dissolved in 25 cc. of chloroform, was added 3.4 g. of bromine. Immediately thereafter there was added a solution of 1.2 g. of sodium hydroxide in 15 cc. of water. After decolorization, the chloroform layer was separated and, without drying, was treated with 4 cc. of styrene. The solution was warmed a little on the water-bath, and the chloroform was removed in a stream of air. The residue was dissolved in 15 cc. of hot absolute alcohol. On cooling, an oil separated. The supernatant solution was decanted, the sirup was washed by decantation with a little alcohol, and was dried in the vacuum desiccator over sulfuric acid. Like the corresponding phenylsulfonylmethylamido compound, this substance did not crystallize, even on standing for several months in the ice-chest.

1-Phenyl-1-bromo-2-(N-benzyl-*p*-toluenesulfonamido)-ethane (XV).—This substance was prepared in exactly the same manner as XIV. A sirup was obtained, which, on standing for two days, crystallized; recrystallization from alcohol.

1-Phenyl-2-(N-benzyl-*p*-toluenesulfonamido)-ethylene (XVI).—A solution of 2.5 g. of (XV) in 25 cc. of 2% sodium ethoxide solution was boiled for one hour. Ten milliliters of hot water was added to the hot solution to redissolve the sodium bromide. The crystalline product that separated on cooling was crystallized from alcohol.

1-Phenyl-2-(N-benzyl-*p*-toluenesulfonamido)-ethane (XVII).—A suspension of 1.4 g. of (XVI) was hydrogenated with 1.5 g. of a 5% palladium–barium sulfate catalyst. In twenty minutes, the required 90 cc. of hydrogen was absorbed. Forty milliliters of benzene was added, the solution filtered from the catalyst, evaporated to dryness, and the residue recrystallized from alcohol.

Benzylphenethylamine.—A solution of 1.8 g. of (XVII) in 60 cc. of amyl alcohol was treated with 3 g. of metallic sodium, as described for the preparation of methyl-2-phenyl-2-hydroxyethylamine, with the exception that 10% sulfuric acid was used to extract the amine from the amyl alcohol solution, and the acid solution was made alkaline without preliminary concentration. The crude benzylphenethylamine hydrochloride isolated was purified by dissolving it in a little water and adding concentrated hydrochloric acid. Pure benzylphenethylamine hydrochloride separated.

1,1-Dimethyl-1-bromo-2-(N-methylbenzenesulfonamido)-ethane (XVIII).—A fairly rapid stream of isobutylene (generated from 5 g. of *t*-butyl alcohol and 5 g. of oxalic acid) was passed through a suspension of 5 g. of N-bromo-N-methylbenzenesulfonamide in 10 cc. of chloroform, at 40°, until a colorless solution resulted. This required about fifteen minutes. A special delivery tube with a large surface exposure was used. The chloroform was allowed to evaporate spontaneously, and the solid residue was recrystallized from 15 cc. of absolute alcohol; yield 4.8 g. This substance may also be prepared by treating liquefied isobutylene in a sealed tube, as described for (XIX).

1,1-Dimethyl-1-bromo-2-(N-methyl-*p*-toluenesulfonamido)-ethane (XIX).—Eight grams of liquefied isobutylene was sealed with 10 g. of N-bromo-N-methyl-*p*-toluenesulfonamide, and the contents were allowed to reach room temperature. After all the bromo compound had dissolved, and the solution was colorless, the tube was cooled in a dry ice–acetone mixture and opened. The excess isobutylene was allowed to escape and the solid residue was recrystallized from 30 cc. of absolute alcohol; yield 9.7 g.

1,1-Dimethyl-2-(N-methylbenzenesulfonamido)-ethylene or 1-Methyl-1-methylene-2-(N-methylbenzenesulfonamido)-ethane (XX).—A solution of 8.4 g. of XVIII in 16 cc. of dry quinoline was boiled for one minute. The solution was then cooled, and acidified with dilute hydrochloric acid, and the oil was extracted with ether. The

(4) Johnson and Guest, *Am. Chem. J.*, **42**, 350 (1909); Becker and Decker, *Ann.*, **395**, 368 (1913).

(5) "Beilstein," 4th ed., Vol. XII, p. 1094.

(6) Johnson and Guest, *Am. Chem. J.*, **42**, 350 (1909).

ethereal solution was dried with calcium chloride and the ether removed by distillation. The residue was distilled *in vacuo*, and practically all of it passed over at 203° at 21 mm. The yield was 3.8 g. of a colorless, viscous oil. The substance reduced permanganate, absorbed bromine, and showed all the reactions of a double bond, including hydrogenation, described below.

Catalytic Reduction of XX, and Hydrolysis to Methylisobutylamine.—A solution of 0.87 g. of (XX) in 6 cc. of alcohol was reduced, with the aid of 0.046 g. of platinum oxide catalyst (Adams). In five minutes, 85 cc., or the theoretical molecular equivalent of hydrogen was absorbed, and further shaking produced no more absorption. The solution was filtered from the catalyst, and the alcohol was distilled. The residue from 2.0 g. of reduced substance was heated with 10 cc. of concentrated hydrochloric acid for two hours at 150°. The amine hydrochloride was isolated as described in the case of the styrene addition product (XI). The substance melted at 178°, which is the melting point recorded in the literature for methylisobutylamine hydrochloride; the melting point of the prepared chloroplatinate (192°) is also in agreement with that recorded. The substance was extremely hygroscopic.

1,1 - Dimethyl - 1 - bromo - 2 - (N-methylbenzylsulfonamido)-ethane (XXI).—Two grams of N-bromo-N-methylbenzylsulfonamide, 6 cc. of chloroform, and 2 cc. of liquid isobutylene were sealed in a Pyrex tube, and the mixture brought to 40°. When the solution had become colorless, the tube was opened, and excess isobutylene allowed to escape. The chloroform was allowed to evaporate spontaneously, and the residue was recrystallized from 40 cc. of absolute alcohol; yield 1.5 g.

1,1-Dimethyl-2-(N-methylbenzylsulfonamido)-ethylene or 1 - Methyl - 1-methylene - 2 - (N - methylbenzylsulfonamido)-ethane (XXII).—On treatment of (XXI) with quinoline, in the usual manner, hydrogen bromide was eliminated, and the unsaturated compound was formed. The substance (XXII) was hydrogenated with platinum oxide (Adams) in alcohol solution, in the usual manner. The resultant N-methyl-N-isobutylbenzylsulfonamide melted at 83°.

1-Bromo-1-chloro-2-(N-methylbenzenesulfonamido)-ethane (XXIII).—Vinyl chloride (15 g.) and 26 g. of N-bromo-N-methylbenzylsulfonamide were sealed up and kept at room temperature until the next day. A colorless solution resulted. Excess vinyl chloride was allowed to escape, and the residue was crystallized from 125 cc. of 95% alcohol; yield 26 g.

1-Bromo-1-chloro-2-(N-methyl-*p*-toluenesulfonamido)-ethane (XXIV).—This substance was prepared in the manner described above.

1 - Chloro - 2 - (N - methyl - *p* - toluenesulfonamido)-ethylene (XXV).—A solution of 1 g. of XXIV in 5 cc. of absolute alcohol was refluxed for fifty minutes with 5 cc. of an alcoholic solution containing 2% of sodium ethoxide. Excess alcohol was removed on the water-bath. To the residue was added water and ether; the ethereal solution was separated and dried with sodium sulfate. The ether was distilled, and the oil was transferred to a desiccator. Several days later it solidified. The material, recrystallized from alcohol, melted at 91°. With the crystalline material at hand, the substance was readily prepared by heating XXIV with sodium ethoxide solution, as described above. After the refluxing was over, water was added to the warm solution to redissolve the inorganic salts, and a crystal was dropped in. On cooling, the substance of m. p. 91° separated.

1 - (N - Methyl - *p* - toluenesulfonamido) - 2 - bromopropane (XXVI).—Ten grams of N-bromo-N-methyl-*p*-toluenesulfonamide was sealed with 10 cc. of liquid propylene and 30 cc. of chloroform. After it had reached room temperature, the bomb tube was heated in a water-bath at 70–80° until the contents became colorless, which required about thirty to forty minutes. Excess propylene was allowed to escape, the chloroform was removed by distillation on the water-bath, and the residue was recrystallized from 40 cc. of absolute alcohol; yield 8.5 g.

Removal of Hydrogen Bromide from XXVI, Catalytic Hydrogenation and Subsequent Hydrolysis to Methylpropylamine.—Eight grams of the addition product XXVI was heated on the water-bath under reflux for two hours with 60 cc. of a 2% sodium ethylate solution in alcohol. The product was then worked up as described in the case of XXV. Evaporation of the ether left a semi-solid mass. The solid could be separated from the oily portion with filter paper. It melted at 54–56.

The oily portion contained 6.12% nitrogen. At 20 mm. the mixture distilled within the range 195–205°. Apparently, we are dealing here with two isomers of the formula $C_{11}H_{15}O_2NS$; $CH_2{=}CHCH_2NCH_3SO_2C_6H_4CH_3$(B) and $CH_3CH{=}CHNCH_3SO_2C_6H_4CH_3$(A). A solution of 1.37 g. of the semi-solid in 8 cc. of methyl alcohol was hydrogenated, with the aid 1.3 g. of 5% palladium–barium sulfate catalyst. After two and one-half hours, 123 cc. of nitrogen was absorbed, or about 90% of the theoretical quantity, for one double bond. After evaporation of the alcohol, the N-methyl-N-*n*-propyl-*p*-toluenesulfonamide was obtained in crystalline form.

One gram of the substance was hydrolyzed, as described previously in the case of the styrene product. The hydrochloride melted at 150°, which is in agreement with the melting point recorded in the literature[7] for methyl-*n*-propylamine hydrochloride. The hydrochloride of methylisopropylamine melts at 77°.

1 - Phenyl - 1 - *p* - toluenesulfonamido - 2 - bromoethane (II).—In an attempted preparation of N-bromo-N-acetyl-*p*-toluenesulfonamide, from N-acetyl-*p*-toluenesulfonamide and sodium hypobromite, N,N-dibromo-*p*-toluenesulfonamide, previously prepared by Chattaway, was obtained. This on interaction with styrene produced simultaneous bromination and addition. The brominated styrene remained in the chloroform solution, and the difficultly soluble addition product separated.

The addition product was conveniently prepared as follows: to 11.5 g. of *p*-toluenesulfonamide was added 6.9 cc. of bromine, the two components being intimately mixed, and then, with cooling and stirring, 27 cc. of 20% sodium hydroxide was added gradually from a separatory funnel. The lower layer containing the reaction product was dissolved in 60 cc. of lukewarm chloroform, and the chloroform layer was separated from the alkaline solution. To the chloroform solution, which was not dried, there was added drop by drop from a buret, at first with cooling and

(7) Chattaway, *J. Chem. Soc.*, **87**, 164 (1905).

stirring, 15 cc. of styrene. Toward the end of the addition, the solution was allowed to warm up, so as to complete the reaction. Usually, a small amount of a yellow substance precipitated from the hot solution toward the end of the styrene addition. This is the sodium salt of the monobromosulfonamide, which is later removed from the addition product by washing with alcohol. On cooling of the chloroform solution with ice water, the addition product separated. It was collected on a filter, washed with 20 cc. of ice-cold chloroform, and then with 30 cc. of cold absolute alcohol, and air-dried. The yield was 14.0 g. of substance, m. p. 163°, which, for the conversion into the imine, is sufficiently pure. Another 4 g. of addition product was obtained by evaporation of the filtrate to dryness, washing of the semi-solid residue with ice-cold alcohol, and recrystallization from alcohol. The bromine in the addition product is held rather firmly; none of it is precipitated by alcoholic silver nitrate solution in the course of twenty-four hours. In the corresponding methylamido addition product (X), the bromine, being attached to a carbon atom holding a phenyl group, is precipitated practically quantitatively during the first five minutes by alcoholic silver nitrate solution. Again, whereas the methylamido compound readily yielded an acetate on heating with sodium acetate and glacial acetic acid for four hours, the amido compound (II), is recovered practically unchanged under the same conditions.

1 - *p* - Anisyl - 1 - *p* - toluenesulfonamido - 2 - bromopropane (XXVII).—To a chloroform solution of the dibromoamide, prepared exactly as described above, was added, with cooling and stirring, 12 cc. of anethole. After the reaction was complete, the solution was cooled in ice water, and the product worked up as in the case of the styrene product.

1 - (3,4 - Methylenedioxyphenyl) - 1 - *p* - toluenesulfonamido - 2 - bromopropane (XXVIII).—The addition product was prepared as described above, from 12 cc. of isosafrole, and the dibromoamide was prepared from 11.5 g. of *p*-toluenesulfonamide. The chloroform solution was set aside in the ice chest for twenty-four hours, since crystallization proceeded very slowly.

1 - Phenyl - 1 - bromo - 2 - [N - (1 - phenyl - 2 - bromoethyl) - *p* - toluenesulfonamido]- ethane (VIII). (Interaction of the Bromo Derivative of 1-Phenyl-1-*p*-toluenesulfonamido-2-bromoethane with Styrene.)—To a solution of 3.5 g. of VI was added 2.5 g. of bromine and then 20% sodium hydroxide solution, drop by drop until almost all the free bromine had disappeared. A trace of free bromine was allowed to remain. At this point, 1.0 g. of unchanged starting material, m. p. 167°, precipitated. It was removed by filtration, and to the chloroform filtrate 1 cc. of styrene was added. The solution was warmed slightly on the water-bath, and the chloroform was removed by a stream of air. The residue still contained "positive" bromine (potassium iodide test). One milliliter of styrene was added, and the mixture was warmed on the water-bath until a test with potassium iodide showed the absence of "positive" halogen. The residue was dissolved in a little chloroform and ligroin was added. The precipitate was recrystallized several times from alcohol.

N-(*p*-Tolylsulfonyl)-styreneimine (IV).—A suspension of 11.5 g. of the styrene addition product (II), m. p. 167°, in 40 cc. of alcohol was brought to boiling on the water-bath. There was then rapidly added, from a pipet, 8 cc. of 20% aqueous sodium hydroxide solution. The addition product dissolved completely. To the hot solution, 8 cc. of warm water was added. On cooling the solution, styreneimine crystallized in glistening plates; yield 8.6 g. An acetone solution of the substance did not decolorize a solution of permanganate in acetone.

1 - Phenyl - 1 - halo - 2 - *p* - toluenesulfonamidoethanes (XXIX–XXXI).—A solution of 1 g. IV in 35 cc. of ether was shaken with 15 cc. of an aqueous hydrobromic acid solution. The ether was allowed to evaporate spontaneously, and the residue was washed with ice-cold alcohol. The addition product (XXIX) crystallized in needles. The corresponding chloro (XXX) and iodo (XXXI) ethanes were also prepared.

Catalytic Hydrogenation of N-(*p*-Tolylsulfonyl)-styreneimine (IV).—A suspension of 2.0 g. of the imine in 6 cc. of methyl alcohol was subjected to hydrogenation, with the aid of 0.5 g. of a 5% palladium–barium sulfate catalyst. In forty-five minutes, the calculated amount of hydrogen (172 cc.) was absorbed, and further treatment caused no more hydrogen to be taken up. The solution was filtered and washed with methyl alcohol, and the filtrate was evaporated to dryness. The N-phenethyl-*p*-toluenesulfonamide (XXXII) was left behind in the form of needles, m. p. 67°. The melting point recorded in the literature is 65–66°.

Hydrolysis of N - Phenethyl - *p* - toluenesulfonamide (XXXII).—On heating 0.7 g. of (XXXII) with 6 cc. of concentrated hydrochloric acid at 150° for two hours, the substance was recovered unchanged. The heating was then repeated for another two hours at 170°, and the hydrochloride of phenethylamine, m. p. 217°, was recovered.

Phenethylamine was obtained in one step by treating IV with an excess of sodium in boiling amyl alcohol solution, in the manner previously described. The same result was obtained by subjecting the styrene addition product (II) to the action of sodium and boiling amyl alcohol.

Treatment of the isosafrole addition product (XXVII), with sodium and amyl alcohol, gave aminoisosafrole; m. p. of hydrochloride 183°.

1-Phenyl-1-bromo-2-(N-phenethyl-*p*-toluenesulfonamido)-ethane (XXXIII).—One gram of XXXII, obtained from the catalytic reduction of IV, was dissolved in 10 cc. of chloroform, and treated successively with 1.2 g. of bromine and 0.6 g. of sodium hydroxide in 10 cc. of water. The chloroform solution was separated and treated with 0.5 cc. of styrene. The chloroform was removed in a stream of air, to the residue was added 0.2 cc. more of styrene, and the mixture was warmed for two to three minutes. It was then dissolved in 4 cc. of absolute alcohol. On cooling, a gum separated. After standing for several days in the ice chest, it solidified. The material was recrystallized several times from alcohol.

N - (2 - Phenyl - 2 - hydroxyethyl) - *p* - toluenesulfonamide (XXXIV).—A suspension of 0.2 g. of IV in 150 cc. of water was boiled under reflux for two hours. On cooling, white needles crystallized.

1 - Phenyl - 1 - trichloroacetoxy - 2 - *p* - toluenesulfonamidoethane (XXXV).—A mixture of 10 g. of IV and 10 g. of trichloroacetic acid was warmed on the water-bath until a homogeneous solution resulted. The gum was poured

in a thin stream into 100 cc. of water contained in a large mortar. The gum was rubbed with a pestle, the supernatant liquor being replaced with fresh water, until crystallization took place. The material, after several recrystallizations from alcohol, melted at 125°. The compound was stable toward boiling water or alcohol but hydrolyzed by alkali to XXXIV.

1 - Phenyl - 1 - ethoxy - 2 - *p* - toluenesulfonamidoethane (XXXVI).—One gram of IV was added to 7 cc. of absolute alcohol which contained 12 drops of concentrated sulfuric acid. The substance immediately dissolved with the evolution of heat. On cooling and scratching of the walls of the container with a glass rod, a precipitate separated. It was collected by filtration and washed with 5 cc. of ice-cold alcohol.

1 - Phenyl - 1 - crotonoxy - 2 - *p* - toluenesulfonamidoethane (XXXVII).—A mixture of 1 g. of IV with 2 g. of crotonic acid was heated at 160° for five minutes. A test

TABLE I

ADDITION COMPOUNDS, [a]THEIR DERIVATIVES, AND [b]CLEAVAGE PRODUCTS

Substance	M. p., °C.	Analyses, % Nitrogen Calcd.	Nitrogen Found	Halogen Calcd.	Halogen Found
1-Phenyl-1-bromo-2-(N-methylbenzenesulfonamido)-ethane (IX)	Sirup	3.95	4.03	22.6	22.6
1-Phenyl-1-bromo-2-(N-methyl-*p*-toluenesulfonamido)-ethane (X)	67	3.80	3.98	21.74	22.60
1-Phenyl-1-acetoxy-2-(N-methyl-*p*-toluenesulfonamido)-ethane (XI)[a]	94	4.03	3.81	...	...
1-Phenyl-1-hydroxy-2-(N-methyl-*p*-toluenesulfonamido)-ethane (XII)[a]	Oil	...	...	...	...
Methyl-(2-phenyl-2-hydroxyethyl)-amine[b]	78	9.27	9.33	...	...
1-Phenyl-2-(N-methyl-*p*-toluenesulfonamido)-ethylene (XIII)[a]	106–7	4.88	4.97	...	...
Methylphenethylamine hydrochloride[b]	162	8.17	8.23	...	...
1-Phenyl-1-bromo-2-(N-benzylbenzenesulfonamido)-ethane (XIV)	Sirup	3.27	3.51	...	...
1-Phenyl-1-bromo-2-(N-benzyl-*p*-toluenesulfonamido)-ethane (XV)	99	3.15	2.92	...	...
1-Phenyl-2-(N-benzyl-*p*-toluenesulfonamido)-ethylene (XVI)[a]	122	3.85	3.94	...	...
1-Phenyl-2-(N-benzyl-*p*-toluenesulfonamido)-ethane (XVII)[a]	105	3.85	4.00	...	...
Benzylphenethylamine hydrochloride[b]	265	...	...	...	...
1,1-Dimethyl-1-bromo-2-(N-methylbenzenesulfonamido)-ethane (XVIII)	95	4.57	4.64	26.1	25.4
1,1-Dimethyl-1-bromo-2-(N-methyl-*p*-toluenesulfonamido)-ethane (XIX)	93	4.37	4.49	25.8	25.2
1,1-Dimethyl-2-(N-methylbenzenesulfonamido)-ethylene (XX)[a] or 1-methyl-1-methylene-2-(N-methylbenzenesulfonamido)-ethane	Oil	6.27	6.44	...	...
Methylisobutylamine hydrochloride[b]	178	11.33	11.34	...	...
1,1-Dimethyl-1-bromo-2-(N-methylbenzylsulfonamido)-ethane (XXI)	123	4.37	4.29	...	...
1,1-Dimethyl-2-(N-methylbenzylsulfonamido)-ethylene (XXII)[a] or 1-methyl-1-methylene-2-(N-methylbenzylsulfonamido)-ethane	60	5.85	5.81	...	...
N-Methyl-N-isobutylbenzylsulfonylamide[a]	83	5.81	5.77	...	...
1-Bromo-1-chloro-2-(N-methylbenzenesulfonamido)-ethane (XXIII)	90	4.48	4.55	...	...
1-Bromo-1-chloro-2-(N-methyl-*p*-toluenesulfonamido)-ethane (XXIV)	90	4.28	4.41	35.33	34.49
1-Chloro-2-(N-methyl-*p*-toluenesulfonamido)-ethylene (XXV)[a]	91	5.70	5.78	14.44	14.05
1-(N-Methyl-*p*-toluenesulfonamido)-2-bromopropane (XXVI)	92	4.58	4.56	...	...
1-(N-Methyl-*p*-toluenesulfonamido)-propylene[a] (A)	54–56	6.22	6.16	...	...
and 3-(N-methyl-*p*-toluenesulfonamido)-propylene (B)	Oil	6.22	6.12	...	...
N-Methyl-N-*n*-propyl-*p*-toluenesulfonamide[a]	40	6.16	6.17	...	...
Methyl-*n*-propylamine hydrochloride[b]	150	12.78	12.60	...	...
1-Phenyl-1-*p*-toluenesulfonamido-2-bromoethane (II)	167	3.95	3.97	...	...
N-(*p*-Tolylsulfonyl)-styreneimine (IV)[a]	95	5.13	5.22	...	...
N-(2-Phenyl-2-hydroxyethyl)-*p*-toluenesulfonamide (XXXIV)[a]	113	4.91	4.89	...	...
2-Phenyl-2-hydroxyethylamine picrate[b]	158	15.30	15.56	...	...
1-Phenyl-1-trichloroacetoxy-2-*p*-toluenesulfonamidoethane (XXXV)[a]	125	3.20	3.47	24.4	23.5
1-Phenyl-1-ethoxy-2-*p*-toluenesulfonamidoethane (XXXVI)[a]	106	4.07	4.30	...	...
1-Phenyl-1-crotonoxy-2-*p*-toluenesulfonamidoethane (XXXVII)[a]	85	3.92	3.93	...	...
1-Phenyl-1-acetoxy-2-*p*-toluenesulfonamidoethane (XXXVIII)[a]	105	...	...	...	...
1-Phenyl-1-bromo-2-*p*-toluenesulfonamidoethane (XXIX)[a]	111	3.95	4.22	...	...
1-Phenyl-1-chloro-2-*p*-toluenesulfonamidoethane (XXX)[a]	95	4.52	4.77	...	...
1-Phenyl-1-iodo-2-*p*-toluenesulfonamidoethane (XXXI)[a]	137	3.49	3.66	...	...
N-Phenethyl-*p*-toluenesulfonamide (XXXII)[a]	67	...	...	...	...
Phenethylamine hydrochloride[b]	217	8.88	8.94	...	...
1-*p*-Anisyl-1-*p*-toluenesulfonamido-2-bromopropane (XXVII)	167	3.95	3.97	...	...
1-(3,4-Methylenedioxyphenyl)-1-*p*-toluenesulfonamido-2-bromopropane (XXVIII)	153	3.40	3.51	...	...
1-Phenyl-1-bromo-2-[N-(1-phenyl-2-bromoethyl)-*p*-toluenesulfonamido]-ethane (VIII)	158	2.60	2.69	...	...
1-Phenyl-1-bromo-2-(N-phenethyl-*p*-toluenesulfonamido)-ethane (XXXIII)	97	3.05	3.09	...	...

with the cooled material showed it to be completely soluble in alkali. The reaction product was treated with sodium carbonate solution, to remove unchanged crotonic acid, the residue was washed with water, and recrystallized from alcohol. When the crotonate was heated on the water-bath for fifteen minutes with 10% sodium hydroxide, and the solution acidified, XXXIV (m. p. 113°) separated.

1 - Phenyl - 1 - acetoxy - 2 - *p* - toluenesulfonamidoethane (XXXVIII).—A solution of 55 g. of IV in 100 cc. of glacial acetic acid was warmed on the water-bath until a test portion showed it to be completely soluble in alkali. This required thirty minutes. Too much heating renders the isolation of a crystalline acetate a difficult matter. The solution was poured in a fine stream into a liter of ice water. After standing for thirty minutes, the crystals were collected by filtration and air-dried. The yield was 65 g. (97% of the theoretical); m. p. 105°. The same acetate was obtained by refluxing for six hours 1 g. of XXIX (m. p. 111°) with 0.4 g. of anhydrous sodium acetate in 10 cc. of glacial acetic acid.

2-Phenyl-2-hydroxyethylamine.—A solution of 10 g. of XXXIV in 250 cc. of amyl alcohol was brought to boiling, and 18 g. of metallic sodium gradually added. The solution was then worked up in the usual manner. The amine was recovered in the form of a semi-solid mass, which when exposed to carbon dioxide yielded the known carbonate, m. p. 115°. The picrate melted at 158°.

Summary

1. Halosulfonamides of the type $R'SO_2NBrR$ react with a large number of olefins to yield products in which the bromine atom takes the same position as the bromine atom in the "normal" addition of hydrogen bromide to these substances.

2. The N,N-dibromosulfonamides, on the other hand, add to olefins to give products in which the bromine atom takes the same position as the bromine atom in the "abnormal" addition of hydrogen bromide to these compounds.

3. The preparation of N-(*p*-tolylsulfonyl)-styreneimine and its reactions with various reagents are reported.

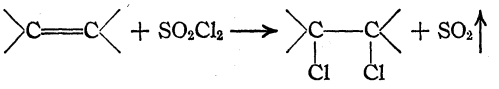
CHICAGO, ILLINOIS RECEIVED AUGUST 31, 1939

[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY OF THE UNIVERSITY OF CHICAGO]

Chlorinations with Sulfuryl Chloride. II. The Peroxide-Catalyzed Reaction of Sulfuryl Chloride with Ethylenic Compounds

BY M. S. KHARASCH AND HERBERT C. BROWN[1]

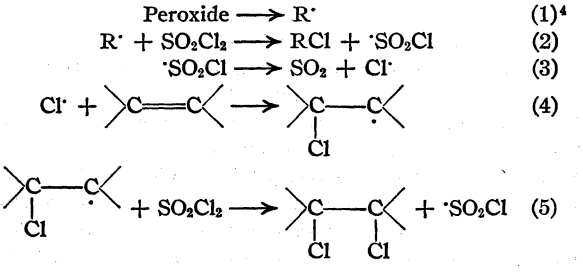
Sulfuryl chloride reacts readily with most ethylenic compounds to yield the saturated dichloro derivatives and sulfur dioxide.



Although this reaction has been used for synthetic purposes,[2] no thorough study has been made of the factors which control these additions.

We have previously shown that the presence of small quantities of organic peroxides brings about a reaction between sulfuryl chloride and saturated aliphatic hydrocarbons.[3] The characteristics of the reaction of sulfuryl chloride with olefins led us to suspect that this reaction is also peroxide-catalyzed. Investigation has confirmed this belief, and the evidence we have obtained indicates that the mechanism of this reaction is similar to that involved in the peroxide-catalyzed reaction of sulfuryl chloride with aliphatic hydrocarbons, a chain reaction involving chlorine atoms.

The following mechanism is in full agreement with the experimental facts and is advanced as representing the most probable course of the reaction in the light of our present-day information.



That the reaction is peroxide-catalyzed is indicated by a number of observations. Thus, an old sample of cyclohexene (which gave a strong test for peroxides) reacted with sulfuryl chloride with explosive violence when the two substances were mixed at room temperature. When the

(1) Eli Lilly Fellow, 1938–1939.

(2) A search of the literature reveals the use of sulfuryl chloride for the chlorination of unsaturated substances in the following instances: (a) chlorination of tetraphenylethylene and its derivatives, Norris, Thomas and Brown, *Ber.*, **43**, 2949 (1910); (b) chlorination of cinnamic acid and cinnamyl aldehyde, Durrans, *J. Chem. Soc.*, **123**, 1424 (1923); (c) chlorination of cyclohexene, Frieze and Djiang, *Ber.*, **71**, 667 (1938); and (d) chlorination of 3-hexene, Spiegler and Tinker, THIS JOURNAL, **61**, 940 (1939).

(3) Kharasch and Brown, *ibid.*, **61**, 2142 (1939).

(4) The dot denotes an unshared electron. The evidence for the assumption that the catalytic effect of peroxides in these chlorinations is due to their decomposition into organic free radicals, is discussed in the first paper of this series: *ibid.*, **61**, 2149 (1939).

cyclohexene was distilled carefully immediately before use (weak peroxide test), a moderate reaction ensued only after an induction period of several minutes. Addition of a drop or two of old cyclohexene, benzaldehyde, or ascaridole to the freshly-distilled cyclohexene catalyzes the reaction and eliminates the initial induction period. Passage of dry air through the relatively inactive cyclohexene also enhances its reactivity. The reactivity of **allyl chloride** is similarly enhanced by peroxidic materials.

Unsaturated compounds which are less sensitive to traces of peroxide can be purified easily to such a degree that no appreciable reaction with sulfuryl chloride occurs in the absence of added peroxide. For example, pure ***sym*-dichloroethylene** can be heated with sulfuryl chloride under reflux for several hours without appreciable reaction. In the presence of a small quantity (0.002 mole) of benzoyl peroxide, however, reaction occurs smoothly to yield *sym*-tetrachloroethane. **Tetrachloroethylene** reacts in a similar manner to form hexachloroethane. This reaction is, however, very slow (15% in five hours) compared to the other olefin chlorinations studied.

Stilbene readily reacts to yield the two isomeric stilbene dichlorides, and **tetraphenylethylene** forms the corresponding dichloride. In previous work on the chlorination of tetraphenylethylene with sulfuryl chloride,[2a] it was reported that different samples of sulfuryl chloride showed different capacities for reacting with tetraphenylethylene. The "inactive" samples could be activated by the addition of small quantities of acetic acid. We have repeated this work and have found that in the dark peroxide-free acetic acid does not catalyze the reaction of sulfuryl chloride, either with this olefin or with any of the others which we have tested (dichloroethylene, tetrachloroethylene, and stilbene). It appears likely that the activation was produced by the presence of peroxidic impurities in the acetic acid.

We have also carried out some preliminary studies of the action of sulfuryl chloride on unsaturated acids and anhydrides, such as crotonic acid, cinnamic acid, and maleic anhydride. However, the reaction which takes place is not the simple peroxide-catalyzed reaction with the double bond mentioned above. Study of this reaction is being continued.

Experimental Part

Chlorination of Cyclohexene.—The chlorination of cyclohexene can be carried out most conveniently by adding the sulfuryl chloride through a condenser to the cyclohexene contained in a flask. It is advisable to use freshly-distilled cyclohexene, adding one or two drops of benzaldehyde or some similar peroxidic material (old cyclohexene, ascaridole) as a catalyst. The reaction is strongly exothermic and the use of a diluent (carbon tetrachloride, methylene chloride, or benzene) to moderate the vigor of the reaction is recommended.

It is also advantageous to use a comparatively volatile solvent and to keep the reaction mixture boiling gently in order to facilitate the escape of the sulfur dioxide from the solution. Otherwise, side reactions of the sulfur dioxide with the olefin decrease the yield.

In a round-bottomed flask fitted with a ground-glass joint were placed 24.6 g. of cyclohexene (0.3 mole) and 30 g. of carbon tetrachloride. The flask was attached to a reflux condenser, and a solution of 27.0 g. of sulfuryl chloride (0.2 mole) in 30 g. of carbon tetrachloride was then added gradually through the condenser in the course of an hour. The heat of the reaction is sufficient to keep the mixture refluxing. After all the sulfuryl chloride had been added, the reaction mixture was heated gently for another hour, and was then fractionated. There was isolated 27.2 g. of dichlorocyclohexane (b. p. 79–80° at 22 mm., $n^{20}D$ 1.4903). This represents a yield of nearly 90% (based on the sulfuryl chloride used).

Chlorination of Allyl Chloride.—The chlorination of allyl chloride is similar to that described above. Yields of 80 to 90% of 1,2,3-trichloropropane are readily obtained.

Chlorination of *sym*-Dichloroethylene.—The chloro derivatives of ethylene are comparatively insensitive to traces of peroxides. For this reason these compounds may be purified easily, and the dependence of the reaction of sulfuryl chloride with the double bond upon peroxide catalysis shown.

Freshly distilled dichloroethylene, b. p. 60–60.5° (19.4 g., 0.2 mole), and sulfuryl chloride (40.5 g., 0.3 mole) were heated under reflux for three hours in the dark. At the end of this time, the reaction mixture was fractionated: no reaction had taken place. The fractions were combined, a small quantity of benzoyl peroxide (0.002 mole) was added, and the refluxing was continued. Slow evolution of sulfur dioxide from the reaction mixture indicated that a reaction was now taking place. At the end of two hours the heating was discontinued, and the mixture was fractionated. There was isolated 29.5 g. of *sym*-tetrachloroethane (b. p. 143–145°, $n^{20}D$ 1.4942). The yield was 85%.

Chlorination of Stilbene.—In the absence of added peroxide, stilbene reacts slowly with sulfuryl chloride. Whether this slow reaction is due to a trace of peroxide, or whether it is a slow thermal bimolecular reaction, could not be determined. The addition of a small quantity of benzaldehyde or ascaridole brings about a rapid, vigorous reaction at room temperature. The yield of crude product (stilbene dichloride) is quantitative. After fractional crystallization of this crude material, first from alcohol to obtain the higher-melting isomer, and then from ligroin to obtain the other isomer, there was obtained a 45% yield of α,α'-stilbene dichloride, m. p. 191–193°, and a 33% yield of the β,β' isomer, m. p. 90–93°.

Chlorination of Tetraphenylethylene.—Tetraphenylethylene, like stilbene, reacts slowly with sulfuryl chloride in the absence of added peroxide. When a trace of a peroxide (benzaldehyde which gives a strong peroxide test, or ascaridole) is added, the reaction is accelerated tremendously. The product formed is the dichloride, m. p. 184–186° (dec.).

Summary

1. Sulfuryl chloride reacts with ethylenic compounds to form the corresponding dichlorides. The following olefins have been chlorinated: cyclohexene, allyl chloride, dichloroethylene, tetrachloroethylene, stilbene, and tetraphenylethylene.

2. The chlorination of these ethylenic compounds by means of sulfuryl chloride is catalyzed by organic peroxides.

3. It is suggested that the reaction proceeds through a chain mechanism involving atoms and free radicals.

CHICAGO, ILLINOIS RECEIVED OCTOBER 11, 1939

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY AND THE WILLIAM G. KERCKHOFF LABORATORIES OF THE BIOLOGICAL SCIENCES, CALIFORNIA INSTITUTE OF TECHNOLOGY]

The Wound Hormones of Plants. IV. Structure and Synthesis of a Traumatin[1]

BY JAMES ENGLISH, JR.,[1a] JAMES BONNER AND A. J. HAAGEN-SMIT

Many plant tissue extracts are capable of inducing renewed growth activity in mature plant cells. These growth inducing extracts are usually obtained from ground or heated tissues, and they are capable of evoking cell division and cell enlargement in unwounded cells. The active principles have therefore been referred to as "wound hormones."[2] The present paper concerns the structure and synthesis of one highly active "wound hormone," 1-decene-1,10-dicarboxylic acid, whose isolation has already been announced.[3] The authors propose that the name "traumatic acid" be used in referring to this substance.

In earlier papers[4] a quantitative bio-assay (the bean test) for wound hormone activity has been described.

Activity tests of the material described below were always carried out in the presence of a "co-factor"[5] mixture.

One-tenth gamma of the pure substance per applied drop elicits a detectable response in the bean test. The pure product, m. p. 165–166°, is optically inactive and yielded an equivalent weight by titration of 118. A micro-Zerewitinoff determination carried out on the dimethyl ester showed the absence of active hydrogen. Catalytic hydrogenation yielded decane-1,10-dicarboxylic acid, identified by melting point and mixed melting point with an authentic sample prepared from decamethylene glycol.[6]

Since the analysis and the result of the hydrogenation experiment indicated the existence of one double bond, an oxidative degradation was carried out. On oxidation of the methyl ester with permanganate in acetone solution, sebacic acid was formed indicating the presence of a double bond in the α-β position. This conclusion was confirmed by the synthesis of 1-decene-1,10-di-

(1) This paper describes work begun under a grant from the Lalor Foundation. Report of work carried out with the coöperation of the Works Progress Administration, Official Project Number 665-07-3-83, Work Project Number 9809.

(1a) Present address: Yale University, New Haven, Conn.

(2) (a) G. Haberlandt, *Beit. z. allgemeinen Botanik*, **2**, 1 (1921); (b) G. Haberlandt, *Biol. Zentr.*, **42**, 145 (1922).

(3) J. English, J. Bonner and A. Haagen-Smit, *Proc. Nat. Acad. Sci.*, **25**, 323 (1939).

(4) J. English and J. Bonner, *Jour. Biol. Chem.*, **121**, 791 (1937); J. Bonner and J. English, *Plant Physiol.*, **13**, 331 (1938).

(5) For a description of the preparation and properties of this co-factor mixture, see note 3. Sucrose and particularly glutamic acid can in part replace the co-factor mixture in augmenting the activity of traumatic acid.

(6) P. Chuit, *Helv. Chim. Acta*, **9**, 264 (1926).

carboxylic acid which proved to be identical with the natural active material. The synthesis was carried out by converting undecylenic acid to the half aldehyde of sebacic acid[7] and condensing this with malonic acid in the presence of pyridine. Carbon dioxide was split off as expected[8] and the unsaturated acid was isolated after hydrolysis of the ester group.

During the course of the investigation a large number of pure organic substances was tested (in the presence of the co-factor mixture noted above) for activity in the bean test. With the exception of certain homologs and analogs of decene-dicarboxylic acid, these materials (indoleacetic acid, vitamins B_1, B_2, B_6, and other known plant growth substances as well as numerous organic acids) were wholly without activity. The hydrogenation product, decane-1,10-dicarboxylic acid, possesses an activity approximately half that of decene-1,10-dicarboxylic acid. The presence of the double bond, therefore, while not essential, nevertheless enhances the activity of this molecule. The saturated dibasic acids possessing 7 or fewer C atoms were without significant activity. Suberic and azelaic acids with 8 and 9 C atoms, respectively, possess slight activity and sebacic acid (10 C atoms) is approximately half as active as decene-1,10-dicarboxylic acid. It is of interest that although succinic acid is completely inactive, maleic acid evokes a small but definite response in the bean test. In this case, as in the case of the C_{12} acids, the presence of one double bond increases wound hormone activity. Lauric acid, with 12 C atoms and but one carboxyl group is completely inactive as are the unsaturated monobasic acids linolic and undecylenic. Two carboxyl groups would therefore appear to be essential for wound hormone activity in the bean test.

The physiological activities of decene-dicarboxylic acid and the related higher dicarboxylic acids are not restricted to the evoking of intumescences in bean pods. Synthetic decene-dicarboxylic acid is capable of evoking intense cell division activity in the "potato test" of Haberlandt.[9] The activity of decene-dicarboxylic acid in this test is further enhanced by the co-factor mixture described above in connection with the bean test. It seems probable therefore that traumatic acid is one of the substances responsible for wound periderm formation in the potato.

Synthetic decene-dicarboxylic acid is also capable of partially inhibiting the germination of seeds, particularly those seeds which are borne in fleshy fruits such as tomato, and it seems possible therefore that traumatic acid is in nature partly responsible for the failure of such seeds to germinate while they remain within the fruit. A fuller account of these physiological investigations will be published elsewhere.

(7) C. R. Noller and R. Adams, THIS JOURNAL, 48, 1074 (1926).

(8) W. J. Hickinbottom, "Reactions of Organic Compounds," Longmans, Green and Co., New York, N. Y., p. 147.

(9) G. Haberlandt, *Sitzber. Kgl. preuss. Akad. Wiss.*, 16, 318 (1913).

Experimental

Isolation Procedure.—The preparation of the crystalline active material was carried out as described in a previous paper with the added precaution that all solvent evaporations were carried out below 35°. In this way there was obtained, after repeated recrystallization from alcohol, 56.6 mg. of pure material, m. p. 165–166°; 40 mg. dissolved in 2 cc. of absolute alcohol showed no measurable optical rotation in a 10-cm. tube.

Hydrogenation.—Nine milligrams of the product was hydrogenated by shaking with hydrogen at atmospheric pressure in glacial acetic acid in the presence of platinum oxide. On filtering the catalyst and removing the solvent, there was obtained a crystalline product which, after one recrystallization from alcohol, melted at 127° and was pure decene-1,10-dicarboxylic acid. Mixture with an authentic sample showed no m. p. depression.

Five milligrams of the pure reduction product was converted to the anilide by heating with thionyl chloride, removing the excess reagent *in vacuo* and adding aniline. After heating on the steam-bath for fifteen minutes the product was worked up in the usual manner. After recrystallization from alcohol, it gave a melting point of 171° and showed no melting point depression with a sample prepared from synthetic decane-1,10-dicarboxylic acid.

Anal.[10] Calcd. for $C_{24}H_{32}O_2N_2$: N, 7.38. Found: N, 7.38, 7.28.

Oxidation.—Eighteen milligrams of the pure crystalline material was dissolved in ether and an ether solution containing an excess of diazomethane was added. The crude methyl ester[4] obtained on evaporation of the ether was dissolved in acetone and oxidized by adding an acetone solution of potassium permanganate at room temperature until an excess was present. The solution was then refluxed and permanganate added until no more was taken up. The acetone was removed under reduced pressure from the filtered solution and the residue was dissolved in 4 normal sodium hydroxide. This solution was then heated on the steam-bath for two hours, cooled, acidified and extracted with ether. Upon evaporation of the ether there was obtained 14 mg. of crude acid which, after recrystallizing twice from alcohol, melted at 133° and was found to be identical with sebacic acid by mixed melting point. This product yielded an amide, m. p. 200°, identical with sebacic acid di-amide.

(10) Microanalysis by G. A. Swinehart.

Synthesis of 1-Decene-1,10-dicarboxylic Acid.—Undecylenic acid methyl ester (b. p. 119–120°, 10 mm.) prepared from Eastman Kodak Co. undecylenic acid was ozonized according to the procedure of Noller and Adams[7] in acetic acid solution and the half aldehyde of methyl sebacate (b. p. 124–125° (4 mm.)) obtained in 40% yield. Thirteen grams of this product was mixed with 15 g. of malonic acid and 15 g. of dry pyridine and heated under reflux for four hours. A vigorous evolution of carbon dioxide was observed in the early stages of the reaction. The resulting clear solution was acidified, poured into water and extracted with ether. After removal of the pyridine by extraction with dilute hydrochloric acid, the ether was evaporated and the crude product hydrolyzed directly by heating under reflux with 3 normal sodium hydroxide for two hours. Upon acidification the 1-decene-1,10-dicarboxylic acid precipitated and was recrystallized from alcohol or acetone, m. p. 165–166°. This product showed no depression of melting point when mixed with the naturally occurring material and was identical with the latter in crystalline form and physiological activity.

Anal. Calcd. for $C_{12}H_{20}O_4$: C, 63.05; H, 8.80. Found: C, 62.98; H, 8.85.

The S-benzyl thiuronium salt of traumatic acid was prepared according to the method of Donleavy.[11]

Anal. Calcd. for $C_{28}H_{40}O_4N_4S_2$: C, 59.96; H, 7.79; N, 9.99. Found: C, 59.78; H, 7.49; N, 9.90.

(11) J. J. Donleavy, THIS JOURNAL, **58**, 1004 (1936).

An oxidation of the synthetic product with permanganate in hot water solution gave sebacic acid, identified by melting point (133°) and mixed melting point.

Summary

The crystalline substance isolated from string bean pods and capable of inducing renewed cell division and cell extension activity in the parenchymatous cells of the bean pod mesocarp is shown to be 1-decene-1,10-dicarboxylic acid. Synthetic 1-decene-1,10-dicarboxylic acid was prepared and shown to be identical with the natural product both in physical properties and in physiological activity. It is proposed that the name "traumatic acid" be used in referring to this substance.

Traumatic acid is also shown to be capable of inducing wound periderm formation in washed disks of potato tuber and to function thus as a wound hormone of the potato. Traumatic acid is also capable of partially replacing the juice of the tomato fruit in reversibly inhibiting the germination of tomato seeds.

PASADENA, CALIF. RECEIVED AUGUST 10, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

The System *n*-Butylmagnesium Bromide–Magnesium Bromide–Ethyl Ether

BY W. E. DOERING AND C. R. NOLLER

The system magnesium bromide–ethyl ether has been investigated by Menschutkin[1] who found that the solubility of the dietherate varied from 1.08% at −8° to 5.80% at 22°. At 22.8° the dietherate melted under ether to give two liquid phases. The composition of the upper layer changed from 6.8% dietherate at 30° to 10.2% at 90° while that of the lower layer changed from 69.8% at 30° to 68.6% at 90°.

During the course of another investigation[2] it was found that quantities of magnesium bromide greatly in excess of its solubility in ether could be added to Grignard solutions without the separation of two phases and in connection with studies on the composition and constitution of Grignard reagents it became desirable to determine quantitatively the effect of Grignard reagents on the solubility of magnesium halides. Table I and Fig. 1 summarize our results on the system *n*-butylmagnesium bromide–magnesium bromide–ethyl ether. Since the molecules of both the Grignard reagent and the magnesium bromide are present in all probability as the dietherates at ordinary temperatures when an excess of ether is present, the numerical values have been calculated on this basis. It is realized of course that the system is more complicated than indicated because of the equilibrium between *n*-butylmagnesium bromide, di-*n*-butylmagnesium and magnesium bromide. Since it is not possible at the present time to determine accurately the position of this equilibrium,[3] all of the active Grignard reagent has been calculated as being in the form of *n*-butylmagnesium bromide.

It can be seen that the presence of *n*-butylmagnesium bromide greatly modifies the solubility of magnesium bromide dietherate. Whereas magnesium bromide dietherate and ether form homogeneous solutions at 25° only when the con-

(1) Menschutkin, *Z. anorg. Chem.*, **49**, 34, 207 (1906).

(2) Probert, Master's Thesis, Stanford University, 1933.

(3) Noller and White, THIS JOURNAL, **59**, 1354 (1937).

TABLE I

COMPOSITION IN WEIGHT PERCENTAGE OF UPPER AND LOWER LAYERS FOR VARIOUS MIXTURES OF *n*-BUTYLMAGNESIUM BROMIDE DIETHERATE, MAGNESIUM BROMIDE DIETHERATE AND DIETHYL ETHER AT 25°

Point[a]	Layer	$C_4H_9MgBr \cdot 2C_4H_{10}O$	$MgBr_2 \cdot 2C_4H_{10}O$	Ether (by diff.)
a	Lower[b]	0.2	72.5	27.3
b	Lower	2.3	73.3	24.4
c	Lower	6.1	70.4	23.5
c′	Upper	.8	5.5	93.7
d	Lower	8.4	67.7	23.9
d′	Upper	1.4	5.8	92.8
e	Lower	13.9	60.7	25.4
e′	Upper	2.9	5.9	91.2
f	Lower	16.1	57.9	26.0
f′	Upper	3.6	5.8	90.6
g	Lower	23.1	39.2	37.7
g′	Upper	10.3	10.9	78.8
h	Lower	22.3	31.4	46.3
h′	Upper	14.4	15.3	70.3

[a] Primed and unprimed letters denote compositions in equilibrium with each other. [b] This is an analysis of the liquid magnesium bromide diethereate saturated with ether. A small amount of basic magnesium was present which was calculated as if it were *n*-butylmagnesium bromide but this readily can be ignored.

centration of the diethereate is greater than 73% or less than 5.5%, if the total concentration of *n*-butylmagnesium bromide diethereate is greater than approximately 23% the ratio of the magnesium bromide diethereate to the ether may be any value without the separation into two phases. It is also of interest that when separation into two phases does occur the concentration of the *n*-butylmagnesium bromide diethereate is always greater in the lower layer than in the upper layer. These two results indicate that the mutual solubility of the two diethereates is greater than their solubility in ether.

Experimental

The liquid magnesium bromide diethereate was prepared by the addition of bromine in slight excess over the calculated amount to pure magnesium turnings[4] under absolute ether. The solutions always darkened somewhat as the reaction progressed. The heavy liquid layer was transferred under nitrogen to a graduated reservoir which was fitted so that the liquid could be transferred to the reaction tubes by pressure. A 2 *N* solution of *n*-butylmagnesium bromide was prepared by the usual procedure and stored in the same way as the magnesium bromide solution.

The reaction vessels were cylindrical tubes of approximately 80 cc. capacity and 3 cm. in diameter fitted with

(4) Aluminum Company of America, No. 651 ingot.

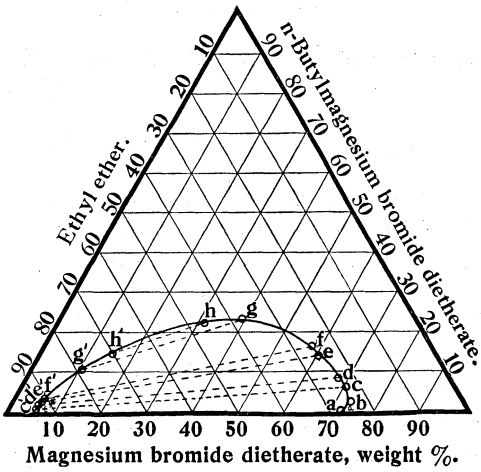


Fig. 1.—System *n*-butylmagnesium bromide–magnesium bromide–ethyl ether.

necks and stoppers made from 10/30 standard taper "No-Lub" ground joints. The stoppers and necks had hooks so that they could be held firmly together by means of rubber bands. The hooks on the necks also permitted the tubes to be suspended above the pan of an analytical balance. Even the "No-Lub" joints permitted the passage of ether by capillarity but this could be prevented by putting a thin line of vaseline around the outermost edge of the stopper. This sealed the air in the ground joint so that the ether did not pass more than a third of the way through the stopper.

Varying amounts of the magnesium bromide diethereate, Grignard solution and absolute ether were added to the flasks under nitrogen and the mixtures shaken for one-half hour at 25 ± 1°. The tubes were then weighed accurately to one centigram and samples of both upper and lower layers rapidly removed by long wash-out pipets, the tubes being reweighed after each withdrawal. The samples were analyzed for Grignard reagent by titration with standard sulfuric acid and for bromine by the Mohr procedure. From these data the weight of *n*-butylmagnesium bromide diethereate and of magnesium bromide diethereate could be calculated and the ether determined by difference. At least duplicate determinations were made of each analysis and the results averaged. The agreement between duplicate determinations was in all cases better than 2%, except in point g′ where the variation was of the order of 5%.

Summary

A study of the system *n*-butylmagnesium bromide–magnesium bromide–ether shows that *n*-butylmagnesium bromide diethereate greatly modifies the solubility of magnesium bromide diethereate in ether and that the mutual solubility of the two diethereates is greater than their solubility in ether.

CAMBRIDGE, MASSACHUSETTS

RECEIVED AUGUST 30, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF MARYLAND]

Ketene in the Friedel–Crafts Reaction. I. Direct Acetylation of Aromatic Hydrocarbons with Ketene[1]

BY JONATHAN W. WILLIAMS[2] AND JAMES M. OSBORN[3]

The use of ketene in the Friedel–Crafts reaction has been the subject of several studies.[4] In each case reported the yield of methyl aryl ketone has been low. In particular, the yield of acetophenone from benzene and ketene has been reported as 20%, or less.

Results of the present investigation show that the yield of acetophenone from ketene and benzene may be increased above previously reported values by the following considerations: (1) use of a considerable excess of ketene; (2) use of ketene which contains minimum amounts of ethylene and carbon monoxide; (3) operation at 0°; (4) addition of aluminum chloride in small portions with rapid stirring; (5) use of at least 1.5 moles of aluminum chloride per mole of hydrocarbon; (6) use of an inert diluent, as carbon disulfide.

The reaction of ketene and naphthalene can be run so that methyl α-naphthyl ketone may be obtained to the practical exclusion of the β-isomer. The use of ketene in the Friedel–Crafts reaction has been extended to the reactions with tetralin and diphenyl.

Experimental Part

Ketene was generated by the pyrolysis of acetone, using a modification[5] of Ott's ketene lamp[4c,6] with an output of 0.45 mole per hour.

Acetophenone.—Ketene was passed into a well-stirred mixture of 100 ml. (1.1 moles) of benzene and 300 ml. of carbon disulfide maintained at 0°. At fifteen-minute intervals approximately 10-g. portions of aluminum chloride were added until 200 g. (1.5 moles) had been used (five hours). Ketene addition and stirring were continued for a total of ten hours (4.5 moles of ketene). The addition complex was decomposed by pouring onto 1 kg. of cracked ice and 30 ml. of concd. hydrochloric acid. After removal of carbon disulfide and benzene from the organic layer, the following fractions were obtained at 22 mm.: (a) 75–105°, 60.1 g.; (b) 105–220°, 30.5 g.: (c) viscous residue, 15 ml. Fraction (a) contained the acetophenone. It was washed with equal volumes of 5% sodium hydroxide solution and water, dried over sodium sulfate, and redistilled. These fractions were obtained at 12 mm.: (a) 75–83°, 1.3 g.; (b) 83–84°, 44.1 g.; (c) residue, 5 ml. Fraction (b) was pure acetophenone; yield, 32.7%.

Methyl α-Naphthyl Ketone.—The procedure was similar to the preparation of acetophenone, using one mole (128 g.) of naphthalene in 600 ml. of carbon disulfide. These fractions were obtained at 7 mm.: (a) 85–90°, 3.0 g.; (b) 145–151°, 70.0 g.; (c) 151–170°, 7.4 g.; (d) viscous residue, 75 ml. Fraction (a) was unchanged naphthalene (2.4%). Fraction (b) was washed with alkali, then with water, dried over sodium sulfate and distilled. A fraction boiling at 150–151° (7 mm.) weighed 59.1 g. This represented a 34.8% yield of methyl α-naphthyl ketone.

The ketone was shown to be the α-isomer by oxidation to α-naphthoic acid[7] and by conversion to the picrate.[4a,8] Fractional crystallization of the picrate showed that the ketone was largely the α-isomer, but that a small amount of the β-isomer was present. For the ketone $n^{27}D$ is 1.6265.

Methyl α-Naphthyl Ketone 2,4-Dinitrophenylhydrazone.—Prepared by the standard procedure and recrystallized from benzene, this substance melted at 259°. *Anal.* Calcd. for $C_{18}H_{14}O_4N_4$: C, 61.71; H, 4.03. Found:[9] C, 61.92, 61.84; H, 4.15, 4.04.

Methyl β-Tetrahydronaphthyl Ketone.—The procedure was similar to that for acetophenone, using one mole (136 ml.) of tetralin in 600 ml. of carbon disulfide. These fractions were obtained at 14 mm.: (a) 85–100°, 25.9 g.; (b) 100–152°, 2.4 g.; (c) 152–172°, 59.5 g.; (d) amorphous residue, 60 ml. Fraction (a) represented 19.6% recovered tetralin. Fraction (c) was redistilled at 14 mm.: (a) 152–159°, 1.7 g.; (b) 159–160°, 42.0 g.: (c) 160–168°, 8.8 g.; (d) viscous residue, 5 ml. Fraction (b) represented a 24.1% yield of methyl β-tetrahydronaphthyl ketone. The ketone was characterized by the preparation of the oxime,[10] m. p. 107°, and tetrahydronaphthalene-β-carboxylic acid,[10] m. p. 150°, obtained by the action of bleaching powder[11] on the ketone. For the ketone $n^{27}D$ is 1.5597.

Methyl β-Tetrahydronaphthyl Ketone 2,4-Dinitrophenylhydrazone.—Recrystallized from benzene, the m. p. was 236°. *Anal.* Calcd. for $C_{18}H_{18}O_4N_4$: N, 15.82. Found:[12] N, 15.97, 16.02.

***p*-Phenylacetophenone.**—Ketene was passed into a solution of one mole (154 g.) of diphenyl in 600 ml. of carbon disulfide at 30° with good stirring for twenty hours (9.0 moles ketene). Two moles (267 g.) of aluminum chloride was added over a ten-hour period. Distillation of the hydrolysis products gave 101.5 g. of material boiling at 140–237° (35 mm.), and which solidified on cooling.

(1) Presented before the Division of Organic Chemistry at the Boston meeting of the American Chemical Society, September, 1939.

(2) Present address: Chemistry Dept., University of North Carolina, Chapel Hill, N. C.

(3) Taken from the M. S. Thesis of James M. Osborn.

(4) (a) Hurd, THIS JOURNAL, **47**, 2777 (1925); (b) Ploeg, *Rec. trav. chim.*, **45**, 342 (1926); (c) Packendorff, Zelinsky and Leder-Packendorff, *Ber.*, **66**, 1069 (1933); (d) Spring and Vickerstaff, *J. Chem. Soc.*, 1873 (1935).

(5) Hurd and Williams, THIS JOURNAL, **58**, 965 (1936).

(6) Ott, Schröter and Packendorff, *J. prakt. Chem.*, **130**, 177 (1931).

(7) Kailan, *Monatsh.*, **28**, 1069 (1907).

(8) Stobbe, *Ann.*, **380**, 95 (1911).

(9) Analysis by E. O. Haenni.

(10) Scharwin, *Ber.*, **35**, 2511 (1902).

(11) Hurd and Thomas, THIS JOURNAL, **55**, 1646 (1933).

(12) Analysis by L. A. Smith.

It was air-dried and redistilled at 20 mm.: (a) 120–150°, 19.4 g.; (b) 150–195°, 11.9 g.; (c) 195–215°, 51.3 g. Fraction (a) contained 10.7 g. of diphenyl, a 7.0% recovery. Fractions (b) and (c) were recrystallized several times from 95% alcohol and yielded 45.9 g. of *p*-phenylacetophenone, m. p. 121°. This represented a 23.4% yield.

Summary

Factors influencing the yield of acetophenone from benzene and ketene have been studied. Conditions have been determined for the preparation of methyl α-naphthyl ketone to the practical exclusion of the β-isomer. The preparations of methyl β-tetrahydronaphthyl ketone and *p*-phenylacetophenone, using ketene, are reported.

COLLEGE PARK, MARYLAND RECEIVED OCTOBER 5, 1939

[CONTRIBUTION FROM THE ORGANIC CHEMISTRY LABORATORIES OF THE UNIVERSITY OF FLORIDA]

alpha,omega-Amino Alcohols. I. N-Phenyl-N'-(ω-hydroxyalkyl)-piperazines from α,ω-Chlorohydrins. Derivatives of Piperazine. XVII

BY GEORGE W. ANDERSON[1] AND C. B. POLLARD

Pyman and Levene[2] have synthesized α,ω-amino alcohols by the reaction of secondary amines with α,ω-chlorohydrins. We have now employed this reaction for the synthesis of a series of N-phenyl-N'-(ω-hydroxyalkyl)-piperazines.

The general procedure followed was to heat 0.2 mole of the chlorohydrin with 0.4 mole of N-phenylpiperazine for five hours on a water-bath. The white solid product was heated with 40 cc. of 5 *M* potassium carbonate, the resulting orange colored oily layer was separated and after it had cooled and solidified, was washed with water and recrystallized from 250 cc. of 60% ethyl alcohol. The white crystals were dried to constant weight in a vacuum over fused potassium hydroxide. Two recrystallizations from ligroin (70–100°) gave a material of constant melting point. The urethans were prepared in hot ligroin solution and were recrystallized from this solvent.

With one exception, the amino alcohols were obtained in a quantitative crude yield. That of N-phenyl-N'-(4-hydroxybutyl)-piperazine was reduced because of the formation of tetramethylene oxide. Neutral equivalents of the amino alcohols and their phenylurethans and analytical data are recorded in Table I.

TABLE I

N-PHENYL-N'-(ω-HYDROXYALKYL)-PIPERAZINES OF THE GENERAL FORMULA $C_6H_5NC_4H_8N(CH_2)_nOH$ AND THEIR PHENYLURETHANS

	Neutral equivalent (methyl orange)					Phenylurethans		
			M. p.,	Anal., % N		M. p.,	Anal., % N	
n	Calcd.	Found	°C. (corr.)	Calcd.	Found	°C. (corr.)	Calcd.	Found
4	234.3	236.0	59.0–60.0	11.96	11.81	91.0–92.0	11.98	11.64
5	248.4	248.3	74.0–75.0	11.28	11.13	100.0–101.5	11.44	11.24
6	262.4	262.7	65.5–67.0	10.68	10.52	91.5–93.0	11.01	10.91
7	276.4	274.9	75.5–76.5	10.14	10.06	96.5–97.5	10.63	10.46
8	290.4	292.1	57.0–58.5	9.65	9.43	99.5–100.5	10.26	10.09
9	304.5	303.1	80.0–80.5	9.20	9.14	94.0–95.0	9.92	9.78
10	318.5	317.1	67.0–68.0	8.80	8.74	95.0–96.0	9.60	9.45

N-Phenyl-N'-(8-hydroxyoctyl)-piperazine readily absorbs water from air to form a monohydrate. The other amino alcohols absorb water less rapidly.

The α,ω-chlorohydrins of four and five carbon atoms were obtained in 35% yield by the method of Kirner and Richter.[3] The higher members were prepared in approximately 65% yield by continuous extraction of the reaction mixtures of the corresponding glycols and hydrochloric acid.[4]

Final purification was effected by fractionation at 10 mm. The boiling points of the α,ω-chlorohydrins showed a regular increase with increasing number of carbon atoms.

Phenyl- or α-naphthylurethans were prepared from the chlorohydrins. New urethans prepared were the α-naphthylurethans of hexamethylene-

(1) This paper is abstracted from a portion of a dissertation submitted by George W. Anderson to the Graduate Council of the University of Florida in partial fulfilment of the requirements for the degree of Doctor of Philosophy, May, 1939.

(2) Pyman and Levene, British Patent 402,159, Nov. 30, 1933, to Boot's Pure Drug Co.

(3) Kirner and Richter, THIS JOURNAL, 51, 2503 (1929).

(4) Bennett and Moses, *J. Chem. Soc.*, 1697 (1931).

α,ω-chlorohydrin, m. p. 49–50°, and of decamethylene-α,ω-chlorohydrin, m. p. 63–64°. The melting point of the phenylurethan of nonamethylene-α,ω-chlorohydrin was 70–70.5°, 3° higher than previously reported.[4]

N-Phenyl-N′-(8-hydroxyoctyl)-piperazine Hydrate.—N-phenyl-N′-(8-hydroxyoctyl)-piperazine of m. p. 57–58.5° and neut. equiv. 292.1 (mol. wt. is 290.4) gave a compound of m. p. 80–82° and neut. equiv. 306.5 (theoretical 308.4 for a monohydrate) upon exposure to air.

Summary

A series of seven new amino alcohols, the N-phenyl-N′-(ω-hydroxyalkyl)-piperazines, with the alkyl group having four through ten carbon atoms, has been synthesized from α,ω-chlorohydrins and N-phenylpiperazine. Their phenylurethans are reported. The formation of the monohydrate of N-phenyl-N′-(8-hydroxyoctyl)-piperazine upon exposure to air has been ascertained.

alpha,omega-Chlorohydrins of four through ten carbon atoms have been made by methods reported in the literature. The phenylurethan of nonamethylene chlorohydrin was found to melt 3° higher than previously reported. The α-naphthylurethans of hexamethylene and decamethylene chlorohydrins are reported for the first time.

GAINESVILLE, FLORIDA RECEIVED JUNE 26, 1939

[CONTRIBUTION FROM THE ORGANIC CHEMISTRY LABORATORIES OF THE UNIVERSITY OF FLORIDA]

alpha,omega-Amino Alcohols. II. Morpholino Alcohols. Derivatives of Morpholine. II

BY GEORGE W. ANDERSON[1] AND C. B. POLLARD

Paden and Adkins[2] in their study of the reaction of amines with glycols at 200–250° in the presence of copper–chromium oxide reported one experiment in which equivalent quantities of phenethylamine and tetramethylene glycol in dioxane solution were heated for half an hour with hydrogen at 200–400 atm. with the production of 35% of 4-(N-phenethylamino)-butanol-1, 19% of 1-phenethylpyrrolidine, and 43% of unchanged amine and glycol.

On the basis of this experiment we have investigated the reaction of morpholine with α,ω-glycols of four through ten carbon atoms and, as was to be expected, have obtained only two products, namely, the morpholino alcohol and the dimorpholinoalkane. Data are shown in Tables I, II and III.

Approximately 0.5 mole of each reactant in 300 cc. of dioxane was heated at 235–270° for six hours at a pressure of 100 atm. After cooling, the dioxane was distilled off at atmospheric pressure and the remainder fractionated in an efficient electrically heated air-jacketed column 2 cm. in bore, 70 cm. long, packed with 6 × 6 mm. Raschig rings, and having a total condensation, variable take-off head. In several cases, a similar column, 1.8 cm. in bore and 30 cm. long, packed with 5 × 5 mm. Raschig rings, and having a total condensation, variable take-off head was used.

The morpholino alcohols, with the exception of 7-morpholinoheptanol-1, were also prepared from morpholine and the corresponding chlorohydrins. Almost quantitative yields were obtained by this method. Physical and analytical data for the seven new morpholino alcohols are recorded in Table II.

The aryl urethans of the morpholino alcohols were prepared by mixing hot solutions of the aryl isocyanate and the alcohol and heating the mix-

TABLE I

MORPHOLINO ALCOHOLS BY ALKYLATION[a]

Glycol	Moles used	Moles of morpholine	Yields[b] of pure compd., % Amino alcohol	Diamine	Cu–Cr–O cat. used
Tetramethylene	0.75	0.94	36	22	22
Pentamethylene	.80	1.0	31	28	24
Hexamethylene	.60	0.60	21	18	20
Heptamethylene	.33	.42	19	28	10
Octamethylene	.50	.75	26	41	15
Nonamethylene	.34	.43	38	28	11
Decamethylene	.40	.40	21	13	9

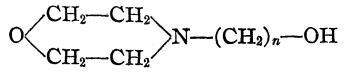
[a] Between 125 and 300 cc. of dioxane was used in each case as solvent. The reaction was carried out under about 100 atm. of hydrogen at 235–270° for six hours. [b] Yields are based on the glycol used. Some of the glycol did not react in each case, but was not recovered pure, so yields were not adjusted for it.

(1) This paper is abstracted from a portion of a dissertation submitted by George W. Anderson to the Graduate Council of the University of Florida in partial fulfilment of the requirements for the degree of Doctor of Philosophy, May, 1939.

(2) Paden and Adkins, THIS JOURNAL, 58, 2487 (1936).

TABLE II

PHYSICAL AND ANALYTICAL DATA FOR THE MORPHOLINO ALCOHOL SERIES

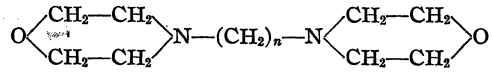
General Formula: 

n	Neut. equiv.[a] Calcd.	Found	B. p., °C. at 5 mm. pressure	Refrac. index	d^{25}_4	M.R. Calcd.	Found	Anal., % N Calcd.	Found
4	159.2	159.3	116.5–7.0	$n^{24}D$ 1.4745	1.018	44.05	43.93	8.81	8.92
5	173.2	173.2	133.0–3.5	$n^{24}D$ 1.4755	1.005	48.67	48.50	8.09	8.09
6	187.3	184.9	146.0–7.0	$n^{25}D$ 1.4750	0.9884	53.29	53.30	7.49	7.34
7	201.3	203.6	155.5–8.0	$n^{25}D$ 1.4747	.9783	57.91	57.80	6.96	6.93
8	215.3	214.7	164.0–4.2	$n^{27}D$ 1.4735	.9675	62.52	62.55	6.51	6.37
9	229.3	227.6	173.0–3.5	M. p. 31°	....	...	...	6.11	5.86
10	243.3	243.5	164.0–5.0[b]	M. p. 39.5–40.5°	....	...	...	5.76	5.66

[a] With methyl orange indicator, using buffer of pH 4.0 for color standard. [b] At 2 mm. pressure.

TABLE III

PHYSICAL AND ANALYTICAL DATA FOR THE DIMORPHOLINOALKANE SERIES

General Formula: 

n	Neut. equiv.[a] Calcd.	Found	B. p., °C. at 5 mm.	Refrac. index or m. p., °C.	d^{25}_4	M.R. Calcd.	Found	Anal., % N Calcd.	Found
4	114.1	114.7	147.5–8.5	51.5–52.5	....	...	...	12.28	12.00
5	121.1	121.3	161.0–2.0	$n^{25}D$ 1.4804	0.9980	69.10	69.29	11.56	11.32
6	128.1	129.3	169.5–171	35.5–38.5	....	...	...	10.93	10.76
7	135.2	136.3	183.0–4.0	$n^{27}D$ 1.4796	0.9789	78.34	78.46	10.37	10.18
8	141.2	141.6	191.5–3.5	46.5–47.5;[b] 48	....	...	...	9.85	9.72
9	149.2	146.7	203.5–4.0	$n^{25}D$ 1.4789	0.9639	87.38	87.42	9.39	9.11
10	156.2	152.5	187.0–9.0[d]	48.0–49.0;[c] 50.5–51.5	....	...	...	8.97	8.87

[a] With methyl orange indicator, using buffer of pH 4.0 for color standard. [b,c] Double melting points. Not complete resolidification after first melting, but distinct crystal formation. [d] At 2 mm. pressure.

ture for half an hour. The urethans separated on cooling and were recrystallized from ligroin until successive crystallizations did not raise the m. p. Physical and analytical data for the urethans are summarized in Table IV.

TABLE IV

ARYL URETHANS OF MORPHOLINO ALCOHOLS

GENERAL FORMULA: $O(CH_2CH_2)_2N$-$(CH_2)_n$-O-CONHR, WHERE R IS EITHER PHENYL OR α-NAPHTHYL

n	R	M. p., °C. (corr.)	Anal., % N Calcd.	Found
4	Phenyl	86.0–87.0	10.07	9.80
5	Phenyl	55.5–57.0	9.58	9.32
6	α-Naphthyl	71.0–72.0	7.86	7.53
7	Phenyl	71.0–72.0	8.74	8.56
8	α-Naphthyl	73.0–74.0	7.29	6.96
9	α-Naphthyl	54.0–56.0	7.03	6.83
10	α-Naphthyl	66.5–67.5	6.79	6.75

Summary

1. A series of seven morpholino alcohols of the type R-$(CH_2)_n$-OH, where R is the morpholine group and n is 4 through 10, has been synthesized by the catalyzed reaction of α,ω-glycols and morpholine, and also by the reaction of chlorohydrins and morpholine except in the case of 7-morpholinoheptanol-1. Their phenyl- or α-naphthylurethans have been made.

2. A series of seven dimorpholinoalkanes of the type R-$(CH_2)_n$-R, where R is the morpholine group and n is 4 through 10, has been obtained as a by-product in the catalyzed reaction of morpholine and α,ω-glycols. Physical and analytical data are reported.

GAINESVILLE, FLORIDA RECEIVED JULY 31, 1939

[CONTRIBUTION FROM THE INTERNATIONAL LEPROSY CENTER, RIO DE JANEIRO, BRASIL]

Analysis of Chaulmoogra Oils. IV. *Hydnocarpus anthelmintica* Oil. V. *Taraktogenos kurzii* (Chaulmoogra) Oil

BY HOWARD IRVING COLE AND HUMBERTO T. CARDOSO

IV. *Hydnocarpus Anthelmintica* Oil

The oil expressed from the seeds of *Hydnocarpus anthelmintica* is extensively used in the treatment of leprosy, ranking next to *H. wightiana* oil in therapeutic importance. *H. anthelmintica* occurs abundantly in Siam, Cambodia, Cochin China, and Laos. It also has been reported from Burma. The tree grows to a height of 20 to 25 meters and is generally found in valleys from sea level to 1300 meters altitude. It has been successfully cultivated in Hawaii and the Belgian Congo. The ripe fruits are more or less globular in shape and vary in size from 8 to 15 centimeters in diameter. The seeds are of approximately the same shape and size as those of *H. wightiana* (1 to 2 centimeters long) but are readily distinguished from the latter because of their smoother and thicker shell. The oil is used by the natives of Siam for cutaneous affections. The seeds form an article of export to China where they are known as Ta-fung-chi or Ta-feng-tzu.

As early as 1905 Power and Barrowcliff[1] attempted to analyze *H. anthelmintica* oil. They reported that the total fatty acids of this oil contained chaulmoogric, hydnocarpic, oleic and palmitic acids. Although several qualitative analyses have been made since, no one has succeeded in making a quantitative analysis due to the difficulty in separating the constituents. We have succeeded in analyzing *H. anthelmintica* oil by the method for chaulmoogra oils given in the first article of this series.[2] The constituents and percentage composition are given in Table I. Besides the acids previously reported as present, our analysis shows that gorlic acid and a small percentage of a lower homolog of hydnocarpic acid are also present.

TABLE I

PERCENTAGE COMPOSITION OF THE FATTY ACIDS OF *H. anthelmintica* AND *T. kurzii* OILS (FROM TABLES II AND III)

Acids	*H. anthelmintica*, %	*T. kurzii*, %
Hydnocarpic	67.8	34.9
Chaulmoogric	8.7	22.5
Gorlic	1.4	22.6
Oleic	12.3	14.6
Palmitic	7.5	4.0
Lower homologs of hydnocarpic acid	0.1	0.4
Loss	2.2	1.0

(1) Power and Barrowcliff, *J. Chem. Soc.*, **87**, 884, 896 (1905).
(2) Cole and Cardoso, THIS JOURNAL, **60**, 614 (1938).

Experimental

The sample of *H. anthelmintica* oil was obtained from a 300-liter drum imported several years ago from Siam by the Departamento de Prophylaxia da Lepra da São Paulo, who generously donated the sample for our analysis. Although the oil was more than five years old, its characteristics indicate that very little decomposition had taken place. The characteristics determined at the time of the analysis were as follows: specific gravity 25/25, 0.952; F. F. A. (as % oleic) 2.9; saponification no., 203.3; iodine no. (Hanus), 89.2; specific optical rotation, $[\alpha]^{25}D$ +49.70; refractive index $[n]^{25}D$ 1.4772; unsaponifiable matter, 0.50%.

Method of Analysis.—Since the medicinal properties of chaulmoogra oils depend upon the percentage of optically active fatty acids, the analysis is reported in per cent. of the various fatty acids present. The sample of oil was saponified and the fatty acids liberated in the usual manner. The solid acids were separated from the liquid acids by crystallization from 80% ethyl alcohol. The two fractions were changed to ethyl esters and then fractionally distilled at 10 mm. in a Podbielniak Model B high temperature fractionating apparatus. The details of the separation and distillation were given in the first article of this series,[2] the only change being that the two final crystallizations for the separation of the liquid acids were made with 80% acetone to prevent the formation of ethyl esters.

Qualitative Analysis

In our analysis of the total fatty acids of *H. anthelmintica* oil we found chaulmoogric, hydnocarpic, gorlic, oleic and palmitic acids besides a very small percentage of a lower homolog of hydnocarpic acid. The acids were identified as follows.

Chaulmoogric Acid.—Pure chaulmoogric acid was obtained readily from the acids from fraction 3, Table III, by crystallization to constant melting point from 80% alcohol. It gave the correct optical rotation, iodine number, neutralization equivalent and melting point for pure chaulmoogric acid.[3]

Hydnocarpic Acid.—This acid was isolated in the pure state from fraction 2, Table III, by repeated crystallization of the acids from 80% alcohol. It gave all the correct constants for pure hydnocarpic acid.[3]

Gorlic Acid.—Ethyl gorlate was isolated by several fractional distillations of those fractions rich in ethyl gorlate such as fraction 3, Table II, by the method previously de-

(3) Cole and Cardoso, THIS JOURNAL, **59**, 963 (1937).

TABLE II

FRACTIONAL DISTILLATION OF ETHYL ESTERS FROM LIQUID ACIDS OF *H. wightiana* AND *T. kurzii* OILS

Fraction	B. p., °C. (10 mm.)	Cc.	Sp. rot.	Iodine no.	% in liquid fraction: Hydnocarpate	Chaulmoograte	Gorlate	Oleate	Palmitate	Lower homologs
H. anthelmintica (17.9% of total fatty acids)										
1	153–187	1.0	36.89	...	...	...	...	...	0.69	0.61
2	187–201	36.0	36.56	82.01	27.60	...	...	16.50	2.66	..
3	201–207	25.0	36.49	94.11	16.24	...	3.20	13.00	..	..
4	207–209	8.0	35.49	98.98	4.47	...	1.66	4.26	..	..
5	209–215	4.5	38.34	104.20	...	2.52	1.53	1.81	..	..
Loss		2.5								
% in liquid fraction					48.31	2.52	6.39	35.57	3.35	0.61
% in total fatty acids					8.64	0.45	1.15	6.37	0.60	0.11
T. kurzii (41.7% of total fatty acids)										
1	161–185	2	30.59	...	...	...	...	...	1.55	0.98
2	185–201	28	34.37	94.78	14.17	...	6.09	12.97	2.20	..
3	201–207	8	40.23	112.8	3.67	...	3.24	3.22	..	..
4	207–217	39.7	48.78	138.3	...	11.87	32.20	6.24	..	..
Residue		1.3								
% in liquid fraction					17.84	11.87	41.53	22.43	3.75	0.98
% in total fatty acids					7.45	4.95	17.3	9.35	1.56	0.41

TABLE III

FRACTIONAL DISTILLATION OF ETHYL ESTERS FROM SOLID ACIDS OF *H. anthelmintica* AND *T. kurzii* OILS

Fraction	B. p., °C. (10 mm.)	Cc.	Sp. rot.	Iodine no.	% in solid fraction: Hydnocarpate	Chaulmoograte	Gorlate	Oleate	Palmitate
H. anthelmintica Oil (82.1% of total fatty acids)									
1	191–201	69	51.10	80.05	57.0	...	..	4.8	7.2
2	201–211	18	51.79	84.08	15.1	...	..	1.7	1.2
3	211–215	11	51.93	84.35	...	10.0	0.31	0.69	..
Loss		2							
% in solid fraction					72.1	10.0	0.31	7.19	8.4
% in total fatty acids					59.2	8.21	0.25	5.90	6.9
T. kurzii Oil (58.3% of total fatty acids)									
1	191–202	41.5	47.67	82.10	32.0	...	..	5.27	4.23
2	202–209	19.3	51.74	94.30	14.94	...	1.35	3.01	..
3	209–217	38.6	54.38	99.05	...	30.11	7.72	0.77	..
Loss		0.6							
% in solid fraction					46.94	30.11	9.07	9.05	4.23
% in total fatty acids					27.37	17.55	5.28	5.28	2.47

scribed.[4] The correct constants were obtained for ethyl gorlate and gorlic acid.[4]

Oleic Acid.—Oleic acid was not obtained pure but its presence was indicated in the liquid fraction by the distillation curve of the ethyl esters and by the correct iodine numbers for mixtures containing ethyl oleate in fractions 2, 3, 4 and 5 of Table II. The elaidic acid test cannot be used in the presence of gorlic acid as the latter gives a similar reaction. Hydrogenation tests were also unsatisfactory in the presence of chaulmoogric or hydnocarpic acid.

Palmitic Acid.—This acid was separated by cooling fractions of ethyl esters rich in palmitate, the latter solidifying at a higher temperature than hydnocarpate. The solid ester was separated and crystallized from ethyl alcohol to constant melting point (24°). Upon changing it to the acid and crystallizing from alcohol, the correct melting point and neutralization equivalent for palmitic acid were obtained.

Lower Homologs.—The presence of at least one homolog of hydnocarpic acid was indicated by the optical rotation and boiling point of fraction 1, Table II. The sample was too small to attempt to identify this compound.

Quantitative Analysis

The total fatty acids of *H. anthelmintica* oil when separated into liquid and solid acids by the method described by us consisted of 17.9% liquid acids and 82.1% solid acids. Although the separation is by no means complete, the breaks in the distillation curves of the ethyl esters made from these two fractions are much more distinct than when the whole esters are used. Complete separation is not necessary as the amounts of the various constituents can be computed by taking advantage of the boiling points, optical rotations and iodine numbers or absence of one or both of the two latter constants as described in Part I of

(4) Cole and Cardoso, THIS JOURNAL, **60**, 612 (1938).

this series of articles. The results of these computations are given in Tables II and III and these are summarized in Table I. Fraction 1, Table II was computed on the assumption that it was a mixture of alepric acid[5] and a saturated acid.

V. *Taraktogenos kurzii* (Chaulmoogra) Oil

Chaulmoogra is the native name for *Taraktogenos kurzii* oil which has been used for centuries in Burma and India in the treatment of leprosy. In recent years, however, the word "chaulmoogra" has been used generically to indicate any oil containing chaulmoogric acid which might be used in the treatment of leprosy, such as *H. wightiana* or *C. brasiliensis* oil. *Taraktogenos kurzii* is a tree widely distributed in Burma. It is also found in Siam, Eastern Bengal and Assam. *T. kurzii*, called by the Burmese, kalaw, grows to a height of 15 to 20 meters in dense forests. The fruits are globular, varying in size from 8 to 15 cm. in diameter. The seeds are larger than those from *H. wightiana* with a smoother and thicker shell. Bears are very fond of the white flesh of the fruit (in which the seeds are imbedded) and large numbers of them are said to roam the forests in search of the kalaw fruits. Collecting the seeds is very dangerous on account of tigers, bears and other wild animals. The fruit ripens in June or July, falls in the rainy season and is usually no longer fresh when gathered. For this reason and because of the long time necessary for transportation to a press for expression of the oil the true chaulmoogra oil of commerce is almost always of poor quality with a very high free fatty acid content. It is often adulterated and other hydnocarpus oils are frequently sold as chaulmoogra oil. Because of these disadvantages its use in leprosy treatment has been largely superseded by authentic *H. wightiana* and *H. anthelmintica* oils, which are cheaper and of better quality. Plantations would eliminate these disadvantages. In fact the oil for this analysis was obtained from a plantation at Vicosa, Minas Geraes, where Dr. Rolfs has succeeded in acclimatizing *T. kurzii* to Brazil. It flourishes there, producing heavy crops of fruits.

The first analysis of chaulmoogra oil was made by Power and Gornall[6] in 1904. They reported that the oil contained both chaulmoogric and hydnocarpic as well as a small amount of palmitic and linolic acids. Other investigators have added very little to our knowledge of chaulmoogra oil. No quantitative analysis has ever been made.

(5) Cole and Cardoso, THIS JOURNAL, **61**, 2349 (1939).

(6) Power and Gornall, *J. Chem. Soc.*, **85**, pt. II, 838, 851 (1904).

We have made an analysis of this oil by the method described in the first article of this series.[2] The constituents and percentage composition of chaulmoogra oil are given in Table I. Besides the acids mentioned by Power and Gornall, we have found that the oil also contains gorlic and oleic acids and a small amount of a lower homolog of hydnocarpic acid. No linolic or linolenic acid was found. The high iodine numbers of certain fractions which led previous investigators to suspect the presence of linolic or linolenic acid are due to the presence of gorlic acid, which has two double bonds. If gorlic acid should prove to be of greater value in leprosy treatment than the other optically active fatty acids, then the true chaulmoogra oil would be preferable to the other oils we have analyzed since it contains the highest percentage of this acid (see Table V).

Previous statements that the oil does not keep well are not true. The bad reputation of the oil is due to the fact that the oil is practically never expressed from fresh dried seeds as mentioned above. Oil from old seeds is always irritating. *T. kurzii* oil which we cold-pressed from fresh, dried seeds has changed very little after standing for three years and is still non-irritating upon injection. We have found this generally true of all the chaulmoogra oils we have analyzed.

Experimental

The sample of oil was obtained by cold pressing of fresh, dried seeds kindly donated by the Escola Superior de Agricultura at Vicosa, Minas Geraes. The sample of oil was three years old before it was analyzed but the characteristics of the oil had changed only very slightly in that time. The characteristics of the oil made at the time of analysis were as follows: specific gravity 25/25, 0.952; F.F.A. (as % oleic), 1.3; saponification no., 200.6; iodine no. (Hanus), 101.5; specific optical rotation $[\alpha]^{25}D$ +49.80; refractive index $[n]^{25}D$ 1.4790; unsaponifiable matter 0.29%.

The analysis was made on the total fatty acid content of the oil since the medicinal properties of the oil depend upon the percentage of the optically active acids present and was made in the same manner as that of *H. anthelmintica* oil.

Qualitative Analysis.—The fatty acids of *T. kurzii* oil were found to contain chaulmoogric, hydnocarpic, gorlic, oleic and palmitic acids with a very small percentage of a lower homolog of hydnocarpic acid. The acids were identified in the same manner as those from *H. anthelmintica* oil.

Quantitative Analysis.—The total fatty acids of *T. kurzii* oil when separated into liquid and solid fatty acids by the method described by us consisted of 41.7% liquid acids and 58.3% solid acids. After distillation of the ethyl esters made from these two fractions, the amounts of the various constituents present were computed as previously

TABLE IV

CHARACTERISTICS OF CHAULMOOGRA OILS

	Hydnocarpus wightiana	*Hydnocarpus anthelmintica*	*Taraktogenos kurzii*	*Carpotroche brasiliensis*	*Oncoba echinata*
Specific gravity 25/25	0.955	0.952	0.952	0.955	...
Free fatty acid (as % oleic)	2.7	2.9	1.3	3.6	4.3
Saponification number	201.0	203.3	200.6	201.8	193.7
Iodine number (Hanus)	98.4	89.2	101.5	108.0	96.4
Spec. optical rotation $[\alpha]^{25}D$	55.0	49.7	49.8	53.8	51.7
Refractive index $[n]^{25}D$	1.4799	1.4772	1.4790	1.4790	...
Unsaponifiable matter, %	0.25	0.50	0.29	....	...

TABLE V

PERCENTAGE COMPOSITION OF TOTAL FATTY ACIDS OF CHAULMOOGRA OILS

Acids	*H. wightiana*	*H. anthelmintica*	*T. kurzii*	*C. Brasiliensis*	*O. echinata*
Hydnocarpic	48.7	67.8	34.9	45.0	None
Chaulmoogric	27.0	8.7	22.5	24.4	74.9
Gorlic	12.2	1.4	22.6	15.4	14.7
Lower homologs of hydnocarpic	3.4	0.1	0.4	?	?
Oleic	6.5	12.3	14.6	6.3	2.2
Palmitic	1.8	7.5	4.0	6.6	7.8
Loss	0.4	2.2	1.0	2.3	0.4

described. The results of these computations are given in Tables II and III and these are summarized in Table I. Fraction 1, Table II, was computed on the assumption that only alepric and palmitic acids were present as the sample was too small to be separated further.

Summary

The qualitative and quantitative analyses of *Hydnocarpus anthelmintica* and *Taraktogenos kurzii* (chaulmoogra) oils have been made by the methods described in the first article of this series. They are the first quantitative analyses that have been made of these two important medicinal oils.

The percentage compositions of these oils are given in Table I.

A summary of the characteristics and percentage compositions of the five oils of the chaulmoogra group so far analyzed in this series of articles is given in Tables IV and V.

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[CONTRIBUTION FROM THE G & A LABORATORIES, INC.]

Studies in the omega-Camphor Series. I. On the Synthesis of 2-Keto-apocamphane-1-acetic Acid

BY TORSTEN HASSELSTROM AND BURT L. HAMPTON

Some time ago one of the authors of this paper described the reaction involved in the formation of the Semmler and Bartelt lactone from teresantalic acid and the synthesis of *cis*-2-keto-apocamphane-7-π-carboxylic acid,[1] the corresponding *trans* acid being previously synthesized.[2] In view of the fact that camphor itself does not exert the cardiostimulating action, but certain π-camphor derivatives,[3] derived therefrom, do, it was of interest to synthesize some corresponding ω-2-substituted camphane derivatives.

The present paper deals with the synthesis of the novel 2-keto-apocamphane-1-acetic acid, some derivatives of it and with the reactions involved in its preparation.

As starting material we used the ω-benzoylborneol (II) of Lipp, *et al.*,[4] who obtained this compound from camphene (I) by combining it with benzoyl chloride by means of the Friedel–Crafts synthesis, whereby the asymmetric camphene nucleus is converted into the symmetric camphor skeleton by the Meerwein–Wagner rearrangement.

On subjecting the oxime of ω-benzoylborneol (III) to the Beckmann rearrangement, we obtained a mixture of 2-hydroxy-apocamphane-1-acetanilide (IV) and the anilide of camphenecarboxylic acid (VI) together with some tarry material of unknown composition and small amounts of benzonitrile which was identified as benzoic acid by hydrolysis.

The 2-hydroxy-apocamphane-1-acetanilide was hydrolyzed with alcoholic potassium hydroxide solution. The resulting product was the lactone of 2-hydroxy-apocamphane-1-acetic acid (XIV)

(1) (a) Hasselstrom, THIS JOURNAL, **53**, 1099 (1931); (b) Asahina and Ishidate, *Ber.*, **66**, 1675 (1933).

(2) (a) Wedekind, *Ber.*, **55**, 1557 (1923); (b) Hasselstrom, *Ann. Acad. Firn.*, **30**, 12 (1929).

(3) Tamura, *Imp. Acad. Japan*, **11**, 4 (1935).

(4) Lipp, Küppers and Holl, *Ber.*, **60**, 1575 (1927).

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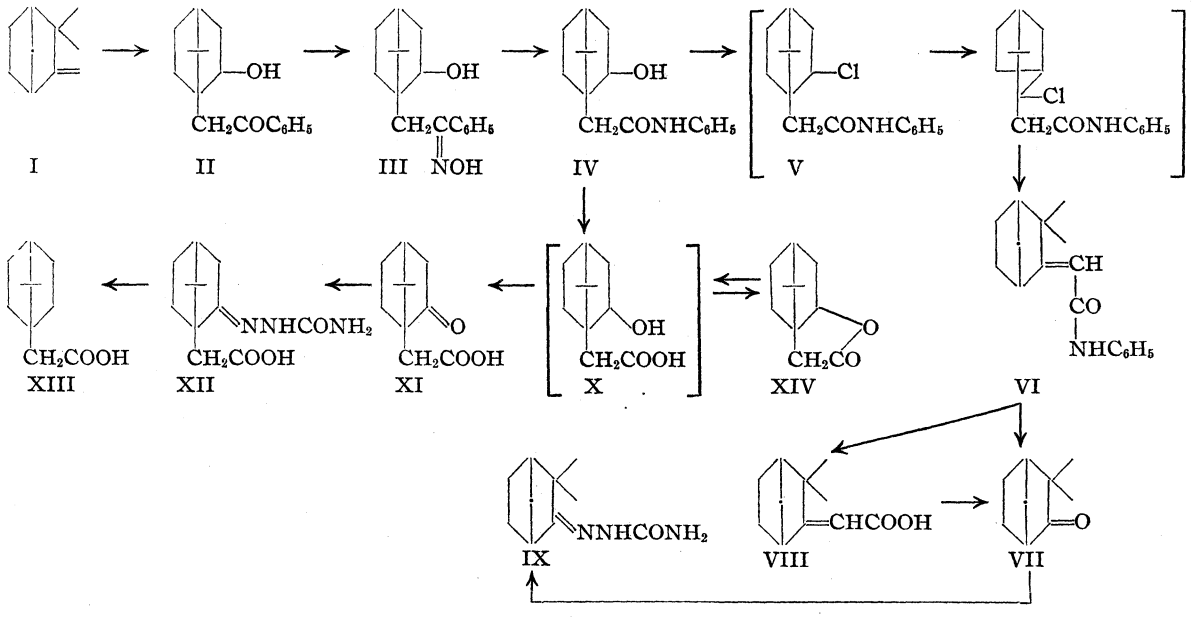

together with aniline which for identification was converted into benzanilide. Attempts to isolate the intermediate hydroxy acid (X) in a pure state failed on account of the ease by which lactone formation takes place. On oxidation with alkaline potassium permanganate solution the potassium salt of 2-hydroxy-apocamphane-1-acetic acid obtained from the lactone by hydrolysis, yielded 2-keto-apocamphene-1-acetic acid (XI). This acid was identified through its semicarbazone (XII), which when subjected to the Wolff–Kishner reaction produced the apocamphane-1-acetic acid (XIII). This series of reactions shows the stability of the hydroxy group of the 2-hydroxy-apocamphane-1-acetanilide in contrast to the corresponding group in ω-benzoylborneol, which on heating is transformed into a furan derivative;[4] this also establishes the evidence that the 2-hydroxy-apocamphane-1-acetanilide and the lactone derived therefrom have the symmetric camphor skeleton.

The camphene-carboxyanilide (VI) obtained as a by-product in the Beckmann rearrangement of the oxime of ω-benzoylborneol is a secondary product apparently formed by way of the Meerwein-Wagner retropinacoline rearrangement from the intermediate 2-chloro-apocamphane-1-acetanilide (V). We observed that on treating 2-hydroxy-apocamphane-1-acetanilide with phosphorus pentachloride in ether solution, the resulting product is camphene-carboxyanilide (VI). On hydrolysis with alcoholic potassium hydroxide solution, this compound yielded camphene-carboxylic acid (VIII) and aniline identified as benzanilide. Since our product showed a higher melting point than the acid recorded by Langlois[5] obtained from ω-bromocamphene by means of the Grignard reaction, for identification it was oxidized with potassium permanganate to camphenilone (VII) whereby oxalic acid was obtained as a by-product. The semicarbazone (IX), prepared subsequently, did not lower the melting point in the mixed melting point test with an authentic sample of camphenilone semicarbazone.

The asymmetric structure of camphene-carboxyanilide was further established by the fact that on direct oxidation with potassium permanganate, it yielded camphenilone which was identified as the semicarbazone, (IX).

Acknowledgment.—Thanks are due to Mr. Ted Calmes of the University of Florida, Gainesville, Florida, for carrying out the Wolff–Kishner reaction.

Experimental

Starting Material.—The camphene was a technical product obtained from E. I. du Pont de Nemours and Company, Wilmington, Del. This material was used in the preparation of ω-benzoylborneol and subsequently for the oxime of this product according to directions by Lipp *et al.*[4]

The Beckmann Rearrangement of the Oxime of ω-Benzoylborneol.—Thirty-five g. (0.12 mole) of the oxime

(5) Langlois, *Ann. chim.*, [IX] **12**, 193, 363 (1919).

(ω-benzoylborneol: m. p. 86–87° (corr.), m. p. 85–86°, Lipp, *et al.;* oxime: m. p. 160–161° (corr.); 159–160° Lipp, *et al.*) was dissolved in 300 cc. of anhydrous ether and 77 g. (0.37 mole) of phosphorus pentachloride was slowly added over a period of one hour to the cooled solution. The temperature of the solution was kept between 20–30° throughout the course of the reaction. After terminating the reaction, the mixture was washed with cold water until the washings were no longer acid to litmus. The ether solution was separated from the water and the ether was removed. The residue was subjected to steam distillation and the distillate extracted with ether. After removal of the ether, 0.5 g. of benzonitrile was isolated and identified by hydrolyzing it to benzoic acid. It was refluxed for three hours with 10 cc. of 20% potassium hydroxide solution. During the reaction some evolution of ammonia took place. After evaporating the alcohol, the solution was acidified with dilute hydrochloric acid and the solid precipitate recrystallized from hexane, m. p. 122.5–123.5° (corr.); it did not lower the melting point when mixed with an authentic sample of benzoic acid.

The residue from the steam distillation was dissolved in a minimum amount of ethanol. After standing in an ice box overnight, a white crystalline precipitate consisting of 2-hydroxy-apocamphane-1-acetanilide was removed by filtration. After two recrystallizations from ethanol, the white rectangular needles melted constantly at 176.5–177.5° (corr.), yield 10 g. (28.2%).

Anal. Calcd. for $C_{17}H_{23}O_2N$: C, 74.9; H, 8.51. Found: C, 74.59; H, 8.72.[6]

The alcoholic mother liquors from the above reaction were evaporated on a steam-bath, leaving 17 g. of an oily residue which was refluxed for three hours with 300 cc. of a 10% alcoholic potassium hydroxide solution. After cooling, the solution was poured into 1200 cc. of ice water and the mixture extracted three times with ether. The ether solution was dried with sodium sulfate and after evaporating the ether, the brownish residue was dissolved in hexane. On standing in the ice box for four hours, a brownish crystalline precipitate was obtained which, after decolorizing with norite, was recrystallized from hexane. After two recrystallizations from hexane and one from dilute ethanol, the solid compound, camphene-carboxyanilide, melted constantly at 154.5–155.5° (corr.); fine white needles; yield 3.3 g. (10.1%).

Anal. Calcd. for $C_{17}H_{21}ON$: C, 80.00; H, 8.28. Found: C, 80.20; H, 8.34.

The hexane filtrates were evaporated, leaving 4.5 g. of a reddish viscous oil which was not identified at this time.

The aqueous alkaline solution was evaporated to a small volume on a hot-plate, carbon dioxide being passed through the solution to prevent oxidation. After filtering, the solution was acidified with dilute hydrochloric acid and extracted with ether. After drying the ether solution with anhydrous sodium sulfate and evaporating the ether, 1.2 g. of a reddish oil was obtained. On standing for about two weeks, it slowly deposited a crystalline solid which after recrystallization from hexane melted constantly at 201.5–202.5° (corr.). It was identified as the lactone of the 2-hydroxy-apocamphane-1-acetic acid since it did not lower the melting point in the mixed melting point test with an authentic sample.

Lactone of 2-Hydroxy-apocamphane-1-acetic Acid.—Four and five-tenths grams of 2-hydroxy-apocamphane-1-acetanilide was refluxed for six hours with 160 cc. of 20% alcoholic potassium hydroxide and, after cooling, poured into 800 cc. of ice water. The solution was then extracted five times with ether. The aqueous layer was evaporated to about 100 cc., carbon dioxide being passed through to prevent oxidation, filtered and, after cooling, acidified with dilute hydrochloric acid. The mixture was now extracted three times with ether and the ether solution dried with anhydrous sodium sulfate. After evaporating the ether, there was obtained a reddish oil which slowly deposited crystals on standing. The semi-solid mass was covered with acetyl chloride and the mixture left standing at room temperature for about fifteen minutes, then the excess of acetyl chloride removed *in vacuo*. The remaining solid was recrystallized from hexane, melting constantly at 201.5–202.5° (corr.); yield, 1.77 g. (60%).

Anal. Calcd. for $C_{11}H_{16}O_2$: C, 72.90; H, 9.45. Found: C, 73.20; H, 9.32.

The ether solution from the extraction of the original alkaline liquors was dried over anhydrous sodium sulfate and distilled, leaving minute quantities of a red oil consisting of aniline since, when treated with benzoyl chloride, it yielded benzanilide melting at 162.5–163.5° (corr.) and did not lower the melting point when mixed with an authentic sample.

2-Keto-apocamphane-1-acetic Acid.—One and seven-tenths grams of the above lactone was dissolved in 34 cc. of a 2% potassium hydroxide solution containing 1.27 g. of potassium permanganate. On refluxing the solution for about fifteen minutes, the permanganate color had disappeared and the mixture was filtered from the precipitated manganese dioxide, evaporated to a small volume on the steam-bath and after cooling to room temperature, acidified with dilute hydrochloric acid and extracted with ether three times. The ether solution was dried with anhydrous sodium sulfate and evaporated, leaving a straw colored oil which was dissolved in a small quantity of water. The precipitated solid melted constantly after three crystallizations from water at 92–93° (corr.), yield 0.6 g. (84.4%).

Anal. Calcd. for $C_{11}H_{16}O_3$: C, 67.33; H, 8.22; neut. equiv., 196.2. Found: C, 67.29; H, 8.20; neut. equiv., 197.1.

Semicarbazone of 2-Keto-apocamphane-1-acetic Acid.—From 0.04 g. of the keto acid, the semicarbazone was prepared in the usual manner, giving an almost quantitative yield. The semicarbazone was recrystallized from ethanol, melting constantly at 199–200° (corr.).

Anal. Calcd. for $C_{12}H_{19}O_4N_3$: C, 56.88; H, 7.56. Found: C, 56.63; H, 7.47.

Apocamphane-1-acetic Acid.—Five-tenths gram of the semicarbazone of 2-keto-apocamphane-1-acetic acid was added to a bomb tube containing sodium ethylate prepared from 0.6 g. of sodium dissolved in 3 cc. of absolute alcohol. After closing the tube, the mixture was heated at 170–180° for fifteen hours. After cooling, the mixture was diluted

(6) All analyses for this paper were done by Mr. S. Gottlieb, Columbia University, New York, N. Y.

with water and the crude acid precipitated with dilute hydrochloric acid; yield 0.3 g. (83.2%). It was dissolved in dilute 20% ethanol, decolorized with norite and recrystallized from the same solvent. After three recrystallizations, it melted constantly at 77–78° (corr.).

Anal. Calcd. for $C_{11}H_{18}O_2$: C, 72.48; H, 9.95; neut. equiv., 182.25. Found: C, 72.53; H, 10.05; neut. equiv., 182.30.

Conversion of 2-Hydroxy-apocamphane-1-acetanilide into Camphene-carboxy-anilide.—Two g. (0.007 mole) of 2-hydroxy-apocamphane-1-acetanilide was suspended in 200 cc. of absolute ether and 1.6 g. (0.007 mole) of phosphorus pentachloride was added slowly, the mixture being cooled during the reaction. The suspended compound gradually went into solution as the reaction progressed and, after completion, the ether solution was washed with cold water until the washings were no longer acid to litmus. The ether solution was dried with anhydrous sodium sulfate and evaporated, leaving a solid which on recrystallization from 85% ethanol melted at 153–154° (corr.); yield 1.2 g. (66%). It did not lower the melting point in the mixed melting point test with an authentic sample of camphene-carboxyanilide.

Camphene-carboxylic Acid.—Eight-tenths gram of camphene-carboxy-anilide was refluxed for thirty-six hours with 100 cc. of 20% alcoholic potassium hydroxide. After cooling, the solution was poured into ice water which was extracted with ether. The aqueous solution was evaporated to about 20 cc. while carbon dioxide was being passed through, filtered and after cooling acidified with dilute hydrochloric acid and extracted with ether. The ether solution was dried with sodium sulfate and evaporated, leaving a brownish solid which was dissolved in hexane, decolorized with norite and recrystallized from the same solvent; melting point 126–127° (corr.); yield, 0.13 g. (23.2%).

Anal. Calcd. for $C_{11}H_{16}O_2$: C, 73.32; H, 8.95; neut. equiv., 180.23. Found: C, 73.41; H, 9.15; neut. equiv., 180.70.

The ether solution obtained by extracting the original alkaline liquors was dried with anhydrous sodium sulfate and evaporated, leaving a residue which partly solidified on cooling. It was washed with a small amount of hexane, leaving a white solid which proved to be identical with the original material; yield 0.282 g. (35%). The hexane washings were evaporated, leaving minute quantities of a residual reddish oil which consisted of aniline since the benzoyl derivative prepared in the usual manner melted at 162.5–163.5° (corr.), and did not lower the melting point when mixed with an authentic sample of benzanilide.

Camphenilone Semicarbazone.—Two and five-tenths grams of camphenecarboxylic acid was dissolved in 75 cc. of water containing 2.61 g. of potassium hydroxide. To this solution was slowly added a solution of 4.38 g. of potassium permanganate solution while steam distilling. A volatile oil of camphoraceous odor was taken up in ether, the solution being dried with anhydrous sodium sulfate. After distilling off the ether, there was obtained 1.5 g. (79%) of camphenilone which was immediately converted into the semicarbazone prepared in the usual manner; yield of semicarbazone 1.8 g. It was recrystallized from dilute ethanol, yielding fine white needles melting at 223–224° (corr.) and did not lower the melting point in the mixed melting point test with an authentic sample.

Anal. Calcd. for $C_{10}H_{17}ON_3$: C, 61.53; H, 8.78 Found: C, 61.34; H, 8.89.

The manganese dioxide was filtered from the aqueous solution, which was evaporated to a small volume, acidified with dilute hydrochloric acid and the precipitate removed by filtration. After recrystallizing from hexane, the acid melted at 126–127° (corr.). The mixed melting point test with the original material showed no lowering; recovery, 0.2 g. A solution of calcium chloride was added to the aqueous solution made alkaline with ammonia after removal of the original acid. The precipitate responded to the usual tests for calcium oxalate.

Three and seven-tenths grams of camphene-carboxyanilide was added to a solution of 6.4 g. of potassium permanganate and 0.8 g. of potassium hydroxide in 230 cc. of water. The mixture was shaken on a machine for fifteen hours and then steam distilled; 200 cc. of distillate was collected to which was added 1 g. of semicarbazide hydrochloride and 1 g. of sodium acetate. On standing *in vacuo* for three days, a crystalline precipitate was separated and recrystallized from ethanol, m. p. 224–225° (corr.). When mixed with an authentic sample of camphenilone semicarbazone, it did not lower the melting point.

Summary

1. When subjected to the Beckmann rearrangement, ω-benzoylborneoloxime yielded 2-hydroxy-apocamphane-1-acetanilide and as secondary product camphene-carboxyanilide, formed apparently by the Meerwein–Wagner rearrangement, and small amounts of benzonitrile, together with some tarry material of unknown composition.

2. The composition of 2-hydroxy-apocamphane-1-acetanilide was established by a series of new ω-homocamphor derivatives: lactone of hydroxy-apocamphane-1-acetic acid, 2-keto-apocamphane-1-acetic acid, semicarbazone of 2-keto-apocamphane-1-acetic acid and apocamphane-1-acetic acid.

3. The Meerwein–Wagner retropinacoline rearrangement on 2-hydroxy-apocamphane-1-acetanilide yielded camphene-carboxyanilide, which was characterized through its oxidation to camphenilone and hydrolysis to camphene-carboxylic acid.

SAVANNAH, GEORGIA RECEIVED SEPTEMBER 18, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF THE GENERAL ELECTRIC CO.]

The Density, Thermal Expansion, Vapor Pressure, and Refractive Index of Styrene, and the Density and Thermal Expansion of Polystyrene

BY WINTON PATNODE AND W. J. SCHEIBER

The density of styrene has been reported by a number of investigators,[1] but the values are not in good agreement. We have measured the density of styrene over the range 30–120° with the aid of a dilatometer, and the results of these measurements are plotted in Fig. 1. The points in circles and triangles are our measurements on two samples, and the lettered points indicate the previously published values.[1] The styrene used was obtained from the Dow Chemical Co. and from the Standard Telephones and Cables, Ltd., in England. Each sample was purified by fractional distillation at 80 mm., the middle fractions of constant boiling point and refractive index being taken for measurement of density.

In Fig. 2 is plotted log vapor pressure *versus* $1/(t + 230)$ of data taken from the literature[2] (lettered points), and of our samples which boiled at 76.2–76.7° at 80 mm. A good straight line can be drawn through these points, and it indicates a boiling point of 145.1° at 760 mm. This is in good agreement with an experimentally determined boiling point on very pure styrene of 145.0–145.4°.[1x]

In Fig. 3 is a plot of refractive index *versus* temperature, the lettered points again referring to the literature.[3] Our measurements, made with the aid of an Abbé refractometer, appear to be somewhat higher than many of the others, which, however, is to be expected if the earlier samples contained saturated impurities such as ethylbenzene. Phenylacetylene, however, would have the opposite effect, but our samples were found to contain less than 0.25% (limit of sensitivity of our test) of this impurity, if any at all.

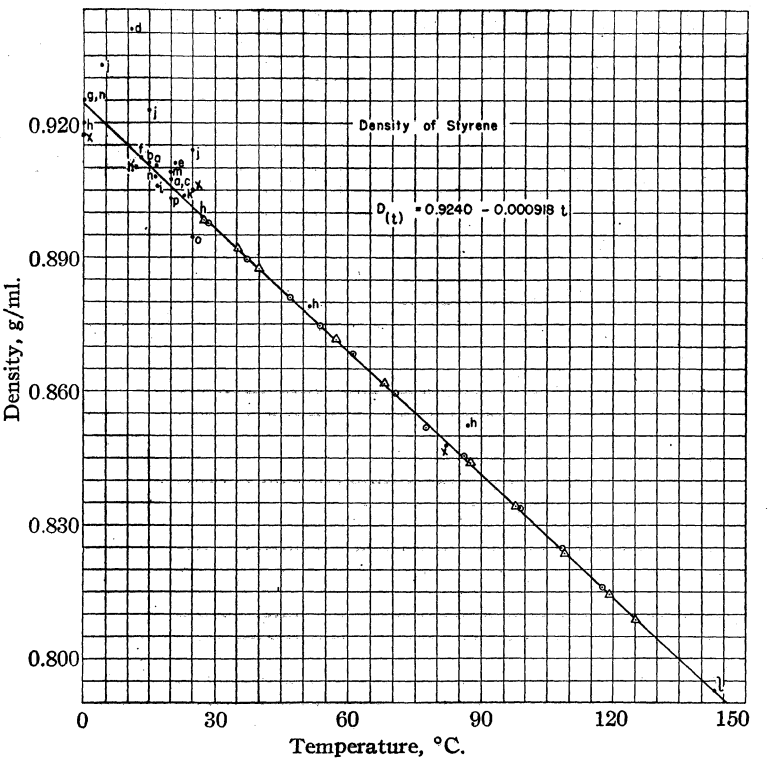

Fig. 1.—Density of styrene.

The density of resinous polystyrene was measured with the aid of a dilatometer for solids, the immersion liquid being mercury. Figure 4 is a plot of density *versus* temperature for two samples. Note that the curves consist of two straight lines that intersect at a point. At the temperature corresponding to this point there is apparently a fundamental change in the structure of the polymer. Sample I was prepared by heating pure, degassed styrene in a sealed tube under pressure

(1) (a) Auwers and Eisenlohr, *J. prakt. Chem.*, [2] **82**, 85 (1910); (b) Biltz, *Ann.*, **A296**, 275 (1897); (c) Brühl, *ibid.*, **235**, 13 (1886); (d) Gladstone, *J. Chem. Soc.*, **45**, 224 (1884); (e) Gladstone, *ibid.*, **59**, 292 (1891); (f) Klages and Keil, *Ber.*, **36**, 1632 (1903); (g) Krakau, *ibid.*, **11**, 1260 (1878); (h) Lemoine, *Compt. rend.*, **125**, 530 (1897); (i) Nasini and Bernheimer, *Gazz. chim. ital.*, **15**, 84 (1885); (j) Perkin, *J. Chem. Soc.*, **69**, 1224 (1896); (k) Sabetay, *Bull. soc. chim.*, **45**, 69–75 (1929); (l) Schiff, *Ann.*, **220**, 93 (1883); (m) Waterman and de Kok, *Rec. trav. chim.*, **53**, 1133 (1934); (n) Weger, *Ann.*, **221**, 69 (1883); (o) Otto and Wenzke, THIS JOURNAL, **57**, 294 (1935); (p) Müller, *Physik. Z.*, **38**, 283 (1937); (x) private communication, Dow Chemical Co.

(2) (q) Fittig and Binder, *Ann.*, **195**, 135 (1879); (r) Auwers, Roth and Eisenlohr, *ibid.*, **282**, (1910); (s) Linder, *J. Phys. Chem.*, **35**, 531 (1931); (t) von Richenberg, "Einfache und fractionierte Distillation," p. 201 (1923); (u) Dolliver, Gresham, Kistiakowsky and Vaughan, THIS JOURNAL, **59**, 831 (1937); (v) Zartman and Adkins, *ibid.*, **54**, 1668 (1932); (w) Gorman, Davis and Gross, *Physik. Z.*, **39**, 181–185 (1938); and Ref. 1b, f, i, k, m, n, o, x.

(3) Ref. 1a, b, e, f, i, k, m, o, x; Ref. 2u, w.

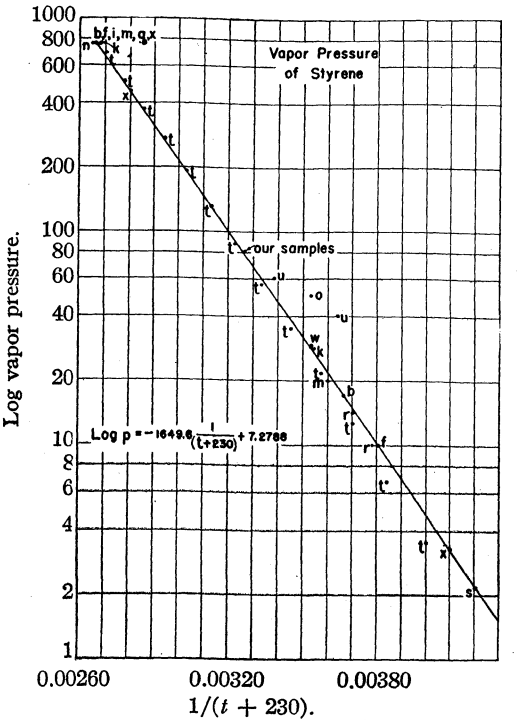

Fig. 2.—Vapor pressure of styrene.

of mercury for several weeks at 100° and then for three additional weeks at 125°. Sample II was prepared by heating for four weeks in a sealed tube at 150°, a piece of polystyrene that had spontaneously polymerized in a bottle at room temperature over a period of about six months. Although the purity of this sample was unknown, it is believed to have been over 98% styrene. As a measure of the relative average molecular weights of the samples measured, their specific viscosities, $\eta_{sp.} = \eta_r - 1$, of 1 g. of polymer in 40 g. of benzene were measured at 26°, and found to be 2.04 for Sample I and 1.42 for Sample II. These values are in contradiction to the general rule that the lower the temperature of polymerization, the higher the molecular weight of the polymer, and

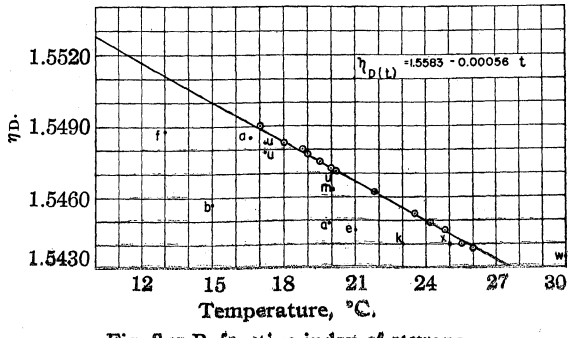

Fig. 3.—Refractive index of styrene.

may be attributed to the fact that Sample II was subsequently heated at 150°, which brings up the interesting question of change in average molecular weight with temperature, and the possibility of equilibria. An attempt to measure the density of the piece of polystyrene that had been formed at room temperature, and had never been heated, was successful at low temperatures only; at 70° and above the volume decreased continuously with time, probably owing to continued polymerization.

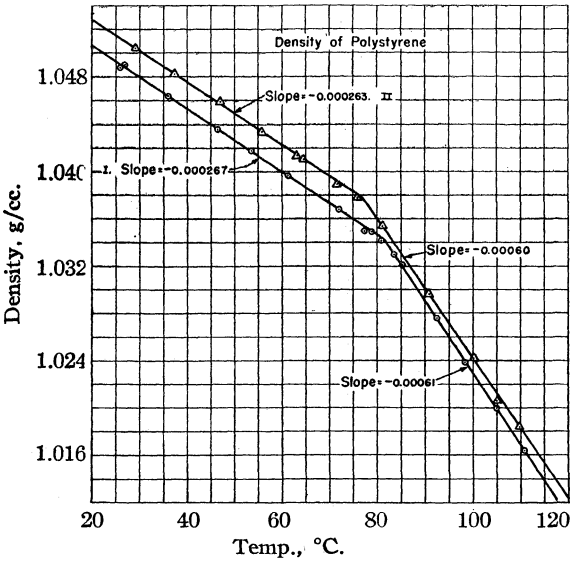

Fig. 4.—Density of polystyrene.

The data plotted in Fig. 4 were readily reproducible, even though the samples were repeatedly heated and cooled. It was necessary, however, to wait for considerable time, sometimes hours, for the volume to become constant at constant temperature, apparently long after temperature equilibrium had been established. This slow, persistent change in volume is a common property of glasses. The relative densities of the two samples are real, although the absolute density of each was found to be about 0.1% higher when measured by weighing in air and in water. The transition temperatures of the two samples are 81.5 and 77.5°. Measurement of the "high elasticity temperatures" of the same two samples by J. J. Russell in this Laboratory gave the values of 86 and 81°. Although these values are not identical with those for the transition temperature, they are in the same relative order. This lends further evidence to the assumption that polystyrene undergoes a fundamental change in struc-

ture at a definite temperature, depending upon the sample, which in some respects resembles the melting of crystals. It is also interesting to observe that although the densities and transition temperatures of these two samples are different, the slopes of the curves are identical.

Recently Jenckel and Ueberreiter[4] published a long paper describing the change in specific volume of polystyrene with temperature which confirms the general phenomena described above, and in addition they conclude that the transition temperature is depressed not only by a low average molecular weight of the polymer, but also by the presence of impurities in the resin such as monomeric styrene, paraffin, or polystyrene of very low molecular weight. Their data indicate an upper limit for transition temperature of slightly above 100° regardless of molecular weight, although their data for transition temperature and molecular weight do not fall upon a smooth curve. Neither do their values for density bear any regular relationship to average molecular weight or to transition temperature, although some such relationship might be expected. And, finally, their values for coefficient of expansion, as indicated by the slopes of the specific volume–temperature curves, show no regular relationship to molecular weight. This lack of regularity may indicate either that their measurements are in error by quantities greater than the differences found, or that the measured properties are influenced greatly by factors which have but little influence upon the viscosities of solutions of the polymers.

This bi-linear thermal expansion of polystyrene, the sharp transition temperature, and the closely accompanying sharp "high elasticity temperature" all point to the conclusion that polystyrene is a body of fairly definite composition and structure. It would be interesting to examine other linear polymers in the light of these observations, and to investigate the effect of cross-linking on the transition temperature.

(4) Jenckel and Ueberreiter, *Z. physik. Chem.*, **182A**, 361 (1938).

Summary

This paper includes the density, thermal expansion, vapor pressure, and refractive index of styrene, and the density and thermal expansion of polystyrene. A discussion of these latter properties is given in relation to other properties of the polymer.

SCHENECTADY, NEW YORK RECEIVED AUGUST 22, 1939

[JOINT CONTRIBUTION FROM THE RESEARCH LABORATORY OF INORGANIC CHEMISTRY,* NO. 75, AND THE GEORGE EASTMAN LABORATORY OF PHYSICS,† MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

The Radioactive Determination of Protactinium in Siliceous Terrestrial and Meteoritic Material

BY WALTER C. SCHUMB,* ROBLEY D. EVANS† AND JANE L. HASTINGS*

In order to test more completely the validity of the general rule that the abundance ratio of the isotopes of any element is a constant, independent of the source or of the mode of combination of the element, it is of interest and importance to determine such abundance ratios in meteorites, which represent the only available specimens of extra-terrestrial matter. Atomic weight or isotopic abundance ratios have been determined for carbon, oxygen, silicon, chlorine, iron, cobalt and nickel, by various workers[1]; and in the case of all the elements studied the isotopic abundance ratios are not measurably different in meteoritic and in terrestrial matter.

In the case of radioactive elements, such as uranium, these abundance ratios assume additional interest, in that by means of them a knowledge may be obtained of the difference in age between these atoms in the meteorite specimen and in terrestrial substances containing the same element. This subject was discussed in some detail by Evans,[2] who on the working assumption that the "isotopic ratio of any element is a constant of nature, and is independent of its place of origin in the galactic system," derived the following expression for the differential age in years of

(1) Baxter and Thorvaldson, THIS JOURNAL, **33**, 337 (1911); Baxter and Hoover, *ibid.*, **34**, 1657 (1912); Baxter and Parsons, *ibid.*, **43**, 507 (1921); Baxter and Hilton, *ibid.*, **45**, 694,(1923); Baxter and Dorcas, *ibid.*, **46**, 357 (1924); Jaeger and Dykstra, *Koninkl Akad. Wetenschappen. Amsterdam*, **27**, 393 (1924); Harkins and Stone, THIS JOURNAL, **48**, 938, 3233 (1926); Baxter and Ishimaru, *ibid.*, **51**, 1729 (1929); Manian, Urey and Bleakney, *ibid.*, **56**, 2601 (1934); Jenkins and King, *Publ. Astr. Soc. Pac.*, **48**, 323 (1936); Nier and Gulbransen, THIS JOURNAL, **61**, 697 (1939).

(2) Evans, *Pop. Astronomy*, **46**, 159–170 (1938).

uranium atoms in a meteorite and in the earth:[3]

$$t_m - t_e = 2.8 \times 10^9 \log (R_e/R_m) \qquad (1)$$

where t_m and t_e are the respective ages in the meteorite and in the earth, R_e is the $_{92}U^{235}:{}_{92}U^{238}$ activity ratio observed in the earth today, and R_m is the same ratio measured in the meteorite.

The present paper reports the results obtained in a portion of a program for the determination of isotopic abundance ratios in meteorites being carried on jointly in these laboratories, in particular, the determination of the isotopic ratio of $_{92}U^{235}$ (or AcU) to $_{92}U^{238}$ (or UI) in a specimen of the Pultusk[4] meteorite, which, because of its reported[2] high heliocentric velocity (56 km. per sec.) has been considered as representing not only extra-terrestrial but possibly extra-solar material.[5] The sample used in this work was very kindly furnished to Professor Evans by Dr. C. C. Gregg and Mr. H. W. Nichols of the Field Museum of Natural History, Chicago. Nier[6] has recently checked the constancy of the isotopic abundance ratio of U^{235}/U^{238} in terrestrial material by means of mass spectroscopic determinations on Pb^{207} and Pb^{206} for twenty-one uranium minerals and on U^{238} and U^{235} for three minerals.

In all but very young rocks radioactive equilibrium has been established in the three radioactive series, that is, the rate of disintegration is equal to the rate of formation of all members of each series derived from the three parent elements, $_{92}U^{238}$, $_{92}U^{235}$ and $_{90}Th^{232}$. Therefore, by determining the amount of any one member of a series present, the quantity of any other may be calculated. Thus the determination of the protactinium content of a specimen permits the calculation of the amount of the parent element AcU, and the determination of the radon content of the sample makes possible the calculation of the amount of the parent element UI present, and from these two values the abundance ratio U^{235}/U^{238} may be obtained.

(3) The numerical factor 2.8 has been changed from 1.46, given in the reference cited, to 2.8 as the result of more recent work on the actinium series branching ratio by A. O. Nier, *Phys. Rev.*, **55**, 150 (1939).

(4) A shower of fragments of a stony meteorite fell in Pultusk, Poland, on Jan. 30, 1868.

(5) Professor C. C. Wylie of the State University of Iowa has kindly communicated to us the results of his recent recalculation of the Pultusk trajectory observations, originally reported by Galle in 1868, following interviews with those who observed the meteorite fall. Professor Wylie's extensive experience in such interviews leads him to reduce the reported height of appearance of the meteorite. This has the effect of reducing the computed velocity so that the Pultusk meteorite would be of solar-system origin rather than extra-solar. Professor Wylie has just summarized his work in *Science*, **9**, 264 (1939).

(6) Nier, *Phys. Rev.*, **55**, 150, 153 (1939).

A method has been worked out by v. Grosse[7] and others for the isolation of protactinium from other radioactive elements. The present method is a modification of that of v. Grosse in that provision had to be made for the elimination of large amounts of silica and some 5% of free metal along with metal sulfides. The chemical analysis of two specimens of the Pultusk meteorite, as given in Farrington's[8] compilation, are presented in Table I.

TABLE I

PREVIOUS ANALYSES OF PULTUSK METEORITE

	G. von Rath, 1869	R. Rammelsberg, 1870
Specimen no.	82	101
SiO_2	41.54	35.85
Al_2O_3	1.17	1.96
FeO	14.04	12.12
CaO	0.28	1.56
Na_2O	1.34	0.95
K_2O	...	0.39
Fe	11.51	15.55
Ni	0.65	2.21
MgO	26.73	24.95

Experimental

Preliminary Work.—The preliminary work for testing the method was carried out on granite of known radium content. All solid reagents to be used were tested separately and a record made of their alpha activity. The efficiency of the method for the removal of radioelements other than protactinium and their isotopes was checked by adding known amounts of solutions of the salts of uranium, thorium, and polonium, respectively, and repeating all operations. These experiments proved that three separations (as described in Table II and the section on analytical procedure) removed 94% of the added uranium, 100% of the thorium and 95% of the polonium. Finally, a small sample of pure protactinium, deposited in zirconium pyrophosphate, and kindly furnished us for the purpose by Dr. v. Grosse, was converted into a highly dilute solution. The alpha activity of a portion of this solution was measured, and a known amount of it was carried through the chemical procedure. The activity of the recovered protactinium was determined, whereby it was demonstrated that 90 ± 6% of the protactinium could be recovered. In view of the many steps required in the analytical procedure employed, this recovery is considered to be satisfactory.

Sampling.—Due to the probability of surface leaching and contamination, only the inner portions of specimens of granite were used. These were ground, first in a steel mortar and finally in agate, both mortars being "rinsed" by grinding inactive sodium carbonate in them before use. After thorough mixing, a third of the finely ground material was reserved in a stoppered bottle for the radon de-

(7) A. v. Grosse, *Phys. Rev.*, **42**, 565 (1932); Francis and Da-Tchang, *Phil. Mag.*, **20**, 623 (1935).

(8) O. C. Farrington, *Field Museum of Natural History, Geological Series*, **3**, 195–229 (1911).

terminations and the remainder used for the separation of protactinium. In the case of the Pultusk meteorite sample, all of the outer black layer, or "skin," was carefully removed and samples of the inner portions were prepared as in the case of the granite.

Analytical Procedure.—A 50-g. sample of the siliceous material was treated with 100 cc. of aqua regia and heated on the steam-bath for a half hour. After cooling, the diluted acid solution was filtered and the residue dried and ignited in platinum. The filtrate was evaporated and the residue dehydrated. The residue was taken up with concd. hydrochloric acid, followed by water, and the silica filtered and combined with the original residue. The dehydration process was then repeated. The combined residues were treated several times with 47% hydrofluoric acid to which a few drops of concd. sulfuric acid had been added, and evaporated to fumes after each treatment. Three times the calculated amount of hydrofluoric acid was used to ensure complete removal of silica, assuming the latter to be 50% of the original sample. The residue then was heated to dull red heat and after cooling was treated with hot, concd. hydrochloric acid followed by hot water. There remained very little residue and this was filtered off and washed with hot water, dried, ignited and reserved for future work, if necessary.

The filtrate was combined with that from the final dehydration and the solution was evaporated to 200 cc. To the cooled solution zirconyl chloride solution was added equivalent to 100 mg. of ZrO_2. An excess of 6 *N* phosphoric acid was added and the solution stirred for several minutes. The precipitate of zirconium phosphate was allowed to stand for at least two hours before filtering. The precipitate was washed with 5% hydrochloric acid, dried, ignited, and weighed. The filtrate was reserved.

To the zirconium pyrophosphate, which contained the protactinium, 20 cc. of 2% hydrofluoric acid was added and the vessel heated until solution was complete. After cooling, solutions of the nitrates of barium, lead, lanthanum, and bismuth, equivalent to 4 mg. of each element, were added. The insoluble sulfates and fluorides of these elements co-precipitate those of radioactive elements other than protactinium, as indicated in Table II.

TABLE II

RADIOACTIVE SEPARATIONS FROM SOLN. OF ZrP_2O_7 + Pa IN 2% HF

Reagent	Radioactive elements and isotopes removed
$Ba(NO_3)_2$	Ra, $MsTh_1$, AcX, ThX
$Pb(NO_3)_2$	RaB, ThB, AcB, RaD, ThD, AcD, RaG
$Bi(NO_3)_3$	Po, RaC, ThC, AcC, RaE
$La(NO_3)_3$	Ac, $MsTh_2$

After standing for one hour, the precipitates were filtered, using hard rubber funnels. The residues were discarded. This operation was carried out three times to assure satisfactory elimination of radioactive contaminants, because blanks on which only two separations had been made occasionally showed residual counts. The third filtrate was evaporated to dryness, the residue ignited at red heat for ten minutes, and after cooling each residue so obtained was placed in a separate desiccator to avoid possible contamination.

A portion of the residue was transferred to an agate mortar and finely ground under alcohol. A suspension of the ground material was made in ethyl alcohol and poured upon a weighed silver disk, which had been sealed to a brass evaporating cylinder by means of rubber cement. The alcohol was evaporated in a heated cabinet in an atmosphere of well-aged and hence radioactively inert nitrogen. When the sample was dry, the cylinder and rubber cement were quantitatively removed from the disk and the disk plus the sample was weighed.

Measurement of Activity.—The weighed disk, containing the protactinium with zirconium pyrophosphate deposit, was placed in the recording alpha counter. An ionization chamber of the parallel plate condenser type was used, the design and operation of which has been discussed fully by Finney and Evans.[9] The ions formed by the alpha rays are collected, the current amplified, and the resulting galvanometer deflections recorded photographically upon sensitized bromide paper contained in a Telechron-driven drum camera which makes one revolution every two hours. Twenty consecutive hours of observation were generally employed in order to minimize the probable error. These could be recorded on a single sheet of 5 × 37.5 in. paper, by using a laterally moving light source.

The inner parts of the ionization chamber are made of spun copper and are easily removable for cleaning. Some contamination is, of course, inevitable, due to radioactive material in the walls of the ionization chamber, so that even without a radioactive sample in the chamber the record obtained will show some countable α-rays. Careful cleaning and the use of inactive silver for the metal disks minimizes this "background."

A blank on all reagents was carried along in parallel with the samples, and this served as a check on the completeness of removal of radioactive contaminants and on the overall manipulative procedures.

Calculated Results and Conclusions.—A sample of granite from Ontario, designated as "K. D. Fine," known to be low in radioactive material, was selected for a representative terrestrial material. The protactinium content was calculated from the observed alpha count per sq. cm. of source by means of the following two equations, discussed in the paper of Finney and Evans.[9]

$$n_a' = \frac{N\mu\tau}{4}\left[\frac{2(R-\rho)-\tau}{(R-\rho)}\right] \qquad (2)$$

in which

n_a' = alpha counts observed per cm.^{2} of source
N = alpha rays per cm.^{3} emitted in the source
R = 3.61 air-cm. = mean range in air at 15° and 760 mm. for alpha particles from Pa
ρ = 0.5 air-cm. (assumed maximum range of short range α-rays not detected)
μ = $15.6 \times 10^{-4}/d$ = ratio of range of α rays in the solid to the range in air
$\mu\tau$ = thickness of source in cm.
τ = mass/(area × density × μ) = source thickness in air-cm.

$$N = \frac{6.02 \times 10^{23} Q.\lambda.d}{W} \qquad (3)$$

(9) Finney and Evans, *Phys. Rev.*, **48**, 503 (1935).

TABLE III

PROTACTINIUM CONTENT OF MINERALS

Sample no.	Original rock sample, g.	ZrP_2O_7 + Pa, mg. Total	Pa, mg. Tested	Observed count: Over background	Observed count: Over blank	Observed count: For sample	Pa in 10^{-12}, g./g. rock
				Granite			
Blank	...	210	41.5	1.7 ± 1.1	.....	.....	.....
No. 1	15.04	199	28.5	0.8 ± 1.3	0.0 ± 1.7	0.0 ± 12	0.00 ± 0.23
			42.1	10.0 ± 1.2	8.3 ± 1.6	39 ± 8	.76 ± .16
No. 2	15.18	231	52.4	5.6 ± 1.0	3.9 ± 1.5	17 ± 7	.32 ± .13
			47.7	7.4 ± 0.9	5.7 ± 1.4	28 ± 7	.52 ± .13
					Mean	24.1 ± 4.6	0.46 ± 0.09
				Pultusk Meteorite			
Blank	...	111	42.7	0.0 ± 0.8	.....	0.0	0.0
Rock	51	110	27.3	0.8 ± 0.6	.....	3.2 ± 2.4	.018 ± 0.013
			34.2	2.7 ± 0.8	.....	8.7 ± 2.6	.049 ± .013
					Mean	6.0 ± 1.7	0.035 ± 0.011

where

W = 231 = at. wt. of Pa
λ = 2.5×10^{-9} hr.$^{-1}$ = decay constant of Pa
Q = concentration of Pa in g. per g. of source
d = density of ZrP_2O_7.

The probable error for each background run and determination of alpha rays due to protactinium was calculated in the usual way:

$$\text{P. E.} = 0.67\left[\frac{\Sigma(x - \bar{x})^2}{n(n-1)}\right]^{1/2}$$

where $\bar{x}$ is the average of n individual observations of x.

Table III summarizes the results obtained with the granite and Pultusk meteorite.

In equation (1) above the quotient of the activity ratios R_e/R_m is equal to the quotient of the mass ratios, since the radioactive decay constants and the atomic weights involved cancel out in the quotient.

The mean values of the radium content of these two specimens, as determined by Mr. Clark Goodman of the Physics Department, are 0.28 ± 0.02 $\times 10^{-12}$ g. Ra per g. for the granite and 0.023 ± 0.005 $\times 10^{-12}$ for the Pultusk meteorite. The corresponding observed weight ratios, Pa/Ra for the granite, and similarly for the meteorite, become 1.64 ± 0.5 and 1.52 ± 0.5, respectively. From these results the conclusion may be drawn that, if the probable errors are considered, there is no appreciable difference in the age of terrestrial uranium atoms and those in this specimen of the Pultusk meteorite.

The observed Pa/Ra ratio, and consequently the U^{235}/U^{238} ratio, is about twice the value observed by Nier[6] in terrestrial uranium minerals. Our probable error is based on the observed fluctuations in the α-ray counting rates, and does not include the contributions of any unknown systematic errors. Our observed Pa/Ra ratio, 1.64 ± 0.5, is higher than Nier's value by 1.5 times our probable error. According to the theory of errors, there is a 30% chance that the true value differs from the observed by more than 1.5 times the probable error. Therefore, the two values are compatible with each other. The differential age estimated from these observations depends (Equation 1) only on the logarithm of the *ratio* of the observations on meteoritic and terrestrial material, and is therefore much more accurate than the observations themselves.

From the chemical standpoint a more definite conclusion may be arrived at: the method employed for the separation and estimation of protactinium has proved satisfactory for as little as 10^{-13} g. of protactinium per g. of siliceous material, and with larger samples this limit probably could be set much lower.

This investigation was materially assisted by a grant from the Cyrus M. Warren Fund of the American Academy of Arts and Sciences, which is hereby gratefully acknowledged.

Summary

The protactinium contents of a granite and of a specimen of a meteorite (Pultusk), both high in silica, have been determined by the co-precipitation of the protactinium with zirconium phosphate, followed by purification of the ignited pyrophosphate, employing a modification of the method of v. Grosse. The alpha activity of the protactinium thus isolated was measured on a re-

cording alpha-counter and the concentration of protactinium in the two specimens of terrestrial and of meteoritic material calculated.

From these data and the corresponding radium concentrations of the same specimens determined independently, the weight ratios Pa/Ra have been derived for the two materials. From these results the conclusion has been reached that within the limits of error the age of the uranium atoms in this specimen of the Pultusk meteorite is the same as for terrestrial uranium.

The method is capable of estimating as little as 10^{-13} g. of Pa per g. of siliceous material, and the limit may probably be lower than this if larger samples are taken.

CAMBRIDGE, MASS. RECEIVED JULY 28, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF PHYSICAL CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY] No. 432]

Rates of the Thermal Reduction of Dichromic Acid by Quinine, Hydroquinine, and Cinchonine in Dilute Sulfuric Acid at 0 to 60°

BY LAWRENCE J. HEIDT

Quinine and ten similar alkaloids reduce dichromic acid when ultraviolet light is absorbed by the alkaloid.[1] This reaction was studied in dilute sulfuric acid at 0 to 30°. The variations in the photochemical efficiencies with structural changes in the alkaloids suggested that the hexavalent chromium was reduced mostly by the secondary hydroxyl group.[1d] The kinetics of the photochemical reaction were also studied and interpreted.[1c] This paper presents a study of the kinetics of the thermal reaction in the same environment.

Materials.—The source and purification of the reagents were the same as in the photochemical work. Acid solutions were standardized by comparison with sample 84 of U. S. Bureau of Standards potassium acid phthalate.

Stock solutions of ferrous ammonium sulfate were made from clear green crystals of Analytical Reagent material and were stored in the dark. They were standardized against dichromate solutions each week they were used and the proper factors at other times interpolated.

Apparatus and Procedure.—One of the two reaction cells is sketched[2] in Fig. 1a. The stirrer was the Pyrex plunger, D. In the cell not sketched, the part of D containing the disks was replaced with a Pyrex ribbon twisted like a screw. The fall of each plunger was cushioned by a Pyrex button fused onto the end that struck the bottom of the cell. An iron nail, B, was sealed into the top of each plunger whereby it was lifted at intervals by an electromagnet and fell when a "flasher" interrupted the current in the magnet. The cell outlet, C, used in the preliminary work, was replaced by a glass joint whose cap contained the male part made of solid glass. An umbrella fused to this cap fit loosely around the joint and extended as far down as the female part illustrated in the sketch. The volume of each cell was 100 cc. Their other characteristics have been published,[3] although these cells and the accompanying apparatus were used first in this research.

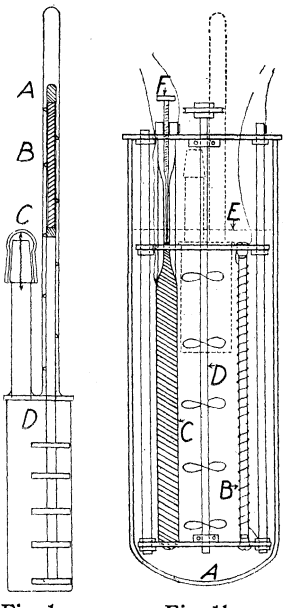

Fig. 1a.

Fig. 1b.

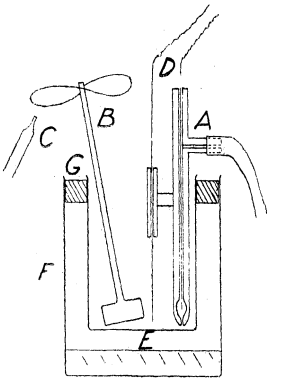

Fig. 1c.

The arrangement of the apparatus in the thermostat is sketched in Fig. 1b. The thermoregulator was a relay operated by a vacuum tube whose grid was in series with the contact, F, made in the glass capillary. This capillary was sealed to a welded steel tube filled with mercury. The quick response of the mercury in the steel tube to changes in the temperature of the bath enabled all adjustments for a new temperature setting to be completed within an hour. The bath then remained within 0.01° for ten hours and within 0.03° for several days. The container was the silvered dewar flask, A. The level of the thermo-

(1) (a) Luther and Forbes, THIS JOURNAL, **31**, 770 (1909); (b) Forbes, Heidt and Boissonas, *ibid.*, **54**, 960 (1932); (c) Forbes, Heidt and Brackett, *ibid.*, **55**, 588 (1933); (d) Forbes and Heidt, *ibid.*, **55**, 2407 (1933); (e) Heidt and Forbes, *ibid.*, **55**, 2701 (1933); and (f) Forbes, *Cold Spring Harbor Symposia Quant. Biol.*, **2**, 1 (1935).

(2) Mr. Arnold J. Levine made the drawings in Fig. 1, with financial aid from the National Youth Administration.

(3) Heidt and Purves, THIS JOURNAL, **60**, 1206 (1938).

stating oil was kept at E. In later work above 60° it became necessary to place the glass capillary outside of A, and connection with the steel tube was made through a piece of steel capillary. The contact with the grid was then made at room temperature—held within 2° to maintain the bath within the ranges of temperature given above.

At 0°, the reaction vessels were placed in a mush of crushed ice and distilled water in a commercial one-gallon (5-liter) vacuum jug fitted with a light-proof cover but without any other apparatus to control the temperature. Nevertheless, T remained at 0.00° in the center of the bath around the reaction cell. Only clear pieces of ice were used and they were washed with distilled water. Stirring of the reacting mixtures was restricted to shaking the cell and contents just before removing a sample, and weighing it out directly for analysis.

Reference (3) describes the way in which temperatures were measured and solutions brought quickly to the temperature of the thermostat. Tared samples of dry alkaloid and stock solutions of sulfuric acid and potassium dichromate were used to make up the reaction mixtures. When less than 10 mg. of alkaloid was required, the appropriate volume of a more concentrated, *freshly prepared* solution was used. This procedure helped avoid any peroxide which might have formed if stock solutions of these alkaloids had been kept in contact with air for long periods.

Reactions were followed by measuring the change in concentration of the substances that oxidized, in acid solution at room temperature, solutions of ferrous ammonium sulfate. Presumably these oxidizing substances were mainly hexavalent chromium, so the measured rate has been taken as $-\Delta(K_2Cr_2O_7)/\Delta t$.

The apparatus sketched in Fig. 1c was used to titrate the weighed samples of the reaction mixtures. These were placed in the inner beaker, E, and thermostated with a water-bath in the outer beaker, F, centered with the cork ring, G. The end-point was taken as the maximum potential difference, p. d., produced between the platinum wires, D, by a drop of titer. This maximum usually occurred within five drops (0.1 ml.) after the bulb (volume about 0.02 ml.) surrounding one of the electrodes had been flushed by blowing repeatedly through A until no p. d. between the electrodes dipping in the solution was measurable. The galvanometer which detected the p. d. had a sensitivity of 45 meg., and a CDRX of 18,000 ohms. Analyses were reproduced to 0.03 g. of 0.001 *M* Mohr salt. Solutions were weighed to 1 mg., and were transferred with clean, dry pipets.

Samples for analyses were taken from tubes at 0° or directly from the reaction cell if at 0°. The tubes were sealed with glass caps ground to fit tightly without grease. Often, two sets of analyses were made upon the samples in the tubes; the first set, within an hour after the sample had been transferred from the reaction cell, and the second set, after the sample had stood overnight at 0°. The difference between the two sets was usually small, so that a linear extrapolation was made to the time when the sample was taken from the reaction cell. When the correction thereby applied to the first set of analyses was less than 0.2%, the second set was omitted for the remaining samples.

The photochemical reaction was made negligible by keeping the reacting solutions in the dark except during sampling and when made up and analyzed in dim, diffuse light.

Results

The initial concentration of the sulfuric acid was fixed at 1.55 *M*, so that only a small fraction of the hydrogen ions was consumed. The *p*H, therefore, remained almost unchanged throughout the reaction. The thermal as well as the photochemical reactions were paralyzed even at 60° in the absence of added acid, and a precipitate appeared when the alkaloid and dichromate concentrations were much greater than 0.0003 *M*.

The increase in the initial rate of the reaction with the concentrations of dichromate and alkaloid are plotted on a logarithmic scale in Figs. 2A and 2B. The abscissa has been adjusted to make the points at 0, 30 and 60° coincide at 0.000167 *M* dichromate and 0.01 *M* alkaloid. The reaction rates were the same in either cell, and each point on the plot represents the average of many experiments, which agreed within 5% in the stirred solutions and within 10% in solutions not stirred. The rates for quinine, hydroquinine, and cinchonine were the same within the limits of error.

The straight lines through the points in Figs. 2A and 2B are given by equation (1) $-\Delta(K_2Cr_2O_7)/\Delta t = k(K_2Cr_2O_7)(\text{alkaloid})^{1/2}$. The average k in kilograms$^{1/2}$ moles$^{-1/2}$ and minutes^{-1} was 0.00055 at 0°, 0.0026 at 30°, and 0.011 at 60°.

The straight line through the points on the plot, in Fig. 2C, of $\log_{10} k$ against $1/T$, is given by equation (2) $\log_{10} k = 4.05 - 2000/T$. $T = 273.2° +$ °C. The energy of activation is 9 kilocalories.

In quinine, the methoxyl group in position six of the quinoline nucleus, and the vinyl group, do not enter the reaction; otherwise, equation (1) would not be expected to hold for all three alkaloids unless the rates of oxidation of these groups were also given by (1). The small activation energy suggests that a large number of degrees of freedom contribute energy to the activation process in accord with the large conjugated system of single and double bonds which transmit energy readily throughout the quinoline part of the alkaloid. It may also mean that the potential of the oxidation–reduction system and the steric factor largely determine these rates. The small value of the frequency factor implies a large steric effect often associated with reactions between complex molecules.[4]

(4) See, for example, H. W. Melville, *Chem. Soc., Annual Reports*, **35**, 69 (1939).

As the thermal reaction proceeded, its rate at first increased slightly as shown, for example, at 30° in Table I, before it began to decrease very slowly as the hexavalent chromium continued to disappear.

TABLE I

Temp., 30.0°; quinine, 0.01 *M*; $K_2Cr_2O_7$, 0.00017 *M*; H_2SO_4, 1.55 *M*.

% Dichromate reduced	$-\Delta(K_2Cr_2O_7)/\Delta t$ (moles/kg./min.) $\times 10^3$	$k \times 10^3$ calculated from equation (1)
1 to 5	4.5	2.7
5 to 48	5.5	4.4
48 to 53	4.0	4.7
53 to 84	3.5	6.5
84 to 89	1.8	8.2

In all cases, the observed rate in the latter stages of the reaction was several times greater than the rate calculated by equation (1) for the initial reaction. The reaction, therefore, was autocatalyzed as are a large number of oxidations involving organic molecules and oxygen, probably due to the formation of peroxides[5] and easily oxidized products such as the ketone.[1d]

In the photochemical reaction, autocatalysis also occurred.[1b,c] The equation for the initial reaction, however, may be written as

$$(1)^* \quad -\Delta(K_2Cr_2O_7)/\Delta t = k^*(K_2Cr_2O_7)^{1/2}\,(\text{alkaloid})^\circ$$

k^* not only varied with the temperature, but also with structural differences in the alkaloids and the wave length and intensity of monochromatic light absorbed by the alkaloids. Light absorbed by the other reactants did not affect the reaction measured. The independence of the photochemical rate upon the concentration of the alkaloid (indicated in (1)* by (alkaloid)°) therefore suggested[1c] that one molecule of alkaloid entered the photochemical reaction. $\text{Log}_{10}\ k^*$ was a linear function of $1/T$ but the slopes of the plots were nearly horizontal, *e. g.*, for quinine at λ 366 mμ, $\log_{10} k^* = a - 370/T$, when other variables were fixed.

A comparison of equations (1)* and (1) shows that the light effective in the photochemical reaction initiates a different reaction (as measured by the disappearance of dichromate) than takes place upon the absorption of thermal energy alone.

Summary

The thermal rates of oxidations of quinine, hydroquinine and cinchonine by dichromic acid in 1.55 *M* sulfuric acid are the same within 5%. The reactions are autocatalytic.

The initial rates are given by the equations

$$-\Delta(K_2Cr_2O_7)/\Delta t = k(K_2Cr_2O_7)\,(\text{alkaloid})^{1/2} \quad (1)$$

and

$$\log_{10} k = 4.05 - 2000/T \quad (2)$$

(5) H. L. J. Bäckstrom, *Medd. Vetenskapsakad. Nobelinst.*, **6**, No. 16, 57 (1927), and his other publications.

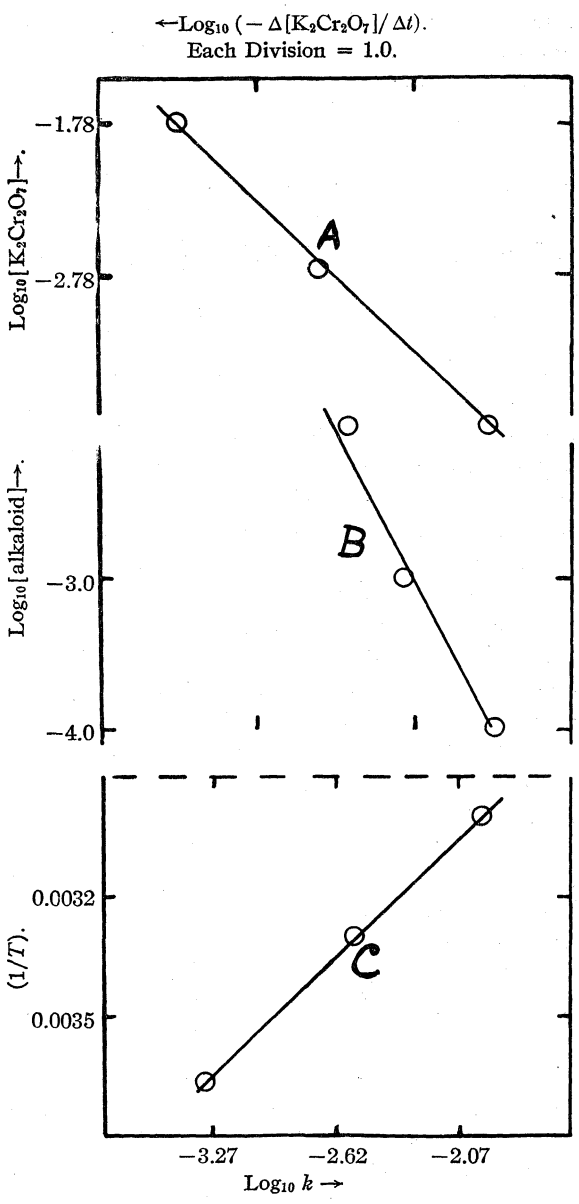

Fig. 2.—The slopes of the lines in plots A and B, when the logarithm of the rate is taken as the dependent variable, give the order of the initial reaction with respect to the reactant whose concentration is varied. In plot A, the concentration of alkaloid was fixed at 0.01 *M* and in plot B, dichromate was fixed at 0.00017 *M*. The activation energy of the reaction equals −4.58 multiplied by the slope of the line in plot C when $\log_{10} k$ is taken as the dependent variable.

when k is expressed in (kilograms of solution)$^{1/2}$ (moles)$^{-1/2}$ (minutes)$^{-1}$.

Light absorbed by the alkaloids initiates a different reaction which is affected very little by thermal energy.

CAMBRIDGE, MASS. RECEIVED OCTOBER 6, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, NO. 204]

The Unesterified Primary Hydroxyls in Acetone Soluble Cellulose Acetate[1]

BY F. B. CRAMER AND C. B. PURVES

It is well known that cellulose triacetate, subjected to a mild hydrolysis, loses some of its original solubilities in organic solvents and acquires new ones, among which a capacity to dissolve in acetone is of great technical importance.[2] Although there have been various opinions as to the cause of this change,[3] it now seems certain that an alteration in the average chain length of the cellulose macromolecule is not necessarily involved.[4] On the other hand, only those acetates which average 2.1 to 2.6 acetyl groups per anhydroglucose unit are soluble in acetone and they must be prepared by the partial hydrolysis of the triacetate rather than by the partial esterification of cellulose.[3,5] These observations suggest that true acetone solubility depends not only upon the numerical ratio of acetyl to hydroxyl groups[6] but also on their relative distribution. Whatever this may be, unesterified hydroxyl is confined to the second, third and sixth positions of the glucose residues and is accordingly of a secondary or a primary alcoholic nature. We have found only one attempt to discriminate chemically between the two possible types of hydroxyl, and this was by determining the molar amount of triphenylmethyl chloride which would condense with commercial acetone-soluble acetate dissolved in pyridine.[7] By assuming that only unesterified primary as opposed to secondary hydroxyls would react under these conditions, approximately one-third of the free hydroxyls were assigned to the primary or sixth position of the glucose units. This assumption was subsequently shown to be unfounded in the case of simple glycosides[8] and the result required confirmation by an independent method.

In the present work, two commercial acetone-soluble cellulose acetates averaging 0.56 and 0.67 mole of free hyroxyl per glucose unit were condensed, in dilute pyridine solution at 20°, with a large excess of *p*-toluenesulfonyl chloride (tosyl chloride). Samples were isolated at intervals and their sulfur content plotted against time (Fig. 1). About one-third of the hydroxyls were rapidly esterified in the first three hours, then the rate decreased markedly and the tosylation reached a maximum between the third and tenth days, when the reaction was about three-quarters complete. An extremely slow replacement of tosyl groups by chlorine progressed during the subsequent months. The tosylation removed no acetyl groups because the products analyzed for acetyl retained the original quota. It was also improbable that acetyl had wandered from one hydroxyl to another during the reaction, the reagents used not having caused this even with partly acetylated glucoses where such wandering was known to occur readily.[9] The tosyl groups were therefore considered to be faithful reproductions of the positions of the hydroxyls in the original cellulose acetate. In order to determine these positions, it was hoped that the tosylated acetate could be degraded to partly tosylated glucoses, the examination of which would give the desired information. Attempts to accomplish this degradation with hydrogen bromide in glacial acetic acid,[10] with cold

(1) Delivered at the Boston meeting of the American Chemical Society, September, 1939.

(2) Berl and Koerber, THIS JOURNAL, **61**, 154 (1939), studied the effect of low temperatures on such solubility relationships.

(3) The earlier work has been reviewed adequately by Krüger in "Zelluloseazetate," Theodor Steinkopff, Dresden-Blasewitz, 1933, pp. 173–178. See also Marsh and Wood, "An Introduction to the Chemistry of Cellulose," Chapman and Hall, Ltd., London, 1938, pp. 200–210.

(4) Staudinger and Daumiller, *Ann.*, **529**, 219 (1937). This paper has many literature references.

(5) Direct partial acetylation may give products of limited or temporary solubility or which are too degraded to be of technical value. They are omitted from consideration throughout the present article.

(6) Highfield, *Trans. Faraday Soc.*, **22**, 57 (1926).

(7) Sakurada and Kitabatake, *J. Soc. Chem. Ind. Japan*, **37**, (supplementary binding) 604 (1934).

(8) Hockett and Hudson, THIS JOURNAL, **56**, 945 (1934).

(9) Helferich, Bredereck and Schneidmüller, *Ann.*, **458**, 111 (1927).

(10) Hess, Littmann and Pfleger, *ibid.*, **507**, 55 (1933), obtained 2,3,6-tritosylacetobromoglucose in 70% yield from tritosyl starch by using this reagent.

72% sulfuric acid,[11] or with cold 43% hydrochloric acid[12] produced dark decomposition products. The use of alcoholic hydrogen chloride in a sealed tube[13] removed the tosyl residues. In these circumstances recourse was had to less drastic methods.

When *p*-toluenesulfonyl esters of glucose were heated with an excess of sodium iodide in acetone, the residues in the primary or sixth position were exclusively and quantitatively replaced by iodine.[14] This method of estimating primary in the presence of secondary hydroxyl proceeded very smoothly in the present case and showed that 0.197 tosyl group was in the sixth position of the anhydroglucose units. Of the available 0.56 hydroxyls in the original acetone soluble acetate, 0.197 or 35% was accordingly of a primary nature. The acetyl and sulfur analyses of the fully tosylated material failed to account for 0.13 mole of original hydroxyl. Failure to reacetylate this completely, together with the presence of traces of chlorine and nitrogen, suggested that the discrepancy was partly due to the accumulation of small analytical errors. The above estimate of 35% primary hydroxyl was therefore a minimum value and the true figure may have been close to 50%.

Pyridinium hydrochloride, in pyridine solution at 100°, rapidly replaced a tosyl group on the primary hydroxyl of methyl glucoside by chlorine.[15] When the fully tosylated cellulose acetate was submitted to this reaction, 0.24 mole of chlorine was introduced and 0.24 or 43% of the original hydroxyls were by inference primary. Thus both estimations went to show that one-third to one-half of the exposed hydroxyls in acetone-soluble acetate were in the sixth position of the anhydroglucose units. It followed that the partial deacetylation of cellulose triacetate to the acetone soluble condition involved the removal of acetyl from primary and secondary positions at approximately the same rate.

The amount of primary hydroxyl corresponded quite closely with the number of tosyl groups entering the cellulose acetate molecule in the initial, rapid reaction. This fact, in conjunction with the occasional preferential reaction of the same group

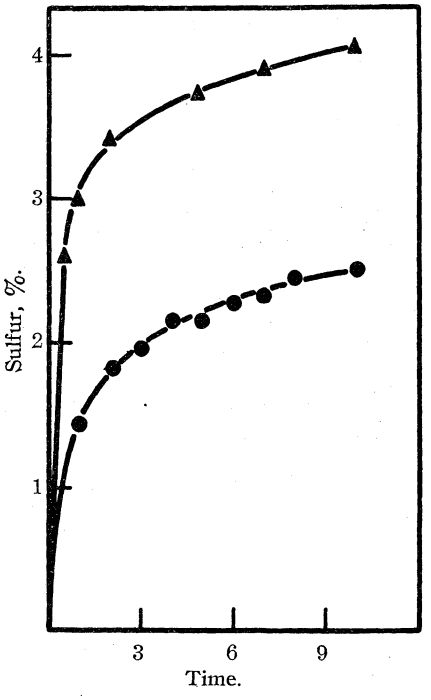

Fig. 1.—Tosylation rate curve of acetone soluble cellulose acetate I. Initial portion, ●; time in hours. Later portion of same curve ▲; time in days.

in methylglycosides,[16] suggested that the product be isolated and examined at the break in the tosylation–rate curve (Fig. 1). Specimens from two different cellulose acetates both contained 0.19 tosyl group per glucose unit, of which no less than 84 and 90% was in the primary position and replaceable by iodine. The form of the tosylation rate curve was thus definitely shown to be determined by the eleven- or twelvefold superiority in reaction velocity of the primary in contrast to the combined rates of the two secondary hydroxyls. There is no reason to believe that this superiority is displayed only toward *p*-toluenesulfonyl chloride. It is therefore probable that other acid chlorides in pyridine solution will acylate up to 0.2 mole of primary hydroxyl in acetone soluble cellulose acetates with rapidity and without causing acetyl wandering. Mixed acylated celluloses of approximately known constitution probably can be prepared in this way.

It is interesting to note that the tosylation rate curve (Fig. 1) is similar in shape to that observed in the heterogeneous acetylation of fibrous cellulose.[17] The break in the latter was considered to

(11) Monier-Williams, *J. Chem. Soc.*, 803 (1921).
(12) Willstätter and Zechmeister, *Ber.*, **62**, 722 (1929).
(13) Irvine and Hirst, *J. Chem. Soc.*, 1585 (1922).
(14) Oldham and Rutherford, THIS JOURNAL, **54**, 366 (1932).
(15) Hess and Stenzel, *Ber.*, **68**, 981 (1935). The fourth position in tosylated methyl glucoside also was chlorinated but in cellulose this is blocked by the glycosidic linking.
(16) Compton, THIS JOURNAL, **60**, 395 (1938); Lieser and Schweitzer, *Ann.*, **519**, 271 (1935).
(17) Hess and Trogus, *Z. physik. Chem.*, **B15**, 157 (1931).

mark the end of a rapid, superficial, intramicellar reaction, involving one-third to one-half of the hydroxyls, and the beginning of a slower reaction governed by the rate of diffusion into the interior of the micelles. As these were undoubtedly penetrated, it is possible that the entire reaction was permutoid in character and conditioned by the greater esterification rate of that third of the hydroxyls which were primary. Such a directly acetylated product might have the same acetyl content and the same average molecular weight as an acetone soluble acetate produced by the partial saponification of the triacetate. The distribution of acetyl and hydroxyl would nonetheless be sharply different, as primary hydroxyl would be present in the latter case and none in the former.[18] Free primary hydroxyl may prove to be necessary for true solubility in acetone.[19]

Attempts were made to confirm the presence of iodine in the primary position of the iodo-cellulose acetate by degrading it to 6-iodoglucose. The iodine atom was as unstable toward the usual reagents as the tosyl group was found to be in the earlier experiments. A highly degraded desoxycellulose acetate was finally prepared in almost quantitative yield by reducing the iodo acetate with a zinc–copper couple. The fact that glucomethylose (isorhamnose) units were present in the desoxy acetate was supported by the formation of methyl furfural on distillation with aqueous acid, and also by the isolation of isorhamnose as the crystalline, well-defined tetraacetate after the degradation had been completed by standard methods. With the exception of these degradations, all the reactions described proceeded practically quantitatively and without significant alteration in the average chain length as measured by Staudinger's viscosity method.[20] The derivatives had a wide range of complete solubility in organic solvents and, chlorinated and degraded products excepted, were fibrous.

Experimental

The Roman numerals refer to the table of viscosities at the end of the article.

Materials.—Two commercial acetone soluble acetates were studied, sample I being an Eastman Kodak Co. and sample II a du Pont Co. product.[21] The acetyl analyses were 39.7 and 38.6%, respectively, corresponding to averages of 2.44 and 2.33 moles per glucose unit. The ash was 0.063 and 0.044%, the sulfur contents were negligible and both specimens dissolved completely in acetone to almost colorless solutions free of opalescence. They were dried over phosphorus pentoxide *in vacuo* at 55–65°.

High grade pyridine was redistilled from barium oxide shortly before use and the *p*-toluenesulfonyl chloride was recrystallized from ether.

Rate of Tosylation.—Twenty grams (1 mole hydroxyl) and 106 g. of pure tosyl chloride (18.3 moles) were separately dissolved in 115 and 240 cc., respectively, of pyridine. The solutions were separately brought to 20°, quickly mixed by shaking and the mixture kept at 20°. At intervals, 30-cc. samples were withdrawn, quickly cooled to 0° and mixed with equal volumes of ice-cold acetone containing more than sufficient water to decompose the excess tosyl chloride. After five minutes of shaking in a bath at 0°, the mixture was stirred into 600 cc. of distilled water and twenty minutes later the precipitate was filtered, washed well with water and dried over anhydrous calcium chloride. Solution in 40 cc. of acetone, filtration to remove impurities, reprecipitation from water, washing and drying followed. The above procedure diminished local heating of the viscid samples during isolation and thus avoided a replacement of tosyl by chlorine. A white, fibrous, acid-free product was obtained in nearly quantitative yield. After a final drying over phosphorus pentoxide *in vacuo*, analyses for sulfur were made by Waters' method,[22] since Carius estimations were erratic and frequently low. The data were plotted in Fig. 1.

The cellulose acetate II gave very similar results, with a sulfur maximum of 4.43% (fourth and eleventh days). This corresponded to a substitution of 2.33 acetyl and 0.46 mole tosyl per glucose unit, *i. e.*, to a substitution of 73% of the original 0.67 mole of hydroxyl. The very slow and partial replacement of primary tosyl by chlorine at 20° was followed on this sample for another four months.

Anal. Calcd. for 2.33 acetyl, 0.39 tosyl and 0.22 chlorine: S, 3.80; Cl, 2.41. Found (III): S, 3.81, 3.79; Cl, 2.40, 2.37.

Maximum Degree of Tosylation.—A 20-g. batch of the acetate, sample I, was withdrawn from the above reaction mixture after ten days, or when the sulfur content was near the maximum. The white, fibrous material was completely soluble in acetone, glacial acetic acid, dioxane, pyridine and chloroform to clear, nearly colorless, viscid solutions. It was insoluble in alcohols, ether and hydrocarbons.

Anal. Calcd. for 2.44 acetyl and 0.43 tosyl groups: acetyl, 31.7; S, 4.16. Found (IV): acetyl, 31.3, 31.5; S, 4.04, 4.08. Nitrogen and chlorine were present in traces.

(18) Spurlin, THIS JOURNAL, **61**, 2222 (1939), dealt mathematically with the arrangement of substituents in cellulose derivatives and reviewed the literature.

(19) The acetone soluble acetate loses this property when heated with glacial acetic acid (U. S. Patent 1,668,946), which probably re-esterifies the primary hydroxyls preferentially. A direct acetylation of cellulose with acid catalysts in presence of sufficient aldehyde may produce acetone soluble products of technical value (U. S. Patent 1,930,145). Here some primary hydroxyls may be protected from acetylation by a prior and selective reaction with the aldehyde.

(20) Staudinger, "Die hochmolekularen organischen Verbindungen," Verlag J. Springer, Berlin, 1932.

(21) We wish to thank Drs. J. W. Hill and F. Schulze of the du Pont Co., for the gift of this acetate. It was part of an individually manufactured lot representing the most uniform type of high grade commercial product. The acetyl quoted was 39.3% and a 24% solution in anhydrous acetone had a viscosity of 375 poises.

(22) Waters, *Ind. Eng. Chem.*, **12**, 482 (1920).

A second preparation (acetyl, 31.4; S, 3.9%) was reacetylated with pyridine and acetic anhydride. *Anal.* Calcd. for complete substitution with 2.57 moles acetyl and 0.43 moles tosyl: acetyl, 33.0. Found (V): acetyl, 31.6, 31.9.

A 6-Chloro-tosyl Cellulose Acetate.—The dry, tosylated acetate (IV), 2 g., dissolved in 20 cc. of pyridine, was added to the suspension made by passing 1.5 g. of dry hydrogen chloride into 30 g. of pyridine. The pyridine hydrochloride dissolved while the mixture was kept at 80–85° in a glass-stoppered flask. After four hours the dark solution was cooled and stirred into 600 cc. of water and the white precipitate, which filtered normally, was well washed and dried. Solution of this precipitate in acetone, filtration and addition of water to the filtrate gave a colloidal suspension which was separated with difficulty. The material dried to a horny mass which behaved in the same way when reprecipitated from acetone by water. Among the cellulose derivatives studied, the 6-chloro-tosyl acetate was the only one with a marked tendency to disperse in this fashion.

Anal. Calcd. for 2.44 acetyl, 0.19 tosyl and 0.24 moles chlorine: S, 2.04; Cl, 2.86. Found (VI): S, 1.89, 1.92; Cl, 2.80.

A 6-Iodo-tosyl Cellulose Acetate.—Ten grams of the tosylated acetate (IV) and 20 g. of sodium iodide were dissolved in 150 cc. of pure dry acetone. The glass-stoppered bottle containing the solution was kept at 100° for two hours in an autoclave containing additional acetone to compensate the pressure within and without the bottle. After cooling and diluting with acetone, the viscid solution was filtered from the insoluble sodium *p*-toluenesulfonate. The acetone filtrate was poured into much distilled water and the precipitate purified by reprecipitation in the usual way. Tests with silver nitrate and starch solutions showed that iodine, either free or combined, was absent from the final supernatant liquors. The iodo-tosyl acetate was fibrous, had a slight yellow tinge and the same solubilities as the parent tosyl derivative.

Anal. Calcd. for 2.44 acetyl, 0.233 tosyl and 0.197 moles iodine: S, 2.31; I, 7.77. Found (VII): S, 2.33, 2.36; I, 7.94, 7.88.

A duplicate iodination on a smaller scale was heated for sixteen hours at 100° without increasing the iodine content of the product, which was therefore the maximum obtainable. Found: I, 7.7.

Partial Tosylation of Cellulose Acetate I.—The mixture already described was used and the tosylation was interrupted after three hours at 20°. The initial, rapid reaction was then almost over (Fig. 1).

Anal. Calcd. for 2.44 acetyl and 0.19 tosyl groups: acetyl, 35.7; S, 2.07. Found (VIII): acetyl, 35.0; S, 2.00.

A 6-Iodo-cellulose Acetate.—The above partially tosylated derivative (VIII) was heated in 10% acetone solution with twice its weight of sodium iodide at 100° for two hours before isolation of the product.

Anal. Calcd. for 2.44 acetyl, 0.031 tosyl and 0.159 iodine: S, 0.35; I, 7.04. Found (IX): S, 0.32; I, 6.55, 6.51.

Of the original tosyl groups, 0.159 or 84% had been replaced by iodine.

A Desoxy-cellulose Acetate.—The partial tosylation of the acetone soluble acetate (II), 162 g., was carried out as before save that only one-tenth of the previous amount of tosyl chloride was used. This economy was compensated by a reaction time of twenty-four hours instead of three. The mixture was then diluted with 1500 cc. of acetone containing 30 cc. of water and after ten minutes was worked up in the ordinary way; yield, 175 g. or 97%.

Anal. Calcd. for 2.33 acetyl and 0.19 tosyl: S, 2.10. Found (X): S, 2.10.

The iodination of 170 g. of this derivative was with 1400 cc. of acetone and 170 g. of sodium iodide: yield of 6-iodo-cellulose acetate, 165 g. or quantitative. *Anal.* Calcd. for 2.33 acetyl, 0.02 tosyl and 0.17 iodine: S, 0.23; I, 7.67. Found (XI): S, 0.17; I, 7.56, 7.53. Here 89.5% of the original tosyl groups had been replaced by iodine.

The iodo acetate, 20-g. lots, dissolved in 300 cc. of glacial acetic acid on the steam-bath, was stirred vigorously while 100 g. of a zinc–copper couple was added during forty-five minutes. Heating and stirring were continued for a total of five hours. The pasty mass, containing zinc acetate, was then poured into 3000 cc. of water and the precipitate was filtered, washed, dried and extracted with acetone. This extract was centrifuged to remove small particles of zinc and the desoxy acetate precipitated by pouring the concentrated solution into cold, dilute hydrochloric acid. As soon as traces of gray, colloidal zinc had dissolved and the powdery product was perfectly white, it was recovered by filtration, washed well with water and dried. An almost quantitative yield (149 g. from 160 g. of the iodo acetate) of iodine free material was obtained.

Anal. Calcd. for 2.33 acetyl, 0.02 tosyl: acetyl 38.6; S, 0.25. Found (XII): acetyl, 38.6; S, 0.14, 0.25. The reduction had not altered the number of acetyl or tosyl groups.[23]

Examination of the Desoxy Cellulose Acetate.—(a) The customary procedure for furfural analysis[24] gave 0.0338 g. of phloroglucide from 0.7377 g. of material. This phloroglucide resembled that of methylfurfural in being completely soluble in alcohol and in having a red-brown color. In the same circumstances pure α-methylisorhamnoside, 0.0496 g., gave 0.0274 g. of a similar phloroglucide. Calculation from this preliminary calibration experiment showed the presence of 8.3% of methylisorhamnoside residues in the desoxy cellulose acetate. Calcd. from the 6-iodo acetate, 11.6%.

(b) The degradation of 100 g. of the desoxy acetate was accomplished by alternately heating under reflux with 2% methyl alcoholic hydrogen chloride and reacetylating the undissolved residue. When all had been dissolved, the combined, neutralized, alcoholic solutions were concentrated and about 50 g. of crystalline methylglucosides were removed. The residual sirup was hydrolyzed to constant rotation with 5% sulfuric acid on the steam-bath (225 min.), the solution was neutralized, fermented to remove glucose and evaporated to dryness. Acetylation of the residue with acetic anhydride and anhydrous sodium

(23) Our thanks are due to Dr. G. E. Murray for these analyses.

(24) *Ind. Eng. Chem.*, **15**, 748 (1923).

acetate gave 2.7 g. of pure glucomethylose (isorhamnose) tetraacetate with a specific dextrorotation of 21.6° in chloroform (sodium light) and m. p. 145–146° (corr.), not depressed by admixture with an authentic specimen. *Anal.* Calcd. for $C_6H_8O_5(COCH_3)_4$: acetyl, 51.8. Found: acetyl, 52.3, 52.5.

This authentic specimen was prepared from α-methylglucomethyloside by hydrolysis and acetylation exactly similar to that employed above. As the yield was only 52%, 100 g. of the desoxy cellulose acetate contained the equivalent of 2.7 × 100/52 or 5.4 g. of the glucomethylose tetraacetate, *i. e.*, about 25% of the calculated amount.

Viscosities of the above Derivatives.—Staudinger's methods[20] were followed, the solvent being glacial acetic acid at 25 ± 0.1° in every case. An Ostwald type viscometer was used and η_{sp}/c became approximately constant in the range c 0.006 to 0.001 molar glucose residues per liter. The Roman numerals in Table I refer to derivatives and analyses already recorded.

TABLE I

VISCOSITIES OF ACETONE SOLUBLE CELLULOSE ACETATES AND VARIOUS DERIVATIVES

	Calcd. mol. wt.	η_{sp}/c
Derivatives of Acetate I		
Acetate I	264	44.1
Fully tosylated IV	331	39.4
IV, reacetylated V	337	42.9
6-Chlorotosyl VI	298	41.2
6-Iodotosyl VII	322	39.6
Partly tosylated VIII	294	49.1
6-Iodo acetate IX	292	46.6
Derivatives of Acetate II		
Acetate II	260	52.5
6-Chlorotosyl III	324	53.3
Partly tosylated X	289	54.3
6-Iodo acetate XI	282	50.5
6-Desoxy acetate XII	260	6.8[a]

[a] c was 0.03 to 0.01 mole per liter.

Summary

1. *p*-Toluenesulfonyl chloride in pyridine at 20° rapidly esterified about one-third of the free hydroxyl groups in commercial, acetone soluble cellulose acetates. The remainder reacted much more slowly. No removal, and probably no wandering, of acetyl groups occurred.

2. Sodium iodide in acetone at 100°, or hydrogen chloride in pyridine at 85°, smoothly substituted iodine or chlorine atoms for *p*-toluenesulfonyl residues derived from primary, as opposed to secondary, hydroxyls. Analyses of the halogenated mixed cellulose esters indicated that at least one-third of the free hydroxyls in acetone soluble cellulose acetate were in the primary (sixth) positions of the anhydroglucose units.

3. The esterification (1) was interrupted at the end of the initial, rapid reaction and the groups introduced were replaceable to the extent of 85 to 90% by iodine. *p*-Toluenesulfonyl chloride had therefore reacted ten or twelve times as rapidly with the free primary as with the free secondary hydroxyl groups (second and third positions).

4. All the above reactions proceeded almost quantitatively and without appreciable degradation of the cellulose as measured by viscosity methods.

5. The position of iodine in a 6-iodocellulose acetate was confirmed by reduction to a degraded iodine-free desoxy acetate. This gave methylfurfural on distillation with mineral acid and glucomethylose (isorhamnose) after complete hydrolysis. Glucomethylose was identified as the crystalline tetraacetate, m. p. 145–146°, with a specific dextrorotation of 21.6° in chloroform.

CAMBRIDGE, MASS. RECEIVED OCTOBER 17, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, NO. 205]

The Unesterified Secondary Hydroxyls in Acetone Soluble Cellulose Acetate[1]

BY F. B. CRAMER, R. C. HOCKETT AND C. B. PURVES

The examination of a commercial acetone soluble cellulose acetate,[2] containing on the average 2.33 moles of acetyl and 0.67 mole of hydroxyl per glucose unit, led to the conclusion that at least 0.22 mole of the hydroxyl occupied the primary or sixth position in the anhydro-glucose residues.[3] This left not more than 0.45 mole distributed between the second and third positions in an unknown manner. If this distribution was a random one, some of the glucose units along the partly acetylated cellulose macromolecule should be devoid of acetyl in both the second and third positions. In other words, they should contain the —CHOH—CHOH— or glycol grouping. Extensive work[4] has shown that many glycols are oxidized quantitatively to two aldehyde groups by one mole of lead tetraacetate, that secondary reactions are very slow and that semi or complete acetylation thoroughly protects the glycol from the reagent. It was possible, therefore, to investigate the occurrence of 2,3 deacetylation in suitable solutions of cellulose acetates by noting their consumption of lead tetraacetate. This was followed easily by the potassium iodide–sodium thiosulfate method.[5] Both the commercial cellulose acetate and the triacetate prepared from it remained dissolved in a 50% chloroform–acetic acid mixture. The triacetate solution utilized no lead tetraacetate over a period of several days and acetylation thus protected the glycol groups of the anhydroglucose units from oxidation in a satisfactory manner. As expected, the normality of the lead tetraacetate in the acetone soluble acetate solution diminished with time but unfortunately the instability of the solvent[6] interfered with a prolonged examination. This was possible when pure glacial acetic acid was used (Fig. 1). By analogy with the similar behavior of many simple glycosides,[7] the break in the curve (Fig. 1, eighty hours) was taken to mark the end of the true glycol oxidation, and the subsequent much slower change was regarded as an oxidation of another type. With this assumption, inspection of the curve showed that each glucose residue in the acetone soluble cellulose acetate averaged $7 - 10 \times 10^{-3}$ mole of glycol grouping, or one such group was present in every 100–150 glucose residues.

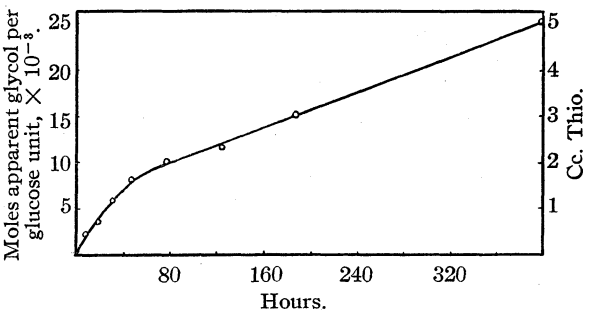

Fig. 1.—Oxidation of acetone soluble cellulose acetate with lead tetraacetate in glacial acetic acid at 25°.

If a partly acetylated cellulose averaged H moles of hydroxyl, randomly distributed along the macromolecule as x moles in the second and $H - x$ moles in the third position, the probability of the glycol grouping is $x(H - x)$ per glucose unit. This probability attains its maximum value of $H^2/4$ when $x = H/2$ or when hydroxyls in the two positions are numerically equal. In the present case, $H = 0.45$ or, at the very least, 0.35 and the probabilities of the glycol group are 0.0506 and 0.0306, respectively, or one occurs in every 20 to 32 glucose residues. The disagreement between this calculated value and the experimental one of one in 100 to 150 shows that the distribution of hydroxyl was by no means a matter of chance.

Although speculation concerning the method of distribution is premature, it seems evident that the assumption of a micellar structure for cellulose acetate in which acetyl had been lost preferentially from the surface of the micelles would lead to calculated ratios lying between 1:2 and 1:32. On the other hand, if the second positions averaged about ten times the number of unesterified hydroxyls as the third, or *vice versa*, calculation would agree approximately with experiment.

(1) Delivered at the Boston meeting of the American Chemical Society, September, 1939.

(2) Kindly given by the du Pont Company. The acetyl content was 38.6%, sulfur 0.007, ash 0.004, and the viscosity in 24% anhydrous acetone solution was 375 poises. It was a high grade sample of the most uniform commercial type.

(3) Cramer and Purves, THIS JOURNAL, **61**, 3458 (1939).

(4) Criegee, *Ber.*, **64**, 260 (1931).

(5) Dimroth and Schweitzer, *ibid.*, **56**, 1375 (1923).

(6) Eventually the thiosulfate blank titration increased and crystalline lead chloride separated owing to slight decomposition of the carefully purified chloroform.

(7) Hockett and McClenahan, THIS JOURNAL, **61**, 1667 (1939).

This would also be true if, in the partial hydrolysis from cellulose triacetate, the loss of acetyl from either one of the two positions tended to stabilize the adjacent group in the same anhydroglucose residue.

Experimental

Materials.—The acetone soluble cellulose acetate was from the batch previously studied[3] and the triacetate was made from it by careful acetylation with pyridine and acetic anhydride. Both were dried over phosphorus pentoxide in a vacuum at 55°.

The chloroform was washed with water and distilled from phosphorus pentoxide while the glacial acetic acid was distilled from chromic anhydride to free it from any aldehyde.

Oxidation with Lead Tetraacetate.—The cellulose acetate, 2.6 g. or 0.01 mole, was dissolved completely in 25 cc. of glacial acetic acid contained in a 100-cc., glass-stoppered volumetric flask. An approximately decinormal solution of lead tetraacetate in the same solvent, 25 cc., was then added at 25° and the volume made up to the mark. The viscid solution required prompt and thorough mixing, after which it was kept at 25 ± 0.5° in the dark. Samples were withdrawn at intervals in a 10-cc. pipet and discharged into 20 cc. of an aqueous solution containing 20 g. of potassium iodide and 250 g. of sodium acetate per liter. The pipet was rinsed well with 5 cc. of the acetic acid and after the addition of the rinsings the liberated iodine was titrated with $N/100$ sodium thiosulfate.[5] Vigorous shaking of the heterogeneous mixtures was necessary during the titrations, which took about five minutes each to complete. The blank on the reagents remained constant at 37.5 cc. of thiosulfate throughout the experiment. Differences from the blank are plotted as the right-hand ordinate in Fig. 1 and at the break in the curve (eighty hours) the 1 millimole sample of cellulose acetate utilized about 2 cc. of $N/100$ sodium thiosulfate. This corresponded to 10^{-5} mole of lead tetraacetate or of glycol. The results of precisely similar experiments, carried out in chloroform–acetic acid solution, are mentioned in the Introduction.

Summary

A commercial acetone soluble cellulose acetate had an average of 0.35 to 0.45 mole of unesterified hydroxyl distributed between the second and third positions of the anhydroglucose units. The unsubstituted —CHOH—CHOH— or glycol groupings it contained were estimated, by means of lead tetraacetate, to occur not more frequently than once in a hundred glucose residues. A significantly greater frequency of once in twenty to thirty was calculated by assuming a purely random distribution of hydroxyl between the two positions.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF FISK UNIVERSITY]

Ricinus communis. I. Oxidation of Ricinoleic Acid

BY ST. ELMO BRADY

The oxidation of ricinoleic acid, its ethyl ester and its isomer, ricinelaidic acid, as well as some of their oxidation products, the trihydroxystearic acids and the *n*-aldehydo-octanoic acid has been studied and the experimental results obtained in these studies are presented in this communication.

Experimental Part

(a) Preparation and Purification of Ricinoleic Acid and Derivatives.—The castor oil was saponified with alcoholic potassium hydroxide, the excess alcohol removed, the potassium salt dissolved in water and the solution exhausted with ether to remove the unsaponifiable materials. These will be the subject of a future investigation. The free fatty acids were liberated with dilute hydrochloric acid, collected and allowed to stand for two days during which time the insoluble acids separated and were removed. The free fatty acids were mixed with an equal volume of alcohol and cooled below zero for several days, when another small portion of insoluble acids separated. The free fatty acids were again converted into the sodium salts using approximately the calculated weight of pure sodium hydroxide dissolved in alcohol. After the removal of the solvent and dilution with water a practically clear solution remained. The barium salt was precipitated from this solution, filtered, dried and refluxed with ether to remove any soluble barium salt present. Several recrystallizations of the barium ricinoleate from alcohol finally gave a white crystalline product that analyzed pure.

The dry salt was suspended in ether and carefully decomposed with dilute hydrochloric acid. After washing thoroughly and drying the ethereal solution over anhydrous sodium sulfate, the solvent was removed in a vacuum desiccator by the aid of the pump. Especial care was exercised not to heat the acid since it polymerizes very easily even at a temperature of 40°. The acid so prepared was of a very slight yellowish tinge, somewhat viscous and perfectly clear. It solidified in the refrigerator at 3–4° to a white waxy solid which melted approximately at 5°.

Anal. Calcd. for $C_{18}H_{34}O_3$: iodine no., 85.1. Found: iodine no., 85.0, 85.1.

Preparation of the Ethyl Ester of Ricinoleic Acid.—The pure ricinoleic acid was dissolved in twice the volume

of absolute alcohol and the temperature reduced to near 0° in a freezing mixture. A stream of dry hydrogen chloride was introduced slowly until the solution was saturated. The solution was then allowed to stand overnight at room temperature. The alcohol was washed out of the solution and the residue taken up with ether. The ethereal solution was shaken several times with a dilute solution of potassium hydroxide, washed with water and dried over anhydrous sodium sulfate. After the removal of the solvent, the ethyl ricinoleate was distilled under reduced pressure and collected at 193–194° (1–2 mm.) or 206° (3–4 mm.). The ester so prepared is water clear.

Anal. Calcd. for $C_{20}H_{38}O_3$: iodine no., 77.91. Found: iodine no. (Hanus), 77.92, 77.93. Refractive index, $n^{25}D$ 1.4595, $n^{26}D$ 1.4590. Specific gravity 20°/20°, 0.9182.

Preparation of the Ethyl Acetylricinoleate.—The ethyl ricinoleate (50 g.) as described above was dissolved in 70 cc. of chloroform, 30 cc. of pyridine added and the solution cooled to 0° in a salt–ice-bath. A slight excess of acetyl chloride was introduced carefully and the solution allowed to remain at the temperature of the bath for two hours and then overnight at room temperature. The excess acid chloride and pyridine were washed out with water, the residue taken up in ether, dried over anhydrous sodium sulfate and the solvent removed. The acetyl derivative was distilled under reduced pressure and collected at 196° (2–3 mm.); refractive index, $n^{27}D$ 1.452; iodine no., 69.1; theoretical, 69.02.

(b) Oxidations. (1) Ethyl Ricinoleate: with Neutral Potassium Permanganate.—Fifty grams of the ester was dissolved in 350 cc. of dry acetone and 200 g. of finely powdered potassium permanganate added during the course of an hour, the solution being refluxed gently during the addition and finally for fifteen hours.

The solvent was then removed, the residue mixed with water and the precipitated oxides of manganese brought into solution by the action of sulfuric acid and sodium bisulfite. After cooling, the acid solution was exhaustively extracted with ether.

The ethereal extract was washed, then repeatedly extracted with sodium carbonate solution (20%) and the combined alkaline extracts shaken with ether to remove any suspended neutral products.

The ethereal solution from the alkaline extract was washed with water, dried, the solvent removed and the resulting oil cooled. The neutral substances amounted to 7.1 g. The odor was somewhat aromatic and pleasant.

Separation of the Acid Products.—The sodium carbonate extract was treated with solid sodium hydroxide dissolved in a little water and heated under the reflux for an hour. This ensured the conversion of any esters into the sodium salts. The cooled solution was acidified and extracted with ether several times. After the removal of the solvent, the residue partially solidified on cooling and amounted to 40.7 g.

The mixture of solid acids was refluxed with five successive portions of petroleum ether (b. p. 40–60°), employing 150 cc. of solvent each time, for one-half hour. The undissolved acids were of a light yellow color and amounted to 22.0 g. About 0.4 g. of solid acid was deposited from the light petroleum which was filtered before the removal of the solvent.

There were 17.1 g. of liquid acids remaining after the evaporation of the petroleum ether. This material was fractionated under reduced pressure several times and the following fractions finally obtained. Fraction 1, b. p. 84–85° (3 mm.), was a colorless, limpid liquid. Calcd. for $C_6H_{11}O_2Ag$: Ag, 48.40; mol. wt., 116. Found: Ag, 48.23; neut. equiv., 128: caproic acid. Fraction 2, b. p. 90–95° (3 mm.), was a colorless liquid, slightly viscous. Calcd. for $C_7H_{13}O_2Ag$: Ag, 45.54; mol. wt., 130. Found: Ag, 45.37; neut. equiv., 128: heptylic acid. Fraction 3, b. p. 95–100° (3 mm.), colorless liquid. Calcd. for $C_8H_{15}O_2Ag$: Ag, 43.00; mol. wt., 147. Found: Ag, 42.87; neut. equiv., 146.8, 146: caprylic acid. Fraction 4, b. p. 159–160 (3 mm.), was a colorless liquid which solidified to a white solid at room temperature. It was recrystallized from petroleum ether and separated in large glistening plates, m. p. 49–50°. Calcd. for $C_9H_{18}O_3$: C, 62.06; H, 10.34; mol. wt., 174. Found: C, 62.15; H, 10.40; mol. wt. (Rast), 176: β-hydroxypelargonic acid.

Purification of the Insoluble Acids.—The crude product insoluble in petroleum ether was dissolved in hot water, filtered from a small quantity of impurities and then heated with decolorizing charcoal. The final filtrate was water-clear and deposited, on cooling, fine needles of m. p. 95°. The crystals had the odor of one of the liquid acids which seemed to persist after several recrystallizations, even though the melting point increased to 104°. To remove this persistent odor, the crystals were refluxed with petroleum ether and filtered hot. The large glistening crystals now had no odor and melted at 106–107°. Further recrystallization did not raise the melting point.

Anal. Calcd. for $C_9H_{14}O_4Ag_2$: Ag, 53.70; mol. wt., 188. Found: Ag, 53.82; neut. equiv., 94; mol. wt. (Rast), 190: azelaic acid.

The dianilide of azelaic acid was prepared and melted at 186.5–187°.

The aqueous filtrate from the above crystallization was evaporated to a small bulk and cooled. A white amorphous solid separated which was removed and dried. This was recrystallized from hot water when small granular crystals separated, m. p. 125–126°. These crystals were thought to contain possibly a small amount of stearic acid and were therefore refluxed with benzene, in which the latter is soluble. On filtering and drying the crystals no increase was noted in the melting point. Because of the variation in the analytical data, the product was recrystallized several times from hot water without any change in the melting point. The crystals were then dissolved in a sufficient volume of ether for the solution and cooled in the refrigerator at 3–4° when a separation of crystals took place. These were filtered off and the solution again cooled for twelve hours when a second crop of crystals was obtained. The solution was then concentrated on the bath and allowed to cool and a third crop of crystals was obtained. The three fractions showed the same melting point, 141°.

Anal. Calcd. for $C_8H_{12}O_4Ag_2$: Ag, 55.64; mol. wt., 174. Found: Ag, 55.52; neut. equiv., 86.4; mol. wt. (Rast), 175: suberic acid.

The ethereal solution from the suberic acid failed to produce additional crystals after standing in the refrigerator for forty-eight hours. The solution was concentrated to a

small bulk and crystals separated which were filtered and dried. These amounted to almost the same weight of the suberic acid and of m. p. 96°. These crystals were not further examined at this time but will be the subject of future investigation as will be true of the neutral products obtained in the oxidation.

(2) **Ricinoleic Acid: with Alkaline Potassium Permanganate.**—Five grams of ricinoleic acid was dissolved in an alkaline solution containing 1.6 g. of potassium hydroxide and made up to 2500 cc. of solution. Ice was then added until the temperature was around 0°. A solution of potassium permanganate (5.3 g. in 250 cc. water) was added hurriedly and the solution stirred for ten minutes, after which time a solution of bisulfite (30 g. in 150 cc. of water) was added and then 70 cc. of 5 *N* hydrochloric acid. During this time ice remained and the stirring was continued until it had melted. The solution amounted to approximately 3000 cc., and was allowed to stand overnight, when a white flocculent precipitate settled. This was collected and dried. The yield of the crude product was practically quantitative.

The crude product was refluxed with petroleum ether (b. p. 40–60°) and the insoluble portion removed. The latter was refluxed with chloroform and the insoluble portion filtered. On cooling the chloroform solution deposited crystals which were filtered and recrystallized from alcohol. On standing, white needle-like crystals separated, m. p. 110°.

Anal. Calcd. for trihydroxystearic acid, $C_{18}H_{36}O_5$: C, 65.06; H, 10.84. Found: C, 65.12; H, 10.90.

The solid insoluble in chloroform was recrystallized from alcohol and white crystals were obtained, m. p. 141°. Recrystallization did not alter the melting point.

Anal. Calcd. for trihydroxystearic acid: mol. wt., 332. Found: neut. equiv., 337, 334; mol. wt. (Rast), 335.

Five grams of ricinoleic acid gave under the conditions of the experiment: 1.80 g. of acid, m. p. 141°; 1.70 g. of acid, m. p. 110°; 1.50 g. of oily product of pleasant odor.

(3) **Ricinelaidic Acid: with Alkaline Potassium Permanganate.**—The ricinelaidic acid was prepared by the action of nitric acid and potassium nitrite on ricinoleic acid. Crystallization from petroleum ether gave a white product, m. p. 51°. The same procedure was used in the oxidation of this acid as with the ricinoleic acid. The product, however, was the acid of m. p. 110° with a very small amount of the acid with m. p. 141°.

(4) **Trihydroxystearic Acid: with Periodic Acid.**—Potassium periodate (6 g.) was dissolved in 200 cc. of *N* sulfuric acid at 20° and was added rapidly to a solution of trihydroxystearic acid, 6 g. in 400 cc. of alcohol at 40°. After ten minutes the clear solution was cooled to 15°, diluted with water to dissolve any potassium sulfate precipitating, and extracted with ether. The ethereal solution, on the removal of the solvent, gave an oily product which was submitted to steam distillation. The aqueous distillate was extracted with ether, the ethereal solution dried over anhydrous sodium sulfate, and the solvent removed. The β-hydroxypelargonic aldehyde gave a semicarbazone, crystallized from alcohol, m. p. 151°. The bisulfite compound crystallized in thin plates, from which the aldehyde was regenerated easily.

The acetyl derivative is a colorless oil, b. p. 61–62°, while the semicarbazone of the β-acetylpelargonic aldehyde forms shining plates from water, m. p. 171°.

Attempted purification of the aldehyde by distillation under reduced pressure resulted in the elimination of water and the formation of an unsaturated aldehyde. This decomposition took place around 100° (3 mm.).

The aqueous solution of the non-volatile product, after the steam distillation, was filtered from a small amount of material and reduced to a small volume. On cooling, an oily product separated which finally solidified on cooling. This was extracted with ether, the ethereal solution dried and the solvent removed. The product was a light yellow solid. The impure *n*-aldehydo-octanoic acid was extracted with boiling petroleum ether (b. p. 40–60°) in which most of the product dissolved. Cooling of the petroleum ether solution in the refrigerator over a long period of time gave small plates which were recrystallized from water and separated in glistening plates, m. p. 40°. The 2,4-dinitrophenylhydrazone crystallized from methyl alcohol in orange prisms, m. p. 121° (King[1] gave 122.5°). The semicarbazone separated immediately in the cold, was recrystallized from alcohol in small, colorless crystals, m. p. 166°, insoluble in light petroleum (Harries and Thieme,[2] gave 166°; King[1] 166.5°).

The oxidation of the trihydroxystearic acid, m. p. 110°, with periodic acid gave the same products and yields equally as good as those obtained from the acid, m. p. 141°.

(5) ***n*-Aldehydo-octanoic Acid: with Acid Permanganate.**—A solution of potassium permanganate containing 2 g. in 100 cc. of water at 50°, was added slowly to a solution of the semialdehyde in 100 cc. of water acidified with sulfuric acid (3.5 g.), until the color of the permanganate persists for several minutes. After decolorizing with a solution of sodium bisulfite, the clear solution was cooled. The deposit of azelaic acid was recrystallized from hot water and gave the characteristic rectangular plates, m. p. 107°, which was unchanged when mixed with an authentic specimen.

Summary

1. Ricinoleic acid and its ethyl ester with theoretical iodine numbers have been prepared.

2. The oxidation of ethyl ricinoleate in dry acetone yields the liquid acids, caproic, heptylic and caprylic; and the solid acids, β-hydroxypelargonic acid, azelaic, suberic, and an acid of m. p. 96°.

3. The oxidation of ricinoleic acid in alkaline permanganate solution at 0° gave two trihydroxystearic acids already known, m. p. 110° and 141°, respectively, in approximately equal amounts. The oxidation of ricinelaidic acid, on the other hand, gave a large percentage of the acid, m. p. 110°, and a small amount of the acid, m. p. 141°.

4. The oxidation of both the trihydroxystearic acids obtained from ricinoleic and ricine-

(1) King, *J. Chem. Soc.*, 1826 (1938).
(2) Harries and Thieme, *Ann.*, **343**, 454 (1905).

laidic acids, respectively, with periodic acid, resulted in the same products, β-hydroxy-pelargonic aldehyde and aldehydo-azelaic acid.

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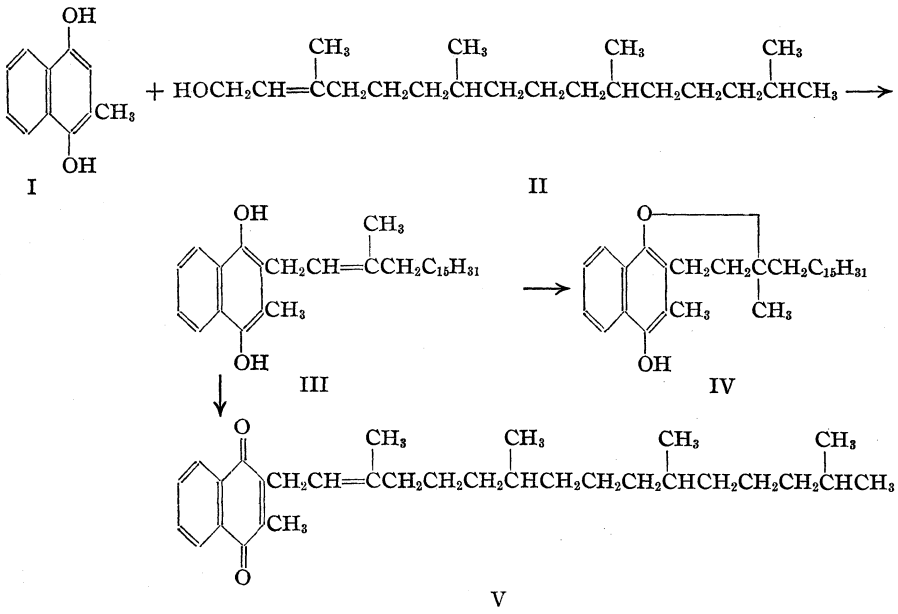
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Synthesis of Vitamin K_1[1]

BY LOUIS F. FIESER

In seeking to apply to the synthesis of vitamin K_1 the method of condensation employed successfully[2] for the synthesis of simple quinones of the structural type postulated[3] for the natural substance, trial was first made[2] of the condensation of 2-methyl-1,4-naphthohydroquinone with an equivalent amount of phytol in molten oxalic acid dihydrate at 140°. A smooth reaction ensued but the product had the properties of the naphthotocopherol IV, rather than of the desired substituted hydroquinone III. The result was much the same on conducting the reaction in the presence of anhydrous oxalic acid in dioxane solution at the reflux temperature.[2] On attempting to avoid the cyclization step by further moderating the conditions, it was found that reaction occurs at a reasonable rate at 75° and there were indications of the formation of 2-methyl-3-phytyl-1,4-naphthohydroquinone (III). A further improvement consisted in using a large excess of methylnaphthohydroquinone (up to 5.7 equivalents) in order to accelerate the bimolecular condensation reaction and thus give it precedence over the monomolecular cyclization. The tabulation of results given in the Experimental Part shows that this definitely increases the yield based upon phytol. The best results were obtained with a reaction time of thirty-six hours; the yield falls off on more prolonged heating, evidently because of cyclization to the naphthotocopherol. The proportion of oxalic acid can be varied considerably without change in the results and this reagent can be replaced by trichloroacetic acid.



The problem of separating the primary product III from the reaction mixture was solved very simply by working with the material in the reduced condition. The unchanged methylnaphthohydroquinone can be separated completely and recovered in a usable condition by extraction of an ethereal solution of the mixture with 1–2% alkali containing sodium hydrosulfite to prevent oxidation, the yellow vat color providing a convenient index of the course of the extraction. The more highly substituted naphthohydroquinone is not extracted from ether even with 25% aqueous alkali, and the separation of the two dihydroxy compounds is therefore very sharp. The impurities retained in the ether, including the naphthotocopherol, phytol, and possibly phytadiene, are all very soluble in petroleum ether whereas methylphytylnaphthohy-

(1) See preliminary communications, THIS JOURNAL, **61**, 2559, 2561 (1939).

(2) Fieser, Campbell, Fry and Gates, *ibid.*, **61**, 2559, 3216 (1939).

(3) Fieser, Bowen, Campbell, M. Fieser, Fry, Jones, Riegel, Schweitzer and Smith, *ibid.*, **61**, 1925 (1939).

droquinone is sparingly soluble in this solvent and separates as a waxy white solid. By repeated centrifugation and digestion with fresh solvent, the substance can be freed completely from contaminants, and no difficulty was experienced in isolating the material from an oil containing as little as 6% of product. Although the substance can be oxidized to the quinone by deliberately shaking an ethereal solution with air, as observed for vitamin K_1 hydroquinone by Doisy, *et al.*,[4,5] no difficulty was experienced in manipulating and evaporating ethereal solutions without protection from the air. When covered with petroleum ether the white solid shows little tendency to undergo air oxidation.

Conversion to the quinone was accomplished by shaking an ethereal solution of the well washed hydroquinone with silver oxide and magnesium sulfate. Evaporation of the filtered yellow solution left a light yellow oil consisting of 2-methyl-3-phytyl-1,4-naphthohydroquinone in a directly pure condition. The substance gives an intense Dam–Karrer color test with alcoholic alkali and the spectrum[1] corresponds closely to the pattern of simple 2,3-dialkyl-1,4-naphthoquinones.[2,3,6,7] That the structure is correctly represented by formula V was inferred from considerations already outlined.[1] The synthesis can be completed in a very short working period and provides a practical method for the preparation of the quinone in quantity. The yield amounts to 44% of the weight of phytol used, or 29% of the theoretical amount.

The synthetic quinone corresponded closely in properties with vitamin K_1 from alfalfa as described by Doisy, *et al.*,[8] and by the Dam–Karrer group.[9] In addition to the properties noted, the substance was found to have high antihemorrhagic activity[1] and to yield a crystalline hydroquinone diacetate. The fully purified derivative melted at 60–61.5° and remelted at 60–60.5°, whereas Doisy's dihydro vitamin K_1 diacetate was reported[4] to melt at 59° (purified sample,[5] m. p. 62–63°). At the time the synthetic diacetate was first isolated in a crystalline condition (Aug. 10) it was known from Doisy's degradative work[10] that the vitamin very probably is either 2-methyl or 2-ethyl-3-phytyl-1,4-naphthoquinone. While Doisy had tentatively favored the latter structure, the close correspondence to the synthetic methyl compound strongly suggested that we had the vitamin in hand. This view was strengthened by the consideration that in this series ethyl compounds melt considerably lower than the methyl homologs, as shown in the following comparison of data previously published.[2] Difference in m. p. between 2-methyl and 2-ethyl compounds:

2-Alkyl-1,4-naphthohydroquinone diacetates	+ 8°
2-Alkyl-1,4-naphthohydroquinone dibenzoates	+16°
2-Alkyl-3-cinnamyl-1,4-naphthohydroquinone diacetates	+44°
2-Alkyl-3-cinnamyl-1,4-naphthoquinones	+ 9°

A direct comparison was of course essential, and it seemed possible that the isolation of the natural vitamin might be accomplished far more easily than heretofore by applying the information and experience gained in the synthesis. While previously reported methods of isolation involve processing the material in the quinone form, it was found that considerable advantage can be taken of the distinctive chemical and physical properties of the vitamin hydroquinone. The starting material was very kindly supplied by Dr. Byron Riegel and consisted of a purified alfalfa concentrate containing 3–5% of vitamin prepared as described by Riegel, Schweitzer and Smith.[11] The vitamin present was reduced by shaking an alcoholic suspension of the concentrate with aqueous sodium hydrosulfite and the material was then extracted with petroleum ether. Unlike the experience of the synthesis, the vitamin hydroquinone did not separate at this point but remained in solution, apparently because of the high proportion and nature of the companion substances. Another method of separation was sought and in trials with pure synthetic 2-methyl-3-phytyl-1,4-naphthohydroquinone it was soon found that this very weakly acidic substance can

(4) Binkley, MacCorquodale, Cheney, Thayer, McKee and Doisy, THIS JOURNAL, **61**, 1612 (1939).

(5) Binkley, MacCorquodale, Thayer and Doisy, *J. Biol. Chem.*, **130**, 219 (1939).

(6) Fieser, Bowen, Campbell, Fry and Gates, THIS JOURNAL, **61**, 1926 (1939).

(7) In this connection belated reference may be made to the extensive study of the spectra of naphthoquinones by Macbeth, Price and Winzor, *J. Chem. Soc.*, 325 (1935). This paper was of considerable value to us in arriving at the conception of vitamins K_1 and K_2 as α-naphthoquinones; the marked similarity of the spectra of the vitamins to that reported by the British investigators for 2,3-diacetoxy-1,4-naphthoquinone was noted by Dr. R. N. Jones on May 19.

(8) McKee, Binkley, MacCorquodale, Thayer and Doisy, THIS JOURNAL, **61**, 1295 (1939).

(9) Dam, Geiger, Glavind, P. Karrer, W. Karrer, Rothschild and Solomon, *Helv. Chim. Acta*, **22**, 310 (1939).

(10) MacCorquodale, Binkley, Thayer and Doisy, THIS JOURNAL, **61**, 1928 (1939).

(11) Riegel, Schweitzer and Smith, *J. Biol. Chem.*, **129**, 495 (1939).

be extracted from petroleum ether with Claisen's alkali (aqueous potassium hydroxide–methanol). When hydrosulfite is added to keep the material in the reduced condition the alkaline liquor acquires a bright yellow vat color which clearly indicates the course of the extraction. The yellow alkaline layer is then separated and merely diluted with water in the presence of ether, when the hydroquinone is liberated from its salt and passes into the ether layer. On processing the reduced concentrate in this way the vitamin hydroquinone was extracted easily and completely, and on evaporation of the ether layer and treatment of the residue with petroleum ether it separated as a white solid. The well washed hydroquinone was then oxidized and afforded a light yellow oil having the characteristics of very pure vitamin K_1. The entire process appears very simple and efficient and avoids difficulties arising from the sensitivity of the vitamin in its oxidized form to heat, light, alkali, and adsorbents.

The sample of natural vitamin K_1 was found by Dr. W. L. Sampson to have the same degree of antihemorrhagic activity as synthetic 2-methyl-3-phytyl-1,4-naphthoquinone. Assayed with chicks by the eighteen-hour procedure,[1] the minimum dose for both substances was approximately 2 γ.[12] The absorption curve determined by D. M. Bowen for the synthetic quinone has already been reported,[1,13] and this corresponds well in form and in the position of the maxima with the curve for vitamin K_1 published by Dam, Karrer, *et al.*[9] A direct comparison of the present samples was kindly made by Dr. T. J. Webb. For the synthetic quinone he found the following maxima (mμ) and log ϵ values (in alcohol): 241(4.18), 248(4.24), 263(4.22), 271(4.23), 330(3.45); the only significant difference between this and Bowen's determination is in placing one of the subsidiary maxima in the region of intense absorption at 263 instead of 260.5 mμ. The maxima for the natural sample occurred at the same wave lengths as above but were slightly lower, the log ϵ values at the several maxima differing by the constant amount of 0.04 unit. This indicates that the natural sample at the time of examination was not quite as pure as the synthetic.

The natural vitamin K_1 gave a crystalline diacetate corresponding in melting point with the synthetic sample and giving no depression when mixed with this substance. While it is perhaps questionable if, among closely related compounds of this series, the absence of a depression in the mixed melting point determination constitutes a rigid proof of identity, it seems significant that the mixture was observed to exhibit the behavior characteristic of both individual samples of solidifying in a few hours and remelting at a sharper and slightly lower temperature. That the synthetic and natural quinone samples give diacetates which thus appear to be identical does not exclude the possibility of the presence in the samples of a certain amount of the geometrical isomer differing from that affording the crystalline diacetate, for the yields of crystalline product in the few reductive acetylations conducted were not quantitative. Although this point merits further investigation, the present indication from the behavior and assay of various samples is that stereoisomerism probably plays a minor role.

Before drawing a final conclusion concerning the identity of the vitamin it seemed desirable to investigate the alternate possibility, and 2-ethyl-naphthohydroquinone was consequently condensed as above with phytol. The reaction proceeded less readily than in the methyl series and the phytyl-substituted hydroquinone proved to be much more soluble in petroleum ether and failed to separate. The method of extraction with Claisen's alkali was successfully applied, but even after removal of all but traces of impurities in this way the substance, in sharp contrast to the behavior noted with both the synthetic methyl compound and the vitamin hydroquinone, did not solidify on treatment with petroleum ether. Oxidation of the unpurified material gave a sample of 2-ethyl-3-phytyl-1,4-naphthoquinone having the characteristic vitamin K type of spectrum but a lower extinction coefficient and estimated from the value found and from the extinction coefficient of the pure synthetic methyl compound to be 95 ± 3% pure (T. J. Webb). Dr. Sampson found this material inactive at a dosage of 160 γ. The lack of activity and the marked contrast in the solubility relationships of the hydroquinone eliminate any possibility of identity with vitamin K_1.

The evidence is therefore conclusive that vitamin K_1 is identical with synthetic 2-methyl-3-phytyl-1,4-naphthoquinone. The conclusion based upon the present synthesis, which was completed before the structure of the vitamin had

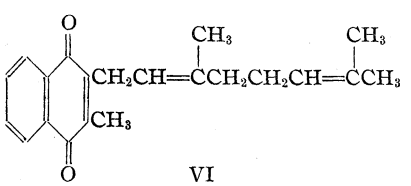
(12) A full account of the assays mentioned in this series of papers will be reported elsewhere by Dr. Sampson.

(13) The log ϵ value for the broad band at 328 mμ was inadvertently printed as 2.42 in place of 3.42.

been established by other evidence, agrees with that reached by Doisy, *et al.*, from degradative experiments[14] and from a further synthesis.[14,15]

In confirmation of a prediction[16] based on the behavior of simpler synthetic models, it has been established that vitamin K_1 (synthetic) yields phthiocol as one product of the Dam–Karrer color reaction with alcoholic alkali.

2,6 - Dimethyl- 3- phytyl - 1,4 - naphthoquinone was synthesized by M. D. Gates, Jr., by the procedure given above and found to be devoid of antihemorrhagic activity at a dosage of 50 γ (W. L. Sampson). D. M. Bowen observed the following absorption maxima (mμ) and log ϵ values in alcohol): 247(4.24), 256.5(4.33), 264.5(4.22), 271-(4.22), 331(3.47). A comparison with Bowen's results[1] for the 2-methyl compound shows that the nuclear methyl group at the 6-position displaces the absorption bands 4.4 mμ (av.) in the direction of longer wave lengths while the logarithm of the extinction coefficient is 0.05 unit higher. A similar shift attending substitution in the benzenoid ring has been observed with simpler models.[16] 2-Methyl-1,4-naphthohydroquinone was condensed under comparable conditions with geraniol and with the diene myrcene, which presumably bears the relationship to geraniol which phytadiene bears to phytol. The reaction proceeded considerably better with the alcohol than with the diene. In each case the substituted hydroquinone separated from petroleum ether in such a gelatinous condition that full purification was not achieved. The quinone obtained from geraniol is referred to as 2-methyl-3-geranyl-1,4-naphthoquinone and assigned the structure VI; it is not yet known whether the product from myrcene is identical with this substance. 2-Methyl-3-geranyl-1,4-naphthoquinone is active at a dosage of 25 γ but not at 5 γ (W. L. Sampson).



VI

(14) Binkley, Cheney, Holcomb, McKee, Thayer, MacCorquodale and Doisy, THIS JOURNAL, **61**, 2558 (1939).

(15) MacCorquodale, McKee, Binkley, Cheney, Holcomb, Thayer and Doisy, *J. Biol. Chem.*, **130**, 433 (1939).

(16) Fieser, Campbell and Fry, THIS JOURNAL, **61**, 2206 (1939). Essentially the same interpretation of the initial phase of the color reaction has been advanced more recently by Karrer, *Helv. Chim. Acta*, **22**, 1146 (1939).

The assay results now available for the series of 2,3-dialkyl-1,4-naphthoquinones for the most part point to a certain specificity in the structures associated with significant antihemorrhagic activity, while the 2,3-dimethyl compound constitutes a rather anomalous example which seems to indicate a lack of such specificity. Since the natural vitamins may be described as 2,3-dialkyl derivatives having at least one long side chain, it is odd that activity[16] should be encountered in the 2,3-dimethyl compound and not in substances more closely related to the vitamins in structure such as the 2,3-diallyl, 2-methyl-3-trimethylallyl, and 2-methyl-3-benzyl compounds. Excepting this anomalous case the results form a consistent picture. Activity begins to appear as the alkyl groups are increased in size beyond the limits just noted (total of 6–8 carbons) and is encountered in the 2-methyl-3-cinnamyl (10 carbons) and 2-methyl-3-geranyl (11 carbons) compounds. Activity reaches a high point in vitamins K_1 and K_2 with a total of 21 and 30 carbon atoms, respectively, in the side chains. The structure 2-methyl-3-phytyl-1,4-naphthoquinone seems highly specific, for the activity is lost on introducing a methyl group into the benzenoid nucleus or enlarging the 2-methyl to an ethyl group.

In view of these indications of specificity it seems very remarkable that the simple and rather remotely related 2-methyl-1,4-naphthoquinone should exhibit striking potency, as first reported by Ansbacher and Fernholz.[17] It is to be noted that early assays in three different laboratories[18,19,20] indicated the compound to be but very weakly active and that the more recent results, while all pointing to a high order of potency, still differ in the exact relative activity assigned to the compound with respect to vitamin K_1. Two groups of investigators[20,21] find the 2-methyl compound about four times as potent as the vitamin, another regards the two compounds as equally active,[22] while according to a third group methylnaphthoquinone "is by no means as active as vitamin K."[23] A possible explanation both for

(17) Ansbacher and Fernholz, THIS JOURNAL, **61**, 1924 (1939).

(18) Thayer, Cheney, Binkley, MacCorquodale and Doisy, *ibid.*, **61**, 1932 (1939).

(19) Almquist and Klose, *ibid.*, **61**, 1923 (1939).

(20) Tishler and Sampson, *ibid.*, **61**, 2563 (1939).

(21) Fernholz and Ansbacher, *Science*, **90**, 215 (1939).

(22) Thayer, Binkley, MacCorquodale, Doisy, Emmett, Brown and Bird, THIS JOURNAL, **61**, 2563 (1939).

(23) Almquist and Klose, *ibid.*, **61**, 2557 (1939). Since this paper was written Almquist and Klose, *J. Biol. Chem.*, **130**, 787 (1939), have observed high potency in the compound when administered orally.

the high potency shown in certain of the chick-assays and for the evident variability of the results is suggested by the present observation that methylnaphthoquinone in the reduced form is a component in a simple synthesis of vitamin K_1 which can be conducted in the laboratory at a moderate temperature and with a mildly active catalyst. It is conceivable that the material administered orally in the assays merely provides one component for a similar synthesis in the organism. The substance in the reduced form may combine with phytol or similar component, available to a greater or less extent according to the nature of the diet and the technique of the assay, giving vitamin K_1 or a related compound. A given amount of the simple quinone could then give rise to as much as 2.6 times its weight of active vitamin, which might account for an apparently greater activity on the weight basis.

The author is indebted to various workers in the Merck Laboratories for their coöperation in conducting the bio-assays and for spectrographic determinations and analyses kindly carried out after the summer closing of the Harvard Laboratory.

Experimental Part[24]

Synthesis of 2-Methyl-3-phytyl-1,4-naphthoquinone.—The procedure found most satisfactory is illustrated by the following experiment. A mixture of 5 g. of 2-methylnaphthohydroquinone, 1 g. of powdered anhydrous oxalic acid, 1.48 g. of phytol, and 15 cc. of dioxane (purified with sodium) was warmed to 75° and shaken to bring the solid into solution. The flask was closed with a stopper carrying a thermometer and heated on a hot-plate for thirty-six hours at 75° (±3–4°). During this time the initially light orange or orange-red solution becomes deep red. The solution was cooled, washed into a separatory with ether, diluted with water, and the mixture extracted with ether. The red ethereal solution was separated, washed with a fresh portion of water, and then extracted with successive 50-cc. portions of 2% potassium hydroxide in which sodium hydrosulfite was dissolved just before use (1–2 g. per 100 cc.). Shaking with the first portion of alkali-hydrosulfite should result in the discharge of the red color and the appearance of a bright yellow alkaline layer; more hydrosulfite is added if the red color persists, while more alkali is used in case the yellow color does not appear. The mixture often forms a rather persistent emulsion and in this case the funnel is kept stoppered until the layers separate in order to avoid oxidation by the air. In the present experiment the unchanged methylnaphthohydroquinone responsible for the yellow vat was nearly all removed in three extractions, and two more were made to eliminate traces of the substance, the fourth being weakly yellow and the fifth colorless. The alkaline extracts were run into a large separatory funnel containing about 50 cc. of ether to protect the solution from oxidation, and after collecting the total yellow liquor in this way it was shaken with the ether and the yellow layer run into another separatory funnel containing 75–100 cc. of ether. Sufficient acetic acid was then added to discharge the yellow color and the liberated methylnaphthohydroquinone was extracted into the ether. The aqueous layer was extracted with a fresh portion of ether and the total extract was dried with magnesium sulfate and evaporated nearly to dryness. The residual cake of hydroquinone was covered with petroleum ether, broken up, collected, and washed with petroleum ether. The recovered material was obtained as a colorless or slightly gray crystalline powder suitable for further use and weighing 3.55 g.

The weakly yellow ethereal solution remaining after extraction with alkali was washed with water and with a small volume of saturated sodium chloride solution, dried with magnesium sulfate and the solvent evaporated, eventually in vacuum, leaving 2.00 g. of a light orange-brown oil. When cooled and rubbed, this had the consistency of a soft wax, and on stirring with 30–50 cc. of petroleum ether (b. p. 20–40°) a fine white solid separated. Lumps of brown wax were disintegrated by rubbing and by digesting the mixture at the boiling point, and the pasty, white suspension was then transferred to centrifuge tubes and cooled in ice. On centrifugation the 2-methyl-3-phytyl-1,4-naphthohydroquinone separated as a white, somewhat waxy, and fairly voluminous sludge. The brownish supernatant liquor was decanted and the solid stirred with a rather liberal quantity of fresh solvent, cooled, and centrifuged, when the liquor was definitely but faintly colored. Evaporation of the combined petroleum ether liquors and washings gave 1.29 g. of residual, dark brown oil.

When the petroleum ether paste of the hydroquinone is covered with a little fresh solvent it may be manipulated or kept for several hours without protection from the air. Two digestions as above seem to give a very pure product, but the substance is so sparingly soluble in cold petroleum ether that the process can be repeated with little loss. The hydroquinone can be dissolved in hot ligroin but separates on cooling as a fine powder which is not easily retained on a filter paper.

For conversion to the quinone the petroleum ether sludge was dissolved in a little dry ether (very soluble) and the colorless solution shaken for twenty minutes with excess silver oxide (1 g.) and magnesium sulfate. The clear yellow solution was evaporated on the hot-plate and the last traces of ether removed in vacuum. (A brownish color observed during the filtration or on evaporation is due to the presence of quinhydrone and indicates incomplete oxidation.) 2-Methyl-3-phytyl-1,4-naphthoquinone was left as a residue in the form of a pure yellow, heavy, but rather mobile oil; yield 0.65 g. (29%, based on phytol). The sample for analysis was dried at 78° and 2 mm. pressure.

Anal. Calcd. for $C_{31}H_{46}O_2$: C, 82.61; H, 10.29. Found: C, 82.76; H, 10.53.

The results of a study of the effect of various changes in the proportions and conditions are given in Table I.

(24) Microanalyses by Lyon Southworth and Herbert S. Wight.

TABLE I

SUMMARY OF YIELDS

Condensation of 1.48 g. (0.005 *m.*) of phytol, or indicated multiple, in dioxane: 10 cc. for 0.86 g. = 0.005 *m.* of the hydroquinone, 15 cc. for larger amounts.

Methylnaphtho-hydroquinone, g.	Condens. agent	Temp., °C.	Time, hrs.	Recov. starting material, g.	Total oil, g.	Residual oil, g.	Yield of quinone, g.
0.86	1 g. $(CO_2H)_2$	Refl.	22	..	1.65	..	0.0
.86	1 g. $(CO_2H)_2$	75	18	0.21	..	1.47	.20
.86	1 g. $(CO_2H)_2$	75	41	.1	1.67	1.49	.11
3	1 g. $(CO_2H)_2$	75	18	1.8	1.97	1.54	.36
3	3 g. $(CO_2H)_2$	75	18	1.92	1.97	1.62	.32
5	1 g. CCl_3CO_2H	75	24	..	1.98	1.40	.53
5[a]	1 g. $(CO_2H)_2$	75	25	3.51	1.96	1.33	.62
5	1 g. $(CO_2H)_2$	75	27	3.56	1.96	1.29	.60
5	1 g. $(CO_2H)_2$	50	27	4.01	1.48	..	.00
5-Fivefold[b]	1 g. $(CO_2H)_2$	75	31	3.35	2.08	1.45	.58
5	1 g. $(CO_2H)_2$	75	36	3.55	2.00	1.29	.65
5-Fourfold	1 g. $(CO_2H)_2$	75	36	3.42	1.98	1.30	.64
5	1 g. $(CO_2H)_2$	75	69	3.72	1.94	1.52	.40

[a] With the addition of 4 g. of anhydrous magnesium sulfate. [b] Exposed to bright sunlight in the daylight hours.

At 50° there was no evidence of reaction and the mobile oil left on extraction with alkali seemed to be unchanged phytol. In the experiment conducted at the reflux temperature the product was a viscous brown oil which gave only a trace of solid when cooled in petroleum ether solution and which evidently consisted very largely of the naphthotocopherol. At the intermediate temperature of 75° the reaction proceeds satisfactorily and the optimum time seems to be about thirty-six hours. The results show that a too prolonged reaction period results in a marked drop in the yield (formation of the naphthotocopherol) and that a large excess of methylnaphthohydroquinone is definitely advantageous. The addition of a drying agent or a threefold increase in the amount of condensing agent does not materially influence the results, and trichloroacetic acid seems to be about as effective as anhydrous oxalic acid. No differences were observed on conducting the condensation on a four- or five-fold scale, or on exposing the solution to bright August sunlight in a Pyrex Erlenmeyer flask. In the latter experiment the solution was flushed with nitrogen at 75° before stoppering the flask.

Properties of the Quinone.—Synthetic 2-methyl-3-phytyl-1,4-naphthoquinone is very soluble in petroleum ether, moderately soluble in acetone, and sparingly soluble in methyl or ethyl alcohol; the solutions are pure yellow. The substance can be caused to separate from acetone in fluffy yellow crystals by cooling in a bath of solid carbon dioxide and rubbing. There was no evidence of decomposition on evaporation of ethereal solutions of the quinone to dryness on the hot-plate, even at atmospheric pressure, or in manipulating the substance in the diffused light of the laboratory, although undue exposure to light was always avoided. On overnight distillation of a 0.7-g. sample with a mercury vapor pump at 150–180° some decomposition occurred, for the distillate was dark reddish-yellow. As initially prepared the quinone has a pure, light yellow color, and a useful test of purity consists in shaking a yellow ethereal solution of the substance with aqueous sodium hydrosulfite. With vigorous shaking the yellow color is slowly discharged and both layers become colorless.

On shaking the quinone with equal volumes of petroleum ether and 90% aqueous methanol, the yellow color seemed to be retained completely in the hydrocarbon layer. Such a distribution was tried as a possible method of isolating the substance from the reaction mixture in the above synthesis. After removal of phenolic starting material the solution was shaken with silver oxide and the total oil (1.91 g.) taken into petroleum ether (40 cc.) and extracted with eight 40-cc. portions of 90% methanol. The extracts were all weakly yellow and when tested by warming with an equal volume of 10% potassium hydroxide the first and second were negative, the third intermediate, and the remainder gave an identical positive response consisting in the appearance of a clear light purple color persisting for one or two minutes. The yellow petroleum ether layer retained 1.41 g. of material which gave a strong but rather dull color test; when shaken with ether–hydrosulfite the color faded slightly to a straw-yellow, and on separation of the hydroquinone from petroleum ether and oxidation there was obtained 0.16 g. of the pure quinone (under the conditions used the total yield should be 0.65 g.). The material collected from the fourth to eighth methanol extracts by back extraction with petroleum ether was a light yellow oil (0.19 g.), but it gave only a weak and dull color with alcoholic alkali and the yellow color was not completely discharged on shaking with ether–hydrosulfite. It therefore appears that while a certain amount of contaminant (phytol?) is removed in one or two distributions between petroleum ether and 90% methanol, the latter solvent then extracts some other (yellow) impurity (naphthotocopherol?) along with small amounts of the quinone.

Dam–Karrer Color Reaction.—The following tests were made with a 10% solution of potassium hydroxide in 95% ethanol. A solution of 1–2 mg. of the quinone in 1 cc. of this solvent when treated with 1–2 drops of the alkali in the cold slowly developed a light purple color (three minutes) which became stronger on warming and then faded in one or two minutes to dull red. On treating a similar solution of the quinone with an equal volume of the alcoholic alkali, a clear intense indigo-blue color appeared

almost at once in the cold. This changed to purple in about one minute and in about three minutes more the dull red end stage had been reached.

In a typical exploratory cleavage experiment 0.62 g. of the quinone was dissolved in 30 cc. of alcohol by warming to about 40° and the solution was treated with 12 cc. of alcoholic potassium hydroxide solution. The solution became indigo blue at once, cloudy (one minute), dull purple (two to three minutes), and then dull red (five minutes). It was diluted, giving a cloudy precipitate, extracted with ether, and the orange-red aqueous layer separated from the brown ethereal solution and acidified. The brown-yellow solution was extracted with ether and the latter shaken with soda solution; the light red extract was acidified and the liberated material taken into ether. Evaporation gave 30–40 mg. of an orange-yellow solid, which was extracted with successive portions of boiling ligroin (b. p. 60–90°). On clarifying and concentrating the solution there was obtained a small amount (2–3 mg.) of a yellow crystallizate melting at 166–168°. The results were not as good when less alkali was used. On conducting the reaction at 0° the indigo-purple phase persisted for about ten minutes. When the alkali was added to the quinone solution at the boiling point the color changes were soon over; the yield of yellow pigment was lower and the bulk of the quinone seemed to be converted into a neutral, bright red oil (isomerization product?).

The combined crude cleavage product from several experiments was further purified by solution in soda and precipitation from the clarified deep cherry-red solution. The crystalline product was then sublimed at 90–105° (2 mm.) and obtained as pure yellow microcrystals, m. p. 170–171°. A mixture of this with a sample of phthiocol, m. p. 171–172°, from the collection of Samuel C. Hooker[25] melted at 171.5–172.5°.

Anal.[26] Calcd. for $C_{11}H_8O_3$: C, 70.21; H, 4.26. Found: C, 70.33; H, 4.29.

2-Methyl-3-phytyl-1,4-naphthohydroquinone Diacetate.—For reductive acetylation 0.50 g. of the synthetic quinone was suspended in 5 cc. of acetic anhydride and treated with 0.5 g. of zinc dust and then, while cooling in ice, with 5 drops of pyridine. A part of the quinone was reduced at once but some adhered to the walls and formed a mat with the zinc. On working this with a spatula under ice cooling the oil soon dissolved to an almost colorless solution leaving the zinc as a clean powder. After ten minutes in the ice-bath and one-half hour at room temperature, acetic acid was added and the mixture boiled and filtered and the residue extracted with acetic acid and with water. After further dilution with water the filtrate was warmed for ten minutes, cooled, and the oily product extracted with ether. After washing with acid, alkali, and water, the solution was dried and evaporated and gave 0.55 g. of the diacetate as a very faintly yellow, viscous oil. An earlier sample prepared in this way and dried at 80° and 2 mm. was analyzed with the following results.

Anal. Calcd. for $C_{35}H_{52}O_4$: C, 78.31; H, 9.77. Found: C, 78.43; H, 10.01.

Even when in a good and analytically pure condition the diacetate often is slow to crystallize. The most successful expedient found was to dissolve the oil in a rather liberal quantity of methanol, cause some of the material to separate as an oil by cooling (well below 0° if necessary), and rub this thoroughly with a stirring rod. Once the oil is obtained in a somewhat waxy condition, solidification usually occurs after standing for a time at room temperature and is further promoted by rubbing and cooling. The first crystallizate was obtained on exposure of an alcoholic solution containing suspended oil to bright sunlight for a few hours in a Pyrex flask, but it now seems likely that the prior rubbing was of more significance than the irradiation. The sample in question melted at 57–59° and the m. p. was the same on forced crystallization from methanol (Found: C, 78.34; H, 9.87). In the experiment referred to above the material crystallized within a few minutes without irradiation and on merely rubbing with methanol and cooling under the tap. The first crop (0.23 g.) softened at 56° and melted at 59.5° to a clear liquid, the behavior resembling that of camphor. Recrystallization from methanol was not very satisfactory, giving a white powder, m. p. 59–60°, and 95% ethanol was used in the further purification with better success. On seeding a not too concentrated alcoholic solution at room temperature and allowing the solution to stand without external cooling, the diacetate slowly formed cottony clusters of fine needles, m. p. (camphor-like) 60.5–63°. The melt solidified within a few hours and remelted sharply at 60–60.5°. After a further crystallization the material had the same appearance and m. p. characteristics. When heated extremely slowly, the sample melted at 60–61.5°; it remelted at 60–60.5°. While the temperature of first remelting seems significant, the m. p. becomes slightly lower on repeating the process, and if the sample is heated to 160° it fails to solidify in the tube.

In duplicate determinations with the best sample of the diacetate, Dr. R. N. Jones found for the extinction coefficient at 230 mμ (absolute ethanol, per cent. by volume) the values $E^{1\%}_{1\,cm.}$ = 1770, 1780. Doisy reports a much lower coefficient (1250,[4] 1300, or 1600[5]). It may be noted that the extinction coefficient for the quinone found both in this Laboratory[1] and by Dr. Webb ($E^{1\%}_{1\,cm.,\ 248\ m\mu}$ = 386) agrees with Doisy's first value (385[8]) but not with that more recently reported (540[4]).

The **dibenzoate** was prepared by adding pyridine to a petroleum ether sludge of the hydroquinone, removing the hydrocarbon solvent in vacuum, and adding benzoyl chloride. After standing overnight water was added and the product extracted with ether. The solution was washed well with dilute acid, 10% alkali and water and afforded a rather yellow, oily product on evaporation. After various trials the dibenzoate was obtained crystalline from alcohol, exposing the solution to direct sunlight, and melted at 85–86°. Recrystallization from methanol gave slightly waxy white nodules of the same m. p. and the small sample was not purified further.

Anal. Calcd. for $C_{45}H_{56}O_4$: C, 81.77; H, 8.54. Found: C, 81.63; H, 8.59.

2,6-Dimethyl-3-phytyl-1,4-naphthoquinone (M. D. Gates, Jr.).—The 2,6-dimethyl-1,4-naphthohydroquinone required as starting material was prepared by reduction of the quinone (11.5 g.) in suspension in alcohol (110 cc.)

(25) S. C. Hooker, THIS JOURNAL, **58**, 1174 (1936).

(26) Microanalysis conducted at the Merck Research Laboratory.

with stannous chloride (45 g.)–hydrochloric acid (50 cc.); water (100 cc.) was added, the solution was boiled with Norite, filtered (with the addition of 50 cc. of alcohol), and diluted with 100 cc. of water. The product separated as fine, slightly pink needles; yield 9.9 g. (85%). A solution of 4 g. of this material, 1.48 g. of phytol, and 1 g. of anhydrous oxalic acid in 15 cc. of dioxane was heated at 70–80° for twenty-four hours. The reaction mixture was worked up exactly as described in the above example, the recovered hydroquinone amounting to 2.37 g. and the yield of quinone being 0.54 g. In another experiment using 5 g. of starting material the yield was 0.59 g. The quinone was obtained as a viscous yellow oil having a slight reddish tinge. The Dam–Karrer color test is the same as with the lower homolog.

Anal. Calcd. for $C_{32}H_{48}O_2$: C, 82.70; H, 10.41. Found: C, 82.53; H, 10.44.

The **hydroquinone diacetate,** prepared as above, was obtained as a solid without difficulty from methanol, but the substance did not form good crystals from either methanol or ethanol. It separated as gelatinous masses which shrank to hard, solid granules on drying. When heated at the ordinary rate the substance melted at 55–56.5°.

Anal. Calcd. for $C_{36}H_{54}O_4$: C, 78.50; H, 9.88. Found: C, 78.84; H, 9.88.

2-Methyl-3-geranyl-1,4-naphthoquinone.—On heating 2 g. of methylnaphthohydroquinone, 1.13 g. of geraniol, 1 g. of anhydrous oxalic acid, and 10 cc. of dioxane at approximately 84° for twenty-four and one-half hours and working up the mixture by the above procedure, 1.0 g. of starting material was recovered and on adding petroleum ether to the alkali-insoluble oil the substituted hydroquinone separated as a voluminous white gel. The precipitated material was so gelatinous that removal of the impurities in the mother liquor was difficult. The substance was stirred and centrifuged with three additional portions of petroleum ether, but probably still retained impurities, as seen from the analysis below. Oxidation with silver oxide gave 0.26 g. of the quinone as a viscous yellow oil tinged slightly with red. A solution of the quinone in alcohol when treated with an equal volume of 10% alcoholic potassium hydroxide gave an intense indigo-blue solution changing to purple and then dull red. Yellow crystals resulted on cooling a methanol solution to −70°.

Anal. Calcd. for $C_{21}H_{24}O_2$: C, 81.78; H, 7.85. Found: C, 81.22; H, 8.01.

A parallel experiment was carried out with the quantities given above but replacing the geraniol by an equivalent quantity of myrcene (1.00 g.). The mixture was kept at 90–95° for twenty-four hours. Extraction with dilute alkali gave 1.31 g. of recovered starting material and left 1.0 g. of dark oil. The latter afforded a very small quantity of substituted hydroquinone as a petroleum ether sludge and on oxidation this afforded 79 mg. of the quinone as a yellow (slightly dark) oil (Found: C, 81.16, 81.24; H, 7.88, 7.99).

2-Ethyl-3-phytyl-1,4-naphthoquinone.—A mixture of 4.8 g. of 2-ethyl-1,4-naphthohydroquinone, 1.48 g. of phytol, 1 g. of anhydrous oxalic acid, and 15 cc. of dioxane was heated at 75° for twenty-four hours, diluted with water, extracted with ether, and the unchanged hydroquinone removed as usual. A brown oil (1.85 g.) of the usual appearance was obtained from the alkali-insoluble fraction, but this dissolved readily in petroleum ether and the substituted hydroquinone failed to separate even on cooling well below 0°. A partial purification was accomplished by shaking this in ether with silver oxide and magnesium sulfate and extracting a petroleum ether solution of the oxidized product with two portions of 90% methanol. Evaporation of the petroleum ether layer gave 1.37 g. of a rather reddish oil giving with alcoholic alkali a strong greenish-blue color changing to purple and then dull red. A fairly sharp separation finally was made by the extraction procedure described in detail below as applied to the isolation of vitamin K_1. Following the same procedure, 1.21 g. of the reddish oil was reduced in alcoholic suspension and a petroleum ether solution of the reduced material extracted with Claisen's alkali and hydrosulfite. On dilution of the yellow liquor with water, extraction with ether, and evaporation there was obtained 0.28 g. of crude substituted hydroquinone as a brownish oil which still failed to yield a solid from petroleum ether and which consequently was oxidized with silver oxide to the quinone (0.27 g.). This was obtained as a yellow (slightly dark) oil giving, when warmed with 5% alcoholic potassium hydroxide, an intense indigo-blue changing to purple and then dull red. On reductive acetylation it gave a clear, nearly colorless oil which failed to crystallize from methanol.

Isolation of Natural Vitamin K_1.—The starting material supplied by Dr. Riegel was described by him as an alfalfa concentrate containing 3–5% vitamin. In the Dam–Karrer test it gave a pale but distinct transient purple in dilute solution and a quite strong purple at higher concentrations. A 5.32 g. portion of the viscous yellow oil was suspended in 90 cc. of alcohol at room temperature, a fresh solution of 4.5 g. of sodium hydrosulfite in 30 cc. of water was added, the flask was stoppered, and the mixture containing oil droplets and precipitated salts was shaken vigorously for ten minutes. After adding 50 cc. of water to dissolve the salts the mixture was shaken again for ten minutes.[27] The suspension of light yellow oil was diluted further and extracted with about 100 cc. of petroleum ether and the weakly yellow solution was shaken thoroughly with 5% potassium hydroxide containing 1–2% of hydrosulfite, the colorless aqueous layer being separated and discarded (no precipitate with acetic acid). The petroleum ether solution was then extracted with 50 cc. of Claisen's alkali[28] to which 3 cc. of saturated aqueous hydrosulfite had been added, the alkaline liquor acquiring a bright yellow color characteristic of the salt of the vitamin hydroquinone. The solution is cloudy and apparently contains suspended salt, but a fairly clean separation is possible. The yellow alkaline layer was drawn off into a separatory funnel containing 50 cc. of ether, and two further extractions were made, the last being only pale yellow. The unextracted material recovered from the petroleum ether was a yellow oil weighing 4.61 g. The total alkaline liquor was shaken with the covering layer of

(27) When the pure synthetic vitamin is reduced by the above procedure the hydroquinone separates at this point as a white solid.

(28) Prepared from 35 g. of potassium hydroxide in 25 cc. of water, diluted to 100 cc. with methanol; Claisen, *Ann.*, **418**, 96 (1919).

ether, adding a little petroleum ether to facilitate the settling of the (colorless) ether layer. (If darkening occurs at any time in the ether layer due to oxidation, more hydrosulfite is added.) The washed yellow liquor was then run into another separatory funnel containing 50 cc. of ether and diluted with 2–3 volumes of 2–4% aqueous hydrosulfite solution (the hydroquinone is particularly sensitive to oxidation when in contact with aqueous alcohol). The dilution results in liberation of the free hydroquinone with disappearance of the yellow color, and on shaking the mixture the substance passes into the ether layer to give a pale yellowish solution. This was separated, washed with aqueous hydrosulfite solution and with water, dried and evaporated. The residual pale reddish-brown oil (0.17 g.) became waxy on cooling, and on adding 10 cc. of petroleum ether the vitamin hydroquinone separated at once as a fine white solid. The suspension was iced and centrifuged and the white sludge stirred with fresh solvent and the process repeated. The purified material was taken up in dry ether and shaken for one-half hour with silver oxide and magnesium sulfate. The filtered yellow solution on evaporation, eventually under vacuum, left a residue of 60 mg. of vitamin K_1 in the form of a pure yellow, rather mobile oil.

Anal.[26] Calcd. for $C_{31}H_{46}O_2$: C, 82.61; H, 10.29. Found: C, 82.64; H, 10.20.

The behavior in the Dam–Karrer test was exactly as described for the synthetic material.

Vitamin K_1 hydroquinone diacetate was obtained by reductive acetylation of 35 mg. of the quinone by the pyridine procedure and obtained initially as a colorless oil (40 mg.). After suitable rubbing in methanol (one hour) this formed waxy, semi-solid masses, and on standing overnight at room temperature with exposure to the morning sun solid particles appeared. On rubbing, the wax all went to a good white powder which was collected after cooling and afforded 6 mg. of material melting at 57–59.5° (camphor-like) and remelting at 57–58.5°. Recrystallized from 95% ethanol the substance formed compact clusters of microneedles, m. p. 58.5–60°.

Anal.[26] Calcd. for $C_{35}H_{52}O_4$: C, 78.31; H, 9.77. Found: C, 78.13; H, 10.11.

A mixture of this substance with the best sample of synthetic 2-methyl-3-phytyl-1,4-naphthohydroquinone diacetate melted at 59.5–61.5°. The melt solidified in about one hour and remelted sharply at 59.5–60°. Dr. E. A. Doisy kindly compared the synthetic diacetate with a sample of the natural vitamin K_1 hydroquinone diacetate prepared in his laboratory (m. p. 61.5–63°) and found that a mixture of equal parts melted at 59.5–61.5°.

Summary

2-Methyl-3-phytyl-1,4-naphthoquinone has been synthesized and found identical with natural vitamin K_1 from alfalfa by a direct comparison of samples with regard to analysis, spectrum, antihemorrhagic activity, color reaction, and the melting point and mixed melting point of a crystalline derivative.

The synthesis is an essentially one-step process utilizing 2-methyl-1,4-naphthohydroquinone and phytol and provides a practical method of preparing the vitamin in quantity. By separating and purifying the product in the reduced form prior to oxidation, the quinone is obtained in a pure condition without recourse to distillation or adsorption. Natural vitamin K_1 can be isolated very easily from alfalfa concentrates by a similar procedure.

Vitamin K_1 yields phthiocol on cleavage with alcoholic alkali.

The 2-ethyl-3-phytyl and 2,6-dimethyl-3-phytyl derivatives of 1,4-naphthoquinone were synthesized and found inactive in the chick-assay, while 2-methyl-3-geranyl-1,4-naphthoquinone shows moderate potency. Indications of a certain structural specificity are discussed and a tentative hypothesis is suggested concerning the action of 2-methyl-1,4-naphthoquinone.

CONVERSE MEMORIAL LABORATORY
CAMBRIDGE, MASSACHUSETTS

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[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. LXXVIII. Sterols from Sow Pregnancy Urine

BY RUSSELL E. MARKER AND EWALD ROHRMANN

The fact that mares pregnancy urine has been shown recently to exhibit some interesting differences[1] from the other pregnancy urines which have been studied indicates the desirability of further investigations of pregnancy urines of other animals.

The present preliminary investigation of sow pregnancy urine indicates that this urine is strikingly different from the other urines studied. Sow pregnancy urine differs from other urines mainly in the absence of the three common pregnanediols which have been found in all of the other pregnancy urines heretofore investigated. However, both pregnanol-3(α)-one-20 and *allo*-pregnanol-3(β)-one-20 were isolated from the ketonic sterol fraction. The presence of these two products and the absence of pregnanediols suggests that the sow in the course of the *in vivo* reduction of progesterone[2] is unable to effect the reduction of a C-20 carbonyl group to a C-20 carbinol. This also receives support from the fact that progesterone has been isolated from sow ovaries.[3]

The *epi*-ketone fraction remaining after the removal of pregnanol-3(α)-one-20 when treated with hydroxylamine acetate yielded an oxime which appears to be identical with androsterone oxime, thus indicating the presence of androsterone. This lends further support to the theory that these products are derived from the adrenal compounds. Callow[4] has recently suggested that *trans*-dehydroandrosterone is probably derived from the adrenal cortical secretions and not from testosterone. It should be pointed out that from the generalizations previously made in regard to the origin of these substances,[2,5] both androsterone and *trans*-dehydroandrosterone may be derived from the adrenal cortical secretions and it is not necessary to assume that they are reduction products of $\Delta^{4,5}$-androstenedione-3,17.

Both cholesterol and the characteristic urinary hydrocarbon[1,6,7] of the composition $C_{28}H_{58}$ were isolated from the sow urine. β-Equistanol[8,9,10] was not encountered.

There appear to be other C-3 beta sterols present in the sow pregnancy urine but these could not be isolated from the quantity of urine studied. No apparent differences were observed in urine collected during the second month of pregnancy and during the last month of pregnancy.

This investigation was supported by a grant from the Committee for Research in Problems of Sex, National Research Council.

Experimental Part

To 30 gallons (110 liters) of sow pregnancy urine, collected from Chester sows during the last month of pregnancy was added enough concentrated hydrochloric acid to bring it to a *p*H of 1. The urine was then heated at 100° for three hours, thoroughly extracted with butanol, and the solvent removed *in vacuo*. The residue, consisting of a black tar, was steam distilled for two hours from aqueous sodium hydroxide. The neutral products were extracted with ether and the solvent removed.

The total neutral fraction (14 g.) was dissolved in pyridine (20 cc.) and 10 g. of succinic anhydride was added. The mixture was heated for ninety minutes on the steam-bath, after which ether and water were added and the pyridine removed by dilute hydrochloric acid. The succinates were removed from the ether by potassium carbonate solution, and hydrolyzed by boiling with alcoholic potassium hydroxide.

Hydrocarbon Fraction.—The non-carbinol fraction was treated with Girard's reagent in alcohol, but only a negligible amount of ketones was obtained. The non-ketonic fraction was then sublimed in high vacuum at 80–100° and the sublimate crystallized from acetone to give white plates, m. p. 60–63°. It gave no depression in melting point when mixed with the urinary hydrocarbon obtained from mares pregnancy and human pregnancy urine, m. p. 61–63°.

Anal. Calcd. for $C_{28}H_{58}$: C, 85.3; H, 14.8. Found: C, 85.1; H, 14.8.

The carbinol fraction was dissolved in a small amount of alcohol and treated with 10 g. of digitonin dissolved in 500 cc. of hot 90% ethanol. The digitonide was allowed to stand overnight, filtered, washed and dried; yield, 8.6 g. The digitonide was heated on the steam-bath for one hour with 25 cc. of dry pyridine and the solution poured into ether and filtered. The pyridine was removed from the filtrate by dilute hydrochloric acid and the ether was evaporated to 1.9 g. of oily residue.

(1) Marker and Rohrmann, THIS JOURNAL, **61**, 2537 (1939).
(2) Marker, THIS JOURNAL, **60**, 1725 (1938).
(3) Fieser, "Chemistry of Natural Products Related to Phenanthrene," 2d ed., Reinhold Publishing Corp., New York, N. Y., 1937, pp. 241 ff.
(4) Callow, *Biochem. J.*, **33**, 559 (1939).
(5) Marker and Lawson, THIS JOURNAL, **60**, 2928 (1938).
(6) Marker, *ibid.*, **60**, 2442 (1938).
(7) Marker, *ibid.*, **61**, 1287 (1939).
(8) Marker, Lawson, Rohrmann and Wittle, *ibid.*, **60**, 1555 (1938).
(9) Marker, Wittle and Lawson, *ibid.*, **60**, 2931 (1938).
(10) Marker and Rohrmann, *ibid.*, **60**, 1565 (1938).

The ketones were spearated from the beta-sterols by means of Girard's reagent in the usual manner. These were sublimed in high vacuum and the fraction distilling from 100–200° was collected. The sublimate was crystallized from ether–pentane to give white crystals, m. p. 191–193°. This gave no depression in melting point when mixed with *allo*-pregnanol-3(β)-20-one, m. p. 193–194°.

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.2; H, 9.9. Found: C, 79.0; H, 9.6.

No other crystalline products could be obtained from the mother liquors.

beta-Non-ketonic Sterols.—The fraction of non-ketonic, digitonin precipitable sterols was sublimed in high vacuum, the fraction subliming at 100–200° being collected. This was crystallized from ether–pentane and then from ethanol, to give white crystals, m. p. 146–147°. This gave no depression in melting point when mixed with an authentic sample of cholesterol, m. p. 147–148.5°.

Anal. Calcd. for $C_{27}H_{46}O$: C, 83.9; H, 12.0. Found: C, 83.8; H, 11.9.

No additional crystalline products were obtained from the mother liquors. The solvent was evaporated and the residual tar oxidized by chromic anhydride in acetic acid at 25°. The small ketone fraction obtained was treated with semicarbazide acetate. None of the extremely insoluble disemicarbazone of *allo*-pregnanedione could be isolated, indicating the absence of *allo*-pregnanediol-3(β), 20(α).

Epimeric Ketones.—The fraction of sterols not precipitated by digitonin was treated with Girard's reagent in alcohol in the usual manner. The hydroxy ketones were sublimed *in vacuo*, the fraction subliming at 100–200° being collected. The sublimate was crystallized repeatedly from ether–pentane to give white crystals, m. p. 139–142°. This gave no depression in melting point when mixed with epipregnanolone, m. p. 144°.

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.2; H, 9.9. Found: C, 79.1; H, 9.7.

The filtrate was evaporated and the residue dissolved in 5 cc. of ethanol. To this was added 600 mg. of sodium acetate and 500 mg. of hydroxylamine hydrochloride and the solution heated four hours at 90°. Water was added and the gum which deposited was crystallized from 60% ethanol and then from 80% acetone to give white crystals, m. p. 210–212°. This gave no depression in melting point when mixed with the oxime of androsterone, m. p. 212–214°.

Anal. Calcd. for $C_{19}H_{31}O_2N$: C, 74.7; H, 10.2. Found: C, 74.2; H, 10.1.

The epimeric non-ketonic sterol fraction was sublimed in high vacuum. The sublimate could not be obtained crystalline. The total sublimate was oxidized by chromic anhydride in acetic acid at 25° and the ketonic fraction isolated from the mixture by means of Girard's reagent. Only a small amount of ketones was obtained which resisted crystallization after sublimation. These were treated with semicarbazide hydrochloride and sodium acetate in alcohol. The semicarbazones which were formed were extremely soluble in cold ethanol. Since *allo*-pregnanedione forms a very insoluble semicarbazone, even in boiling alcohol, the absence of this product is indicated.

Fifteen gallons (55 liters) of urine collected during the second month of pregnancy of the hogs gave the same results as those reported above.

Summary

Sow pregnancy urine differs from other pregnancy urines studied in that the pregnanediols appear to be absent.

Pregnanol-3(α)-one-20, *allo*-pregnanol-3(β)-one-20, cholesterol and the urinary hydrocarbon were isolated.

Evidence of the presence of androsterone was obtained.

STATE COLLEGE, PENNA. RECEIVED OCTOBER 23, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. LXXIX. Oxidation Products of Dihydrosarsasapogenin

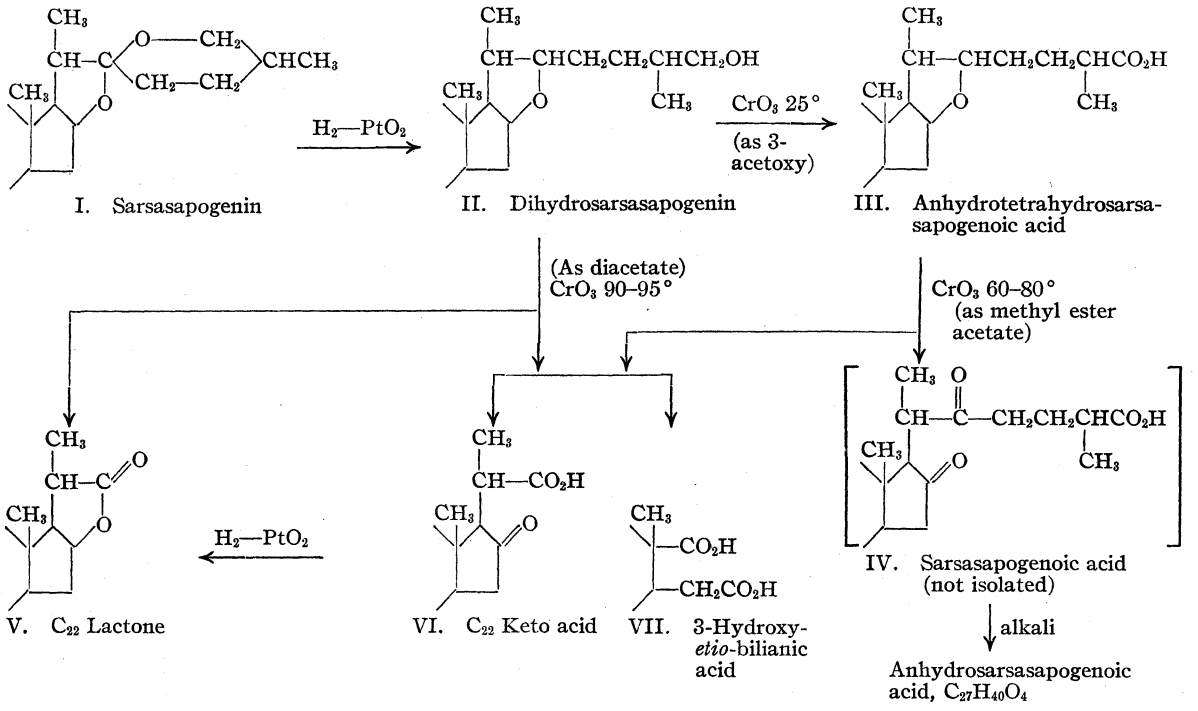
BY RUSSELL E. MARKER AND EWALD ROHRMANN

In order to obtain further evidence concerning the structure of the side chain of sarsasapogenin (I),[1] we have oxidized with chromic anhydride the methyl ester acetate of anhydrotetrahydrosarsasapogenoic acid (III) (obtained both from sarsasapogenoic acid by catalytic hydrogenation and from 3-acetoxydihydrosarsasapogenin by mild oxidation) and by treatment of the neutral fraction from the oxidation with aqueous ethanolic alkali have obtained a good yield of an acid identical with anhydrosarsasapogenoic acid. This indicates that the methyl ester acetate of sarsasapogenoic acid was formed in the oxidation and was in turn converted to the anhydro acid by the alkali treatment. In this reaction sarsasapogenoic acid could only have arisen from the oxidative opening of an oxide ring to yield a diketo compound, thus supporting IV which we recently proposed[2] for sarsasapogenoic acid.

Further support of the structure assigned to di-

(1) Marker and Rohrmann, THIS JOURNAL, **61**, 846 (1939).

(2) Marker and Rohrmann, THIS JOURNAL, **61**, 2072 (1939).



hydrosarsasapogenin[1] (II) has been obtained from a study of its oxidation products. The oxidation of the diacetate with chromic anhydride at 90–95° yielded a neutral fraction from which the C_{22} lactone[3] was isolated. The acidic fraction (extractable with 3% sodium hydroxide) yielded the C_{22} keto acid[4] (IV) and the C_{19} dibasic acid[5] (VII).

We wish to thank Parke, Davis and Company for the generous help and assistance rendered during the course of this work.

Experimental Part[6]

Oxidation of the Diacetate of Dihydrosarsasapogenin.—A mixture of 20 g. of dihydrosarsasapogenin, m. p. 165–166°, and 200 cc. of acetic anhydride was refluxed for thirty minutes. The acetic anhydride was evaporated *in vacuo* and the residual sirup dissolved in 400 cc. of acetic acid. The well stirred solution was heated at 90–95° on a steam-bath while 44 g. of chromic anhydride in 250 cc. of 80% acetic acid was added over a period of two hours, after which the mixture was heated for an additional two hours. The mixture was concentrated *in vacuo* to a volume of about 100 cc. The residual material was diluted with water and the precipitated solids taken up in ether. The ethereal solution, after thorough washing with water, was washed twice with 3% sodium hydroxide solution to remove the acidic fraction.

The ether solution containing the neutral material was evaporated to a sirup which was hydrolyzed by refluxing with an excess of ethanolic potassium hydroxide. The resulting solution was diluted with water and the precipitated solid taken up in ether. The alkaline water layer was washed several times with ether. Evaporation of the combined ether extracts gave approximately 2 g. of a neutral sirup which was not investigated further. The alkaline water layer was acidified with hydrochloric acid and the mixture extracted with ether. Evaporation of the ether gave almost 600 mg. of crude lactonic material (noncrystalline). This was sublimed in high vacuum and the material distilling at 140–160° was crystallized from ether–pentane to give fine white needles, m. p. 200–201.5°. This gave no depression with the hydroxy lactone of sarsasapogenin, m. p. 200–201.5°.

Anal. Calcd. for $C_{22}H_{34}O_3$: C, 76.25; H, 9.9. Found: C, 76.1; H, 9.9.

The sodium hydroxide washings containing the acidic material from the oxidation was heated on the steam-bath for twenty minutes to complete the hydrolysis. The cooled mixture was acidified with hydrochloric acid and the precipitated acids taken up in ether. Upon standing the ethereal solution deposited 600 mg. of small compact white crystals which were recrystallized once from methanol to give a product, m. p. 285–288° dec. This gave no depression with a sample of the C_{22} keto acid previously reported,[4] m. p. 285–287° dec.

Anal. Calcd. for $C_{22}H_{34}O_4$: C, 72.9; H, 9.5. Found: C, 72.5; H, 9.3.

The filtrate remaining after removal of the C_{22} keto acid was evaporated and the residual sirup crystallized from chloroform to give 1.9 g. of white crystals, m. p. 219–222°. This gave no depression with a sample of the C_{19} dibasic acid,[5] m. p. 220–222°.

Anal. Calcd. for $C_{19}H_{30}O_5$: C, 67.4; H, 8.9. Found: C, 67.2; H, 9.0.

When refluxed for thirty minutes with acetic anhydride

(3) Farmer and Kon, *J. Chem. Soc.*, 414 (1937).
(4) Marker and Rohrmann, THIS JOURNAL, **61**, 1285 (1939).
(5) Marker and Rohrmann, *ibid.*, **61**, 2722 (1939).
(6) Micro-analyses by Dr. John R. Adams, Jr., of this Laboratory.

the acid formed the **acetate anhydride,** m. p. 202–203.5°. This gave no depression with a previously reported sample,[5] m. p. 203–204°.

Anal. Calcd. for $C_{21}H_{30}O_5$: C, 69.6; H, 8.3. Found: C, 69.7; H, 8.3.

Conversion of Anhydrotetrahydrosarsasapogenoic Acid to Anhydrosarsasapogenoic Acid.—The methyl ester of anhydrotetrahydrosarsasapogenoic acid was prepared by refluxing the acid (prepared from 3-acetoxydihydrosarsasapogenin) in methanol solution acidified with sulfuric acid. The ester, m. p. 124–126°, was identical with that obtained by the action of diazomethane on the acid.

A mixture of 7 g. of the methyl ester and 60 cc. of acetic anhydride was refluxed for thirty minutes. The acetic anhydride was evaporated *in vacuo* and the residual sirup dissolved in 200 cc. of acetic acid. To this well-stirred solution heated at 55–60° was added 10 g. of chromic anhydride in 80 cc. of 80% acetic acid over a period of two hours. The mixture was heated for an additional two hours at 55–60° and then for one hour at 80°. The excess chromic anhydride was destroyed with 5 cc. of ethanol and the mixture was evaporated *in vacuo* to a volume of approximately 75 cc. The mixture was diluted with water and the solid extracted with ether. The ethereal extract was washed with water and then twice with 3% sodium hydroxide solution.

The ethereal solution containing the neutral material was evaporated to give approximately 2 g. of sirup. This was dissolved in 30 cc. of 95% ethanol and to this solution was added 3 g. of potassium hydroxide and 15 cc. of water. The solution, after refluxing for two hours, was diluted with water and the resulting clear solution acidified with hydrochloric acid. The precipitated acid was taken up in ether. The ethereal solution was evaporated to a volume of about 30 cc. when 575 mg. of compact white crystals separated. These were recrystallized once from methanol–ether to give a product with m. p. 243–245° dec. This gave no depression with a sample of anhydrosarsasapogenoic acid prepared from sarsasapogenoic acid, m. p. 242–244°.

Anal. Calcd. for $C_{27}H_{40}O_4$: C, 75.7; H, 9.4. Found: C, 75.6; H, 9.4.

The acidic fraction from the oxidation yielded the C_{22} keto acid, m. p. 283–285°.

A similar oxidation of the methyl ester acetate of anhydrotetrahydrosarsasapogenoic acid (1.45 g.) prepared from sarsasapogenoic acid by catalytic hydrogenation yielded the C_{22} keto acid, m. p. 284–286° dec.

Anal. Calcd. for $C_{22}H_{34}O_4$: C, 72.9; H, 9.5. Found: C, 72.6; H, 9.4.

The acidic filtrate from this yielded 3-hydroxy-*etio*-bilianic acid, m. p. 219–221°.

Anal. Calcd. for $C_{19}H_{30}O_5$: C, 67.4; H, 8.9. Found: C, 67.2; H, 9.0.

The neutral fraction from the oxidation upon treatment with aqueous ethanolic potassium hydroxide as described previously yielded anhydrosarsasapogenoic acid, m. p. 243–245° dec.

Anal. Calcd. for $C_{27}H_{40}O_4$: C, 75.7; H, 9.4. Found: C, 75.9; H, 9.4.

Summary

The chromic anhydride oxidation products of dihydrosarsasapogenin have been studied.

STATE COLLEGE, PENNSYLVANIA
RECEIVED SEPTEMBER 25, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

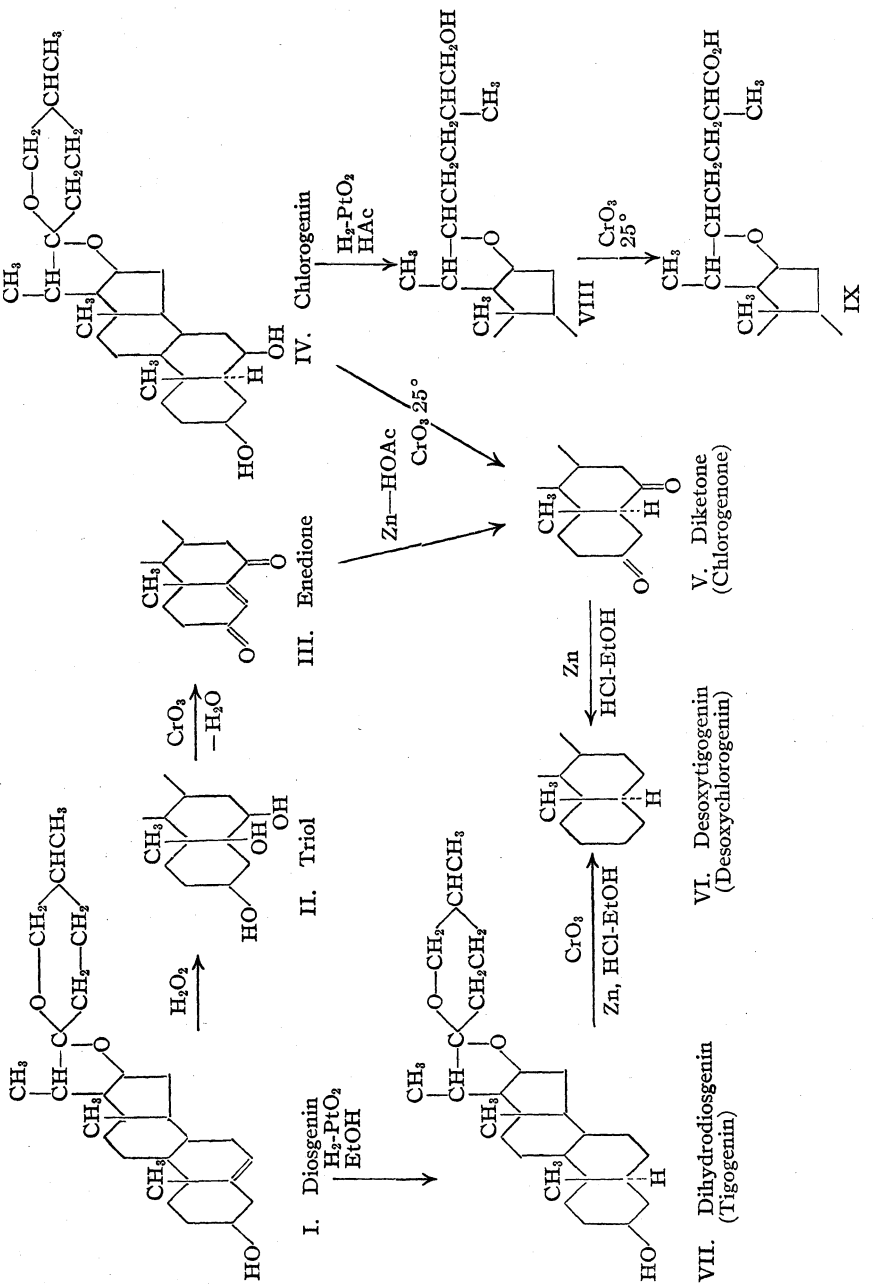
Sterols. LXXX. Reactions of Chlorogenin

BY RUSSELL E. MARKER AND EWALD ROHRMANN

In a previous paper[1] we presented evidence indicating that the nuclear hydroxyl groups of the steroid sapogenin, chlorogenin,[2] were located at C-3 and C-6 and that the hydroxyl group at C-3 was of the β-configuration. Noller[3] had previously postulated that the hydroxyl groups were at C-3 and C-12 and that the group at C-3 was of the α-configuration. We also presented evidence indicating that chlorogenin belongs to the *allo* series in its configuration at C-5. Further evidence concerning the nuclear structure is afforded by the fact that tigogenone and chlorogenone upon Clemmensen reduction yield the same desoxy compound.[4] The catalytic hydrogenation of the desoxy compounds in an acidic medium likewise gives the same dihydrodesoxy compound. This indicates that chlorogenin differs from tigogenin only in the presence of an additional hydroxyl group.

In a previous paper[4] we alluded to the highly interesting studies of Tsukamoto, Ueno and Ota[5] on diosgenin (I), an unsaturated steroid sapogenin which yields tigogenin upon reduction. Of especial interest are the experiments of Tsukamoto, Ueno, Ota and Tschesche[6] on the oxidation of dios-

(1) Marker and Rohrmann, THIS JOURNAL, **61**, 946 (1939).
(2) Liang and Noller, *ibid.*, **57**, 525 (1935).
(3) Noller, *ibid.*, **59**, 1092 (1937).
(4) Marker and Rohrmann, *ibid.*, **61**, 1516 (1939).
(5) Tsukamoto, Ueno and Ota, *C. A.*, **31**, 3493 (1937); *ibid.*, **32**, 2537 (1938); Tsukamoto and Ueno, *ibid.*, **32**, 7470 (1938).
(6) Tsukamoto, Ueno, Ota and Tschesche, *J. Pharm. Soc., Japan*, **57**, 283 (1937).



genin with hydrogen peroxide. The product of this reaction is a triol (II) which upon oxidation with chromic anhydride and subsequent dehydration yielded an enedione (III). Reduction of this product with zinc and acetic acid yielded a diketone (V), $C_{27}H_{40}O_4$, m. p. 234°. This diketone yielded a crystalline pyridazine derivative, $C_{27}H_{40}O_2N_2$, dec. 308°.

Professor T. Tsukamoto has kindly compared a sample of chlorogenone, m. p. 234°, with the saturated diketone (V) obtained from diosgenin. The substances appeared to be identical in properties and the mixed melting point showed no depression.

It now appears that the only objection which can be advanced against the formulation of chlorogenin as a 3,6-dihydroxy compound is the fact that on mild oxidation with chromic anhydride, Noller[3] obtained a keto dibasic acid which he stated to be different from digitogenic acid, the chromic anhydride oxidation product of digitogenin. However, no direct comparison of the acids was reported. We have pointed out previously[7] that the chemistry of the oxidation of digitogenin is in a rather confused state. In nearly all of the work on digitogenic acid and its alkali isomerization product, digitoic acid, there appears to be a lack of adequate data on the purity of the acids.

The relationships existing between diosgenin, tigogenin and chlorogenin raise many interesting questions in regard to the biogenesis of the steroidal saponins.

In the present work chlorogenin has been subjected to the reactions characteristic of sarsasapogenin.[8] As would be expected, chlorogenin resembles tigogenin more closely than it does sarsasapogenin in its various reactions involving the side chain. It shows little tendency to undergo isomerization with hydrochloric acid in ethanol solution. Attempts to reduce the substance by the Clemmensen method were unsuccessful.

(7) Marker and Rohrmann, THIS JOURNAL, **61**, 2724 (1939).
(8) Marker and Rohrmann, *ibid.*, **61**, 746 (1939).

Chlorogenin upon catalytic hydrogenation in acetic acid yielded dihydrochlorogenin (VIII), a substance analogous to dihydrosarsasapogenin. Dihydrochlorogenin formed a tris-3,5-dinitrobenzoate, indicating the presence of a third hydroxyl group. Mild oxidation of dihydrochlorogenin with chromic anhydride readily yielded an acid, $C_{27}H_{40}O_5$, which formed a disemicarbazone and a methyl ester. This acid (IX) has been designated tentatively as 3,6-dehydroanhydrotetrahydrochlorogenoic acid[9] because of its analogy to 3-dehydroanhydrotetrahydrosarsasapogenoic acid.[9]

Chlorogenin diacetate reacted readily with one mole of bromine in acetic acid to yield bromochlorogenin diacetate. Reduction of the bromo compound with sodium and ethanol yielded chlorogenin.[8,10]

McMillan and Noller,[11] in their studies on the oxidation of chlorogenin diacetate with chromic anhydride under relatively mild conditions, obtained the chlorogenin lactone diacetate as one of the products. Both their lactone diacetate and the hydroxy lactone were crystallized from methanol and their analyses indicated the presence of methanol of crystallization. We have oxidized chlorogenin diacetate with chromic anhydride under somewhat more vigorous conditions to obtain the lactone diacetate in yields comparable to the lactone yields obtained in an analogous oxidation of sarsasapogenin acetate. Analyses of our lactone diacetate, dihydroxy lactone, lactone dibenzoate and diketo lactone, none of which were crystallized from methanol, indicated the absence of any solvent of crystallization. From the acidic products of the oxidation there was obtained a small amount of an acid which analyses indicated as analogous to the C_{22} keto acid obtained by a similar oxidation of sarsasapogenin acetate.[12] Unfortunately, the yield of this acid was too low to permit further characterization.

We wish to thank Parke, Davis and Company for their generous help and assistance in the various phases of this work. We are especially grateful to Professor T. Tsukamoto of Kanazawa University, Kanazawa, Japan, for comparing a sample of chlorogenone with the saturated diketone derived from diosgenin. We also wish to thank Mr. Paul H. Williams, and Drs. Elmer J. Lawson and H. C. Benedict for their assistance in obtaining the bulbs of *Chlorogalum pomeridianum*.

(9) Marker and Rohrmann, THIS JOURNAL, **61**, 2072 (1939).
(10) Marker and Rohrmann, *ibid.*, **61**, 1921 (1939).
(11) McMillan and Noller, *ibid.*, **60**, 1630 (1938).
(12) Marker and Rohrmann, *ibid.*, **61**, 1285 (1939).

Experimental Part

The chlorogenin was isolated from *Chlorogalum pomeridianum* by the procedure described by Liang and Noller.[2] The material was crystallized from methanol as white needles, m. p. 265–268°.

A sample of chlorogenin (1 g.), m. p. 265–268°, was refluxed for fifty hours with 150 cc. of 95% ethanol and 30 cc. of concentrated hydrochloric acid. The product (800 mg.) recovered from the reaction melted at 258–265°. A mixture with chlorogenin melted at 260–267°.

Chlorogenin was recovered essentially unchanged after treatment with amalgamated zinc in ethanol–hydrochloric acid solution. When heated at 80° with an acetic acid solution of selenium dioxide a red precipitate formed almost at once. No product was isolated.

Dihydrochlorogenin.—A mixture of 7 g. of chlorogenin, 1 g. of Adams catalyst and 160 cc. of glacial acetic acid was shaken with hydrogen at 70° and 3 atmospheres for sixteen hours. The mixture was filtered and the filtrate evaporated *in vacuo*. The residual sirup, which would not crystallize, was refluxed on the steam-bath for thirty minutes with an excess of alcoholic potassium hydroxide. The resulting solution was diluted with water. The precipitate was collected, washed with water and dried. The white residue was crystallized from 95% ethanol to give 5 g. of white needles, m. p. 233–235°, sparingly soluble in ether.

Anal. Calcd. for $C_{27}H_{46}O_4$: C, 74.6; H, 10.7. Found: C, 74.8; H, 10.6.

It gave a precipitate with a 2% ethanolic solution of digitonin but did not react with bromine or selenium dioxide.

Tris-3,5-dinitrobenzoate of Dihydrochlorogenin.—To a solution of 400 mg. of dihydrochlorogenin in 15 cc. of dry pyridine was added 800 mg. of 3,5-dinitrobenzoyl chloride. The resulting solution was allowed to stand at room temperature for eight hours. It was then heated at 60° for three hours and the material poured into an excess of dilute hydrochloric acid. The resulting precipitated mixture, after standing overnight, was collected, washed with water, dried, and crystallized from acetone to give white crystals, m. p. 210–212°.

Anal. Calcd. for $C_{41}H_{50}O_{14}N_4$: C, 68.1; H, 7.0. Calcd. for $C_{48}H_{52}O_{19}N_6$: C, 56.7; H, 5.2. Found: C, 57.1; H, 5.1.

Oxidation of Dihydrochlorogenin.—To a solution of 1.5 g. of dihydrochlorogenin in 60 cc. of glacial acetic acid was added a solution of 1.5 g. of chromic anhydride in 30 cc. of 80% acetic acid. After standing at room temperature for two hours the solution was diluted with water and the mixture extracted with ether. The ethereal extract was washed first with water and then with dilute sodium carbonate solution. The sodium carbonate washings were acidified with hydrochloric acid and the white precipitate which separated was collected and washed with water. The dried material was crystallized from acetone as white plates, m. p. 202–204°.

Anal. Calcd. for $C_{27}H_{40}O_5$: C, 72.9; H, 9.1; neut. equiv., 454. Found: C, 73.1; H, 9.1; neut. equiv., 460.

The acid reacted with an ethanolic solution of semicarbazide acetate under the usual conditions to yield a **disemicarbazone** which was crystallized from ethanol to give a product, with m. p. 240° dec.

Anal. Calcd. for $C_{29}H_{46}O_5N_6$: C, 62.3; H, 8.3. Found: C, 62.5; H, 8.4.

With diazomethane the acid yielded a **methyl ester** which was crystallized from ether–pentane as white needles, m. p. 156.5–158°.

Anal. Calcd. for $C_{28}H_{42}O_5$: C, 73.3; H, 9.2. Found: C, 73.5; H, 9.4.

Bromochlorogenin Diacetate.—To a solution of 500 mg. of chlorogenin diacetate in 40 cc. of glacial acetic acid containing two drops of 48% hydrobromic acid was added 1.1 cc. of 1.05 *M* bromine in glacial acetic acid as rapidly as the bromine was absorbed. Hydrogen bromide was liberated. The solution was poured into water and the precipitate collected and washed with water. The dried white residue was crystallized from methanol to give white crystals, m. p. 200° with slight decomposition.

Anal. Calcd. for $C_{31}H_{47}O_6Br$: C, 62.5; H, 7.9. Found: C, 62.5; H, 7.8.

Dihydrodesoxychlorogenin (Dihydrodesoxytigogenin).—A mixture of 100 mg. of desoxychlorogenin, m. p. 173–175°, prepared by Clemmensen reduction of chlorogenone with amalgamated zinc, 120 cc. of acetic acid and 500 mg. of Adams catalyst was shaken with hydrogen at 3 atmospheres pressure for sixteen hours at 25°. The product was worked up as described for dihydrochlorogenin. Crystallization from ether–pentane gave white needles, m. p. 92.5–93.5°. This gave no depression with a sample of dihydrodesoxytigogenin,[4] m. p. 92.5°.

Anal. Calcd. for $C_{27}H_{46}O_2$: C, 80.5; H, 11.5. Found: C, 80.4, 80.5; H, 11.6, 11.6.

Oxidation of Chlorogenin Diacetate.—To a solution of 4 g. of chlorogenin diacetate in 175 cc. of glacial acetic acid heated on the steam-bath at 90–95° was added 5.5 g. of chromic anhydride in 50 cc. of 80% acetic acid over a period of one hour. The mixture was heated for an additional ninety minutes. After evaporating to a volume of approximately 50 cc. *in vacuo* the mixture was diluted with water and the precipitated solids taken up in ether. The ethereal extract was washed with water and then with 3% sodium hydroxide solution to remove acidic products.

The sodium hydroxide solution was heated for fifteen minutes on the steam-bath, cooled and acidified with hydrochloric acid. The precipitated acids were taken up in ether and crystallized from acetone to give a small amount of white crystals, m. p. 224–226°.

Anal. Calcd. for $C_{22}H_{34}O_5$: C, 69.8; H, 9.0. Found: C, 69.6, 69.4; H, 9.1, 9.0.

The ethereal solution containing the neutral fraction was evaporated and the residue crystallized from ether–pentane–acetone to give white needles, m. p. 247–250°, of the **lactone diacetate.**

Anal. Calcd. for $C_{26}H_{38}O_6$: C, 69.9; H, 8.6. Found: C, 69.9; H, 8.6.

Hydrolysis of the lactone diacetate with ethanolic potassium hydroxide gave **chlorogenin lactone** which crystallized from ether–acetone as white needles, m. p. 250–251.5°.

Anal. Calcd. for $C_{22}H_{34}O_4$: C, 72.9; H, 9.5. Found: C, 72.6; H, 9.7.

Oxidation of chlorogenin lactone with chromic anhydride in acetic acid at 25° for one hour gave the **diketo lactone** which crystallized from ether–pentane as compact white crystals, m. p. 243–245°.

Anal. Calcd. for $C_{22}H_{30}O_4$: C, 73.7; H, 8.4. Found: C, 73.6; H, 8.2.

Treatment of chlorogenin lactone with benzoyl chloride in pyridine at 25° for twenty hours gave the **lactone dibenzoate** which crystallized from aqueous acetone as white needles, m. p. 278–280°.

Anal. Calcd. for $C_{36}H_{42}O_6$: C, 75.75; H, 7.4. Found: C, 75.4; H, 7.4.

Summary

Chlorogenone prepared by the oxidation of chlorogenin appears to be identical with the 3,6-diketone of diosgenin.

Chlorogenin was reduced catalytically to give dihydrochlorogenin, mild oxidation of which gave an acid, $C_{27}H_{40}O_5$, which formed a disemicarbazone and a methyl ester.

Chlorogenin formed a monobromo derivative with bromine in acetic acid. Reduction of this gave back chlorogenin.

The lactone diacetate, dihydroxy lactone, lactone dibenzoate and diketo lactone were prepared from chlorogenin.

STATE COLLEGE, PENNSYLVANIA
RECEIVED SEPTEMBER 25, 1939

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY OF PRINCETON UNIVERSITY]

Molecular Rearrangements in the Sterols. IV. The Structure of *i*-Cholestanone[1]

BY KURT LADENBURG,[2] PURNENDU NATH CHAKRAVORTY[3] AND EVERETT S. WALLIS

In parts I, II and III[4,5,6] of this series, experiments on the preparation and on the determination of the structure of a new isomer of cholesterol, designated by us as *i*-cholesterol, and shown to be the parent alcohol of the isomeric dextrorotatory cholesteryl ethers, have been described. Although our experimental results were confirmed at once by other investigators,[7] our interpretation and proposed formulation of the structure of this new isomer was sharply questioned.

In this paper we wish to report the results of certain experiments which establish more rigidly the original formulation proposed in this Laboratory of the structure of these highly interesting compounds. Before the existence of *i*-cholesterol was suspected, Windaus and Dalmer[8] had treated α-3-chlorocholestanone-6 with alcoholic potassium hydroxide, and had obtained a halogen-free ketone which they believed to contain a true double bond, and which they named "heterocholestenone." That this "heterocholestenone" was in reality *i*-cholestanone was first pointed out by Heilbron and co-workers,[9] who prepared *i*-cholestanone not only by the method of Wallis, *et al.*,[4] by oxidation of *i*-cholesterol, but also obtained it from *i*-cholesteryl acetate and from *i*-cholesterol methyl ether. We are now able to report that we have prepared the isomer of *i*-cholestanone containing a true double bond by refluxing α-3-bromocholestanone-6 with quinoline. The double bond so produced by the removal of hydrogen bromide shifts from the C_3:C_4 position to the position conjugated to the ketone group as is indicated by its absorption spectra; the compound shows absorption in the ultraviolet, maximum at 2450 Å., the wave length characteristic for conjugation across two rings. Therefore, we have assigned to it the structural formula III. This new ketone melts at 105°; its oxime melts at 185°. The same compound is also obtained in somewhat smaller yields from α-3-chlorocholestanone-6 by treatment with quinoline. It is, thus, the "true heterocholestenone."

In Part III of this series it was shown that the cyclopropane ring of *i*-cholestanone can be opened without difficulty. Thus when treated with dry hydrogen chloride α-3-chloro-cholestanone-6 is formed. We have found that a similar reaction takes place when aqueous hydrogen bromide is added to an acetic acid solution of *i*-cholestanone; α-3-bromo-cholestanone-6 (m. p. 123°) crystallizes out quantitatively. Another interesting observation is the fact that when an acetic acid solution of *i*-cholestanone is refluxed with dilute sulfuric acid, it is converted into β-3-hydroxy-cholestanone-6 (m. p. 142–143°) identical with the compound prepared by the method of Windaus.[10]

To establish further proof of the structure of *i*-cholestanone (II), a study of degradative oxidations of this ketone has been made. The following experiments show that there is no double bond in the molecule. Hydrogen peroxide, when heated with an acetic acid solution of the ketone, has no effect. Neither is the compound oxidized by neutral or alkaline potassium permanganate, reagents which attack violently compounds containing a double bond. However, when a pyridine solution of *i*-cholestanone is shaken for twenty-four hours with an aqueous solution of potassium hypobromite, an acid (IV) is obtained. This acid melts at 233°. It is dibasic and does not decolorize bromine solution nor does it give an active Liebermann reaction. Unlike the ketone, it does not add water or halogen acid; its analysis agrees with the assigned formula IV.

The facts mentioned above show the marked difference in the stability of the cyclopropane ring in the series: *i*-cholesterol, *i*-cholestanone, *i*-cholestane diacid. *i*-Cholesterol has been prepared from cholesterol by molecular rearrangement, and can be converted back into cholesterol under certain conditions; *i. e.*, the cyclopropane linkage can shift to a double bond and *vice versa*. *i*-Cho-

(1) The experimental results herein described were placed before the Society in a paper read before the Division of Organic Chemistry at the Society meeting in Boston, September 11–15, 1939.

(2) Harvard Fellow in Chemistry.

(3) Research Assistant on special funds from The Rockefeller Foundation.

(4) Wallis, Fernholz and Gephart, THIS JOURNAL, **59**, 137 (1937).

(5) Ford and Wallis, *ibid.*, **59**, 1415 (1937).

(6) Ford, Chakravorty and Wallis, *ibid.*, **60**, 413 (1938).

(7) Beynon, Heilbron and Spring, *J. Chem. Soc.*, 1459 (1937); see also, Heilbron, Hodges and Spring, *ibid.*, 759 (1938).

(8) Windaus and Dalmer, *Ber.*, **52**, 168 (1919).

(9) Heilbron, Hodges and Spring, *J. Chem. Soc.*, 759 (1938).

(10) Windaus, *Ber.*, **36**, 3754 (1903).

lestanone does not undergo isomerization. The cyclopropane linkage, however, can be opened without difficulty. In the dicarboxylic acid the cyclopropane linkage exhibits the greatest stability and resists strongly efforts to rupture it. Thus, it can be concluded that the stability of the cyclopropane ring depends on the nature of the state of oxidation of the C_6 carbon atom. Exactly the same relationship has been observed with sabina ketone and its derivatives.[11]

In an attempt to relate the above diacid (IV) to a known compound, β-3-chloro-cholestane-diacid-6,7 (VI) was prepared from β-3-chlorocholestanone-6 (V) according to the method of Windaus and Stein.[12] When this compound is treated with alcoholic potassium hydroxide, hydrogen chloride is not removed. Treatment with sodium ethylate, however, at higher temperature results in a halogen-free dicarboxylic acid (VII), m. p. 231°. This compound gives no reaction characteristic of the ethylenic double bond but exhibits all those properties associated with the presence of a cyclopropane ring. Experiments show that it is not identical with the acid obtained from *i*-cholestanone. Thus this second acid is an isomer of *i*-cholestane-diacid (IV).

This isomerism can be explained as being due to the relative positions of the groups at C_3, since the two acids were obtained from the α- and β-chloro ketones, respectively. However, the isomerism may be due to the relative positions of the groups at C_5.

The following experiments show that the stereochemical positions of both asymmetric centers, C_3 and C_5, are involved.

In order to establish the isomeric relationship of the above dicarboxylic acids, α-3-chlorocholestane-diacid-6,7 (VIII) was prepared from α-3-chlorocholestanone-6 according to Windaus and Staden.[13] This diacid loses hydrogen chloride with greater difficulty than the other halogen compounds studied in this series. But it can be removed when the acid is treated with sodium ethylate at 150°. When this procedure is followed, a halogen-free diabasic acid (IX), melting at 265°, is obtained. This third acid also gives no reactions of the double bond and is an isomer of the other two. Since, like the diacid (IV), it also has been derived from α-3-chlorocholestanone-6, the steric position of the hydrogen at C_3 with respect to the methyl group at C_{10} should be the same in these two diacids (IV and IX), and the latter will be designated as α_2-*i*-cholestane-diacid-6,7. We believe that its non-identity with the α_1-*i*-cholestane-diacid-6,7 (IV) is due to a difference in the steric position of the carboxyl group at C_5, the inversion being caused by the influence of the alkaline reagent on α-3-chlorocholestane-diacid-6,7 (VIII). The mechanism of such an inversion may be explained by the formation of an enol. Thus, the carboxyl group at C_5 in the diacid (IX) is believed to have a *trans* orientation with respect to the methyl group at C_{10}. In the diacid (IV), however, the carboxyl group at C_5 should be in *cis* position to the methyl group at C_{10} since in the oxidation of the ketone (II) to the acid (IV) inversion cannot take place, there being no available hydrogen at C_5.

Theoretically there should exist a fourth isomeric acid of the structure (XI) which should be obtained by the oxidation of the isomer of *i*-cholestanone (X). As yet this acid has not been prepared. This diacid (XI) should have the same stereochemical configuration at C_3 as the diacid (VII) but would differ from the latter in the steric position of the carboxyl group at C_5. In accordance with the naming of the α-diacids, the diacid (VII) will be designated as β_2-*i*-cholestane-diacid-6,7. The method of preparation of the β_1-*i*-cholestane-diacid-6,7 is being studied at the present time.

The chart contains in outline the reactions discussed.

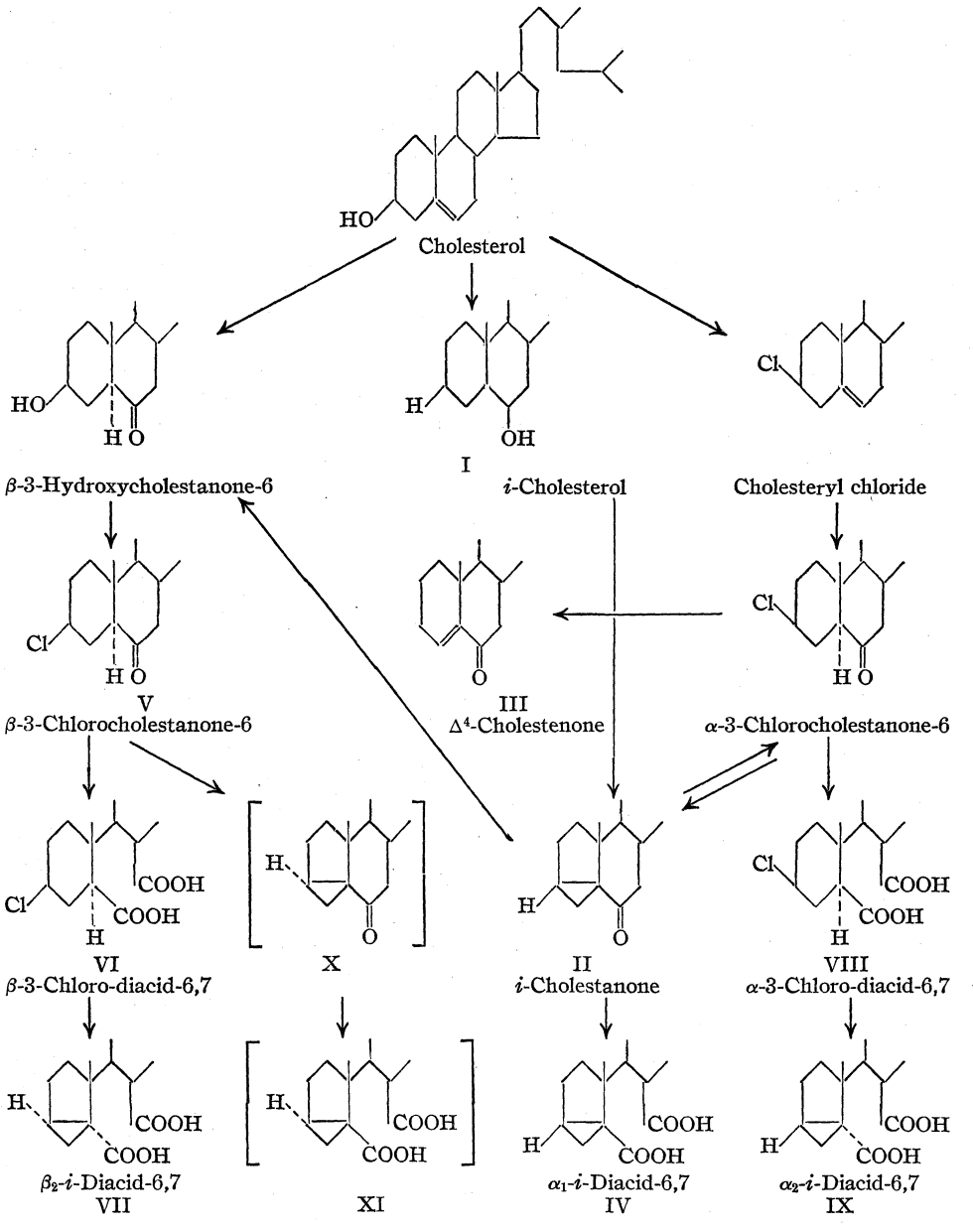
While the nature of the isomeric relationship between these acids is clear, the assignment of the steric position of the hydrogen at C_3 and of the carboxyl at C_5 is difficult. It is possible, however, to make certain deductions based on some observations of other investigators[14] in closely allied fields. If one considers for example the α- and β-cholestanols, one sees that these two compounds each yield different chlorides depending on whether they are treated with phosphorus pentachloride or with thionyl chloride. With cholesterol, however, the same product in each case results. Ruzicka assumes that the β-cholestyl chloride (m. p. 105°) is the *trans* form and the α-isomeride (m. p. 116°) is the *cis* form, basing his assumption on the fact that in the cholestanols

(11) Wallach, *Ann.*, **359**, 265 (1908); Thomson, *J. Chem. Soc.*, **97**, 1502 (1910).

(12) Windaus and Stein, *Ber.*, **37**, 3699 (1904).

(13) Windaus and Staden, *Ber.*, **54**, 1059 (1921).

(14) Ruzicka, Wirz and Meyer, *Helv. Chim. Acta*, **18**, 998 (1935); Marker, Whitmore and Kamm, THIS JOURNAL, **57**, 1755, 2358 (1935).



the α-form (*cis* or *epi*) has a higher melting point than the β-form (*trans* or normal). It must be remembered that *cis* and *trans* here refer to the position of the functional group at C_3 with respect to the hydrogen at C_5. Therefore, if this be true, it follows that a Walden inversion takes place in the chlorination of cholesterol with either phosphorus pentachloride or thionyl chloride, whereas with the cholestanols only chlorination with thionyl chloride causes an inversion.

If we apply these relationships to the reactions described in this paper and assume inversion to take place in the chlorination of cholesterol but not with cholestanol, a *cis*- or *epi* configuration should be assigned to the α-chlorocholestanone-6 (m. p. 129°) and a *trans*- or normal configuration to the β-chloro ketone (m. p. 181°). It should be pointed out that this leads to confusion, when considered in the light of Ruzicka's rule, which assumes that of the two isomers the one of higher melting point has the *epi*- or *cis* configuration. It is interesting to note, however, that the two chloro diacids obtained from the α- and β-ketones, respectively, are in accordance with Ruzicka's assumption, the α-chloro diacid melting at 263° and the β-form melting at 243°.

We also can state that the stereochemical configurations so assigned to the α- and β-3-chlorocholestanone-6 are supported by certain experimental observations. Windaus[8] has observed that hydrogen chloride may be removed from the α-chloro ketone without difficulty by simply warming with alcoholic potassium hydroxide, whereas a similar or even more drastic treatment leaves the β-chloro ketone unchanged. Since it is now believed that the removal of the hydrogen chloride with an alkaline reagent involves the hydrogen atom at C_5 and not, as Windaus assumed, at C_4, the difference of the α- and β-chloro ketones in this particular reaction may well be attributed to the *cis* orientation of the chlorine atom to the hydrogen at C_5 in the α-compound and to the *trans* orientation in the β-isomer. It is also possible to follow this argument through to the 3-chloro diacids. If we consider that sodium ethylate first produces an inversion of the carboxyl group at C_5 before removal of hydrogen chloride from the chloro acids is attained, then the reaction would be expected to proceed more easily in the case of the β-form than in the case of the α-isomeride. This expectation is substantiated by the experiments.

Experimental Part

Preparation of *i*-Cholestanone (II) from *i*-Cholestanone-oxime.—*i*-Cholestanone-oxime (m. p. 143–144°) prepared by the method of Wallis, Fernholz, and Gephart was hydrolyzed with dilute sulfuric acid in alcohol solution. The solution was boiled for three hours, diluted with water, and extracted several times with ether. Evaporation of the ether and recrystallization of the residue gave a crystalline ketone which melted at 96°.[15] When mixed with an authentic specimen of the halogen-free ketone of m. p. 96° (oxime 143°) prepared from α-3-chlorocholestanone-6 by the Windaus and Dalmer method, no depression of the melting point was observed.

Preparation of β-3-Hydroxycholestanone-6 from *i*-Cholestanone.—One gram of *i*-cholestanone was dissolved in 200 cc. of acetic acid and 50 cc. of 5 *N* sulfuric acid. The solution was refluxed for two hours, diluted with water, and extracted with ether. After removing the solvent, the residue was taken up in alcoholic sodium hydroxide and refluxed for one hour to hydrolyze any acetate formed in the reaction. The hydroxy ketone was precipitated with water, filtered, and recrystallized from alcohol; yield 0.95 g. (91%), m. p. 142–143°. The acetate was prepared by refluxing 0.1 g. of the material with acetic anhydride for one hour. On making up the product in the usual manner, crystals were obtained from alcohol which melted at 127–128°. No depression of the melting point of the free hydroxy ketone as well as of its acetate could be observed when these compounds were mixed with specimens prepared according to Windaus.[10]

Preparation of the Oxime of β-3-Acetoxycholestanone-6.—The oxime was prepared in the usual manner. It melted at 194–195°.

Anal. Calcd. for $C_{29}H_{49}O_3N$: C, 75.77; H, 10.74; N, 3.04. Found: C, 75.96; H, 10.49; N, 3.08.

Preparation of α-3-Bromocholestanone-6.—To a solution of 0.25 g. of *i*-cholestanone in acetic acid, 2.5 cc. of a 34% aqueous hydrobromic acid solution was added. After standing overnight at room temperature, a crystalline product separated which was filtered and recrystallized from dilute acetic acid and alcohol. It melted at 123°, yield quantitative.

Anal. Calcd. for $C_{27}H_{45}OBr$: C, 69.65; H, 9.74; Br, 17.17. Found: C, 69.76; H, 9.84; Br, 17.47.

Preparation of Δ^4-Cholestanone-6 (III).—Four grams of α-3-bromocholestanone-6 (m. p. 123°) was dissolved in 60 cc. of freshly distilled quinoline and the solution refluxed for one hour in an atmosphere of nitrogen. The product was precipitated with water and extracted with ether. The quinoline was removed with dilute sulfuric acid. The solvent was evaporated, and the residue was crystallized from alcohol. Crystals were obtained which melted at 104–105°, yield 2.6 g. (79%).

Anal. Calcd. for $C_{27}H_{44}O$: C, 84.31; H, 11.53. Found: C, 84.24; H, 11.31.

The oxime of Δ^4-cholestenone-6 was prepared in the usual way, giving crystals from alcohol which melted at 184–185°.

Anal. Calcd. for $C_{27}H_{45}ON$: C, 81.14; H, 11.35; N, 3.51. Found: C, 80.98; H, 11.16; N, 3.72.

Preparation of α_1-*i*-Cholestane-diacid-6,7 (IV).—To a solution of 100 cc. of 10% potassium hydroxide and 2.5 cc. of bromine, 2.5 g. of *i*-cholestanone-6 (II) was added; the temperature was raised to about 50° so that all of the solid material became properly suspended. After cooling to room temperature, 250 cc. of pyridine was added and the solution was shaken vigorously for twenty-four hours; the solution was clear and almost colorless. After cooling to 0° sulfuric acid was added until the smell of pyridine was no longer noticeable, and the precipitate was taken up in ether. The ether was extracted with dilute alkali and the acidic product was precipitated with sulfuric acid. The precipitate was filtered and the product was recrystallized from dilute alcohol. Crystals were obtained which melted at 232–233°, yield quantitative, 18.1 mg. in 2 cc. of absolute acetone, α_D +0.16, $[\alpha]^{25}_D$ +18° in absolute acetone.

Anal. Calcd. for $C_{27}H_{44}O_4$: C, 74.95; H, 10.25; neut. equiv., 216. Found: C, 74.72; H, 10.13; neut. equiv., 216.

Preparation of β-*i*-Cholestane-diacid-6,7 (VII).—Two grams of metallic sodium was dissolved in 25 cc. of absolute alcohol in a bomb tube. To the clear solution 1 g. of β-3-chlorocholestane-diacid-6,7 (m. p. 243°), prepared according to Windaus and Stein, was added. The tube was sealed and heated in a furnace at 120° for one hour. A

(15) In the original recording of the melting point of this compound an error was made. We believe, however, that we are correct in our statement that the oxime melts at 143–144° and not at 122–123° as later reported by Heilbron, Hodges and Spring.[9] We have prepared this oxime many times by both methods, and never have we been able to obtain the melting point recorded by them.

successful reaction was indicated by the precipitation of sodium chloride. Water was added and the acidic reaction product was precipitated with sulfuric acid, filtered and recrystallized from dilute alcohol and dilute acetic acid. The crystals melted at 230–231°, 17.4 mg. in 2 cc. absolute acetone, α_D + 0.48, $[\alpha]^{24}D$ +55°. Experiment showed that this halogen-free dicarboxylic acid crystallizes with one molecule of water, which is still retained after drying in vacuum at 110°.

Anal. Calcd. for $C_{27}H_{44}O_4 \cdot H_2O$: C, 71.97; H, 10.29; neut. equiv., 226. Found: C, 72.16; H, 10.28; neut. equiv., 230.

Preparation of α_2-*i*-Cholestane-diacid-6,7 (IX).—This acid was prepared from α-3-chlorocholestane-diacid-6,7 (m. p. 263°) in a manner similar to the one described above. In this case, however, the reaction had to be carried out at 150°, and the time had to be increased to eight hours. The halogen-free dicarboxylic acid melts at 265°, 18.8 mg. in absolute dioxane, α_D +0.43, $[\alpha]^{25}D$ +46° in dioxane.

Anal. Calcd. for $C_{27}H_{44}O$: C, 74.95; H, 10.25; neut. equiv., 216. Found: C, 75.03; H, 10.46; neut. equiv., 217.

We wish to take this opportunity to express our thanks to Merck and Company, Inc., of Rahway, New Jersey, for the analyses published in this paper, for the determination of the absorption of Δ^4-cholestenone and for the cholesterol used as the starting material.

Summary

Further evidence has been given to show that Windaus' method of removing hydrogen chloride from α-3-chlorocholestanone-6 gives *i*-cholestanone and not the unsaturated ketone heterocholestenone.

The true heterocholestenone, Δ^4-cholestenone-6, has been obtained and characterized.

A new dicarboxylic acid, m. p. 233°, has been prepared from *i*-cholestanone. This acid has been shown to be an isomer of another new acid, m. p. 231°, obtained from β-3-chlorocholestanone-6. A third isomeric acid, m. p. 265°, has been prepared from α-3-chlorocholestanone-6.

A detailed discussion of the stereochemical relationships of these compounds has been given.

PRINCETON, N. J. RECEIVED SEPTEMBER 29, 1939

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF TEMPLE UNIVERSITY]

The Oxidation of Certain Heteronuclear-Substituted Polybromodiphenyls

BY FRANCIS H. CASE

In the course of various investigations in this Laboratory dealing with the structures of certain heteronuclear polybromodiphenyls, it seemed desirable to obtain more information as to the behavior of these compounds on oxidation. Although it is known, in general, that in the case of those diphenyls substituted by bromine in one ring only, the unsubstituted ring is destroyed by oxidation, there appears to be no information concerning the oxidation of those compounds in which bromine is a substituent in both rings. The method of oxidation employed utilizes chromic anhydride in approximately 75% acetic acid solution.[1] In each case a considerable amount of the total molecule was destroyed.

The oxidation of 3,4′-[2] and of 2,3′-dibromodiphenyls yielded *p*- and *m*-bromobenzoic acids, respectively, as the sole resulting products. The tribromodiphenyls investigated may (with the exception of 2,4,6-tribromodiphenyl) be divided into two groups in each of which the dibromo substituted nucleus remains the same, while the position of the monobromo substituent in the other nucleus is varied. Group A consists of 2,3′,5′-(I),[3] 3,3′,5′-(II), and 3′,4,5′-(III) tribromodiphenyls. Group B contains 2,2′,5′-(IV), 2′,3,5′-(V) and 2′,4,5′-(VI) tribromodiphenyls. The results of the oxidation of these six isomers are as follows: I and II yield only 3,5-dibromobenzoic acid; III, only *p*-bromobenzoic acid; IV, only 2,5-dibromobenzoic acid; V, both *m*-bromobenzoic and 2,5-dibromobenzoic acid; VI, both *p*-bromobenzoic and 2,5-dibromobenzoic acid.

The oxidation of 2,4,4′,6-tetrabromodiphenyl was found to yield only *p*-bromobenzoic acid, while 2,4,6-tribromodiphenyl, subjected to the same treatment, also yielded a certain amount of *p*-bromobenzoic acid. This surprising result was at first attributed to the presence of a small amount of 2,4,4′,6-tetrabromo-3-aminodiphenyl in the 2,4,6-tribromo-3-aminodiphenyl from which the 2,4,6-tribromodiphenyl was obtained by deamination. However, this explanation had to be

(1) L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., Inc., Boston, Mass., 1935, p. 230.

(2) Case, THIS JOURNAL, **60**, 424 (1938).

(3) Case, THIS JOURNAL, **61**, 767 (1939).

discarded when it was found that 2,4,6-tribromodiphenyl prepared by Ullmann's reaction from 2,4,6-tribromoiodobenzene and iodobenzene yielded the same product on oxidation. It is possible that bromine liberated during the oxidation of the tribromo compound attacks the unsubstituted nucleus of some of the still unoxidized material, thus producing momentarily the tetrabromo derivative.

The synthesis of 2,4,6-tribromodiphenyl by Ullmann's reaction and the establishment of its identity with that produced by the method of Blakey and Scarborough[4] leave no further doubt as to the structure of the latter. The structure of 2,4,4',6-tetrabromodiphenyl, obtained by bromination of 4-bromo-3'-aminodiphenyl,[4] followed by deamination, is based on analogy with that of 2,4,6-tribromodiphenyl obtained similarly from 3-aminodiphenyl.

As a result of these studies of the oxidation of various polybromo substituted diphenyls, it is possible to arrange the various bromo-substituted phenyl radicals in the order of decreasing stability toward oxidation as follows: 4-bromo-, 3,5-dibromo-, (2,5-dibromo- and 3-bromo-), 2-bromo-, and 2,4,6-tribromo- phenyl.

The 2,3'-dibromodiphenyl used in this work was prepared by the deamination of 2,3'-dibromo-4'-aminodiphenyl.[3]

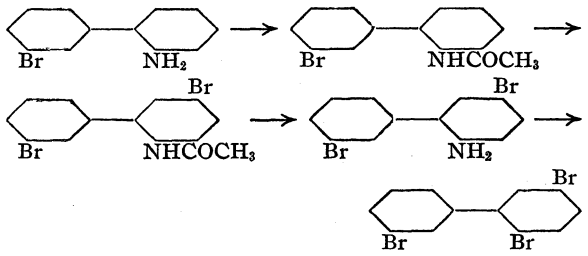
3,3',5'-Tribromodiphenyl was obtained by the following series of reactions: 2-amino-3'-bromodiphenyl[8] ⟶ 2-amino-3,3',5-tribromodiphenyl ⟶ 3,3',5'-tribromodiphenyl. Since on oxidation 3,3',5'-tribromodiphenyl yields 3,5-dibromobenzoic acid, the positions taken by the two entering bromine atoms in the dibromination of 2-amino-3'-bromodiphenyl are proved.

3',4,5'-Tribromodiphenyl was prepared by deamination of 3',4,5'-tribromo-4'-aminodiphenyl.[5] It evidently is identical with the tribromodiphenyl synthesized by Bellavita[6] from 2-amino-3,5-dibromo-4'-nitrodiphenyl.

2',4,5'-Tribromodiphenyl was synthesized by the following series of reactions: 4-bromo-3'-acetaminodiphenyl[4] ⟶ 2',4-dibromo-5'-acetaminodiphenyl ⟶ 2',4-dibromo-5'-aminodiphenyl ⟶ 2',4,5'-tribromodiphenyl.

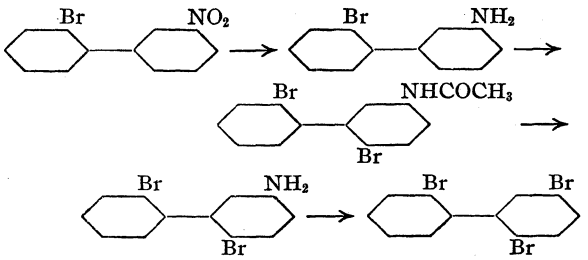
The structure of the dibromo base was proved by its conversion to 2,4'-dibromodiphenyl on deamination. The final product is evidently identical with the tribromodiphenyl prepared by Bellavita[7] from *o*, *p*'-bianiline.

2',3,5'-Tribromodiphenyl was prepared in the manner indicated[8]



The structure of the dibromo base was proved by its conversion to 3,3'-dibromodiphenyl on deamination.

The synthesis of 2,2',5'-tribromodiphenyl was effected by the following procedure[2]



The structure of the dibromo base was proved by its conversion to 2,2'-dibromodiphenyl on deamination.

Attempts to prepare 3,3',5'-tribromodiphenyl from 3-nitrobenzidine[9] by monobromination of the corresponding diurethan, removal of the urethano groups, reduction of the resulting 3-bromo-3'-nitrodiphenyl, followed by acetylation, monobromination, hydrolysis, and replacement of amino by bromine were unsuccessful, as it was found that 3-nitrobenzidine formed only a monourethan under the experimental conditions. This product upon monobromination, hydrolysis and deamination yielded 3-bromo-5-nitrodiphenyl, whose structure is proved by the fact that on reduction, replacement of amino by bromine and oxidation, 3,5-dibromobenzoic acid was formed. This bromonitrodiphenyl is evidently identical with that obtained by Scarborough and Waters[10] by deamination of 5-bromo-3-nitro-4-aminodiphenyl.

Experimental Part

The compounds described in Table I, grouped according to their generic relationships, were

(4) Blakey and Scarborough, *J. Chem. Soc.*, 3000 (1927).
(5) Scarborough and Waters, *ibid.*, 557 (1926).
(6) Bellavita, *Gazz. chim. ital.*, **67**, 574 (1937).
(7) Bellavita, *ibid.*, **65**, 632 (1935).
(8) Lesslie and Turner, *J. Chem. Soc.*, 1590 (1933).
(9) Le Fèvre and Turner, *ibid.*, 245 (1928).
(10) Scarborough and Waters, *ibid.*, 1138 (1927).

TABLE I

Compound	Crystallizing solvent	M. p. or b. p., °C.	Anal. for bromine, % Calcd.	Found
2,3′-Dibromodiphenyl		B. p. 165–168 (3 mm.)	51.28	51.51
2-Amino-3,3′,5-tribromodiphenyl	Methanol	M. p. 111–112	59.08	59.29
Acetyl derivative	Ethanol	M. p. 185–186	53.53	53.60
3,3′,5′-Tribromodiphenyl	Ethanol	M. p. 112–113	61.34	61.49
3′,4,5′-Tribromodiphenyl	Ethanol	M. p. 102–103	61.34	61.48
2,4,4′,6-Tetrabromo-3-aminodiphenyl[a]	Ethanol	M. p. 93–94	66.18	65.95
Acetyl derivative	Ethanol	M. p. 260–261	60.69	60.88
2,4,4′,6-Tetrabromodiphenyl	Ethanol	M. p. 105–106	68.06	67.86
3-Amino-5-bromodiphenyl	Bz–pet. ether	M. p. 89–90	32.26	32.19
Acetyl derivative	Benzene	M. p. 142–143	27.56	27.34
2-Acetamino-3′-bromodiphenyl	Ether–pet. ether	M. p. 93–94	27.56	27.79
3,3′-Dibromo-6′-acetaminodiphenyl[b]	Bz–pet. ether	M. p. 145–146	43.35	43.11
2′,3,5′-Tribromodiphenyl		B. p. 213–216 (6 mm.)	61.34	61.08
2,6′-Dibromo-3′-acetaminodiphenyl[b]	EtOH–water	M. p. 142	43.35	43.32
2,2′,5′-Tribromodiphenyl	Pet. ether	M. p. 77–78	61.34	61.13
2′,4-Dibromo-5′-aminodiphenyl	Bz–pet. ether	M. p. 91–92	48.89	49.07
Acetyl derivative	Ethanol	M. p. 163–164	43.35	43.62
2′,4,5′-Tribromodiphenyl	Methanol	M. p. 77–78	61.34	61.75

[a] Blakey and Scarborough[4] record m. p. 104° for this compound. [b] Free base not isolated.

prepared by the following general methods according to the scheme already indicated: (1) reduction of nitro compounds was effected by stannous chloride in ethanol; (2) acetylation of amines by means of an acetic acid–acetic anhydride mixture in the presence of a small amount of sulfuric acid; (3) bromination of acetamino derivatives by the use of one mole of bromine in acetic acid solution containing sodium acetate; (4) deamination of amines by means of saturated sodium nitrite solution in a boiling alcoholic solution of the amine containing dilute sulfuric acid; (5) hydrolysis of acetamino compounds by alcoholic hydrobromic acid.

2,4,6-Tribromodiphenyl.—To 45 g. of iodobenzene heated to 180°, was added gradually a mixture of 44 g. of 2,4,6-tribromoiodobenzene and 40 g. of copper powder. The mixture was heated for two hours at 200° with stirring. After cooling, the mass was extracted with ether and the ether residue distilled. From it was obtained, after two distillations, 17.5 g. of a fraction, b. p. 190–198° (4 mm.), which after crystallization from petroleum ether yielded a pure tribromodiphenyl, m. p. 65–66°.

Anal. Calcd. for $C_{12}H_7Br_3$: Br, 61.34. Found: Br, 61.45.

This product melted unchanged when mixed with 2,4,6-tribromodiphenyl prepared by the method of Blakey and Scarborough.[4] The tribromodiphenyl prepared by either method yields on oxidation only *p*-bromobenzoic acid.

3-Nitrobenzidine.—The following method was found superior to that of Le Fèvre and Turner.[9] Twenty grams of 3,4′-dinitro-4-aminodiphenyl,[9] dissolved in 200 cc. of dioxane, was treated with 4 g. of sulfur and 24 g. of hydrated sodium sulfide and the mixture heated on the steam-bath for ten hours. After removal of the dioxane on the steam-bath by means of an aspirator, the residue was purified by washing with hot water, followed by extraction with hot 1–1 acetic acid. The base was precipitated by ammonia from the acetic acid solution, and not further purified; yield of crude base, 17 g.

Monourethan of 3-Nitrobenzidine.—A boiling solution of 121 g. of crude 3-nitrobenzidine and 169 g. of diethylaniline in 1250 cc. of ethanol was treated gradually with 146 g. of ethyl chlorocarbonate. The mixture was boiled for ten minutes after the reaction had subsided, and then poured into a large volume of water. The resulting precipitate was crystallized from benzene: yield, 88 g. of a product melting at 163–164°. The pure monourethan melts at 167–168°.

Anal. Calcd. for $C_{15}H_{15}N_3O_4$: C, 59.77; H, 5.02. Found: C, 59.58; H, 4.81.

Monourethan of 3-Nitro-5-bromobenzidine.—This was prepared by the bromination of the monourethan of 3-nitrobenzidine in glacial acetic acid containing anhydrous sodium acetate. It was crystallized from benzene, m. p. 167–168°.

Anal. Calcd. for $C_{15}H_{14}O_4N_3Br$: Br, 21.03. Found: Br, 21.24.

3-Nitro-5-bromobenzidine.—The crude base was prepared from the urethan by hydrolysis with hot 60% sulfuric acid.

3-Nitro-5-bromodiphenyl.[10]—Eighty grams of crude 3-nitro-5-bromobenzidine was dissolved in 326 cc. of concd. sulfuric acid, and the mixture diluted with 300 cc. of water. Diazotization was then effected by the slow addition of 80 g. of sodium nitrite, keeping the temperature below 10°. Following this, the mixture was treated with 300 cc. of 20% oleum at a temperature below 30°, and poured into 2 liters of boiling alcohol. After refluxing for two hours, the alcohol was removed and water added. The desired product was extracted with ether, and, after removal of ether, distilled *in vacuo*, yielding 31 g., b. p. 200–242°

(5 mm.). The crude distillate was recrystallized from methanol: yield, 10.5 g.; m. p. 71–72°.

Anal. Calcd. for $C_{12}H_8NO_2Br$: Br, 28.75. Found: Br, 29.12.

Summary

1. A study has been made of the oxidation products of the following polybromodiphenyls: 2,3′- and 3,4′-dibromodiphenyl, 2,3′,5′-, 3,3′,5′-, 3′,4,5′-, 2,2′,5′-, 2′,3,5′-, 2′,4,5′- and 2,4,6-tribromodiphenyls, and 2,4,4′,6-tetrabromodiphenyl.

2. The preparation of those polybromodiphenyls not previously recorded is described.

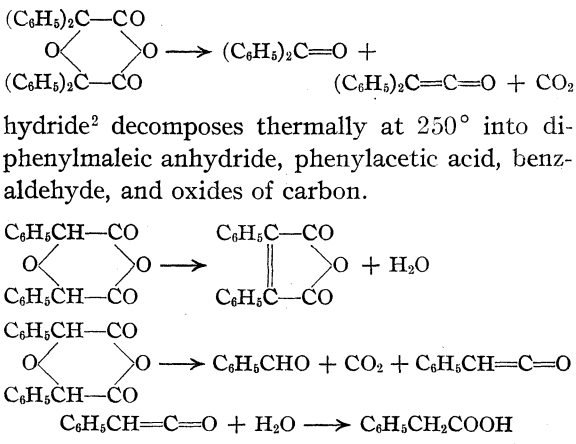
PHILADELPHIA, PENNA. RECEIVED SEPTEMBER 8, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

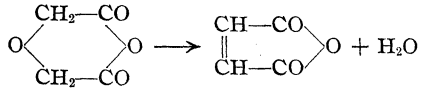
The Pyrolysis of Diglycolic Anhydride

BY CHARLES D. HURD AND HOWARD G. GLASS

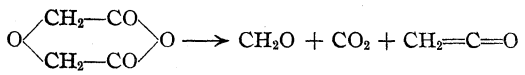
On pyrolysis, dibenzilic anhydride[1] yields benzophenone and diphenylketene. Dimandelic anhydride[2] decomposes thermally at 250° into diphenylmaleic anhydride, phenylacetic acid, benzaldehyde, and oxides of carbon.



The present work deals with diglycolic anhydride. From the above one would predict for it a bidirectional breakdown on heating. One reaction should give rise to maleic anhydride



whereas the other should yield ketene



A good yield of maleic anhydride was obtained at 450–500°. Some ketene was observed too, but since water was formed in this reaction it must have changed much of the ketene into acetic acid.

The production of maleic anhydride from diglycolic anhydride involves lengthening of the carbon chain. This is an interesting, unusual method of bringing about such an effect.

(1) Staudinger, *Ber.*, **44**, 543 (1911).

(2) Hurd and Raterink, THIS JOURNAL, **55**, 1541 (1933).

Experimental

Diglycolic Anhydride.—To 35 g. of diglycolic acid was added 65 g. of acetic anhydride and the mixture was refluxed four hours. Then 35 g. of acetic acid was distilled off, 30 g. more of acetic anhydride added and the mixture was refluxed for two hours longer. On distillation 5 g. more of acetic acid was collected and 61 g. of acetic anhydride was recovered. The residue was vacuum distilled. There was collected 32 g. (94% yield) of diglycolic anhydride at 130° and 20 mm. It solidified on cooling; m. p. 94–95°. The derivative with aniline, diglycolic phenylimide, was prepared. Its melting point of 109–110° confirmed Anschütz' value[3] of 111°.

Analysis of Mixtures of Maleic and Diglycolic Anhydrides.—The separation of these two anhydrides was accomplished satisfactorily by the selective solvent action of benzene. Both anhydrides were soluble in hot benzene whereas diglycolic anhydride separated on cooling the solution to 6°. After concentrating the filtrate and cooling till crystals of this compound no longer appeared, furan was added to the solution. After a time, crystals of the addition product of furan and maleic anhydride separated.[4] This material melted at 122–124° and at 125° after recrystallization (literature, 125°).

In various mixtures, recovery of the diglycolic anhydride was almost quantitative and recovery of the maleic anhydride derivative was 89–95%. The results are presented in Table I.

TABLE I

SEPARATION OF MALEIC AND DIGLYCOLIC ANHYDRIDES

Mixture, g.		Diglycolic anhydride found		Maleic anhydride found	
Maleic anhydride	Diglycolic anhydride	G.	%	Furan deriv. G.	%
3.0	12.0	11.6	97	4.75	94
1.0	1.0	1.0	100	1.6	95
0.8	1.0	0.97	97	1.25	93
.6	1.0	.95	95	0.90	89
.4	1.0	.96	96	.60	89
.2	1.0	.97	97	.30	89

Pyrolysis of Diglycolic Anhydride.—The sample of diglycolic anhydride was placed in a test-tube with a side

(3) Anschütz, *Ann.*, **273**, 66 (1892).

(4) Diels and Alder, *Ber.*, **62**, 554 (1929).

arm capillary. An oil-bath at 100° kept the anhydride melted and mercury, which was dropped in through a capillary jet, forced the anhydride at a uniform rate into the top of the vertical hot reaction tube. The reaction products were condensed in a side-arm flask, attached to the bottom of the tube. The flask was cooled in ice and connected to a gas collecting bottle. The tube was flushed out with nitrogen before each run.

The effective hot volume of the reaction tube was 87 cc. This volume makes allowance for the volume of the thermocouple well. The tube was electrically heated in a furnace whose temperature was recorded and controlled by a Leeds and Northrup potentiometer-type recorder-controller.

In the first run at 450°, 20 g. of diglycolic anhydride was passed through the tube during eighty minutes (contact time, about forty seconds). From the reaction products was obtained 15.5 g. of diglycolic anhydride and 1.2 g. of diglycolic acid. Hence, 3.3 g. of the anhydride was the amount pyrolyzed. The furan derivative weighed 3.2 g. From Table I it may be assumed that this represents 95% of the maleic anhydride present. Hence, the corrected yield of maleic anhydride, based on the diglycolic anhydride not recovered, was 71%.

The second run was performed also with 20 g. of diglycolic anhydride during eighty-seven minutes (contact time, forty-two seconds). There was recovered 10.2 g. of the anhydride and 1.5 g. of diglycolic acid; therefore, 8.3 g. of the anhydride was pyrolyzed. The furan derivative weighed 4.9 g. With the 95% correction factor, this represents a 44% yield of maleic anhydride.

The gas evolved in runs 1 and 2, respectively, measured 600 and 2500 cc. The gas was analyzed for CO_2, unsaturates, H_2 and CO. These relative amounts were formed in run 1 (% by volume): 16.6, 4.7, 20.7, 58.0. In run 2: 13.1, 21.6, 20.7, 44.6.

Ketene in the Products.—An 8-g. sample of diglycolic anhydride was pyrolyzed in the same apparatus at 500°. The gases which were evolved were passed through a low-pitched coil condenser cooled to −15° by ice and salt, and the uncondensed gas was conducted through standard alkali. The ketene in the gas stream neutralized 0.56 cc. of 2.218 *N* sodium hydroxide. This represents 0.00124 mole of ketene or 0.052 g. This is a 4% yield, calculated on the basis of 3.3 g. of unrecovered diglycolic anhydride.

Summary

Diglycolic anhydride undergoes pyrolysis at 450–500° into maleic anhydride. This reaction involves lengthening of the carbon chain. Concurrently, a small yield of ketene is obtained. A method for the separation of mixtures of diglycolic anhydride and maleic anhydride is included.

EVANSTON, ILLINOIS RECEIVED OCTOBER 25, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DEPAUW UNIVERSITY]

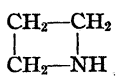
Azetidine Derivatives. I. 2,4-Diketo-3-hydroxy-3-arylazetidines

BY J. L. RIEBSOMER, HOWARD BURKETT, THOMAS HODGSON AND FRED SENOUR

The five- and six-membered heterocyclic compounds are well known since they are found in such important substances as pyrrole and pyridine. Interest in the structure and synthesis of such compounds has been fostered by the study of natural products in which these basic structures are often found.

On the other hand, four-membered heterocyclic compounds containing nitrogen in the ring have been found difficult to prepare and since no relationship between their structure and important natural products has been observed, this field of chemistry has been almost neglected.

Azetidine, or trimethyleneimine, has been known since about 1890[1] when it was prepared by the distillation of trimethylenediamine hydrochloride and by heating γ-bromopropylamine with alkali.[2]

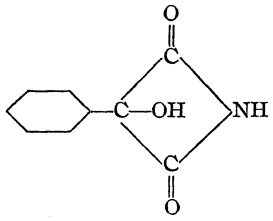


A few syntheses of substituted azetidines have been reported such as the synthesis of 3,3-dimethylazetidine,[3] N-phenyl-3,3-diphenyl-2,4-diketo-azetidine,[4] O-methylol-O-benzyleneimine,[5] 3-hydroxy-3-2,4,6-trimethoxyphenyl-2,4-diketo-azetidine,[6] and others.[7,8,9,10]

The purpose of this paper is to present a new method for the synthesis of substituted diketo-azetidines and to report certain pharmacological studies of these new compounds.

In an attempt to condense phenylhydroxymalonic esters[11] with urea in the presence of sodium ethylate to produce the corresponding barbituric acid derivatives, there were produced instead imides or azetidine derivatives such as

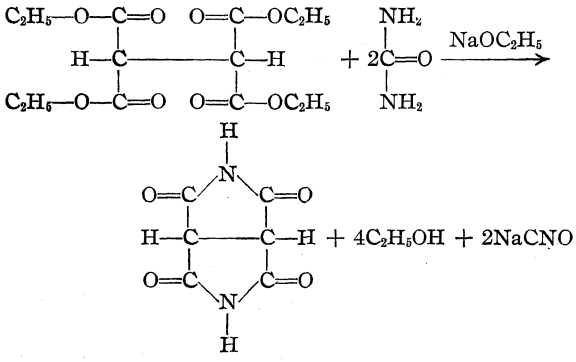
(1) Ladenburg and Sieber, *Ber.*, **23**, 2727 (1890).
(2) Gabriel and Weiner, *ibid.*, **21**, 2675 (1888).
(3) Komppa and Sevon, *Ann. Acad. Sci. Fennicae*, **37A**, 7, 8 (1933).
(4) Staudinger, Göhring and Schöller, *Ber.*, **47**, 46 (1914); Staudinger and Becker, *ibid.*, **50**, 1016 (1917).
(5) Orlov, *Chem. Zentr.*, **76**, 674 (1905); **77**, 1413 (1906).
(6) Szeki, *Ber.*, **56**, 2464 (1923).
(7) Gibbs and Marvel, THIS JOURNAL, **56**, 725 (1934); *ibid.*, **57**, 1137 (1935).
(8) Govaert, *Proc. Acad. Sci. Amsterdam*, **37**, 156 (1934).
(9) LeFèvre, *J. Chem. Soc.*, 733 (1929).
(10) Warren and Briggs, *Ber.*, **64B**, 26 (1931).
(11) Riebsomer, Irvine and Andrews, THIS JOURNAL, **60**, 1015 (1938).



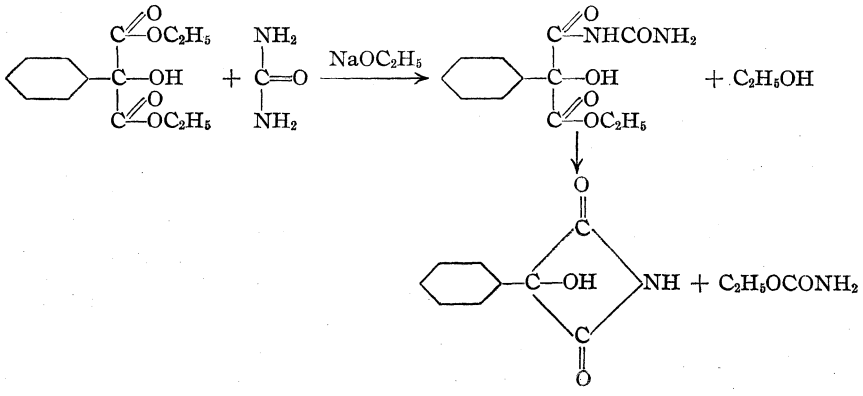
Further investigation proved that gaseous ammonia passed into the mixture of substituted malonic ester, and sodium ethylate dissolved in alcohol, produced the same substituted azetidines as when urea was added, though in lower yields.

This formation of azetidine derivatives is not so unusual as might be expected when one considers that urea has been used under similar conditions to synthesize five-membered heterocyclic nitrogen compounds.

Roeder[12] treated diethyl succinate with urea in the presence of sodium ethylate and produced succinimide. In the same publication Roeder reported a reaction very similar to the one by which we have prepared substituted azetidines and wrote the equation

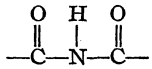


On the basis of such experience it would seem reasonable to represent the reactions by which we have prepared azetidine derivatives thus



Or since ammonia may be substituted for urea to produce the same azetidine derivatives one might reasonably postulate that urea is first decomposed by the sodium ethylate to produce ammonia which would then react to give the imide and ethyl alcohol.

Since these azetidine derivatives contain the grouping



which is associated with many compounds possessing hypnotic activity,[13] it seemed justifiable to expect some hypnotic activity when these compounds were administered to animals. All the compounds prepared in this series, however, proved to be inactive as hypnotics when given to rabbits. Not only are they inactive as hypnotics but they are toxic to rabbits in relatively small doses.

Experimental

General Method of Preparation.—Since these compounds were all prepared by essentially the same procedure, it is necessary to describe in detail the preparation of only one. For the preparation of 2,4-diketo-3-phenyl-3-hydroxy-azetidine, 25 g. of phenylhydroxymalonic ester was added to a sodium ethylate solution prepared from 80 g. of absolute alcohol and 7.5 g. of sodium. The mixture was placed in a 3-necked flask equipped with a stirrer, condenser and addition tube and was heated to 115–120° with an oil-bath and 10 g. of urea was added. After stirring at 115–120° for five hours 10 g. more urea was added and the stirring and heating continued for about eleven hours.

When the reaction was finished, the excess alcohol was evaporated to complete dryness. The dried product was dissolved in 100 cc. of water. To this solution was added 50 g. of ice and 10% hydrochloric acid was introduced slowly with stirring until the solution was acid to litmus. A large excess of acid should be avoided. The acidified solution was extracted with three 50-cc. portions of ether, and the ether solution dried over anhydrous sodium sulfate and filtered. The ether solution then was evaporated and the oily residue crystallized from a benzene–petroleum ether mixture. The yield of 2,4-diketo-3-hydroxy-3-phenylazetidine was 4.3 g., or 17% of the theoretical based on the quantity of ester used. In some cases the final purification was rather difficult and involved several crystallizations.

(12) Roeder, *Ber.*, **46**, 2561 (1913).

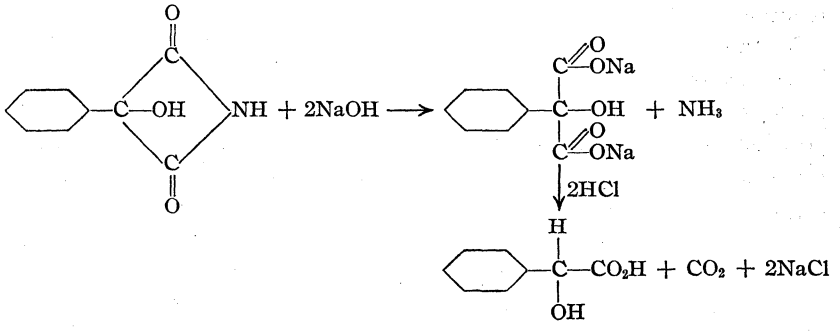
(13) Shonle, *Ind. Eng. Chem.*, **23**, 1104 (1931).

TABLE I

2,4-Diketo-3-hydroxy-3-arylazetidine	M. p., °C.	Analyses, Kjeldahl, % Calcd.	Found	Combustion analyses,% Calcd. C	H	Found C	H	Yield azetidine deriv., %	M. p. (acid produced upon sapon.), °C.
Phenyl	107.5–108	7.91	7.94	61.02	3.95	61.01	4.23	17	118
p-Tolyl	131	7.33	7.23	62.82	5.23	62.62	5.41	9	145
p-Ethyl	105–106	6.83	7.06	64.39	5.37	64.30	5.60	24	141–142
2,5-Dimethyl	135–136	6.83	6.70	64.39	5.37	63.98	5.45	37	116–117
Mesityl	151–152	6.39	6.29	65.75	5.94	65.79	6.02	6	147
p-*s*-Butyl	89–90	6.01	5.86	66.85	6.43	66.74	6.52	38	105–106

Synthesis Using Ammonia Instead of Urea.—In this synthesis the procedure was the same as outlined above except that dry ammonia gas was bubbled slowly into the arylhydroxymalonic ester–sodium ethylate mixture instead of adding the urea. This procedure was carried out in three different cases using phenylhydroxymalonic ester, *p*-tolylhydroxymalonic ester and *p*-ethylphenylhydroxymalonic ester as starting materials. The corresponding azetidine derivatives were formed in yields of about 3%. The melting points, mixed melting points and N, C and H analyses checked with the compounds produced from urea and the corresponding malonic esters.

Proof of Structure.—A sample of 1–2 g. of each of the substituted azetidines was saponified with excess 20% aqueous sodium hydroxide by boiling the mixture for four hours. Ammonia gas was evolved, which would be anticipated from such treatment of imides. The saponified product was strongly acidified with hydrochloric acid and boiled for four hours during which time carbon dioxide was evolved. The acidified solution was extracted with ether, the ether evaporated and the residue crystallized from benzene. The resulting products were shown by their melting points and mixed melting points to be the corresponding mandelic acids. The reactions may be explained by the typical equations shown.



A summary of the data obtained from the compounds prepared is assembled in Table I.

The authors are indebted to Dr. Robert S. Shelton of the William S. Merrell Company for the pharmacological data, and to Dean William M. Blanchard of DePauw University who was instrumental in obtaining financial aid from The National Research Council, and from Mr. J. K. Lilly of Indianapolis, Indiana.

Summary

1. Six 2,4-diketo-3-hydroxy-3-arylazetidines have been prepared by the condensation of arylhydroxymalonic esters and urea.

2. These compounds failed to show any hypnotic activity when administered to rabbits. They did prove to be moderately toxic.

GREENCASTLE, INDIANA RECEIVED AUGUST 18, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF HOWARD UNIVERSITY AND QUEENS COLLEGE]

The Addition of Methoxyamine to α,β-Unsaturated Ketones and the Rearrangement of β-Methoxyaminoketones[1]

BY A. H. BLATT

We have found from some experiments designed to determine the usefulness of methoxyamine[2] as a reagent for carbonyl compounds that, while methoxyamine hydrochloride reacts readily with both aldehydes and ketones to form oxime methyl ethers, the free base reacts in this fashion only with aldehydes and the more reactive ketones. This observation, which is in qualitative agreement with studies on the rate of oxime formation in relation to the *p*H of the reaction medium,[3] suggested that methoxyamine might, like numerous other basic nitrogen compounds,[4] add to the conjugated system present in α,β-unsaturated ketones. Such addition, we have found, does take place and in the following paragraphs we report on one portion of a study of this addition reaction and the resulting addition products.

Methoxyamine adds readily and reversibly to benzalacetophenone and to a number of its analogs which contain a substituent in the *p* or *p'* position to furnish saturated β-methoxyamino ketones such as (I).

$$C_6H_5CH{=}CHCOC_6H_5 + CH_3ONH_2 \rightleftharpoons \underset{\displaystyle NHOCH_3}{\overset{\displaystyle C_6H_5CHCH_2COC_6H_5}{|}}$$

I

Methoxyamino-*bis*-propiophenones, such as VII, occasionally are formed also and from one unsaturated ketone, *p*-methylbenzalacetophenone, a *bis* compound of this type is the only product. The addition reaction is in itself unusual because it takes place in the absence of any added catalyst and because, when a strong base is added as a catalyst, the reaction does not stop with the formation of a β-methoxyamino ketone. Up to the present time the addition of methoxyamine to benzalacetophenone and eight substituted benzalacetophenones has been examined (see Table I). With every ketone, addition takes place. There are considerable variations in the yields of addition products obtained but differences in the solubilities of the products as well as in the position of equilibrium must be considered in order to account for the actual yields obtained, and there is no indication as yet of any regular influence on the addition reaction exerted by the substituent present in the unsaturated ketone.

In view of the large amount of information already available on the addition reactions of α,β-unsaturated ketones, there can be little doubt but that the addition of methoxyamine to these unsaturated ketones is 1,4 and that the addition products are constituted like that from benzalacetophenone whose structure is shown in formula (I). However, the rearrangement which takes place on treatment of these addition products with strong bases, and which will be described shortly, makes it imperative to secure unequivocal evidence for the structures assigned to the addition products. This evidence was obtained for the addition product of methoxyamine to benzalacetophenone, β-phenyl-β-methoxyaminopropiophenone (I), by oxidizing the material to a product whose structure was established by two independent syntheses.

When β-phenyl-β-methoxyaminopropiophenone, as its hydrochloride (II), is oxidized by hypochlorous acid,[5] it furnishes the monoxime methyl ether of dibenzoylmethane (III).

$$\left[\underset{\displaystyle NH_2OCH_3}{\overset{\displaystyle C_6H_5CHCH_2COC_6H_5}{|}}\right]Cl + HOCl \longrightarrow$$

II

$$C_6H_5C(=NOCH_3)CH_2COC_6H_5{}^{6} + 2HCl + H_2O$$

III

The structure of the oxime ether (III) is estab-

(1) Presented in part at the Milwaukee meeting of the American Chemical Society, September, 1938.

(2) The name methoxyamine is both more concise and more clearly descriptive than the usual name, α-methylhydroxylamine. Dr. E. J. Crane, Editor of *Chemical Abstracts*, to whom we are indebted for assistance in naming the methoxyamine addition products described in this paper, has also informed us that methoxyamine is the correct name. Compare Patterson, THIS JOURNAL, **55**, 3918 (1933).

(3) Ölander, *Z. physik. Chem.*, **129**, 1 (1927); Huckel and Sachs, *Ann.*, **498**, 176 (1932).

(4) (a) Ammonia and amines: Tambor and Wildi, *Ber.*, **31**, 349 (1898); Kohn and Morgenstern, *Monatsh.*, **28**, 485 (1907); Smith and Adkins, THIS JOURNAL, **60**, 407 (1938). (b) Piperidine: Georgi and Schwyzer, *J. prakt. Chem.*, **86**, 273 (1912). (c) Piperazine and morpholine: Stewart and Pollard, THIS JOURNAL, **58**, 1980 (1936); **59**, 2006, 2702 (1937). (d) Hydroxylamine: Harries, *Ann.*, **330**, 191 (1904)

(5) Boese, Jones and Major, THIS JOURNAL, **53**, 3530 (1931).

(6) The configuration assigned to this oxime ether is purely arbitrary.

lished by its preparation, accompanied by the dioxime dimethyl ether (IV), from methoxyamine hydrochloride and dibenzoylmethane (a synthesis which takes advantage of the fact mentioned previously that methoxyamine hydrochloride, in contrast with the free base, reacts with ketonic carbonyl groups).

$$C_6H_5COCH_2COC_6H_5 \xrightarrow{CH_3ONH_3Cl} C_6H_5CCH_2COC_6H_5 + C_6H_5C(NOCH_3)CH_2C(NOCH_3)C_6H_5$$
(III: $C_6H_5CCH_2COC_6H_5$, $NOCH_3$; IV: $C_6H_5C(NOCH_3)CH_2C(NOCH_3)C_6H_5$)

This set of reactions, it should particularly be noted, establishes the location of the nitrogen atom in the addition product as attached to the carbon atom in the β-position to the carbonyl group.

A second synthesis of the monoxime methyl ether of dibenzoylmethane, which establishes at the same time that methoxyamine adds also to acetylenic ketones, is furnished by the reaction between methoxyamine and benzoylphenylacetylene. The 1,4-addition of methoxyamine to this ketone would furnish a product (V) which, as the eneamine tautomer of an oxime methyl ether, should rearrange to the same substance, (III), that was obtained by the oxidation of β-phenyl-β-methoxyaminopropiophenone (I). This expectation is realized for the addition of methoxyamine to benzoylphenylacetylene furnishes directly the monoxime methyl ether of dibenzoylmethane (III).

$$C_6H_5C{\equiv}CCOC_6H_5 + CH_3ONH_2 \longrightarrow \left[C_6H_5C(NHOCH_3){=}CHCOC_6H_5\right] \longrightarrow C_6H_5CCH_2COC_6H_5$$
(V: $C_6H_5C(NHOCH_3){=}CHCOC_6H_5$; III: $C_6H_5CCH_2COC_6H_5$, $NOCH_3$)

Finally, the fact may be mentioned, as corroborative negative evidence for 1,4-addition, that β-phenylbenzalacetophenone which does not undergo the customary 1,4-addition reactions[7] does not add methoxyamine.

It was stated earlier that the addition of methoxyamine to α,β-unsaturated ketones is reversible. This is shown by the behavior of the addition products on heating, either alone or in the presence of a methoxyamine acceptor. Usually the addition products can be distilled in a high vacuum but when they are heated at only moderately reduced pressures they dissociate to regenerate methoxyamine and an α,β-unsaturated ketone. The equilibrium in the addition reactions usually is quite favorable to the formation of the addition products and this is true whether the addition is carried out at room temperature or near the boiling point of the solvent, alcohol. Consequently the addition products can be heated in alcoholic solution to the boiling point of the solution without appreciable change. If, however, a methoxyamine acceptor, for example, benzaldehyde which as an aldehyde will react with the free base, is present, then the addition reaction is reversed and the unsaturated ketone is regenerated. In effect, this process utilizes the addition products as oximating agents.

$$C_6H_5CH(NHOCH_3)CH_2COC_6H_4Br\text{-}p + C_6H_5CHO \longrightarrow$$
(VI: $C_6H_5CH(NHOCH_3)CH_2COC_6H_4Br\text{-}p$)

$$C_6H_5CH{=}CHCOC_6H_4Br\text{-}p + C_6H_5CH{=}NOCH_3 + H_2O$$

The β-methoxyaminopropiophenones produced by the addition of methoxyamine to α,β-unsaturated ketones are O,N-disubstituted hydroxylamines and as such are weak bases. They will add to a second molecule of unsaturated ketone, they can be readily acetylated, and they form easily hydrolyzed salts with the halogen acids. Addition to a second molecule of unsaturated ketone furnishes methoxyimino-*bis*-propiophenones such as (VII). These *bis* compounds or trimolecular products are relatively unreactive, high melting and sparingly soluble substances.

$$C_6H_5CH(NHOCH_3)CH_2COC_6H_5 + C_6H_5CH{=}CHCOC_6H_5 \longrightarrow$$
(VII: $C_6H_5CH(NOCH_3)CH_2COC_6H_5$)

The acetyl derivatives of the β-methoxyaminopropiophenones (see Table II, p. 3498), which are formed in quantitative yield simply by dissolving the parent substances in acetic anhydride, are more sparingly soluble and crystallize better than do the addition products. The acetyl derivatives, like the parent compounds, regenerate α,β-unsaturated ketones on heating; unlike the parent compounds they also regenerate α,β-unsaturated compounds on treatment with sodium methylate. The salts formed by the addition compounds with the halogen acids can be hydrolyzed by solution in alcohol and dilution with water. If, however, these salts in alcoholic solution or the addition products in alcoholic acid are heated, the addition

(7) Kohler, *Am. Chem. J.*, **38**, 515 (1907).

reaction is reversed. And, since methoxyamine hydrochloride reacts with ketonic carbonyl groups the oxime methyl ether of the unsaturated ketone, as well as the unsaturated ketone, is formed. The process is illustrated by the equation

$$C_6H_5CHCH_2COC_6H_4Br\text{-}p + HCl \longrightarrow$$
$$\quad\quad |$$
$$\quad NHOCH_3$$
$$C_6H_5CH{=}CHCOC_6H_4Br\text{-}p + CH_3ONH_3Cl \longrightarrow$$
$$C_6H_5CH{=}CHCC_6H_4Br\text{-}p^6 + HCl + H_2O$$
$$\quad\quad\quad

TABLE I

Notes to Table I. All the products described are colorless solids; the β-methoxyaminopropiophenones are readily soluble in all the common solvents save petroleum ether. The letters in the column "Temperature" indicate that addition was made near the boiling point of the solution (H) or at room temperature (C). The yields reported refer to crude, washed addition products. No yields are reported for the *bis* compounds as they were obtained only in small amounts from reaction mixtures which had been allowed to stand for long periods of time. The addition product from anisalacetophenone could not be obtained solid; the oil left after evaporating the solvent and excess methoxyamine furnished a crystalline acetyl derivative, see Table II. The addition product from benzal-*p*-methylacetophenone was difficult to obtain as a solid and to handle once solid; the oil left after evaporating the solvent and excess methoxyamine was used to prepare the acetyl derivative, Table II, and the unsaturated amine, Table III.

Unsaturated ketone	Product	Temp.,	Yield, %	M. p., °C.	Crystallized from	Formula	OCH_3 Anal., % Calcd.	Found
		H	78					
$C_6H_5CH{=}CHCOC_6H_5$	$C_6H_5CH(NHOCH_3)CH_2COC_6H_5$	C	64	54–55	Ethanol	$C_{16}H_{17}NO_2$	12.15	11.9
	$C_6H_5CHCH_2COC_6H_5$ | $NOCH_3$ | $C_6H_5CHCH_2COC_6H_5$	C	..	178–179	Ethanol	$C_{31}H_{29}NO_3$	6.7	6.7
$C_6H_5CH{=}CHCOC_6H_4CH_3$-*p*	$C_6H_5CH(NHOCH_3)CH_2COC_6H_4CH_3$-*p*	C	60	43–44	Ether–pet. ether	$C_{17}H_{19}NO_2$	11.5	11.45
p-$CH_3C_6H_4CH{=}CHCOC_6H_5$	*p*-$CH_3C_6H_4CHCH_2COC_6H_5$ | $NOCH_3$ | *p*-$CH_3C_6H_4CHCH_2COC_6H_5$	C	..	185–186	Methanol	$C_{33}H_{33}NO_3$	6.3	6.3
$C_6H_5CH{=}CHCOC_6H_4Cl$-*p*	$C_6H_5CH(NHOCH_3)CH_2COC_6H_4Cl$-*p*	C	70	51–52	Ether–pet. ether	$C_{16}H_{16}ClNO_2$	10.7	10.66
p-$ClC_6H_4CH{=}CHCOC_6H_5$	*p*-$ClC_6H_4CH(NHOCH_3)CH_2COC_6H_5$	H	86	67–68	Ethanol	$C_{16}H_{16}ClNO_2$	10.7	10.7
$C_6H_5CH{=}CHCOC_6H_4OCH_3$-*p*	$C_6H_5CH(NHOCH_3)CH_2COC_6H_4OCH_3$-*p*	H	65	52–53	Ethanol	$C_{17}H_{19}NO_3$	21.75	21.4
	$C_6H_5CHCH_2COC_6H_4OCH_3$-*p* | $NOCH_3$ | $C_6H_5CHCH_2COC_6H_4OCH_3$-*p*	C	..	183–184	Ethanol	$C_{33}H_{33}NO_5$	17.8	18.1
$C_6H_5CH{=}CHCOC_6H_4Br$-*p*	$C_6H_5CH(NHOCH_3)CH_2COC_6H_4Br$-*p*	C	83	66–67	Ethanol	$C_{16}H_{16}BrNO_2$	9.3	8.9
p-$BrC_6H_4CH{=}CHCOC_6H_5$	*p*-$BrC_6H_4CH(NHOCH_3)CH_2COC_6H_5$	H	63	52–53	Ethanol	$C_{16}H_{16}BrNO_2$	9.3	9.1

product by a molecular weight determination (calcd. for $C_{31}H_{29}NO_3$: mol. wt., 463. Found: mol. wt. (camphor), 458) and by a synthesis from β-phenyl-β-methoxyaminopropiophenone (I) and benzalacetophenone. For this purpose 1.0 g. of the unsaturated ketone and 1.2 g. of the methoxyamino ketone were dissolved in 15 cc. of alcohol and left for sixty-seven days at room temperature. During this time, 0.6 g. of the sparingly soluble *bis* compound precipitated. On high vacuum distillation this material furnished benzalacetophenone.

The effect of acids on the β-methoxyaminopropiophenones and the reversal of the addition reaction which leads to their formation were examined using β-phenyl-β-methoxyamino-*p*-bromopropiophenone (VI), since the products obtained from the compound were easily handled. When a solution of 1.0 g. of the propiophenone (VI) in 16 cc. of alcohol, 1 cc. of concd. hydrochloric acid and 3 cc. of water was boiled for three hours then chilled, it deposited 0.35 g. of benzal-*p*-bromoacetophenone (mixed m. p.). The filtrate, after removal of the unsaturated ketone, left on slow evaporation benzal-*p*-bromoacetophenoneoxime methyl ether (VIII). This material was identified by comparison with a sample prepared by boiling for three hours an alcoholic solution containing benzal-*p*-bromoacetophenone and an equivalent amount of methoxyamine hydrochloride. The oxime ether (VIII), obtained by evaporating an ether extract of the reaction mixture, crystallizes from alcohol in long silky needles which melt at 77–78°.

Anal. Calcd. for $C_{16}H_{14}BrNO_2$: OCH_3, 9.8. Found: OCH_3, 9.6.

When 1.65 g. of β-phenyl-β-methoxyamino-*p*-bromopropiophenone in 5 cc. of methyl alcohol was boiled for forty-eight hours with two equivalents of benzaldehyde, the solution on cooling set to a paste. Filtration furnished 0.5 g. of benzal-*p*-bromoacetophenone, identified by comparison with an authentic sample.

Oxidation of β-Phenyl-β-methoxyaminopropiophenone (I).—One-half gram of the hydrochloride (II) was stirred into 50 cc. of cold water, and 20 cc. of cold sodium hypochlorite solution ("Oxol") was added. Dilute hydrochloric acid in excess was next added and the reaction mixture was stirred for an hour. The precipitated solid, which was slightly sticky and weighed 0.5 g., was crystallized from alcohol. It then melted at 114–115° and was shown to be the monoxime methyl ether of dibenzoylmethane (III) by a mixed melting point with a synthetic sample of that material.

Synthesis of the Monoxime Methyl Ether of Dibenzoylmethane (III).—A. When a solution of 4.5 g. of dibenzoylmethane and 1.7 g. of methoxyamine hydrochloride in 20 cc. of alcohol was boiled for two hours, then cooled, it deposited 3.4 g. of colorless solid which melted over the range 70–100°. Crystallization from alcohol furnished the pure monoxime ether (III) in fine silky needles which melted at 114–115°.

Anal. Calcd. for $C_{16}H_{15}NO_2$: OCH_3, 11.79. Found: OCH_3, 11.85.

The impurity accompanying the monoxime ether (III) and responsible for the low melting point of the crude product is the dioxime dimethyl ether of dibenzoylmethane (IV). The dioxime dimethyl ether can be prepared directly from dibenzoylmethane and two equivalents of methoxyamine hydrochloride or from the monoxime

TABLE II

Substance	M. p., °C.	Crystallized from	Compn.	OCH_3 anal., % Calcd.	Found
$C_6H_5CH(N(COCH_3)(OCH_3))CH_2COC_6H_5$	94.5–95.5	EtOH–water	$C_{18}H_{19}NO_3$	10.44	10.2
$C_6H_5CH(N(COCH_3)(OCH_3))CH_2COC_6H_4CH_3$-$p$	118–119	Methanol	$C_{19}H_{21}NO_3$	10.0	10.0
$C_6H_5CH(N(COCH_3)(OCH_3))CH_2COC_6H_4Cl$-$p$	142–143	Methanol	$C_{18}H_{18}ClNO_3$	9.35	9.35
p-$ClC_6H_4CH(N(COCH_3)(OCH_3))CH_2COC_6H_5$	91–92	Ethanol	$C_{18}H_{18}ClNO_3$	9.35	9.1
$C_6H_5CH(N(COCH_3)(OCH_3))CH_2COC_6H_4OCH_3$-$p$	115–116	Ethanol	$C_{19}H_{21}NO_4$	19.3	19.75
p-$CH_3OC_6H_4CH(N(COCH_3)(OCH_3))CH_2COC_6H_5$	130–131	Ethanol	$C_{19}H_{21}NO_3$	19.3	19.6
$C_6H_5CH(N(COCH_3)(OCH_3))CH_2COC_6H_4Br$-$p$	157–158	Ethanol	$C_{18}H_{18}BrNO_3$	8.24	8.0
p-$BrC_6H_4CH(N(COCH_3)(OCH_3))CH_2COC_6H_5$	91–92	Ethanol	$C_{18}H_{18}BrNO_3$	8.24	8.37

TABLE III

Substance	Yield, %	Crystallized from	M. p., °C.	Compn.	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
$C_6H_5CH{=}C(NH_2)COC_6H_5$	94	Methanol	100–101	$C_{15}H_{13}NO$	80.73	81.08	5.8	5.8
$C_6H_5CH{=}C(NH_2)COC_6H_4CH_3$-$p$	64	Methanol	92–93	$C_{16}H_{15}NO$	81.0	80.64	6.3	6.4
$C_6H_5CH{=}C(NH_2)COC_6H_4Cl$-$p$	66	Ethanol	81–82	$C_{15}H_{12}ClNO$	69.9	69.8	4.7	5.2
p-$ClC_6H_4CH{=}C(NH_2)COC_6H_5$	80	Ethanol	88–89	$C_{15}H_{12}ClNO$	69.9	70.1	4.7	4.8
$C_6H_5CH{=}C(NH_2)COC_6H_4Br$-$p$	83	Methanol	103–104	$C_{15}H_{12}BrNO$	59.6	60.0	4.0	4.2
p-$BrC_6H_4CH{=}C(NH_2)COC_6H_5$	90	Methanol	114–115	$C_{15}H_{12}BrNO$	59.6	59.7	4.0	4.4

α-Aminobenzalacetophenone can also be prepared, less satisfactorily, in a single reaction using benzalacetophenone, methoxyamine and alcoholic potassium hydroxide. α-Aminobenzal-p-methylacetophenone was prepared from the crude oily product obtained from benzal-p-methylacetophenone and methoxyamine. The yield of this amino ketone is, therefore, based on the unsaturated ketone used and is the over-all yield of two reactions. The amino ketone from β-phenyl-β-methoxyamino-p-methoxypropiophenone was an intractable oil.

methyl ether with the same reagent. The pure dioxime ether, crystallized from alcohol, melts at 57.5–58.5°.

Anal. Calcd. for $C_{17}H_{18}N_2O_2$: OCH_3, 21.98. Found: OCH_3, 21.4.

B. One gram of benzoylphenylacetylene[9] was dissolved in 5 cc. of warm methanol and 0.3 g. of methoxyamine was added. After eighteen hours at room temperature the solution set solid when rubbed with a stirring rod. On chilling and filtering, 1.0 g. of crude oxime ether, identified by comparison with a sample prepared from dibenzoylmethane, was obtained.

Acetylation of the β-methoxyaminopropiophenones takes place on dissolving them in excess acetic anhydride. In some cases, solution occurs at room temperature while in other cases gentle warming on the steam-bath for a minute or two is required. The acetyl derivatives crystallize when the reaction mixtures, after cooling to room temperature, are stirred with water to destroy the excess anhydride. The yields are quantitative and the products are all colorless solids. Detailed information about the acetylation products is summarized in Table II.

When the acetyl derivative of β-phenyl-β-methoxyamino-p-bromopropiophenone was distilled at 15 mm., it furnished benzal-p-bromoacetophenone. The same product, in quantitative yield, was obtained when this acetyl derivative suspended in methyl alcohol was treated in the cold with one equivalent of sodium methylate.

Rearrangement of the β-Methoxyaminopropiophenones to α-Aminobenzalacetophenones.—Although the conversion of the β-methoxyaminopropiophenones to unsaturated α-amino ketones can be effected using a rather wide range of concentrations, temperatures and reaction times, we have found it most convenient to dissolve one equivalent of the methoxyamino ketone in two equivalents of 2 *N* sodium methylate solution at about 60°, adding absolute methyl alcohol when necessary to bring about complete solution. The reaction mixture is kept warm until it develops a yellow to orange color, usually about ten minutes is required, then left to stand overnight. Next day on chilling, the α-amino ketone crystallizes. The transformation is probably finished in less time but this procedure ensures completeness of reaction. Estimates of the amounts of α-amino ketones which remain dissolved in the reaction mixture, based on rough determinations of the solubility of the α-amino ketones, indicate that the rearrangement is essentially quantitative. We shall describe in detail the conversion of two β-methoxyamino ketones to α-amino ketones for illustrative purposes. Other data on the rearrangements and products are given in Table III.

When 2.55 g. (0.01 mole) of β-phenyl-β-methoxyamino-

(9) We are indebted to Dr. R. C. Fuson for a sample of this ketone.

propiophenone (I) was dissolved by warming to 60° for ten minutes in 10 cc. of sodium methylate solution containing 0.46 g. (0.02 mole) of sodium and the orange-yellow solution was left for eighteen hours, it deposited on chilling 2.19 of α-aminobenzalacetophenone (IX); yield, 94%. The product, after crystallization from methyl alcohol, melted at 100–101°. This amino ketone, which had previously been prepared by a different method,[8] was identified by analysis, by the formation of a hydrochloride melting with decomposition at 180° (instantaneous melting point, 185°), and by hydrolysis on warming with dilute hydrochloric acid to phenylbenzylglyoxal which was isolated and characterized as the antimony derivative, m. p. and mixed m. p. 174–175°.

When 6.7 g. (0.02 mole) of β-phenyl-β-methoxyamino-*p*-bromopropiophenone (VI) was dissolved in 20 cc. of warm sodium methylate, containing 0.92 g. of sodium (0.04 mole), plus 20 cc. of absolute methyl alcohol and warmed for fifteen minutes the orange reaction mixture set solid on cooling. Chilling and filtering furnished 5.0 g. of α-aminobenzal-*p*-bromoacetophenone, a yield of 83%.

Summary

Methoxyamine adds to benzalacetophenone and its *p* or *p'* substituted analogs to furnish β-methoxyaminopropiophenones and β,β'-methoxyimino-*bis*-propiophenones. The same reagent adds also to benzoylphenylacetylene. The addition reaction has been shown to be reversible and the structures of the addition products have been established. The chemical behavior of the addition products has been described and it has been shown that the β-methoxyaminopropiophenones on treatment with strong bases lose a molecule of alcohol and rearrange to form α-amino unsaturated ketones.

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[A COMMUNICATION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Preparation of Certain Amines

BY EDWARD J. SCHWOEGLER AND HOMER ADKINS

Alcohols react with primary and secondary amines under the influence of such hydrogenating and dehydrogenating catalysts as nickel,[1,2] palladium[3] and copper chromite[4,5] with the formation of secondary and tertiary amines.

$$ROH + R'NH_2 \longrightarrow RNHR' + H_2O \quad (1)$$
$$ROH + R'_2NH \longrightarrow RNR'_2 + H_2O \quad (2)$$

Since tertiary alcohols do not show this type of reaction it is plausible to asume that the primary function of the catalyst is to dehydrogenate the alcohol to an aldehyde or ketone. The latter would then react with an amine to give a product which is readily hydrogenated to an amine.

$$R_2CHOH \longrightarrow R_2CO + H_2 \quad (3)$$
$$R_2CO + R'NH_2 \longrightarrow R_2C(OH)(NHR') \quad (4)$$
$$R_2C(OH)(NHR) + H_2 \longrightarrow R_2CHNHR + H_2O \quad (5)$$

An alternative series of reactions depending upon the dehydrogenation of the original amine instead of the alcohol is not plausible for the product of reactions similar to (3), (4) and (5) would be an ether:

$$RCH_2NH_2 \longrightarrow RCH{=}NH + H_2 \quad (6)$$
$$RCH{=}NH + R'OH \longrightarrow RCH(NH_2)(OR') \quad (7)$$
$$RCH(NH_2)(OR') + H_2 \longrightarrow RCH_2OR' + NH_3 \quad (8)$$

However, a dehydrogenation as shown in (6) probably occurs, for secondary amines having the same alkyl groups as the primary amine are readily formed over palladium,[3] nickel[2] and copper chromite.[4] In fact this reaction constitutes an important side reaction when it is desired to combine an alcohol and an amine according to the type reactions (1) and (2). The series of probable reactions is

$$RCH_2NH_2 \longrightarrow RCH{=}NH + H_2 \quad (9)$$
$$RCH{=}NH + RCH_2NH_2 \longrightarrow RCH(NH_2)(NHCH_2R) \quad (10)$$
$$RCH(NH_2)(NHCH_2R) + H_2 \longrightarrow (RCH_2)_2NH + NH_3 \quad (11)$$

Reactions of the type shown in (1) and (2) go smoothly and almost quantitatively in certain cases, but this is by no means always true. It seemed desirable therefore to ascertain the optimum conditions for the reaction of representative alcohols and aliphatic amines. The data given in Table I indicate the yields which have been obtained under the specified conditions. A consid-

(1) Adkins and Cramer, THIS JOURNAL, **52**, 4350 (1930).
(2) Winans and Adkins, *ibid.*, **54**, 306 (1932).
(3) Kindler, *Ann.*, **485**, 113 (1931).
(4) Paden and Adkins, THIS JOURNAL, **58**, 2487 (1936).
(5) Hill and Adkins, *ibid.*, **60**, 1033 (1938).

erable number of variations in the experimental conditions have been made and the ones specified for the various reactants gave the highest yields among those tried. It is probable that variations in the temperature and duration of reaction, ratio of catalyst to reactants, etc., would give even higher yields of the desired products.

The data in the table show very clearly that the optimum conditions vary with the alcohol and with the amine. The optimum yield varies over

TABLE I

YIELDS OF AMINES BY REACTION OF ALCOHOLS AND AMINES[a]

Alcohols	Amines							
	n-Amylamine		Piperidine		Phenethylamine		2-Me-4-aminopentane	
Ethyl	39%	a	82%	c	67%	b	53%	g
			31	d				
n-Propyl	15	a	63	d	26	b	61	a
i-Propyl	43	a	46	d	67	b	50	a
n-Butyl	6	a	70	c	60	b	48	j
			83	f				
n-Hexyl	....		84	d	....		...	
Cyclohexyl	57	e	59	d	58	b	37	h
2-Ethylhexyl	....		29	i	....		....	
n-Dodecyl	0	a	69	c	14	b	47	h
			78	d				

[a] Equimolecular quantities (usually 0.2 mole) of amine and alcohol and 4 g. of copper chromite were used except in (c) where 3 to 4 g. of Raney nickel and (f) and (j) where 8 g. of copper chromite was the catalyst. Eighty ml. of dioxane was used as a solvent for 0.2 mole of amine except in (c) where an excess of alcohol, and (a) and (g) where diethyl ether was the reaction medium. All reactions were carried out under 125 atm. of hydrogen at the temperatures and for the duration of time indicated below: (a) and (e) twelve hours at 180°, (b) and (c) three and one-half hours at 200°, (d) and (f) three and one-half hours at 250°, (g), (h) and (j) twelve hours at 200°, (i) twelve hours at 250°.

wide limits even if comparisons are made with the same amine and different alcohols or the same alcohol with different amines. Among the four amines, the best yields were with piperidine while the poorest were with *n*-amylamine. This may be correlated with the fact that higher temperatures could be used with piperidine than with *n*-amylamine. The higher temperature which may be used with piperidine as contrasted with the primary amines is probably due to the fact that the latter may form secondary amines through reactions (9), (10) and (11). For example, yields as high as 52% of diphenethylamine were obtained at 250° over copper chromite. At 200° no appreciable amount of diphenethylamine was formed.

Mignonac was the first to prepare amines by the hydrogenation of aqueous ammoniacal or amine solutions of aldehydes and ketones.[6] Later it was shown that better yields of the amines were obtained if the ammonia or amine addition product of the aldehyde were isolated and the hydrogenation carried out in an organic solvent.[7] However, there has been described no practical method for preparing primary amines directly from aldehydes or ketones and ammonia.[8] The most satisfactory method for converting an aldehyde or ketone to a primary amine has been through the preparation of the oxime.[7,9]

Representative ketones and aldehydes have now been converted in good yields to the corresponding primary amines by dissolving the carbonyl compound in a mixture of methanol and liquid ammonia and hydrogenating over Raney nickel. The reaction mixture in most cases consisted of 0.5 mole of carbonyl compound, 0.7 mole of ammonia, 50 ml. of methanol and 3 to 4 g. of Raney nickel under 150 atm. of hydrogen. Preparations were also made on a slightly smaller scale and on quantities six times as large as those specified above. Except for benzaldehyde (125°) and furfural (125 to 140°) the temperature for reaction was 150°. The period of reaction was usually about one hour, though furfural was complete after ten minutes, while benzophenone was heated for three and one-half hours before the absorption of hydrogen ceased.

Among the compounds which have given good results are heptaldehyde, benzaldehyde, acetophenone, pinacolone and several dialkyl ketones. The yields of various amines were as follows: 2-methyl-4-aminopentane, 65%; α-phenethylamine, 64%; benzhydrylamine, 19%; 2,2-dimethyl-3-aminobutane, 51%; 5-aminononane, 72%; 2,4-dimethyl-3-aminopentane, 48%; benzylamine, 48%; *n*-heptylamine, 59%; and furfurylamine, 60%. Acetonylacetone under the same conditions gave 2,5-dimethylpyrrolidine, 28%, and 2,5-dimethylpyrrole, 59%, while acetylacetone underwent aminolysis to give acetamide in quantitative yield.

Secondary amines are formed in very consider-

(6) Mignonac, *Compt. rend.*, **172**, 275 (1921).

(7) Winans and Adkins, THIS JOURNAL, **55**, 2051 (1933).

(8) Since the completion of the experimental work described herein a U. S. patent 2,109,159, Feb. 22, 1938, has been issued to C. F. Winans covering the hydrogenation of a mixture of furfural and ammonia in an inert organic solvent with the production of furfurylamines.

(9) Martha E. Smith and Adkins, THIS JOURNAL, **60**, 660 (1938).

TABLE II

PHYSICAL PROPERTIES AND ANALYTICAL DATA

Amine	Formula	Amines B. p., °C.	Mm.	$n^{25}D$	Nitrogen, % Calcd.	Found	Hydrochlorides M. p., °C.	Chlorine, % Calcd.	Found
N-2-Ethylhexylpiperidine	$C_{13}H_{17}N$	141	42	1.4520	7.10	6.99	162–163	15.17	15.24
N-*n*-Propyl-β-phenethylamine	$C_{11}H_{17}N$	102	16	1.4998	8.59	8.47	218	17.76	17.81
N-Isopropyl-β-phenethylamine	$C_{11}H_{17}N$	112	21	1.4990	8.59	8.44	163–164	17.76	17.59
N-Ethyl-*n*-amylamine	$C_7H_{17}N$	136		1.4111	12.17	12.38	195	23.48	23.51
N-*n*-Propyl-*n*-amylamine	$C_8H_{19}N$	155		1.4161	10.85	11.01	247(d)	21.41	21.21
N-Isopropyl-*n*-amylamine	$C_8H_{19}N$	146		1.4113	10.85	10.81	167–167.5	21.41	21.45
N-Cyclohexyl-*n*-amylamine	$C_{11}H_{23}N$	118	30	1.4500	8.28	8.08			
N-Ethyl-2-Me-4-aminopentane	$C_8H_{19}N$	136		1.4105	10.84	10.67	144–145	21.41	21.55
N-*n*-Propyl-2-Me-4-aminopentane	$C_9H_{21}N$	162		1.4148	9.78	9.73	139	19.73	19.59
N-*n*-Butyl-2-Me-4-aminopentane	$C_{10}H_{23}N$	179		1.4192	8.91	8.79	149–150	18.31	18.23
N-Dodecyl-2-Me-4-aminopentane	$C_{18}H_{39}N$	170–172	12	1.4410	5.20	5.04	124.5–125	11.60	11.66
N-Cyclohexyl-2-Me-4-aminopentane	$C_{12}H_{25}N$	106	21	1.4530	7.65	7.91	198–199	16.07	16.03
N-Isopropyl-2-Me-4-aminopentane	$C_9H_{21}N$	146		1.4098	9.78	9.80	158.5	19.73	19.88
2-Me-4-aminopentane	$C_6H_{15}N$	108–109		1.4063			139.5	25.77	25.76
N-Ethyl-β-phenethylamine	$C_{10}H_{15}N$	85	8				183.5–184	19.11	19.00
		81	6						
N-*n*-Butyl-β-phenethylamine	$C_{12}H_{19}N$	113.5	6					16.60	16.44
2,4-Di-Me-3-aminopentane	$C_7H_{17}N$	129					196	25.77	25.75
2,2-Di-Me-3-aminobutane	$C_6H_{15}N$	102					296–297 (subl.)	25.77	25.78
2,5-Di-Me-pyrrolidine	$C_6H_{13}N$	113–118					201–202	26.15	26.20
Picrate of isopropylpiperidine	$C_{14}H_{20}N_4O_4$	(M. p.) 153			15.73	15.91			
Phenyl isocyanate deriv. of N-cyclohexyl-*n*-amylamine	$C_{18}H_{28}N_2O$	(M. p.) 110			9.72	9.78			

able yields through the hydrogenation of cyanides. Seldom is the ratio of primary to secondary amine greater than 3 to 1 and in some instances it is not more than 2 to 1. The formation of the secondary amine probably results from the following series of reactions as originally suggested by von Braun[2]

$$RCN + H_2 \longrightarrow RCH{=}NH \quad (12)$$

$$RCH{=}NH + H_2 \longrightarrow RCH_2NH_2 \quad (13)$$

$$RCH{=}NH + RCH_2NH_2 \longrightarrow RCH\begin{matrix}NH_2\\NHCH_2R\end{matrix} \quad (14)$$

$$RCH\begin{matrix}NH_2\\NHCH_2R\end{matrix} + H_2 \longrightarrow (RCH_2)_2NH + NH_3 \quad (15)$$

It seemed possible therefore to minimize the formation of secondary amines by carrying out the hydrogenation in the presence of ammonia. The imine formed according to reaction (12) would then have less opportunity to undergo reaction (13) because ammonia would also add to the imine

$$RCH{=}NH + NH_3 \longrightarrow RCH\begin{matrix}NH_2\\NH_2\end{matrix} \quad (16)$$

The hydrogenolysis (17) of the product of reaction (16) would give a primary amine and not a secondary amine as would be produced by reaction (15) from the addition product of reaction (14).[10]

$$RCH\begin{matrix}NH_2\\NH_2\end{matrix} + H_2 \longrightarrow RCH_2NH_2 + NH_3 \quad (17)$$

The results of hydrogenating *n*-butyl cyanide and *n*-hexyl cyanide in the presence of ammonia at 125° over Raney nickel supported this hypothesis. The yields of secondary amine were less than 5% and the yields of the primary amines, $C_5H_{11}NH_2$ and $C_7H_{15}NH_2$, were from 90 to 95%. In these experiments from 0.4 to 0.7 mole of the cyanide was hydrogenated mixed with from 0.9 to 1.6 mole of ammonia.

The reactions were carried out in steel reaction vessels using standard equipment, procedures and catalysts.[11] The products were usually separated by fractionation through a modified Widmer column having a spiral 18 cm. in length with one turn of the helix per cm.[9] The technique for

(10) There is no evidence as to whether the reactions shown in (5), (11), (15) and (17) proceed through hydrogenolysis as indicated or through a loss of ammonia and the hydrogenation of the resulting imine.

(11) Adkins, "Reactions of Hydrogen, etc.," University of Wisconsin Press, Madison, Wisconsin, 1937.

using liquid ammonia has been described in connection with the preparation of diacetoneamine.[12]

Alcohols, amines, ketones, aldehydes and cyanides were freed of any halogen-containing impurity by means of Raney nickel before they were submitted to reaction. In other respects these compounds were prepared and purified by the usual procedures.

Amines distilling over with solvents were recovered as the hydrochlorides and the amines regenerated with alkali and purified by fractional distillation. Amines were characterized by analysis and by the formation of solid derivatives. Neutral equivalents were determined upon all the amines reported.

Analytical data and physical properties of several amines and their derivatives not previously reported are given in Table II. References for certain other amines and their derivatives are given herewith: N-ethylpiperidine,[13] N-*n*-propylpiperidine,[13] N-*i*-propylpiperidine,[13] N-*n*-butylpiperidine,[14] N-*n*-hexylpiperidine,[15] N-cyclohexylpiperidine,[2] N-*n*-dodecylpiperidine,[16] N-cyclohexylphenethylamine,[17] N-*n*-dodecylphenethylamine,[18] α-phenethylamine,[19] benzhydrylamine,[20] 5-aminononane,[21] benzylamine,[22] *n*-heptylamine,[23] furfurylamine,[8] 2,5-di-Me-pyrrole, N-*n*-butyl-*n*-amylamine,[24] 2,2-di-Me-3-aminopentane,[25] 2,4-di-Me-3-aminopentane.[26]

(12) Martha E. Smith and Adkins, THIS JOURNAL, **60**, 408 (1938).
(13) Evans, *J. Chem. Soc.*, **71**, 524 (1897).
(14) Von Braun, *Ber.*, **40**, 3930 (1907).
(15) Von Braun and Buckman, *ibid.*, **64B**, 2610 (1931).
(16) Wojcik and Adkins, THIS JOURNAL, **56**, 2419 (1934).
(17) Wieland, Schopf and Hermsen, *Ann.*, **444**, 40 (1925).
(18) Wojcik and Adkins, THIS JOURNAL, **56**, 2424 (1934).

Summary

Favorable conditions for the reaction of eight representative alcohols with four different amines to give secondary and tertiary amines have been ascertained.

It has been found that representative aldehydes, dialkyl ketones and alkyl aryl ketones may be directly converted in good yields to primary amines by hydrogenating them over Raney nickel in an ammonia–methanol mixture.

The formation of secondary amines in the hydrogenation of cyanides over Raney nickel may be almost entirely prevented by carrying out the hydrogenation in the presence of sufficient ammonia.

(19) Tafel, *Ber.*, **19**, 1929 (1886).
(20) Heilbron, "Dictionary of Organic Compounds," Vol. I, Eyre and Spottiswoode, London, 1934, p. 49.
(21) Unpublished work by G. M. Whitman.
(22) Hoogewerff, *Rec. trav. chim.*, **5**, 253 (1886).
(23) Mulliken, "Identification of Pure Organic Compounds," Vol. II, John Wiley and Sons, New York, N. Y., 1916, p. 140.
(24) Ochiai and Tsuda, *J. Pharm. Soc. Japan*, **56**, 352 (1936).
(25) Markownikoff, *Ber.*, **32**, 1448 (1899).
(26) Mailhe, *Bull. soc. chim.*, **27**, 541 (1920).

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

The Conjugation of Amino Acids with Isocyanates of the Anthracene and 1,2-Benzanthracene Series[1]

BY LOUIS F. FIESER AND HUGH J. CREECH[2]

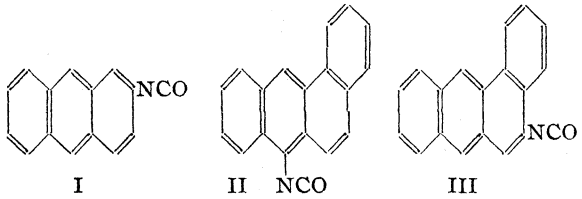
This communication describes results obtained in an extension of the program of research initiated by Franks and one of us[3,4,5] on the problem of conjugating carcinogenic hydrocarbons with proteins and investigating their possible immunizing action against hydrocarbon carcinogenesis. In the previous work the meso isocyanate derivatives of anthracene and 1,2,5,6-dibenzanthracene were prepared, characterized by reaction with simple amines and alcohols, and linked to various proteins by interaction in aqueous dioxane solution. The conjugated proteins were found to possess definite antigenic properties, varying with the nature of the prosthetic group, and experiments with preparations of 1,2,5,6-dibenzanthryl-9-carbamido-casein afforded some indications of an immunization against the action of dibenzanthracene. The material was also found to be mildly carcinogenic, and this property was discovered also in the conjugate from dibenzanthryl isocyanate and glycine.

As one step in the extension of this work we have prepared and characterized the isocyanates resulting from the interaction of phosgene with

(1) The investigations in this series were undertaken in coöperation with Dr. W. R. Franks of the Banting Institute and have been supported by a grant from the International Cancer Research Foundation.
(2) Research Fellow of the University of Toronto.
(3) Creech and Franks, *Am. J. Cancer*, **30**, 555 (1937).
(4) Creech and Franks, THIS JOURNAL, **60**, 127 (1938).
(5) Franks and Creech, *Am. J. Cancer*, **35**, 203 (1939).

β-anthramine, 10-amino-1,2-benzanthracene[6] and 3-amino-1,2-benzanthracene.[7] These starting materials were selected largely because of their availability. While it is desirable eventually to produce protein derivatives having affixed residues to which can be ascribed both carcinogenic and non-carcinogenic characteristics, the information at hand provides little basis for foretelling the biological properties of simple functional derivatives of even the much studied 1,2-benzanthracene. Since the potently carcinogenic 10-methyl-1,2-benzanthracene contrasts sharply with the inactive 3-isomer while the 10- and 3-methoxy compounds are both weakly carcinogenic[8] the relationship between corresponding isomeric carbamido derivatives is entirely problematical and seemed worthy of investigation.

In order to provide samples for biological assay, and as a prelude to preparation of the protein derivatives, the isocyanates I–III were converted into



I II III

the methyl and ethyl carbamates (ArNHCOOR), the substituted ureas ($ArNHCONH_2$), disubstituted ureas (ArNHCONHAr), and carbamido ethanol derivatives ($ArNHCONHCH_2CH_2OH$). The 10-substituted 1,2-benzanthracene derivatives contrasted sharply with the corresponding compounds in the other two series in tending to separate in a gelatinous condition. Crystalline samples were obtained only after tedious manipulation, whereas the derivatives from I and III and also from 1,2,5,6-dibenzanthryl-9-isocyanate crystallized readily. It may be noted that Badger and Cook[9] encountered similar difficulties with other 10-substituted 1,2-benzanthracenes.

The preparation of carbamido acids by linking the isocyanates to amino acids is of interest as a possible route to water-soluble carcinogens[3,10] and because of Boyland and Levi's[11] observation that certain polynuclear aromatic hydrocarbons fed to animals are excreted in part in conjugation with amino acids. Furthermore, the experiments of White and White[12] suggest a possible interaction of amino acids with carcinogenic hydrocarbons in the organism, and the striking discovery of Kögl and Erxleben[13] of the presence of amino acids of "unnatural" configuration in the hydrolyzates from tumor tissue gives impetus to the extensive study of the rôle of amino acids in respect to malignant growth. The reaction of the isocyanates I–III with glycine and with ε-aminocaproic acid was studied in aqueous dioxane solution in order to gain further experience with a procedure which could be employed for conjugating the compounds with proteins.[3,5] The condensations proceeded satisfactorily under very mild conditions, and pure reaction products were obtained in a crystalline condition in the experiments with β-anthryl- and 1,2-benzanthryl-3-isocyanate and also from the reaction of 1,2,5,6-dibenzanthryl-9-isocyanate with each of the above amino acids; the dibenzanthryl carbamido acetic acid previously assayed[3] had not been isolated in a pure state. A tendency to form gels was again encountered in the 10-substituted 1,2-benzanthracene series and the carbamido acetic and caproic acids were not obtained crystalline. Suitable processes of precipitation gave amorphous preparations of satisfactory analysis, and the ethyl ester of the former compound was isolated in a crystalline form. The glycine conjugates are sensitive substances and decompose below the melting point or when heated in organic solvents at temperatures above about 50–60°. The caproic acid derivatives are more easily purified and melt sharply without decomposition.

The present experiments provide some assurance that the method of conjugation in aqueous dioxane solution is suitable for application to proteins, and results to be reported later have borne out this expectation. In a trial of pyridine as the solvent it was found that 1,2-benzanthryl-10-isocyanate in the absence of any other reagent is polymerized rapidly by pyridine at room temperature to an amorphous, high-melting product (dimer?[14]).

Experimental Part[15]

β-Anthryl Isocyanate.—β-Aminoanthracene was prepared in 40% yield from commercial β-aminoanthra-

(6) Fieser and Hershberg, THIS JOURNAL, **60**, 1893 (1938).
(7) Fieser, Hershberg, Long and Newman, *ibid.*, **59**, 475 (1937).
(8) Summary: Fieser, *Am. J. Cancer*, **34**, 37 (1938).
(9) Badger and Cook, *J. Chem. Soc.*, 802 (1939).
(10) Bachmann and Cole, *J. Org. Chem.*, **4**, 60 (1939).
(11) Boyland and Levi, *Biochem. J.*, **30**, 1225 (1936).
(12) White and White, *Proc. Soc. Expil. Biol. Med.*, **39**, 527 (1938).
(13) Kögl and Erxleben, *Z. physiol. Chem.*, **258**, 57 (1939).
(14) van Hoogstraten, *Rec. trav. chim.*, **51**, 414 (1932).
(15) Melting points below 275° are corrected; more reliable results often were obtained using an evacuated capillary. Microanalyses by Lyon Southworth.

quinone by the method of von Braun and Bayer.[16] After several crystallizations from acetone, methanol, and benzene–ligroin, the amine was obtained as bright greenish-yellow plates, m. p. 243.5–244.5° (in vacuum: 245–245.5°).[17]

Gradual addition of excess phosgene (20 g.) in toluene to a solution of the purified amine (3 g.) in benzene produced a flocculent white precipitate of the amine hydrochloride which disappeared after refluxing for about one-half hour. The solution was evaporated at diminished pressure (100 mm.) in an atmosphere of nitrogen until it became opalescent, and it was then filtered and transferred to a vacuum desiccator. The isocyanate crystallized on further removal of the solvent and recrystallization from benzene and from carbon tetrachloride gave 2.4 g. (70%) of small, faintly yellow needles, m. p. 207.5–208°.

Anal. Calcd. for $C_{15}H_9ON$: N, 6.39; C, 82.17; H, 4.14. Found: N, 6.66 (Kjeldahl), 6.64 (Dumas); C, 81.98; H, 4.10.

In the preparation of the derivatives listed below the crude reaction products were obtained in very nearly quantitative yield.

Methyl β-anthrylcarbamate was prepared by refluxing a solution of the isocyanate (100 mg.) in methanol (10 cc.) for one-half hour. Crystallized from methanol–ligroin the substance formed lustrous, weakly yellow plates, m. p. 231–231.5°.

Anal. Calcd. for $C_{16}H_{13}O_2N$: N, 5.57. Found: N, 5.59.

The **ethyl carbamate,** obtained by refluxing the isocyanate (200 mg.) in chloroform (20 cc.) with absolute ethanol (10 cc.) for fifteen minutes, formed glistening light yellow plates from ethanol–ligroin, m. p. 216–216.5°.

Anal. Calcd. for $C_{17}H_{15}O_2N$: N, 5.28. Found: N, 5.31.

β-Anthrylcarbamidoethanol.—On adding a solution of 250 mg. of the isocyanate in 20 cc. of chloroform to 0.25 cc. of β-aminoethanol in 10 cc. of chloroform an amorphous greenish precipitate formed at once; after short warming to 40° it was cooled and the product collected and washed with 35 cc. of warm chloroform. Crystallization from 75 cc. of ethanol containing 3 cc. of dioxane gave slender, bright yellow needles. In an evacuated capillary the substance darkened at 310° and melted at about 350°.

Anal. Calcd. for $C_{17}H_{15}O_2N_2$: N, 9.99; C, 72.84; H, 5.75. Found: N, 9.82; C, 73.10; H, 5.76.

β-Anthryl Urea.—To 150 mg. of the isocyanate in 15 cc. of dioxane there was added 5 cc. of dioxane containing several drops of concentrated ammonium hydroxide. The greenish-yellow material which precipitated was crystallized from dioxane, forming small yellow plates (unmelted at 360°).

Anal. Calcd. for $C_{15}H_{12}ON_2$: N, 11.80. Found: N, 11.74.

N,N'-Di-β-anthryl Urea.—A mixture of benzene solutions of the isocyanate and β-anthramine was refluxed for twenty minutes and cooled. The yellowish-brown precipitate was washed, dried and purified by solution in dioxane and precipitation with benzene or by evaporation. Crystals were not obtained; the amorphous material was unmelted at 340° (Calcd.: N, 6.79; found: 6.02, 6.06).

β-Anthrylcarbamidoacetic Acid.—A solution of 75 mg. of glycine in 3 cc. of water was brought to *p*H 8.5 (colorimetric) by suitable addition of sodium hydroxide and added with stirring to 200 mg. of β-anthryl isocyanate in 25 cc. of dioxane. A greenish precipitate appeared at once, and after ten minutes a large volume of water was added, the mixture was warmed to 40°, alkali was added to bring the *p*H to 8.5, and the solution was filtered. Dilute hydrochloric acid was added to the opalescent filtrate to bring the *p*H to 3.0, and the greenish-white, flocculent precipitate, separated by centrifugation, was dissolved either in 500 cc. of water adjusted to *p*H 8.5 or in 1% sodium carbonate solution. Filtration through a No. 50 Whatman paper removed a trace of insoluble material. The conjugate was reprecipitated and washed with copious amounts of slightly acidified water. The process of solution and precipitation was repeated twice and the product dried in a vacuum desiccator. Further purification of the amorphous material was accomplished using water–dioxane–ethanol (5:1:2) and cooling very slowly. Eventually the substance was obtained as slender yellow needles. In an evacuated capillary the substance darkened at 250° and melted at about 310° with decomposition.

Anal. Calcd. for $C_{17}H_{14}O_3N_2$: N, 9.51; C, 69.38; H, 4.80. Found: N, 9.70; C, 68.99; H, 4.74.

ε-(β-Anthrylcarbamido)-caproic acid was prepared by conjugation of the isocyanate with ε-aminocaproic acid[18] by the above procedure and the material purified by repeated precipitation was crystallized from water–dioxane–alcohol (2:1:3) and obtained as short, dull yellow needles which darkened slightly at 260° and melted at 285–286° (vacuum).

Anal. Calcd. for $C_{21}H_{22}O_3N_2$: N, 7.98. Found: N, 8.07.

Nitration of 1,2-Benzanthracene.—A nearly colorless commercial sample of the hydrocarbon, m. p. 161–162.5° (Fraenkel and Landau), and a yellowish sample, m. p. 159–161.5° (Dominion Tar and Chemical Co.), were found unsatisfactory for the reaction, apparently because of the presence of significant quantities of chrysene. A supply of pure 1,2-benzanthracene was consequently synthesized according to Bachmann,[19,20] the hydrolysis of the intermediate naphthyl tolyl ketimine being conducted by the procedure of Fieser and Seligman.[21] Purification of the crude yellow pyrolysis product (m. p. 158.5–160°) by filtration of a benzene solution through an alumina tower removed some of the color and raised the m. p. (160–161°), but subsequent treatment with maleic anhydride[19] gave blue-fluorescent colorless plates, m. p. 160.5–161° in 30% over-all yield.

On nitrating 50 g. of the pure hydrocarbon in six lots

(16) von Braun and Bayer, *Ann.*, **472**, 116 (1929).

(17) The uncorrected m. p. is reported as 236–237°, or 238°: Liebermann and Bollert, *Ber.*, **15**, 226 (1882); Roemer, *ibid.*, **15**, 224 (1882).

(18) Eck, *Org. Syntheses*, **17**, 7 (1937).

(19) Bachmann, *J. Org. Chem.*, **1**, 349 (1936).

(20) See also Fieser and Hershberg, THIS JOURNAL, **59**, 2502 (1937).

(21) Fieser and Seligman, *ibid.*, **58**, 2486 (1936).

by the procedure of the literature[6,22] with some trial variations the yields were from 25 to 45% and the combined yield of pure 10-nitro-1,2-benzanthracene, m. p. 164–164.5°, was 20.2 g. (33%). No pure products were isolated from the mother liquors.

10-Amino-1,2-benzanthracene.—Since hydrogenation[6] of the nitro compound did not appear practical for preparative purposes, other methods were tried. Using phenylhydrazine for the reduction, the yield was only 20%, but satisfactory results were obtained with stannous chloride. In a typical run a solution of 6 g. of the pure nitro compound in 250 cc. of hot glacial acetic acid was treated with 50 g. of stannous chloride in 60 cc. of hot concentrated hydrochloric acid. After refluxing for one-half hour with mechanical stirring, 50 cc. of glacial acetic acid was added to bring about complete solution. On cooling the yellow tin double salt crystallized and was washed with acetic acid, dilute hydrochloric acid, alcohol and ether. The dried solid (7.8 g.) was decomposed by stirring with 175 cc. of 1 *N* ammonium hydroxide at 5° for one-half hour and at room temperature for one and one-half hours. The yellow solid was dried and crystallized twice from ether–petroleum ether, giving 4.1 g. (77%) of yellow needles of the amine, m. p. 175.5–176° (176–176.5° in an evacuated tube).

1,2-Benzanthryl-10-isocyanate.—On proceeding as above, 7.5 g. of the amine gave 6.5 g. (78%) of the isocyanate as slightly yellow diamond-shaped plates, m. p. 144–144.5°, after crystallization from benzene–toluene and benzene–ligroin.

Anal. Calcd. for $C_{19}H_{11}ON$: N, 5.20; C, 84.74; H, 4.12. Found: N, 5.25; C, 84.68; H, 4.10.

The purification of the carbamates described below presented considerable difficulty because of their marked tendency to separate in a gelatinous condition. A similar property was noted by Morgan and Pettet[23] in methyl and ethyl *p*-xenylcarbamates. The substances are very soluble in methanol, chloroform, ether, benzene and carbon tetrachloride and on evaporation nearly to dryness separate as amorphous powders; the addition of petroleum ether, in which the solublity is slight, invariably led to separation as a gel.

Methyl 1,2-Benzanthryl-10-carbamate.—The isocyanate was refluxed with methanol for fifteen minutes, the solution was evaporated to dryness, and the yellowish-white residue washed with methanol (m. p. 224–225°). On evaporation of a solution of the substance in ether the solid separating on the walls melted at 223–224.5° and that deposited on the bottom melted at 226–227°. Another preparation, after repeated precipitation as a gel from dioxane, methanol, or benzene by suitable addition of petroleum ether or ligroin, dried to a white powder, m. p. 226–227°. This eventually was crystallized from methanol as tiny white needles, m. p. 227–227.5°.

Anal. Calcd. for $C_{20}H_{15}O_2N$: N, 4.65. Found: N, 4.78.

The **ethyl carbamate** after similar tedious manipulation finally crystallized from absolute ethanol as rosets of small, colorless needles, m. p. 204–204.5°.

Anal. Calcd. for $C_{21}H_{17}O_2N$: N, 4.44. Found: N, 4.63.

1,2-Benzanthryl-10-carbamidoethanol also initially formed a gel but eventually was obtained from absolute ethanol–dioxane as slender white needles, m. p. 247–248° (in vacuum), with slight darkening at 240°.

Anal. Calcd. for $C_{21}H_{18}O_2N_2$: N, 8.47. Found: N, 8.37.

1,2-Benzanthryl-10-urea.—Slow cooling of a solution of the dried gelatinous reaction product in dioxane–ethyl acetate gave fine, colorless needles, m. p. (in vacuum) 334–336°, dec.

Anal. Calcd. for $C_{19}H_{14}ON_2$: N, 9.78. Found: N, 9.42.

N,N′-Di-(1,2-benzanthryl-10)-urea.—The dried powder from the flocculent brown precipitate resulting from the interaction of the 10-isocyanate and the 10-amine was repeatedly deposited from dioxane in an amorphous condition but failed to crystallize (unmelted at 330°).

Anal. Calcd. for $C_{37}H_{24}ON_2$: N, 5.47. Found: N, 5.38.

Polymerization of 1,2-Benzanthryl-10-isocyanate.—Since difficulties were encountered in attempts to prepare derivatives of aromatic isocyanates in pyridine solution, trial was made of the action of this solvent on pure 1,2-benzanthryl-10-isocyanate. The substance (100 mg.) dissolved at once at room temperature in purified anhydrous pyridine (5 cc.) to give a yellow solution, and in a few minutes the polymer began to separate. Collected and washed with ether, this was obtained as a slightly yellow powder, m. p. 305–307° (vacuum), very sparingly soluble in dioxane or benzene and only moderately soluble in pyridine. The absence of unpolymerized material was shown by the observation that boiling alcohol dissolved only a trace of material and left a residue of the same melting point.

Anal. Calcd. for $(C_{19}H_{11}ON)_x$: N, 5.20. Found: N, 5.57.

1,2-Benzanthryl-10-carbamidoacetic Acid.—The conjugate prepared from 0.5 g. of the isocyanate and 0.2 g. of glycine by the above procedure separated on acidification of the aqueous solution as a gel, which on drying afforded 0.6 g. of a light brown powder (calcd.: N, 8.13; found: 8.78). After two more precipitations, the dried material (N, 7.49) was washed with cold ether to an almost colorless powder (N, 8.16). The substance decomposed when heated in organic solvents. The addition of petroleum ether to solutions of the conjugate in cold acetone–dioxane or aqueous dioxane gave light brown amorphous precipitates which darkened at 230–240° and melted with decomposition in the region 270–275° (found for different samples: N, 7.68, 7.77). The substance was not obtained crystalline.

The **ethyl ester** was prepared by adding 0.13 g. of glycine ethyl ester in 5 cc. of benzene to 325 mg. of the isocyanate in 15 cc. of benzene at 35°. A gelatinous precipitate separated at once and after shaking for fifteen minutes this was collected, dried and washed with benzene. The yellowish solid (0.4 g.) was dissolved in pyridine at 50°; on cooling a granular product separated and was washed with ether (0.24 g., colorless; attempted concentration

(22) Barnett and Mathews, *Chem. News*, **130**, 339 (1925).
(23) Morgan and Pettet, *J. Chem. Soc.*, 1124 (1931).

of the filtrate led to decomposition). On slow cooling of a solution of this substance in ethanol–dioxane colorless microcrystals were obtained, m. p. 245–245.5°. Hydrolysis to the free acid was tried without success (decomposition).

Anal. Calcd. for $C_{23}H_{20}O_3N_2$: N, 7.52; C, 74.17; H, 5.41. Found: N, 7.67; C, 74.44; H, 5.34.

ε-(1,2-Benzanthryl-10-carbamido)-caproic acid was obtained initially as a flocculent precipitate. It formed a gel on the first two treatments with dioxane–ethanol–water and then was obtained as an amorphous precipitate giving when dried an almost colorless powder, m. p. 265–267°, with slight darkening at 200°.

Anal. Calcd. for $C_{25}H_{24}O_3N_2$: N, 7.00. Found: N, 7.06.

1,2,5,6-Dibenzanthryl-9-urea was prepared as above and obtained from dioxane in a colorless microcrystalline condition, m. p. 360–363°, dec. (vacuum).

Anal. Calcd. for $C_{23}H_{16}ON_2$: N, 8.33. Found: N, 8.19.

1,2,5,6-Dibenzanthryl-9-carbamidoacetic Acid.—This previously reported[3] substance has now been crystallized from dioxane–ethanol–water and obtained as slightly yellow needles darkening at 270° and melting at about 300° with decomposition.

Anal. Calcd. for $C_{25}H_{18}O_3N_2$: N, 7.10. Found: N, 6.64.

ε-(1,2,5,6-Dibenzanthryl-9-carbamido)-caproic acid crystallized from dioxane–ethanol–water as colorless plates which turned yellow at about 250°; m. p. about 305°.

Anal. Calcd. for $C_{29}H_{26}O_3N_2$: N, 6.21. Found: N, 6.07.

Attempted Formation of Ureas.—On refluxing a benzene solution of the 9-isocyanate and the 9-amine of 1,2,5,6-dibenzanthracene for two hours there was no evidence of reaction and both starting materials were isolated from the solution. The isocyanate reacted readily with aniline, however, giving an amorphous powder which was not obtained in a satisfactory condition. It was further found that the reaction proceeds readily with the corresponding *meso*-anthracene derivatives, giving **N,N'-di-(anthryl-9)-urea** (m. p. above 360°. Calcd.: N, 6.79. Found: N, 6.51). It therefore appears that the failure of the reaction between the two *meso*-dibenzanthracene derivatives is attributable to steric hindrance.[6,24]

1,2-Benzanthryl-3-isocyanate.—A supply of the 3-amine kindly synthesized by F. C. Novello by the previously described method[7] was recrystallized from ethanol and from benzene–ligroin, giving yellow needles, m. p. 211–212° (213.5–214° in an evacuated capillary). The isocyanate was prepared as usual (73% yield, pure) and obtained from benzene–ligroin as light yellow needles, m. p. 163–163.5°.

Anal. Calcd. for $C_{19}H_{11}ON$: N, 5.20; C, 84.74; H, 4.12. Found: N, 4.99; C, 84.83; H, 4.06.

Treated with pyridine at 25° the substance gave an amorphous, high melting polymer.

Methyl 1,2-benzanthryl-3-carbamate crystallized readily from methanol as slender white needles, m. p. 203.5–204°.

Anal. Calcd. for $C_{20}H_{15}O_2N$: N, 4.65; C, 79.71; H, 5.02. Found: N, 4.84; C, 79.57; H, 4.92.

The **ethyl carbamate** formed long, colorless needles from ethanol, m. p. 211.5–212° (Calcd.: N, 4.44. Found: N, 4.62).

1,2-Benzanthryl-3-carbamidoethanol at first separated from dioxane–ethanol in a flocculent condition but eventually formed colorless needles, m. p. 343–345° (vacuum).

Anal. Calcd. for $C_{21}H_{18}O_2N_2$: N, 8.47. Found: N, 8.50.

1,2-Benzanthryl-3-urea formed fine white needles, m. p. above 350°, from dioxane.

Anal. Calcd. for $C_{19}H_{14}ON_2$: N, 9.78. Found: N, 9.89.

The **N,N'-disubstituted urea** was obtained only as a light brown powder, m. p. above 350° (Calcd.: N, 5.47. Found: N, 5.31.).

1,2-Benzanthryl-3-carbamidoacetic acid separated from dioxane–ethanol–water as fragile, slightly yellow needles, m. p. about 310°, dec. (vacuum).

Anal. Calcd. for $C_{21}H_{16}O_3N_2$: N, 8.13. Found: N, 7.91.

ε-(1,2-Benzanthryl-3-carbamido)-caproic acid crystallized readily from dioxane–ethanol–water as glistening white needles, m. p. 295–297° (some darkening at 230°).

Anal. Calcd. for $C_{25}H_{24}O_3N_2$: N, 7.00; C, 74.97; H, 6.04. Found: N, 7.01; C, 74.84; H, 5.54.

Summary

β-Anthryl-, 1,2-benzanthryl-3- and 1,2-benzanthryl-10-isocyanate have been prepared and characterized by conversion to various carbamates and substituted ureas. The isocyanates were coupled with glycine and with ε-aminocaproic acid to give alkali-soluble substances some of which are being tested for carcinogenic activity. The method of conjugation in aqueous dioxane was found suitable for application to proteins.

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(24) Fieser and Hershberg, THIS JOURNAL, **60**, 2542 (1938).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

The Synthesis of 5,6-Dimethylglucose

BY M. R. SALMON AND GARFIELD POWELL

In the synthesis of the various partially methylated sugars investigators have attempted to use a number of blocking agents in what may be termed an indirect synthesis from the acetone sugars or related cyclic acetals, that is to say, reagents which will block certain hydroxyl groups while the acetone, etc., residues are removed and replaced by methyl or other substituents. The esters of the carboxylic acids are not satisfactory blocking agents for this type of synthesis because of their tendency to migrate and to be removed under the basic conditions of methylation, and the toluenesulfonates sometimes have the undesirable property of causing Walden inversions upon removal. While the acetates, benzoates and tosylates occasionally have been used for syntheses of this type, it seems desirable to have alternative procedures available for more general use.

Most promising of the blocking agents which have been proposed appear to be the nitro groups used by a number of English investigators,[1] and the benzyl groups of Freudenberg[2] and Zemplén[3] and their co-workers, both of which lack the ability to migrate and may be removed readily by reduction. Since it is desirable to have several blocking agents with different properties available for use as occasion demands, we are presenting in this paper a study of the use of the benzoxymethyl group in the synthesis of the previously unknown 5,6-dimethylglucose. This group appears to be somewhat more stable to alkali than the nitro group and to be introduced into the sugar molecule under somewhat less drastic conditions than the benzyl group, but like these groups is readily removable by reduction. This reduction could be performed either with sodium and alcohol or catalytically. By analogy with the results of other investigations on the reductive scission of compounds containing the O-benzyl group we would expect the primary reduction products of the benzoxymethyl group to be toluene and formaldehyde, but our results indicate the production of methyl alcohol rather than formaldehyde by reduction with sodium and alcohol.

Chloromethyl benzyl ether reacts with diacetoneglucose either with the method used by Freudenberg or that used by Zemplén for the introduction of benzyl groups, but in boiling ether instead of at the higher temperatures necessary with benzyl chloride. The resulting 3-benzoxymethyldiacetoneglucose (I) was hydrolyzed under the usual conditions to 3-benzoxymethylmonoacetoneglucose (II) which was methylated to 5,6-dimethyl - 3 - benzoxymethyl - monoacetoneglucose (III). Reduction of this compound with sodium and alcohol gave 5,6-dimethyl-monoacetoneglucose (IV) and acid hydrolysis gave 5,6-dimethylglucose (V). To verify the structures we have assigned to these compounds we have degraded 5,6-dimethylglucose to dimethylglyceric acid by a method similar to that used by Jackson and Hudson[4] in the degradation of several glycosides. The dimethylglyceric acid was identified by a comparison of its derivatives with those of a sample of dimethylglyceric acid prepared by the methylation of glyceric acid.

It is interesting to compare 5,6-dimethylglucose with the 5-methylglucose described by von Vargha,[5] since neither of these compounds can form the normal pyranose ring. Both sugars have a very low rotation, they rapidly reduce cold Fehling solution and cold neutral permanganate and color the Schiff aldehyde reagent; properties which have been taken by von Vargha to indicate the presence of a considerable amount of the open chain aldehyde form.

We found that phenyl isocyanate formed readily crystallizable, easily purified derivatives with two intermediates (II and IV) which failed to form crystalline acetates or tosylates. We were able to crystallize 5,6-dimethyl-monoacetoneglucose only by seeding with crystals obtained by the hydrolysis of the corresponding urethan. The preparation of polyurethans of some free sugars and glycosides with phenyl isocyanate has been described,[6] but the products were amorphous and difficult to purify.

(1) Oldham, *J. Chem. Soc.*, **127**, 2840 (1925); Irvine and Rutherford, THIS JOURNAL, **54**, 1491 (1932); Bell, *J. Chem. Soc.*, 1553 (1936); Bell and Synge, *ibid.*, 1711 (1937); 833, 836 (1938).

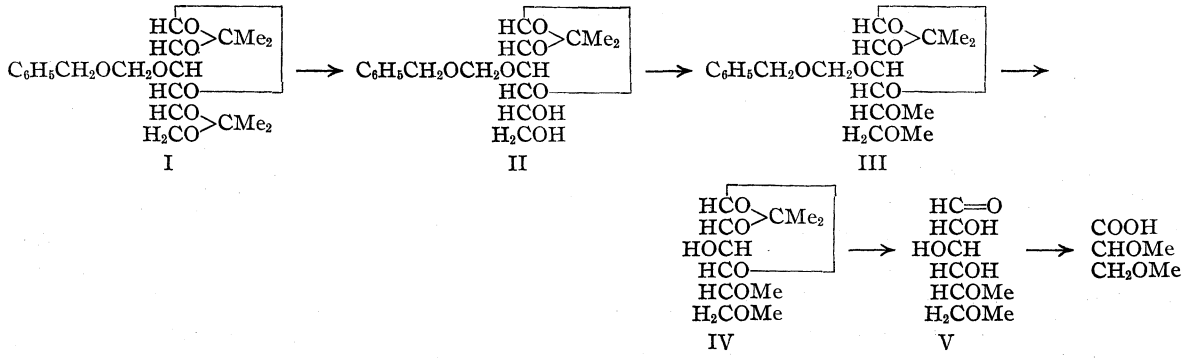
(2) Freudenberg, Hochstetter and Engels, *Ber.*, **58**, 666 (1925); Freudenberg, Dürr and Hochstetter, *ibid.*, **61**, 1735 (1928); Freudenberg and Plankenhorn, *Ann.*, **536**, 257 (1938).

(3) Zemplén, Csürös and Angyal, *Ber.*, **70**, 1848 (1937).

(4) Jackson and Hudson, THIS JOURNAL, **59**, 994 (1937).

(5) Von Vargha, *Ber.*, **69**, 2098 (1936).

(6) Maquenne and Goodwin, *Bull. soc. chim.*, (3) **31**, 430 (1904); Jolles and Botrini, *Gazz. chim. ital.*, **65**, 1217 (1935).



Experimental

Chloromethyl benzyl ether was prepared by the method of Hill and Keach.[7] This method is known to give variable results[7,8] and we obtained a large percentage of failures. By the addition of an equal volume of petroleum ether to the chloromethyl benzyl ether after separation of the water layer, the danger of decomposition on distillation was diminished and a good yield was obtained in the great majority of attempts at preparation.

3-Benzoxymethyl-diacetoneglucose. Method A.—Fifteen grams of diacetoneglucose was dissolved in 40 cc. of dry ether and allowed to react with the theoretical amount of sodium. The reaction took about two days at room temperature. When the reaction was complete traces of unreacted sodium were removed with a spatula and the theoretical amount of chloromethyl benzyl ether was added slowly. Considerable heat was evolved. When the reaction slowed down the ether was refluxed for a few hours and allowed to stand overnight. The ether solution was washed with aqueous sodium carbonate and then with water, dried over potassium carbonate and after removing the solvent the residue was distilled in vacuum. After a fore-run of diacetoneglucose the main fraction distilled at 163–177° at 0.2 mm. with a bath temperature of 214–245°; yield 12 g. or 55%.

Anal. Calcd. for $C_{20}H_{28}O_7$: C, 63.2; H, 7.4. Found: C, 63.3; H, 7.3.

In other preparations of this material the product was subjected to a careful fractionation in an unsuccessful attempt to obtain a crystalline product. The course of one of these fractionations was followed by analysis and it was found that the lower boiling fractions were several per cent. too high and the higher boiling fractions about 1% too low in carbon content. Diacetoneglucose is not the principal impurity. We believe the analysis quoted is in good agreement with theory only because of the accidental compensation of incidental impurities of higher and lower carbon contents.

All distillations recorded in this paper were carried out in flasks with wide, low side arms. Bumping was prevented by packing the boiling chamber with glass wool.

3-Benzoxymethyl-diacetoneglucose prepared in this way is a yellowish, slightly viscous oil. On reduction by the method described later in the preparation of 5,6-dimethyl-monoacetoneglucose we obtained diacetoneglucose in 78% yield based on the crude product. Reduction in hydrogen with palladium black in acid solution also gave diacetoneglucose. Colorless 3-benzoxymethyl-diacetoneglucose can be obtained by refluxing with aqueous alcoholic potassium hydroxide and redistilling.

Method B.—Ten grams of 3-acetyl-diacetoneglucose[9] was dissolved in 100 cc. of ether and 21 g. of chloromethyl benzyl ether was added. Eighty-five grams of powdered potassium hydroxide was added over the course of an hour while the mixture was stirred vigorously with a mechanical stirrer. The ether was refluxed for an hour and a half after the addition of the potassium hydroxide. Water sufficient to dissolve the inorganic materials was added and the two layers separated. The water layer was washed with a little ether, the combined ether extracts washed with a little water and dried over potassium carbonate. The residue after evaporation of the ether was distilled and the fraction boiling at 150–160° at 0.14 mm. was collected. This was redistilled and 4.5 g. was collected at 157–160° at 0.15 mm., bath temperature 210–230°. Hydrolysis with aqueous alcoholic hydrochloric acid gave 70% of the theoretical amount of formaldehyde, isolated as the dimethyldihydroresorcinol condensation product.[10]

3-Benzoxymethyl-monoacetoneglucose.—Ninety-six grams of 3-benzoxymethyl-diacetoneglucose (Method A, b. p. 150–170° at 0.1 mm.) was dissolved in 300 cc. of glacial acetic acid and 30 cc. of water was added. After standing for fourteen hours at room temperature the solvent was distilled off in vacuum and the residue dissolved in an additional 300 cc. of glacial acetic acid to which was added 50 cc. of water. This was allowed to stand for nine hours at room temperature, the solvents distilled off in vacuum, the residue mixed with water and sodium carbonate added in the amount necessary to neutralize the remaining acetic acid. The two layers were separated and the water layer extracted with 90 cc. of chloroform. A small amount of the chloroform solution was dried with sodium carbonate, the chloroform distilled off and the oily residue dried at 56° in vacuum for two hours.

Anal. Calcd. for $C_{17}H_{24}O_7$: C, 60.0; H, 7.1. Found: C, 58.2; H, 6.9.

3-Benzoxymethyl-monoacetoneglucose (1.23 g.) was reduced with sodium and absolute alcohol under the conditions described later in the preparation of 5,6-dimethyl-

(7) Hill and Keach, THIS JOURNAL, **48**, 257 (1926).

(8) Carré, *Compt. rend.*, **186**, 1629 (1928); *Bull. soc. chim.*, **43**, 767 (1928).

(9) Fischer, *Ber.*, **51**, 321 (1918).

(10) Vorländer, *Z. anal. Chem.*, **77**, 241, 321 (1929).

monoacetoneglucose. Monoacetoneglucose was isolated from the product in a yield of 68% calculated on the crude product. 3-Benzoxymethyl-monoacetoneglucose (0.9 g.) was dissolved in 2 cc. of dry benzene and 0.75 g. of phenyl isocyanate was added. The solution was warmed in a bath at 85° for three hours. A few drops of absolute alcohol were added and the solution again warmed for a few minutes. The benzene was evaporated and the residue crystallized from aqueous alcohol. The crystals so obtained were dissolved in chloroform and filtered from a small amount of diphenylurea which was obtained as a by-product. After recrystallization from aqueous alcohol or benzene the product melted at 148–148.5° (corr.); yield about 0.7 g. crude or 0.4 g. of pure product. The same 5,6-dicarbanilyl-3-benzoxymethyl-monoacetoneglucose was obtained from 3-benzoxymethyl-diacetoneglucose prepared by either method A or B. For analysis the preparation was dried at 100° in a vacuum for two hours.

Anal. Calcd. for $C_{31}H_{34}N_2O_9$: C, 64.3; H, 5.9; N, 4.84. Found: C, 64.3; H, 5.8; N, 4.95.

5,6 - Dimethyl - 3 - benzoxymethyl - monoacetoneglucose.—Eighty-six grams of 3-benzoxymethyl-monoacetoneglucose was methylated twice with 300 cc. of dimethyl sulfate and 288 g. of sodium hydroxide each time, using the general conditions described by West and Holden.[11] The product from these methylations was methylated twice with silver oxide and 170 g. of methyl iodide each time. We are unable to account for the extreme difficulty of methylating this compound. The product was distilled twice in vacuum, the second time it was collected at 155–163° at 0.12 mm. with a bath temperature of 185–200°; yield 49 g.

Anal. Calcd. for $C_{17}H_{22}O_5(OCH_3)_2$: C, 62.0; H, 7.7; OCH_3, 16.85. Found: C, 62.6; H, 7.6; OCH_3, 13.85.

5,6-Dimethyl-monoacetoneglucose.—To 42 g. of 5,6-dimethyl-3-benzoxymethyl-monoacetoneglucose was added 57 g. of sodium. The flask was heated on the steam-bath under a reflux condenser and absolute alcohol was added over a period of six hours until all the sodium had been decomposed. Several hundred cc. of water was added and the solution almost neutralized with acetic acid. Most of the alcohol was distilled off on a steam-bath and the aqueous solution was extracted six times with 100 cc. of chloroform each time. The chloroform was distilled off and the residue was dissolved in 300 cc. of 90% acetic acid and allowed to hydrolyze for eighteen hours at room temperature to remove traces of diacetoneglucose which might still be present. The solvents were removed in vacuum, the residue taken up in water, neutralized with sodium carbonate and extracted with chloroform. The product distilled at 105–110° at 0.15 mm. with a bath temperature of 145–160°; yield 20 g. or 71%. When seeded with crystalline material obtained as described below it crystallized in rods completely and immediately with a rise in temperature. After recrystallization from low boiling ligroin it melted at 56–56.5° (corr.); $[\alpha]^{30}D$ −12.8 (water, c = 4.18).

Anal. Calcd. for $C_9H_{14}O_4(OCH_3)_2$: C, 53.2; H, 8.1; OCH_3, 25.0. Found: C, 53.2; H, 8.2; OCH_3, 23.2.

Crystallization of 5,6-Dimethyl-monoacetoneglucose.—One gram of non-crystalline 5,6-dimethyl-monoacetoneglucose was dissolved in 2 cc. of dry benzene and 0.5 g. of phenyl isocyanate added. The mixture was held in a water-bath at 85° for three hours. A few drops of absolute alcohol were added and the solution warmed for a few minutes. The benzene was evaporated and the product crystallized from aqueous alcohol; yield 0.7 g. of crude material. It was purified with very little loss by digesting with a few cc. of 20–40° petroleum ether. After two treatments it melted at 88–89° (corr.) and this value was unchanged by further treatment. The compound crystallized in flat plates or prisms from petroleum ether, in buttons from a mixture of benzene and petroleum ether, and from aqueous alcohol in long needles which melted several degrees lower; $[\alpha]^{30}D$ −12.3 (95% alcohol, c = 3.25).

Anal. Calcd. for $C_{16}H_{19}NO_5(OCH_3)_2$: C, 58.9; H, 6.9; N, 3.8; OCH_3, 16.9. Found: C, 59.5; H, 7.2; N, 3.9; OCH_3, 16.2.

In one preparation in which we used a drop of pyridine as a catalyst, we obtained another derivative which melted at 241–242° after recrystallization from acetone–alcohol, and gave an analysis corresponding approximately to the N,N′-diphenylallophanate of 5,6-dimethyl-monoacetoneglucose.

Anal. Calcd. for $C_{25}H_{30}N_2O_8$: C, 61.7; H, 6.2; N, 5.75. Found: C, 61.1; H, 6.2; N, 6.24.

One hundred and thirty mg. of sodium was dissolved in 5 cc. of absolute methyl alcohol and to this was added 750 mg. of 3-carbanilyl-5,6-dimethyl-monoacetoneglucose described above. The mixture was refluxed for one hour, water added to the appearance of a slight turbidity, the mixture seeded with phenyl methyl urethan and placed in the ice box. The next day phenyl methyl urethan had crystallized out in 50% of the theoretical quantity. The alcohol was evaporated off and the residue taken up with water and placed in the ice box to remove a further small crop of phenyl methyl urethan. This was filtered off and the filtrate extracted ten times with a third of its volume of petroleum ether to remove the last traces of phenyl methyl urethan. The water layer was treated with norite, filtered, and the sugar extracted with chloroform. The chloroform was distilled off in vacuum and the last traces of water were removed by distilling with a mixture of absolute alcohol and benzene. The residue crystallized on cooling and scratching with a glass rod. These crystals were used to seed the main crop of 5,6-dimethyl-monoacetoneglucose.

5,6-Dimethylglucose.—Two grams of 5,6-dimethyl-monoacetoneglucose was dissolved in 10 cc. of *N* hydrochloric acid and held in a bath at 80° for thirty minutes. The solution was cooled and the acid neutralized with silver carbonate. The filtrate was treated with hydrogen sulfide to remove the last traces of silver, shaken with carbon, filtered and evaporated to dryness in vacuum. The sugar is a colorless or light greenish-yellow oil which so far has failed to crystallize. When treated with Fehling solution at room temperature the solution becomes cloudy almost immediately and yellow copper oxide settles in about half an hour. Neutral potassium permanganate is decolorized instantly at room temperature. The sugar reddens fuchsin–sulfurous acid but the color does not develop as rapidly nor is it as deep as is typical of true aldehydes.

(11) West and Holden, THIS JOURNAL, **56**, 930 (1934).

After drying for one week in a vacuum desiccator over phosphorus pentoxide it showed $[\alpha]^{32}D$ +4.0 ± 0.3° (water, c = 2.4). No mutarotation was observed.

5,6-Dimethylglucose retains water so tenaciously that we were unable to get a satisfactory analysis. After two weeks in a vacuum desiccator over phosphorus pentoxide, the carbon and hydrogen analysis corresponded to a little more than half a mole of water per mole of sugar. The osazone was oily. The *p*-bromophenyl osazone was treated with carbon and recrystallized in poor yield from 95% alcohol. It formed very fine yellow needles melting at 155.5–156° dec. (corr.). It was dried for one hour in vacuum at 100° for analysis.

Anal. Calcd. for $C_{18}H_{18}Br_2N_4O_2(OCH_3)_2$: C, 44.1; H, 4.5; N, 10.3. Found: C, 44.3; H, 4.8; N, 10.4.

Glyceric acid was prepared by the method of Debus.[12] We failed to resolve it with brucine by the method reported in the literature to have given resolution.[13] The *d,l* mixture was methylated with silver oxide and methyl iodide and the product distilled in a vacuum.

Anal. Calcd. for $C_3H_3O(OCH_3)_3$: OCH_3, 62.8. Found: OCH_3, 55.2.

The ester was hydrolyzed with barium hydroxide, the excess barium removed with carbon dioxide, the solution of the barium salt of dimethylglyceric acid acidified with an excess of concentrated hydrochloric acid and extracted with chloroform for four hours in a continuous extraction apparatus. The chloroform extract was covered with a layer of water, the water layer made slightly basic to litmus with sodium hydroxide and then just acid to litmus with hydrochloric acid. The solution was evaporated to dryness in a vacuum but the sodium salt of dimethylglyceric acid failed to crystallize.

Sodium dimethylglycerate was converted to the *p*-bromophenacyl ester by warming with slightly less than the theoretical quantity of *p*-bromophenacyl bromide in alcohol for three hours. The ester was recrystallized to constant melting point by crystallizing alternately from 80% alcohol and from petroleum ether containing about 20% of benzene. It melted at 66.5–67.5° (corr.). The *p*-phenylphenacyl ester, prepared in the same way, was treated with carbon and recrystallized from alcohol by the very slow addition of water at 0°, m. p. 62.5–63° (corr.). Both esters were dried for analysis at 35° in vacuum for two hours.

Anal. Calcd. for $C_{13}H_{15}BrO_5$: C, 47.1; H, 4.6. Found: C, 47.4; H, 4.6. Calcd. for $C_{17}H_{14}O_3(OCH_3)_2$: C, 69.5; H, 6.1; OCH_3, 18.9. Found: C, 69.3; H, 5.9; OCH_3, 18.9.

Degradation of 5,6-dimethylglucose was carried out in a manner similar to that used by Jackson and Hudson[4] with several glycosides. When the degradation is carried out with large amounts of materials or in concentrated solutions, there is a tendency for the reaction mixture to become warm with the separation of iodine. This happened to some extent in one run using 1.5 g. of the sugar and 7 g. of periodic acid, but it apparently did not affect the course of the reaction. After standing overnight at room temperature, the oxidation mixture was filtered from the iodine which had separated and extracted with chloroform for twelve hours in a continuous extractor. The chloroform extract was covered with a layer of water, the chloroform evaporated on the steam-bath and the water solution filtered from more iodine which had separated. Excess bromine was added and the solution allowed to stand overnight at room temperature. The water was distilled down to a volume of 10–15 cc. in vacuum, 5 g. of hydrated barium hydroxide was added, the solution protected from the air with a tube of soda lime and heated on the steam-bath for a total period of ten hours to racemize the *d*-dimethylglyceric acid to the *d,l* mixture. The solution was diluted to a volume of several hundred cc. and the excess barium was removed with carbon dioxide. The filtrate from the barium carbonate was evaporated in a vacuum, acidified with concentrated hydrochloric acid, and extracted with chloroform in a continuous extractor. The chloroform extract was covered with a layer of water, the water solution made faintly alkaline to litmus with sodium hydroxide and then just acid with hydrochloric acid. The solvents were removed in vacuum and the product converted to the *p*-bromophenacyl ester and the *p*-phenylphenacyl ester. The *p*-bromophenacyl ester melted at 65.5–66.5° (corr.) after recrystallization and the mixed melting point with the *p*-bromophenacyl ester of dimethylglyceric acid was 66–67° (corr.). The *p*-phenylphenacyl ester melted at 62.5–63° (corr.) after recrystallization and the mixed melting point with the *p*-phenylphenacyl ester of dimethylglyceric acid was also 62.5–63° (corr.).

Anal. Calcd. for $C_{13}H_{15}BrO_5$: C, 47.1; H, 4.6. Found: C, 47.2; H, 4.6. Calcd. for $C_{17}H_{14}O_3(OCH_3)_2$: C, 69.5; H, 6.1; OCH_3, 18.9. Found: C, 69.8; H, 6.3; OCH_3, 18.2.

We wish to thank Mr. Saul Gottlieb for the microanalyses reported in this paper.

Summary

5,6-Dimethylglucose has been synthesized from diacetoneglucose using the benzoxymethyl group as a substituent for blocking the third hydroxyl group.

Urethans prepared with phenyl isocyanate were found to have many desirable properties as crystalline derivatives of some of our intermediates.

NEW YORK, N. Y. RECEIVED OCTOBER 6, 1939

(12) Debus, *Ann.*, **106**, 79 (1858).

(13) Neuberg and Silbermann, *Ber.*, **37**, 339 (1904); Frankland and Done, *J. Chem. Soc.*, **87**, 618 (1905).

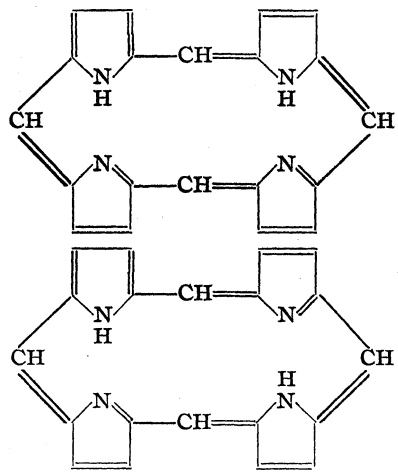
[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Infrared Studies of the Porphyrin Molecule

BY C. S. VESTLING AND J. R. DOWNING

The work of Hans Fischer and associates[1] has furnished strong evidence that Kuster's formulation of the porphyrin nucleus is the correct one. There are some details, however, which are lacking.

Corwin and Quattlebaum[2] exclude "resonance isomers" and discuss the possibility of *cis* or *trans* N-isomers in the porphyrin series



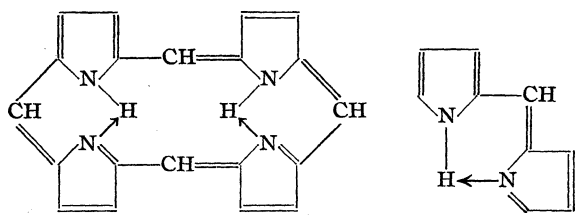
Fischer[3] has suggested the possibility of N-isomerism in dipyrrylmethenes. Conant and Bailey,[4] however, were unable to demonstrate N-isomerism in isomeric porphyrins by preparation of metallic complexes. The electrometric titrations of Conant, Chow and Dietz[5] in glacial acetic acid have been accepted as evidence for the presence of *two* basic groups in the prophyrins.

Preliminary examination of molecular models of the porphyrin nucleus indicates atomic distances which are distinctly favorable for the presence of N–H–N bonding. Hence it was decided to examine this problem using the method of infrared spectroscopy, originally proposed by Wulf.[6]

Infrared absorption spectra studies in this Laboratory[7] have proved to be of great value in structural work on organic acids, amides, and other compounds.[8,9] It is possible with this technique to identify various characteristic bonding frequencies. Their presence or absence can be demonstrated rather conclusively. Further, the method is especially applicable to small quantities of materials.

The problem was, therefore, that of noting the presence or absence of characteristic absorption peaks in a study of synthetic etioporphyrin I, iron etioporphyrin I chloride (etiohemin chloride), two dipyrrylmethenes, and the copper complex of one of them.

The data shown in the curves to follow suggest that hydrogen bonding *may* result in the structures below, which account for the observed lack of isomerism



Experimental

The prism spectrograph used in this work has been described.[10] The source of radiation was a 220-volt Nernst glower. The instrument was calibrated to 0.01 μ with reference to the 2.673 μ band of water vapor. Solutions in carbon tetrachloride were measured with carbon tetrachloride as a blank, and the molar absorption coefficient, K, was plotted against wave numbers (cm.$^{-1}$). K was calculated from the expression

$$K = \frac{1}{cd} \log \frac{I_0}{I}$$

where I is the intensity through the solution; I_0 is the intensity through an equal thickness of pure solvent; c is the molar concentration; and d the cell length. In cases where the concentration was indefinite because of low solubility, the absorption (log I_0/I) was plotted instead of the molar absorption coefficient.

The materials used in this investigation were carefully purified. Where possible, analyses of important compounds are reported.

The authors are indebted to Dr. R. E. Ellingson for a

(1) H. Fischer and H. Orth, "Die Chemie des Pyrrols," Vol. II, Akademische Verlagsgesellschaft m. b. H., Leipzig, 1937.

(2) A. H. Corwin and W. M. Quattlebaum, Jr., THIS JOURNAL, **58**, 1083 (1936).

(3) H. Fischer, *Z. physiol. Chem.*, **128**, 63 (1923).

(4) J. B. Conant and C. F. Bailey, THIS JOURNAL, **55**, 796 (1933).

(5) J. B. Conant, B. F. Chow and E. M. Dietz, *ibid.*, **56**, 2185 (1934).

(6) G. E. Hilbert, O. R. Wulf, S. B. Hendricks and U. Liddel, *ibid.*, **58**, 548 (1936).

(7) W. H. Rodebush and A. M. Buswell, *J. Phys. Chem.*, **43**, 219 (1939).

(8) A. M. Buswell, W. H. Rodebush and M. F. Roy, THIS JOURNAL, **60**, 2239 (1938).

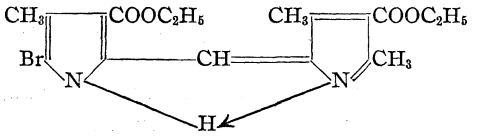
(9) A. M. Buswell, W. H. Rodebush and M. F. Roy, *ibid.*, **60**, 2444 (1938).

(10) A. M. Buswell, V. Deitz and W. H. Rodebush, *J. Chem. Phys.*, **5**, 501 (1937).

supply of 3,5,3′,5′-tetramethyl-4,4′-dicarbethoxydipyrrylmethene (Piloty's). Beautiful red needles of this compound were recrystallized from benzene–hexane; they decomposed at 190°. Hydrogenation with Adams platinum catalyst yielded white crystals of the dipyrrylmethane which melted at 228–229° (uncorr.) with some decomposition.

Anal. Calcd. for $C_{19}H_{24}O_4N_2$: N, 8.14. Found: N, 8.16.

3,4′,5 - Trimethyl - 3′,4 - dicarbethoxy - 5′ - bromodipyrrylmethane was synthesized as described below.



It must be pointed out that the exact structure of this compound is not conclusively proved, although the mode of synthesis and analysis suggest the structure given. 2,4-Dimethyl-3-carbethoxypyrrole was freshly recrystallized from cold methanol, dissolved in cold, dry ether (ice–salt temperature), and treated slowly with two moles of bromine (Baker C. P.) in cold ether. At first a flocculent light-colored precipitate formed; when one mole of bromine had been added, the system suddenly turned red. A vigorous evolution of hydrogen bromide took place throughout. The reaction product was a light red amorphous methene hydrobromide. The free base was obtained by grinding with cold concentrated ammonium hydroxide in a mortar and extracting with boiling hexane to yield after slow crystallization long (2 mm.), red needles.

Anal. Calcd. for $C_{18}H_{21}O_4N_2Br$: N, 6.85. Found: N, 6.89.

The copper complex of this material was prepared by prolonged shaking of a chloroform solution of the dipyrrylmethene hydrobromide with concentrated aqueous $CuSO_4 \cdot NH_4OH$. Macroscopic green crystals of the copper complex were obtained in good yield and used without analysis.

Etioporphyrin I (1,3,5,7-tetramethyl-2,4,6,8-tetraethylporphin) was synthesized by Walter Schlesinger according to the methods of Fischer, *et al.*[1] The absorption maxima of the purified crystalline material in chloroform are: I, 484–508 mμ; II, 524–536 mμ; III, 560–570 mμ; IV, 610–618 mμ; order of intensity: I, II, III, IV.

Anal. (recrystallized material). Calcd. for $C_{32}H_{38}N_4$: C, 60.33; H, 7.94; N, 11.71. Found: C, 80.99, 79.83; H, 8.17, 7.93; N, 11.83.

The preparation of iron etioporphyrin I chloride will be described elsewhere. Beautiful macroscopic octagonal platelets of metallic luster were obtained porphyrin-free in better than 90% yields. Their purity was indicated by a series of reductive titrations.[11]

In the curves shown, the peaks at 3.30–3.50 μ are due to aliphatic C–H vibrations, since they are identical in frequency with absorption peaks observed in numerous other compounds containing such groups.

The significant peaks from the standpoint of this research are those at 3.03 μ in Fig. 1 (I), 3.11 μ in Fig. 1 (II) and 3.01 μ in Fig. 2 (I). The complete disappearance of these peaks (Figs. 1 (III) and 2 (II)) when metallic derivatives are formed by replacement of the hydrogens of the N–H groups shows that they are absorption maxima caused by N–H vibrations. In the case of etiohemin I (Fig. 2 (II)) the complete disappearance of the N–H peak indicates conclusively that both hydrogens attached to nitrogens in the porphyrin nucleus are replaced by the iron upon substitution.

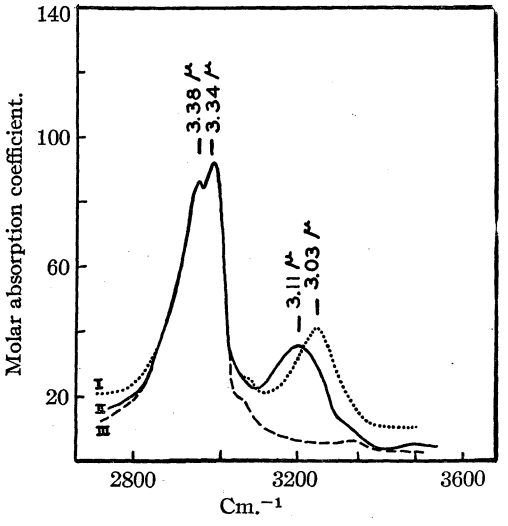


Fig. 1.—I, 3,4′,5-Trimethyl-3′,4-dicarbethoxy-5′-bromodipyrrylmethene (0.002 *M* in 10.180 cm. cell). II, 3,5,3′,5′-Tetramethyl-4,4′-dicarbethoxydipyrryl methene (0.008 *M* in 2.532 cm. cell). III, Copper complex of 3,4′,5-trimethyl-3′,4-dicarbethoxy-5′-bromodipyrrylmethene (0.002 *M* in 10.180 cm. cell.)

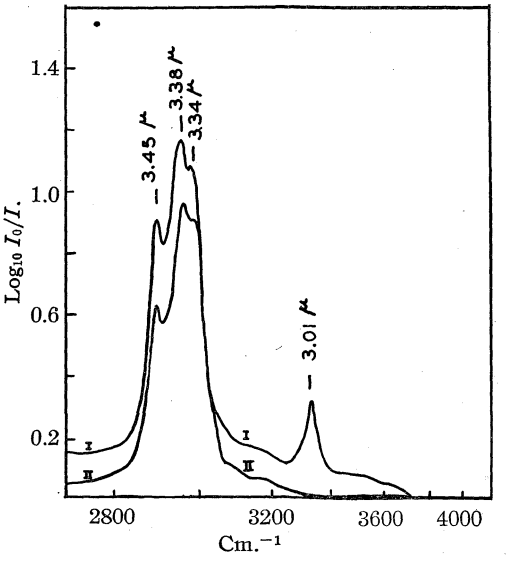


Fig. 2.—I, Etioporphyrin I (<0.001 *M* in 10.180 cm. cell). II, Etiohemin I (<0.0005 *M* in 10.180 cm. cell).

(11) C. S. Vestling, unpublished data.

The question of whether or not these peaks may be assigned to N–H–N bonding between the secondary pyrrole nitrogens and the tertiary nitrogens in these compounds arises from a consideration of the structures involved. It must be stated at once that infrared spectroscopy can only give evidence for *intra*molecular bonding when a set of absorption frequencies can be compared with those exhibited by like acceptors and donors in different molecules. On the other hand, *inter*molecular bonding between molecules of like or unlike species may be demonstrated conclusively by observing the effect of concentration changes in solution upon "bonded" or "unbonded" peaks. This criterion of course becomes inapplicable in testing for intramolecular bonding.

Since the absorption peaks in question differ markedly from the pyrrole N–H peak at 2.85 μ,[12] one is inclined to suggest that N–H–N bonding exists in these molecules. However, this is unproved as yet, since the character of the substituted pyrrole rings may have been changed in the formation of these compounds. This seems possible in light of the recent work on unbonded N–H frequencies.[13] Hence we can only state at present that the absorption peaks occur at frequencies which might be expected[12] if N–H–N bonding were existent in the porphin and dipyrrylmethene nuclei.

(12) A. M. Buswell, J. R. Downing and W. H. Rodebush, THIS JOURNAL, **61**, 3252 (1939).

The authors wish to express their gratitude to Professors A. M. Buswell and W. H. Rodebush for use of the infrared apparatus and for timely suggestions.

Summary

1. The infrared absorption of two dipyrrylmethenes, the copper complex of one of them, etioporphyrin I, and etiohemin I chloride has been measured. Replacement of acidic hydrogens with metal atoms eliminated nitrogen–hydrogen absorption in the dipyrrylmethenes and in etioporphyrin I.

2. The possibility of N–H–N bonding in these compounds is discussed.

(13) A. M. Buswell, G. W. McMillan, W. H. Rodebush and F. T. Wall, *ibid.*, **61**, 2809 (1939).

URBANA, ILLINOIS RECEIVED SEPTEMBER 30, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORY, GENERAL ELECTRIC COMPANY]

The Hydrolysis of Bromine. The Hydration of the Halogens. The Mechanism of Certain Halogen Reactions

BY HERMAN A. LIEBHAFSKY

Corrections.—Jones and Baeckstrom[1] and Liebhafsky[2] have independently established 5.8 (10^{-9}) as the value of K_1, the equilibrium constant of the bromine hydrolysis, at 25°. The temperature coefficients of this reaction (*cf.* Ref. 2, Table II, last column) are probably more accurately known than is K_1 at any temperature except 25°. For these reasons, it is especially desirable to correct a computational error that Professors R. H. Gillette and H. A. Young of the Division of Chemistry, University of California at Davis, have kindly called to my attention. Through some mischance, 11.9(10^{-9}) at 35°, the result for Series 5, instead of 11.3(10^{-9}), the result for Series 7 (*cf.* Ref. 2, Table II), was used in deriving an incorrect equation for K_1 as a function of temperature. A table and a conclusion in Ref. 2 consequently should be changed to read as follows.

(1) Jones and Baeckstrom, THIS JOURNAL, **56**, 1517 (1934).
(2) Liebhafsky, *ibid.*, **56**, 1500 (1934).

TABLE IV (Ref. 2)

SUMMARY OF BEST VALUES FOR $K_1 \times 10^{-9}$ AT DIFFERENT TEMPERATURES

	0°	10°	25°	30°	35°
Liebhafsky	0.69	1.76	5.8	8.2	11.3
Computed	.88	1.95	(5.8)[a]	8.14	(11.3)[a]
Selected[b]	.70	1.78	5.8	8.3	11.3

[a] Value assumed in deriving the equation $\log K_1 = 0.6876 - 2660.3/T$ from which computed values were obtained. [b] Only these finally selected values for K_1 are expressed in activities. (Similar changes are to be made in Ref. 3, p. 95, Table I.)

Summary (Ref. 2)

4. The temperature variation of the K_1 for bromine is anomalous in the neighborhood of 10°; but the departure of $d(\log K_1)/d(1/T)$ from constancy is less pronounced than that observed by Jakowkin in the case of chlorine.

Also, the line "a. Measurements at 0° by Jones and Hartmann" has been omitted above the first row of data in Table III.

Hydration of the Halogens.—The temperature coefficients of halogen equilibria involving aqueous solutions are generally anomalous.[3] When the corresponding equilibrium constants are calculated in the usual manner—that is, by using (X_2), the concentration of free halogen in the aqueous solution—the log K_{X_2} *vs.* $1/T$ plot approaches a limiting straight line at higher temperatures but bends more and more sharply to the $1/T$ axis as 0° is approached. Figure 1 illustrates this behavior. While D', the distribution ratio of iodine between air and carbon tetrachloride, shows the orthodox temperature dependence, D, the distribution ratio between air and water, behaves anomalously.[4] This anomaly has found a reasonably satisfactory quantitative explanation in the assumption that the degree of hydration of the halogen is changing in the temperature region where the anomaly occurs; as 0° is approached, the equilibrium

$$\mathrm{U} + (h - u)\,\mathrm{H_2O} \rightleftarrows \mathrm{H} \qquad (1)$$
$$(\mathrm{H}) + (\mathrm{U}) = (X_2)$$

shifts so as to increase (H), the concentration of the more hydrated form. (The formula of U is $I_2 \cdot uH_2O$; that of H, $I_2 \cdot hH_2O$.) The correction of the above error tends to strengthen this explanation and has a bearing on the important problem of correlating kinetic and equilibrium data (cf. Ref. 3, p. 111). The data in Table 2d, Ref. 3, for the bromine hydrolysis should be:

d. For bromine from reaction 12 (*cf.* Table I)

T, °C.	35.0	25.0	10.0	0.0
$10^9 \times K_{Br_2}$ (measd.)	11.3	5.8	1.76	.69
d	(d = 0 assumed)		0.045	.106
(H)/(U)			.109	.276

$d = \log K_{Br_2}$ (calcd.) $- \log K_{Br_2}$ (measd.)
$\log K_{Br_2}$ (calcd.) $= 0.6876 - 2660.3/T$
$\Delta H_{H_2} = -14300$ cal.

The difference between d for 0° from kinetic (0.21) and equilibrium data (new value, 0.11) is now cut virtually in half (*cf.* Ref. 3, p. 95, last paragraph).

(3) Liebhafsky, *Chem. Rev.*, **17**, 89 (1935).

(4) The data for aqueous solutions have been reproduced from Ref. 3, where the original sources are cited. D' has been obtained for each temperature by dividing the vapor pressure of iodine in mm. of mercury [Baxter and Grose, THIS JOURNAL, **37**, 1061 (1915)] by the solubility in mole fractions of iodine for that solvent [Hildebrand and Jenks, *ibid.*, **42**, 2180 (1920)].

The calculated values[3] of the heats of hydration (Equilibrium 1) now are:

Type of measurement	Chlorine	Bromine	Iodine
Equilibrium (distribution between air and H_2O)	− 9,700 cal.	−13,100 cal.	−11,800 cal.
Equilibrium (hydrolysis of the halogen)	− 9,900 cal.	−14,300 cal.	
Equilibrium (distribution between CCl_4 and H_2O)	−10,700 cal.		
Kinetic (see text below)		−25,000 cal.	−22,800 cal.

The new value for bromine is in good agreement with the other value derived from equilibrium data.

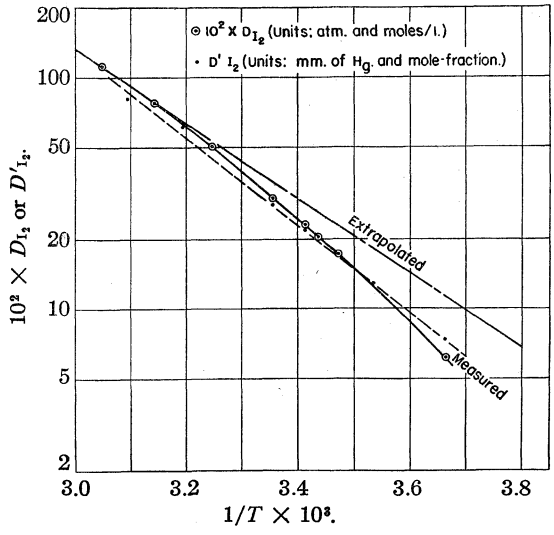


Fig. 1.—Distribution ratios for iodine between air and water (D, anomalous temperature coefficient), and between air and carbon tetrachloride (D', normal temperature coefficient). The plot is semi-logarithmic.

The specific rates at which hydrogen peroxide is oxidized by each of the three halogens, X_2, are the kinetic data from which heats of hydration were deduced. For bromine and iodine, these large (and, perhaps, unreasonably large) heats are obtained because the downward curvatures in the $1/T$ plots are more pronounced for the kinetic than for the equilibrium measurements. These unexplained minor inconsistencies should not be permitted to obscure the more important fact that for bromine and iodine both types of measurements reveal the existence of similar temperature coefficient anomalies. This fact indicates that the assumed mechanisms, which are of the type

Rapid equilibria

$$\mathrm{U} + \mathrm{H_2O} \rightleftarrows \mathrm{HXO} + \mathrm{H^+} + \mathrm{X^-} + u\mathrm{H_2O} \qquad (2a)$$
$$\mathrm{H} \rightleftarrows \mathrm{HXO} + \mathrm{H^+} + \mathrm{X^-} + (h - 1)\mathrm{H_2O} \qquad (2b)$$

Rate-determining

$$\text{step } \mathrm{H_2O_2} + \mathrm{HXO} \longrightarrow \mathrm{H_2O} + \mathrm{O_2} + \mathrm{H^+} + \mathrm{X^-} \qquad (3)$$

are in the main correct, for mechanisms of this

type will reflect a change in the ratio (H)/(U) because such a change necessarily causes a change in the ratio (HXO)/(X_2).

The reaction between chlorine and hydrogen peroxide,[5] however, does not appear to proceed mainly by such a mechanism; for the kinetic data give a linear log k *vs.* $1/T$ plot from 0 to 25°. (The temperature coefficient of the chlorine hydrolysis equilibrium is nearly twice as great at 0° as at the higher temperature.[6]) This conclusion is strengthened greatly by the experimental fact that hypochlorous acid when mixed directly with hydrogen peroxide reacted at approximately one-millionth the rate to be expected from kinetic measurements on the chlorine–hydrogen peroxide reaction.[7] The difficulty has been thoroughly discussed by Makower, who presented this conclusion as a third alternative explanation; the evidence from other reactions[3] seems convincing enough to warrant rejection of the other two. To summarize: The rate of the chlorine–hydrogen peroxide reaction, unlike the rates of the corresponding bromine and iodine reactions, is unaffected by the shift from U to H which occurs when the temperature of an aqueous X_2 solution is lowered. The mechanism of this reaction must therefore differ from the mechanisms of the other two.

The Reaction between Arsenious Acid and Iodine.—Roebuck's classical investigation[8a,b] of the reaction

$$H_3AsO_3 + I_3^- + H_2O = H_3AsO_4 + 2H^+ + 3I^- \quad (4)$$

was the first complete experimental demonstration of the relation obtaining between chemical kinetics and chemical equilibrium. The mechanism for the forward reaction

$$\text{Rapid equilibrium:} \quad I_3^- \rightleftarrows I_2 + I^- \quad (5)$$

$$\text{Rapid equilibrium:} \quad I_2 + H_2O \rightleftarrows HIO + H^+ + I^- \quad (6)$$

$$\text{Rate-determining step:} \quad HIO + H_3AsO_3 \longrightarrow H_3AsO_4 + H^+ + I^- \quad (7)$$

does not appear to have been questioned seriously although the work of Makower and Liebhafsky[9] left little doubt that further verification was desirable. Since hypoiodous acid is so unstable that it can scarcely be treated directly with arsenious acid in the absence of iodine, this verification was sought in a study of the temperature coefficient of the forward reaction.

The following measurements were made in 1932 in the Chemical Laboratory of the University of California at Berkeley. Since the rate law of the forward reaction has been established, it sufficed to perform the experiments under conditions such that no concentration except that of total iodine changed greatly during the course of an experiment. Sodium iodide, sodium meta-arsenite and perchloric acid solutions were mixed, diluted and placed in a thermostat; the reaction was begun by adding sodium triiodide solution that was also at thermostat temperature. The rate was measured by rapidly titrating samples of the reaction mixture withdrawn from time to time, with 0.02 N sodium thiosulfate. The detailed data for Experiment 5 are given in Fig. 2, where the thiosulfate titer is plotted on semi-logarithmic paper against the time. The initial

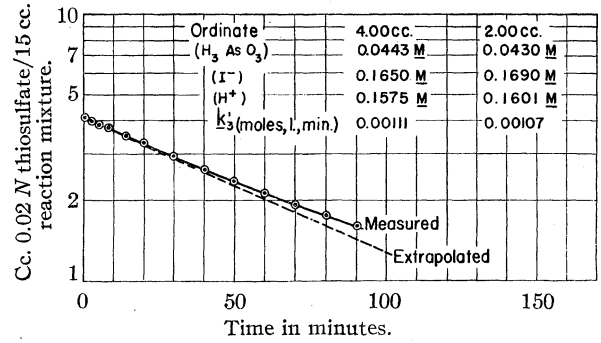


Fig. 2.—Detailed results for expt. 5 on the rate of reaction 4. The plot is semi-logarithmic.

concentrations for all experiments were nearly identical, except that the concentration of arsenious acid was cut in half for the experiments at the two highest temperatures. Under the concentration conditions chosen, the reaction is approximately first order; the deviations from straight lines in the log $\Sigma(I_2)$ *vs.* t plots were satisfactorily removed by correcting for the changes in (H^+), (I^-) and (H_3AsO_3) that occurred as the reaction proceeded. (The change in (H^+) caused by mixing meta-arsenite and perchloric acid was of course allowed for.) In other words, the rate law

$$-d(I_3^-)/dt = k_3' \frac{(I_3^-)}{(H^+)(I^-)^2}(H_3AsO_3) \quad (8)$$

was obeyed satisfactorily. The temperatures and results are summarized in Table I.

(5) Makower, THIS JOURNAL, **56**, 1315 (1934).
(6) Jakowkin, *Z. physik. Chem.*, **29**, 613 (1899).
(7) Bray, *Chem. Rev.*, **10**, 175 (1932).
(8) (a) Roebuck, *J. Phys. Chem.*, **6**, 365 (1902), and (b) **9**, 727 (1905); (c) Liebhafsky, *ibid.*, **35**, 1648 (1931); references to other work will be found in Ref. 8c.
(9) Makower and Liebhafsky, *Trans. Faraday Soc.*, **29**, 597 (1933).

Comparison of the last two columns in Table I shows that here, as in the chlorine–hydrogen peroxide reaction, the logarithm of the specific rate is a linear function of $1/T$ to within the experimental error. Roebuck's[8c] value for k_3' at 0° in sulfuric acid solution is 9.4(10^{-4}) (units: moles, liters, minutes); this result, when corrected for the decreased acid concentration due to the presence of HSO_4^-, is in good agreement with the Table I value.[10] Roebuck gives several values for the temperature coefficient of k_3' between 0 and 10°; his highest value, 3.5,[8a] corresponds to a heat of activation $Q = +19{,}200$ cal.; his lowest, 3.17,[8b] to +17,710 cal., which is in fair agreement with +16,970 cal., the value from Table I.

TABLE I

TEMPERATURE COEFFICIENT DATA FOR THE ARSENIOUS ACID–IODINE REACTION

Experiment	T, °K.	$10^4 \times k_3'$ (meas.)	$10^4 \times k_3'$ (calcd.)[a]
3	273.1	6.7	6.6
4	273.1	6.5	6.6
5	277.7	10.9	11.2
6	283.5	21.6	21.1
7	288.1	36	34
8	293.1	58	57

[a] Calculated values from the equation $\log k_3' = 10.411 - (3710.0/T)$.

The magnitude of Q and its constancy (or near constancy) both suggest the necessity of revising the mechanism of the arsenious acid–iodine reaction. The heat of dissociation of triiodide ion (+4320 cal.)[8c] and the heat of hydrolysis of iodine (+22,700 cal.)[8c] must both be included in Q if the accepted mechanism is correct; on this basis the heat of activation for the rate-determining step between hypoiodous and arsenious acids would have a *negative* heat of activation of 10,000 cal. When Roebuck's work was reexamined some years ago,[8c] it was not known that a constant Q was in conflict with most of the data for aqueous halogen solutions[3]; as it now appears, the previous conclusion[11] that the rate-determining step has a negative temperature coefficient must be rejected, and the mechanism for the arsenious acid–iodine reaction revised.

The revised mechanism must meet the requirement that the rate at all temperatures be independent of the ratio (H)/(U). Perhaps the simplest mechanism that can be devised to meet this requirement is

Rapid equilibria

$$U + H_3AsO_3 \rightleftarrows A + H^+ + I^- \quad (9)$$

$$H + H_3AsO_3 \rightleftarrows B + H^+ + I^- \quad (10)$$

Rate-determining steps of identical specific rate

$$A \xrightarrow{k_1} H_3AsO_4 + H^+ + I^- \quad (11a)$$

$$B \xrightarrow{k_1} H_3AsO_4 + H^+ + I^- \quad (11b)$$

The device of having A and B decompose at the same (or nearly the same) specific rate is saved from being an obvious artifice by the fact that these two intermediate products differ only in the degree of hydration. An analogous mechanism would eliminate the conflict between equilibrium and kinetic data for the chlorine–hydrogen peroxide reaction.

A detailed discussion of the arguments for and against this mechanism is scarcely warranted. Accurate measurements of the equilibrium constant for the iodine hydrolysis over the temperature range in question would be more valuable than such a discussion; but these data, especially for the lower temperatures, will be difficult to obtain. The existence of accurate hydrolysis equilibrium measurements for the analogous chlorine–hydrogen peroxide reaction to some extent compensates this difficulty.

It may be pointed out, finally, that the equilibrium constant of a halogen reaction could, if heat capacity terms are ignored, be a linear function of $1/T$. This linearity will result if the forward (reverse) reaction has a mechanism like that outlined for the arsenious acid, while the reverse (forward) reaction proceeds by a mechanism whose temperature coefficient is normal. The triiodide equilibrium (Reaction 5) appears to be one case of this kind, and Equilibrium 4 another. Further experimental work to test these ideas is highly desirable.

Light Absorption by Iodine Solutions.—The General Electric recording spectrophotometer[12] was used to establish whether a characteristic change in the absorption of visible light accompanied the change in the hydration of iodine between 0 and 75°. For purposes of comparison, carbon tetrachloride solutions were also investigated at different temperatures. The ease with which iodine volatilizes from aqueous solutions is well known; this difficulty was minimized by filling the cell (5.15 cm. long) with the warm or

(10) (a) The dissociation constant at 25° of HSO_4^- in concentration units for the above reaction mixtures is near 0.03: Noyes and Sherrill, THIS JOURNAL, **48**, 186 (1926). (b) The corresponding heat of dissociation is small; Hamer, *ibid.*, **56**, 860 (1934).

(11) (a) Ref. 8c; (b) *cf.* also, Moelwyn-Hughes, "Kinetics of Reactions in Solution," Clarendon Press, Oxford, 1933, p. 207.

(12) Michaelson and Liebhafsky, *Gen. Elec. Rev.*, **39**, 445 (1936).

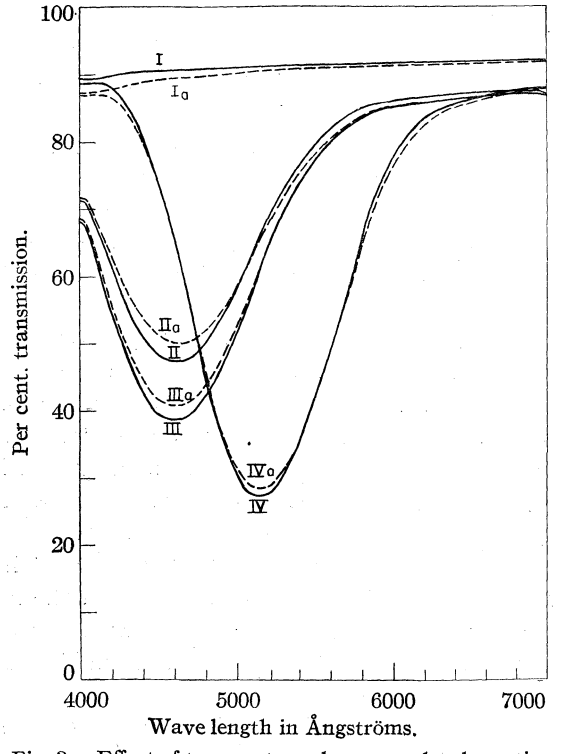


Fig. 3.—Effect of temperature change on the absorption of visible light by iodine solutions:

Curve	Solvent	Moles I_2/l.	T, °C.
I	CCl_4	None	25
Ia	CCl_4	None	50
II	H_2O	6×10^{-5}	24
IIa	H_2O	6×10^{-5}	76
III	H_2O	9×10^{-5}	0.3
IIIa	H_2O	9×10^{-5}	24
IV	CCl_4	9.5×10^{-5}	25
IVa	CCl_4	9.5×10^{-5}	51

cold solution, tracing its transmission curve (less than three minutes is required), and permitting the covered cell to stand until its contents reached room temperature, when the transmission was again measured. Some of the curves obtained are shown in Fig. 3; that the effect of changing temperature on the water-filled cell is very small is obvious from the uppermost curves in Fig. 4.

Figure 1 shows clearly that aqueous iodine solutions show anomalous temperature coefficients while carbon tetrachloride solutions do not; Fig. 3 shows that changing temperature affects light absorption by both solutions almost identically when the change in the absorption by carbon tetrachloride itself is allowed for. It follows, therefore, that the change in hydration presumably responsible for the curvature in Fig. 1 cannot be detected on the spectrophotometer, and that U is itself hydrated. The noticeable displacement toward longer wave lengths of Curve IIa, Fig. 3, indicates that the complete dehydration of iodine is beginning at 76°.

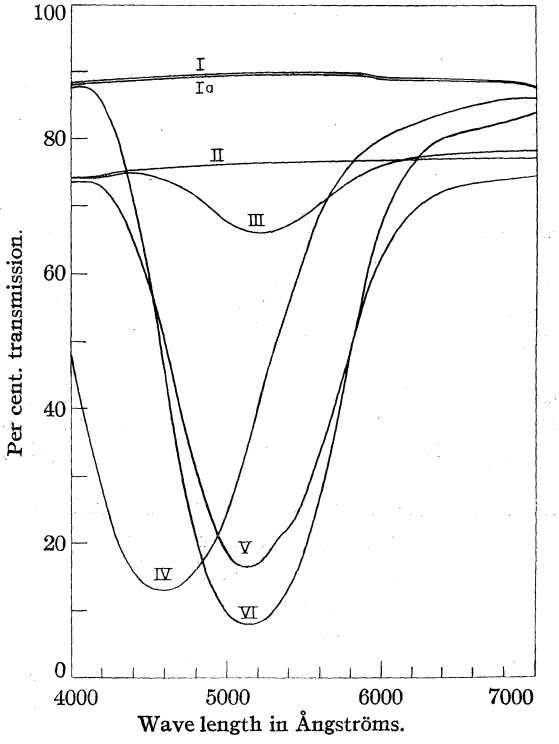


Fig. 4.—Absorption of visible light by gaseous and dissolved iodine:

Curve	Solvent	Moles I_2/l.	T, °C.
I	H_2O	None	25
Ia	H_2O	None	50
II	Air	None	25
III	Air	1.6×10^{-5}	25
IV	H_2O	2.36×10^{-4}	25
V	Air	Unknown	25
VI	CCl_4	2.39×10^{-4}	25

The small decrease in absorption with increasing temperature shown in Fig. 3 doubtless results from the concomitant increase in the number of iodine molecules in the first vibrational level, an explanation that Gibson, Rice and Bayliss[13] have shown to be quantitatively satisfactory in the case of gaseous chlorine. The fact that this decrease occurs to about the same extent for aqueous as for carbon tetrachloride solutions indicates that light absorption leads to comparable processes in both kinds of solutions, even though water probably forms definite solvates with iodine and carbon tetrachloride does not.

The failure of the spectrophotometer to detect the shift from U to H (which, according to results

(13) (a) Gibson and Bayliss, *Phys. Rev.*, **44**, 188 (1933); (b) Gibson, Rice and Bayliss, *ibid.*, p. 193.

given above, involves some 10,000 cal. at least) suggested that transmission curves be obtained for iodine vapor.[14] The vapor was generated by heating the quartz cell, into which a crystal of iodine had been placed, so that the ends remained hotter than the other portions. The room temperature curve was obtained after the cell had cooled; the corresponding concentration of iodine was calculated from its vapor pressure.[4] The data derived from the various curves in Fig. 4 are ($\log I_0/I = \epsilon \times 1 \times$ moles/liter):

Source	Solvent	$\lambda_{max.}$, Å.	$\epsilon_{max.}$	Width, W, at $\epsilon = 1/2\ \epsilon_{max.}$, Å.	Product $W \times \epsilon_{max.}$, Å.
Curve V	Air	5120	..	860	..
Curve III	Air	5200	810	850	$69(10^4)$
Curve VI	CCl_4	5140	870	860	$75(10^4)$
Curve IV	H_2O	4600	690	1010	$70(10^4)$
Ref 14	Inert gases	5200	830	880	$73(10^4)$

Although the work was done with reasonable care, extreme accuracy is not claimed for the $\epsilon_{max.}$ values; relative ϵ values and the positions of the absorption maxima are more reliable. A detailed comparison with the large amount of earlier work is not feasible—among other things, because the effects of differences in cell thickness and in concentration would have to be known. The parameters in the last two columns are given in an effort to describe the curves without listing the individual ϵ values. The product in the last column should be approximately proportional to the area under the curve, and its departure from constancy may be a partial measure of solvent influence.

The data from Curve III are obviously in good agreement with those derived from the "limiting" curve of Rabinowitsch and Wood.[14] In Curve V, the limiting conditions are probably not quite reached because of the higher pressure of iodine vapor; the slight "hump" near 5400 Å. results, as they have pointed out, from the superposition on the main band series of the series due to the first vibrational state. They state: "It is noteworthy that these humps appear in *solutions* of Br_2 and I_2 as well, showing that the vibrational quanta of these molecules are not strongly affected by dissolution in carbon tetrachloride and similar solvents." The spectrophotometric curves, published and unpublished, obtained in this Laboratory for iodine–carbon tetrachloride solutions do not support this conclusion since they do not show the "hump" in question. A small spectroscope that resolved the bands of iodine vapor showed no structure whatever in the absorption by a carbon tetrachloride solution. This empirical evidence of how completely the interaction of solvent with solute molecules modifies quantum restrictions could not, of course, have been obtained with the spectrophotometer, which has a slit width of 100 Å.

Figure 1 shows that approximately 9000 cal./mole is evolved when an infinitesimal amount of iodine vapor is dissolved in a saturated carbon tetrachloride solution. The spectrophotometric curves for vapor and solution are virtually identical, except that the solution shows a somewhat higher transition probability (higher value of $\epsilon_{max.}$ and of the product $W \times \epsilon_{max.}$).[15] The failure of the spectrophotometer to reflect the interaction of carbon tetrachloride with iodine makes its failure to detect the shift from U to H seem less serious.

The following differences in visible light absorption exist between solutions of iodine in carbon tetrachloride (in which there are no definite solvates) and solutions in water (in which definite hydrates are present): the absorption maximum in water 5–600 Å. further toward the violet; $\epsilon_{max.}$ is smaller; the absorption curve is broader (the product $W \times \epsilon_{max.}$, however, is approximately the same for both solutions). It is probable that these differences result from the formation of definite iodine–solvent compounds, but how and why is uncertain. Further work is necessary.

Summary

Certain corrections of earlier work on the bromine hydrolysis have strengthened the case for the hypothesis that the anomalous temperature coefficients associated with aqueous halogen solutions result from shifts in the hydration equilibria.

Temperature coefficient data for the arsenious acid–iodine reaction have been given.

Evidence against the conventional mechanisms

(14) Rabinowitsch and Wood, *Trans. Faraday Soc.*, **32**, 540 (1936). Professor H. Sponer kindly called this valuable paper to the author's attention after his own experimental work was completed.

(15) Rabinowitsch and Wood[14] hold a weakening of the selection rules by the electric fields of the solvent molecules responsible for the increase in transition probability. If this explanation and the work of Groh and Papp [*Z. physik. Chem.*, **A149**, 153 (1930)] are correct, the order of increasing influence by these electric fields for several solvents is carbon tetrachloride, hexane, carbon bisulfide, with only small differences among the three. Moreover, if water has a similar effect, this effect must be masked by others as the table above shows. The data for chlorine, which should show the effect most strongly, are worth consulting in this connection (*cf.* Fergusson, Slotin and Style, *Trans. Faraday Soc.*, **32**, 956 (1936), Fig. 2).

for this and the chlorine–hydrogen peroxide reaction seems strong enough to warrant their revision. One such revision has been carried out.

Anomalies in the temperature coefficients of processes in aqueous iodine solutions find no counterpart in the absorption of visible light by these solutions. Gaseous iodine in air and iodine dissolved in carbon tetrachloride are virtually indistinguishable with a spectrophotometer. Aqueous iodine solutions differ from them in three spectrophotometrically measurable ways.

SCHENECTADY, N. Y. RECEIVED AUGUST 19, 1939

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY No. 735]

Thermal and Photochemical Exchange Reactions of Bromine

BY J. NORTON WILSON AND ROSCOE G. DICKINSON

Several reactions involving exchange of bromine atoms between elementary bromine and bromine compounds in carbon tetrachloride solutions have been investigated in this Laboratory with the use of radioactive bromine. The results obtained from the study of the thermal reactions between bromine and arsenious bromide, stannic bromide, ethylene bromide, and trichlorobromomethane and the photochemical reaction between bromine and trichlorobromomethane are here described.

Experimental Method.—The thermal exchanges were investigated in general as follows. A solution of radioactive bromine in carbon tetrachloride was divided into two portions: the bromine was extracted from one of these portions and converted to silver bromide for electroscopic measurements; the other portion of the solution was mixed with a solution of the bromine compound to be investigated, and the mixture, hereafter referred to as the reaction mixture, was kept at a definite temperature for a convenient time; a precipitate of silver bromide was then prepared from either the bromine or the bromine compound in the mixture. The extent of exchange was then calculated from the known composition of the reaction mixture and the relative electroscopic activities of the two silver bromide precipitates, and is reported here as percentage of complete exchange. The electroscopic measurements were made by a method described elsewhere.[1]

The method used to prepare the dilute highly radioactive solutions of bromine used in the photochemical experiments may be of interest: a small amount of highly radioactive sodium bromide was prepared by the method of Erbacher and Philipp[2] from a large amount of ethylene bromide which had been exposed to slow neutrons from a radon–beryllium source. The sodium bromide, dissolved in a small amount of water, was shaken with a dilute solution of bromine in carbon tetrachloride. As was expected from the known rapidity of the exchange between bromine and bromide ion in aqueous solution,[3] exchange was rapid; the resulting solution of radioactive bromine was dried with phosphorus pentoxide, distilled and diluted to the desired concentration with carbon tetrachloride.

Experiments with Stannic and Arsenious Bromides.—The reaction mixtures were subjected immediately after mixing to vacuum distillation at 25° to remove bromine. The residue of metallic bromide was then hydrolyzed and the resulting bromide ion was precipitated as silver bromide for radioactivity measurements. Exchange was apparently complete with solutions containing 4 mole per cent. of bromine and 2 mole per cent. of either metallic bromide. Since the extent of exchange was calculated on the basis of the initial composition of the solution, exchange was probably completed before an appreciable fraction of the bromine had distilled away, *i. e.*, within about ten minutes. The time elapsing between the initial mixing of the solutions and the conclusion of the distillation was about thirty minutes.

Experiments with Ethylene Bromide.—The reaction mixtures were sealed in glass ampoules and kept in the dark at the desired temperature for a convenient time; the bromine was then extracted with sodium nitrite solution and converted to silver bromide. No exchange beyond the limits of experimental error was detected in a solution of the composition 24 mole per cent. Br_2, 28 mole per cent. $C_2H_4Br_2$, which was kept at 100° for sixty-five minutes. Experiments using lower concentrations and temperatures similarly indicated no exchange. In no experiment was the apparent extent of exchange greater than 3%; this value is less than the estimated experimental error.

Experiments with Trichlorobromomethane.—The thermal reactions were carried out similarly to those involving ethylene bromide. At concentrations of approximately 0.3 moles of bromine and 1 mole of CCl_3Br per liter, the apparent extents of exchange observed in solutions kept for four minutes at 25°, forty minutes at 95° and fifty minutes at 115° were, respectively, −5, 7 and 9%. These measurements are obviously uncertain by at least 5% of

(1) Wilson and Dickinson, THIS JOURNAL, **59**, 1358 (1937).

(2) Erbacher and Philipp, *Z. physik. Chem.*, **A176**, 169 (1936).

(3) Roginskii and Gophstein, *Physik. Z. Sowjetunion*, **7**, 672 (1935).

complete exchange and possibly more; it is doubtful whether any appreciable exchange occurred.

The photochemical experiments were carried out as follows. A solution of radioactive bromine and trichlorobromomethane in carbon tetrachloride was frozen with liquid air; the space above the solution was evacuated in order that oxygen might be largely removed. The solution was melted and separated *in vacuo* into two approximately equal portions which were then sealed off. One portion was thermostated and illuminated for a measured time with filtered radiation from a 500-watt tungsten lamp; the filter transmitted chiefly in the range 5000 to 6100 Å. The other portion was kept in the dark at the same temperature for the same time. After the illumination was completed, both solutions were cooled in the dark; the bromine was extracted from the same volume of each and converted to silver bromide for electroscopic measurements. A small volume of each solution was also analyzed for bromine.

A thermal exchange experiment was performed using the same technique: the solution was separated *in vacuo* into two portions; bromine from one portion was converted immediately to silver bromide; the other portion was kept in the dark at a high temperature for some time before the bromine extraction.

The results obtained with solutions containing about 0.003 mole of bromine and 0.08 mole of trichlorobromomethane per liter were as follows: thermal, solution heated at 76° for seventy-five minutes, −3% exchange; photochemical, solution illuminated at 76° for seventy minutes, 98% exchange. Two experiments in which solutions containing 0.003 mole of bromine and 0.02 mole of trichlorobromomethane per liter were illuminated at 76° for twenty minutes resulted in 86 and 97% exchange. Other experiments at higher temperatures or with longer illumination times also gave 85 to 100% exchange.

Summary

Investigation of the exchange of bromine between radioactive bromine and various bromine compounds has led to the following results: a rapid exchange occurs with arsenious bromide and with stannic bromide at room temperature in carbon tetrachloride solution (!); in the same solvent no exchange beyond the limits of experimental uncertainty was observed to occur with either ethylene bromide or trichlorobromomethane in the dark at 100°; a rapid exchange with trichlorobromomethane is induced by green light at 76°.

A convenient method has been described for the preparation of dilute and highly radioactive solutions of bromine in carbon tetrachloride.

PASADENA, CALIFORNIA RECEIVED SEPTEMBER 21, 1939

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, NO. 743]

The Molecular Structures of Glyoxal and Dimethylglyoxal by the Electron Diffraction Method

BY JAMES E. LUVALLE[1] AND VERNER SCHOMAKER

Introduction.—Extension to open chain hetero-atomic aliphatic compounds of the structural investigations[2] of the constitutional effect of different bonds upon adjacent bonds should provide useful information concerning the electronic structures and the extent of resonance in these molecules. The recent electron diffraction studies of formaldehyde[3] and acetaldehyde[4] have given a reliable value for the carbon–oxygen double bond distance. We have now extended the investigation of compounds containing the carbonyl group to glyoxal and dimethylglyoxal, both of which contain a pair of conjugated carbon–oxygen double bonds and present the possibility of free rotation around the carbon–carbon bond connecting the adjacent carbonyl groups. Furthermore, both substances are colored, glyoxal being the simplest colored compound whose molecules have a conjugated system. Of the compounds glyoxal, dimethylglyoxal, oxalyl chloride, oxamide, and oxalic acid, it is found that glyoxal and dimethylglyoxal are colored whereas the remaining compounds are colorless. All five of these compounds may be represented by the formula RCORCO and the difference in color between the first two compounds and the remaining three compounds suggests that there may be a structural difference between the two groups of compounds. Oxalyl chloride is now under investigation in these Laboratories by the electron diffraction method, and the X-ray study of crystals of oxamide is also under way.

(1) Julius Rosenwald Fellow.

(2) (a) L. Pauling, L. O. Brockway and J. Y. Beach, THIS JOURNAL, **57**, 2705 (1935); (b) L. Pauling and L. O. Brockway, *ibid.*, **59**, 1223 (1937); (c) L. Pauling, H. D. Springall and K. J. Palmer *ibid.*, **61**, 927 (1939); (d) V. Schomaker and L. Pauling *ibid.*, **61**, 1769 (1939).

(3) D. P. Stevenson, J. E. LuValle and V. Schomaker, *ibid.*, **61**, 2508 (1939).

(4) D. P. Stevenson, H. D. Burnham and V. Schomaker, *ibid.*, **61**, 2922 (1939).

Experimental.—Glyoxal was prepared by the oxidation of ethylene with selenium dioxide after the method of Riley and Friend.[5] The ethylene was oxidized in a 3 × 30 cm. Pyrex tube containing equal amounts by weight of phosphorus pentoxide and finely-ground selenium dioxide placed in alternating layers. At the ends of the tube there were longer (7 cm.) columns of phosphorus pentoxide and plugs of "Pyrex wool" (No. 9930). Gentle heating was necessary for starting the reaction. The glyoxal was collected in a trap at −60°. The ethylene was obtained from the Ohio Chemical Company and the selenium dioxide from the Eimer and Amend Company, New York.

Eastman "white label" dimethylglyoxal (b. p. 87–88.5°) was used without further purification.

The electron diffraction photographs were prepared with the apparatus described by Brockway.[6] The values of $s_0 = (4\pi/\lambda)\sin\theta/2$ given in the tables are averages of the values found by visual measurement of the ring diameters for ten or more films. The wave length of the electrons determined from transmission pictures of gold foil (a = 4.070 Å.) was 0.0611 Å. and the camera distance was 10.84 cm. The radial distribution functions[7] were calculated using the s_0 values of both the maxima and minima, and the coefficients, C_K, were determined from these s_0 values and the visually estimated intensities, I_K, according to the method recommended by Schomaker.[8]

Glyoxal.—The photographs of glyoxal are very good, extending to s_0 = 27 and showing thirteen maxima and shelves. The radial distribution curve (Fig. 1) calculated with the C_K and s_0 values of Table I shows four principal peaks at 1.18, 1.48, 2.34 and 3.45 Å., the last two peaks being more reliable than the first two. The peak at 1.18 Å. corresponds to the carbon–oxygen double bond distance, that at 1.48 Å. to the carbon–carbon distance, and that at 2.34 Å. to the long carbon–oxygen distance. These distances indicate a value of about 121° for the C—C=O angle. Resonance probably causes the molecule to be coplanar. Of the two coplanar configurations, the *trans* form is suggested by the strong radial distribution peak at 3.45 Å., this value being very close to that calculated for a *trans* model having the above parameters (3.41 Å.). The remaining small radial distribution peaks are probably without significance.

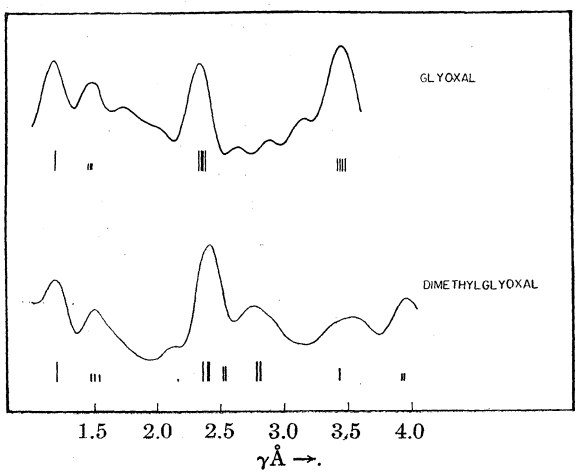


Fig. 1.—Radial distribution curves for glyoxal and dimethylglyoxal. The vertical lines beneath the curves show the various interatomic distances of the models used in the final determination of distances by the correlation method.

Twenty-four intensity curves were calculated with the ratio C—C/C=O varying from 1.38/1.20 to 1.52/1.20 and the angle C—C=O varying from 116° to 128°. The eight intensity curves of Fig. 2 were calculated for coplanar *trans* models with the distance C—H = 1.09 Å. and the angle H—C—C = 114°. A temperature factor was introduced into all the hydrogen terms in the intensity function.[6] If the C—H parameter here assumed were in error by 0.03 Å. the change would not be detected since the contribution of the hydrogen terms is small. The H—C—C angle parameter is likewise unimportant. The longer carbon–oxygen distance and the oxygen–oxygen distance in these models are compatible with the strong radial distribution peaks at 2.34 Å. and 3.45 Å. The faint seventh and tenth shelves which were measured and used in the radial distribution function cannot be distinguished definitely on any of the theoretical curves; however, this is shown by the work of Schomaker and Stevenson[9] on the interpretation of electron diffraction photographs not to be especially surprising.

Curves D and F of Fig. 2 reproduce the photographs satisfactorily, and curves C and E are nearly as good; in the final evaluation of parameters all four models have been used with models

(5) H. L. Riley and N. A. C. Friend, *J. Chem. Soc.*, 2342 (1932).

(6) L. O. Brockway, *Rev. Mod. Physics*, **8**, 231 (1936).

(7) L. Pauling and L. O. Brockway, THIS JOURNAL, **57**, 2684 (1935).

(8) Verner Schomaker, American Chemical Society Meeting, Baltimore, April, 1939.

(9) V. Schomaker and D. P. Stevenson, to be published.

TABLE I

GLYOXAL

Max.	Min.	I	C_K	s_0	Model C[a] s	Model C s/s_0	Model D s	Model D s/s_0	Model E s	Model E s/s_0	Model F s	Model F s/s_0
	1	−10	− 6	3.16	3.20	(1.013)[b]	3.30	(1.044)	3.20	(1.013)	3.30	(1.044)
1		4	2	4.02	3.50	(0.871)	3.60	(0.896)	3.40	(0.846)	3.50	(0.871)
	2	− 6	− 6	4.87	4.48	(0.920)	4.32	(0.930)	4.55	(0.934)	4.50	(0.928)
2		10	6	6.06	6.07	1.002	6.10	1.007	6.06	1.000	6.08	1.003
	3	− 5	− 6	7.26	7.40	(1.019)	7.60	(1.047)	7.40	1.019	7.60	1.047
3		5	5	8.12	7.90	(0.973)	8.00	(0.985)	7.90	(0.974)	8.00	(0.985)
	4	− 2	− 3	8.81	8.80	0.999	8.80	0.999	8.77	0.995	8.80	0.999
4		3	4	9.51	9.10	0.957	9.50	0.999	9.22	0.970	9.20	0.967
	5	− 7	− 8	10.34	9.95	(0.962)	10.07	(0.974)	9.90	(0.957)	10.00	(0.962)
5		8	12	11.54	11.40	0.988	11.52	0.998	11.32	0.981	11.49	0.996
	6	− 4	− 6	12.53	12.66	1.010	12.87	1.027	12.47	0.987	12.64	1.009
6		3	5	13.40	13.32	0.994	13.50	1.007	13.28	0.991	13.38	0.999
	7	− 1	− 1	14.36[d]	...[c]	...	...	...	...	...	...	...
7		2	3	15.06[d]	...[c]	...	...	...	...	...	...	...
	8	− 8	−13	15.28	15.30	(1.001)	15.40	(1.008)	15.22	(0.996)	15.22	(0.996)
8		7	12	16.90	16.83	0.996	17.05	1.009	16.77	0.992	16.90	1.000
	9	− 2	− 3	17.76	18.05	(1.016)	18.33	(1.032)	17.90	(1.008)	18.22	(1.026)
9		1	2	18.67	18.58	0.995	18.80	1.007	18.40	0.986	18.73	1.003
	10	− ½	− 1	19.47[d]	...[c]	...	...	...	...	...	...	...
10		½	1	20.18[d]	...[c]	...	...	...	...	...	...	...
	11	− 8	−10	20.37	20.05	(0.984)	20.05	(0.984)	20.70	(1.016)	20.05	(0.984)
11		5	8	22.25	22.18	0.997	22.40	1.007	22.08	0.992	22.25	1.000
	12	− 8	− 8	23.50	23.60	1.004	23.90	1.017	23.54	1.002	23.70	1.009
12		2	3	24.38	24.10	0.989	24.60	1.009	23.90	0.980	24.40	1.001
	13	− 3	− 2	25.53	25.20	(0.976)	25.35	(0.991)	25.10	(0.984)	25.24	(0.987)
13		3	4	27.08	27.43	(1.013)	27.63	(1.020)	27.28	(1.007)	27.60	(1.019)
	Average					0.994		1.008		0.989		0.999
	Average deviation					0.008		0.006		0.008		0.006
	(C=O) = 1.20 × $(\overline{s/s_0})$					1.193		1.208		1.187		1.199
	(C—C) = 1.46 × $(\overline{s/s_0})$					1.451		1.472				
	= 1.48 × $(\overline{s/s_0})$									1.464		1.479
	(C=O) = 1.20 ± 0.01 Å.											
	(C—C) = 1.47 ± 0.02 Å.											

[a] The models are described in the legend to Fig. 2. [b] Less reliable values, not included in taking the averages, are shown in parentheses. [c] The theoretical curve indicates no precisely measurable feature at this point. [d] The values of s_0 used in the radial distribution function were somewhat different than the ones given here; the weights show these terms were relatively unimportant.

D and F assigned weights three times as great as models C and E. Curves A, B, G and H are not at all satisfactory and the corresponding models were discarded.

It is concluded that the glyoxal molecule has the configuration and distances described by the following parameters: C—H = 1.09 Å. (assumed), C=O = 1.20 ± 0.01 Å., C—C = 1.47 ± 0.02 Å., angle C—C=O = 123° ± 2°. The molecule is probably coplanar and *trans;* the evidence for this view provided by the radial distribution function is supported by a strong dependence of the intensity curves upon the relative orientation of the carbonyl groups of the glyoxal molecule. Theoretical considerations[10] indicate that resonating systems tend to be coplanar. The electron diffraction data are not incompatible with a mixture containing a small fraction of molecules with the *cis* configuration. The data indicate that the amplitude of libration around the carbon–carbon bond is small.

Dimethylglyoxal.—The photographs of dimethylglyoxal are excellent, extending out to s_0 = 27 and showing eleven maxima and shelves. The s_0, I_K, and C_K values are given in Table II. The radial distribution curve (Fig. 1), calculated with the s_0 and C_K values of this table, has peaks at 1.19, (1.50), (2.12), 2.41, 2.75, (3.56), and 3.95 Å. (The less reliable peaks are enclosed in parentheses.) We can assume coplanarity of the molecule as it possesses a resonating system. The peak at 1.19 Å. corresponds to the carbon–oxygen

(10) L. Pauling and J. Sherman, *J. Chem. Phys.*, **1**, 679 (1933); W. G. Penney, *Proc. Roy. Soc.* (London), **A158**, 306 (1937).

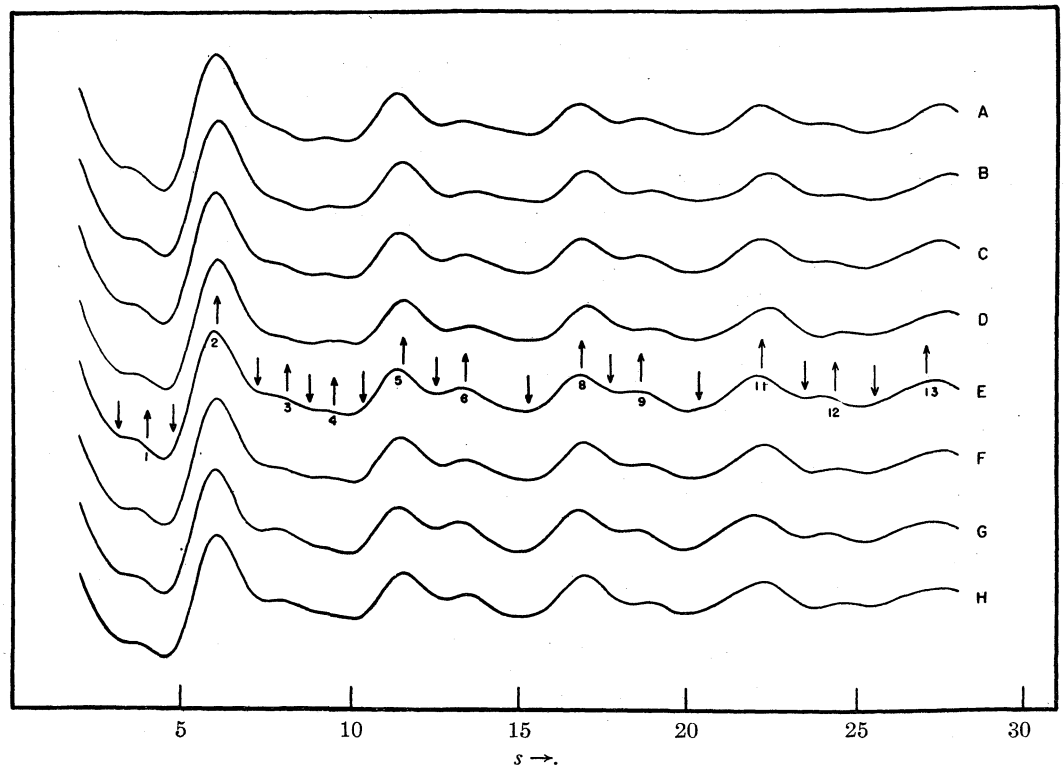


Fig. 2.—Theoretical intensity curves for glyoxal. Denoting the C—C=O by α and the ratio of the C—C distance to the C=O distance by ρ:

Curve A, $\alpha = 128°$, $\rho = 1.42/1.20$; Curve B, $\alpha = 125°$, $\rho = 1.42/1.20$;
Curve C, $\alpha = 125°$, $\rho = 1.46/1.20$; Curve D, $\alpha = 122°$, $\rho = 1.46/1.20$;
Curve E, $\alpha = 125°$, $\rho = 1.48/1.20$; Curve F, $\alpha = 122°$, $\rho = 1.48/1.20$;
Curve G, $\alpha = 122°$, $\rho = 1.52/1.20$; Curve H, $\alpha = 119°$, $\rho = 1.52/1.20$.

TABLE II

DIMETHYLGLYOXAL

Max.	Min.	I	C_K	s_0	Model C[a] s	Model C[a] s/s_0	Model D s	Model D s/s_0
1		50	4	3.05	2.94	(0.964)	2.90	(0.951)
	2	−100	−10	4.36	4.27	(0.979)	4.25	(0.975)
2		100	12	5.59	5.75	(1.028)	5.82	(1.041)
	3	− 30	− 2	7.35	7.23	0.984	7.30	0.993
3		60	11	8.20	8.27	1.008	8.30	1.012
	4	− 10	− 2	8.86	...[b]	...	...	...
4		5	1	9.37	9.30	0.993	9.30	0.993
	5	− 50	−12	10.23	10.20	0.997	10.26	1.003
5		50	12	11.44	11.52	1.007	11.50	1.005
	6	− 40	−11	12.37	12.43	1.005	12.42	1.004
6		55	14	13.44	13.46	1.001	13.42	0.999
	7	− 60	−24	15.29	15.13	0.990	15.10	0.988
7		60	17	16.21	16.77	(1.035)	16.64	(1.027)
	8	− 30	−10	17.64	17.73	1.005	17.57	0.996
8		20	5	18.84	18.47	(0.980)	18.34	(0.973)
	9	− 60	−15	20.19	19.90	0.986	19.88	0.985
9		45	13	21.48	21.50	1.001	22.30	1.038
	10	− 20	− 7	23.26	23.80	1.023	23.63	1.017
10		10	3	24.34	24.70	(1.015)	24.40	(1.002)
	11	− 25	− 7	25.23	25.05	(0.993)	25.60	(1.015)
11		30	8	26.87	27.53	(1.025)	27.35	(1.018)
		Average				0.998		1.001
		Average deviation				0.007		0.010

[a] The models are described in the legend to Fig. 3. [b] The theoretical curves do not show a precisely measurable feature at this point.

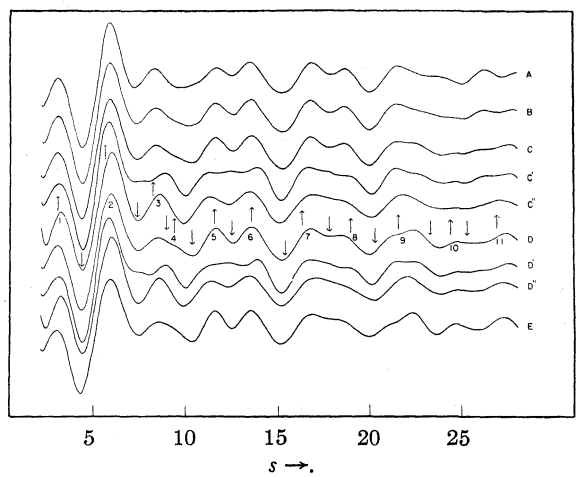


Fig. 3.—Theoretical intensity curves for dimethylglyoxal. All the curves have the following parameters in common: C—H = 1.09 Å. (assumed), C=O = 1.20 Å., C_2—C_3 = 1.47 Å., C_1—C_2 = 1.54 Å., and angle CO—C=O (α) = 123° ± 2°. Denoting angle CH_3—C=O by β we have: Curve A, $\beta = 125°$; Curve B, $\beta = 124°$; Curves C, C′, and C″, $\beta = 123°$; Curves D, D′, and D″, $\beta = 122°$; Curve E, $\beta = 121°$.

double bond distance, that at 1.50 Å. to the 2–3 carbon–carbon distance and the two 1–2 carbon–carbon distances, and that at 2.41 Å. to the 1–3 carbon–carbon distance and the two carbon–oxygen distances. The peak at 2.75 Å. may be attributed to the long carbon–oxygen distance of the molecule with the *trans* configuration or possibly to the long carbon–carbon distance for the *cis* configuration, and the broad peak at 3.56 Å. may represent the oxygen–oxygen distance for the *trans* configuration or the long carbon–oxygen distance for the *cis* configuration. However, the peak at 3.95 Å. can be attributed only to the long carbon–carbon (1–4) distance of the *trans* form, which indicates strongly that the molecule has the *trans* configuration.

Assuming that the distances and the C—C=O angle found for glyoxal hold for dimethylglyoxal, five models were set up and fifteen intensity curves calculated, five for the *cis* form, five for the *trans* form, and five in which the terms dependent upon the relative orientation of the acetyl groups were omitted from the intensity function. The angle β was varied from 119 to 125°.

Of the curves shown in Fig. 3, A, B, C, D and E are for the *trans* models, C′ and D′ are for the *cis* models, and C″ and D″ are the incomplete intensity curves corresponding to C and D, respectively. Curves C and D both give satisfactory agreement with the photographs except for the ninth and tenth maxima. On curve C, the ninth maximum is observed to have shifted to a smaller s value than that measured and the tenth maximum is too weak, whereas on curve D, the ninth maximum is observed to have shifted to a larger s value than that measured and the tenth maximum is too strong. The best model accordingly lies between model C and D. Examination of Fig. 3 shows that the remaining *trans* models, A, B, and E, are unsatisfactory and the *cis* models C′ and D′ are out of the question. Curves C″ and D″ show that the libration around the 2–3 carbon–carbon bond is not of great amplitude.

It is concluded that the dimethylglyoxal molecule is essentially coplanar and *trans* with the following parameter values: C—H = 1.09 Å., C_2—C_3 = 1.47 ± 0.02 Å., C_1—C_2 = 1.54 ± 0.02 Å., C=O = 1.20 ± 0.02 Å., angle CO—C=O (α) = 123° ± 2°, and angle CH_3—C=O (β) = 122.5° ± 1°. The electron diffraction data are not incompatible with a mixture containing a small fraction of *cis* molecules. The data indicate that the amplitude of libration around the (C_2–C_3) carbon–carbon bond is small. It must be emphasized that the determination of the configuration and distances in dimethylglyoxal is not as precise as that for glyoxal. The radial distribution curve strongly indicates this model but a model in which the 2–3 carbon–carbon bond is somewhat lengthened and the 1–2 and 3–4 carbon–carbon bonds are slightly shortened cannot be eliminated by the qualitative comparison, but such a model does not agree with the radial distribution function as well as our final model.

Discussion.—The observed shortening in both molecules of 0.07 Å. for the carbon–carbon bond connecting the adjacent carbonyl groups corresponds to 15 or 20% double bond character,[2b] and is nearly the same as that (1.46 Å.) reported for butadiene.[2d] The electron diffraction data for both glyoxal and dimethylglyoxal indicate restricted rotation around the carbonyl–carbonyl bond.

Calculation of the potential restricting rotation around the 2–3 carbon–carbon bond in dimethylglyoxal by the method of Beach and Stevenson[11] using Zahn's values[12] of the dipole moment and Smyth's values[13] of the group moments indicates that the potential barrier restricting rotation is steeper than a parabolic barrier and greater than 12 kcal. in height. Zahn[12] finds an amplitude of approximately 30° for the libration in dimethylglyoxal. Dipole moment data are not available for glyoxal, so that the corresponding calculation could not be made; however, the potential barrier should be of the same order of magnitude for both substances.

Calculation of the coulombic interactions for the *cis* and *trans* models of glyoxal and dimethylglyoxal using Smyth's values[13] of the bond moments shows that the *trans* glyoxal molecule is about 6.9 kcal./mole more stable than the *cis* configuration and that the *trans* dimethylglyoxal molecule is about 1.7 kcal./mole more stable than the *cis* configuration. Calculations of the ratio of the partition functions of *cis* to *trans* glyoxal and dimethylglyoxal are simplified by the assumption that the vibrational partition functions are the same for both the *cis* and *trans* configurations, the translational partition functions are the same; therefore, the calculation becomes the cal-

(11) J. Y. Beach and D. P. Stevenson, *J. Chem. Phys.*, **6**, 635 (1938).

(12) C. T. Zahn, *Phys. Rev.*, **40**, 291 (1932).

(13) C. P. Smyth, *J. Phys. Chem.*, **41**, 209 (1937).

culation of the square root of the ratio of the product of the three principal moments of inertia for the two configurations. The ratios $[(I_1I_2I_3)_{cis}/(I_1I_2I_3)_{trans}]^{1/2}$ for the glyoxal and dimethylglyoxal molecules are 1.15 and 1.00, respectively. For the equilibrium *cis* $\rightleftarrows$ *trans* these values combined with the ΔE values given above correspond to equilibrium constants of 87,000 and 20 for glyoxal and dimethylglyoxal, respectively; that is, the fraction of *cis* glyoxal is negligible and that of *cis* dimethylglyoxal may be about 5%. These results agree with our electron diffraction investigations.

We express our thanks to Dr. Linus Pauling for his helpful criticism and discussion and to Dr. D. P. Stevenson for assistance with the calculations and helpful discussion.

Summary

The configurations of glyoxal and dimethylglyoxal as determined by the electron diffraction method are given by the following parameters:

Glyoxal: C—H = 1.09 Å. (assumed), C=O = 1.20 ± 0.01 Å., C—C = 1.47 ± 0.02 Å., angle C—C=O = 123° ± 2°

Dimethylglyoxal: C—H = 1.09 Å. (assumed), C=O = 1.20 ± 0.02 Å., C_2—C_3 = 1.47 ± 0.02 Å., C_1—C_2 = 1.54 ± 0.02 Å., angle CO—C=O = 123° ± 2°, angle CH_3—C=O = 122.5° ± 1°

The electron diffraction data and the dipole moment data as well as chemical information indicate uniformly that both molecules are coplanar with the *trans* configuration and that rotation around the carbon–carbon bond connecting the adjacent carbonyl groups is restricted.

PASADENA, CALIFORNIA RECEIVED OCTOBER 23, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF BOTANY AND DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Quantum Efficiency of Photosynthesis in Chlorella. II

BY H. G. PETERING,[1] B. M. DUGGAR AND FARRINGTON DANIELS

Photosynthesis in algae has been the object of an extended investigation in these laboratories. The quantum efficiency was found to be of the order of 0.05 molecule per quantum,[2] much lower than the older value of 0.25 reported by Warburg and Negelein.[3] In order to study further the reasons for this large discrepancy, a new method was developed[4] for the rapid determination of dissolved oxygen making use of the dropping mercury electrode. The respiration correction seemed to be the most important source of error, and the manometric method used by Warburg and Negelein involves a considerable time lag in determining the rate of respiration and of photosynthesis. If respiration is faster under the conditions imposed by photosynthesis, then a prompt determination of respiration after the light is turned off is necessary if arbitrary assumptions are to be minimized. Results obtained with the dropping mercury electrode are given here. They agree essentially with those reported earlier[2] and are in definite disagreement with those of Warburg and Negelein.[3] Recently Rieke[5] has reported a value of 0.24 obtained with the manometric method in agreement with Warburg and Negelein.

Experimental Procedure

The material was *Chlorella pyrenoidosa*, of the same strain as used before.[2] It was grown in pure culture on agar slants and periodically transferred to fresh slants or to liquid media. The liquid culture was essentially the salt nutrient recommended by Warburg and Negelein.[3] The composition was:

Agar medium, g.		Liquid nutrient, *M*	
$NaNO_3$	0.25	$MgSO_4$	0.020
$CaCl_2$	.25	KNO_3	.005
KH_2PO_4	.25	KH_2PO_4	.018
$MgSO_4$	.25	$FeSO_4$	.00001
Cane sugar	2.00		
Water	1 liter		

Distilled water from a block tin condenser was used in most of the experiments but no differences were noted when in some of the experiments tap water from Lake Mendota was used. The algae were grown in 300-cc. flasks on a water-cooled rack illuminated from the bottom, while air, to which had been added 5% carbon dioxide, was bubbled through. Warburg's recommendations were followed in a general way, exposing algal cultures to bright light (four 200-watt filament lamps at 30 cm.) for a week and then to weaker light (six 25-watt lamps at 45 cm.).

(1) Present address: Chemical Section, Michigan Experiment Station, East Lansing, Michigan.

(2) W. M. Manning, J. F. Stauffer, B. M. Duggar and F. Daniels, THIS JOURNAL, **60**, 266 (1938).

(3) O. Warburg and E. Negelein, *Z. physik. Chem.*, **106**, 191 (1923).

(4) H. G. Petering and F. Daniels, THIS JOURNAL, **60**, 2796 (1938).

(5) F. F. Rieke, *J. Chem. Phys.*, **7**, 238 (1939).

The cultures were not used after they were more than fourteen days old. A normal growth curve was obtained for the algae under these conditions, showing rapid growth from the fourth to the eighth day.

In preparing a sample for measurements the supernatant liquid was decanted and the remaining algal solution was diluted immediately with fresh nutrient solution, which had been passed through filter paper to provide sufficient organic material for proper action of the dropping mercury electrode. The *p*H of the solution was adjusted to 5.5, the value attained by the growing algae in about a week. In some earlier experiments the algae were concentrated by centrifuging and then diluting but in later experiments this was avoided since it may affect the respiration. The algae were diluted until 50–75% of the light was transmitted by a solution 1.6 cm. thick. This usually required the addition of ten volumes or more of the fresh nutrient solution.

A 500-watt projection lamp was used with a lens and filter system giving parallel light chiefly between 6100 and 7200 Å. with a sharp maximum at about 6400 Å. A Corning No. 243 signal red filter was used together with 9 cm. of an 0.05 *N* copper sulfate solution. In some of the experiments with higher light intensity the copper sulfate was 0.025 *N* and tests showed that 10 to 15% of the total radiation might have been in the longer red and short infrared, but very little of this could have been absorbed by passage through the 1.6 cm. cell.

The incident and transmitted light were measured with a large-area thermopile having thirty junctions. Calibration was effected with a U. S. Bureau of Standards radiation lamp and corrections were made for reflections at the windows. Each cm. deflection of the thermopile-galvanometer was equivalent to 72.5 ergs per second per sq. cm. The room was thermostated between 24 and 26°. All of the light falling on the reaction cell was homogeneous with respect to both color and intensity. The entire cell was illuminated and half or more of the light was transmitted. Since most of the transmitted light was scattered, the thermopile was placed as close behind the reaction cell as possible. Tests showed that the thermopile could be moved from side to side over a wide range and forward and backward for several millimeters without changing the galvanometer deflections. The total light transmitted was calculated by multiplying the light falling on the thermopile by the ratio of the area of the reaction cell to that of the thermopile.

The reaction cell, 4.5 × 3.1 cm. in cross section and 1.6 cm. in thickness,[6] was placed in front of the thermopile. The narrow neck at the top of the cell permitted the insertion of the thin capillary tip of the dropping mercury electrode and the U-tube at the bottom kept at constant level the anode pool of mercury, 1 sq. cm. in area. The algal suspension was added until it over-flowed the cell and then the cathode tip was inserted at the center without forming air bubbles. The mercury dropped at the rate of about 1 drop per second[7] and the galvanometer readings were taken at 1.00 volt and at 0.10 volt. The difference in galvanometer readings at the two voltages was a straight line function of the oxygen concentration[8] as determined by the Winkler chemical analysis for dissolved oxygen. At 25° the calibration gave 9×10^{-9} mole of oxygen per cc. for each cm. deflection. The algae were not stirred because the whole cell was illuminated and the algae did not settle appreciably during the time of the determination. Experiments in which the cell was shaken between measurements showed that the stirring was not necessary.

(6) Fig. 2B of reference 4.

(7) It is necessary to keep the dropping rate constant and the temperature of the room should not vary by more than 1 or 2°, particularly if a galvanometer shunt is used. It is essential that the drops of mercury coalesce immediately with the anode pool of mercury. If organic matter prevents this coalescence it is necessary to use an external anode connected through a salt bridge in agar.

Results

A series of twenty-nine determinations was first obtained with the Winkler titration method and the quantum yields were between 0.02 and 0.07 in agreement with the earlier work.[2] However, it was found that the rate of oxygen consumption after illumination changed with time and the method was abandoned in favor of the rapid electrical method described here which permits a prompt determination of the rates of

TABLE I

QUANTUM YIELDS IN PHOTOSYNTHESIS

Expt.	Age culture in days, light intense + weak	Incident intensity (ergs/sec. sq. cm.)	% Absorption	Molecules per quantum
1	11 + 5	2210	26.7	0.069
2	3 + 0	2080	23.3	.069
3[a]	3 + 0	2080	23.3	.065
4	9 + 7	1820	27.2	.070
5[a]	9 + 7	1820	27.2	.068
6	3 + 0	1490	42.0	.070
7	3 + 0	1490	42.0	.085
8	4 + 0	1860	48.0	.080
9	4 + 0	1860	48.0	.063
10A	7 + 5	1460	34.1	.100
10B	7 + 5	1460	34.1	.086
10C	7 + 5	1460	34.1	.067
11A	5 + 5	1100	36.9	(.096)[b]
11B	5 + 5	1100	36.9	.069
11C	5 + 5	1100	36.9	(.064)[b]
12A[a]	5 + 5	1100	36.9	(.135)[b]
12B[a]	5 + 5	1100	36.9	.059
19	5 + 5	1770	40.0	.068
13A	7 + 2	6080	40.0	.059
13B	7 + 2	6080	40.0	.054
14[a]	7 + 2	6080	40.0	.066
15	6 + 5	4530	31.0	.059
16A	8 + 5	4690	41.0	.045
16B	8 + 5	2410	41.0	.048
17A[a]	8 + 5	4630	44.0	.063
17B[a]	8 + 5	2380	44.0	.061
18A[a]	8 + 5	4660	42.5	.073
18B[a]	8 + 5	4660	42.5	.079
19	8 + 5	1773	33.8	.068

[a] Glucose or sodium glycolate added. [b] Calculations by the method of Warburg and Negelein are indicated by parentheses.

(8) Curve D, Fig. 4, ref. 4.

respiration and photosynthesis. An example of these measurements has been given.[9] The mercury was shown not to affect the living algae under the conditions of the experiment.

The results are shown in Figs. 1, 2, and 3 and in Table I. The temperature was always 24–26°.

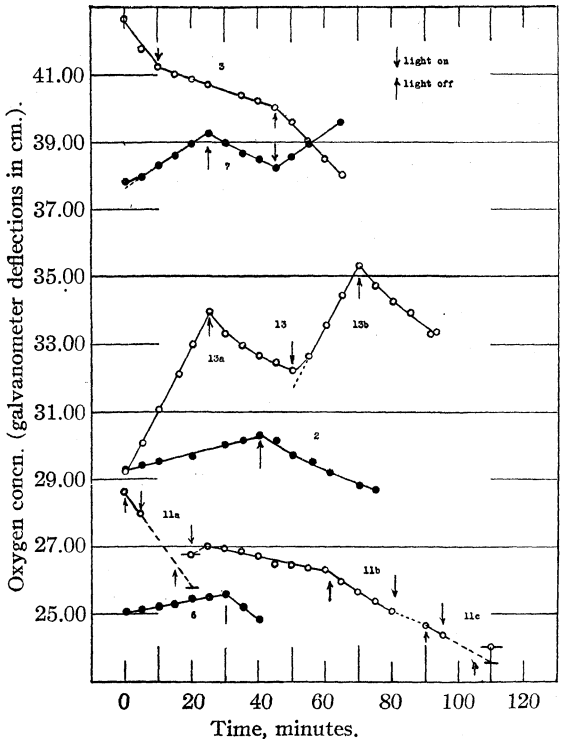


Fig. 1.—Oxygen concentration during photosynthesis and respiration.

Experiments with lower light intensities ranging from 1100 to 2200 ergs per second per sq. cm. are given first. The quantum yields range from 0.059 to 0.10. In expts. 13 to 18 the intensity was higher, 4500 to 6000, except that in expts. 16B and 17B the light intensity was reduced to about half the value in 16A and 17A by the introduction of a wire screen.

In expts. 3, 5 and 14, about 1% of glucose was added. In expt. 12, 1.0% of sodium glycolate was added. Experiments 16, 17 and 18 were practically the same except that in expt. 17 the solution was 0.05 *M* in sodium glycolate and in 18 it was 0.025 *M* in sodium glycolate and 0.025 *M* in glucose.

The method of calculation is illustrated with the data of experiment 13A.

Rate of oxygen change in light

$$\frac{(33.95 - 32.95)\text{ cm.}}{(25.0 - 20.0)\text{ min.}} = 0.20\text{ cm./min.}$$

Rate of oxygen change in dark

$$\frac{(33.30 - 33.95)\text{ cm.}}{(25.0 - 30.0)\text{ min.}} = -0.13\text{ cm./min.}$$

Rate of photosynthesis (corrected for respiration) = 0.20 − (−0.13) = 0.33 cm./min. In some experiments the calculations were made from tangents to the curves rather than from individual data.

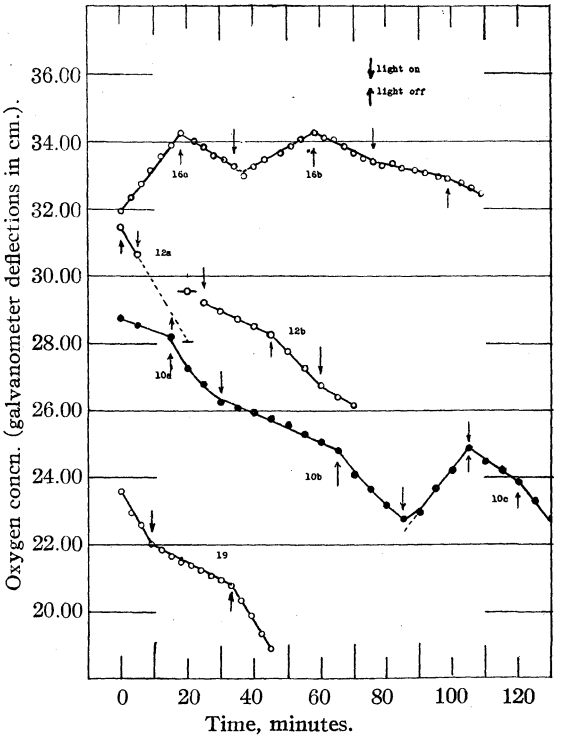


Fig. 2.—Oxygen concentration during photosynthesis and respiration.

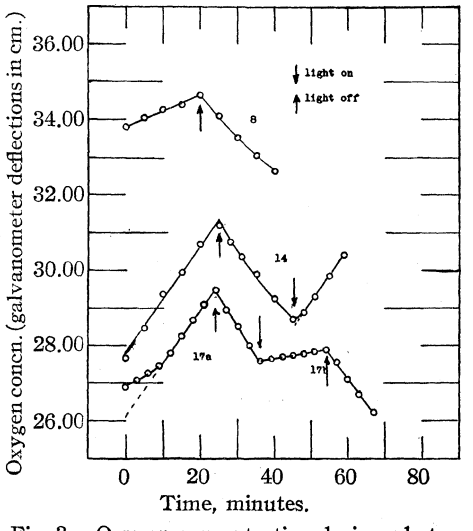


Fig. 3.—Oxygen concentration during photosynthesis and respiration.

(9) Reference 4, Fig. 5.

One unit cell volume is taken as 1 sq. cm. surface multiplied by the thickness of the cell, or 1.60 cc. One cm. deflection (difference between galvanometer reading with 1.00 volt and 0.100 volt) is equivalent to 9×10^{-9} mole of oxygen per cc. or 8.68×10^{15} molecules of oxygen per unit cell volume. The deflection of the thermopile back of the reaction cell was 45.0 cm. and 80.3 cm. when the cell was removed. With corrections for reflections, the incident light was 6080 ergs per second and the transmitted light 3620, giving an absorption per unit cell volume of 2460 ergs per second. At 6500 Å. one quantum contains 3.03×10^{-12} erg. Then the quantum yield is

$$\Phi = \frac{0.33 \times 8.68 \times 10^{15}}{2460 \times 60/3.03 \times 10^{-12}} = 0.059 \text{ molecule per quantum}$$

An hour later with the same light intensity, at 13B the slope was 0.18 cm. per minute in the light and −0.12 cm. in the dark, leading to a photosynthesis value of 0.30 cm. per minute and a quantum yield of 0.054.

The steady rate of respiration attained between the thirty-fifth and fiftieth minutes might be considered the significant rate, leading to a still lower quantum yield. In this period the slope is −0.05 cm. per minute. Combining this with the rate of oxygen uptake for the first exposure to a light a quantum yield of 0.045 is obtained; and combining it with the slope during the second exposure a value of 0.041. However, since there is disagreement regarding the value of quantum yields in photosynthesis, only the highest values are recorded in Table I. When the respiration rate decreased with time, the rate immediately after illumination was used in the calculations. The biologically significant and continuing quantum yields may be lower.

Discussion

A wide variety of conditions are covered by the data of Table I and Figs. 1, 2, 3, and yet the quantum yields are always low, *i. e.*, less than 0.10,[10] except in the case of 12A which was calculated in a different way. No correlation could be found between the quantum yield and the age or concentration of the algae or other factors. Many factors seem to influence the rate of respiration, such as the concentration of algae, the addition of glucose or glycolate and exposure to light, but the effect is compensated for in photosynthesis. When the slope for the oxygen change in the light is added to the slope for the oxygen change in the dark and combined with the amount of light absorbed, the quantum yields are almost always between 0.04 and 0.09. When the concentration of cells is low and the intensity of light is high, oxygen is evolved rapidly giving a positive slope but when the concentration is high and the light low, the respiration may be so great that illumination simply lessens the rate at which the oxygen is consumed and the slope of the oxygen-concentration–time curve remains negative but less steep.

Although the rate of respiration in the dark may change, it is seen that the amount of oxygen evolved in the light is a linear function of the time at constant light intensity. Apparently in the light a steady state of intermediate products may be reached which assures a uniform rate of respiration, at least over moderate time intervals.

In expts. 16B and 17B the light intensity was reduced by half, giving a slower rate of assimilation. However, the respiration was slower also with the result that the quantum yields are the same as in experiments 16A and 17A, respectively. Under these conditions the light must be the limiting factor because the rate of photosynthesis is directly proportional to the intensity.

It is well known that the addition of glucose accelerates respiration and in expts. 3, 5, 14, 17 and 18 this tendency is shown by the steeper curves. At low light intensities the quantum yields are not affected by this increased respiration but in expts. 14, 17 and 18 at higher light intensities there is evidence of an increase.

The discrepancy between the results obtained in this Laboratory and those obtained by Warburg and Negelein[2] and by Rieke[4] may be explained in part by the different methods of measurements. These investigators measured the oxygen change with a manometer and it is difficult under these conditions to obtain separately the actual rates of oxygen change in the light and in the dark on account of the time lag involved during the attainment of equilibrium between the gas phase and solution. Accordingly, a method of extrapolation was used[11] based on a few measurements and on the assumption that the rate of

(10) In new experiments, by Mr. W. E. Moore, to be reported later, algae from a different source have been used, the water has been specially purified and various inorganic and organic substances have been added. The same low quantum yields have been obtained consistently.

(11) This method is illustrated by Rieke in Fig. 1 of ref. 3.

respiration does not change. Periods of illumination and dark were chosen which were found experimentally to be favorable for the development of high apparent quantum yields.

Determinations 11A, 11C and 12A have been calculated by this extrapolation method as shown by the dotted lines in Fig. 1. After a period of illumination the algal suspension was kept in the dark for a period of five minutes. Oxygen concentrations were determined at the beginning of this dark period and at the end of the fifth minute. The light was turned on from the fifth to the fifteenth minute, and after five minutes in the dark the final reading was taken at the twentieth minute. The difference between this oxygen concentration and the value extrapolated from the fifth to the twentieth minute (assuming constant respiration), was used in calculating the amount of oxygen evolved during the ten-minute exposure to light. In 11A and 12A high values were obtained by this method of calculation. In 11C where the extrapolation sequence was started only after the algae had come to equilibrium with the light, as defined by a uniform rate of oxygen change (straight line), the calculations by the extrapolation method and the differential rate method are the same, and both are low.

The authors are glad to acknowledge the support of the Wisconsin Alumni Research Foundation in this investigation.

Summary

Quantum yields in photosynthesis by algae have been measured under a variety of conditions, making use of the dropping mercury electrode for the rapid measurement of dissolved oxygen. The results show that at 25°, 0.04 to 0.1 molecule of oxygen is evolved in photosynthesis by chlorella per quantum of red light absorbed. This efficiency is much lower than the efficiency 0.25 which has been hitherto accepted.

MADISON, WISCONSIN RECEIVED OCTOBER 13, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

A Photocalorimeter. The Quantum Efficiency of Photosynthesis in Algae

BY JOHN L. MAGEE, THOMAS W. DEWITT, ELIZABETH COOLIDGE SMITH AND FARRINGTON DANIELS

The calorimeter described in this paper is designed to measure heat changes accompanying photochemical reactions. It was developed originally for determining thermally the quantum efficiency of photosynthesis by *Chlorella*. The hitherto accepted value of 0.25 molecule of carbon dioxide converted per quantum absorbed was obtained by Warburg and Negelein[1] with a differential manometer. Work originally undertaken in this Laboratory to extend the investigation of Warburg led to a much lower quantum yield, of the order of 0.05 molecule per quantum.[2] It was thus desirable to measure the quantum yield by other methods. Warburg's high efficiency demands that a large fraction of the absorbed radiation be converted into chemical energy while the lower efficiencies of Manning, Stauffer, Duggar and Daniels require that most of the radiation be dissipated as heat. A calorimetric method was suggested as an independent check on the work. The calorimeter consists of a small thin-walled quartz cell mounted in a cylindrical aluminum container. A multijunction thermocouple measures the temperature difference between the cell and container. A double thermostat keeps the latter at constant temperature. A thermopile placed behind the cell measures the amount of radiation transmitted. The calorimeter is calibrated at different light intensities by filling it with a solution of india ink or other chemically-inert, opaque liquid, and plotting galvanometer deflections against time until a steady state is reached. The heat evolved or absorbed in a chemical reaction can then be obtained by comparing the galvanometer–time curve with the curve for a chemically inert material under similar conditions.[2a]

(1) Warburg and E. Negelein, *Z. physik. Chem.*, **106**, 191 (1923).

(2) W. M. Manning, J. F. Stauffer, B. M. Duggar, and F. Daniels, THIS JOURNAL, **60**, 266 (1938).

Experimental Procedure

Apparatus.—The construction of the photocalorimeter is shown in Fig. 1. The cylindrical quartz cell with pol-

(2a) Dr. William A. Arnold of the Hopkins Marine Station of Stanford University at Pacific Grove, Calif., has developed independently a microcalorimeter which in August, 1938, was giving quantum yields with algae slightly greater than those obtained in this investigation.

ished ends, 2.3 cm. long and 1.3 cm. in diameter with two glass-stoppered openings in the top, has a capacity of 2.9 cc. It is supported by four fiber points in a hollow, cylindrical aluminum case 6.3 cm. long and 7.5 cm. in diameter having a central hole 4.5 cm. in diameter. The top of the case is removable for filling and emptying the reaction cell. Except for the front and rear faces, the quartz cell is silvered on the outside and covered with glyptal lacquer. The fifty copper–constantan thermocouple junctions, coated with glyptal lacquer, are fastened to the cell with de Khotinsky cement and the cold ends are attached in the same manner to the lacquered aluminum casing. The copper wire is no. 40 and the constantan wire no. 36, giving a total resistance of 34 ohms. The thermopile placed immediately behind the photocalorimeter has a surface larger than that of the calorimeter. It absorbs and measures all the transmitted light. It has twenty-eight junctions attached to the single, large, circular receiver and is enclosed in an aluminum block with a quartz window. The galvanometer (10 mm. per microvolt) is connected by a double pole switch to either the calorimeter or the thermopile.

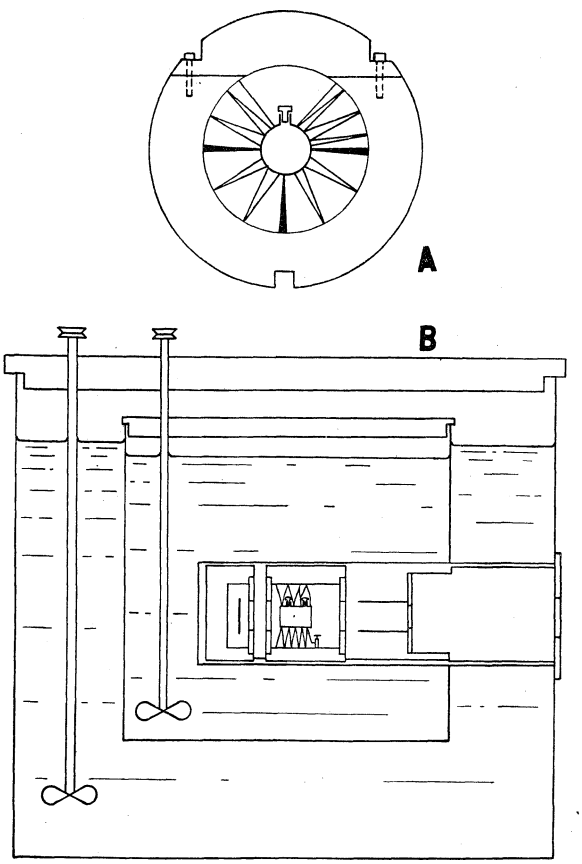


Fig. 1.—Photocalorimeter: A, end view; B, side view in thermostat.

A deflection of 1 cm. in the scale corresponds to a difference of 0.0003° in the calorimeter and it is essential therefore to have the cold junctions maintained at a very constant temperature. The problem was solved only after using a double thermostat, an outer one of water with a mercury regulator and stirrer, constant to 0.003°, and an inner one of oil supplied with a slow stirrer but no heater. The bottoms of the thermopile and calorimeter are slotted and run into the center of the inner thermostat along a track in a horizontal submarine tube as shown in Fig. 1B. In this way the cell is readily removed, filled and replaced in an exact position. After the thermopile and calorimeter are in position, a cylinder with quartz windows is telescoped inside of the thermostated tube and pushed flush with the outside of the thermostat. In this way circulation of cooler air is prevented. Thermal equilibrium is reached in about two hours after inserting the calorimeter and closing the tube.

For the measurements on *Chlorella*, a 500-watt projection lamp was used with a lens and three filters—a 10 cm. filter solution of 0.5% $CuSO_4$, 5 cm. of water, and a Corning signal red #243 filter. The parallel beam of light is diaphragmed down until it barely fills the whole calorimeter cell. The calorimeter is filled and emptied with micropipets having capillary outlets. The top of the aluminum block is removed and a piece of filter paper is placed over the top of the quartz calorimeter cell. The stoppers of the cell are allowed to protrude through holes in the filter paper and when they are replaced, the rims are dried and covered with a trace of glycerol. A slight variation in the calibration value from day to day was traced to different humidity of the laboratory air. Occasionally the galvanometer deflection in the dark was abnormal due to evaporation of traces of moisture, but this difficulty was corrected by sweeping through a current of dry air.

Calibration.—The thermopile registered 1 cm. deflection for each 102 ergs per second, as measured with a Bureau of Standards radiation lamp, after correction for the reflection at the quartz window. The calorimeter was calibrated with a beam of light and the thermopile as shown in Table I where R is the thermopile reading with the calorimeter removed and r is the thermopile reading when the light is partially absorbed by the calorimeter cell. The energies absorbed as shown in the third column contain small corrections for reflections at the rear window back into the calorimeter. A slight cloudiness on the calorimeter windows necessitated another correction when

TABLE I

CALIBRATION OF PHOTOCALORIMETER

Absorbing material	R	r	Energy absorbed, ergs/cm./sec.	Calorimeter deflection, cm.	Energy absorbed per sec. per cm. deflection
Water	29.0	23.4	776	9.0	85
Water	68.7	56.6	1720	20.6	82
India ink	33.6	15.3	1885	21.2	85
Colloidal silver	25.5	9.5	1833	23.0	80
India ink	35.5	13.8	2491	30.0	83
India ink	33.3	10.5	2591	31.2	83
Colloidal silver	48.5	18.5	3442	40.8	84
Colloidal silver	41.3	7.3	3808	45.8	83
Colloidal silver	48.1	11.8	4093	49.0	84
Colloidal silver	46.6	7.9	4332	49.6	88
India ink	74.7	26.8	5476	62.0	88
India ink	85.0	37.5	5505	63.4	87
				Average	84.4

measuring the heat of chemical reactions. The calorimeter–galvanometer deflections are given in the fourth column for the different energy imputs. These steady-state values are reached a few minutes after the light is introduced and remain constant indefinitely, as long as the intensity of light being absorbed remains constant. Under these conditions, the rate of absorption of radiant heat is exactly offset by the rate at which heat is lost to the colder aluminum block. Different absorbing materials were used, india ink and colloidal silver, and since both gave the same calibration value, it is safe to assume that they are chemically inert.

The calorimeter–galvanometer deflections are straight line functions of the amount of energy being absorbed, at least in the range 600 to 5300 ergs per second. The averaged result shows that each cm. deflection, in the steady state, corresponds to an absorption of 84.4 ergs per second.

The calibration described here was made before and during the first eleven experiments reported in Table II. Calibration measurements were repeated from time to time and it was found that the sensitivity of the calorimeter decreased slowly with use. The de Khotinsky cement was apparently unable to keep constant the thermal contact between the thermocouples and cell. The last determinations were made nine months later and in these, 1 cm. deflection corresponds to the absorption of 96 ergs per second.

The calorimeter was tested with the inversion of cane sugar and a value in good agreement with accepted values was obtained.[3] This reaction is, of course, thermal and serves as an entirely independent check on the calibration.

Measurements on Photosynthesis.—The algae used were *Chlorella vulgaris* or *Chlorella pyrenoidosa* grown under standard conditions in Warburg nutrient solution. The Department of Botany coöperated in this work. The details of the growing conditions are given elsewhere.[2,4] The light treatment was about the same for all: namely, one week at a high light intensity and one week at a lower light intensity.

Preliminary measurements indicated that the algae use only a small fraction of the absorbed energy in photosynthesis, about 20%. These measurements were made on suspensions of algal cells (approximately 15,000,000 cells per cc.) in the Warburg nutrient solution and were complicated by the settling of the algae. The time required for the calorimeter system to reach equilibrium was so long that settling began to take place and it was impossible to obtain very accurate values of the thermal efficiency. The qualitative results, however, indicated that the low quantum yields were real.

It was found that the addition of less than 0.1% agar rendered the settling of the algae much slower. A gel was not formed. Agar was used in all of the reported work. Quantum yield measurements made with the dropping mercury electrode on these algae indicated that they behaved normally.[4]

Measurement of the steady-state deflections for the illuminated algae had to be delayed two hours for the calorimeter system to come to complete equilibrium. Enough carbon dioxide was present so that there was no danger of its exhaustion; accordingly the samples were usually illuminated while the equilibrium was being reached. In some experiments, the algae were left in the dark for the first hour and then illuminated the second hour. Photosynthesis steady-state values will be designated P.

In order to obtain the thermal efficiency of photosynthesizing algae, the rate of heat evolution due to respiration also must be known. The difference between the steady-state deflection during photosynthesis and the deflection caused by the respiration gives the net amount of absorbed radiation being dissipated as heat by the algae per unit time. The total absorption of energy is measured by means of the thermopile. The fraction of absorbed energy dissipated as heat is the ratio of these two quantities. A difficulty in determining the respiration value arises from the slowness of the calorimeter in reaching a steady-state value when illumination is started or discontinued. The algae, being in a closed cell, use up their oxygen and the respiration falls to a lower value before the proper deflection is reached. This difficulty was met by determining the rate of cooling immediately after the light is turned off.

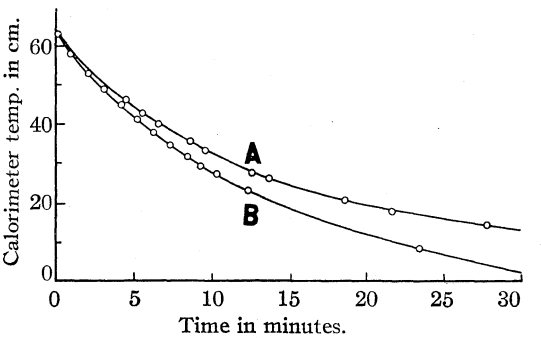


Fig. 2.—Cooling curves: A, with inert material; B, with respiring algae.

A cooling curve with inert material in the calorimeter is given at B in Fig. 2 and the cooling curve of algae after being illuminated is given at A. The slower rate of cooling of A is due to the heat added from respiration of the algae. Whereas curve B approaches zero deflection asymptotically, curve A approaches asymptotically a fixed deflection (temperature). This fixed deflection a is a measure of the respiration and is calculated from deflections shortly after turning off the light, since, at that time, the heat effect is not complicated by the settling of the algae nor the decreas-

(3) J. L. Magee and F. Daniels, forthcoming publication.

(4) H. G. Petering, B. M. Duggar and F. Daniels, *ibid.*, **61**, 3525 (1939).

TABLE II

FRACTION OF RADIATION CONVERTED INTO CHEMICAL ENERGY DURING PHOTOSYNTHESIS

1	2	3	4	5	6	7	8	9
Incident intensity, ergs/sec.	Total absorption, ergs/sec.	Absorption by algae, ergs/sec.	Photosynthesis defl. (P), cm.	Respiration defl. (a), cm.	Total heat evolved in calorimeter, ergs per sec., $(P - a) \times 85$ or $(P - a) \times 96$	Energy used in chem. reacn., ergs/sec. (2) − (6)	Energy efficiency (7)/(3) = f	Quantum yield $\Phi = 43f/112$
6740	5595	5109	63.5	10.0	4548	1047	0.205	0.079
3640	2291	2028	22.5	2.0	1743	548	.270	.104
3490	2539	2283	23.5	2.0	1981	558	.244	.094
1300	961	856	11.0	1.0	850	111	.130	.054
3830	2092	1805	24.2	4.0	1717	375	.208	.080
1450	816	707	12.5	4.0	723	93	.132	.051
8350	4857	4147	49.3	5.0	3766	1091	.263	.101
2640	1553	1354	17.8	3.5	1216	337	.249	.096
950	310	204	3.6	0.0	306	4	.019	.007
1890	948	801	9.3	.0	791	157	.196	.075
1830	1233	1099	10.8	.0	918	315	.287	.110
2825	1888	1514	15.4	.0	1478	410	.270	.104
2482	1653	1354	14.9	1.1	1325	328	.242	.094
2370	1606	1312	15.2	1.1	1354	252	.192	.075
2090	1494	1267	14.3	1.7	1210	284	.224	.086[a]
1420	1175	1047	12.0	1.3	1027	148	.141	.054
1240	1041	942	10.6	1.0	922	119	.126	.049

Average 0.077

[a] A determination on this sample with the dropping mercury electrode gave a quantum yield of 0.073.

ing rate of respiration caused by the gradual exhaustion of oxygen.

The calorimeter deflections, x, which are proportional to temperature differences, obey approximately the cooling law

$$\frac{-dx}{dt} = k(x - a)$$

or

$$\ln \frac{x - a}{x_0 - a} = -kt$$

where x_0 is the value of x when the time t is zero.

Then in the form

$$a = \frac{x - x_0 e^{-kt}}{1 - e^{-kt}}$$

it is easy to evaluate a from a few readings near the beginning of a cooling curve with algae. Constant k is evaluated from the slope of the straight line produced by plotting log x against t when the calorimeter is filled with an inert material, as in curve B.

In order to calculate the quantum yield from the thermal efficiency, an assumption regarding the chemical reaction must be made. It is generally believed that the photosynthesis reaction is

$$CO_2 + H_2O + Nh\nu \longrightarrow 1/6\ (C_6H_{12}O_2) + O_2 \qquad \Delta H = 112{,}000 \text{ cal.}$$

The energy of an einstein of the light used (approximately 6500 Å.) was roughly 43,000 cal. per mole. Thus, for the above reaction with 100% energy efficiency a maximum quantum yield of 43,000/112,000 = 0.38 is obtained. The observed energy efficiency multiplied by 0.38 gives the values listed as quantum yields.

The data are given in Table II for the seventeen experiments carried out in this way. The incident energy given in the first column is only slightly less than the incident energy per square cm. since the cell window is about 1 sq. cm.

An examination of the data of Table II shows that the conditions were varied over a considerable range, the incident light intensity ranging from 950 to 6700 ergs per second and the energy absorption by algae from 200 to 5100 ergs per second. The absorption of energy in the photocalorimeter is determined by the concentration of algae as well as by the intensity of incident light. The difference between the second and third columns is due partly to reflection and partly to a correction for energy absorbed in the imperfect face of the photocalorimeter. In some of the experiments the concentration of algae was so low that respiration was hardly detectable and the results cannot be considered accurate. In these experiments, there may have been a slight evaporation of moisture from the cell which balanced the heat

of respiration. Only the difference $P - a$ is important in determining the efficiency, however, and such errors cancel in the result.

In some cases the quantum efficiencies were determined also by the dropping mercury electrode,[4] using the same cultures of algae. The average quantum yield of the last six determinations is 0.077 by the calorimeter, and 0.063 by the dropping mercury electrode. In the third from the last, the two different measurements were made on samples of the same solution of algae at the same time. The agreement is within the experimental error.

Discussion

The average of the quantum yields obtained in Table II, namely, 0.08 molecule of carbon dioxide consumed per quantum absorbed, is in good agreement with other investigations in this Laboratory[2,4] and gives a much lower value than the generally accepted value of 0.25.[1]

The respiration corrections work in the direction to increase the efficiency and most of the uncertainty in the calculations of the quantum yield is connected with the measurements of this quantity. When the oxygen is partially depleted by respiration, the respiration is slower and subject to larger variations. Under these conditions, the rate of respiration may be affected by factors which do not matter when the oxygen supply is larger. After sufficient photosynthesis, there is, of course, an ample supply of oxygen, corresponding to saturation of oxygen.

The quantum yields apparently do not depend greatly upon the factors which change respiration rates.[5] The rate of respiration is not proportional to oxygen concentration or rate of photosynthesis, although at very low concentrations it tends to increase with both. The concentration of oxidizable intermediates is, of course, increased with increasing rate of photosynthesis, and so the general tendency is for respiration to increase with light intensity.

This work corroborates the low quantum yields in photosynthesis obtained in the Wisconsin laboratory and indicates that the algae are much less efficient than expected on the basis of Warburg's results. These efficiencies based on thermal measurements appear to run slightly higher than those based on measurements of oxygen. If such a difference should be definitely established, it might indicate the existence of intermediate steps involving less heat absorption than that which is involved in combining carbon dioxide and water to give oxygen and carbohydrate.

The authors wish to express their appreciation to Professor B. M. Duggar of the Department of Botany for advice; and to Dr. W. M. Manning, Dr. H. G. Petering, and Mr. W. E. Moore for advice and experimental assistance. The dropping mercury electrode measurements were made by Mr. Moore. They wish also to thank the Wisconsin Alumni Research Foundation for aid in carrying out this investigation.

Summary

1. A small calorimeter is described capable of measuring a rate of heat change as small as a millionth of a calorie per second. It is designed to admit light and thus give a measurement of heat changes accompanying photochemical reactions.

2. The thermal efficiency of photosynthesis by green algae has been measured. About four-fifths of the red light absorbed in living algae is converted into heat, leading to a quantum yield of about 0.08 molecule per quantum absorbed.

MADISON, WISCONSIN RECEIVED OCTOBER 13, 1939

(5) See Reference 4, Petering, Duggar and Daniels. This fact has been corroborated by the results of Mr. W. E. Moore, in more recent experiments.

[JOINT CONTRIBUTION FROM THE CHEMISTRY LABORATORIES OF CANISIUS COLLEGE AND OF THE UNIVERSITY OF MARYLAND]

The Critical Increment of Ionic Reactions. IV. The Influence of Dielectric Constant and Ionic Strength[1]

BY LOUIS RAMPINO[2] AND W. J. SVIRBELY

In this investigation the conversion of ammonium cyanate to urea has been carried out over a temperature range of 30 to 60° in isodielectric mixtures of water with isopropanol over a dielectric range of 63.5 to 20. The critical increments obtained from the corresponding rate constants are compared with those obtained from theoretical equations previously derived and used.[3] Comparison is also made with other existing kinetics theories.

TABLE I

SUMMARY OF DATA AT ZERO IONIC STRENGTH IN CONSTANT DIELECTRIC CONSTANT MEDIA

Temp. °C.	Wt. % *i*-PrOH	k_0 Eq. 1	k_0 Eq. 3	Wt. % *i*-PrOH	k_0 Eq. 1	k_0 Eq. 3
		At 63.5			At 60	
30	18.70	0.0105	0.0103	23.50	0.0125	0.0128
40	14.15	.0313	.0309	19.30	.0372	.0384
50	9.65	.0852	.0865	14.8	.114[a]	.108
60	4.98	.223	.228	10.50	.279	.285
log K_0 (eq. 3)		12.95			13.08	
E (eq. 3)		20,750			20,800	
E (eq. 9)		(20,750)			20,590	
		At 55			At 50	
30	30.65	0.0165	0.0168	37.75	0.0234	0.0234
40	26.58	.0502	.0505	33.90	.0709	.0702
50	22.60	.145[a]	.142	30.20	.210[a]	.197
60	18.30	.378	.376	26.16	.516	.518
log K_0 (eq. 3)		13.22			13.30	
E (eq. 3)		20,830			20,740	
E (eq. 9)		20,350			20,050	
		At 45			At 40	
30	44.85	0.0331	0.0332	51.90	0.0479	0.0493
40	41.25	.0975	.0994	48.65	.147	.148
50	37.80	.273[a]	.278	45.40	.397[a]	.414
60	34.17	.725	.731	42.10	1.094	1.091
log K_0 (eq. 3)		13.43			13.63	
E (eq. 3)		20,710			20,750	
E (eq. 9)		19,670			19,220	
		At 35			At 30	
30	59.05	0.0762	0.756	66.35	0.135	0.134
40	56.10	.233	.229	63.90	.408	.406
50	53.05	.642	.644	60.90	1.122	1.146
60	50.10	1.71	1.71	58.15	3.030	3.038
log K_0 (eq. 3)		13.91			14.16	
E (eq. 3)		20,880			20,880	
E (eq. 9)		18,620			17,830	
		At 25			At 20	
30	75.55	0.296	0.296	88.80	0.954	0.956
40	72.40	.856	.853	84.20	2.470	2.45
50	69.60	2.290	2.30	80.60	5.940	5.92
60	66.82	5.840	5.880	77.60	13.51	13.59
log K_0 (eq. 3)		13.89			12.75	
E (eq. 3)		20,030			17,780	
E (eq. 9)		16,730			15,070	

[a] k_0 value from work of Warner and Warrick, ref. 6.

TABLE II

SUMMARY OF DATA AT $\sqrt{\mu}$ = 0.194 IN CONSTANT DIELECTRIC CONSTANT MEDIA

Temp. °C.	k_1 Eq. 2	k_1 Eq. 3	k_1 Eq. 2	k_1 Eq. 3
	At 63.5		At 60	
30	0.00654	0.00646	0.00753	0.00769
40	.0198	.0198	.0229	.0235
50	.0548	.0563	.0712	.0672
60	.146	.151	.177	.180
log K (eq. 3)	13.00		13.09	
E (eq. 3)	21,100		21,120	
E (eq. 6 at 50°)	21,090		21,160	
	At 55		At 50	
30	0.00941	0.00974	0.0125	0.0126
40	.0293	.0299	.0388	.0387
50	.0861	.0857	.118	.111
60	.229	.231	.294	.297
log K (eq. 3)	13.25		13.32	
E (eq. 3)	21,200		21,140	
E (eq. 6 at 50°)	21,220		21,170	
	At 45		At 40	
30	0.0164	0.0164	0.0215	0.0219
40	.0496	.0503	.0683	.0676
50	.142	.144	.188	.195
60	.385	.385	.533	.525
log K (eq. 3)	13.42		13.66	
E (eq. 3)	21,120		21,280	
E (eq. 6 at 50°)	21,180		21,260	
	At 35		At 30	
30	0.0307	0.0309	0.0471	0.0468
40	.0967	.0958	.147	.145
50	.274	.277	.416	.421
60	.749	.749	1.157	1.145
log K (eq. 3)	13.86		14.09	
E (eq. 3)	21,350		21,420	
E (eq. 6 at 50°)	21,430		21,490	
	At 25		At 20	
30	0.0857	0.0852	0.215	0.214
40	.256	.253	.578	.572
50	.710	.705	1.445	1.442
60	1.867	1.845	3.395	3.437
log K (eq. 3)	13.76		12.72	
E (eq. 3)	20,600		18,600	
E (eq. 6 at 50°)	20,700		18,510	

Experimental and Discussion

The isopropanol[4] was refluxed over calcium oxide and anhydrous potassium carbonate for twenty hours and then fractionally distilled. The center portion was redistilled over a small amount

(1) Presented at the Baltimore meeting of the American Chemical Society, April, 1939.

(2) From the thesis presented to the Graduate Committee of Canisius College by Louis Rampino in partial fulfilment of the requirements for the degree of Master of Science, June, 1939.

(3) Lander and Svirbely, THIS JOURNAL, **60**, 1613 (1938), previous paper of the series.

(4) Grateful acknowledgment is made to the Union Carbide and Carbon Corp., N. Y. for providing the isopropanol used.

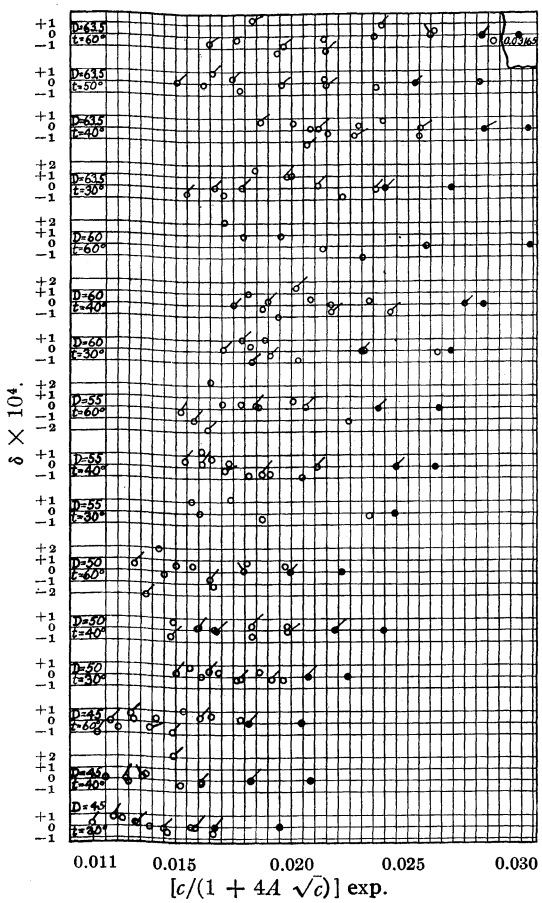


Fig. 1.—Isopropyl alcohol–water mixtures.

of sodium, the boiling point being 82° (uncorr.). All other materials were prepared or purified as described in previous papers,[3] which also describe the procedure used in this investigation. Temperatures were checked against a thermometer calibrated by the Bureau of Standards. Thermostat temperatures were maintained constant within ±0.01°. Dielectric constants for the isopropanol–water mixtures were taken from the work of Åkerlöf.[5]

Average values of the limiting velocity constant at $\mu = 0$ listed in Table I were obtained by means of the usual equation[3,6]

$$k_0 t = \left(\frac{1 + 4A\sqrt{C}}{C}\right) - \left(\frac{1 + 4A\sqrt{C^0}}{C^0}\right) \quad (1)$$

Derivations (δ) of the experimental value of $C/(1 + 4A\sqrt{C})$ from the value calculated from the average k_0 are plotted[3,6] against the experimental values of this function in Figs. 1 and 2. In Table II we give velocity constants (k_1) at $\sqrt{\mu} = 0.194$ obtained from k_0 by the relation[3,6]

$$k_1 = \frac{k_0}{1 + 2A\sqrt{\mu}} \quad (2)$$

If log k_0 is plotted against $1/T$ for the various isodielectric mixtures, then one may express the linear plots as well as those of log k_1 against $1/T$ by means of the general equation

$$\log k = \log K - (E/4.58T) \quad (3)$$

Values of log K_0 and E_0 and of log K_1 and E_1 obtained by means of equation (3) are listed in Tables I and II, respectively. Values of k_0 and k_1 calculated by equation (3) using the tabulated values of log K and E are also shown in the tables.

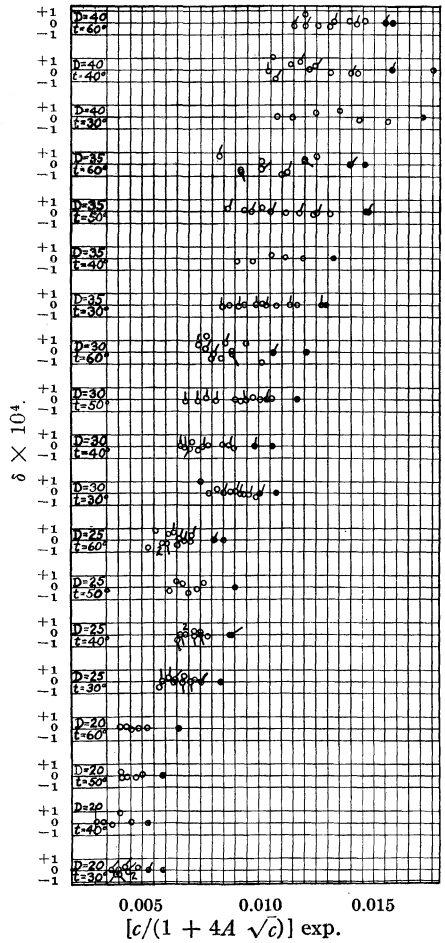


Fig. 2.—Isopropyl alcohol–water mixtures.

From the equation[3]

$$(E^0)\text{fixed comp.} = (E^{0*}_D) + 2.3RT^2\left(\frac{\partial \log k_0}{\partial D}\right)\frac{dD}{dT} \quad (4)$$

one obtains in this case using water as the solvent of fixed composition

$$(E^0)_{H_2O} - (E^{0*}_D) = 620T/D \quad (5)$$

At 50°, using equation (5), one calculates the difference between the two critical increments to be

(5) Åkerlöf, THIS JOURNAL, **54**, 4125 (1932).
(6) Warner and Warrick, *ibid.*, **57**, 1491 (1935).

2860 cal. Using the experimental values of the E_0's given in Table I and taking E_0 in water[3] to be 23,580 cal., one observes that the difference between the two critical increments varies between 2830 to 2700 cal. in the isodielectric mixtures from 63.5 to 30. The difference becomes larger at the dielectric values of 25 and 20. Thus E^{0*}_D apparently is independent of the dielectric constant over the major portion of the dielectric range covered.

One may calculate the critical increment at a fixed ionic strength by means of the equation[3]

$$E = E^0 + \frac{(12.5 \times 10^6 \sqrt{\mu} RT)}{(TD)^{3/2} + 8.36 \times 10^6 \sqrt{\mu}} \left(1 + \frac{\mathrm{d} \ln D}{\mathrm{d} \ln T}\right) \quad (6)$$

The values for E at $\sqrt{\mu} = 0.194$ have been obtained using equation (6) and are listed in Table II. These results are in good agreement with the E's obtained by equation (3).

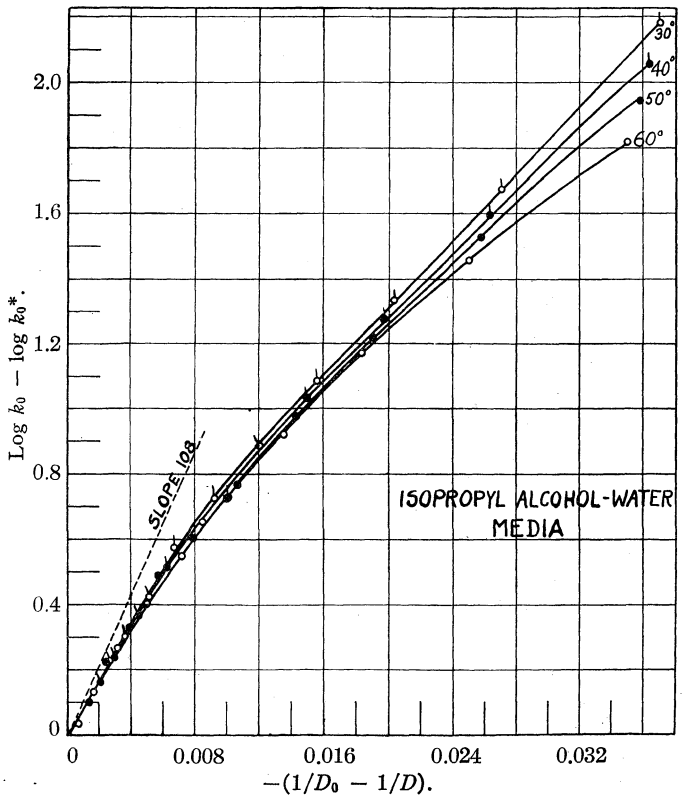


Fig. 3.

Deviations from the linearity predicted by Scatchard's[7] equation

$$\log k_0 - \log k_0^* = \frac{e^2 Z_A Z_B}{2.3KTr}\left(\frac{1}{D^0} - \frac{1}{D}\right) \quad (7)$$

are obtained when (log k_0 − log k_0*) are plotted against $(1/D^0 - 1/D)$. These plots are shown in Fig. 3 at the various temperatures. The limiting slopes of the curves are in fair agreement with the predicted values assuming $r = 2 \times 10^{-8}$ cm.

As pointed out before, an empirical relation can be obtained between the dielectric effect and the temperature effect on the value of the limiting velocity constant, namely

$$\left(\frac{\Delta k_0}{\Delta D}\right)_T = -C\left(\frac{\Delta k_0}{\Delta T}\right)_D \quad (8)$$

Using the values in Table I, one observes that C has an average value[8] of 0.52 from $D = 60$ to $D = 40$. On going to lower dielectrics C increases reaching an average value of 2.80 at $D = 20$.

Referring to the values of log K_0 and log K in Tables I and II, it is observed that for any isodielectric mixture the two values are fairly constant. However, as one goes to lower dielectrics (D = 63.5 to $D = 30$) a continual increase is obtained. This behavior of log K_0 is similar to that observed in the isodielectric glycol–water mixtures[3] and also in isodielectric dioxane–water mixtures (forthcoming paper). La Mer's[9] treatment for reactions predicts constancy[10] for the log K's (B in his notation).

Taking into account the various factors which should influence the critical increment, La Mer[9] developed an equation which in isodielectric media and at zero ionic strength becomes

$$(\Delta E^{0*}_D)_{\sqrt{\mu}=0} = \Delta E_0 + \frac{Z_A Z_B N e^2}{D}\left(\frac{1}{r_A + r_B}\right) \quad (9)$$

where (ΔE^{0*}_D) is the critical increment in isodielectric media, ΔE_0^* refers to the energy contribution for the reactants as uncharged molecules and the other terms have the usual meanings. Using the experimental values of ΔE^{0*}_D at $D = 63.5$ one calculates ΔE_0^* to be 23,360 cal. Values of ΔE^{0*}_D calculated from this value of ΔE_0^* by means of equation (9) assuming $(r_A + r_B) = 2 \times 10^{-8}$ cm. are given in Table I. The agreement at the higher dielectric constants is as good as should be expected considering the limitations imposed

(7) Scatchard, *Chem. Rev.*, **10**, 229 (1932).

(8) We wish to point out an error in the paper using glycol–water mixtures, Ref. 3, where C should be 0.55.

(9) Amis and La Mer, THIS JOURNAL, **61**, 905 (1939).

(10) It should be pointed out that this constancy is obeyed for this reaction in isodielectric methanol media.

on equation (9), especially due to the assumption of a constant value for $r_A + r_B$.[11]

In testing the collision theory in terms of the thermodynamic theory as developed by La Mer[9] the following equation is obtained when the P factor is assumed = 1

$$\frac{RT}{Nh} e^{\Delta S^*/R} = \frac{N}{1000} \sigma_{12}^2 \left[8\pi RT \left(\frac{1}{M_1} + \frac{1}{M_2}\right)\right]^{1/2} \quad (10)$$

where N = Avogadro's number, h = Planck's constant, M_1 and M_2 are the molecular weights of the reactants and σ_{12} is the distance of the approach between centers of reactants for an effective collision. Substituting in the various values at $t = 60°$ using $M_1 = 18$, $M_2 = 42$, and clearing one obtains

$$\log \sigma_{12} = {}^1/_2(\Delta S^*/2.3R) - 6.7125 \quad (11)$$

which in turn[9] leads to

$$\log \sigma_{12} = {}^1/_2 (\log K_0 - \log (RT/hN)) - 6.7125 \quad (12)$$

Since $\log RT/hN = 14.1520$ (min.$^{-1}$) at 60° then equation (12) becomes

$$\log \sigma_{12} = \frac{\log K_0}{2} - 13.791 \quad (13)$$

Using the values of $\log K_0$ given in Table I, σ_{12} can be determined in the various isodielectric media by means of equation (13). This method gives $\sigma_{12} = 4.83$ Å. at $D = 63.5$, and then σ_{12} increases to a maximum value of 19.4 Å. at $D = 30$. Thus at the higher dielectrics the collision theory is in satisfactory agreement with the thermodynamic treatment although at the lower dielectrics the agreement is less satisfactory.

Finally as to the behavior of this reaction in $D = 25$ and $D = 20$ media as evidenced by the very marked drop in ΔE and in $\log K_0$, we can offer no definite answer. Undoubtedly association plays some part as the dielectric constant is decreased and probably the mechanism of the reaction itself changes. Due to this uncertainty concerning the mechanism and the inadequacy of equations (1) and (2) in the solvents of lower dielectric constant, we are presenting the actual time–concentration data in Table III on typical experiments at 40° in solvents of dielectric constants 30, 25 and 20, along with the second order constants calculated for a mean ionic strength at various concentration ranges by the graphical method.[6]

TABLE III

RATE OF CONVERSION OF AMMONIUM CYANATE INTO UREA AT 40°

D	t, min.	C, moles/liter	Range of concn.	$\sqrt{\mu}$	Bimolecular k, (graphical)
30	0	0.05686			
	43	.04264	0.050–0.045	0.218	0.130
	60	.03885	.045– .040	.206	.147
	84	.03412	.040– .035	.194	.156
	101	.03100	.035– .030	.180	.169
	115	.02949			
25	0	.06032	.06 – .05	.2343	.220
	16	.04938	.050– .045	.218	.229
	24	.04557			
	29	.04315	.045– .040	.206	.252
	37	.03962			
	45	.03622	.040– .035	.194	.295
20	0	.04035	.040– .035	.194	.526
	12	.03144	.035– .030	.180	.618
	21	.02571	.030– .025	.166	.661
	32	.02203	.025– .020	.150	.703
	44	.01863			
	54	.01625			

(11) In glycol–water media the agreement between ΔE^*_D calculated and ΔE^*_D by experiment is comparable to that found in this investigation. It is rather surprising that considerably better agreement is found in methanol–water media.

Finally as to the behavior of this reaction in $D = 25$ and $D = 20$ media as evidenced by the very marked drop in ΔE and in $\log K_0$, we can offer no definite answer. Undoubtedly association plays some part as the dielectric constant is decreased and probably the mechanism of the reaction itself changes. Due to this uncertainty concerning the mechanism and the inadequacy of equations (1) and (2) in the solvents of lower dielectric constant, we are presenting the actual time–concentration data in Table III on typical experiments at 40° in solvents of dielectric constants 30, 25 and 20, along with the second order constants calculated for a mean ionic strength at various concentration ranges by the graphical method.[6]

Summary

1. The rate of conversion of ammonium cyanate to urea has been studied over the temperature range 30 to 60° in isodielectric mixtures of isopropanol with water over the dielectric range of 63.5 to 20.

2. The influence of ionic strength upon the observed critical increments at zero ionic strength is in good agreement with equations previously derived. It is observed that the critical increment is apparently independent of the dielectric constant in isodielectric mixtures over the major portion of the range investigated.

3. From $D = 63.5$ to $D = 40$, the following empirical relation holds

$$\left(\frac{\Delta k_0}{\Delta D}\right)_T = -0.52 \left(\frac{\Delta k_0}{\Delta T}\right)_D$$

4. At the higher dielectric constants, the influence of the dielectric constant of the solvent upon the rate constants is in as good agreement with the Scatchard–Christiansen theory as can reasonably be expected.

5. The value of the collision factor Z in the Arrhenius theory varies with dielectric constant.

6. Comparisons are made between the observed critical increments and those calculated by the thermodynamic treatment of La Mer.

7. The collision theory is shown to be in satisfactory agreement with the thermodynamic treatment at the higher dielectrics used.

BUFFALO, N. Y.
COLLEGE PARK, MARYLAND RECEIVED AUGUST 4, 1939

[JOINT CONTRIBUTION FROM THE CHEMISTRY LABORATORIES OF THE UNIVERSITY OF MARYLAND AND OF CANISIUS COLLEGE]

The Critical Increment of Ionic Reactions. V. The Influence of Dielectric Constant and Ionic Strength[1]

BY W. J. SVIRBELY AND JAMES LANDER

The investigation of the conversion of ammonium cyanate to urea in isodielectric mixtures of various solvent–water media has been continued in this research using isodielectric mixtures of dioxane–water. The reaction has been studied over a temperature range of 30 to 60° in isodielectric media having a dielectric constant range of 63.5 to 5. The critical increments obtained from the experimental data are compared with those calculated from theoretical equations previously given.[2] Comparison is also made with other existing solution kinetics theories.

Experimental and Discussion

The dioxane was refluxed over calcium oxide and over sodium for about twenty-four hours. It was then distilled twice, the middle portions of each run being collected. The final fraction had a freezing point of 11.72°. The preparation of other materials, purification, experimental procedure, etc., have already been described.[2] Dielectric constants for the dioxane–water media were taken from the work of Åkerlöf and Short.[3] In the preceding paper[2] of this series, these equations were given

$$k_0 t = \left(\frac{1 + 4A\sqrt{C}}{C}\right) - \left(\frac{1 + 4A\sqrt{C^0}}{C^0}\right) \quad (1)$$

$$k_1 = \frac{k_0}{1 + 2A\sqrt{\mu}} \quad (2)$$

$$\log k = \log K - \frac{E}{4.58T} \quad (3)$$

$$(E^0)_{\text{fixed comp.}} = (E^{0*}_D) + \frac{2.3RT^2}{} \left(\frac{\partial \log k_0}{\partial D}\right) \frac{dD}{dT} \quad (4)$$

$$E = E^0 + \frac{12.5 \times 10^6 \sqrt{\mu}\, RT}{(TD)^{3/2} + 8.36 \times 10^6 \sqrt{\mu}} \left(1 + \frac{\text{d ln } D}{\text{d ln } T}\right) \quad (5)$$

From equation (4) one obtains in dioxane–water media with water as the solvent of fixed composition the relation

$$(E^0)_{H_2O} - (E^{0*}_D) = 587T/D \quad (6)$$

Equation (6) leads to a difference of 2720 cal. between the two critical increments at 50°. The experimental differences using 23,580 cal.[2] for $(E^0)_{H_2O}$ and using the values of the E^{0*}_D's given in Table I vary from 3570 cal. at $D = 63.5$ to 4810 cal. at $D = 20$ and then they decrease again.

TABLE I

SUMMARY OF DATA AT ZERO IONIC STRENGTH IN CONSTANT DIELECTRIC CONSTANT MEDIA

Temp. °C.	Wt. % Diox.	k_0 Eq. 1	k_0 Eq. 3	Wt. % Diox.	k_0 Eq. 1	k_0 Eq. 3
		At 63.5			At 60	
30	15.0	0.0111	0.0113	19.0	0.0140	0.0138
40	11.50	.0327	.0327	15.65	.0393	.0400
50	7.70	.0896	.0884	12.05	.1075	.108
60	3.85	.223	.225	8.30	.266	.274
log K_0 (eq. 3)		12.46			12.54	
E (eq. 3)		20,010			20,000	
E (eq. 9)		(20,010)			19,850	
		At 55			At 50	
30	24.8	0.0181	0.0187	30.5	0.0262	0.0259
40	21.65	.0524	.0537	27.65	.0734	.0737
50	18.06	.140	.144	24.26	.196	.196
60	14.75	.370	.367	21.20	.488	.492
log K_0 (eq. 3)		12.64			12.61	
E (eq. 3)		19,960			19,720	
E (eq. 9)		19,610			19,310	
		At 45			At 40	
30	36.2	0.0381	0.0378	42.0	0.0567	0.0561
40	33.75	.1071	.107	39.70	.160	.156
50	30.55	.279	.282	36.8	.421	.407
60	27.60	.708	.704	34.0	.997	1.002
log K_0 (eq. 3)		12.68			12.65	
E (eq. 3)		19,590			19,310	
E (eq. 9)		18,930			18,480	
		At 35			At 30	
30	47.8	0.0769	0.0771	53.80	0.163	0.160
40	45.75	.224	.215	51.80	.438	.440
50	42.95	.555	.561	49.50	1.145	1.14
60	40.45	1.490	1.38	47.25	2.79	2.77
log K_0 (eq. 3)		12.81			12.94	
E (eq. 3)		19,340			19,080	
E (eq. 9)		17,880			17,090	
		At 25			At 20	
30	59.80	0.324	0.323	66.10	0.671	0.673
40	58.30	.874	.874	64.90	1.83	1.82
50	56.30	2.19	2.22	63.30	4.57	4.61
60	54.50	5.38	5.35	61.60	11.00	11.08
log K_0 (eq. 3)		13.05			13.34	
E (eq. 3)		18,810			18,770	
E (eq. 9)		15,990				
		At 15			At 10	
30	72.75	1.62	1.61	80.70	5.26	5.25
40	71.80	4.47	4.48	79.90	14.5	14.70
50	70.5	11.30	11.30	79.10	38.50	38.50
log K_0 (eq. 3)		13.85			14.70	
E (eq. 3)		18,940			19,420	
		At 5				
30	91.20	37.2	37.0			
35	90.95	62.4	63.3			
40	90.70	106.0	106.7			
log K_0 (eq. 3)		15.98				
E (eq. 3)		20,000				

(1) Presented at the Baltimore meeting of the A. C. S. April, 1939.

(2) Rampino and Svirbely, THIS JOURNAL, **61**, 3534 (1939), was the previous paper of the series.

(3) Åkerlöf and Short, *ibid.*, **58**, 1241 (1936).

Reference to Table I shows that E^{0*}_D is apparently constant over part of the higher dielectic range, then it decreases until a minimum value around $D = 20$ is reached and after that a rapid increase occurs. We shall show later that even if we use a more extended equation for calculating the k_0's and consequently should get more reliable E_0's at the lower dielectrics, nevertheless the minimum still exists.

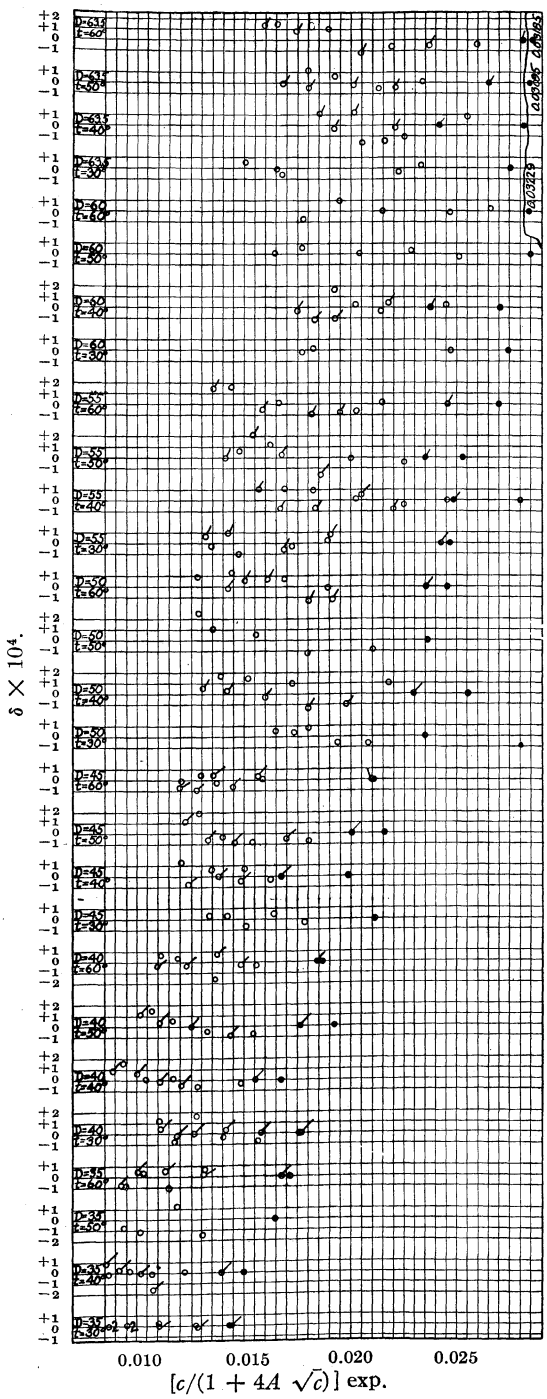


Fig. 1.—Dioxane–water mixtures.

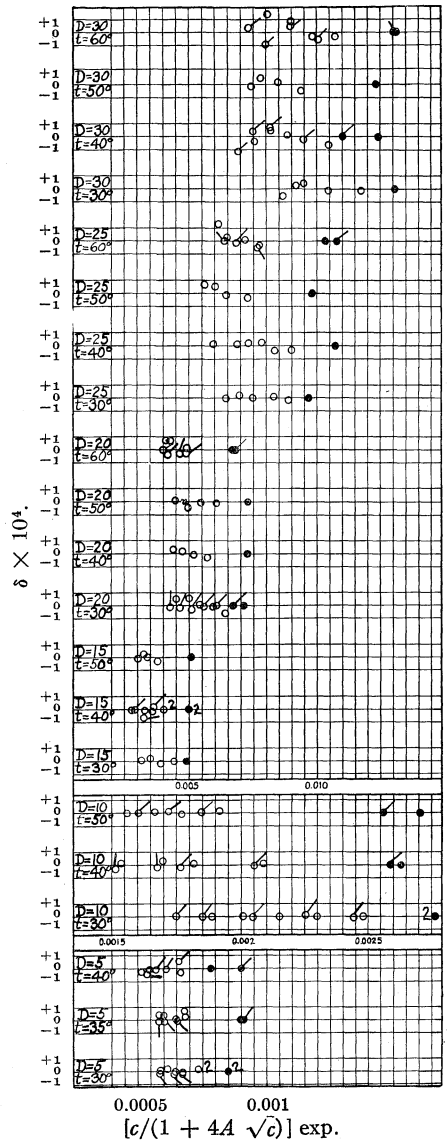


Fig. 2.—Dioxane–water mixtures.

Using equation 5, the values of E at $\sqrt{\mu} = 0.194$ have been calculated and collected in Table II. These results are in good agreement with the experimental E's.

Similarly to the results in the other solvent–water mixtures, we find in this case deviations from the linearity predicted by Scatchard's equation[4]

$$\log k_0 - \log k_0^* = \frac{e^2 Z_A Z_B}{2.3KTr}\left(\frac{1}{D^0} - \frac{1}{D}\right) \qquad (7)$$

when $(\log k_0 - \log k_0^*)$ is plotted against $(1/D^0 - 1/D)$. These plots are shown in Fig. 3 at the

(4) Scatchard, *Chem. Rev.*, **10**, 229 (1932).

TABLE II

SUMMARY OF DATA AT $\sqrt{\mu} = 0.194$ FOR CONSTANT DIELECTRIC CONSTANT MEDIA

Temp. °C.	k_1 Eq. 2	k_1 Eq. 3	k_1 Eq. 2	k_1 Eq. 3	k_1 Eq. 2	k_1 Eq. 3
	At 63.5		At 60		At 55	
30	0.00691	0.00699	0.00843	0.00827	0.01032	0.0106
40	.0207	.0206	.0241	.0243	.0305	.0311
50	.0577	.0567	.0672	.0667	.0831	.0853
60	.146	.147	.169	.172	.224	.220
log K (eq. 3)	12.53		12.56		12.64	
E (eq. 3)	20,400		20,340		20,300	
E (eq. 5 at 50°)	20,350		20,410		20,350	
	At 50		At 45		At 40	
30	0.0140	0.0140	0.0189	0.0187	0.0255	0.0258
40	.0402	.0405	.0544	.0540	.0743	.0737
50	.110	.109	.145	.146	.200	.197
60	.278	.279	.376	.371	.486	.498
log K (eq. 3)	12.58		12.67		12.68	
E (eq. 3)	20,050		20,000		19,820	
E (eq. 5 at 50°)	20,150		20,050		19,820	
	At 35		At 30		At 25	
30	0.0310	0.0318	0.0568	0.0568	0.0938	0.0938
40	.0929	.0907	.158	.161	.262	.263
50	.236	.242	.424	.426	.678	.694
60	.612	.612	1.064	1.067	1.720	1.720
log K (eq. 3)	12.77		12.90		13.01	
E (eq. 3)	19,820		19,650		19,500	
E (eq. 5 at 50°)	19,890		19,690		19,480	
	At 20		At 15		At 10	
30	0.151	0.152	0.258	0.263	0.494	0.491
40	.428	.427	.744	.745	1.417	1.43
50	1.111	1.113	1.954	1.980	3.93	3.91
60	2.77	2.80				
log K (eq. 3)	13.22		13.58		14.24	
E (eq. 3)	19,500		19,670		20,210	
E (eq. 5 at 50°)	19,500		19,740		20,290	
			At 5			
30			1.31	1.30		
40			3.92	3.94		
log K (eq. 3)			15.21			
E (eq. 3)			20,970			
E (eq. 5 at 50°)			20,950			

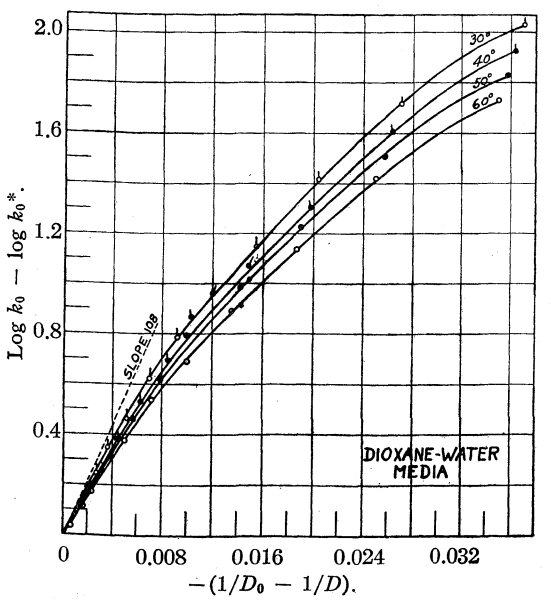


Fig. 3.

various temperatures. The limiting slopes of the curves are in good agreement with the predicted values assuming $r = 2 \times 10^{-8}$ cm. In Fig. 3 we have not shown all of the data obtained. The complete curves tend to flatten out although the slopes are still finite.

The effect of dielectric change and of temperature change on the limiting velocity constant can be expressed by the empirical relation[2]

$$\left(\frac{\Delta k_0}{\Delta D}\right)_T = -C\left(\frac{\Delta k_0}{\Delta T}\right)_D \qquad (8)$$

Using the values of k_0 listed in Table I, it can be shown that C has an average value of 0.61 from $D = 60$ to $D = 35$. On going to lower dielectrics the value of C increases, reaching a value of 14 at $D = 5$.

La Mer's[5] thermodynamic treatment of reactions predicts constancy for the log K's shown in Tables I and II. It is observed that the agreement between the log K's in the two tables in the same isodielectric mixture down to $D = 25$ is good. There is however a tendency toward increased values of the log K's as the dielectric constant is decreased. The increase is not as large however as in the isopropanol–water mixtures.[2]

In calculating critical increments La Mer[5] developed an equation which in isodielectric media and at zero ionic strength becomes

$$(\Delta E^{0*}_D)_{\sqrt{\mu}=0} = \Delta E_0{}^* + \frac{Z_A Z_B N e^2}{D}\left(\frac{1}{r_A + r_B}\right) \qquad (9)$$

$\Delta E_0{}^*$, the energy contribution for the reactants as uncharged molecules can be calculated from the value of (ΔE^{0*}_D) at $D = 63.5$ and is 22,620 cal. Using this value of $\Delta E_0{}^*$, values of ΔE^{0*}_D have been determined by means of equation (9) assuming $(r_A + r_B) = 2 \times 10^{-8}$ cm. and are given in Table I. Here again, as in the previous investigation, the agreement between ΔE^*_D calculated and ΔE^*_D by experiment is as good at the higher dielectric constants as could reasonably be expected.

Using La Mer's method[5] for testing the collision theory in terms of the thermodynamic theory, one can calculate σ_{12}, the distance of nearest approach between the centers of the reactants for an effective collision, by means of the equation[2]

$$\log \sigma_{12} = \log K_0/2 - 13.791 \qquad (10)$$

Using the values of log K_0 in Table I, one obtains $\sigma_{12} = 2.75$ Å. at $D = 63.5$. The values then increase to $\sigma_{12} = 5.42$ Å. at $D = 25$. It is interest-

(5) Amis and La Mer, THIS JOURNAL, **61**, 905 (1939).

ing to observe that using equation (10) at the higher dielectrics where it should hold best one obtains a variety of σ_{12} values for the reactants in the various solvent–water mixtures in which this reaction has been studied. For example, at D = 63.5, σ_{12} equals 1.24 Å., 3.54 Å., 4.83 Å., 2.75 Å. in methanol, glycol, isopropanol and dioxane mixtures, respectively. It is possible that specific solvent influences may be responsible for these variations.

One may compare the percentages by weight of the non-aqueous solvents in the solvent–water mixtures just mentioned at each temperature and at each dielectric value with the values of the limiting velocity constant obtained in order to observe whether the variation in the k_0's seems to depend on the amount of non-aqueous solvent added. No correlation is observed. Plots of log k_0 *versus* $1/D$ are shown in Fig. 4. It is seen that the dioxane, isopropanol, and glycol curves are fairly close to each other at each temperature although the order of the curves is not the same at all of the temperatures. However, placing each solvent in the order of increasing percentage of non-aqueous solvent, we have dioxane, isopropanol, methanol and glycol, respectively.

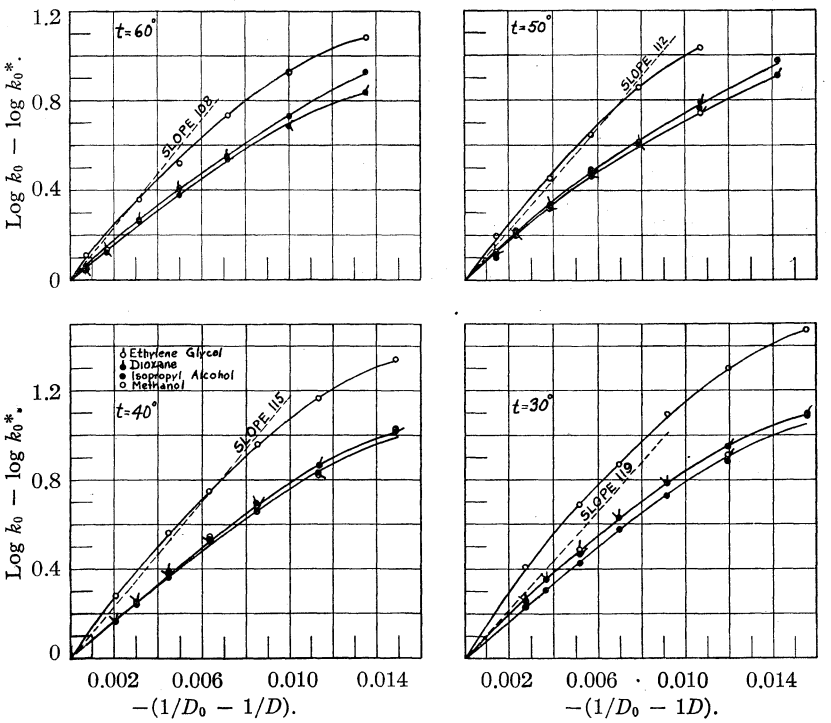


Fig. 4.

It was considered worth while to develop a more accurate method of calculating the limiting velocity constant and observe whether or not the new results would influence the conclusions previously drawn. Starting with the equation[4]

$$\ln k = \ln k_0 + \frac{2.3e^2Z_AZ_B\kappa}{DKT\ (1 + \kappa b)} \qquad (11)$$

substituting in the various terms and using the well-known relation

$$k = k_0 \frac{\gamma_A\gamma_B}{\gamma_x} \qquad (12)$$

one obtains

$$\frac{\gamma_A\gamma_B}{\gamma_x} = e - a\sqrt{\mu}/(b + d\sqrt{\mu}) \qquad (13)$$

where

$$a = 8.35 \times 10^6$$
$$b = (DT)^{3/2}$$
$$d = 100\ DT$$

Following Scatchard's[6] method equation (13) becomes

$$\frac{\gamma_A\gamma_B}{\gamma_x} = \frac{b + d\sqrt{\mu}}{b + d\sqrt{\mu} + a\sqrt{\mu}} \qquad (14)$$

Applying Scatchard's[6] treatment of the rate of reaction in a changing environment, the Brönsted rate equation on using equation 14 becomes

$$\frac{dx}{dt} = \frac{k_0C_0(1 - x)^2\ (b + d\sqrt{C_0}\sqrt{1 - x})}{b + (a + d)\sqrt{C_0}\sqrt{1 - x}} \qquad (15)$$

where $x = (C_0 - C)/C_0$. Clearing and integrating by parts equation (15) becomes

$$\left(\frac{2A\sqrt{C_0}}{b} + 1\right)\left(\frac{1}{C} - \frac{1}{C_0}\right) + \frac{2ad}{b^2}\ln\frac{\sqrt{C}\ (b + d\sqrt{C_0})}{\sqrt{C_0}\ (b + d\sqrt{C})} = k_0t \qquad (16)$$

Using equation (16) values of k_0 were calculated for some of the isodielectric media and are given in Table III. Comparison of the values of k_0 in Tables I and III shows that with equation (16) one obtains higher values of k_0 than with equation (1). However, the values of ΔE are not affected down to D = 25. The increase in log K_0

(6) Scatchard, THIS JOURNAL, **52**, 52 (1930).

TABLE III

k_0 VALUES USING EQ. 16 IN ISODIELECTRIC MEDIA

Temp., °C.	63.5	60	55	25	5
30	0.0167	0.0211	0.0283	0.58	71
40	.0470	.0574	.0813	1.63	221
50	.131	.158	.211	4.14	
60	.330	.401	.561	10.1	
E (eq. 3)	20,000	19,950	19,950	18,750	21,700
log K_0 (eq. 3)	12.63	12.67	12.82	13.29	17.47

is still obtained. The minimum in ΔE is emphasized more than before due to the large increase in ΔE at $D = 5$. This increase may only be an apparent one due to the method of calculation and it may be necessary for an entirely new treatment in low dielectrics to allow for association effects.

TABLE IV

RATE OF CONVERSION OF AMMONIUM CYANATE INTO UREA AT 40°

D	t, min.	C, moles/liter	Range of concn.	$\sqrt{\mu}$	Bimolecular, k (graphical)
25	0	0.08648	0.07 –0.06	0.255	0.218
	20	.06348	.06 – .05	.2343	.225
	30	.05550			
	40	.04971	.05 – .045	.218	.227
	50	.04434	.045– .04	.206	.247
	60	.03994	.04 – .035	.194	.255
	87	.03102	.035– .030	.180	.269
20	0	.07294	.07 – .06	.255	.335
			.06 – .05	.2343	.370
	20	.04740	.05 – .045	.218	.383
	30	.03995	.045– .04	.206	.402
	40	.03426	.04 – .035	.194	.425
	50	.02992	.035– .030	.180	.434
15	0	.07170	.07 – .06	.255	.627
			.06 – .05	.2343	.640
	10	.04966	.05 – .045	.218	.660
	16	.04093	.045– .04	.206	.692
	21	.03570	.04 – .035	.194	.700
	34	.02587	.035– .030	.180	.768
10	0	.06782	.06 – .05	.2343	1.15
			.05 – .045	.218	1.28
	7	.04356	.045– .04	.206	1.32
	12	.03333	.04 – .035	.194	1.43
	15	.02937	.035– .030	.180	1.53
	19	.02436	.030– .025	.166	1.59
5	0	.06003	.06 – .05	.2343	2.77
			.05 – .045	.218	3.03
			.045– .04	.206	3.65
			.04 – .035	.194	4.02
	4	.03263	.035– .030	.180	4.62
	5	.02794			
	6	.02467	.030– .025	.166	5.04
	7	.02210			

In solvents of $D \geqq 25$, calculations by equation (1) and by (16) lead to essentially the same values for E and log K_0 and we therefore could see no advantage in recalculating all of our results by the use of equation (16). Equation (16) apparently represents only a slight improvement over equation (1) and neither equation is adequate for calculating true k_0 values in the solvents of lower dielectric constant. We, therefore, are giving the actual time–concentration data for typical experiments at 40° in solvents of dielectric constants 25, 20, 15, 10 and 5 in Table IV. The ordinary bimolecular constants over finite ranges of concentration are also given in the table.

Summary

1. The rate of conversion of ammonium cyanate to urea has been studied over the temperature range 30 to 60° in isodielectric mixtures of dioxane with water over a dielectric range 63.5 to 5.

2. The influence of ionic strength upon the observed critical increments at zero ionic strength is in good agreement with the theory. It is observed that the critical increment first decreases somewhat with the dielectric constant and then increases, with a minimum appearing at about $D = 20$.

3. From $D = 63.5$ to $D = 35$, the following empirical relation holds

$$\left(\frac{\Delta k_0}{\Delta D}\right)_T = -0.61 \left(\frac{\Delta k_0}{\Delta T}\right)_D$$

4. The influence of the dielectric constant upon the rate constants is in reasonably good agreement with the Scatchard–Christiansen theory at the higher dielectric constants.

5. The value of the collision factor Z varies somewhat with the dielectric constant, especially at the lower dielectric constants.

6. The collision theory is shown to be in satisfactory agreement with the thermodynamic treatment in the higher isodielectric mixtures.

7. The new method of calculating the limiting velocity constants leads to higher values but does not influence the conclusions previously drawn.

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[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY OF STANFORD UNIVERSITY AND SAN JOSE STATE COLLEGE]

Thermal Data on Organic Compounds. XIX. Modern Combustion Data for Some Non-volatile Compounds Containing Carbon, Hydrogen and Oxygen

BY J. WILFRED RICHARDSON AND GEORGE S. PARKS

The heat of combustion of an organic compound constitutes a very important quantity in the calculation of the free energy of formation of the compound by means of the third law of thermodynamics and the fundamental equation $\Delta F = \Delta H - T\Delta S$. Unfortunately, until very recently it has often been the most serious source of error in the resulting free energy value because most of the available combustion data were determined prior to 1900 when calorimetric methods and the purification of substances had not reached so high a standard as at present. For this reason there is now a very urgent need for new combustion data on organic compounds, and accordingly an extensive program of such thermochemical studies has been undertaken at Stanford University.

In this paper we shall summarize the data obtained in an investigation of the heats of combustion of β-methylnaphthalene, phthalic anhydride, phthalic acid, anthracene, phenanthrene, stilbene, pyrene, *n*-hexadecane, cetyl alcohol, 1,3,5-triphenylbenzene, and a sample of polyisobutylene.

Method and Apparatus

The bomb calorimeter was chosen as the type to be used in this investigation because it is best suited for work with solids or liquids of low volatility. After considerable preliminary experimentation our calorimetric apparatus was finally patterned very closely after that described by Huffman and Ellis[1] and our entire procedure became essentially the same as theirs. For this reason we shall forego here any detailed description of our calorimetry and merely present the important characteristics of the apparatus and one or two minor differences from the methods of Huffman.

Our "Parr bomb" had a capacity of 390 ml. Platinum wire was employed as the ignition medium to avoid the somewhat uncertain correction due to oxidation of the iron wire, which is so often used; and the electrical energy introduced in the ignition process was determined accurately by measurements of time, current, and voltage. A small piece of cotton string (instead of the filter paper in Huffman's procedure) was ignited by the platinum wire and this in turn ignited the sample of material under study, which had been placed in a platinum crucible. The heat of combustion of the string was found to be 4169 (±2) cal. per gram, weighed in air. Before each combustion 1 ml. of water was placed in the bomb, which was then filled with pure commercial oxygen to a pressure of 30 atm. at 22°.

In many of the experiments the air initially in the bomb was washed out by filling the bomb at least twice with oxygen to a pressure of 5 atm. and then allowing it to escape until the pressure was reduced to 1 atm. However, there was always present a small quantity of nitrogen within the bomb and the consequent nitric acid produced in the combustion process was titrated with $N/14.55$ sodium carbonate solution. The magnitude of the thermal correction for this nitric acid, calculated on the basis of an evolution of 14,550 cal. per mole of aqueous nitric acid formed, was about 10 calories if the air was not previously washed out and about 1 calorie if it was washed out.

Water for the calorimeter, ordinarily 2780 g., was weighed to 0.05 g. on a high capacity balance. The mass of the material to be burned was determined to 0.00001 g. on a Kuhlmann microchemical balance.

The temperature rise in the calorimeter was measured by a platinum resistance thermometer calibrated by the Bureau of Standards, a Mueller thermometer bridge, a high sensitivity galvanometer, and a lamp-and-scale reading device, all supplied by the Leeds and Northrup Co. The sensitivity of the system was such that a change of 0.00001 ohm (0.0001°) in the resistance of the thermometer caused the reflection from the galvanometer mirror to shift 2 mm. on the scale. The galvanometer was used as a null point instrument in conjunction with a chronograph precise to 0.1 second.

The corrected temperature rise was calculated by the method described by Dickinson.[2] From this temperature rise and the sum of the energies supplied the energy equivalent of the system at 25° was calculated in the calibration experiments; and conversely with the aid of this last quantity the various combustion results were subsequently derived.

Units.—The unit of energy throughout this paper is the defined conventional calorie which has been derived from the international joule by multiplying by the factor 1.0004/4.185. The unit of mass is the gram true mass which is derived from the weight in air against brass weights by use of a suitable correction factor for buoyancy. In cases where the density of the material in question was not available in the literature, we have made rough estimates from the mass and volume of the pelleted substances. The molecular weights used are based on the 1939 table of atomic weights.[3]

Calibration of the Calorimeter.—Benzoic acid (sample 39e) supplied by the United States Bureau of Standards was burned in the bomb, under approximately the standard calorimetric conditions of Washburn,[4] to determine the energy equivalent of the calorimeter at 25°. For this sample Jessup and Green[5] have obtained a combustion

(1) Huffman and Ellis, THIS JOURNAL, **57**, 41 (1935).

(2) Dickinson, *Bull. Bureau of Standards*, **11**, 189 (1914).

(3) Baxter, Guichard, Hönigschmid and Whytlaw-Gray, THIS JOURNAL, **61**, 223 (1939).

(4) Washburn, *Bur. Standards J. Research*, **10**, 525 (1933).

(5) Jessup and Green, *J. Research Nat. Bur. Standards*, **13**, 469 (1934).

value of 26,419 international joules (equal to 6315.3 cal.) per gram under these standard conditions.

TABLE I

CALIBRATIONS WITH OXYGEN CYLINDER 2

$\Delta\theta$, corr. rise °C.	True mass, benzoic acid, g.	Cal. from b. a.	Cal. from HNO_3	Cal. from string $+ EIt$	Energy equiv., cal. per °C.	Dev. from mean, %
1.7932	0.90756	5731.4	9.3	17.4	3211.0	−0.009
1.7959	.90871	5738.6	9.8	19.9	3211.9	+ .019
1.7835	.90301	5702.7	9.9	15.1	3211.5	+ .006
1.7916	.90662	5725.5	9.5	17.0	3210.5	− .025
1.7399	.88080	5562.4	9.5	16.5	3211.9	+ .019
1.9722	.99918	6310.0	0.8	18.6	3211.3[a]	.000
1.9124	.96871	6117.6	1.2	18.0	3211.0[a]	− .009
				Mean	3211.3	± .012

[a] This calibration was made with 2.0 g. less water in the calorimeter and hence 2.0 cal. have been added to the experimental result to bring it up to the "standard" conditions for our calorimeter.

Three different cylinders of oxygen were used during the course of the present investigation and two other cylinders have been used in subsequent work in this Laboratory. With each cylinder of oxygen a series of calibrations of the calorimeter was carried out with the standard benzoic acid. Usually the individual runs in a series were made at different stages of pressure during the use of the cylinder and in this connection no significant changes appeared during the decrease of the oxygen pressure. Table I contains the details for seven calibrations with Cylinder 2, which was used in about 60% of the combustions in the present study. The other four series of calibrations were similarly concordant among themselves and yielded means in excellent agreement with that tabulated here.

Purification of the Compounds

Highest purity Eastman Kodak Co. chemicals were the starting materials in the preparation of all the samples except those of pyrene and polyisobutylene. They were further purified in our Laboratory by recrystallization from suitable solvents and subsequent drying in an electric oven. After such preparation all crystalline materials were kept in desiccators over "dehydrite" and, for at least three days prior to combustion determinations, in vacuum desiccators with frequent evacuation. Ash determinations were made on all substances but, except in the cases of phenanthrene and sample 3 of pyrene, the results were negligible. In these two cases suitable corrections were made in the combustion values.

β-Methylnaphthalene.—Two samples were prepared independently by three successive crystallizations from absolute ethyl alcohol.

Phthalic Anhydride.—Four samples were prepared as follows. (1) The material was crystallized once from a mixture of equal parts of pure benzene and petroleum ether and then sublimed before use. (2) One crystallization was made in this case from a 50–50 mixture of benzene and isoöctane and this was followed by sublimation. (3) The third sample was subjected to one crystallization from "hexone"; the crystals were washed with benzene and then crystallized once from benzene. The product was then sublimed three times before using. (4) This sample was crystallized from "hexone," washed with benzene, then twice crystallized from benzene, and finally sublimed twice.

***o*-Phthalic Acid.**—Two separate samples were prepared by three crystallizations from specially distilled water.

Anthracene.—The original Eastman Kodak Co. product was a muddy yellow. After three crystallizations from benzene the material was of a light yellow color.

Phenanthrene.—This sample was the product of three crystallizations from benzene; it had 0.007% ash content.

Stilbene.—This sample was prepared by crystallizing three times from benzene.

Pyrene.—From the material purified by Jacobs and Parks[6] three samples, all light green in color, were prepared for these combustion measurements. (1) This was the product of one crystallization from benzene followed by one from "hexone." (2) For this sample the procedure was reversed, benzene being used for the solvent after "hexone." (3) Another quantity of pyrene was subjected to three crystallizations from benzene. Ash determinations on this sample showed 0.016% non-combustible.

***n*-Hexadecane.**—The Eastman Kodak Co. product (m. p. 16°) was used in its original form for sample 1. Sample 2 was prepared from some of this material by four crystallizations from a 50–50 mixture of *n*-propyl alcohol and methyl alcohol, followed by six crystallizations from ethylene dichloride. A careful qualitative test for chlorine in the final product (m. p. 17.0°) was negative.

Cetyl Alcohol.—Two samples were prepared. (1) The material (m. p. 48°) was recrystallized twice from methyl alcohol. In spite of being dried for several days in a vacuum desiccator, this sample had a pronounced odor and yielded combustion values averaging 0.071% lower than sample 2. As this indicated incomplete removal of the methyl alcohol, the data obtained for it have not been used in computing the final results in Table III. (2) This sample was prepared by two crystallizations from benzene as a solvent with subsequent drying.

1,3,5-Triphenylbenzene.—Four samples were prepared as follows. (1) This was the product of a crystallization from glacial acetic acid, followed by washing with ethyl alcohol and two crystallizations from ethyl alcohol. (2 and 3) These samples were crystallized three times from absolute ethyl alcohol. They were prepared separately at different stages of this study. (4) This material was twice crystallized from benzene.

Polyisobutylene.—This material was furnished in a very pure form by the Shell Development Company and was not subjected to any additional treatment before use. Its properties have been previously described by Ferry and Parks.[7] Its apparent molecular weight was about 4900, although of course it was a mixture of many polymers.

The Heats of Combustion and Derived Data

The experimental data for the combustions on the two samples of β-methylnaphthalene are presented in Table II. The energy evolved in the isothermal bomb process per g. at 25.0° is represented by $-\Delta U_B/m$ and the deviations of the

(6) Jacobs and Parks, THIS JOURNAL, **56**, 1513 (1934).

(7) Ferry and Parks, *J. Chem. Physics*, **4**, 70 (1936).

individual runs from the mean by Δ. The detailed experimental data for the remaining ten substances are essentially similar in character; they have been omitted here for reasons of spatial economy. Except in the case of cetyl alcohol previously cited, the different samples of any substance yielded extremely concordant combustion values.

TABLE II

THE EXPERIMENTAL DATA FOR β-METHYLNAPHTHALENE AT 25°

Sample	True mass, g.	Total heat evolved, cal.	Cal. from HNO_3	Cal. from string and *Eit*	$-\Delta U_B/m$, cal. $g.^{-1}$	Δ
1	0.58994	5766.1	10.7	15.3	9730.0	+2.0
1	.58946	5759.4	10.6	15.4	9726.5	−1.5
1	.59188	5783.8	10.0	15.0	9729.6	+1.6
1	.59176	5781.6	10.4	15.2	9726.9	−1.1
1	.59236	5788.3	10.7	15.5	9727.3	−0.7
2	.59251	5788.9	10.5	15.1	9726.9	−1.1
2	.59067	5774.2	11.1	14.8	9731.8	+3.8
2	.59076	5770.3	10.7	14.4	9725.1	−2.9
				Mean	9728.0	±1.8

Table III contains a summary of the experimental data for the heats of combustion of the eleven substances together with some important thermal data calculated therefrom. The number of combustions made in each particular case is given in the fifth column; the resulting mean values for $-\Delta U_B/m$ and the mean deviations (Δ) appear in the succeeding column. The values of the bomb process were then calculated per mole and corrected to the standard constant-volume process where the reactants and products are each at 1 atmosphere by means of the equations of Washburn.[4] The energy evolved in this hypothetical standard process is designated by the symbol $-\Delta U_R$. From this quantity $-\Delta H_R$, the heat evolved in the isobaric process at 1 atm., was obtained by addition of the proper work term. Finally, $-\Delta H^\circ_f$, the heat of formation of the compounds from the elements, was then calculated from $-\Delta H_R$ by use of 68,318 cal.[8] and 94,030 cal.[9] for the heats of formation of water and carbon dioxide, respectively.

The two liquids, *n*-hexadecane and polyisobutylene, were never evacuated in the vacuum desiccators and undoubtedly contained dissolved air. According to the solubility data in the "International Critical Tables"[10] and the more recent study of Frolich,[11] this dissolved air at saturation would amount to about 0.02% by weight; and therefore the values for $-\Delta U_R$ in Table III for these two substances have been arbitrarily increased by this percentage in the course of the calculation from the values of $-\Delta U_B/m$.

The uncertainties attached to the values of $-\Delta U_R$ have been calculated by use of the "precision error" described by Rossini.[12] This includes not only the "reaction error" for the combustion of the particular compound but also our "calibration error" of 0.012%, an "assigned error" (by Jessup and Green) of 0.023% on the standardizing substance, and an arbitrary allowance for a 10% uncertainty in the Washburn correction. In the cases of *n*-hexadecane and polyisobutylene an additional 20% uncertainty in the correction for air saturation was assumed.

TABLE III

SUMMARY OF EXPERIMENTAL AND DERIVED DATA AT 25°

Substance	Formula	Mol. wt.	Density	No. of comb.	$-\Delta U_B/m$ and Δ, cal. $g.^{-1}$	$-\Delta U_R$, kcal. $mole^{-1}$	$-\Delta H_R$, kcal. $mole^{-1}$	$-\Delta H^\circ_f$, kcal. $mole^{-1}$
β-Methylnaphthalene (s)	$C_{11}H_{10}$	142.19	1.029	8	9728.0 ± 1.8	1382.43 ± 0.52	1383.91	− 7.99
Phthalic anhydride (s)	$C_8H_4O_3$	148.11	1.527	10	5265.4 ± 2.6	779.04 ± .45	778.74	+110.14
Phthalic acid (s)	$C_8H_6O_4$	166.13	1.593	5	4642.9 ± 0.6	770.51 ± .32	770.21	+186.98
Anthracene (s)	$C_{14}H_{10}$	178.22	1.25	6	9451.0 ± .5	1683.27 ± .58	1684.75	− 16.94
Phenanthrene (s)	$C_{14}H_{10}$	178.22	1.025	4	9396. ± .9	1673.47 ± .61	1674.95	− 26.74
Stilbene (s)	$C_{14}H_{12}$	180.24	1.14	6	9754.1 ± 1.3	1757.02 ± .67	1758.80	− 32.47
Pyrene (s)	$C_{16}H_{10}$	202.24	1.25	11	9260.1 ± 3.4	1871.49 ± .84	1872.97	− 26.90
n-Hexadecane (l)	$C_{16}H_{34}$	226.44	0.775	9	11266.8 ± 1.9	2551.07 ± .97	2556.11	+109.78
Cetyl alcohol (s)	$C_{16}H_{34}O$	242.44	.90	7	10302.7 ± 2.0	2497.04 ± .90	2501.78	+164.11
Triphenylbenzene (s)	$C_{24}H_{18}$	306.39	1.206	12	9542.4 ± 3.2	2921.83 ± 1.27	2924.50	− 52.92
Polyisobutylene (l)	$(C_4H_8)_n$	n(56.105)	0.907	6	11175.8 ± 1.3	626.95 ± 0.23	628.14	+ 21.25

Previous Work

We have found no record of previous combustion measurements for β-methylnaphthalene, pyrene and polyisobutylene.

(8) Rossini, *J. Research Nat. Bur. Standards*, **22**, 407 (1939).

(9) Rossini and Jessup, *ibid.*, **21**, 491 (1938).

(10) "International Critical Tables," Vol. III, McGraw-Hill Book Co., Inc., New York, N. Y., p. 261.

(11) Frolich, Tauch, Hogan and Perr, *Ind. Eng. Chem.*, **23**, 548 (1931).

(12) Rossini, *Chem. Rev.*, **18**, 252 (1936).

For the remaining eight substances there are available in the literature a fair number of early values, mostly obtained around 1890, and a few really modern results. The early values[13] include determinations on all eight substances by Stohmann and his collaborators and a few results by Luginin and by Berthelot. Today it is practically impossible to translate these early data over to our modern standards. As published, they tend to run higher than our present results by amounts ranging up to 1.4%.

Coming to the modern data, where it is possible to put the heats of combustion on a better comparative basis with our new values, we find that Beckers'[14] results for cetyl alcohol and anthracene differ from ours by only −0.05 and +0.02%, respectively, the values of Verkade and Coops[15] for phthalic acid and phthalic anhydride exceed ours by 0.02 and 0.51%, and that of Swietoslawski[15] for phthalic anhydride is 0.04% above our result. In the case of stilbene Roth's value[13] exceeds the present result by 0.17%, that of Berner[16] by 0.07%. For phenanthrene other recent values[17] differ from that given here by −0.06 and +0.45%, and correspondingly for anthracene by +0.03 and +0.17%. For triphenylbenzene Professor Huffman at the California Institute of Technology has kindly made a pair of determinations on our original material with his own calorimetric apparatus. His mean result is 0.02% above that reported in this paper.

Acknowledgment.—Before concluding, we wish to thank Professor H. M. Huffman for his valuable advice and aid so generously given on many occasions during this investigation. We also desire to acknowledge our indebtedness to Mr. George E. Moore for purifying the samples of *n*-hexadecane and cetyl alcohol and making several of the combustions on these materials.

Summary

1. A bomb calorimeter has been calibrated and then used for precise measurements of the heats of combustion of the following eleven substances at 25° and constant volume: β-methylnaphthalene, phthalic anhydride, phthalic acid, anthracene, phenanthrene, stilbene, pyrene, *n*-hexadecane, cetyl alcohol, triphenylbenzene and polyisobutylene.

2. From these experimental results the corresponding heats of combustion and heats of formation at constant pressure have been calculated.

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(13) Landolt–Börnstein–Roth–Scheel, "Tabellen," Julius Springer, Berlin, 1923, p. 1587.

(14) Beckers, *Bull. soc. chim. Belg.*, **40**, 518 (1931).

(15) Verkade and Coops, *Rec. trav. chim.*, **47**, 606 (1928).

(16) Berner, *Arch. Math. Naturvidenskab*, **39**, No. 6 (1926).

(17) Milone and Rossignoli, *Gazz. chim. ital.*, **62**, 644 (1932); Fries, Walter and Schilling, *Ann.*, **516**, 248 (1935).

[CONTRIBUTION FROM THE CHEMICAL AND PHYSICAL LABORATORIES, ARMOUR INSTITUTE OF TECHNOLOGY]

Raman Spectra of Acetylenes. II. Displacements and Depolarization Factors for Phenylacetylene and Derivatives of the Type $C_6H_5C{\equiv}CR$[1]

BY M. J. MURRAY AND FORREST F. CLEVELAND

As was indicated in the first paper of this series[2] (subsequently referred to as I) the line near 2200 cm.$^{-1}$ in disubstituted acetylenes is not single, but is split into two or more parts. To explain this doubling, Gredy[3] postulates the co-existence of two molecular forms each of which gives its own characteristic frequency. Kohlrausch, Pongratz and Seka[4] give some support to this hypothesis by the statement that more than one frequency, if only one molecular form is present, is difficult to understand. Badger[5] attributes the splitting to a Fermi resonance interaction between the fundamental in this region and an overtone of a frequency near 750 or 1100 cm.$^{-1}$, the latter of which should not appear in the Raman spectra. Glockler and Davis[6] accounted for the two lines in dimethylacetylene by supposing that one is due to a symmetrical, the other to an asymmetrical, vibration. If this is true for disubstituted acetylenes in general, the two frequencies in this region should have strikingly

(1) Much of the experimental work discussed in this paper was carried out at Lynchburg College.

(2) M. J. Murray and Forrest F. Cleveland, THIS JOURNAL, **60**, 2664 (1938).

(3) Blanche Gredy, Thèses, Paris, 1935.

(4) K. W. F. Kohlrausch, A. Pongratz and R. Seka, *Sitzber. Akad. Wiss. Wien.*, Abt. IIb, **146**, 218 (1937).

(5) R. M. Badger, *J. Chem. Phys.*, **5**, 178 (1937).

(6) G. Glockler and H. W. Davis, *ibid.*, **2**, 881 (1934).

different depolarization factors. The present investigation was designed to test this point with a number of available derivatives of phenylacetylene.

Experimental Procedure

The method used in determining the depolarization factors has been described elsewhere.[7] Since the spectra of phenylacetylene derivatives are more intense than those of the compounds therein measured, it was possible to decrease the slit width (thus giving better resolution) and to reduce to ninety minutes the time for each exposure.

The Raman frequencies of several of these compounds were reported in I.[2] Since in the present investigation a superior filter[8] and a spectrograph[7] having better optical parts and greater dispersion were used, it has been possible to obtain some of the frequencies with a greater degree of certainty than before. This remark applies especially to the frequencies near 3000 cm.$^{-1}$. Much of the improvement in this region, however, is due also to the use of a different photographic emulsion (Agfa Super Plenachrome Press) which was more sensitive to the green wave lengths. Since the acetylenic compounds used undergo photochemical decomposition rapidly when exposed to light of short wave length and since the filter used was exceedingly efficient in isolating Hg 4358 Å., it was necessary and desirable to use only this frequency for excitation. For example, with this filter the strongest line in the spectra (the 2200 cm.$^{-1}$ line) did not appear on the spectrograms as excited by Hg 4047 Å. Furthermore, all the mercury lines near 5000 Å. were completely eliminated by the filter except Hg 4916 Å. and Hg 4960 Å. which were severely weakened, the latter being observable with great difficulty on long exposures.

In certain cases, noted in the data, the material available was insufficient to fill the Raman tube, and it was necessary to add carbon tetrachloride. Experience proved that this had no observable effect upon the spectra. In a few instances where a carbon tetrachloride line chanced to coincide with one of the lines of the acetylenic compound, it was impossible to read the depolarization factor.

Results

In the tabulation of results the displacement in cm.$^{-1}$ is written first, followed by the estimated intensity in parentheses, which in turn is followed by the depolarization factor, except in cases where low intensity or other cause prevented its measurement. Lines which are unusually broad are designated by the letter b following the intensity notation. Data in regard to which there is some uncertainty are enclosed in brackets. Frequencies which were observed both as Stokes and anti-Stokes lines are designated by the sign ±. In the case of those compounds studied in I,[2] the present tabulation includes those frequencies for which depolarization factors have now been obtained, frequencies which have been redetermined with greater precision, and some frequencies not previously observed. Each new or revised value is indicated by an asterisk. The present estimated intensities are regarded as somewhat more reliable than those reported in I.[2] Because of improvements in technique given above which greatly facilitate measurement in the 3000 cm.$^{-1}$ region, the present values of frequencies above 2800 cm.$^{-1}$ should replace in entirety those given in I.[2]

1. Phenylacetylene ($C_6H_5C{\equiv}CH$).—Synthesized from bromostyrene,[9] b. p. 142°; previous data, Bourguel,[10] and Bourguel and Daure.[11]

$\Delta\nu$ = ±164(6).9; ±353(4).9; ±465(3)<.7; 517(2); ±530(3).9; 621(4b).9; 760(5).5; 1001(7).2; 1027(2)<.6; 1155(2); 1176(4).5; 1196(6).4; 1230(1); 1281(1); 1337(1); [1380(1)]; 1447(1); 1489(2b); 1601(9).8; 2113(10).6; 3066(8).5; 3142(1); 3288(3).

2. 1-Phenylpropyne-1 ($C_6H_5C{\equiv}CCH_3$).—Synthesized by action of dimethyl sulfate on sodium phenylacetylide in ether solution, b. p. 72–73° (15 mm.); previous data, Gredy,[12] Bourguel,[10] and Bourguel and Daure.[11]

$\Delta\nu$ = 149(2); 298(3).8; 388(4).7; 401(2); 510(1); 528(3).9; 626(3); 701(3); 758(2); 953(1); 971(6).3; 1001(7).3; 1030(2); 1053(½); 1160(4) and 1181(4)<.5; 1245(1); 1262(8).3; 1286(2); 1328(1); 1382(4b).9; 1436(3) and 1450(3).7; 1489(4) and 1500(4).7; 1601(9).7; 2214(9).6; 2231(4); 2246(10) and 2262(6).6; 2913(4) and 2930(3).4; 2955(1); 3066(4b).6; 3111(1); 3143(1).

2231 was measured on three different spectrograms, but only when the camera lens was diaphragmed to 1.0 cm. did 2246 and 2262 appear resolved.

3. 1-Chloro-2-phenylethyne ($C_6H_5C{\equiv}CCl$).—Synthesized by action of *p*-toluenesulfonyl chloride on sodium phenylacetylide, b. p. 73° (16 mm.); previous data, Bourguel and Daure.[11] Carbon tetrachloride added.

$\Delta\nu$ = 284(4); 334(3); 364(5).9; 500(2); 521(4); 619(3); 654(1); 754(2); 882(4); 1000(8).3; 1161(3); 1175(3); 1208(1); 1224(2); 1248(6).4; 1487(2); 1599(8).7; 2203(2); 2222(10).6; 3065(3) and 3079(2)<.8.

4. 3-Chloro-1-phenylpropyne-1 ($C_6H_5C{\equiv}CCH_2Cl$).—Carbon tetrachloride added; for previous data, see I.[2]

$\Delta\nu$ = 690(6b).5; 718(4).9; 980(7).4; 1006(2)<.9; 1159(3) and 1174(3).8; 1251(8).5; 1491(4)<.9; 1600(9).8; 2214(10) and 2231(10).7; 2263(4).7; 2956(3).6; 3064(5).6.

5. 3-Phenyl-2-propynol-1 ($C_6H_5C{\equiv}CCH_2OH$).—For previous data, see I.[2]

$\Delta\nu$ = ±188(4b).9; ±270(3) and 282(3).9; 366(3) and 382(5).6; 530(5).7; 573(4).9; 625(5).7; 713*(4).7; 756*(5).8; 956(6).3; ±1000(8).2; 1023*(4) and 1038*(2).3; 1158*(4).9; 1179(5).6; 1258(7).4; 1447*(4b).7; 1490*(5).6; 1603(9).7; 2202(6).6; 2242(10).7; 2278*(2); 2300*(2); 2433*(1); 2510*(1); 2555*(2); 2868*(4)<.6; 2914*(5) and 2935*(4).5; 3061(7).5.

(7) Forrest F. Cleveland and M. J. Murray, *J. Chem. Phys.*, **7**, 396 (1939).

(8) J. T. Edsall and E. B. Wilson, Jr., *ibid.*, **6**, 124 (1938). The present authors have approximately doubled the strength recommended.

(9) "Org. Syntheses," Coll. Vol. I, 1932, p. 428.

(10) M. Bourguel, *Compt. rend.*, **195**, 311 (1932).

(11) M. Bourguel and P. Daure, *Bull. soc. chim.*, **47**, 1349 (1930).

(12) B. Gredy, *Compt. rend.*, **196**, 1119 (1933).

6. 3-Bromo-1-phenylpropyne-1 ($C_6H_5C{\equiv}CCH_2Br$).—Carbon tetrachloride added; for previous data, see I.[2]

$\Delta\nu$ = 609(6b).6; 987(6).4; 1206(5).6; 1269(3).8; 1599(8).7; 2226(10).6; 2265(4).6; 2950*(3)<.6; 3064(5).4.

7. 1-Phenylbutyne-1 ($C_6H_5C{\equiv}CCH_2CH_3$).—Synthesized by action of sodium phenylacetylide on ethyl *p*-toluenesulfonate, b. p. 83° (9 mm.); for previous data, see Gredy.[12]

$\Delta\nu$ = 180(2b).8; 383(3).7; 528(2) and 539(3).7; 624(2).9; 694(1).9; 757(2).9; 893(3)<.6; 999(8).3; 1016(2); 1069(1); 1161(3).7; 1184(4).6; 1240(2) and 1258(6).5; 1330(1).9; 1384(1).8; 1438(1b).8; 1493(2).7; 1599(8).8; 2206(4).7; 2238(10).7; 2839(1)<.7; 2914(3).6; 2931(3)[.3]; 2978(1b).9; 3061(5).6.

A few of Gredy's assignments appear open to some question: 470 e (e = Hg 4358 Å.) is probably 2238 k (k = Hg 4047 Å.).[13] 942 e, reported as a strong line by Gredy, appeared with small intensity and is likely 999 f (f = Hg 4347 Å.). 3025 k is probably 1258 e and 2944 k is probably 1177 e.

8. 4-Chloro-1-phenylbutyne-1 ($C_6H_5C{\equiv}CCH_2CH_2Cl$).—Carbon tetrachloride added; for previous data, see I.[2]

$\Delta\nu$ = 520(4) and 535(4).9; 624(3).9; 646(3) and 665(4).7; 700(3).9; 902*(2).6; 968*(2); 1000(6).3; 1023*(3)<.7; 1153*(3) and 1181(3).7; 1244(5).9; 1263(6).5; 1424(3).8; 1447(4).7; 1491(4).8; 1603(9).7; 2221(10) and 2246(10).6; 2918*(3b).5; 2959*(2); 2979*(2); 3063(6).5.

The frequency 987, previously reported, was not found in the present study.

9. 4-Phenyl-3-butynol-1 ($C_6H_5C{\equiv}CCH_2CH_2OH$).—Carbon tetrachloride added; for previous data, see I.[2]

$\Delta\nu$ = 386(2).9; 528(3b).9; 936(2)<.7; 980(2)<.9; 1000(7).3; 1162(3).9; 1181(3).6; 1241(5) and 1259(5).5; 1432(3) and 1440(3).7; 1602(9).8; 2214(4) and 2233(10).5; 2943*(3) and 2987*(3).5; 3063*(6).6.

10. 5-Chloro-1-phenylpentyne-1 ($C_6H_5C{\equiv}CCH_2CH_2CH_2Cl$).—Carbon tetrachloride added; for previous data, see I.[2]

$\Delta\nu$ = 373(3) and 408(1).7; 521(3).7; 625(3).7; 654(4).7; 693(3).7; 1000(7).2; 1154(3).9; 1177(3).6; 1258(7).5; 1435(4).7; 1489(3).7; 1600(8).7; 2220(10) and 2236(10).6; 2837*(1).8; 2913*(4).4; 2956(3).7; 3063(6).5.

11. 1,3-Diphenylpropyne ($C_6H_5C{\equiv}CCH_2C_6H_5$).—Synthesized by action of benzyl *p*-toluenesulfonate (2 moles) upon phenylacetylenemagnesium bromide (1 mole)[14]; b. p. 135–145° (2–3 mm.) (probably somewhat high due to superheating). Not distilled in column. Previous data, none.

$\Delta\nu$ = ±209(5).8; 279(1b); 327(1b); ±379(5); 488(1); 513(1); 528(4)<.9; 602(4) and 622(5).9; 712(1b); 757(3)<.6; 797(4).9; 813(3); 840(1); 850(1); 910(1b); 947(1); 981(8).2; 1005(8).1; 1032(4).6; 1156(4).9; 1181(6).6; 1249(8b).5; 1287(1b); 1328(1); 1422(3) and 1445(2)<.9; 1493(5).7; 1601(9).7; 2212(8).5; 2238(10).5; 2277(1b); 2317(1); 2435(1); 2558(1); 2817(1); 2883(5) and 2898(3).5; 3065(8b).5; [3202(1)].

12. 1-Phenyl-1-butynol-3 ($C_6H_5C{\equiv}CCHOHCH_3$).—Synthesized by action of acetaldehyde upon phenylacetylenemagnesium bromide, b. p. 123° (9 mm.); for previous data, see Gredy.[15]

$\Delta\nu$ = 174(4b) and 189(4).8; 260(1); 298(1); 349(1); 360(3).9; 433(1); 524(1); 546(4).8; 582(2).9; 621(2).9; 707(1b).9; 756(2).9; 850(1); 935(5).4; 1001(8).3; 1024(1); 1077(1); 1112(2b)<.6; 1158(4).6; 1175(4).6; 1237(1); 1255(7).4; 1276(1); 1323(1); 1385(1); 1445(2).7; 1491(3).7; 1599(9).7; 2198(4).7; 2233(10).6; 2870(2b).5; 2936(3b).4; 2985(2b).7; 3062(5).6.

Gredy's 463 e is probably 2233 k. 489 e was not observed in the present study. 1485 e may be a misprint for 1445 e.

A graphical presentation of those lines for which definite depolarization factors were obtained is given in Fig. 1. The broad lines in the figure correspond to cases in which two lines were not clearly separated on the polarization film. The depolarization factor, multiplied by 10 in order to simplify the diagram, is written near the line to which it corresponds. The height of the line is proportional to its intensity.

Discussion of Results

The data clearly indicate that in the seven cases where it was possible to distinguish two lines on the polarization film in the 2200 cm.$^{-1}$ region, they were both depolarized to the same degree, within experimental error. Since symmetrical vibrations are in general strongly polarized, asymmetrical vibrations strongly depolarized, it is thus impossible to account for the lines observed in the present study by supposing that they correspond one to a symmetrical, the other to an asymmetrical, vibration, as Glockler and Davis[6] state to be the case for dimethylacetylene.

The two molecular forms proposed by Gredy[3] to account for the splitting are $RC{\equiv}CR'$ and $\begin{matrix}R\\R'\end{matrix}\!\!>\!C^+{\equiv}C^-$. The presence of any appreciable portion of the latter compound seems to be ruled out, on a purely physical basis, however, by the extremely small dipole moments obtained for many symmetrical disubstituted acetylenes, such as diphenyl-, di-*n*-butyl-, and di-*n*-amylacetylene. Wenzke and Allard[16] conclude that the simplest structure consistent with zero moment is $RC{\equiv}CR'$ and state that "the presence of an appreciable portion of the acetylidene compound is obviated." Furthermore, the acetylidene form is very difficult to justify on the basis of the facts of organic chemistry.

In regard to Badger's suggestion that the split-

(13) 468 e in $C_6H_5C{\equiv}CCH_2CH_2CH_3$, measured by Gredy, is also probably 2238 k.

(14) J. R. Johnson, A. M. Schwartz and T. L. Jacobs, THIS JOURNAL, **60**, 1885 (1938).

(15) B. Gredy, *Ann. chim.*, [11] **4**, 5 (1935).

(16) H. H. Wenzke and R. P. Allard, THIS JOURNAL, **56**, 859 (1934).

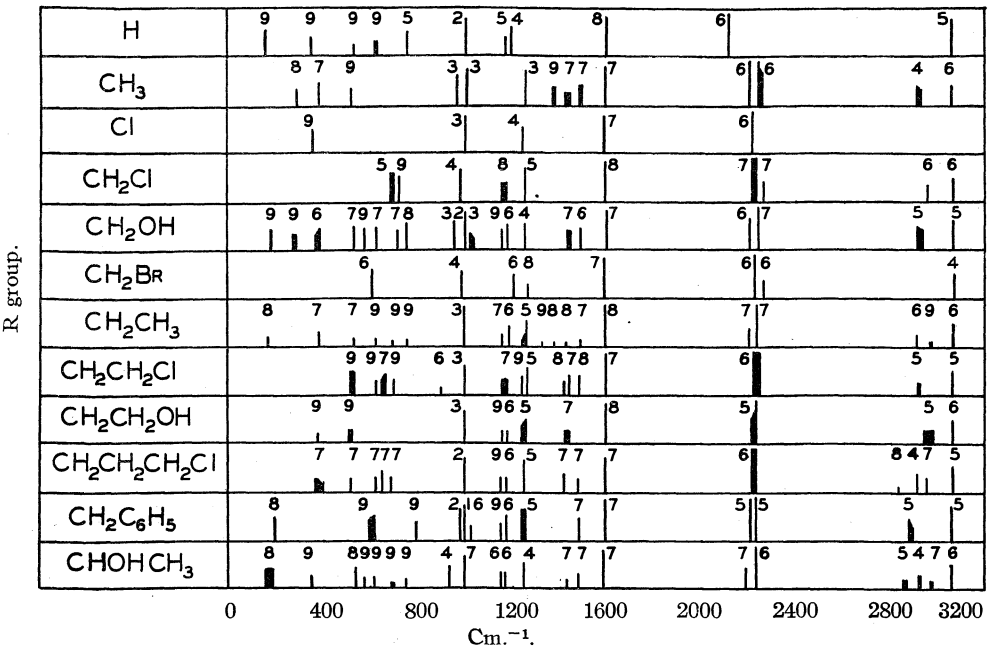


Fig. 1.—Raman spectra of compounds of the type $C_6H_5C{\equiv}CR$.

ting is due to a Fermi resonance interaction, it may be noted that there occurs in the present results no frequency whose first overtone would lie in the 2200 cm.$^{-1}$ region. This is in agreement with Badger's prediction that the frequency near 1100 cm.$^{-1}$ would not be active in the Raman effect. There is, however, a frequency at 756 cm.$^{-1}$ whose second overtone falls at approximately the same frequency as the mean of the two lines near 2200 cm.$^{-1}$. The extent of the agreement for the various compounds is indicated in Table I. It will be noticed that the frequency of the overtone is somewhat greater than the mean of the two frequencies in each case and although the 756 cm.$^{-1}$ frequency appears with remarkable constancy in the spectra of derivatives of phenylacetylene, it has not been observed with similar constancy in the spectra of other disubstituted acetylenes as would need be the case if it is to provide a universal cause for the splitting in acetylenic compounds. The investigation of Badger's hypothesis is being continued by studies in both Raman and infrared absorption spectra.[17]

TABLE I

FREQUENCY RELATIONS IN ACETYLENES OF TYPE $C_6H_5C{\equiv}CR$

R	"Triple bond" frequencies		Mean	Second overtone
CH_3	2214	2254	2234	2274
CH_2Cl	2222	2263	2243	2268
CH_2Br	2226	2265	2246	2271
CH_2OH	2202	2242	2222	2268
CH_2CH_3	2206	2238	2222	2271
CH_2CH_2Cl	2204	2233	2218	2262
$CH_2C_6H_5$	2212	2238	2225	2271
$CHOHCH_3$	2198	2233	2215	2268

Acknowledgment.—It is a pleasure to acknowledge grants in aid of this research program by the American Association for the Advancement of Science, Sigma Xi, and the Virginia Academy of Science.

Summary

1. Raman frequencies and depolarization factors are reported for twelve acetylenic compounds of the type $C_6H_5C{\equiv}CR$, where R is H, Cl, CH_3, C_2H_5, CH_2OH, CH_2Cl, CH_2Br, CH_2CH_2OH, CH_2CH_2Cl, $CHOHCH_3$, $CH_2C_6H_5$, and $CH_2CH_2CH_2Cl$.

2. The two lines near 2200 cm.$^{-1}$ were found to have the same depolarization factors, thus indicating that one frequency cannot correspond to a symmetrical, the other to an asymmetrical, vibration as Glockler and Davis have stated to be the case for dimethylacetylene.

CHICAGO, ILLINOIS RECEIVED SEPTEMBER 25, 1939

(17) In a recent paper on the Raman and infrared absorption spectra of dimethylacetylene, Crawford [*J. Chem. Phys.*, **7**, 555–562 (1939)] reports a weak frequency at 1126 cm.$^{-1}$ in the infrared spectrum which he regards as the fundamental whose first overtone interacts with the fundamental near 2270 cm.$^{-1}$ to produce the doublet 2233, 2310 observed in the Raman spectrum. In this case, the frequency of the overtone is less than the mean of the doublet, rather than greater as in the compounds discussed above.

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS, AND THE WILLIAMS OIL-O-MATIC HEATING CORPORATION]

Hydrogen Bonds Involving the C–H Link. VIII.[1] The Solubilities of Completely Halogenated Methanes in Organic Solvents

BY M. J. COPLEY, G. F. ZELLHOEFER AND C. S. MARVEL

A study[2] of the solubility of halogenated methanes in various organic solvents has shown that compounds of the type CHX_3 and CH_2X_2 (where X is either a chlorine or a fluorine atom) are more soluble in donor solvents which do not contain active hydrogen atoms than would be predicted from Raoult's law. To account for this increase in solubility over the calculated value, it has been postulated that C–H ⟵ O and C–H ⟵ N bonds are formed by the hydrogen of the halogenated methane and the oxygen and nitrogen atoms of the solvent molecules. If this explanation is the correct one, it is obvious that completely halogenated methanes (CX_4) would not show this enhanced solubility in donor solvents. The present paper contains solubility data on CCl_3F and CCl_2F_2 in a wide range of solvents. The solubilities are almost always lower than would be calculated, thus showing that compound formation between solvent and solute does not occur.

Solubility Data

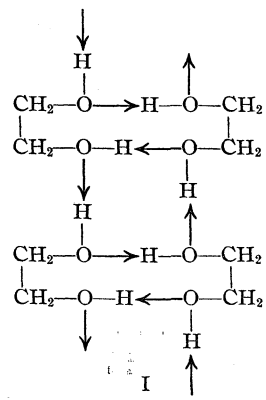
The procedure followed in making the solubility measurements was described in a preceding publication.[2a] The solvents were carefully purified by distillation and their boiling or melting points were checked. The solubilities were measured at 32.2° over a limited pressure range. With few exceptions the vapor pressures of the solvents were negligible when compared with the solute pressures at which measurements were made. Where the vapor pressure of a solvent was appreciable, a correction was applied in obtaining the solubility. The experimental values of the solubility were reproducible to within 1%. The variation of solubility with change in pressure obeyed Henry's law to within the limits of experimental error in practically all cases.

The observed gram per gram and mole fraction solubilities of CCl_2F_2 and CCl_3F at pressures equal to their vapor pressure at 4.5° are given in Table I. Corresponding data for CH_2Cl_2 and $CHCl_2F$, taken from previous papers[2b,c] by the authors, are given wherever available. The statement in the table that the solubility is *very low* in acetamide and in phenol is based on the observation that when these solvents, which are solids at 32.2°, were melted, insufficient solute dissolved in the working pressure range to lower the melting point noticeably. The "ideal" or theoretical mole fractions stated at the top of Table I were calculated using Raoult's law and are the ratios of the vapor pressures[2b] at 4.5° to those[2b] at 32.2°.

Discussion

In practically every solvent examined the solubility of the CX_4 type is less than that calculated from Raoult's law. The very marked difference in the solubility of the CX_4 types in ethers from that of the CHX_3 and CH_2X_2 types in the same solvents emphasizes the role of hydrogen bonding in the solubility process. In solvents which are not characterized by the presence of donor atoms, the solubilities of the hydrogen containing halogenated methanes do not differ widely from the completely halogenated derivatives. In alcohols which are associated through O–H ⟵ O bonds the CX_4 type has a very low solubility as compared with $CHCl_2F$ and CH_2Cl_2. This suggests that although OH ⟵ O bonds are stronger than CH ⟵ O bonds, at equilibrium an appreciable number of CH ⟵ O bonds are present in a solution of a hydrogen containing halogenated methane in alcohol.

Both types of halogenated methanes have ex-



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(1) For the seventh communication of this series see THIS JOURNAL, **61**, 3161 (1939).

(2) (a) Zellhoefer, *Ind. Eng. Chem.*, **29**, 584 (1937); (b) Zellhoefer, Copley and Marvel, THIS JOURNAL, **60**, 1337 (1938); (c) Copley, Zellhoefer and Marvel, *ibid.*, **60**, 2666, 2714 (1938).

TABLE I

SOLUBILITY OF HALOGENATED METHANES IN ORGANIC SOLVENTS

Solvents	CCl_2F_2 G./g.	CCl_2F_2 Mole fr.	CCl_3F G./g.	CCl_3F Mole fr.	$CHCl_2F$ G./g.	$CHCl_2F$ Mole fr.	CH_2Cl_2 G./g.	CH_2Cl_2 Mole fr.
Theoretical		0.453		0.356		0.381		0.311
Alcohols and Ethers								
n-Hexyl alcohol, $C_6H_{13}OH$	0.291	0.197	0.287	0.176	0.425	0.296		
Cyclohexanol, $C_6H_{11}OH$	.170	.123	.229	.143	.388	.274		
Phenol, C_6H_5OH	Very low		Very low		.269	.197	0.210	0.130
Ethylene glycol, $HOCH_2CH_2OH$	.0118	.00602	.0150	.00677	.100	.055		
Trimethylene glycol, $HOCH_2CH_2CH_2OH$	.0223	.0138	.0309	.0168	.106	.073		
Cyclohexyl methyl ether, $C_6H_{11}OCH_3$	.648	.380	.637	.346	.900	.498		
Anisole, $C_6H_5OCH_3$	.318	.220	.415	.244	.673	.415	.385	.328
Tetraethylene glycol dimethyl ether, $CH_3O(CH_2CH_2O)_4CH_3$	.223	.290	.312	.336	1.110	.706	.580	.602
Acids and Esters								
Acetic acid, CH_3COOH	.310	.133	.251	.0986	.688	.286	.280	.174
Propionic acid, C_2H_5COOH	.467	.223	.420	.185	.665	.330	.320	.218
Ethyl laurate, $C_{11}H_{23}COOC_2H_5$	.399	.430	.420	.412	.561	.556		
Ethyl caprylate, $C_7H_{15}COOC_2H_5$	.480	.406	.474	.373	.754	.557		
Aldehydes and Ketones								
Heptaldehyde, $C_6H_{13}CHO$	.525	.327	.534	.304	.979	.519	.473	.388
Cyclohexanone, $C_6H_{10}O$	.381	.236	.486	.257	1.278	.548	.630	.421
Acetylacetone, $CH_3COCH_2COCH_3$	.386	.242	.400	.226	1.023	.499	.455	.394
Acetonylacetone, $CH_3COCH_2CH_2COCH_3$	.185	.147	.247	.170	1.163	.563	.572	.434
Nitrogen Compounds								
Cyclohexylamine, $C_6H_{11}NH_2$	.581	.322			1.070	.506	.520	.377
Aniline, $C_6H_5NH_2$	.0604	.0442	.113	.0706	.385	.258		
Dimethylcyclohexylamine, $C_6H_{11}N(CH_3)_2$	.576	.377	.640	.372	.807	.500		
Dimethylaniline, $C_6H_5N(CH_3)_2$	.262	.208	.382	.252	.695	.425		
Quinoline, C_9H_7N	.119	.113	.229	.177	.633	.443		
Acetamide, CH_3CONH_2	Very low		Very low		Very low		Very low	
N-Methylacetamide, $CH_3CONHCH_3$	.181	.0984	.256	.120	.955	.403	.427	.269
N,N-Dimethylacetamide, $CH_3CON(CH_3)_2$	.305	.180	.326	.171	1.870	.614	1.808	.452
Valeronitrile, C_4H_9CN	.470	.245			1.280	.550	0.630	.351
Benzonitrile, C_6H_5CN					.783	.438		
Nitrobutane, $C_4H_9NO_2$			.356	.210	.780	.438		
Nitrobenzene, $C_6H_5NO_2$					.471	.360		
Ethylmethylketoxime, $C_2H_5(CH_3)C{=}NOH$	.327	.190	.352	.182	.650	.338	.315	.244
Hydrocarbons and Bromides								
n-Decane, $C_{10}H_{22}$	.602	.415	.537	.357	.324	.309		
Mesitylene, $C_6H_3(CH_3)_3$	.532	.346	.568	.332	.668	.437	.328	.317
Bromobenzene, C_6H_5Br	.210	.214	.299	.255	.335	.338		
n-Hexyl bromide, $C_6H_{13}Br$	.367	.333	.396	.322	.398	.390		

tremely low solubility in glycols. This indicates that association in the glycols is more complex than in simple alcohols. The association in glycols may be such as that shown in I in which dimer units are fused together by cross linkages into complex molecules very similar to the type previously suggested for simple amides.[2c]

Th esolubilities of the completely halogenated methanes in ethyl laurate and ethyl caprylate are higher than had been expected. In fact trichloromonofluoromethane has a solubility in excess of that calculated from Raoult's law in both of the esters. It is possible that this exception is due to the fact that the solubility calculated from the ratio of vapor pressures is lower than the value which would be obtained if fugacities were used.

The data on acetylacetone and acetonylacetone show that chelation in the former increases the solubility of the CX_4 type, whereas it decreases solubility of hydrogen containing halogenated methanes. Chelation undoubtedly renders acetylacetone less polar than the unchelated diketone

and the CX_4 type is consistently more soluble in the less polar solvents.

The extremely low solubilities of CCl_2F_2 and CCl_3F in aniline as compared to their solubilities in dimethylaniline and aliphatic amines support the suggestion made in an earlier paper that there is considerable association in primary aromatic amines.[2b]

The solubilities of $CHCl_2F$ in nitro compounds and nitriles show that these groups act as donor centers although when they are attached to a phenyl group[2b] they are much less effective donors than when attached to an alkyl group. A rather surprising case of solubility above the calculated amount was found in the case of $CHCl_2F$ in mesitylene.

Summary

The solubilities of CCl_2F_2 and of CCl_3F have been measured over a range of pressures in a wide variety of organic solvents. In practically every case the solubility was lower than that calculated from Raoult's law. These observations support the earlier postulation that intermolecular association through hydrogen bonding is an important factor in producing solubility of hydrogen containing halogenated methanes.

URBANA, ILLINOIS RECEIVED OCTOBER 6, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF DUKE UNIVERSITY]

The Action of Elementary Fluorine on Organic Compounds. VI. The Vapor Phase Reaction between Ethane and Fluorine in Progressively Varying Proportions

BY JOHN D. CALFEE,[1] NOBUKAZU FUKUHARA AND LUCIUS A. BIGELOW

In a preceding communication (IV),[2] we have described preliminary experiments dealing with the vapor phase fluorination of ethane over a copper gauze catalyst, and the subsequent isolation of hexafluoroethane and other products. The present report describes a further study of this important reaction in which ethane and fluorine reacted in progressively varying proportions, and the more important products subsequently were separated and rectified. In each case, a perfectly quiet continuous change took place, which could be duplicated readily in every essential respect.

The Apparatus.—The fluorination chamber consisted of a section of brass pipe filled with small squares of 20-mesh copper gauze, essentially the same as that described before.[2] However, two tubes filled with sodium fluoride were used instead of one to absorb hydrogen fluoride, and special precautions were taken to make certain that no air whatever was drawn into the apparatus when the condensing trap was cooled with liquid air. Also, the quantities of the reacting gases were measured carefully; the ethane by means of a calibrated flowmeter, and the fluorine through the known electrical efficiency of the generator, recently measured by Lewis[3] and shown to be nearly constant at about 80% during most of the life of the charge. Furthermore, the products were not passed through potassium hydroxide solution, but were distilled directly, since in general the ethane was in excess; thus no free fluorine was present.

The complete Booth–Podbielniak low-temperature rectification unit which was used to separate the products was constructed according to the principles described by Booth and Bozarth.[4] A diagram of the apparatus as adapted to our work, to be described in this and subsequent papers, is illustrated in Fig. 1. The unit consisted of three main parts, first, the boiler OO, the Podbielniak low-temperature column M, and the control manometer S with its contacts 1 and 2, together with the liquid air supply O and other accessories. Beyond the control valve K were the collecting system UU, VV, T, with manometers, and the melting point apparatus W. Finally came the gas density balance FF, with its thermostat, and an absolute manometer AA to measure accurately the pressures in the balance, as well as in any part of the receiving system. The temperature at the head of the column was measured by means of a thermocouple F, in connection with a recording potentiometer; and the boiler as well as the melting point apparatus was provided with a magnetic stirrer. The operating technique for this type of unit, together with the theoretical considerations involved, have been described before.[4]

Results and Discussion.—Four separate fluorinations of ethane were made in the manner already described, and the products condensed and rectified. There were isolated carbon tetrafluoride (b. p. −128°), two azeotropic mixtures, A and B, with constant boiling points, constant molecular weights, but wide melting ranges, ethane (b. p. −88°), hexafluoroethane (b. p. −78°), and some higher boiling material.

When azeotrope B (b. p. −96°, mol. wt. 64) was passed repeatedly through a 10% sodium hydroxide solution,

(1) This paper, and also III and IV of this series, have been constructed wholly or in part, from Mr. Calfee's Doctorate Thesis, presented to the Graduate School of Duke University in May, 1938.

(2) Calfee and Bigelow, THIS JOURNAL, **59**, 2072 (1937).

(3) Hubert M. Lewis, unpublished work.

(4) Booth and Bozarth, *Ind. Eng. Chem.*, **29**, 476 (1937).

dried and redistilled, it boiled at −92°, with a mol. wt. of 62. The difference was due undoubtedly to the removal of a small amount of impurity, presumably carbon dioxide, which could have come from the generator. No evidence was found to indicate the presence of silicon tetrafluoride in this product, but when the sample boiling at −92° was mixed with considerable carbon dioxide and distilled again, it boiled from −98° to −96°. The azeotrope was shown by direct synthesis to consist of ethane and hexafluoroethane, in the approximate molecular ratio of 2:1, since a known mixture of these compounds had a constant boiling point of −92°, and a constant mol. wt. of 64.

Azeotrope A was less simple, however. Its boiling point was −104° at atmospheric pressure (mol. wt. 54), −91 to −90° at 1140 mm. (mol. wt. 52) and −108° at 390 mm. (mol. wt. 52). It did not contain ethylene (b. p. −103°), since it was inert to bromine; and it was not a mixture of ethane and fluoroform, which yielded an azeotrope boiling at −96° (mol. wt. 46).

When it was passed through a 10% solution of sodium hydroxide ten times, dried and redistilled, silica was deposited immediately in the alkaline solution, and the remaining material separated sharply into two fractions, one boiling at −92° (mol. wt. 62), and the other at about −87° (mol. wt. 31). These properties correspond to those of azeotrope B and ethane, respectively. From this it was clear that azeotrope A consisted of ethane, hexafluoroethane and silicon tetrafluoride, in the approximate molecular ratio of 6:1:1, corresponding to an average mol. wt. of 53.

Table I gives the collected results of the fluorinations in the form of a comparison of the volume ratios of the reacting gases with the quantities of the various fractions separated, these last being expressed in liquid volume % of the total condensate obtained in the same run.

TABLE I

THE COLLECTED RESULTS OF THE LOW TEMPERATURE FRACTIONATION OF THE FLUORINATED ETHANE

Liquid volume per cent. of:	Gas volume ratios of fluorine to ethane 1:1	2.3:1	4:1	6:1
Carbon tetrafluoride	5	12	21	12
Azeotrope A	11	17	21	18
Azeotrope B	31	52	14	0
Ethane	42	0	0	0
Hexafluoroethane	0	6	32	41
Residue b. p. > −78°	12	17	14	29

The total volumes of liquid condensate obtained in these runs were 88, 40, 28 and 17 ml., respectively, on a twenty-hour operating basis, and previous to rectification. The figures in the table are to be considered as semi-quantitative, since the measurement of liquid volumes at low temperatures had to be made on a comparison basis, the error being estimated as not greater than ± 3 units in the extreme case. When the fluorine to ethane ratio of 6:1 was used, free fluorine appeared in the condensate, giving it an orange color. It was necessary to remove this halogen before rectification, by repeated melting, freezing and exhausting the product, which may have affected somewhat the values observed in this case.

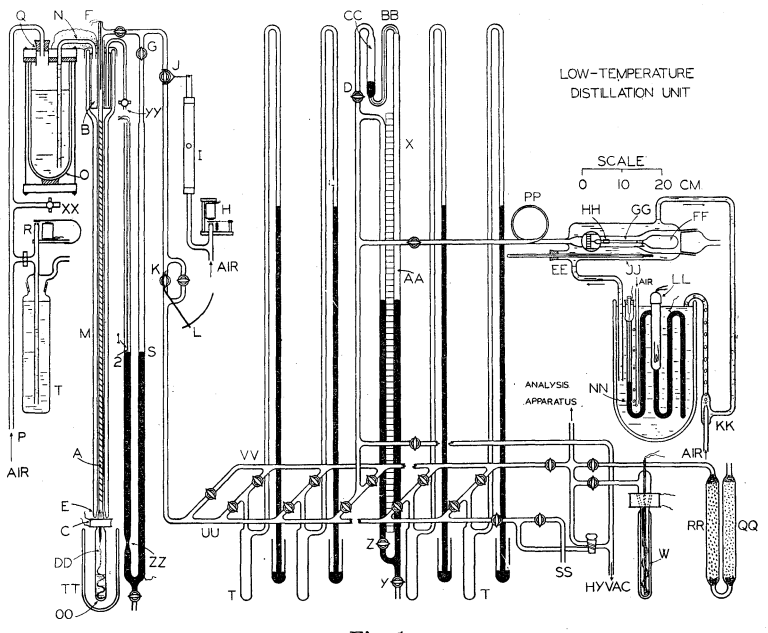


Fig. 1.

The trend of the results was quite clear, however. As the proportion of fluorine in the reaction mixture increased, the quantities of carbon tetrafluoride and hexafluoroethane increased, while the amount of ethane recovered decreased, as would be expected. Also azeotrope B was formed in maximum quantity under conditions when both of its components would be expected to be present in considerable proportions at the same time. The results also compare favorably with the preliminary observations reported earlier,[2] if the marked improvements in technique developed since then are considered. On the whole, it appears that direct fluorination is more similar to chlorination than has been supposed hitherto. A study of the influence upon this reaction of diluting the fluorine with nitrogen is now in progress.

The writers are glad to express here their thanks to Dr. H. S. Booth of Western Reserve University for timely suggestions during the early stages of this work.

Summary

Ethane has been fluorinated in the vapor phase, using progressively changing proportions of the reacting gases.

The more important products have been identified, and the approximate proportions in which they were formed have been determined.

DURHAM, NORTH CAROLINA RECEIVED JULY 21, 1939

[CONTRIBUTION FROM THE LAKESIDE LABORATORIES, MILWAUKEE, AND THE DEPARTMENT OF PHYSIOLOGICAL CHEMISTRY OF THE CHICAGO MEDICAL SCHOOL]

Studies on Proteins in Liquid Ammonia. V. Reaction of Sodium in Liquid Ammonia with Peptones and Related Substances[1]

BY CLEMMY O. MILLER AND RICHARD G. ROBERTS

From previous work[2,3] reported in this series, it is known that certain amino acids, peptides, proteins and related substances are acidic in liquid ammonia. A preliminary report[4] on peptones studied under similar conditions has been made. In this paper we have compared the reactions of Armour's Meat Peptone, Merck's Meat Peptone and Witte's Peptone when metallic sodium is added to them in liquid ammonia by determining the hydrogen evolved from them, and correlating it with their nitrogen content. This method is also used to follow the course of an acid digestion of silk fibroin through several of its peptones, since it reveals the presence of certain compounds and reactive groups that do not affect a Sörensen formol titration or a Van Slyke amino nitrogen determination greatly. It has been noted by others[5] that certain procedures carried out in non-aqueous solvents can reveal groups that do not ordinarily dissociate in aqueous solutions.

Experimental

Method.—The manner of drying the liquid ammonia over sodium and of drying the peptones and related substances has been described previously, as has also been the apparatus for collecting and analyzing the hydrogen.[2,3] The silk peptones were prepared by treating silk fibroin with 70% sulfuric acid at room temperature for one, two, three, four and ten days according to the method described by Morrow[6] for the preparation of four day silk peptones. The synthetic silk peptone was simply a mixture of glycine, alanine and tyrosine made up in the proportions found in silk fibroin.

(1) Some of the data presented here were collected in the laboratories of the Northwestern University Medical School.

(2) C. O. Miller and R. G. Roberts, THIS JOURNAL, **56**, 935 (1934).

(3) R. G. Roberts and C. O. Miller, *ibid.*, **58**, 309 (1936).

(4) R. G. Roberts and C. O. Miller, *Proc. Soc. Exptl. Biol. Med.*, **30**, 821 (1933).

(5) E. J. Cohn, *Ann. Rev. Biochem.*, **4**, 141 (1935).

(6) C. A. Morrow, "Biochemical Laboratory Methods," John Wiley and Sons, Inc., New York, N. Y., 1927.

Discussion

Our work on amino acids showed that a linear curve rising at a forty-five degree angle was obtained when the varying amounts of sodium added were plotted against the hydrogen evolved for one nitrogen equivalent of the substances used. With dipeptides such as glycylglycine or glycyl-*dl*-alanine the curve is linear, but the slope is less than for the amino acids. The curve with proteins can be divided into three segments, one and three roughly paralleling the base line, while segment two roughly parallels the rising curve of the amino acids. Protein curves in general resemble a one-day digestion silk peptone (Fig. 1, curve III). Diketopiperazine gives a curve similar to the proteins except that segment two rises only about 50% as high on the average as the latter. In general the curves of peptones resemble the curve of diketopiperazine. As shown in Fig. 1 Armour's peptone (curve I) gives a smooth curve, while Witte's peptone (curve II) gives sharp segments as if a definite amount of sodium or hydrogen had to be absorbed before a definite quantity of acidic hydrogen could be liberated. For one to one ratios of sodium to nitrogen, Merck peptone is relatively more acidic than either Armour or Witte peptone. Curve III of the one-day digestion silk peptone resembles the curve of silk fibroin; it is still acting like a protein. By the second day, however, the acidity has dropped to that which is characteristic of peptones and the three-day digestion gives a typical peptone curve (IV). By the fourth day the digest has become increasingly acidic again, about equal to that of the one-day digest. The ten-day digest is more acidic than the four-day digest, and gives a curve characteristic of amino acids (V). The ten-day digest seems to be the limit of acidity for a silk fibroin hydrolyzed by sulfuric acid, since a mixture (glycine 53.3%, alanine 31.1% and tyrosine 15.6%), the proportions found in silk fibroin, and

the ten-day digest have the same acidity in liquid ammonia.

The acidic properties of silk fibroin, some of its peptones, and mixtures of its constituent amino acids with themselves and with diketopiperazine can be compared by taking the moles of hydrogen evolved from one nitrogen equivalent of these substances when they are treated with an excess of sodium in liquid ammonia. (For the meaning of above terms, see legend of Fig. 1.) Silk fibroin would start at a high level (0.339) remain at 0.294 for the one-day digest, pass through a minimum for the two-day (0.134) and three-day (0.144) digests and approach a maximum in the four-day (0.320) and in the ten-day (0.359) digests and synthetic mixture (0.358) which is of the same order of acidity as the original silk fibroin (0.339). That other mixtures of amino acids do not evolve the same quantity of hydrogen as the theoretical maximum (0.580) is shown by the equimolar mixture of glycine and tyrosine (0.385). The very marked effect of diketopiperazine in reducing the amount of hydrogen evolved is shown by the equimolar mixture of glycylglycine and diketopiperazine (0.021). That these last two substances tend to form a new compound is made evident by a change in the crystalline form, the solubility and the melting point of the new product. Tyrosine and glycine react in this way also since they do not liberate hydrogen additively when mixed, and likewise form a new compound as described above and before the sodium is added. Another interpretation of these results is that the rings present are more easily reduced by hydrogen in the presence of another acidic substance. However, Roberts and Horvitz have shown recently[7,8] by bio-assay of blood pressure in dogs that adrenalin forms a fairly stable conjugate with glycine in liquid ammonia that will not form at all in water.

If one follows the digestion of a protein by the methods of Sörensen or of Van Slyke, the carboxyl and amino groups would be found to increase even if some diketopiperazine were liberated or were formed during the process. However, in liquid ammonia the acidity as determined by the method described here would not increase, but would actually decrease during digestion if diketopiperazine were liberated or formed during the process of acid digestion or the following ammonolysis, since it would combine in liquid ammonia with the amino acids or peptides present. One interpretation of our data would indicate that diketopiperazines are liberated or formed during an acid digestion up to the three-day period, after which they are broken down to form peptides and amino acids.

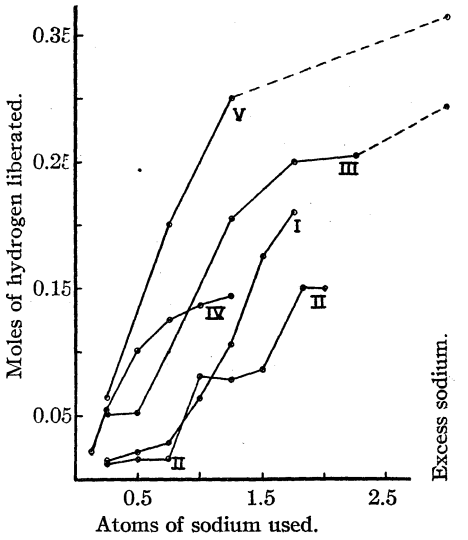


Fig. 1.—Curve I, Armour meat peptone; Curve II, Witte peptone; Curve III, 1-day digestion silk peptone; Curve IV, 3-day digestion silk peptone; Curve V, 10-day digestion silk peptone. In practice 1-g. samples were used, the sodium was added in small pieces and the hydrogen evolved varied from a few cc. to 0.1 l. or more. For convenience in plotting, the sodium is shown in gram atoms (23 g.) and the hydrogen in gram moles (2 g.) for 1 equivalent of nitrogen (14 g.) of the peptones. For a peptone containing 16% nitrogen by the method of Kjeldahl this would represent a sample of 62.5 g. The excess sodium represents an amount necessary to keep the liquid ammonia solution blue after the evolution of hydrogen has ceased. The excess may vary.

The relatively high acidity of native proteins in liquid ammonia is rather puzzling. However, this might be due to the acidity of the peptide hydrogen in long chains, if they are bent or folded in such a way as to bring phenyl or carbonyl groups into the immediate neighborhood of the nitrogen to which the replaceable hydrogen is attached. We did not find the peptide hydrogen of glycylglycine or glycyl-*dl*-alanine to be acidic. It might also come from other groups such as the hydrogen of the tertiary carbon in leucine or the hydrogen of the phenolic group in tyrosine. We have found both leucine and tyrosine to be more acidic in liquid ammonia than glycine or alanine. In his work with hydrocarbons, Wooster[9] found that

(7) R. G. Roberts and H. J. Horvitz, *Am. J. Physiol.*, **119**, 391 (1937).

(8) R. G. Roberts and H. J. Horvitz, *Trans. Illinois State Acad. Sci.*, **31**, 141 (1938).

(9) C. B. Wooster, *Chem. Rev.*, **11**, 1 (1932).

hydrogen attached to a tertiary carbon atom is not replaceable by sodium in liquid ammonia unless at least two phenyl groups are attached to the same carbon. Hydrogen might also be evolved from side chains attached to the longer peptide chains or from diketopiperazines. We regard the variation in acidity as due to the nature of the starting material, and to the conditions of the digestion. We think of both proteins and peptones as being built up of peptides and diketopiperazines with the peptones containing a relatively large amount of diketopiperazines.

Summary

1. A study of the reaction of sodium in liquid ammonia with certain peptones has been made.

2. Peptones are acidic in liquid ammonia, and liberate hydrogen when sodium is added to them.

3. Peptones are more acidic in liquid ammonia than diketopiperazine, but less acidic than proteins or amino acids.

4. Silk peptones prepared by digesting silk fibroin for ten days pass through a minimum acidity on the second and third days.

5. Peptones are more closely related to diketopiperazine than are proteins in their acid reactions in liquid ammonia.

6. Peptones react in liquid ammonia as if they contained relatively more diketopiperazines than do proteins.

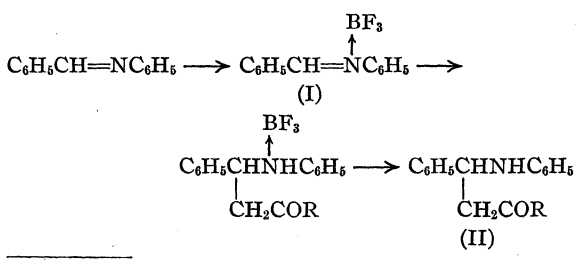
CHICAGO, ILLINOIS RECEIVED JULY 22, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Reactions of Anils. II. Addition of Methyl Ketones to Benzalaniline in the Presence of Boron Fluoride

BY H. R. SNYDER, H. A. KORNBERG AND J. R. ROMIG

In connection with a study of the reactions of anils,[1] it became desirable to effect the addition of methyl ketones to these substances. The reaction has been known for several years,[2] but in many cases it is a very slow process. Boron fluoride would be expected[3] to combine with an anil to produce the linkage $>C=N\rightarrow BF_3$, in which the double bond must be highly polarized because of the charge on the nitrogen atom. As a consequence of the increased polarization the complex should undergo addition reactions more readily than the anil. These predictions now have been realized. The coördination compound (I) is obtained readily and its rapid reaction with methyl ketones affords a convenient method of preparing amino ketones corresponding to (II).



(1) Snyder, Levin and Wiley, THIS JOURNAL, **60**, 2025 (1938).

(2) Mayer, *Bull. soc. chim.*, [3] **31**, 953, 985 (1904); [3] **33**, 157, 498 (1905); [4] **19**, 452 (1916).

(3) Kraus and Brown, THIS JOURNAL, **51**, 2690 (1929).

Procedure. Preparation of Benzalaniline–Boron Fluoride.—To a solution of 2.86 g. of benzalaniline in 155 cc. of dry ether was added 2 cc. of boron fluoride etherate. The precipitate which appeared was separated; analysis showed it to be high in boron. The mother liquor, after standing for several hours in a closed flask, deposited yellow needles, m. p. 135–145° (dec.). The product was analyzed for boron by the hydrogen peroxide oxidation method of Snyder, Kuck and Johnson.[4]

Anal. Calcd. for $C_{13}H_{11}NBF_3$: B, 4.35. Found: B, 4.44.

Addition of Methyl Ketones to Benzalaniline–Boron Fluoride.—One and one-half grams of the coördination compound was dissolved in 25 cc. of acetone. The solution warmed slightly. After a few minutes water was added and the mixture was cooled. The colorless needles of 1-anilino-1-phenylbutan-3-one were collected and recrystallized three times from dilute alcohol; yield, 0.5 g., m. p. 87–88°.

Anal. Calcd. for $C_{16}H_{17}ON$: N, 5.86; mol. wt., 239. Found: N, 5.86, 5.90; mol. wt., 251.

Substitution of ethyl methyl ketone for acetone gave 1-anilino-1-phenylpentan-3-one.[2] When the experiments were repeated with benzalaniline instead of the boron fluoride complex the anil was recovered.

For the preparation of amino ketones by this method the isolation of the coördination compound (I) is unnecessary. The reaction is effected more conveniently by adding boron fluoride etherate to a solution of the anil in an excess of the

(4) Snyder, Kuck and Johnson, THIS JOURNAL, **60**, 110 (1938).

TABLE I

ADDITION OF KETONES TO BENZALANILINE–BORON FLUORIDE

No.	Ketone added[a]	Amino ketone, $RCOCH_2CH(C_6H_5)NHC_6H_5$: No. of recrystallizations from	M. p., °C.	Yield, %	Molecular formula	Nitrogen, % Calcd.	Found	
1	Acetone	1, ligroin[b]	88–89	67	$C_{16}H_{17}ON$	5.86	5.86	5.90
2	Ethyl methyl ketone	1, ligroin[b]	120–121	66	Ref. 2			
3	Isobutyl methyl ketone	2, ligroin	80–81	61	$C_{19}H_{23}ON$	4.98	4.99	5.03
4	*n*-Amyl methyl ketone	2, ligroin	78–79	38	$C_{18}H_{25}ON$	4.75	4.71	4.85
5	4-Methyl-2-hexanone	2, ligroin						
		2, aq. MeOH	72–73	38	$C_{20}H_{25}ON$	4.75	4.81	4.83
6	Benzylacetone	4, ethanol	98–99.5	26	$C_{23}H_{23}ON$	4.26	4.15	4.09
7	Pinacolone	1, ethanol	148–149	71	$C_{19}H_{23}ON$	4.98	4.94	5.16
8	Cyclopentanone[c]	2, aq. MeOH						
		2, aq. acetone	163–164	42	$C_{18}H_{19}ON$	5.28	5.25	5.18
9	Acetophenone	3, aq. MeOH	166–167[d]	62	Ref. 2			
10	Malonic ester[e]	3, aq. MeOH	98–99	6	Ref. 5			

[a] The procedure employed was as follows. A solution of 3.6 g. of benzalaniline in four times the equivalent amount of the ketone was stirred in an ice-bath while 2.8 g. of boron fluoride etherate was added. After standing in the ice-bath for five minutes the solution was poured into 100 cc. of ice and water. The oil which separated soon solidified and was recrystallized as indicated in the second column. [b] These compounds were dissolved in 5% hydrochloric acid, filtered and reprecipitated by sodium bicarbonate prior to crystallization. [c] The solid obtained when cyclohexanone was used could not be purified. [d] Mayer[2] gives 173° as the melting point of this compound. [e] Equivalent amounts of malonic ester and benzalaniline were used.

ketone. A summary of the results obtained by this method is given in the table. It should be mentioned that boron fluoride is not a true catalyst. For example, in variations of Expt. 9 of the table in which the molecular ratios of boron fluoride to benzalaniline were 0.1, 0.32, 0.50 and 0.75, the yields of crude amino ketone were 0, 20, 38 and 68%, respectively.

Of the methyl ketones tested, all but acetomesitylene, mesityl oxide and benzyl methyl ketone gave the expected products. Whereas cyclopentanone reacted readily, cyclohexanone[6] gave only a trace of solid product and α-tetralone gave none at all. Butyraldehyde, the only aldehyde tested, did not give a solid product. Of several compounds containing active methylene groups, only malonic ester gave an addition product. Methone and methyl cyanoacetate gave the benzal derivatives and dibenzoylmethane gave the enolic derivative, dibenzoylmethane boron difluoride.[7] From acetoacetic ester there was obtained only an intractable oil. The symmetrical ketones, diethyl ketone, di-*n*-butyl ketone and di-*n*-nonyl ketone, did not react under the conditions employed with methyl ketones. Benzyl cyanide, phenylacetylene, ethyl acetate and nitromethane likewise failed to give solid products.

(5) Goldstein, *Ber.*, **28**, 145 (1895).

(6) Pirrone describes the preparation of the amino ketone directly from cyclohexanone, benzaldehyde and aniline; *Gazz. chim. ital.*, **66**, 429 (1936).

(7) Morgan and Smith, *J. Chem. Soc.*, **125**, 1963 (1924).

Since the benzal derivatives of methone and methyl cyanoacetate were isolated, it seemed possible that the formation of amino ketones by this method might involve hydrolysis of the anil, reaction of the liberated aldehyde with the ketone, and addition of aniline to the unsaturated ketone so formed.[8] To test this possibility an experiment parallel to no. 1 was run, employing benzalacetone and aniline. Since none of the amino ketone was obtained, the alternate mechanism of direct addition of the ketone to the boron fluoride complex must be accepted.

In order to determine whether the addition of methyl ketones to benzalaniline–boron fluoride is reversible, a small amount of 1-anilino-1-phenylbutan-3-one (II, R = CH_3) was dissolved in an excess of pinacolone and treated with boron fluoride. In a similar experiment 1-anilino-1-phenyl-4,4-dimethylpentan-3-one (II, R = $(CH_3)_3C$) was treated with acetone and boron fluoride. The solutions were allowed to stand for one hour at room temperature. The starting material was recovered almost quantitatively from each, showing that the reaction is not reversible.

Summary

Benzalaniline and boron fluoride react in ether solution to give a coördination compound containing one molecule of each component.

The benzalaniline–boron fluoride complex un-

(8) Tambor and Weld, *Ber.*, **31**, 352 (1898).

dergoes rapid addition of methyl ketones and cyclopentanone. The reaction affords a convenient method of preparation of certain β-amino ketones.

The addition of methyl ketones to benzalaniline in the presence of boron fluoride is not a reversible process.

URBANA, ILLINOIS RECEIVED JULY 5, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Reactions of Anils. III.[1] A New Type of Diels–Alder Reaction

BY H. R. SNYDER, R. B. HASBROUCK AND J. F. RICHARDSON

The reaction of maleic anhydride on compounds containing the structural unit >C=C—C=N— has now been examined in the course of a general study of the behavior in the Diels–Alder reaction of open-chain unsaturated systems containing nitrogen.[2] Since 2-ethyl-2-hexenalaniline (I) is easily available, it was selected for the study.

2-Ethyl-2-hexenalaniline reacts readily with maleic anhydride in boiling benzene. The product is a monobasic acid of the composition corresponding to one molecule of each reagent. This acid could not be reduced by sodium amalgam; hydrogen and platinum converted it into a dihydro derivative which could not be further hydrogenated. Both the original acid and the dihydro acids are extremely stable to hydrolysis, either with acids or bases. Fusion of the original acid with alkali brought about its decomposition into aniline and an acid of the composition $C_{11}H_{14}O_2$. Oxidation of the latter gave trimesic acid.

Since the condensation product is a monobasic acid, 1,4-addition of maleic anhydride to give the heterocyclic substance (II) is immediately excluded. An acid of the correct composition might be formed by addition to maleic anhydride, as has been observed in the case of certain pyrroles.[3] The primary addition product (III), by tautomerization and intramolecular amide formation, could then be transformed into the monobasic acid (IV). However, a substance having the formula (IV) should be reduced by sodium amalgam and should take up four hydrogen atoms on catalytic reduction. Furthermore, this formula does not account for the formation of an acid $C_{11}H_{14}O_2$ which can be oxidized to trimesic acid.

The formation of the condensation product and all its properties can be accounted for readily on the basis of an aldimine–eneamine tautomerism, involving a 1,5-shift of hydrogen, in the original anil (I ⇄ V). This transformation is not surprising, since the system —CH_2—C=C—C=N— is a vinylog of —CH_2—C=N— in which tautomerism is well known. Addition of maleic anhydride to the diene system of the tautomer gives the substance (VI) which, since it is at once an anhydride and a secondary amine, rearranges to form the bicyclic amido acid (VII).

A compound of the formula (VII) would be expected to resist the action of sodium amalgam and to give only a dihydro derivative on hydrogenation. Vigorous hydrolysis with alkali opens the amide ring to give the β-anilino acid salt (VIII). Loss of a molecule of aniline results in the formation of the dihydrobenzene derivative (IX). The latter is unstable; by expelling a molecule of potassium formate it is converted into the salt of 3,5-diethylbenzoic acid, $C_{11}H_{14}O_2$, (X). Oxidation of the latter gives trimesic acid (XI).

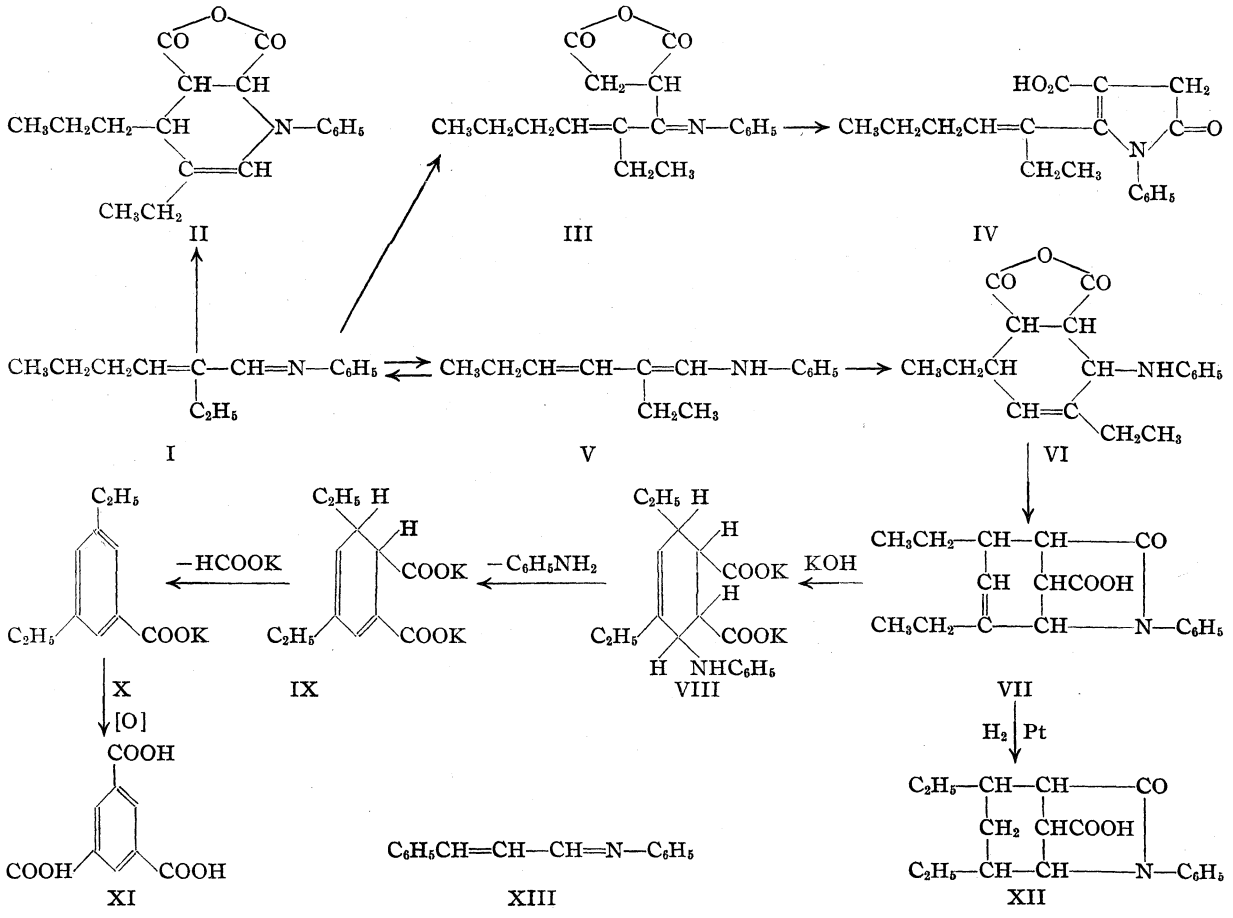
When this work was nearly complete, Bergmann[4] reported that cinnamalaniline (XIII) and maleic anhydride give only maleanilic acid and cinnamaldehyde. We have carefully reëxamined this case; the results have been in harmony with those of Bergmann, except that under highly anhydrous conditions the yield of maleanilic acid was negligible, as might have been expected from the observation[2] that, in reactions of this kind, the first step is addition of water to the carbon–nitrogen double bond. The failure of cinnamalaniline to undergo condensation supports the formulation given for the reaction of 2-ethyl-2-hexenalaniline; because the ε-carbon atom is part of the benzene ring, cinnamalaniline is unable to undergo the initial tautomerization.

(1) For the preceding paper in this series see Snyder, Kornberg and Romig, THIS JOURNAL, **61**, 3556 (1939).

(2) Snyder, Levin and Wiley, *ibid.*, **60**, 2025 (1938).

(3) Diels and Alder, *Ann.*, **486**, 211 (1931).

(4) Bergmann, THIS JOURNAL, **60**, 2811 (1938).



Experimental

Cinnamalaniline and maleic anhydride reacting in ether gave maleanilic acid, m. p. 193–195°, in yields varying from less than 2% (when dry ether was used) to 96% (when the theoretical amount of water was added). Similar results were obtained with benzene and dioxane solutions.

Preparation of 2-Ethyl-2-hexenalaniline.—To 40.2 g. of 2-ethyl-2-hexenal (Carbide and Carbon Chemicals Corporation) was added 30 g. of aniline. The solution was heated on the steam-bath for one minute and, after cooling, was allowed to stand at room temperature for fifteen minutes. The product was separated from the water layer by extraction with 100 cc. of benzene. After removal of the benzene, 48 g. (75%) of 2-ethyl-2-hexenalaniline (I) was distilled at 127–128° (2 mm.) (or 139.5–140.5° (6 mm.)); d^{20}_{20} 0.9379; $n^{20}D$ 1.5596; M_D calcd., 68.77, M_D found, 69.29.

Anal. Calcd. for $C_{14}H_{19}N$: C, 83.52; H, 9.52; N, 6.96. Found: C, 83.58; H, 9.42; N, 7.11.

Maleic anhydride and 2-ethyl-2-hexenalaniline in equilmolecular amounts, were dissolved in anhydrous benzene (1300 cc. per mole of anhydride). After standing for two hours in a closed flask the solution was filtered from a small amount of maleanilic acid. The clear solution was refluxed for three hours, atmospheric moisture being excluded by a calcium chloride tube. After standing for several days, or immediately after seeding, the solution deposited white crystals. After recrystallization from alcohol the product, 5,7-diethyl-2-phenyl-2-azabicyclo-(2,3,1)-oct-6-ene-3-one-8-carboxylic acid (VII), melting at 145–146°, was obtained in 75–80% yield.

Anal. Calcd. for $C_{18}H_{21}O_3N$: C, 72.24; H, 7.08; N, 4.68; neut. equiv., 299.2. Found: C, 72.46; H, 7.09; N, 4.78; neut. equiv., 302.

Catalytic Reduction of the Condensation Product.—A solution of 55 g. (0.184 mole) of the acid in 200 cc. of absolute alcohol was reduced at three atmospheres pressure over Adams platinum oxide catalyst. The pressure drop corresponded to 0.188 mole of hydrogen. The solution was filtered, treated with fresh catalyst and returned to the apparatus; no further reduction occurred. The dihydro acid (XII) was crystallized from dilute alcohol; yield 50 g. (90%). The air-dried material was a monohydrate; it decomposed at 120–130° and melted again at 177°; the neutral equivalent was found to be 322.5, as compared to a theoretical value of 319.2 for the monohydrate. Samples dried *in vacuo* melted at 177° and were anhydrous.

Anal. Calcd. for $C_{18}H_{23}O_3N$: C, 71.7; H, 7.70; N, 4.65; neut. equiv., 301.2. Found: C, 71.8; H, 7.73; N, 4.60; neut. equiv., 300.

The dihydro acid was converted to the chloride by treatment with thionyl chloride. Dry ammonia was

bubbled through a benzene solution of the crude chloride to give an 80% yield of the amide, recrystallized from alcohol, m. p. 187–188°.

Anal. Calcd. for $C_{18}H_{24}O_2N_2$: N, 9.33. Found: N, 9.33.

Hydrolysis of the Condensation Product (VII).—A number of attempts to hydrolyze the acid and its dihydro derivative by boiling with acids and bases were unsuccessful; the starting materials were recovered even after boiling for ten days with 10% sodium hydroxide.

To a solution of 20 g. of potassium hydroxide in 20 cc. of water in a nickel crucible was added 20 g. of (VII). The crucible was heated over a free flame while the mixture was carefully stirred. As water was driven off the mixture solidified; it then melted again and evolved aniline (identified as the benzoyl derivative from a run carried out in glass apparatus). When the evolution of aniline had stopped the hot mixture again solidified. It was dissolved in water and boiled with charcoal. The filtrate, on acidification, gave a yellow solid. This was dried and extracted with three 25-cc. portions of hot chloroform. The residue from evaporation of the chloroform was decolorized in methyl alcohol; after three recrystallizations from dilute methyl alcohol the product, 3,5-diethylbenzoic acid (X), melting at 133°, weighed 2.5 g.

Anal. Calcd. for $C_{11}H_{14}O_2$: C, 74.20; H, 7.87; neut. equiv., 178. Found: C, 74.05; H, 8.04; neut. equiv., 174.

Trimesic Acid (XI).—To a solution of 1 g. of 3,5-diethylbenzoic acid and 1 g. of potassium carbonate in about 50 cc. of water was added 7.0 g. of potassium permanganate. The mixture was heated until a vigorous reaction occurred; when the reaction subsided the mixture was heated for about ten minutes longer. The clear solution obtained after treatment with sulfur dioxide was acidified with hydrochloric acid and cooled in ice–salt. The white solid was collected, dissolved in aqueous potassium carbonate, precipitated with hydrochloric acid and dried. It did not melt at 300°. One-half gram of the acid was converted to the methyl ester by treatment with phosphorus pentachloride and methyl alcohol. After three crystallizations from methyl alcohol the ester melted at 146–147°. A sample prepared from authentic trimesic acid melted at 146–147°; mixtures of the two samples melted at 146–147°.

Anal. Calcd. for $C_{12}H_{12}O_6$: C, 57.1; H, 4.76. Found: C, 57.0; H, 4.87.

Summary

2-Ethyl-2-hexenalaniline and maleic anhydride give 75–80% yields of 5,7-diethyl-2-phenyl-2-azabicyclo-(2,3,1)-oct-6-ene-3-one-8-carboxylic acid. The structure of this product has been proved by reduction to the dihydro derivative, and by degradation to 3,5-diethylbenzoic acid which was oxidized to trimesic acid.

The reaction has been shown to occur through tautomerization of the anil and addition of maleic anhydride to the diene system of the resulting eneamine.

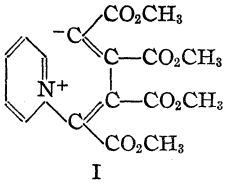
URBANA, ILLINOIS RECEIVED JULY 12, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Reactions of Anils. IV.[1] The Reactions of Benzalaniline and Cinnamalaniline with Methyl Acetylenedicarboxylate

BY H. R. SNYDER, HARRY COHEN AND WM. J. TAPP

The behavior of simple anils toward methyl acetylenedicarboxylate is of interest in connection with the novel structure (I) assigned by Diels and Alder[2] to the labile isomer obtained from pyridine and this reagent. Since only the carbon–nitrogen double bond appears to be involved in the formation of this substance and its stable isomer (II), other compounds containing this linkage might be expected to give similar products.



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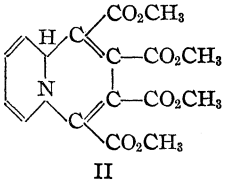


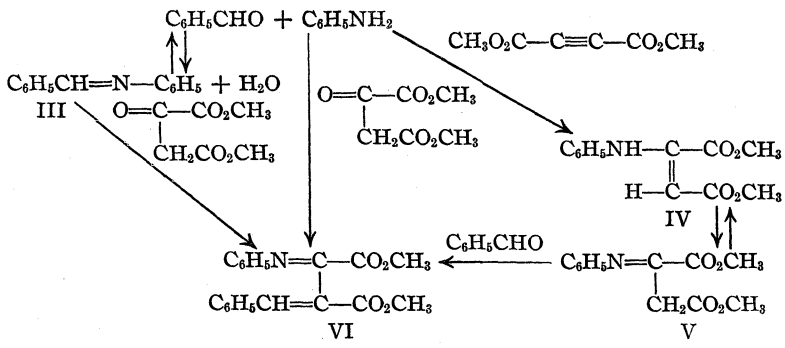
II

It has been found that benzalaniline and the acetylenic ester, reacting in commercial ether, give low yields of a substance (VI) having the composition corresponding to the addition of one molecule of the anil to one of the ester. However, the fact that the yields were greatly improved by the presence of a small amount of water suggested that the reaction involved hydrolysis of the anil. Addition of the liberated aniline to the acetylenic bond of the ester would give (IV), which by tautomerization (IV $\rightleftarrows$ V) and condensation with benzaldehyde would give (VI).

That the compound obtained has the structure (VI) was shown by its formation from methyl oxalacetate, benzaldehyde and aniline. It also could be obtained from methyl oxalacetate and benzalaniline in the presence of a trace of water, and from benzaldehyde, aniline and methyl acetyl-

(1) For the third communication in this series see THIS JOURNAL, 61, 3558 (1939).

(2) Diels and Alder, *Ann.*, 510, 87 (1934).



enedicarboxylate. The substance has the interesting property of dissolving in warm dilute alkali, and may be recovered unchanged from such a solution by acidification. This weakly acidic property must derive from the highly unsaturated character of the molecule.

Cinnamalaniline, $C_6H_5CH{=}CHCH{=}NC_6H_5$, which approximates more nearly the structural features of pyridine, reacts with the acetylenic ester to give two isomeric products of the composition corresponding to the addition of two molecules of the ester to one of the anil. This is the composition to be expected by analogy to the products from pyridine. When carried out in the absence of a solvent the reaction is highly exothermic, resembling in this respect also the reaction of pyridine and the ester. These compounds have not yet been obtained in quantities great enough to permit structural studies; since the work must be interrupted for a year it is being reported in its present status.

Experimental

Benzalaniline and Methyl Acetylenedicarboxylate.—A mixture of 8 g. of methyl acetylenedicarboxylate, 14 g. of benzalaniline, 2 g. of water and 50 cc. of absolute ether was allowed to stand for two days at room temperature. Filtration gave 3.8 g. of white crystals; after recrystallization from toluene the product, methyl α-benzal-α′-phenyliminosuccinate, melted at 192–193°. Similar results were obtained from aniline, benzaldehyde and methyl acetylenedicarboxylate in anhydrous ether.

Anal. Calcd. for $C_{19}H_{17}O_4N$: C, 70.6; H, 5.27; N, 4.34; methoxyl, 19.4; mol. wt., 323. Found: C, 70.44; H, 5.38; N, 4.34; methoxyl, 19.2; mol. wt., 353.

Benzalaniline and Methyl Oxalacetate.—A solution of 0.1 g. of methyl oxalacetate and 0.1 g. of benzalaniline in 1.0 cc. of wet ether deposited crystals after a few hours at room temperature. After two days these were removed by filtration and recrystallized from toluene; m. p. 192–193°; this melting point was not affected by admixture of the product described above.

Benzaldehyde, Aniline and Methyl Oxalacetate.—A solution of 0.1 g. of aniline, 0.1 g. of benzaldehyde and 0.2 g. of methyl oxalacetate in 3.0 cc. of absolute ether deposited crystals after a few hours. After recrystallization from toluene the product melted at 192–193°. The melting point was not affected by admixture of the above samples.

Cinnamalaniline and Methyl Acetylenedicarboxylate.—A solution of 2.8 g. of the ester and 4.0 g. of the anil in 70 cc. of petroleum ether was heated under reflux for two days. After decantation of the solvent, the residue was washed with petroleum ether and crystallized several times from methanol. The yellow crystals weighed 1.1 g. (23%) and melted at 166–167°.

Anal. Calcd. for $C_{27}H_{25}O_8N$: C, 66.0; H, 5.13; N, 2.86; methoxyl, 27.7; mol. wt., 491. Found: C, 66.10; H, 5.29; N, 3.13; methoxyl, 27.4; mol. wt., 441.

The higher-melting isomer was obtained by the following procedure. A flask containing 1.4 g. of the ester was cooled in an ice-bath and 2.0 g. of the anil was added with stirring. The mixture was kept in the ice-bath for four hours and was then allowed to stand at room temperature for two weeks. After washing with petroleum ether, the residue was dissolved in 15 cc. of toluene. The yellow crystals which separated from this solution after about two hours were collected and recrystallized from methanol; m. p. 309–310°, yield 0.05 to 0.10 g.

Anal. Calcd. for $C_{27}H_{25}O_8N$: C, 66.0; H, 5.13; N, 2.86; mol. wt., 491. Found: C, 66.2; H, 5.17; N, 2.90; mol. wt., 436.

Addition of petroleum ether to the toluene mother liquor caused precipitation of the low-melting isomer, which after crystallization from methanol melted at 166–167°; yield 0.5 g. (20%).

Summary

Benzalaniline reacts with methyl acetylenedicarboxylate in the presence of water to give methyl α-benzal-α′-phenyliminosuccinate. The same product may be obtained from benzaldehyde, aniline and methyl oxalacetate or from benzalaniline and methyl oxalacetate.

Cinnamalaniline and methyl acetylenedicarboxylate react to give two isomeric products of composition corresponding to one molecule of anil to two of the ester. The structures of these products have not been determined.

URBANA, ILLINOIS RECEIVED AUGUST 21, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE POLYTECHNIC INSTITUTE OF BROOKLYN]

Preparation of Aminobenzoic Acid Esters of Substituted Monoalkylamino Alcohols[1]

BY SAMUEL D. GOLDBERG, WILLIAM F. RINGK AND PAUL E. SPOERRI

In previous papers, the preparation[2] and the pharmacological properties[3] of two new series of anesthetic compounds were described.

The result of the pharmacological work on these compounds suggested the investigation of the properties of a series of esters in which the side chain was limited to two carbon atoms, one carbon atom carrying two alkyl substituents, thus forming a branched side chain.

The preparation of a series of β-alkylamino-α,α-dimethylethanols, $HOC(CH_3)_2CH_2NHR$, where R represents an alkyl group, was therefore undertaken.

The preparation of these amino alcohols required the use of β-chloro-α,α-dimethylethanol which was synthesized according to the methods of Krassuski[4] and Michael and Leighton,[5] using the addition of hypochlorous acid to isobutylene.

The β-chloro-α,α-dimethylethanol together with an excess of a primary amine in a suitable solvent was refluxed for several hours and then carefully fractionated. The average yield of β-alkylamino-α,α-dimethylethanol was 52%.

The *p*-nitrobenzoic acid esters of the amino alcohols were obtained through the condensation of the amino alcohols with *p*-nitrobenzoyl chloride in an aqueous alkaline medium. The temperature of this reaction must be maintained between 30 to 40° for optimum yields. The nitro esters are all yellow solids.

These nitro esters were reduced with tin and hydrochloric acid to the anesthetic amino bases.

The hydrochlorides of the higher members of the series of the amino bases were in all cases very viscous yellow oils; the sulfates, on the other hand, were all white crystalline solids.

Two members of another series of amino alcohols were prepared utilizing the reaction between a Grignard reagent and a chloro ester[6] or a chloro ketone.[7,8] With ethylmagnesium iodide there is obtained β-chloro-α,α-diethylethanol which on reacting with *n*-butyl- and *i*-butylamines yields the corresponding amino alcohols.

When methylmagnesium iodide is used, these two methods of preparation serve as alternative methods for making β-chloro-α,α-dimethylethanol.

Experimental

β-Ethylamino-α,α-dimethylethanol, $HOC(CH_3)_2CH_2NHC_2H_5$.—In a 250-cc. pressure bottle was placed 31.4 g. (0.23 mole) of a 33% aqueous solution of monoethylamine and 100 cc. of water. To this was added 20 g. (0.18 mole) of β-chloro-α,α-dimethylethanol, the bottle immediately stoppered and shaken occasionally during the next twenty-four hours. The reaction mixture was treated with solid sodium hydroxide and cooled, the upper layer extracted with ether, the ether layer separated and dried over anhydrous sodium sulfate. The ether was evaporated and the residue distilled. Two fractionations of the distillate gave 12 g. (56%) of a water-white liquid with a slight ammoniacal odor, boiling at 152–153°.

Preparation of the Other Members of this Series.—The preparations of the β-methyl- and β-ethylamino-α,α-dimethylethanols were carried out as described above. The higher members of this series of amino alcohols, namely, the β-*n*-propyl-, β-*i*-propyl-, β-*n*-butyl-, β-*i*-butyl-, β-*n*-amyl- and β-*i*-amylamino-α,α-dimethylethanols were prepared in a slightly different manner. 95% ethyl alcohol was used as a solvent for the reactants and the mixtures refluxed from three to twenty-four hours. The reaction mixture was acidified with concentrated hydrochloric acid and vacuum distilled almost to dryness. To the cold residue in the flask was added cold 30% sodium hydroxide solution and the same procedure used for the purification.

In Table I are summarized the physical constants of this series of amino alcohols, the molecular refraction (using Eisenlohr's[9] atomic refraction values) and the analyses of the picrates. The picrates were crystallized from either benzene or xylene.

The nitro esters are prepared by condensing the amino alcohols with *p*-nitrobenzoyl chloride as follows:

β-*i*-Butylamino-α-dimethylethyl *p*-Nitrobenzoate, (iso)-$C_4H_9NHCH_2C(CH_3)_2COOC_6H_4NO_2$.—To 10 g. (0.069 mole) of β-isobutylamino-α,α-dimethylethanol and 5 g. of sodium hydroxide in 250 cc. of water was added with stirring 13 g. (0.07 mole) of powdered *p*-nitrobenzoyl chloride in one amount. The temperature of the reaction was controlled so that it did not go above 40°. An oil was soon formed which finally solidified after one-half

(1) Submitted in partial fulfillment of the requirements for the degree of Master of Science in Chemistry, June, 1936, by William F. Ringk.

(2) Samuel D. Goldberg and Willet F. Whitmore, THIS JOURNAL, **59**, 2280 (1937).

(3) David I. Abramson and Samuel D. Goldberg, *J. Pharmacol.*, **62**, 69–87 (1938).

(4) K. Krassuski, *J. prakt. Chem.*, [2] **75**, 241 (1907).

(5) A. Michael and V. L. Leighton, *Ber.*, **39**, 2157 (1906); *J. prakt. Chem.*, [2] **64**, 103 (1901).

(6) E. Susskind, *Ber.*, **39**, 225 (1906)

(7) Tiffeneau, *Compt. rend.*, **134**, 775 (1902).

(8) Henry, *ibid.*, **142**, 131, 494 (1906); *Rec. trav. chim.*, **26**, 149 (1906).

(9) Eisenlohr, *Z. physik. Chem.*, **75**, 585 (1910); **83**, 429 (1914).

TABLE I

β-ALKYLAMINO-α,α-DIMETHYLETHANOLS ($RHNCH_2C(CH_3)_2OH$)

Alkyl group	B. p., °C.	Sp. gr.	$n^{20}D$	M. p. of picrates, °C.	M_R Calcd.	M_R Found	Formula	Analyses of picrates Carbon, % Calcd.	Found	Hydrogen, % Calcd.	Found
Methyl	142–143	0.8875^{23}	1.4338	137–138	30.361	30.212	$C_{11}H_{16}O_8N_4$	39.76	39.87	4.82	4.84
Ethyl	152–153	$.8777^{19}$	1.4344	132–133	34.979	34.742	$C_{12}H_{18}O_8N_4$	41.62	41.81	5.20	5.41
n-Propyl	169–171	$.8646^{19}$	1.4335	128–129	39.597	39.417	$C_{13}H_{20}O_8N_4$	43.33	43.18	5.56	5.69
i-Propyl	158–160	$.8528^{19}$	1.4288	166–167	39.597	39.586	$C_{13}H_{20}O_8N_4$	43.33	43.22	5.56	5.54
n-Butyl	186–187	$.8586^{20}$	1.4362	121.5–122.5	44.215	44.175	$C_{14}H_{22}O_8N_4$	44.92	45.01	5.88	5.97
i-Butyl	180–181	$.8490^{20}$	1.4309	138–139	44.215	44.201	$C_{14}H_{22}O_8N_4$	44.92	44.68	5.88	6.22
n-Amyl	205–208	$.8543^{20}$	1.4388	109–110	48.833	48.933	$C_{15}H_{24}O_8N_4$	46.39	46.53	6.19	6.29
i-Amyl	202–204	$.8580^{19}$	1.4380	145–146	48.833	48.645	$C_{15}H_{24}O_8N_4$	46.39	46.56	6.19	6.45
β-Alkylamino-α,α-diethylethanols ($RHNCH_2C(C_2H_5)_2OH$)											
n-Butyl	216–220	0.8629^{26}	1.4433 at 23°C.	127–128	53.451	53.182	$C_{16}H_{26}O_8N_4$	47.76	47.87	6.47	6.68
i-Butyl	214–216	$.8621^{26}$	1.4410	130.5–131.5	53.451	52.973	$C_{16}H_{26}O_8N_4$	47.76	47.91	6.47	6.70

TABLE II

β-ALKYLAMINO-α-DIMETHYLETHYL *p*-NITRO- AND *p*-AMINOBENZOATES

Alkyl group	Nitro esters, m. p., °C.	Amino esters, m. p., °C.	Amino ester sulfates m. p., °C.	Formula	Analyses of sulfates Carbon, % Calcd.	Found	Hydrogen, % Calcd.	Found	Nitrogen, % Calcd.	Found
n-Propyl-	108–109	123–124	138–140 150–153	$C_{28}H_{46}O_8N_4S$	56.19	56.37	7.69	7.94	9.36	9.16
n-Butyl-	87–88	116–119	$1H_2O$ Cryst.	$C_{30}H_{52}O_9N_4S$	55.91	56.14	8.07	8.43	8.37	8.19
i-Butyl-	130–131	83.5–84.5	142–143 158.5–159.5	$C_{30}H_{50}O_8N_4S$	57.51	57.39	7.99	8.39	8.95	8.81
n-Amyl-	107–109	93–95	Anhyd. 163–166 $1H_2O$	$C_{32}H_{54}O_8N_4S$	58.72	58.77	8.26	8.23	8.56	8.46
i-Amyl-	112–113	Oil	146–148	$C_{32}H_{54}O_8N_4S$	58.72	57.81	8.26	9.02	8.56	7.82
β-Alkylamino-α-diethylethyl *p*-Nitro- and *p*-Aminobenzoates										
i-Butyl-	.....	122–123	131–133	$C_{34}H_{62}O_8N_4S$	59.46	59.63	9.04	9.29	8.16	8.03

hour of stirring. The solid nitro ester was filtered off and washed with water until free of alkali. The nitro ester was recrystallized from benzene, m. p. 130–131°. The solid nitro ester was then reduced with tin and hydrochloric acid in the usual manner.

All of the esters were made similarly. In Table II are given the constants of the nitro and amino esters, as well as the analyses of the amino ester sulfates.

Pharmacology.—A preliminary pharmacological investigation of the sulfates of the β-*n*-propyl-, β-*n*-butyl, β-*i*-butyl-, and β-*n*-amyl-amino-α-dimethylethyl *p*-aminobenzoates was carried out. As a result of this investigation it was found that this series of anesthetics apparently was too toxic for injection purposes. However, the β-*n*-amyl derivative showed surface anesthetic activity to a high degree and was therefore tested further.[10]

Table III summarizes the toxicity tests of the sulfate of β-*n*-amylamino-α-dimethylethyl *p*-amino benzoate (abbreviated to *n*-amyl sulfate), Cocaine and Butyn.

In an anesthetized dog, *n*-amyl sulfate causes a slight reduction in blood pressure and a slight increase in pulse rate upon intravenous injection of a 1% solution. The intravenous toxicity for dogs is 20 mg./kg.

TABLE III

SUBCUTANEOUS TOXICITY

Compd.	Concn., %	Animal	No. of animals	M. L. D. mg./kg.	% died at M. L. D. indicated
n-Amyl sulfate	1	White mice	64	45	10
Cocaine	1	White mice	41	75–100	0–18
Cocaine	4	White mice	19	100–150	0–25
Butyn	1	White mice	26	25–50	0–12.5
Butyn	5	White mice	26	Approx. 50	14
n-Amyl sulfate	1	Guinea pigs	43	35–40	0–27
Intravenous Toxicity					
n-Amyl sulfate	1	White mice	9	10–15	0–100

Corneal anesthesia in the rabbit's eye, using a 1% *n*-amyl sulfate solution, a 4% cocaine solution and a 2% butyn solution produces anesthesia averaging eighty-seven, sixty-six and seventy-nine minutes, respectively, when from one to five drops of the solution are instilled into the rabbit's eyes. Immediate anesthesia was produced in all cases and no demonstrable irritations found in any treated eye. *n*-Amyl sulfate caused practically no mydriasis and no corneal erosion. Application of one drop of a 1% solution of *n*-amyl sulfate to the cornea of the rabbit's eye produces anesthesia last-

(10) We are indebted to Dr. Donald C. A. Butts of Philadelphia for the pharmacological investigation of this compound.

ing forty-three minutes while a 0.05% (1:2000) solution anesthetizes for six minutes. *n*-Amyl sulfate does not alter the intraocular tension of the rabbit's eye when used in 1% concentrations.

Summary

A series of new β-alkylamino-α,α-dimethylethanols has been prepared.

From these alcohols, as well as two β-alkylamino-α,α-diethylethanols, by combination with *p*-nitrobenzoyl chloride and reduction, there has been prepared a series of new esters.

A pharmacological study of one ester shows it to have interesting surface anesthetic properties.

BROOKLYN, NEW YORK RECEIVED OCTOBER 13, 1939

[A CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE GOODYEAR TIRE & RUBBER CO.]

Nickel as a Catalyst for the Hydrogenation of Aromatic Halogen Compounds

BY CHARLES F. WINANS*

The catalytic hydrogenation of *o*-nitrochlorobenzene over nickel was first attempted by Sabatier and Mailhe[1] who, however, obtained aniline hydrochloride as a result of a combined hydrogenation and dehalogenation. Furthermore, Sabatier and Espel[2] found that small amounts of halogen compounds did not interfere with the vapor phase reduction of benzene provided that some nickel remained in catalytically active form after a portion had been converted to nickel halide in removing the impurity. The simultaneous hydrogenation and dehalogenation of organic compounds has been effected by several workers[3] using platinum and palladium catalysts, and certain others have effected hydrogenation without the removal of halogen. Ellis[4] describes the preparation of a reduced nickel catalyst suitable for the production of chlorinated aromatic amines from the corresponding nitro compounds. Strangely, very little has appeared in the recent literature concerning the use of nickel for the hydrogenation of halogen compounds. The present paper attempts to demonstrate that the hydrogenation of these compounds is a general reaction which is applicable in an efficient and economical process.

The success of this conversion depends upon the choice of a stable halide, the use of a temperature below that at which dehalogenation occurs, and the use of a catalyst with sufficient mass of metal. These conditions have been met in the hydrogenation of aromatic halogen compounds at temperatures below 150° with Raney[5] nickel.

The substituents reducible below 150° which may be attached to the halogenated aromatic nucleus include the olefinic, acetylenic, nitro, nitroso, cyano, oximino, azido, azo, and carbonyl groups. Anils and hydro-amides may also be treated. It has not been possible to hydrogenate chlorobenzene to chlorocyclohexane, for at the temperature required to saturate the benzenoid ring halogen was removed giving rise to benzene in small amounts. Benzyl chloride gave some diphenylethane under similar conditions. In the aliphatic series 1-chloropropene, ω-chlorostyrene, *sym*-dichloroethylene, and tetrachloroethylene resisted saturation of the olefin bond.

The accompanying table gives the names of hydrogen acceptors and reaction products with physical properties and yields for fourteen different halogen compounds illustrating the behavior of several types. Most of the products were distilled from the reaction mixture. Others were obtained in crystalline form as solid product or hydrochloride derivative. All products were identified by the formation of known characteristic derivatives or by analysis.

The relative strength of attachment of chlorine, bromine, and iodine to the aromatic nucleus was demonstrated in the reduction of the halogenated nitrobenzenes. *p*-Chloronitrobenzene gave rise to *p*-chloroaniline even at 150° in nearly quantitative yield. *p*-Bromonitrobenzene was not quite so stable, but still the predominant product was *p*-bromaniline. *o*-Iodonitrobenzene was largely dehalogenated during reduction to aniline, only a small amount of *o*-iodoaniline being isolated from

* Present address: Mellon Institute, Pittsburgh, Pa.

(1) Sabatier and Mailhe, *Compt. rend.*, **138**, 245 (1904).

(2) Sabatier and Espel, *Bull. soc. chim.*, **15**, 778 (1914).

(3) For a complete résumé of the prior work in hydrogenation of organic halogen compounds, see Ellis, "Hydrogenation of Organic Substances," 3d. ed., D. Van Nostrand Co., Inc., New York, N. Y., 1930.

(4) Page 259 of Reference 3.

(5) Murray Raney, U. S. Patent 1,628,190, May 10, 1927.

TABLE I

Hydrogen acceptor	Product	B. p. °C.	Mm.	Yield, %
o-Chloronitrobenzene	*o*-Chloroaniline[a]	95–100	8	96.5
m-Chloronitrobenzene	*m*-Chloroaniline[b]	95–100	9	90.3
p-Chloronitrobenzene	*p*-Chloroaniline[c]	100–110	8	97.0
p-Bromonitrobenzene	*p*-Bromoaniline[d]	M. p. 60		83.0
o-Iodonitrobenzene	*o*-Iodoaniline[e]	M. p. 52		23.0
2,5-Dichloronitrobenzene	2,5-Dichloroaniline[f]	120–125	10	97.0
2,4-Dinitrochlorobenzene	*m*-Phenylenediamine[g]	135–140	5	91.0
o-Chlorobenzaldazine	*o*-Chlorobenzylamine[h]	95–100	9	81.0
o-Chlorobenzalaniline	*o*-Chlorobenzylaniline[i]	.....		65.5
Benzal-2,5-dichloroanil	Benzyl-2,5-dichloroaniline[j]	M. p. 44–45		91.0
o-Chlorobenzaldehyde and excess ammonia	*o*-Chlorobenzylamine[h]	90–95	8	87.5
p-Bromobenzophenone	*p*-Bromobenzhydrol	M. p. 61–62		72.0
p-Bromobenzophenone oxime	*p*-Bromobenzhydrylamine[k]	M. p. 126		88.5
p-Chlorobenzonitrile	*p*-Chlorobenzylamine[l]	98–102	10	64.0
	Di-*p*-chlorobenzylamine[m]	.....		21.0

[a] Hydrochloride, m. p. 230–235°. [b] Benzoyl deriv., m. p. 118–119°. [c] Benzoyl deriv., m. p. 187–188°. [d] Benzoyl deriv., m. p. 201–202°. [e] Acetyl deriv., m. p. 105–107°. [f] Hydrochloride, m. p. 190–191°. [g] Benzoyl deriv., m. p. 237–238°. [h] Benzoyl deriv., m. p. 115–116°. [i] Isolated as hydrochloride, m. p. 185–186°. [j] *Anal.* Calcd. for $C_{13}H_{11}NCl_2$: N, 5.55; Cl, 28.2. Found: N, 5.6; Cl, 27.7. [k] *Anal.* Calcd. for $C_{13}H_{12}NBr$: N, 5.34; Br, 30.5. Found: N, 5.49; Br, 29.6. [l] Hydrochloride, m. p. 238–240°. [m] Isolated as hydrochloride, m. p. 286–288°.

the reaction mixture. Dinitrochlorobenzene lost chlorine to give *m*-phenylenediamine on reduction, even when the reaction temperature was maintained below 40°. On the other hand, the presence of two chlorine atoms in dichloronitrobenzene did not interfere at all in the conversion to dichloroaniline and similarly benzal-2,5-dichloroanil was reduced to benzyl-2,5-dichloroaniline.

When operating with a readily reducible compound such as *p*-chloronitrobenzene a single portion of catalyst has been used in six successive reductions with only slight diminution in activity as judged by reaction time and temperature. In addition, several catalysts which were no longer sufficiently active for more difficult hydrogenations served very well in these simpler conversions.

Experimental

Apparatus and Catalysts.—The shaking autoclave in which these reactions were carried out had a capacity of 900 ml. and was similar in design to those described by Adkins.[6] The reactants were placed directly in the steel autoclave, no liners of copper or glass being employed. The nickel catalyst was prepared from Raney alloy according to the method of Covert and Adkins.[7]

Manipulation.—All hydrogenations were run in ethanol solution, although other solvents which are compatible with reducible compound, product, and water may also be used. When the hydrogenations were attempted in aqueous suspension, the reaction stopped far short of completion. In general, 5% of catalyst based on the weight of the reducible compound was used, although amounts as low as 2% may be used with accompanying slower reaction rate. Temperature was maintained below 150°, and preferably below 125°. Hydrogen pressures as low as 20 atm. were satisfactory in these hydrogenations, but the reaction rate was quite slow. With pressures of 100 atm. or more the reaction was very vigorous and much heat was evolved.

The following description of an experiment in the hydrogenation of *p*-chloronitrobenzene is quite typical. A mixture of 300 g. of *p*-chloronitrobenzene (tech.), 400 ml. of alcohol, and 15 g. of Raney nickel was charged into the autoclave under 100 atm. hydrogen pressure. The autoclave was shaken and slowly heated above room temperature. At 50° absorption of hydrogen as judged by drop in gage pressure was quite rapid and external heating was discontinued. When the pressure had fallen to 20 atm. more hydrogen was admitted from the storage cylinder. After twenty-three minutes the theoretical amount of hydrogen had been absorbed at a maximum temperature of 100°. The cooled reaction mixture, after removal from the autoclave, was filtered from the catalyst and distilled to give 236 g. (97%) *p*-chloroaniline, b. p. 100–110° (8 mm.). The recovered catalyst could be used repeatedly in subsequent hydrogenations.

Summary

The hydrogenation of certain readily reducible groups attached to a halogenated aromatic nucleus has been accomplished with nickel catalyst. These halogenated compounds behave just as do their unhalogenated analogs in regard to time, temperature, and completeness of hydrogenation.

AKRON, OHIO RECEIVED OCTOBER 30, 1939

(6) Adkins, *Ind. Eng. Chem., Anal. Ed.*, **4**, 342 (1932).
(7) Covert and Adkins, THIS JOURNAL, **54**, 4116 (1932).

[A CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE GOODYEAR TIRE & RUBBER CO.]

Hydrogenation of Aldehydes in the Presence of Ammonia

BY CHARLES F. WINANS*

The catalytic hydrogenation of hydro-amides derived from aldehydes such as benzaldehyde, furfuraldehyde, and trimethylacetaldehyde is known to give rise to equimolecular amounts of the corresponding primary and secondary amines.[1] The chemical reactions in the formation of hydrobenzamide are considered to be

$$RCHO + NH_3 \rightleftarrows RCH{=}NH + H_2O \quad (1)$$

$$3RCH{=}NH \rightleftarrows (RCH{=}N)_2CHR + NH_3 \quad (2)$$

These reactions are reversible as shown by Lach[2] who obtained Schiff bases and ammonia by treating hydrobenzamide with amines. The result of adding excess ammonia to hydrobenzamide should be to displace the equilibrium to the left, giving larger amounts of benzalimine which is readily reducible with nickel catalysts to benzylamine. Such is the case, and at the same time there is always produced a small amount of dibenzylamine which arises from the hydrogenation of that hydrobenzamide which has not been decomposed by ammonia.

The addition of one mole of benzaldehyde to one mole of hydrobenzamide with subsequent hydrogenation gives rise to predominant amounts of dibenzylamine. In this case the mechanism is considered to be different, in that the reaction involves, first, the hydrogenation of hydrobenzamide

$$(RCH{=}N)_2CHR + 3H_2 \longrightarrow (RCH_2)_2NH + RCH_2NH_2 \quad (3)$$

second, the reaction of benzaldehyde with benzyl amine

$$RCH_2NH_2 + RCHO \longrightarrow RCH_2N{=}CHR + H_2O \quad (4)$$

and, finally, the hydrogenation of the Schiff base to dibenzylamine

$$RCH_2N{=}CHR + H_2 \longrightarrow (RCH_2)_2NH \quad (5)$$

The use of preformed hydrobenzamide is not necessary, since the hydrogenation of mixtures of benzaldehyde and ammonia gives the same results. Thus, a mixture of 2 moles of aldehyde and 1 mole of ammonia produces the secondary amine predominantly on hydrogenation. A ratio of 3 moles of aldehyde to 2 moles of ammonia gives equimolecular amounts of primary and secondary amines, as if hydrobenzamide itself had been used. Finally, a mixture of one mole of aldehyde and one or more moles of ammonia produces mainly primary amine.

In this way a very effective method for controlling the type of hydrogenation product is made available. It is possible to obtain good yields only with those aldehydes which have no hydrogen on the alpha carbon atom. The use of aliphatic aldehydes should presumably lead to similar results, but the formation of tarry by-products through the aldol reaction or other condensation largely masks the production of amines.

Table I presents the results of several hydrogenations of benzaldehyde, *o*-methylbenzaldehyde, *o*-chlorobenzaldehyde, and furfuraldehyde with varying amounts of ammonia, showing the changes in proportions of products with changes in the aldehyde–ammonia ratio. Where low amounts of ammonia were used, the primary amine fraction contained some of the corresponding alcohol produced by direct hydrogenation of the aldehyde. Titration with standard acid gave the true amine content which is reported. In the other cases the products were substantially pure.

Table II gives summarizing data on the hydrogenation of preformed hydroamides in the presence of aldehydes or of ammonia. These results agree quite well with those of Table I for corresponding ratios of aldehyde and ammonia, and demonstrate that the proportions of products depend on the ratio of reactants and not on the method of addition.

Experimental

All hydrogenations were carried out in a steel shaking autoclave of the type described by Adkins.[3] Hydrogen pressure as low as 20 atmospheres has been quite satisfactory although higher pressures up to 100 atmospheres generally were used. Raney nickel in the amount of 3% on the aldehyde was very active, and a single portion of catalyst could be used a dozen times or more in successive hydrogenations. Temperatures in the range of 40–75° have been effective in these conversions.

Ammonia was most conveniently added as a standard alcoholic solution in those cases where accurately measured amounts were needed. For additions of ammonia in ex-

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(1) Winans and Adkins, THIS JOURNAL, **54**, 306 (1932); **55**, 2054 (1933).

(2) Lach, *Monatsh.*, **9**, 695 (1888).

(3) Adkins, *Ind. Eng. Chem., Anal. Ed.*, **4**, 342 (1932).

TABLE I

HYDROGENATION OF ALDEHYDES WITH AMMONIA

Aldehyde	Moles	Yield of amine product,[a] % ½ Eq. NH_3 Primary	½ Eq. NH_3 Secondary	⅔ Eq. NH_3 Primary	⅔ Eq. NH_3 Secondary	1 Eq. NH_3 Primary	1 Eq. NH_3 Secondary
Benz-	3	11.8	80.8	30.5(91.6)	62.6(94.0)	89.4	7.1
o-Me-benz-	1.67	11.2	81.7	30.8(92.1)	63.1(94.5)	82.6	15.5
o-Chlorobenz-	0.5	3.6	84.6	.. ..	.. ..	87.5	7.6
Furfur-	1.5	12.2	65.5	30.3(91)	66.5(94.1)	79	6.0

[a] The figures in parenthesis are yields computed on the assumption of hydro-amide as starting material. All other figures are based on the aldehyde used.

TABLE II

HYDROGENATION OF MIXTURES

Mixture	Moles	Product	Yield[a]
Hydrobenzamide	0.33	Benzylamine	30.7 (92.5)
		Dibenzylamine	60.9 (92.4)
Hydrobenzamide	0.33	Benzylamine	81
Ammonia	Excess	Dibenzylamine	8
Hydrobenzamide	0.37	Benzylamine	11.7
Benzaldehyde	0.37	Dibenzylamine	67
Hydrofuramide	0.75	Furfurylamine	29.4 (88.7)
		Difurfurylamine	62.8 (94.0)
Hydrofuramide	0.75	Furfurylamine	62.5
Ammonia	Excess	Difurfurylamine	12.4
Hydrofuramide	0.75	Furfurylamine	16.4
Furfural	0.75	Difurfurylamine	60.5

[a] Yield data are based on the aldehyde equivalent of hydro-amide used. Figures in parentheses are based on hydro-amide directly.

cess, the gas was led from a storage cylinder through high pressure connections directly into the autoclave.

A typical hydrogenation is described in detail. Three gram moles of benzaldehyde was added to a solution of 51 g. (3 moles) of ammonia in 300 ml. of cooled alcohol in the hydrogenation autoclave with 10 g. of Raney catalyst. Under an initial pressure of 90 atmospheres hydrogen absorption started at 40° and in half an hour was complete at a final temperature of 70°. Distillation of the filtered reaction product gave 287 g. (89.4%) of benzylamine, b. p. 70–80° (8 mm.), and 21.7 g. (7.1%) of dibenzylamine, b. p. 140–150° (7 mm.).

Ethyl alcohol was used as reaction medium throughout because it is miscible with both starting materials and products. A solvent of this type is necessary to maintain homogeneity where water is one of the products.

Acknowledgment.—The writer is grateful to Messrs. L. B. Sebrell and R. P. Dinsmore of the Goodyear Tire and Rubber Company for their interest in this work and for permission to publish the results.

Summary

The hydrogenation of aldehydes, such as benzaldehyde, containing no reactive hydrogen on the alpha carbon atom, in alcoholic ammonia solution may be accomplished at temperatures below 75°. By suitable control of the ratio of aldehyde to ammonia, the product may be predominantly primary amine or secondary amine.

AKRON, OHIO RECEIVED OCTOBER 30, 1939

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF DUKE UNIVERSITY]

Condensations Brought about by Bases. VII. The Acylation of Ethyl Isobutyryl-isobutyrate and the Cyclization of a 3,5-Diketo-ester by Means of Sodium Triphenylmethyl[1]

BY BOYD E. HUDSON, JR., AND CHARLES R. HAUSER

Ethyl isobutyryl-isobutyrate is readily synthesized in good yield either from the enolate of ethyl isobutyrate (prepared from the ester and sodium triphenylmethyl) and isobutyryl chloride,[2] or from ethyl α-bromoisobutyrate and magnesium[3]; the former method gives a purer product.[4]

Ethyl isobutyryl-isobutyrate (I) on treatment with sodium triphenylmethyl is converted into its sodium enolate, which is readily acylated. The enolate of (I) with acetyl chloride gives presumably compound (II), and with isobutyryl chloride gives compound (III).

In connection with the preparation of com-

(1) This work was supported in part by a grant from the Duke University Research Council.

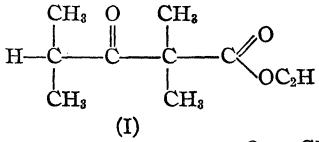
(2) (a) See Hauser and Renfrow, THIS JOURNAL, **59**, 1826 (1937); (b) See also Hauser and Renfrow, "Organic Syntheses," Vol. XIX, John Wiley and Sons, Inc., New York, N. Y., 1939, p. 44.

(3) Salkind, *Chem. Zentr.*, **77**, II, 315 (1906); Zeltner, *Ber.*, **41**, 592 (1908).

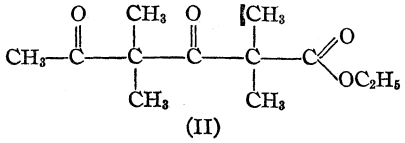
(4) Ethyl isobutyryl-isobutyrate also has been prepared by the self-condensation of ethyl isobutyrate in the presence of sodium triphenylmethyl, see Ref. 2a, p. 1823.

pound (III), it has been shown that this diketo ester is obtained when the reaction mixture, resulting from the self-condensation of ethyl isobutyrate[4] in the presence of sodium triphenylmethyl, is treated with isobutyryl chloride. The yield (42%) of compound (III) isolated in this case was only slightly less than that (46%) obtained when ethyl isobutyryl-isobutyrate was converted into its enolate, and the latter treated with isobutyryl chloride as discussed above. Since the free β-keto-ester does not condense with the acid chloride, this result shows that the ethyl isobutyryl-isobutyrate produced by the self-condensation of ethyl isobutyrate by means of sodium triphenylmethyl (even in the presence of excess ethyl isobutyrate) is in the form of its sodium enolate as postulated previously.[4]

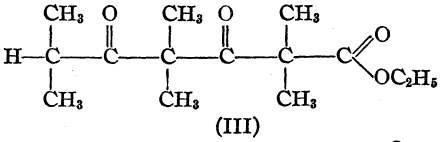
Compound (III) on treatment with sodium triphenylmethyl undergoes cyclization to give compound (IV). Compound (III) on treatment with sodium ethoxide undergoes cleavage, forming ethyl isobutyrate. Attempts to cyclize compound (II) with sodium ethoxide and with sodium triphenylmethyl apparently were unsuccessful; in both cases an alkali-soluble oil that could not be crystallized was obtained. Reisch[5] reported that the tetramethylphloroglucinol, which should result from cyclization of compound (II), is a solid melting at 187–188°.



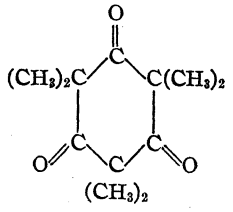
(I)



(II)



(III)



(IV)

The cyclization of compound (III) to give hexamethylphloroglucinol (IV) by means of sodium triphenylmethyl is of interest in connection with the acetoacetic ester condensation. In most ester-condensations of this type the β-keto-ester formed is converted into its enolate. However, similar to the case recently reported in which ethyl isobutyrate was condensed with ethyl benzoate,[6] the cyclization of compound (III) is an instance in which the Claisen[7] or acetoacetic ester type of condensation occurs even though the product formed cannot be converted into an enolate. It should be pointed out that neither of these condensations takes place in the presence of sodium ethoxide as condensing agent, and that they have been effected only by means of a stronger base, sodium triphenylmethyl.

Experimental[8]

Preparation of Ethyl Isobutyryl-isobutyrate. (a) From the Enolate of Ethyl Isobutyrate and Isobutyryl Chloride.[2]—To an ether solution of sodium triphenylmethyl[9] prepared from 63 g. of triphenylchloromethane (m. p. 112–113°), 1500 cc. of dry ether (dried with sodium), and 2000 g. of 1% sodium amalgam was added 21 g. (0.18 mole) of purified ethyl isobutyrate (b. p. 111–112°). After the solution had stood for ten minutes at room temperature with occasional shaking, 19.5 g. (0.18 mole) of isobutyryl chloride (Eastman Kodak Co.) was added rapidly with shaking. After standing in a closed flask for several hours, the reaction mixture was worked up by extracting with water, washing with 10% sodium carbonate solution, and drying first with anhydrous sodium sulfate and then with "Drierite." The solution was filtered and the ether distilled off until the volume of the residue was approximately 75 cc. The residue was chilled overnight in the refrigerator. The triphenylmethane which crystallized out was filtered off and washed with a small quantity of ether, the washings being added to the filtrate. After all the ether was removed by distillation at atmospheric pressure, the filtrate was vacuum-distilled, collecting up to 160° at 15 mm. The distillate was refractionated and the fraction boiling at 93.5–94.5° at 15 mm. collected; yield, 19 g., 55% of the theoretical amount.

(b) From Ethyl α-Bromoisobutyrate and Magnesium.[3]—A solution of 100 g. (0.52 mole) of ethyl α-bromoisobutyrate (Eastman) in an equal volume of dry ether was added to 16.6 g. (0.68 mole) of fresh magnesium turnings contained in a round-bottomed flask equipped with a reflux condenser. The reaction was started by adding a small crystal of iodine and warming the flask gently. After the reaction started, vigorous refluxing took place spontaneously. The reflux rate was moderated by the occasional application of an ice-bath. When spontaneous refluxing ceased, heat was applied and the mixture re-

(5) Reisch, *Monatsh.*, **20**, 488 (1899).

(6) Renfrow and Hauser, THIS JOURNAL, **60**, 463 (1938).

(7) For a general discussion of the Claisen type of condensation, see Hauser, *ibid.*, **60**, 1957 (1938).

(8) All melting points and boiling points given are corrected.

(9) Renfrow and Hauser, "Organic Syntheses," Vol. XIX, John Wiley and Sons, Inc., New York, N. Y., 1939, p. 83; See also Ref. (2a), p. 1825.

fluxed for three hours longer. At the end of that time the reaction mixture was worked up by the cautious addition of ice, followed by dilute sulfuric acid. The ether layer was separated, washed with 10% sodium carbonate solution, and dried with anhydrous sodium sulfate. The ether was distilled off and the residue was vacuum-distilled on a metal-bath from a round-bottomed flask equipped with a six-inch (15 cm.) Widmer column. The fraction boiling at 90–94° at 15 mm. was collected; yield, 34 g., 72% of the theoretical amount.

Reaction of the Enolate of Ethyl Isobutyryl-isobutyrate with Isobutyryl Chloride.—To an ether solution of sodium triphenylmethyl[9] (containing 0.085 mole of base), prepared from 28 g. of triphenylchloromethane, 1000 g. of 1% sodium amalgam, and 750 cc. of dry ether, was added with shaking 16 g. (0.086 mole) of ethyl isobutyryl-isobutyrate. The flask was stoppered and the mixture allowed to stand at room temperature for four hours with frequent shaking. At the end of this time, the mixture was poured rapidly into a solution of 15 g. (0.14 mole) of isobutyryl chloride (Eastman) in 500 cc. of dry ether, the latter being agitated vigorously with a mechanical stirrer. The vessel was closed and the reaction mixture allowed to stand for four hours longer. Then the mixture was extracted twice with water, washed several times with 10% sodium carbonate solution, and dried with anhydrous sodium sulfate followed by "Drierite." The solution was filtered and most of the ether distilled off. The residue (approximately 40 cc.) was chilled overnight in the refrigerator. The triphenylmethane which had crystallized out was filtered off and washed with a small quantity of ether, the washings being added to the filtrate. After all of the ether was removed by distillation at atmospheric pressure, the filtrate was vacuum-distilled, collecting up to 160° at 15 mm. The distillate was refractionated and the fraction of ethyl 2,2,4,4,6-pentamethyl-3,5-diketoheptanoate (III) boiling at 136–138° at 15 mm. was collected; yield, 10 g., 46% of the theoretical amount based on the quantity of either ethyl isobutyryl-isobutyrate or of sodium triphenylmethyl used. A portion of the diketo-ester boiling at 137–138° was analyzed.

Anal.[10] Calcd. for $C_{14}H_{24}O_4$: C, 65.6; H, 9.45. Found: C, 65.2, 65.0; H, 9.57, 9.77.

Cyclization of Ethyl 2,2,4,4,6-Pentamethyl-3,5-diketoheptanoate to Hexamethylphloroglucinol.—Seven and one-half grams (0.029 mole) of the pentamethyl-diketoheptanoate was added to 250 cc. of an ether solution of sodium triphenylmethyl (containing about 0.03 mole of base) prepared as described in the preceding experiment. The red color of the base disappeared immediately with the formation of a precipitate. The reaction flask was stoppered and allowed to stand for three days with occasional shaking. At the end of this time, the mixture was acidified with excess glacial acetic acid, extracted with water, washed with 10% sodium carbonate solution, and dried with anhydrous sodium sulfate. The ether was distilled off and the residue vacuum-distilled. A fraction which solidified in the condenser came over at about 130–140° at 15 mm. The crystalline material was washed from the condenser with ether. The ether was evaporated and the residue recrystallized by dissolving in a minimum of ligroin (90–120°) at about 40° and chilling in a mixture of ice and acetone. A yield of 1.85 g. (30% of the theoretical amount) of hexamethylphloroglucinol melting at 79–80° was obtained. This melting point is in agreement with that reported in the literature for hexamethylphloroglucinol,[11] and was not lowered by the addition of an authentic specimen of that compound prepared[11] by the methylation of phloroglucinol.

Evidence that the Ethyl Isobutyryl-isobutyrate Obtained from Ethyl Isobutyrate and Sodium Triphenylmethyl is in the Form of its Enolate.—To an ether solution of sodium triphenylmethyl[9] (containing approximately 0.18 mole of base) prepared from 63 g. of triphenylchloromethane (m. p. 112–113°), 1500 cc. of dry ether (dried with sodium), and 2000 g. of 1% sodium amalgam was added 45 g. (0.39 mole) of purified ethyl isobutyrate (b. p. 111–112°). The flask was stoppered and allowed to stand for twenty-four hours with occasional shaking. At the end of that time the mixture was poured into a solution of 24 g. (0.22 mole) of isobutyryl chloride (Eastman) in 500 cc. of dry ether with vigorous mechanical stirring. The reaction mixture was allowed to stand in a closed vessel for an hour. It was then extracted with water, washed with several portions of 10% sodium carbonate solution, and dried with anhydrous sodium sulfate followed by "Drierite." The solution was filtered and the ether distilled off until the volume of the residue was approximately 75 cc. The liquid remaining was chilled overnight in the refrigerator. The crystallized triphenylmethane was filtered off and washed with a small quantity of ether, the washings being added to the filtrate. After the ether was removed by distillation (up to 50°), the remaining liquid was distilled, collecting up to 150° at atmospheric pressure. The residue was then vacuum-distilled, collecting up to 180° at 15 mm. Refractionation of the two distillates yielded the following fractions: (a) 106–121° at atm. press., 22 g. (ethyl isobutyrate); (b) 120° at atm. press. to 131° at 15 mm., 3 g.; (c) 136–138° at 15 mm., 6.3 g. (ethyl 2,2,4,4,6-pentamethyl-3,5-diketoheptanoate); (d) 131–139° at 15 mm., 2.2 g. (impure heptanoate).

Fraction (a) consisted practically entirely of ethyl isobutyrate; on redistillation most of the fraction boiled within the range commonly reported for this ester. Fraction (b) may have contained a little ethyl isobutyryl-isobutyrate but because of the wide boiling range and small quantity obtained no attempt was made to isolate this compound. It should be pointed out that ethyl isobutyryl-isobutyrate would be expected if the isobutyryl chloride used contained any isobutyric acid, since the latter would immediately convert the enolate into the free β-keto-ester.

Fraction (c) was regarded as pure ethyl 2,2,4,4,6-pentamethyl-3,5-diketoheptanoate, while fraction (d) probably consisted largely of this compound. The yield of heptanoate in fractions (c) and (d) was 42% of the theoretical amount, based on the quantity of sodium triphenylmethyl used. In the calculation of this yield it was taken into account that one-half the sodium triphenylmethyl was consumed in condensing ethyl isobutyrate with itself, and

(10) Micro-analysis by R. L. Peck.

(11) Spitzer, *Monatsh.*, **11**, 104 (1890).

that only the remaining half of the base served to enolize the condensation product, ethyl isobutyryl-isobutyrate. The heptanoate was cyclized to hexamethylphloroglucinol as described above; the latter was identified by the mixed melting point method.

Cleavage of Ethyl 2,2,4,4,6-Pentamethyl-3,5-diketoheptanoate by Sodium Ethoxide.—Sodium ethoxide was prepared by dissolving 1.80 g. (0.078 mole) of sodium in 150 cc. of absolute alcohol[12] contained in a flask equipped with a ground-glass joint. The excess alcohol was distilled off on an oil-bath and the residue heated for thirty minutes at 200° under a pressure of 10 mm. Dry nitrogen was admitted into the flask which was then allowed to cool to room temperature. To the sodium ethoxide was added a solution of 5.75 g. (0.022 mole) of ethyl 2,2,4,4,6-pentamethyl-3,5-diketoheptanoate in 500 cc. of dry ether. Several pieces of glass tubing about 2 cm. long were dropped into the flask and a well lubricated glass stopper was inserted and clamped in place. The flask was shaken vigorously until most of the cake of sodium ethoxide had been changed to a fine suspension. The mixture was allowed to stand for seven days with occasional shaking. At the end of that time the reaction mixture was acidified with 7 cc. of glacial acetic acid, extracted with water, washed with 10% sodium carbonate solution, and dried with anhydrous magnesium sulfate. Ether was distilled off through a six-inch (15-cm.) Widmer column. Practically all of the residue distilled over at 100–112°; yield, 5.5 g. This material was presumably ethyl isobutyrate; on redistillation most of it boiled at 109–112°, which is the boiling point commonly reported for this ester. The yield of 5.5 g. of ethyl isobutyrate obtained corresponds to 74% of the theoretical amount.

Reaction of Enolate of Ethyl Isobutyryl-isobutyrate with Acetyl Chloride.—To an ether solution of sodium triphenylmethyl,[9] prepared from 28 g. of triphenylchloromethane, 1000 g. of 1% sodium amalgam, and 750 cc. of dry ether, was added 15.6 g. (0.084 mole) of ethyl isobutyryl-isobutyrate. After standing for thirty minutes, the mixture was poured, with vigorous stirring, into a solution of 10 g. (0.126 mole) of acetyl chloride (Baker and Adamson, reagent grade) in 500 cc. of dry ether. After standing for thirty minutes longer, the mixture was extracted with water, washed several times with 10% sodium carbonate solution, and dried with anhydrous sodium sulfate followed by "Drierite." The solution was filtered, the ether distilled off, and the residue vacuum-distilled, collecting up to 160° at 15 mm. The distillate was vacuum-fractionated on a metal-bath, using a flask equipped with a five-inch (13-cm.) Vigreux column, and without the use of an ebullition tube. The fraction boiling at 122–124° at 15 mm., presumably ethyl 2,2,4,4-tetramethyl-3,5-diketohexanoate (II), was collected; yield, 10 g., 52% of the theoretical amount.

Anal.[10] Calcd. for $C_{12}H_{20}O_4$: C, 63.1; H, 8.83. Found: C, 62.9, 63.6; H, 8.92, 8.78.

Attempts to cyclize the compound synthesized above were unsuccessful. Five grams (0.022 mole) of the compound was added to an ether solution of sodium triphenylmethyl containing approximately 0.044 mole of base. The red color of the base disappeared immediately with the formation of a precipitate. The reaction mixture was allowed to stand overnight; it was then acidified with excess dilute hydrochloric acid and extracted with water. The resulting ether solution was extracted three times with 20% sodium hydroxide solution. The combined alkaline extracts were acidified with dilute hydrochloric acid and extracted with ether. Evaporation of the ether left an oily residue (2–3 g.) which could not be made to crystallize. A similar alkali-soluble oil was obtained when the reaction mixture was acidified ten minutes after the addition of the sodium triphenylmethyl. An alkali-soluble oil also was obtained when an ether solution of the compound was allowed to stand for four days with sodium ethoxide. The oil isolated in these experiments has not yet been identified. The reaction will be studied further.

Summary

1. The sodium enolate of ethyl isobutyryl-isobutyrate has been acylated with acetyl chloride and with isobutyryl chloride. The 3,5-diketo-ester, obtained with the latter acid chloride, on treatment with sodium triphenylmethyl undergoes cyclization to form hexamethylphloroglucinol. This cyclization does not take place in the presence of sodium ethoxide.

2. The significance of the cyclization reaction in relation to the acetoacetic ester type of condensation is discussed.

3. Evidence is presented that the ethyl isobutyryl-isobutyrate obtained from the self-condensation of ethyl isobutyrate by means of sodium triphenylmethyl is in the form of its sodium enolate.

4. Two syntheses of ethyl isobutyryl-isobutyrate are described.

DURHAM, NORTH CAROLINA
RECEIVED SEPTEMBER 25, 1939

(12) Prepared by the method of Lund and Bjerrum, *Ber.*, **64**, 210 (1931).

[A CONTRIBUTION FROM THE RIVERSIDE LABORATORY OF THE UNIVERSAL OIL PRODUCTS COMPANY]

The Catalytic Cracking of Aliphatic Hydrocarbons*

BY GUSTAV EGLOFF, J. C. MORRELL, CHARLES L. THOMAS AND HERMAN S. BLOCH

The thermal decomposition of long-chain aliphatic hydrocarbons is characterized by non-selective chain scission which is undesirable from a utilitarian viewpoint; but little systematic work has been done to develop catalysts which would induce a selective chain splitting. A review of the field[1] led to the conclusion that difficultly reducible refractory oxides were the best potential catalysts for carbon–carbon bond scission. In the present work the effect of an activated silica–alumina mass on the reactions of *n*-butenes, *n*-pentenes, *n*-octenes, cetene, *n*-octane and cetane was studied under conditions which allowed comparisons between (1) the catalyzed and the uncatalyzed reactions; (2) the cracking of paraffins and olefins of the same chain length and (3) homologs in both the paraffin and the olefin series.

Reactions of *n*-Butenes.—A mixture of *n*-butenes has been reported to isomerize to isobutene in the presence of a catalyst consisting of phosphoric acid on various supports.[2,3] Frost and co-workers[2] found that the reversible isomerization of butenes-1 and -2 to isobutene followed the equilibrium equation

$$\log K_p = \frac{304}{T} 0.528 \pm 0.020$$

At 300° the equilibrium mixture contained equal amounts of straight chain and branched chain butenes.

In our experiments the *n*-butenes were passed over the catalyst at temperatures varying from 385 to 600°; the results are summarized in Table I.

It is apparent that under the conditions employed considerable polymerization to higher-boiling materials and decomposition to lighter gases accompanies the isomerization to isobutene. The yield of liquid products reached a maximum of about 25% at 450° (at flow rates of 200–230 volumes of gas per volume of catalyst per hour) and then declined; the yield of light gases increased steadily with rise of temperature, but sharply decreased with rise of flow rate.

At space velocity 200–230, the isomerization was not sensitive to temperature change between 450 and 600°; the C_4 fraction of the product contained 24.1 ± 1.5% of isobutene. The total isobutene yield was raised, however, by increasing the space velocity at 600°, since the side reactions were cut down while the isobutene content of the C_4 product was unchanged. The fact that a 5.7-fold increase of space velocity produced no change in the isobutene content points to the attainment of a pseudo-equilibrium; that true equilibrium was not reached is indicated by the isobutene/*n*-butene ratio, which never exceeded 0.40, although according to the equation of Frost and co-workers[2] the equilibrium ratio ranges from 1.0 at 300° to 0.66 at 600°.

Reactions of *n*-Pentenes.—The catalytic isomerization study was extended to the next higher homologs, *n*-pentenes. Although the thermal isomerization of both pentene-1 and -2 into isopentenes has been reported,[4] the work was not corroborated in a later publication by the same author,[5] and no reliable evidence of such isomerization, either thermal or catalytic, has been published[6]; the inter-isomerization of pentene-1 and -2, however, has been definitely established.[4,5]

n-Pentenes prepared by the catalytic dehydration of *n*-amyl alcohol were passed over the present catalyst at 400° with the results shown in Table II.

Distillation of the C_5 fraction after it had been hydrogenated over a nickel catalyst at 100° showed that it contained 82% of isopentane and 18% of *n*-pentane. The conversion of *n*-pentenes to methylbutenes, therefore, was 53%[7]; at the same time about 8% of gas and 17% of material boiling above pentenes were formed. Since the molar ratio of C_4 to C_6 hydrocarbons recovered was about 1.2, it seems likely that the major portion of these hydrocarbons was formed by the decomposition of pentene dimer.

* Published with the financial assistance of the Universal Oil Products Co.

(1) Egloff and Bloch, *Proc. Second World Petroleum Congr., Paris, France*, **2** (II), 461 (1937).

(2) Frost, Rudkovskiĭ and Serebryakova, *Compt. rend. acad. sci. U. R. S. S.* (N. S.), **4**, 373 (1936); Serebryakova and Frost, *J. Gen. Chem.* (*U. S. S. R.*), **7**, 122 (1937).

(3) N. V. Bataafsche Petroleum Maatschappij, French Patent 823,545, Jan. 21, 1938.

(4) Hurd, *Ind. Eng. Chem.*, **26**, 51 (1934).

(5) Hurd, Goodyear and Goldsby, THIS JOURNAL, **58**, 235 (1936).

(6) Norris and Reuter, THIS JOURNAL, **49**, 2626 (1927).

(7) Allowing for 12.5% of isopentenes present in the charging stock; see Experimental Part.

TABLE I

ISOMERIZATION OF *n*-BUTENES

Furnace temp., °C.		385	400	450	500	550	600	600
Duration, hr.		0.75	2	2	2	2	2	0.5
Space velocity (gas), av.		525	200	230	230	225	205	1160
Wt. % of charge	H.-b. prods.	14	20.2	24.3	20.5	14.4	8.9	12.7
	Gas	86	79.8	75.7	79.5	85.6	91.1	87.3
	Light gas (C_3 and lower)	2.8	7.2	13.1	17.1	21.0	31.4	15.7
	Isobutene	8.0	11.6	14.1	15.9	15.0	14.2	17.1
C_4 fraction, % isobutene		9.6	16.1	22.6	25.6	23.3	23.8	23.8
Ratio isobutene/*n*-butenes		0.11	0.20	0.33	0.40	0.37	0.38	0.34
Gas anal., vol. %	H_2	0.0	0.5	0.0	0.0	4.9	17.5	1.3
	CH_4	0.0	0.3	0.0	0.0	8.7	18.6	3.1
	C_2H_4	0.0	0.0	0.0	0.1	2.2	2.8	0.4
	C_2H_6	0.0	0.0	0.0	1.1	2.1	3.4	1.6
	C_3H_6	3.5	10.4	17.9	22.6	18.7	14.0	17.3
	C_3H_8	0.7	1.0	3.9	3.3	1.7	2.5	1.8
	i-C_4H_8	9.2	14.1	17.7	18.7	14.4	9.8	17.8
	n-C_4H_8		69.4	53.0	46.5	38.9		52.9
		85.6					25.7	
	C_4H_6		0.6	0.2	0.4	0.3		0.9
	C_4H_{10}	1.0	3.7	7.3	7.4	8.2	5.6	3.0

TABLE II

CATALYTIC DECOMPOSITION OF *n*-PENTANES[a]

Furnace temp., °C.		400
Duration, hr.		0.75
Space velocity		3.2
Pentenes charged, g.		150
Products, wt. % of charge	Gas, b. p. <15°	7.6
	C_5, b. p. 15–45°	71.7
	C_6, b. p. 45–72°	7.7
	C_7-C_9, b. p. 72–150°	3.8
	C_{10} and bottoms, b. p. >150°	5.1
	Unaccounted	4.1
Gas analysis, vol. %	H_2	4
	C_2H_4	3
	C_3H_6	5
	i-C_4H_8	34
	n-C_4H_8	28
	C_nH_{2n+2} (index = 2.21)	26

[a] Contains 12.5% or less of *iso*-pentenes.

TABLE III

CATALYTIC CRACKING OF *n*-OCTENES

Furnace temp., °C.		375	385	400
Duration, hr.		2.45	0.5	0.5
Space velocity		4.1	4.2	4.1
n-Octenes charged, g.		720	151	148
Liquid recovered, g.		646	125	117
Liquid product, wt. % of charge	$C_5 + C_6 + C_7$, b. p. 10–95°	10.9	8.3	
	i-C_8, b. p. 95–121.5°	58.2	60.5	
	n-C_8, b. p. >121.5°	20.6	14.7	
Gaseous product	Weight % of charge	8.5	14.4[a]	17.5[a]
	Volume, liters (N. T. P.)	27.0	9.6	11.3
	Molecular weight	50.6	51.1	51.3
Anal., vol. %	H_2	0.1	0.0	0.0
	CH_4	0.8	0.0	0.0
	C_3H_6	35.7	27.5	32.4
	C_3H_8	2.1	1.7	1.9
	i-C_4H_8	30.6	32.5	27.8
	n-C_4H_8	22.4	32.3	28.9
	C_4H_{10}	8.3	6.0	9.0
Unaccounted, wt. % of charge		1.8	2.1	3.4

[a] These gasifications correspond to an initial period of high catalytic activity.

Reactions of *n*-Octenes.—*n*-Octenes (prepared by the catalytic dehydration of octanol-2) not only isomerized when passed over the catalyst but also decomposed. The 20% cracking at 375° is in striking contrast to the 0.4% reaction of *n*-octenes obtained thermally at 364–369° by Hugel and Szayna[8] and the 7% obtained by them at 438–444°. The results of the catalytic cracking at 375, 385 and 400° are summarized in Table III.

The composition of the gases produced catalytically is in sharp contrast to that obtained by Hugel and Szayna in thermal cracking. At 438–444°, the gas formed in the latter process contained over 90% of paraffins and hydrogen; the gas obtained by catalytic cracking contained approximately 90% of propene and butenes, and only traces of materials lighter than the three-carbon hydrocarbons. The composition of the catalytically produced gas is unusual also for the fact that approximately equal quantities of normal and isobutene were present; this was especially true of the runs at 385 and 400°. This isobutene could be formed in at least three ways: (1) direct cracking of the *n*-octenes to give two straight-chain butenes followed by the isomerization of the *n*-butenes; (2) direct cracking of the *n*-octenes into two straight-chain C_4 radicals which are isomerized before rearranging to the

(8) Hugel and Szayna, *Ann. combustibles liquides*, **1**, 781 (1926).

olefin, and (3) the isomerization of the *n*-octenes to *iso*-octenes followed by cracking of the iso-octenes to yield isobutene.

Since this catalyst was also studied with *n*-butenes under similar conditions without producing equal amounts of iso- and *n*-butenes, hypothesis (1) seems unlikely. We have no direct evidence for or against hypothesis (2). Since iso-octenes were isolated there is little doubt that hypothesis (3) is entirely possible. Thus, although we are not able to exclude hypothesis (2), we are inclined to favor hypothesis (3).

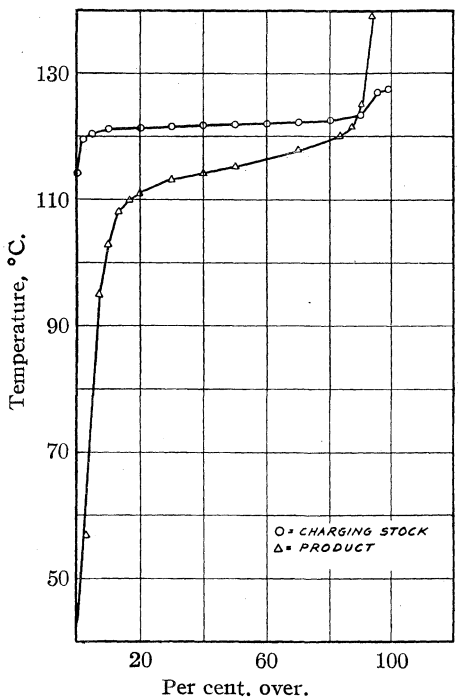


Fig. 1.—Catalytic decomposition of octenes -1 and -2 at 385°.

A study of the distillation curve of the liquid product obtained at 385° (Fig. 1) confirms the isomerization of the octenes; approximately 80% of the octene fraction consisted of iso-octenes boiling lower than the original but boiling above any C_7 olefins. In the 375° run, approximately 75% of the octene fraction consisted of these isoöctenes, as shown in Table III. The catalyst employed in this work was a more effective isomerizing agent than zinc chloride or phosphoric acid on pumice, which, according to Petrov and Cheltsova,[9] converted a mixture of octenes-1 and -2 to a maximum of 45–47% of isoöctenes, under comparable temperature conditions, but with much longer periods of contact.

To determine the constituents of the isoöctene fraction obtained at 375°, all of the product boiling below 121.5° was hydrogenated in the presence of a nickel catalyst at 100° and 100 kg./sq. cm. pressure, and the saturated product distilled on a 50 bubble-plate column of the Bruun type.[10] The distillation curve is shown in Fig. 2. From this curve and refractive indices of several of the fractions, the following hydrocarbons are suggested as likely constituents.[11]

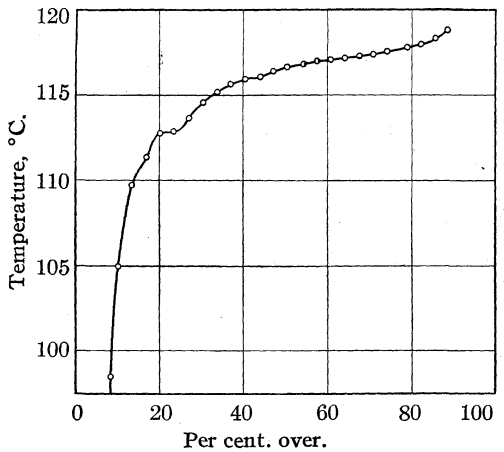


Fig. 2.—Hydrogenated isoöctenes formed from octenes-1 and -2 at 375°.

2,3,4-Trimethylpentane (b. p. 113.8°) corresponding to the first plateau (113.8–113.9°), is the only octane boiling between 111.5 and 114.6° except 2-methyl-3-ethylpentane (b. p. 114°) which is another possibility but is considered less likely.

2-Methylheptane (b. p. 117.2°) corresponds to the second plateau (117.0–117.1 corr.).

4-Methylheptane (b. p. 118.0°) and/or 3,4-dimethylhexane (b. p. 117.9°). The fraction boiling at 117.0–118.0° (corr.) had a refractive index (n^{20}D 1.3987) which indicated that it was probably a mixture of 2-methylheptane (n^{20}D 1.3936) and one or both of the above (n^{20}D 1.4035 and 1.4044, respectively). It seems less likely to contain 3-ethylhexane (b. p. 118.6°, n^{20}D 1.4014) and unlikely to be 3-methyl-3-ethylpentane (b. p. 118.4°, n^{20}D 1.4081).

3-Methylheptane (b. p. 119.0°, n^{20}D 1.3982). The fraction boiling at 118.0–118.8° (corr.) had a

(9) Petrov and Cheltsova, *Compt. rend. acad. sci. U. R. S. S.*, **15**, 79 (1937).

(10) Bruun, *Ind. Eng. Chem., Anal. Ed.*, **8**, 224 (1936).

(11) Grosse and Egloff, "Physical Constants of Paraffin Hydrocarbons," published by Universal Oil Products Co., Chicago, Ill., 1938.

refractive index $n^{20}D$ 1.3982, lower than that of the preceding fraction, and the fraction boiling at 118.8–119.8° (corr.) had an index $n^{20}D$ 1.3987. Since 3-methylheptane is the only octane boiling in this range with a refractive index below 1.4, considerable amounts of this hydrocarbon must have been present.

The over-all picture indicates that the catalyst effects extensive isomerization of *n*-octenes to methylheptenes, dimethylhexenes, and trimethylpentenes, probably by the migration both of alkyl groups and of the double bond. The isoöctenes then crack under the influence of the catalyst, principally to *n*- and isobutenes and to propene and pentenes.

The octene product was hydrogenated and fractionated into an isoöctane cut boiling at 106–119° (corr.). The A. S. T. M. octane number of this cut was 48.5; that of *n*-octane (obtained by hydrogenating the *n*-octenes used in these experiments) in the same engine was −20. This is additional proof that the carbon skeleton of the octene has been changed since, in general, the higher octane number of a given molecular weight paraffin is usually associated with the most highly branched isomer.

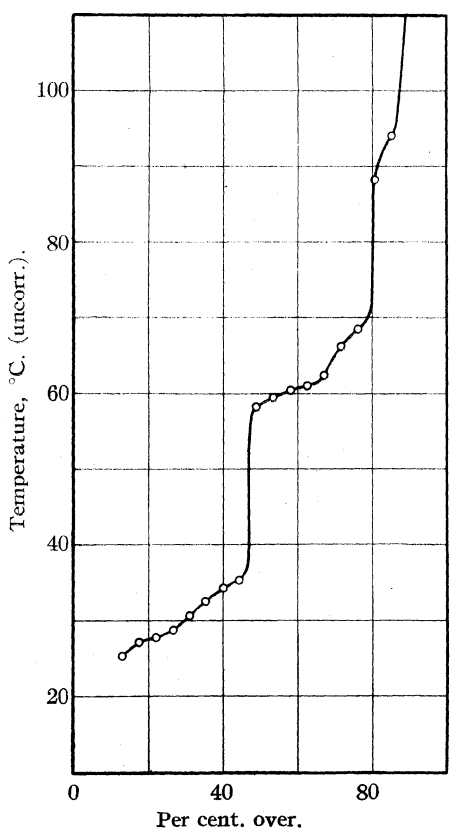


Fig. 3.—Distillation of hydrogenated gasoline from catalytic cracking of cetane.

Cetene Cracking.—From a study of the thermal reactions of cetene at 350 to 725°, Gault and his co-workers[12] concluded that at the lower temperatures olefinic products predominated, while at higher temperatures alicyclic and aromatic hydrocarbons were formed in increasing amounts. The maximum production of olefinic gases (66–68% of the gaseous product) occurred at 575 to 700°, while initial cracking of the cetene began at 450 to 550°, depending on the contact time. Hugel and Goldthorpe[13] found that metallic catalysts lowered the temperature at which reaction began.

With the catalyst used in the present work cetene showed incipient reaction at 300° with a liquid space velocity of four. The gasification under these conditions was only 0.07%, but 8% of the product (neglecting a small amount of residue) boiled over a 6° range immediately below the original boiling range (at reduced pressure). At 350° about 5.5% of the charge was cracked to gasoline and gas; but of the hexadecenes recovered, almost 50% boiled within a 9° range just below that of the original cetene. This fraction was believed to consist of lower-boiling isohexadecenes, since there were no gaseous products such as would have accompanied the formation of 14- and 15-carbon molecules. In run B-331 this lower-boiling hexadecene fraction was catalytically cracked at 350° under the same conditions as were employed for the original cetene; three times as much cracking was effected. These results tend to confirm the tentative conclusions reached in the *n*-octene experiments, namely, that the cracking of normally liquid straight-chain olefins over the present catalyst is largely preceded by isomerization.

The data obtained in the cracking of cetene at 300° to 450° are summarized in Table IV.

It will be noted that the proportion of low-boiling hexadecenes in the C_{16} fraction increases with rising temperature, until practically no cetene is left in the hexadecene fraction of the 450° run.

In order to approximate the course of the reactions, the products were expressed as moles formed per 100 moles of cetene converted to

(12) Gault and Altchidjian, *Compt. rend.*, **178**, 2092 (1924); *Ann. chim.*, (10) **2**, 209 (1924); Gault, Hessel and Altchidjian, *Compt. rend.*, **178**, 1562 (1924).

(13) Hugel and Goldthorpe, *Ann. combustibles liquides*, **3**, 613 (1928).

TABLE IV

CATALYTIC CRACKING OF CETENE

Furnace temp., °C.		300	350	350[a]	400	450
Duration, hr.		3.93	4.0	2.67	4.0	2.78
Space velocity		4.0	4.0	4.0	4.1	4.0
Cetene charged, g.		1230	1255	830	1270	885
Liquid products, wt. % of charge	Total	99	99.5	98.5	95	84
	Gasoline, b. p. 10–200°	0.0	5.1	15.1	43.0	59.5
	Octane number (A. S. T. M.)	...	...	..	77.8	80.6
	Octane number after hydrogenation	...	...	..	34.1	51.6
	Intermed. fr., 200° (750) to 125° (14 mm.)	0.0	0.6	1.1	5.8	8.0
	Low-boiling hexadecenes	8.0	44.9	70.9	26.9	13.0
	Cetene and bottoms	91.0	47.5	9.9	18.3	1.1
Gaseous product	Weight % of charge	0.07	0.44	1.1	4.5	14.1
	Molecular weight	49.2	51	51.5	51	51.2
Anal., vol. %	H_2	0.0	0.0	1.5	0.0	0.0
	CH_4	0.0	0.0	1.2	0.0	0.0
	C_2H_4	20.3	0.7	0.0	3.9	0.0
	C_2H_6		7.3	0.9	0.9	0.0
	C_3H_6	3.5	12.2	18.1	25.8	32.8
	C_3H_8	29.7	17.0	4.6	2.1	3.2
	i-C_4H_8	5.6	14.6	29.5	28.6	27.4
	n-C_4H_8		16.8	36.2	29.2	29.8
	C_4H_{10}	41.0	31.4	8.0	9.4	6.9
Unaccounted, wt. % of charge (including distillation losses)		0.9	1.6	1.9	1.6	4.3

[a] Charge contained 90% of low-boiling hexadecenes, 10% of cetene.

lower-boiling products (other than hexadecenes). The results are shown in Table V.

TABLE V

PRODUCTS OF CETENE DECOMPOSITION

Furnace temp., °C.		350	350[a]	400	450
Decomposition, %		6.1	17.3	53.3	81.6
Moles per 100 moles of cracked cetene	H_2	0.0	0.4	0.0	0.0
	CH_4	0.0	0.3	0.0	0.0
	C_2H_4	0.2	0.0	1.4	0.0
	C_2H_6	2.0	0.2	0.3	0.0
	C_3H_6	3.9	4.8	9.2	25.0
	C_3H_8	5.4	1.2	0.8	2.4
	i-C_4H_8	4.7	7.8	10.2	21
	n-C_4H_8	5.4	9.6	10.4	23
	C_4H_{10}	10.2	2.1	3.4	5.2
	C_5	16[b]	18.8[c]	22.6	36
	C_6	14.7	18.2	26.1	40
	C_7	18.0	19.5	23.7	32
	C_8	34.2	27.0	25.6	24
	C_9	25.2	21.0	23.3	16
	C_{10}			17.3	
	C_{11}	51.4	58.0	10.7	18
	C_{12}			10.0	
	C_{13}				6.2
	C_{14}	11.6	6.7	13.0	0.0
	C_{15}	0.0		0.0	0.0
	Total	202.9	195.6	208.0	248.8

[a] From low-boiling hexadecenes. [b] Of which only 10.2 were recovered, 5.8 assumed lost. [c] Of which only 6.8 were recovered, 12 assumed lost.

In both runs at 350° and in the test at 400°, approximately 200 moles of products were recovered from the cracking of 100 moles of hexadecenes. Practically all of the reaction taking place, therefore, must have been primary. At 450°, on the other hand, of the 200 moles formed by the primary reactions, 50 were cracked in secondary reactions, making it difficult to determine which products are primary and which secondary. For the other three runs, however, a reasonably complete picture of the primary reactions can be given, as shown in Table VI.

The parenthetical figures given for the 400° experiment represent alternate reactions which would also agree with the experimental results, but which would correspond to the different secondary reactions also shown in parentheses. Still others could be devised, but there is no basis for preferring any one set of secondary reactions. Since the amount of secondary reaction is small, however, the over-all picture of the primary reaction is not greatly altered.

The values given in Table VI are in excellent agreement with the molar values given in Table V. The close agreement between the results found for the cetene and the low boiling hexadecenes shows that the products derived from cetene are the same as those from the i-hexadecenes, and confirms the conclusion that the cracking of the former is preceded by isomerization.

TABLE VI

REACTIONS OCCURRING IN CRACKING OF CETENE

Primary cracking reaction	Moles reacting per 100 moles of cetene cracked 350°	350°[a]	400°	Secondary cracking reaction	Moles of primary product reacting per 100 moles of cetene cracked at 400°
$C_{16} \longrightarrow H_2 + C_{16}$	0.0	0.4	0.0		
$C_{16} \longrightarrow C_1 + C_{15}$	0.0	0.3	0.0		
$C_{16} \longrightarrow C_2 + C_{14}$	2	0.2	2		
$C_{16} \longrightarrow C_3 + C_{13}$	9	6	10		
$C_{16} \longrightarrow C_4 + C_{12}$	20	20	12 (17)		
$C_{16} \longrightarrow C_5 + C_{11}$	16	19	17	$C_{11} \longrightarrow C_5 + C_6$	6
$C_{16} \longrightarrow C_6 + C_{10}$	15	18	19 (17)	$C_{10} \longrightarrow C_4 + C_6$ ($C_{12} \longrightarrow 2C_6$)	2 (2)
$C_{16} \longrightarrow C_7 + C_9$	22	20	24		
$C_{16} \longrightarrow 2C_8$	17	14	16 (13)	$C_8 \longrightarrow 2C_4$ ($C_{12} \longrightarrow 3C_4$)	6 (3)

[a] Charging stock: isomerized hexadecenes.

The distillation curves (obtained with a 17-plate vapor-jacketed column[14]) for the hydrogenated gasolines produced at 400 and 450° (Figs. 4 and 5) show plateaus at the same temperatures; but the lower plateaus are broader and the higher plateaus narrower in the 450° curve, corresponding to more secondary cracking of the higher-boiling primary products. This increase in the amount of low-boiling products is probably also responsible for the higher octane numbers found for both the unsaturated and the hydrogenated gasolines produced at 450°, as compared with the 400° product (see Table IV).

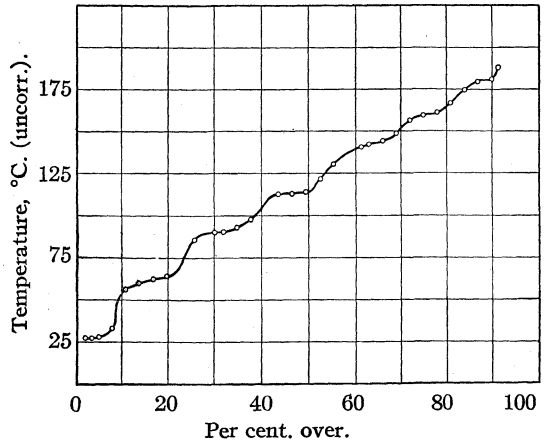


Fig. 4.—Distillation of hydrogenated gasoline from catalytic cracking of cetene at 400°.

The plateaus in the distillation curves indicate the presence of isopentane (28°), 2-methylpentane (60°) and possibly 3-methylpentane (63°) and 2,3-dimethylbutane (58°), the methylhexanes (90–92°) and possibly 2,3-dimethylpentane (90°), the methylheptanes (117–119°) and possibly 2,3-dimethylhexane (116°), the methyloctanes (about 142°), the methylnonanes (about 160–165°) or dimethyloctanes (about 156–160°), and the methyldecanes or dimethylnonanes (about 175–183°). The refractive indices and boiling points obtained at 450° are given in Table VII.

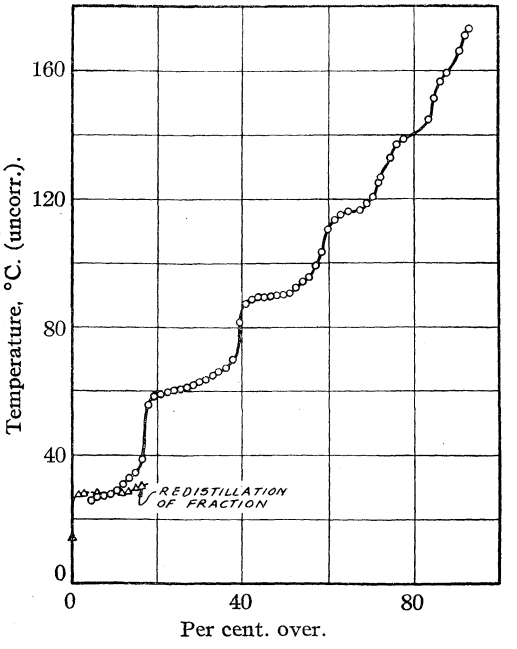


Fig. 5.—Distillation of hydrogenated gasoline from catalytic cracking of cetene at 450°.

It is significant that no appreciable amounts of normal paraffins were present in any fraction of the gasoline, showing that both fragments resulting from the cetene cracking are isomerized. Since thermal scission of an olefin molecule may be expected[4] to occur chiefly at the bond β to the double bond (an observation borne out in this

(14) Tongberg, Quiggle and Fenske, *Ind. Eng. Chem.*, **26**, 1212 (1934).

TABLE VII

SUGGESTED COMPD. IN GASOLINE OBTAINED FROM CETENE AT 450°

Compound	Found B. p., °C. (uncorr.)	Found $n^{20}D$	Literature (11) B. p., °C.	Literature (11) $n^{20}D$
Isopentane	27.8–28.2	1.3543	28.0	1.3552
2-Methylpentane	59.2–60.0	1.3730–1.3736	60.2	1.3717
3-Methylpentane	63.8–64.0	1.3755	63.2	1.3765
2-Methylhexane	89.4	1.3880	90.0	1.3851
3-Methylhexane	90.0	1.3889	91.8	1.3887
2,3-Dimethylhexane	115.6	1.3999	115.8	1.4015
4-Methylheptane	116.4	1.4007	118.0	1.4035
3-Methylheptane	120.2	1.4020	119.0	1.3982
(3-Ethylhexane)			118.6	1.4014

catalytic work by the absence of appreciable quantities of gaseous products containing fewer than three carbon atoms) and since it is further apparent from Table VI that scission takes place to an almost equal extent at each C—C bond of the molecule (except at the three bonds nearest each end of the chain) we may conclude that cetene is catalytically cracked chiefly according to the following successive steps: (1) isomerization of cetene to lower-boiling branched-chain hexadecenes, either with or without migration of the double bond; (2) scission of the chain to an almost equal extent at each bond except those near the extremities of the molecule; (3) isomerization of any normally liquid olefinic products to isoölefins; and (4) with longer contact times or at higher temperatures, secondary decomposition of the longer-chained primary products as in steps 2 and 3, so that the products having fewer than eight carbon atoms increase in amount, while those having more than eight carbon atoms decrease in amount.

It should further be pointed out that small amounts of paraffinic products are formed, and that corresponding to these there should also be either diolefins (not necessarily conjugated), acetylenes, cyclo-olefins, or aromatics in the product. Alternatively a small amount of carbon deposit on the catalyst accounts for the liberation of sufficient hydrogen to hydrogenate a portion of the olefinic product.

Cracking of *n*-Octane.—The previous work on the catalytic and pyrolytic decomposition of *n*-octane has already been adequately summarized.[15,16] In none of the catalytic work were refractory oxide catalysts employed; of the pyrolytic work, that of Marschner[16] is the most complete and was carried out under temperature conditions similar to the present work, so that his results are comparable.

The catalytic decomposition of *n*-octane was carried out at 525, 540, 555 and 570°, at a liquid space velocity of four volumes of liquid octane per volume of catalyst per hour. The results are summarized in Table VIII.

TABLE VIII

CATALYTIC CRACKING OF *n*-OCTANE

Furnace temp., °C.		525	540	555	570
Duration, hr.		0.5	0.5	0.5	0.5
Space velocity		4.1	4.3	4.2	4.2
n-Octane charged, g.		144	152	147	147
Liquid recovered, g.		141	148.4	142	138
Gaseous product[d]	Weight % of charge	1.8	2.7	4.0	5.4
	Volume, liters (N. T. P.)	2.0	2.9	4.1	5.7
	Molecular weight	34.5	36.8	36.5	36.7
	Anal., vol. % H_2	16.3	15.1	12.9	9.0
	Anal., vol. % CH_4	34.9[a]	32.5[c]	8.8	6.1
	Anal., vol. % C_2H_4	20.3	15.0	13.3	12.6
	Anal., vol. % C_2H_6			7.2	7.0
	Anal., vol. % C_3H_6	26.7[b]	32.4[b]	20.4	34.5
	Anal., vol. % C_3H_8			16.5	11.5
	Anal., vol. % i-C_4H_8	2.0	7.3	5.1	6.1
	Anal., vol. % n-C_4H_8			12.4	8.5
	Anal., vol. % C_4H_{10}			3.5	4.9
Unaccounted, wt. % of charge		0.0	−0.7	−1.0	0.0

[a] Total paraffins; index 2.30. [b] Includes *n*-butenes. [c] Total paraffins; index 2.51. [d] Does not include gas dissolved in the liquid product which may amount to 1–2% of the octane charged.

Because of the small amount of reaction and of materials used, a complete analysis of the products was made only in the case of the 570° run. The results are shown in Table IX, together with comparable thermal results calculated from the data of Marschner.

TABLE IX

CATALYTIC AND PYROLYTIC CRACKING OF *n*-OCTANE

		Catalytic	Marschner, pyrolytic
Furnace temp., °C.		570	570
Contact time, seconds		1.0	12.7
Decompn., %		11.0	19.4
Moles of products per mole of octane cracked		2.4	3.2
Complete product analysis, moles per 100 moles of octane cracked	H_2	13	0.3
	CH_4	9	77
	C_2H_4	19	86
	C_2H_6	11	55
	C_3H_6	52	46
	C_3H_8	18	6.5
	C_4H_8	22	18
	C_4H_{10}	7	1.3
	C_5	73	15
	$C_6 + C_7$	16	21
Unaccounted, wt. % of charge		2.2	0.8

Although the degree of cracking in the two runs differs considerably, a comparison is justifiable because of Marschner's conclusion that for pyro-

(15) Egloff, "Reactions of Pure Hydrocarbons," Reinhold Publishing Co., New York, 1937.

(16) Marschner, *Ind. Eng. Chem.*, **30**, 554 (1938).

lytic decomposition "the product analyses were the same when decomposition was increased from 18 to 33%, . . . and differed but little from those obtained at 538°" where 11% cracking was obtained. Furthermore, the incomplete analyses of Dintzes and Zherko[17] for 13% conversion at 570° check closely those of Marschner for 19% decomposition at the same temperature, indicating that essentially the same reactions occur over a rather wide range of temperature and conversion.

It is clear from Table IX that the pyrolytic cracking results in a greater yield of methane, ethane and ethylene than the catalytic reaction, and a far smaller yield of C_5–C_7 hydrocarbons and of hydrogen. Furthermore, from the work of Marschner and of Dintzes and Zherko, it is estimated that to attain a pyrolytic cracking of 11% at 570°, a contact time of seven or eight seconds would be necessary. The catalyst therefore shortens the time of the reaction seven- to eightfold. It is also significant that the *n*-octenes decomposed so much more easily over the catalyst that at 375° there was twice as much cracking as with *n*-octane at 570° with comparable feed rates.

Cetane Cracking.—The cracking of cetane has been studied both thermally[12,18] and catalytically[19] by Gault and his associates, who concluded that in the absence of catalysts the carbon chain was broken indiscriminately at any point, but that with rising temperature the point of scission approached the chain end. The use of quartz or pumice tube-packing lowered the cracking temperature somewhat. This temperature lowering is probably due to more efficient heat transfer to the reacting system rather than to any catalytic properties of the quartz or pumice. The catalysts studied by Gault were of the metallic (*e. g.*, nickel) type so that the reactions produced involved the carbon–hydrogen bonds rather than the carbon–carbon bonds. Such catalytic results are not comparable with the present work.

In the present study cetane was cracked catalytically at 500° and liquid space velocity four. Because of the small amount of reaction and the limited amount of cetane available, the cetane recovered from the first pass (boiling in the original boiling range) was recycled and that recovered from the second pass was further recycled. The low-boiling liquid products of the three passes were combined and hydrogenated; the gases were separately analyzed, but showed substantially the same composition. The composite results are shown in Tables X and XI.

TABLE X

CATALYTIC CRACKING OF CETANE AT 500° (COMPOSITE OF THREE PASSES)

Duration, hr.	8.74
Space velocity, cc./cc. cat./hr.	4.0
Total cetane charged, g.	2728
Liquid product (b. p. >10°), wt. % of charge	88.5
Gasoline, b. p. 10–200°, wt. % of charge	6.9
Intermediate fraction, b. p. 200° (750 mm.) — 144° (13 mm.)	3.6
Cetane, b. p. 144-147° (13 mm.)	76.4
Bottoms	1.6
Gaseous product	
Weight % of charge	11.1
Volume, liters (N. T. P.)	147
Molecular weight	48
Unaccounted, wt. % of charge	0.4

TABLE XI

PRODUCTS OF CETANE CRACKING

Product	Volume %		Moles per 100 moles of cetane decompd.
H_2	1.5	Gas	3.7
CH_4	1.7		4.2
C_2H_4	1.0		2.4
C_2H_6	2.0		4.9
C_3H_6	32.8		80
C_3H_8	12.6		31
i-C_4H_8	11.5		28
n-C_4H_8	21.0		51
C_4H_{10}	16.0		39
C_5	42	Gasoline	41
C_6	28		25
C_7	11		8.3
C_8-C_{12}[a]	19		11.4
C_{13}-C_{15}[b]			18.5

[a] Assumed molecular weight, 130. [b] Assumed molecular weight, 196.

From the fact that approximately 350 moles of reaction products was formed from 100 moles of cracked cetane, it is apparent that these are not the primary products, and no definite reaction mechanism can be postulated. It is interesting, however, that every mole reacting yielded approximately one mole each of C_3, C_4 and gasoline boiling-range hydrocarbons, indicating a selectivity of the catalyst for the formation of three-carbon and four-carbon fragments. In this respect the results differ from those of Gault[12,18] on thermal cracking, since his products led him to conclude that the initial step in the decomposition

(17) Dintzes and Zherko, *J. Gen. Chem.* (*U. S. S. R.*), **6**, 68 (1936).

(18) Gault and Barmann, *Ann. combustibles liquides*, **1**, 77 (1926); Gault and Hessel, *Compt. rend.*, **179**, 171 (1924); *Ann. chim.*, (10) **2**, 319 (1924).

(19) Gault and Sigwalt, *Ann. combustibles liquides*, **2**, 309, 543 (1927).

was the breaking-off of terminal groups forming methane and ethylene. Although exact comparisons with Gault's work are not possible due to the incompleteness of his data, it appears that in the experiments carried out in empty and packed tubes higher temperatures or longer contact times were required to attain the degree of cracking found in our experiments.

The preponderance of small molecules in the present study and the analytical data indicate either that the primary reaction products are more unstable than cetane itself, and that they are 75 to 100% decomposed to secondary products as compared with the 20% decomposition of cetane, or that the cetane molecule is ruptured at several points simultaneously.

The greater stability of *n*-octane as compared with cetane is indicated by the 11% decomposition of the former with the same catalyst and space velocity at a temperature 70° higher (570°) than that required to produce 20% decomposition of cetane.

The hydrogenated gasoline from the cetane decomposition had an A. S. T. M. octane number of 70. Distillation of this hydrogenated product on a 17-theoretical plate column of the vapor jacket[14] type, gave the curve shown in Fig. 3 and indicated the presence of isopentane (b. p. 28°), *n*-pentane (b. p. 36°), 2-methylpentane (b. p. 60°), *n*-hexane (b. p. 60°), and 2-methylhexane (b. p. 90°); 3-methylhexane (b. p. 92°) and 2,3-dimethylpentane (b. p. 90°) also may be present. No *n*-heptane appeared to be present; higher boiling constituents could not be determined because of the small amount of gasoline available. Isopentane, isohexane and isoheptane were all present in greater amounts than the corresponding normal compounds.

Experimental Part

Materials.—*n*-Butenes were prepared by the dehydration of butanol-2 over activated alumina. Low-temperature fractionation showed the following percentage composition: C_3 hydrocarbons 0.2, butene-1 fraction 15.2, butene-2 fraction 83.8, C_5 and higher 0.8. A small amount of isobutene and butanes may also have been present; the C_4 fraction showed 1.8% absorption in 64% sulfuric acid and 95% absorption in 87% sulfuric acid.

Pentene-1 was prepared from a selected cut (134.0–135.8°) of Eastman Technical pentanol-1 by dehydration over activated alumina at 400°. The pentene fraction was separated from the unreacted amyl alcohol and redistilled over sodium hydroxide in a 50-bubble cap column of the Bruun type.[10] The fraction used in this work boiled at 28–31°, and had a refractive index $n^{20}D$ 1.3720, as compared with the literature value of $n^{20}D$ 1.3711.[20] After hydrogenation the refractive index was $n^{20}D$ 1.3574 as compared with the literature value for *n*-pentane of $n^{20}D$ 1.3576. Distillation with a column of 17 theoretical plates efficiency, however, showed the presence of a maximum of 12.5% of isopentane and a minimum of 87.5% of *n*-pentane.

***n*-Octenes and *n*-Octane.**—The *n*-octenes used in the experiments at 385 and 400° were prepared by the dehydration of capryl alcohol over activated alumina at 400° and purified by distillation through a Hempel column. The distillation curve with a small laboratory column of 5 to 10 theoretical plates[21] is shown in Fig. 1. Approximately 10% boiled below 121°, and 7.5% above 125°; the refractive index was $n^{20}D$ 1.4131. The *n*-octenes used in the experiment at 375° were the fraction of the above octenes boiling at 121.2–124.9°, and had an index of refraction $n^{20}D$ 1.4133.

The *n*-octane was prepared by hydrogenation of the Hempel cut of *n*-octenes, and had a refractive index $n^{20}D$ 1.3978, as compared with the value[11] of 1.3980. The melting point was −58°.

Cetane.—Dupont Diesel Standard cetane was used without further purification.

Cetene.—Dupont cetene (technical) was redistilled *in vacuo* in a Claisen flask fitted with a 6-inch (15-cm.) Vigreux side-arm, and the fraction boiling at 148–151° at 7 mm. (d_4^{20} 0.778) was employed in this work; 13.5% of lower-boiling and 12% of higher-boiling material were discarded. All of the vacuum distillations analyzing the products were made in the same Claisen flask as that described above.

Experimental Procedure.—The charging stock was pumped by a copper-bellows pump[22] to an electrically heated preheater of stainless steel tubing maintained at such a temperature that the emergent vapor was at the reaction temperature, and thence into a 100-cc. stainless steel reaction chamber filled with 6–10 mesh granules of catalyst in a bed 15 cm. long. Although the catalyst chamber was supported in an electrically heated aluminum-bronze block which was maintained at a temperature constant to within ±1°, the actual temperature of the catalyst bed (which was read with a movable iron–constantan thermocouple) varied considerably because of the character of the reaction. For example, in the run with cetene at 450°, the reaction was endothermic and a temperature drop of 40° existed between the top of the bed and a point near the bottom. In the pentene run, however, there was a temperature rise in the first portion of the catalyst bed followed by a temperature drop so that although the furnace was maintained at 400°, the actual catalyst temperature varied between 448 and 370°. In the butene runs a temperature rise was observed also. A number of hypotheses have been considered to explain these unexpectedly large temperature changes, but as yet none of them is satisfactory.

The reaction products were led through a water condenser and a vertical ice reflux condenser fitted above a

(20) Leendertse, Tulleners and Waterman, *Rec. trav. chim.*, **53**, 715 (1934).

(21) Thomas, Bloch and Hoekstra, *Ind. Eng. Chem., Anal. Ed.*, **10**, 153 (1938).

(22) Tropsch and Mattox, *Ind. Eng. Chem.*, **26**, 1338 (1934).

receiving flask for the liquid product. The gases were analyzed by a combined low-temperature fractionation and absorption analysis. In the analysis of the butenes 63% sulfuric acid was used to absorb isobutene and 87% acid the *n*-butenes. The condensable portion of the gases was collected in a dry-ice–trichloroethylene trap, and the C_5 and higher-boiling hydrocarbons recovered by a low-temperature distillation with the column previously described.[21] The dissolved gas was removed from the liquid product by the same column and separately analyzed, although in some cases a weighted composite sample of all the gaseous products was analyzed. Maleic anhydride absorption was used in butadiene determination.[23]

Summary

A number of hydrocarbons cracked at atmospheric pressure in the presence of an activated silica–alumina catalyst showed the following behavior:

1. A mixture of *n*-butenes underwent extensive catalytic isomerization to isobutene in the temperature range 385 to 600°, accompanied by polymerization and cracking. Between 450 and 600° the isobutene content of the C_4-product was 24.1 ± 1.5%.

2. *n*-Pentenes showed reactions similar to those of the butenes, yielding 50% of isopentenes at 400°.

3. A mixture of *n*-octenes underwent both catalytic isomerization to isoöctenes and catalytic cracking to gaseous products consisting principally of equal amounts of normal and isobutene. The results are consistent with the theory that isomerization precedes cracking. In the temperature range 375 to 400° the conversion was over 80%.

4. The primary catalytic reaction of cetene in the range 300 to 450° was isomerization to isohexadecenes; the secondary reaction was cracking to lower-boiling olefins, accompanied by isomerization of normal olefinic products to isoolefins. The isohexadecenes catalytically cracked approximately three times as rapidly as cetene itself.

5. *n*-Octane catalytically cracked seven to eight times as rapidly as in thermal decomposition, and the catalytic products contained more C_5–C_7 hydrocarbons and less methane, ethane, and ethylene than the pyrolytic products. The temperature required for the catalytic cracking of octane was 200° higher than that required for *n*-octenes.

6. Cetane was catalytically cracked largely to C_3, C_4 and C_5 hydrocarbons. The gasoline boiling-range products contained both branched-chain and straight-chain hydrocarbons, in contrast to the products of cetene cracking, which were essentially all branched-chain.

Although the behavior in thermal cracking of cetane and cetene is quite similar, cetane is far more stable toward catalytic cracking than cetene. In both cases, the products of catalytic cracking are quite different from those of pyrolytic cracking.

CHICAGO, ILLINOIS RECEIVED APRIL 24, 1939

(23) Tropsch and Mattox, *Ind. Eng. Chem., Anal. Ed.*, **6**, 104 (1934).

[CONTRIBUTION NO. 58 FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF UTAH]

The Adsorption of Hydrogen by Copper Dispersed in Calcium Oxide

BY JOHN R. LEWIS, LAWRENCE J. E. HOFER AND HOWARD WHITEHEAD

Recently a paper[1] by Lewis and Taylor appeared in which the data for the adsorption of hydrogen by copper dispersed in magnesia were given. Papers by Joris, Verhulst and Taylor[2] and by Taylor and Joris[3] showed (1) that copper, when prepared by the method[1] of Lewis and Taylor, is highly dispersed in magnesia, and (2) that this dispersed copper is an excellent catalyst for hydrogenation reactions.

Because of the chemical similarity of magnesia and calcium oxide, one would expect that calcium oxide, like magnesia, would be an excellent dispersing medium for copper and therefore adsorption measurements and catalytic studies on copper dispersed in calcium oxide would prove to be of special interest.

This paper presents the data for the adsorption of hydrogen (1) on pure calcium oxide, and (2) on copper dispersed in calcium oxide.

(1) Lewis and Taylor, THIS JOURNAL, **60**, 877 (1938).

(2) Joris, Verhulst and Taylor, *Bull. soc. chim. Belg.*, **46**, 393 (1937).

(3) Taylor and Joris, *ibid.*, **46**, 241 (1937).

Experimental

Apparatus.—The apparatus used for this work is a modified form of that used in Princeton for similar investigations.

Gases.—Hydrogen was prepared by the electrolysis of a 15% sodium hydroxide solution using nickel electrodes.

The gas was purified and dried by first passing it through anhydrous calcium chloride and then through an electrically heated tube (350°) containing platinized pumice, and finally through a phosphorus pentoxide drying tube.

Nitrogen, used to determine the dead space of the adsorption tube, was prepared by the reaction of ammonium chloride on sodium nitrite. The gas was purified and dried by first passing it over anhydrous calcium chloride, then over finely divided copper maintained at 500°, and finally through a phosphorus pentoxide drying tube.

Preparation of Adsorbents.—Adsorbent No. 1: Copper dispersed in calcium oxide.—A solution of copper ion and calcium ion in the ratio of approximately one Cu^{++} to four Ca^{++} was precipitated by the dropwise addition of the hydroxide while the solution was stirred vigorously. The precipitate was washed by decantation and then treated as follows: first it was heated at 120° for forty-eight hours, then at 350° for forty-eight hours. Finally the dried precipitate was placed in a suitable tube and sealed to the adsorption apparatus. The temperature was raised to 434° and a stream of hydrogen, 25 to 30 bubbles per minute, was passed through the tube for forty hours. At this point the copper oxide was completely reduced to metallic copper. Chemical analysis showed this adsorbent to contain 22.5% copper.

Adsorbent No. 1a: Pure calcium oxide.—This adsorbent was prepared in a manner similar to that used for adsorbent No. 1 except no copper was present. The temperatures and the times of drying were the same as for Adsorbent No. 1.

Adsorbent No. 2: Copper dispersed in calcium oxide.—A solution containing copper ion and calcium ion in the ratio of approximately one Cu^{++} to four Ca^{++} was precipitated as before. It was dried at 60° for twenty-four hours, then at 90° for three hours, then at 120° for ten hours and finally at 360° for seventy-two hours. The dried precipitate was then placed in a reaction tube and sealed to the adsorption apparatus. The tube and contents were heated to 210° with the "Hyvac" oil pump in operation. This was continued for twenty-four hours, after which a stream of hydrogen was passed through the tube containing the mixed oxides, temperature remaining at 210°, for one hundred and sixty-eight hours. At this point reduction of the copper oxide was complete. Chemical analysis showed this adsorbent to contain 19.3% copper.

Adsorbent No. 2a: Pure calcium oxide.—This adsorbent was prepared in exactly the same way as Adsorbent No. 2 except that copper was not present. The temperatures and times of drying were the same.

Experimental Results

The quantities of hydrogen, in cubic centimeters, which were adsorbed at 650 mm. and at various temperatures have been calculated to standard temperature and pressure (S. T. P.) and placed in Table I, and also shown graphically in Fig. 1. Due to the very slow rate at which equilibrium is reached, the quantities reported are not necessarily the true equilibrium values. Some measurements extended over a period of seventy-two hours before readings became sensibly constant. Duplicate runs checked within 10%.

TABLE I

THE VOLUME[a] OF HYDROGEN ADSORBED ON PURE CALCIUM OXIDE AND ON COPPER DISPERSED IN CALCIUM OXIDE

CC. PER GRAM (S. T. P.)

Temp., °A.	Adsorbent 1	Adsorbent 1a	Adsorbent 2	Adsorbent 2a
273	0.101	0.006	0.076	0.016
298	.107	.002	...	...
348	.206	.008	.321	.014
369	.172	.006	.191	.014
399	.132	.007	.162	.014
451	.106	.008	...	...
483	.079	.027	.032	.004
570	.184	.155	.072	.024
707	.097	.160	.064	.095

[a] The measurements were made on 25.94 g. of Adsorbent 1, 20.52 g. of Adsorbent 1a, 19.47 g. of Adsorbent 2, and 19.85 g. of Adsorbent 2a. From these were calculated the data which are given in this table.

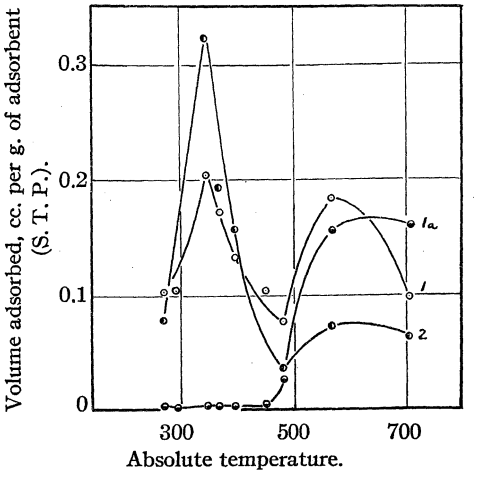


Fig. 1.—The adsorption of hydrogen on calcium oxide and on copper dispersed in calcium oxide at 650 mm. and at various temperatures: Curve 1a, cc. of gas on 1 g. of adsorbent 1a (pure calcium oxide); Curve 1, cc. of gas on 1 g. of adsorbent 1 (copper dispersed in calcium oxide); Curve 2, cc. of gas on 1 g. of adsorbent 2 (copper dispersed in calcium oxide).

The data in Table II and curves 1 and 2 in Fig. 2 were obtained by applying a correction to the values given in Table I. These corrected values were obtained by means of the equation

$$A_t = A_{Cu}F_{Cu} + A_{CaO}F_{CaO} \qquad (1)$$

where A_t is the total adsorption in cc. of hydrogen per g. of adsorbent. A_{Cu} is the adsorption due to copper; F_{Cu} is the fraction, by weight, of copper in the adsorbent; A_{CaO} is the adsorption of hydrogen in cc. per g. of pure calcium oxide; F_{CaO} is the

fraction by weight of calcium oxide in the adsorbent. The assumptions necessary to use Equation I are: (a) the adsorptive capacity of calcium oxide is the same in the pure state and when it is mixed with dispersed copper. (b) For each adsorbent, all the dispersed copper particles are in the same physical state, and their adsorptive capacity is not impaired until the sintering temperature is reached.

TABLE II

THE VOLUME OF HYDROGEN ADSORBED ON DISPERSED COPPER. CC. PER GRAM (S. T. P.) AS GIVEN BY EQUATION 1

	Temperature, °A.								
	273	298	348	369	399	451	483	570	707
1	0.43	0.47	0.89	0.74	0.56	0.44	0.26	0.28	(−0.12)
2	0.32	..	1.56	0.91	0.76	..	0.15	0.27	(−0.06)

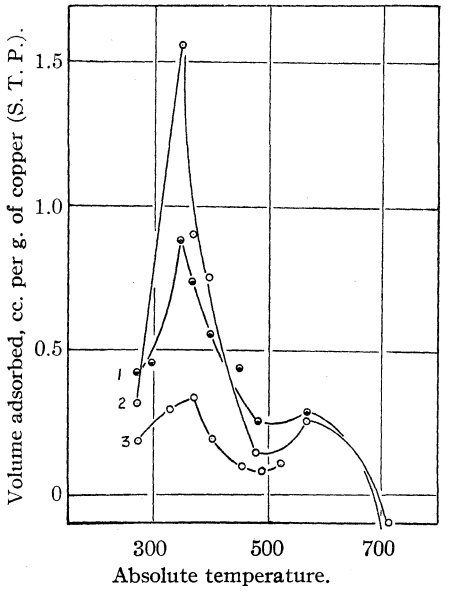


Fig. 2.—The adsorption of hydrogen on pure copper and on copper dispersed in calcium oxide at 650 mm. pressure and at various temperatures and corrected for the hydrogen adsorbed on the calcium oxide by the use of Equation (1). Curve 1 shows the cc. of gas per gram of copper dispersed in adsorbent 1; Curve 2 shows cc. of gas per g. of copper dispersed in adsorbent 2; Curve 3 is for pure copper and was taken from the paper by Lewis and Taylor for purposes of comparison.

Discussion of Results

An examination of the data in Table I and the curves in Fig. 1 show: (1) calcium oxide, curve 1a, is a poor adsorbent over the temperature range 300 to 475° A., but at 475° A. the adsorption increases rapidly with temperature rise until 570° A. is reached. From there on up to 707° A. the slope of the curve decreases. In general we can say that calcium oxide resembles magnesia in its ability to adsorb hydrogen.

Curve 1, Fig. 1, shows the adsorption on adsorbent 1, while curve 2 shows the adsorption on adsorbent 2. The difference in the amounts adsorbed by the two adsorbents, at the various temperatures, is attributed to the different methods used in their preparation. It is interesting to observe, however, that maximum and minimum adsorptions for each adsorbent come at practically the same temperatures. This indicates that the same type of activated adsorption is taking place on each adsorbent. It is also interesting to observe that adsorbent 2 is more effective at 348° A., whereas adsorbent 1 is more effective at 570° A. The higher adsorptive capacity of adsorbent 2 at 348° A. is attributed to the higher activity of the copper.[4,5] It is more active because (1) it was prepared by the reduction of the oxide at 210°, whereas the copper in adsorbent 1 was obtained by reducing the oxide at 434°, and (2) adsorbent 2 was always degassed at 210°, rather than at 434° the temperature used in degassing adsorbent 1. The higher adsorptive capacity of adsorbent 1 at 570° A. is due to the fact that it was completely dehydrated, whereas adsorbent 2 was not.

Using the equation as given above, the data in Table II and the curves in Fig. 2 were obtained. Curve 3, Fig. 2, was taken from the data obtained by Lewis and Taylor[6] for purposes of comparison. It will be observed that, when the adsorption on calcium oxide is corrected for, by use of the equation, the dispersed copper is a much more effective adsorbing agent than is the pure copper. The apparent negative adsorption for adsorbents 1 and 2 at 707° A. may be due to the fact that the calcium oxide is not adsorbing as much hydrogen at that temperature when it is mixed with the copper, as when it is pure. Also, at 707° A. copper may have lost part of its capacity for adsorbing hydrogen, due perhaps to the adsorption curve passing through a temperature minimum. The third possibility is that part of the calcium oxide is covered with copper, which makes that part of the oxide unavailable to the hydrogen.

Summary

1. The adsorption of hydrogen on pure calcium oxide and on copper dispersed in calcium

(4) Gauger and Taylor, THIS JOURNAL, **45**, 920 (1923).
(5) Pease, *ibid.*, **45**, 2296 (1923).
(6) Lewis and Taylor, *ibid.*, **60**, 877 (1938).

oxide has been measured at 650 mm. and at various temperatures.

2. Copper, when dispersed in calcium oxide, is a better adsorbent for hydrogen than is the pure copper.

3. In general the activated adsorption of hydrogen on calcium oxide and on copper dispersed in calcium oxide resembles the adsorption of hydrogen on magnesia and on copper dispersed in magnesia.

4. An equation has been suggested, the use of which permits the more uniform treatment of the data for copper dispersed in oxides.

SALT LAKE CITY, UTAH RECEIVED AUGUST 21, 1939

NOTES

Note on the Dipole Moment of 1-Chloroanthraquinone

BY ERNST BERGMANN AND ANNA WEIZMANN

In connection with a stereochemical investigation in the series of anthracene dichlorides, we reported, a short time ago,[1] some figures on the dipole moment of chloroanthraquinone, which we calculated to 1.9 *D*. Fischer and Rogowski[2] arrived recently at lower figures of 1.53 (in benzene) and 1.55 (in dioxane), respectively. Although without influence on the general results put forward in our paper, we have reinvestigated 1-chloroanthraquinone both in benzene and again in dioxane solution and have found 1.8 and 1.9 *D*, respectively. Following the procedure of the German authors, we have taken the average of the (atomic and) orientation polarization in order to calculate the electric moment, instead of extrapolating to infinite dilution, which would have given even a slightly higher figure.

The *significance* of figures in the tables is as in previous communications.

τ	ρ	ϵ	n^2	$P_{1/2}$	$P_{E^{1/2}}$	P	P_E	P_{A+O}
			Dioxane solution; t = 24.2°					
0	1.0276	2.2553	2.0135	25.2628	21.6250	....	...	...
0.00906	1.0350	2.3200	2.0278	26.3919	22.0405	149.91	67.51	82.40
.01566	1.0404	2.3562	2.0392	27.0544	22.3584	139.62	68.43	71.19
.01739	1.0418	2.3645	2.0415	27.2100	22.4300	137.23	67.90	69.31
			P^{∞}_{A+O} = 74.30; μ = 1.9 *D*					
			Benzene solution; t = 24.6°					
0	0.8732	2.2747	2.2404	26.6302	26.1288	....	...	...
0.00914	.8832	2.3220	2.2506	27.5327	26.4831	124.69	64.88	59.81
.01282	.8872	2.3468	2.2570	27.9744	26.6447	131.06	66.39	64.67
.01817	.8930	2.3923	2.2627	28.7420	26.8606	142.53	66.40	76.13
			P^{∞}_{A+O} = 66.87; μ = 1.8 *D*					

THE DANIEL SIEFF RESEARCH INSTITUTE
REHOVOTH, PALESTINE RECEIVED JULY 5, 1939

(1) E. Bergmann and A. Weizmann, THIS JOURNAL, **60**, 1801 (1938).

(2) Fischer and Rogowski, *Physik. Z.*, **40**, 331 (1939).

The Optical Activity of α-Bromopropionitrile

BY KENNETH L. BERRY AND JULIAN M. STURTEVANT

In connection with recent physical theories of optical rotatory power,[1,2] it would be of interest to know the optical properties of one or more compounds of simple, fixed structure, *i. e.*, compounds containing one asymmetric carbon atom substituted by four groups having optical axes of symmetry parallel with the valence bonds to the asymmetric carbon atom.

(1) Kirkwood, *J. Chem. Phys.*, **5**, 479 (1937).

(2) Condon, Altar and Eyring, *ibid.*, **5**, 753 (1937).

The simplest molecule heretofore available for purposes of comparison of theory with experiment is secondary butyl alcohol.[1,3,4] In view of the uncertainties introduced by the non-linearity of the ethyl and hydroxyl groups, this substance has proved not too satisfactory. Therefore, α-bromopropionitrile has been prepared in an optically active form, since it appears reasonable to assume that each of the groups attached to the asymmetric carbon atom has cylindrical symmetry. Strong evidence in favor of this assumption in the case of the nitrile group is given by Brockway,[5] who demonstrated the linearity of C—C≡N in methyl cyanide by the electron diffraction method, and by Weissberger and Sängewald,[6] who found a zero dipole moment for *p*-dicyanobenzene. The result of Bretscher[7] attributing a relatively large moment to 4,4′-dicyanodiphenyl has been considered anomalous by Le Fèvre and Vine,[8] and as not proving any lack of axial symmetry in this molecule.

Kirkwood's theory leads to the following simple expression for the rotatory parameter of an active molecule in terms of the geometrical configuration and the polarizability tensors of its constituent groups

$$g = g^{(0)} + g^{(1)} + \sum_{k=1}^{N+1} g_k$$

In molecules with only one asymmetric center the g_k vanish. Each term in $g^{(0)}$ vanishes if the optical axes of symmetry of the groups are parallel to the respective bonds linking them to the asymmetric carbon atom. The rotatory power must then be sought in higher terms which are considered by Kirkwood to be relatively unimportant. Thus α-bromopropionitrile might be expected to have a small specific rotation.

l-α-Bromopropionitrile was prepared from *l*-α-bromopropionic acid by asymmetric conversion. The rotation of the acid indicated it to be 67.1% levo and 32.9% dextro. It was converted to the amide and the latter dehydrated with phosphorus pentoxide to obtain the nitrile. After one distillation the nitrile had a specific rotation $[\alpha]^{25}D$ −5.29°, and after a second distillation $[\alpha]^{25}D$ −5.25°. The final product analyzed 10.44, 10.50, and 10.49% nitrogen (calcd. for $CH_3CHBrCN$, 10.46%). On the assumption that no racemization occurred during the synthesis, the calculated specific rotation for the optically pure compound is $[\alpha]^{25}D$ −15.33°. The true value would, of course, be higher if some racemization had occurred.

On first sight, this result indicates that greater importance should be attached to the higher approximations of the polarizability theory. Kirkwood[9] points out, however, that it is not unquestionable evidence since lateral optical anisotropy of sufficient magnitude to account for the observed rotation could be induced in the CN group, probably by the C-Br dipole.

Since this molecule is of considerable interest from a theoretical point of view, efforts will be made to prepare it in a state of higher optical purity. The refractive and rotatory dispersion behavior of the substance in the visible region will be determined.

A more unambiguous test of the importance of the higher terms in Kirkwood's theory would presumably be furnished by a molecule having only monatomic groups attached to the asymmetric carbon atom. Because of this fact and its general theoretical interest, fluorochlorobromomethane, CHFClBr, has been prepared. Attempts are at present being made to resolve it by various methods.

(3) Gorin, Walter and Eyring, *J. Chem. Phys.*, **6**, 824 (1938).
(4) Kuhn, *Z. physik. Chem.*, **B31**, 23 (1936).
(5) Brockway, THIS JOURNAL, **58**, 2516 (1936).
(6) Weissberger and Sängewald, *J. Chem. Soc.*, 855 (1935).
(7) Bretscher, *Helv. Phys. Acta*, **2**, 257 (1929).
(8) Le Fèvre and Vine, *J. Chem. Soc.*, 1878 (1938).
(9) Kirkwood, private communication.

STERLING CHEMISTRY LABORATORY
YALE UNIVERSITY
NEW HAVEN, CONN.
RECEIVED OCTOBER 20, 1939

Desoxycholamine

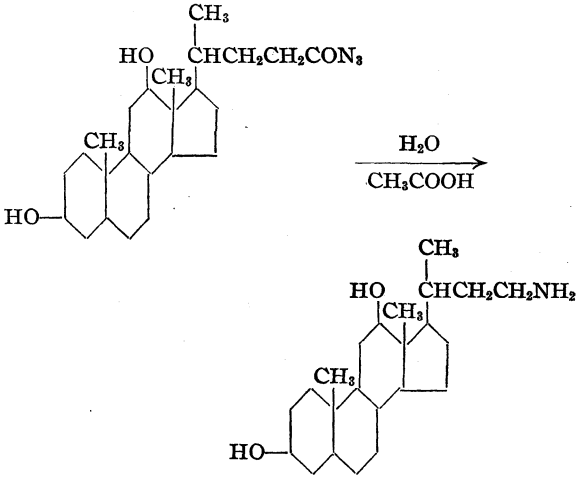
BY WILLIAM T. CALDWELL

In an article describing the preparation of cholamine by Lindemann's modification of the Curtius reaction,[1] attention was called to the fact that Borsche and Schwarz had distilled with caustic potash the urethan derived from cholylazide without, however, obtaining any of the desired amine by this application of the usual Curtius degradation. It was very interesting, therefore, to receive from Dr. Mihail Vanghelovici, in a private communication which he kindly sent, a description of a desoxycholamine whose preparation he reported to the Rumanian Academy of Sciences. He observed that, since his desoxycholamine had been prepared by the Curtius method, working at a pressure of 2 mm., it appeared to be

(1) Caldwell, THIS JOURNAL, **60**, 991 (1938).

much stabler than cholamine. The crude base, m. p. about 90°, yielded a microcrystalline solid, m. p. 118°, after repeated purification; it was strongly alkaline to red litmus moistened with methyl or ethyl alcohol and formed a hydrochloride, m. p. 247°, whose aqueous solution was extremely bitter.

Since I had prepared a desoxycholamine which differed from that described by Dr. Vanghelovici in the melting points, both of the free base and its hydrochloride, as well as in the comparative ease with which it could be obtained in nicely crystalline form from methanol, I am submitting a description of its preparation and some of its characteristics. Although there are differences in melting points, the two amines are alike in being strongly alkaline to red litmus moistened with methyl or ethyl alcohol and in the striking bitterness of their hydrochlorides. It appears not illogical to assume that they are stereoisomers; possibly epimerization occurred during the alkaline hydrolysis used in the Curtius degradation, since this type of change is effected by other alkaline reagents such as sodium alcoholate or metallic sodium in xylene.



Experimental Part

Twenty-two grams of desoxycholylhydrazide, m. p. 203°, was dissolved in 67 cc. of normal hydrochloric acid and 400 cc. of water. After adding 400 g. of ice, sodium nitrite (4.2 g.) in 50 cc. of water was added slowly with good stirring. The mixture was then stirred for an additional fifteen minutes and the azide filtered off with suction. The pressed, wet cake containing approximately 150 g. of water was transferred immediately to 210 g. of glacial acetic acid; it did not all dissolve but, upon gently warming on the steam-bath, the undissolved portion melted; evolution of gas began at about 45°, becoming more vigorous in the neighborhood of 60°; at the same time the amount of oil decreased but even after heating for four hours a small amount (about 1 g.) was visible. After cooling, the solution was filtered through a sintered glass funnel and cold aqueous potassium hydroxide added until the mixture became alkaline to phenolphthalein. The precipitate was then dissolved in alcoholic potassium hydroxide; after warming, this solution was diluted with a large amount of water and the precipitate washed by decantation with water until the aqueous washings gave no alkaline reaction with red litmus. The residual gum still contained a relatively large amount of non-basic material which was not investigated further; after its removal, the amine was purified by several recrystallizations from absolute methanol, from which it separated easily as fine, white crystals upon chilling and scratching the moderately concentrated solution.

Although these crystals were well formed and homogeneous, they did not melt sharply, their behavior depending upon the rate of heating; after beginning to soften at about 70°, they resolidified upon raising the temperature very slowly; finally, however, the substance melted sharply at 157–158°; yield, 3 g. The amine is so insoluble in water that it gives no basic reaction to red litmus moistened with water, at least within a reasonable length of time; on the other hand, it imparts a bright blue color at once to red litmus moistened with methyl or ethyl alcohol.

Analysis of the crystals, dried at room temperature over soda-lime and calcium chloride, indicated that they contained one molecule of methanol of crystallization.

Anal. Calcd. for $C_{23}H_{41}O_2N \cdot CH_3OH$: C, 72.86; H, 11.46. Found: C, 72.63; H, 11.60.

The free base, m. p. 158–159°, after warming for three hours in a drying pistol over metallic sodium at 5 mm. and 100°, was analyzed.

Anal. Calcd. for $C_{23}H_{41}O_2N$: C, 75.97; H, 11.36; N, 3.85. Found: C, 75.31, 75.84; H, 11.39, 11.44; N, 3.87, 3.77. Vanghelovici found: C, 75.37; H, 12.00; N, 3.82.

The hydrochloride, made by passing gaseous hydrogen chloride into a methyl alcoholic solution of the base, melted at 306° after sintering slightly at 300°. Unlike the base it is easily soluble in water.

Anal. Calcd. for $C_{23}H_{41}O_2N \cdot HCl$: Cl, 8.88. Found: Cl, 8.48. Vanghelovici calcd.: N, 3.50. Found: N, 3.80.

CHEMICAL LABORATORY
TEMPLE UNIVERSITY
PHILADELPHIA, PA.

RECEIVED OCTOBER 19, 1939

The Preparation of Primary Amines

BY ALEXANDER GALAT AND GERTRUDE ELION

The transformation of alkyl halides into primary amines by the formation of a double compound with hexamethylenetetramine, followed by alcoholysis in the presence of hydrogen chloride, affords a very convenient means for the preparation of primary amines.[1,2,3] As this method has

(1) Delépine, *Compt. rend.*, **120**, 501 (1895); **124**, 292 (1897); *Bull. soc. chim.*, [3] **17**, 290 (1897); [4] **31**, 108 (1922).
(2) Mannich and Hahn, *Ber.*, **44**, 1542 (1911).
(3) Foldi, *ibid.*, **53**, 1836 (1920).

been practiced in the past, the alkyl halide is added to a solution of hexamethylenetetramine in chloroform, and the addition compound, after it has precipitated, is filtered off. The alkyl iodides react with reasonable rapidity, but the chlorides and bromides react much more slowly, and if they are to be used as starting materials, they should be converted into the iodide by addition of sodium iodide in acetone solution.

This procedure has now been simplified by operating in a single solvent, alcohol, without isolation of the addition compound. The new procedure is as follows.

To a solution of 1 mole of hexamethylenetetramine in eight to ten times its weight of hot 95% alcohol slightly more than 1 mole of sodium iodide is added. One mole of the alkyl chloride or bromide is then added and the solution is allowed to stand until the precipitation is complete. The period of precipitation will vary from a few minutes to several weeks depending upon the substance. The longer the carbon chain the longer is the time required for the precipitation. The mixture containing the precipitate is saturated with hydrogen chloride gas, whereupon the precipitate dissolves and ammonium chloride precipitates. When the latter has been filtered off and the alcohol removed by distillation, the resultant impure hydrochloride is converted into the pure amine by distillation with an excess of sodium hydroxide.

The times of precipitation and the yields of several of the amines obtained were as follows: methylamine, one week, 72%; ethylamine, eight days, 82.5%; benzylamine, two hours, 82.5%; *p*-nitrobenzylamine, one day, 61%; phenylethylamine, three weeks, 54%. The products obtained were of high purity, having melting points closely in accord with the values given in the literature.

THE DENVER CHEMICAL MANUFACTURING COMPANY
163 VARICK STREET
NEW YORK, N. Y. RECEIVED SEPTEMBER 13, 1939

Synthesis of Organobismuth Compounds

BY HENRY GILMAN AND ALEXIS C. SVIGOON

Numerous methods are available for the preparation of organobismuth compounds. However, none among them starts with the diazonium complexes of bismuth salts, although such complexes have been described. Challenger and Wilkinson[1] have reported the preparation of benzenediazonium chloride–bismuth chloride and *p*-toluenediazonium chloride–bismuth chloride complexes; and Supniewski and Adams[2] the benzenediazonium chloride–bismuth chloride complex. No organobismuth compound is formed by interaction of *metallic* bismuth with benzenediazonium chloride.[3]

We are now reporting the conversion of these and other related complexes to the corresponding organobismuth compounds.

In a typical preparation (tri-*p*-tolylbismuth), an ice-cold solution of 0.1 mole of bismuth chloride in 16 cc. of concd. hydrochloric acid was added with stirring to an iced solution of 0.1 mole of *p*-toluenediazonium chloride prepared in the customary manner by diazotization of 10.7 g. of *p*-toluidine. The mixture became quite pasty and of a solid-like consistency as the complex formed. On the addition of 300 cc. of an ice-cold mixture of methyl and ethyl alcohols, a flaky white complex was precipitated. This diazonium complex was filtered, washed with cold methyl alcohol, and dried. The yield was 32.5 g.

Anal. Calcd. for $C_{21}H_{21}N_6BiCl_6$: Bi, 26.9. Found: Bi, 27.2 and 27.0.

A suspension of the *p*-toluenediazonium–bismuth chloride complex (32.5 g.) in 100 cc. of cold acetone was treated with 52.8 g. of copper powder. An evolution of gas took place in several minutes, and the solution became dark brown in color. After one-half hour an equal volume of 25% ammonium hydroxide was added, and then the mixture was diluted to 450 cc. with water. After standing for one hour the solid which had precipitated was filtered, dried, and extracted with dry chloroform. The solid remaining after removal of the chloroform was crystallized from methyl alcohol. The yield of pure tri-*p*-tolylbismuth was 3.07 g. and identification was completed by a mixed melting point determination (m. p., 116–117°) with an authentic specimen which melted at 116–117°.

The diazonium complexes were precipitated by methyl alcohol, ethyl alcohol, and more effectively by mixtures of methyl and ethyl alcohols. Higher alcohols may be better precipitants, and these are being examined together with media other than acetone for decomposing the complexes. A later report will give details on organobismuth compounds not now available, particularly those with solubilizing groups and groups of interest in connection with the cleavage and relative reactivities of unsymmetrical organobismuth compounds.

DEPARTMENT OF CHEMISTRY
IOWA STATE COLLEGE
AMES, IOWA RECEIVED OCTOBER 16, 1939

(1) Challenger and Wilkinson, *J. Chem. Soc.*, **121**, 91 (1922).

(2) Supniewski and Adams, THIS JOURNAL, **48**, 507 (1926). See also, Kharrier, *Atti Accad. Lincei*, [6] **5**, 889 (1927); Nesmeyanov, Kocheshkov and Klimova, *Ber.*, **68B**, 1877 (1935); and Kocheshkov and Nesmeyanov, *J. Gen. Chem.*, (U. S. S. R.) **6**, 144 (1936).

(3) Waters, *J. Chem. Soc.*, 864 (1939).

Preparation of Tricaprylin

BY E. B. HERSHBERG

Pure tricaprylin was required in quantity for use as a solvent medium in animal experiments now being conducted by Dr. Shields Warren with the carcinogenic compounds produced in this Laboratory.[1] The technical 90% caprylic acid produced by Armour and Company (Neo-Fat No. 7) proved to be a suitable source of the acid component. Purification is best effected by conversion with thionyl chloride to the acid chloride, for on careful fractionation octanoyl chloride can be obtained in a state of high purity. A large supply of the technical acid chloride was kindly supplied for the present work by the Armour and Company through the courtesy of H. M. Corley.

A detailed procedure for condensing octanoyl chloride with glycerol in the presence of quinoline was kindly made available to us by Dr. H. H. Young, Swift and Company, who obtained tricaprylin, m. p. 8.6–8.8°, by this method in 82% yield based on glycerol. A disadvantage of this process, noted by Dr. Young and in this Laboratory, is that the crude glyceride is contaminated with a yellow impurity which is retained on distillation and which is rather troublesome to eliminate by adsorption from solution when working with large quantities.

On trying the Schotten–Baumann method under conditions recommended by Menalda[2] it was found that the crude reaction product is completely colorless and that very pure tricaprylin can be obtained in this way in nearly 90% yield.

The technical (90%) octanoyl chloride was first distilled from a Claisen flask at a pressure of 10–30 mm. to make a rough separation and then carefully fractionated in a 1-meter column packed with glass helices. The material used boiled at 89.3–89.6° at 20 mm. (about 80% of the total). A 5-l., three-necked flask was charged with 73.5 g. of anhydrous[3] (vacuum distilled) glycerol, which was washed in with 25–50 cc. of water, and fitted with a Chromel wire stirrer[4] working through a wide glass tube mounted in the center opening to prevent loss by splashing. One of the side openings was fitted with a cork carrying a toluene thermometer and a small glass funnel; the other was equipped with a similar funnel. Simultaneous addition was then made of 410 g. of octanoyl chloride through one funnel and of a solution of 181 g. of 85% potassium hydroxide pellets in 375 cc. of water through the other. The liquids were run from constant-rate funnels[5] under a common air pressure of about 5 lb., which facilitated regulation. Since troublesome emulsions sometimes result from the presence of excess alkali, it is well to keep the acid chloride addition 25–50 cc. ahead of the alkali. The reagents were added in the course of about one hour, controlling the temperature to −5 to 0° by ice–salt cooling. Toward the end a stable emulsion formed; 75–100 cc. of ether was added to thin the mixture and provide better temperature distribution. Vigorous stirring was continued for three hours after the addition at a temperature of −10 to −5°; water and ether (1–1.5 l.) were then added and the layers separated. The ether layer was washed once with water and once with saturated sodium chloride solution and then filtered through a paper covered with a little anhydrous sodium sulfate.

After evaporation of the ether the colorless residue was distilled in a modified Claisen flask[6] connected with a ground-glass joint to a receiver (water cooling not required). After separation of a small fore-run (14 g., b. p. 150–233°) of mono- and diglycerides, the main fraction was distilled rapidly with a free flame and a good vacuum to avoid cracking. There was obtained 333 g. of colorless tricaprylin; as registered in the rapid distillation the b. p. was 233–235° at 1 mm. The yield is 89% based on the glycerol and 84% calculated from the acid chloride used. Careful distillation of a small sample gave the b. p. 233–233.5° corr. at 1.0 mm. (oil manometer[7]), freezing point 9.8–10.1° (compare 8–8.3°,[8] 9.45°[9]). Further purification by partial freezing and centrifugation was repeated twice without altering the freezing point.

When stirring was continued for only two hours

(1) We are indebted to Drs. M. J. Shear and M. B. Shimkin of the U. S. Public Health Service for making a trial of certain possible substitutes for lard as a medium for the injection of carcinogens, including the triglycerides suggested [Fieser, *Am. J. Cancer*, **34**, 37 (1938)] and certain other more readily available esters. In the first experiments with commercial esters, purified where required by Dr. Hershberg, tricaprylin appeared particularly satisfactory and large-scale tests with this glyceride were then initiated by Dr. Shimkin using a quantity of tricaprylin kindly prepared for us by Dr. H. H. Young of the Swift and Co. Research Laboratories.—L. F. FIESER.

(2) Menalda, *Rec. trav. chim.*, **49**, 967 (1930).

(3) Wet glycerol is suitable if the water content is determined from the density.

(4) Hershberg, *Ind. Eng. Chem., Anal. Ed.*, **8**, 313 (1936).

(5) Hershberg, *Org. Syn.*, **18**, 16 (1938).

(6) Adams and Marvel, *ibid.*, Coll. Vol. I, 1932, p. 125.

(7) Chadwick and Palkin, *Ind. Eng. Chem., Anal. Ed.*, **10**, 399 (1938).

(8) Scheij, *Rec. trav. chim.*, **18**, 193 (1899).

(9) Verkade and Willigen, *ibid.*, **54**, 353 (1935).

after the addition, the yield was slightly lower (324 g. or 86%). Substitution of sodium for potassium hydroxide in equivalent amount did not alter the results.

CONVERSE MEMORIAL LABORATORY
HARVARD UNIVERSITY
CAMBRIDGE, MASS. RECEIVED OCTOBER 20, 1939

A Photosensitized Production of Reducing Sugars from Starch

BY LAWRENCE J. HEIDT

Substances which reduce the Shaffer–Hartmann–Somogyi reagent are produced when light is absorbed by aqueous solutions containing uranyl sulfate and *starch*. The apparatus used to illuminate the solutions is described in *Science*, **90,** 473 (1939). The experimental procedure was the same as that given in THIS JOURNAL, **61,** 3223 (1939), for *sucrose*–uranyl solutions.

The ml. of hypo entered in Table I are calculated from the differences between S.–H.–S. estimations made simultaneously on the illuminated portions of a solution and on a portion kept in the dark, at the same temperature. When 5 ml. of water was added to 5 ml. of the S.–H.–S. reagent, the titration required 46.2 ml. of hypo, but 5 ml. of the unphotolyzed portions in Expts. 1, 2, 3, 4, 5 and 6 required 43.0, 45.5, 45.7, 42.8, 44.8 and 44.8 ml. of hypo, respectively. The potato starch, kindly supplied by Professor C. B. Purves, therefore contained very little reducing sugar, and both the illuminated and unphotolyzed solutions of starch in Expt. 4 appeared water-white.

Solutions were irradiated in quartz tubes at 21° with 8.5×10^{18} photons of λ 254 mμ per minute incident on each 11 ml. sample. The starch solutions were 0.008 *M* in uranyl sulfate in Expts. 1, 2 and 3; 0.0004 *M* in quinine sulfate in Expt. 5; 0.0003 *M* in the sodium salt of fluorescein (Eastman Kodak Technical Grade) in Expt. 6 and contained only starch and water in Expt. 4. Each ml. of hypo entered in Table I was equivalent to 5.7×10^{-5} g. of glucose in the uranyl sulfate solutions and to 5.5×10^{-5} g. of glucose in the others.

The experiments with quinine and fluorescein were undertaken to discover for this reaction other photosensitizers—preferably dyes and natural products that absorb sunlight. The amount of reducing substances produced when quinine or fluorescein was present, however, was less or little more than when they were absent and very much less than when uranyl sulfate was used. The intense blue fluorescence initially present in Expt. 5b disappeared toward the end of this photolysis and a light straw solution was formed, but in Expt. 6b the yellow fluorescence was only diminished. This also occurred in parallel experiments with solutions of quinine and fluorescein without starch and the *p*H likewise decreased but in the quinine solution the amount of reducing substances produced was less than 10% of that formed in Expt. 5b and none was formed from the fluorescein or from the uranyl sulfate alone in water.

TABLE I

Expt.	Starch in 50 ml., g.	*p*H in soln. before photolysis	*p*H in soln. after photolysis	Min. photolyzed	Ml. of hypo	ϕ
1a	0.5024	3.0	2.8	21.5	85	0.09
b			2.9	7.2	38	.12
c			2.9	5.0	29.5	.13
d			...	1.45	14.1	.22
2a	.1935	3.35	3.25	8.5	25.5	.07
b			...	4.0	18.0	.10
c			...	3.0	16.0	.12
d			...	2.0	12.1	.14
3a	.0658	3.5	3.4	24.0	26.0	.024
b			...	12.0	17.8	.033
c			...	6.0	13.2	.050
d			...	3.0	8.8	.066
4	.4894	4.35	3.55	860.0	34.5	...
5a	.1935	3.9	3.6	49.5	4.0	<.002
b			3.0	624.0	79.0	<.002
6a	.1956	6.2	6.2	94.5	2.5	
b			5.6	283.0	6.6	

Quantum yields, ϕ, represent the number of oxygen bridges (linking the glucose units) broken per photon of λ 254 mμ absorbed by the system if the measured product is glucose and one bridge is broken per molecule of glucose produced. This may be too simple an hypothesis except, perhaps, for the initial reaction.

In Expts. 4 and 6, ϕ is not given because the extinction coefficients of these solutions were not known at this wave length. Nevertheless, Expt. 4 shows that the measured reaction in Expts. 1, 2 and 3 is mainly a photosensitized reaction. Also in Expts. 1, 2 and 3, ϕ is smaller and falls more rapidly than for the photosensitized decomposition of sucrose at the same concentration of oxygen bridges, if there is one bridge per sucrose molecule and one per glucose unit in starch. This decrease in ϕ probably is due to the colloidal nature of starch solutions and the chain character of the starch molecule, both of which

protect some of the chemical bonds in starch that would otherwise enter the measured reaction.

CONTRIBUTION NO. 433 FROM THE
RESEARCH LABORATORY OF PHYSICAL CHEMISTRY
MASSACHUSETTS INSTITUTE OF TECHNOLOGY
CAMBRIDGE, MASS. RECEIVED OCTOBER 23, 1939

A New Method for the Cleavage of Unsaturated Fatty Acids[1]

BY CHI-YI HSING AND KOU-JEN CHANG

The methods for the cleavage of unsaturated fatty acids reported in the literature are either by energetic oxidations or by ozonization. On account of the side reactions, the degradation products are usually complex mixtures and the yields are very low.

Lead tetraacetate has been introduced by Criegee[2] as a reagent for the cleavage of glycols with excellent results. This oxidizing agent should be equally effective in oxidizing polyhydroxy fatty acids which in turn can be prepared easily from the corresponding unsaturated fatty acids by means of oxidation with alkaline potassium permanganate. It was found that 9,10-dihydroxyoctadecanoic acid (from oleic acid) was oxidized completely in twenty-four hours by lead tetraacetate in glacial acetic acid. As reaction products, pelargonic aldehyde and azelaic semialdehyde were isolated in the form of semicarbazones, each in a yield of about 85%. By using benzene as a solvent, 9,10,12-trihydroxyoctadecanoic acid (from ricinoleic acid, m. p. 111–112°) oxidized in four hours and about 90% of azelaic semi-aldehyde semicarbazone and a product melting at 112–113°, the character of which has not yet been determined, were obtained. A mixed melting point with starting material indicated it was different. The supposition is it may be β-hydroxypelargonic aldehyde semicarbazone or a related compound.

A more extensive study of this method for cleavage of unsaturated fatty acids of known and unknown structure will be reported later.

Experimental

In 10 cc. of glacial acetic acid which had been distilled over phosphorus pentoxide, was suspended 0.6740 g. of 9,10-dihydroxyoctadecanoic acid and to the mixture 0.95 g. of lead tetraacetate was added. This was shaken for twenty-four hours at room temperature. The solution was filtered and heated in a water-bath at 45° for five minutes. It was then treated with 15 cc. of water and a concentrated aqueous solution of 0.5 g. of semicarbazide hydrochloride and 0.6 g. of sodium acetate was added. To the reaction mixture was now introduced a few drops of methanol and it was then vigorously shaken. After standing in an ice box for twenty hours, the semicarbazones separated as a white precipitate. The precipitate was filtered and shaken with cold dilute aqueous sodium hydroxide to dissolve the azelaic semialdehyde semicarbazone. Undissolved, impure pelargonic aldehyde semicarbazone was filtered and washed with water. The alkaline filtrate was acidified with 2% hydrochloric acid. The precipitated azelaic semialdehyde semicarbazone was filtered, washed and dried, yield 0.434 g. (90%). After purification by crystallization from ethanol it melted at 163–164° (Harries and Thieme[3] reported 163°).

The alkali insoluble part consisted of lead chloride and pelargonic aldehyde semicarbazone. It was dissolved in methanol and the lead chloride was filtered. On evaporating the solution to a small volume, the semicarbazone separated as fine crystals melting at 99–100.5° (Bagard and Harries and Turk[4] reported 100°). The yield was 0.348 g. (82%).

(1) Presented at the 7th Anniversary Meeting of the Chinese Chemical Society, held at Kunming, China, August 29, 1939.

(2) R. Criegee, *Ber.*, **64**, 260 (1931); *Ann.*, **481**, 263 (1930); **507**, 159 (1933).

(3) C. Harries and C. Thieme, *Ann.*, **343**, 359 (1905).

(4) P. Bagard, *Bull. soc. chim.*, **4**, I, 346 (1907); C. Harries and H. O. Turk, *Ber.*, **40**, 2756 (1907).

NATIONAL RESEARCH INSTITUTE OF CHEMISTRY
ACADEMIA SINICA
KUNMING, CHINA RECEIVED NOVEMBER 2, 1939

Dependence of Conductance on Field Strength

BY DARWIN J. MEAD AND RAYMOND M. FUOSS

We recently reported the field dependence of the conductance of tetrabutylammonium picrate in diphenyl ether at 50° [THIS JOURNAL, **61**, 2047 (1939)]. We are indebted to Dr. L. Tonks of this Laboratory for calling to our attention a correction which we neglected. The limit approached by the Wien coefficient at zero concentration now agrees with Onsager's theoretical value, when the correction factor of $8/3\ \pi$ is applied.

Our measurements were made in a bridge circuit, in which balance is indicated by zero current in a detector circuit fed through a low-pass filter. Our solutions were non-linear impedances, and the detector showed balance for only the fundamental frequency. According to theory, the specific conductance κ is given by

$$\kappa(t) = \kappa_0 + A V_m \mid \sin \omega t \mid \qquad (1)$$

where κ_0 is the low voltage conductance, A is Onsager's coefficient and V_m is the peak voltage of the sinusoidal input at frequency f, with $\omega = 2\pi f$. The unit current then is

$$i(t) = \kappa_0 V_m \sin \omega t + A V_m^2 \sin \omega t \mid \sin \omega t \mid \qquad (2)$$

In order to find the fundamental in the non-linear term of (2), we simply expand it in a Fourier series

$$f(x) = \sin x \mid \sin x \mid = \Sigma a_n \sin nx$$

and take the first term, for which $a_1 = 8/3\ \pi$. Then from the point of view of the bridge detector

$$i(t) = V_m \sin \omega t\ (\kappa_0 + 8A\,V_m/3\pi) \qquad (3)$$

whence

$$\kappa = \kappa_0 + 8A\,V_m/3\pi \qquad (4)$$

Our experimental result was

$$\kappa = \kappa_0 + B\overline{V} \qquad (5)$$

where B is the experimental slope and $\overline{V} = 2\ V_m/\pi$ is the linear average voltage. Comparison of (4) and (5) gives

$$A = 3B/4 \qquad (6)$$

which brings our experimental result into exact agreement with the theoretical value.

RESEARCH LABORATORY OF
THE GENERAL ELECTRIC COMPANY
SCHENECTADY, NEW YORK RECEIVED NOVEMBER 7, 1939

The Viscosity of Liquid Ammonia

BY C. J. PLANK AND HERSCHEL HUNT

The viscosity of liquid ammonia is reported by Stakelbeck[1] to be 0.00218 g./cm. sec. at 20°, 0.00229 at 10°, 0.00238 at 0° and 0.00252 at −20°. He used the Lawaczec falling ball method. At −33.5° two values are reported, 0.002543[2] poise and 0.00260[3] poise.

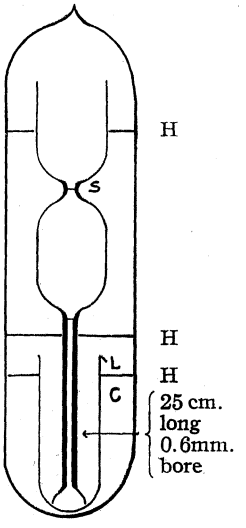


Fig. 1.—Viscometer.

The viscosity of ammonia at room temperature is important. Since Stakelbeck's results have a small temperature coefficient, we redetermined the viscosity at 5, 15 and 25°. Our apparatus is shown in Fig. 1. The apparatus was carefully dried by heating it under reduced pressure. It was calibrated with pure dry carbon disulfide and carbon tetrachloride. The following viscosities[4] and densities of these compounds were used.

Temp.	Carbon disulfide Density	Carbon disulfide Viscosity	Carbon tetrachloride Density	Carbon tetrachloride Viscosity
5°	1.2856	0.004125	1.6230	0.01233
15°	1.2750	.003805	1.6037	.010476
25°	1.2554	.003565	1.5843	.009027

The constants, C and C', of the equation

$$\eta = C\rho t - C'\rho/t$$

were determined at each temperature. The ammonia was dried over sodium and distilled under reduced pressure into the apparatus. After the outside jacket was sealed the apparatus could be rotated in order to fill the viscometer with the liquid. The supports, H's, held the viscometer perfectly vertical and rigid within the jacket when the outside jacket was placed in a vertical position.

The determinations were made in an air thermostat whose temperature was regulated to 0.05°. The time was measured with an accurately calibrated stop watch. Since the time of flow was in the neighborhood of four to eight minutes for the calibration and almost four minutes for the ammonia, the error in the measurement of time was not over 0.02%.

The apparatus was designed as shown because a closed system was necessary, and by having container C full of liquid when the meniscus passes S, a constant head was ensured. A fine lip, L, on C ensured a delivery of the liquids at the same level, so that a change in surface tension of the liquids did not interfere. The small head also increased the time of flow. It is difficult to fill the apparatus with cold ammonia by distillation and get the desired hydrostatic head when the liquid becomes warm. Two viscometers were used and the results are in excellent agreement. The viscosities and densities at the three temperatures are:

Temp., °C.	Density g./cc.	Viscometer number 1	Viscometer number 2	Viscosity of NH_3 (av., g./cm. sec.)
5°	0.63197	0.001628	0.001607	0.001618
15°	.61821	.001468	.001446	.001457
25°	.60427	.001350	.001350	.001350

The densities were determined by the pycnometer method. These data, if we can judge by the long extrapolation, are in good agreement with the low temperature values in the literature. Stakelbeck's results would indicate that the temperature coefficient of viscosity for ammonia is much smaller than the coefficient for any other known liquid. His results agree with ours if we multiply

(1) Stakelbeck, *Z. Kälte-Ind.*, **40**, 33–40 (1933).
(2) Fitzgerald, *J. Phys. Chem.*, **16**, 621 (1912).
(3) Elsey, THIS JOURNAL, **42**, 2454 (1920).
(4) Thorpe and Rodger, *Trans. Roy. Soc. (London)*, **(A)185**, 397 (1895).

his values by the density of ammonia, an odd coincidence.

DEPARTMENT OF CHEMISTRY
PURDUE UNIVERSITY
LAFAYETTE, INDIANA RECEIVED JULY 3, 1939

The Preparation of Grignard Reagents from Magnesium Amalgams

BY EUGENE G. ROCHOW

Magnesium amalgams have been used for the preparation of magnesium alkyls and aryls,[1] and for the coupling of ketones with chloro-esters and chloro-ethers.[2,3,4] In view of the high reactivity of dilute amalgams of magnesium toward oxygen and water, it seemed interesting to investigate the formation of methylmagnesium halides from such amalgams, and then to follow with experiments on other less reactive halides.

The phase diagram for the system Mg–Hg shows two compounds, $MgHg_2$ and MgHg. Below 168° the equilibrium condition at the low magnesium end is a mixture of $MgHg_2$ crystals and liquid, and hence the reported solubility of magnesium in mercury (3% at 250°, 1% at 100° and probably 0.1% at room temp.) must refer to the solubility of $MgHg_2$. Since $MgHg_2$ contains 5.71% magnesium by weight, amalgams of this or greater concentration of magnesium will be solids, and amalgams in the range 5 to 0.1% magnesium will normally be mixtures of $MgHg_2$ with increasing proportions of liquid.

Amalgams containing from 0.1 to 1.0% of magnesium were prepared in an all-glass apparatus under an atmosphere of purified nitrogen.[5] The dissolution of magnesium in mercury is strongly exothermic, so no external heating was required. After cooling in the stream of nitrogen, 50 cc. of a 0.1 *N* solution of methylmagnesium chloride was added through the condenser and methyl bromide was admitted. The purpose of the methylmagnesium chloride was to eliminate difficulties in starting, which would have confused the results obtained.

After refluxing the amalgam with the solution of methyl bromide for several hours, samples of the ether layer were withdrawn for determination of total CH_3MgX by evolution of methane with water. The increase of CH_3MgX over that added at the start was calculated as % yield based on the magnesium. Typical results were:

% Mg in amalgam	Yield of RMgX, %
0.1	0
0.5	4.1
1.0	25.3

Unreacted magnesium was evident in the mercury layer in each case as soon as the amalgam was exposed to the air. Attempts were made to displace a possible equilibrium between $MgHg_2$ and RMgX, but the results indicated that there was no such equilibrium. Dilute magnesium amalgams did not seem to react at all with methyl chloride, and the iodide is reported to form the R_2Mg compound under such conditions.[1]

The odor of mercury dimethyl was detected in some of the experiments. Metallic mercury does not react with RMgX to form R_2Hg,[6] but mercury halides would do so readily, and such halides might have been formed in small quantity.

The experiments indicate that the yield of RMgX from magnesium amalgams increases with the concentration of magnesium in the amalgam, and with the increasing possibility of free magnesium in the amalgam mixture. It may be concluded that $MgHg_2$ does not participate in the Grignard reaction as readily as magnesium, and that mercury therefore has an inhibiting effect on the reaction.

(1) Fleck, *Ann.*, **276**, 129 (1893).

(2) Sommelet, *Ann. chim. phys.*, (8) **9**, 484 (1906). Superficial amalgamation by addition of a trace of $HgCl_2$ was used here to start the reaction.

(3) Darzens, *Compt. rend.*, **151**, 883 (1910).

(4) Grignard, *Bull. soc. chim.*, **128**, 1285 (1926).

(5) The dilute amalgams are very sensitive to traces of oxygen and moisture, and it was found that the ordinary purification methods had to be supplemented by passing the gas through a 1% Mg amalgam before use.

(6) Gilman, "Organic Chemistry," Vol. I, John Wiley and Sons, Inc., New York, N. Y., Chapter 4.

RESEARCH LABORATORY
GENERAL ELECTRIC COMPANY
SCHENECTADY, NEW YORK RECEIVED OCTOBER 13, 1939

Addition of Compounds of Dicyclohexylamine

BY CHARLES F. WINANS

In the hydrogenation of cyclohexanone in the presence of ammonia to form cyclohexylamine, a crystalline compound, m. p. 46°, formed in the cooled residue after distilling cyclohexylamine. This solid was found only when there was an insufficient amount of ammonia for complete reaction of the carbonyl group. Distillation of this product separated it into equivalent amounts of cyclohexanol and dicyclohexylamine, which recombined with evolution of heat to give the original crystalline material.

The preparation of a number of analogous addition compounds was attempted with several amines and hydroxy compounds. Usually a solid formed on mixing equimolecular amounts of the materials at room temperature, but sometimes chilling was required. Recrystallization was effected by cooling a solution of the addition compound in ether or petroleum ether.

A typical example of the preparation of these compounds is as follows. A solution of 10 g. of dicyclohexylamine in 10 ml. of petroleum ether was mixed with 5 g. of cyclohexanol in 10 ml. of petroleum ether. The clear solution was strongly chilled to deposit crystals which were filtered out, washed with petroleum ether and dried in air; m. p. 47–48°. *Anal.* Calcd. for $(C_6H_{11})_2NH \cdot C_6H_{11}OH$: N, 4.99. Found: N, 4.87.

The table gives data on a number of these materials. Several recrystallized products melted below room temperature, but the existence of a compound is shown by the analysis of the melt.

The only known reference[1] on this subject is an article by Fougue, who described the formation of a hydrate (m. p. 23°) and an alcoholate (m. p. 28°) of dicyclohexylamine, but who did not discover the apparent generality of this behavior. It is, furthermore, quite surprising that these materials were not found earlier in view of the large amount of work done on reactions of cyclohexanol with ammonia and of cyclohexanone and hydrogen with ammonia, where conditions for isolation of an addition compound must have been at least as favorable as in this case.

(1) Fougue, *Compt. rend.*, **166**, 394 (1918).

TABLE I

AMINE–ALCOHOL ADDITION COMPOUNDS

Amine	Alcohol	M. p., °C.	Nitrogen, % Calcd.	Found
Dicyclohexyl-	Cyclohexanol	47–48	4.99	4.87
Dicyclohexyl-	2-Me-cyclohexanol	59–60	4.74	4.65
Dicyclohexyl-	1,2-Cyclohexanediol	64–66	4.72	4.72
Dicyclohexyl-	1,3-Cyclohexanediol	64–66	4.72	4.72
Dicyclohexyl-	1,4-Cyclohexanediol	90–91	4.72	4.59
Dicyclohexyl-	o-Cyclohexylcyclohexanol	43–45	3.86	3.61
Dicyclohexyl-	*p-t*-Butylcyclohexanol	75–76	4.15	4.12
Dicyclohexyl-	β-Phenethyl alcohol	Below	4.62	4.27
Dicyclohexyl-	1,3-Butanediol	room	5.16	5.10
Dicyclohexyl-	Benzyl alcohol	temp.	4.84	4.72
Dibenzyl-	Cyclohexanol	Below	4.72	4.63
Piperidine	1,3-Cyclohexanediol	room	6.96	6.78
Cyclohexyl-	Cyclohexanol	temp.	7.04	6.84

RESEARCH LABORATORIES
THE GOODYEAR TIRE & RUBBER COMPANY
AKRON, OHIO

RECEIVED OCTOBER 30, 1939

COMMUNICATIONS TO THE EDITOR

STEROLS. LXXXI. CONVERSION OF SARSASAPOGENIN TO PREGNANEDIOL-3(α),20(α)

Sir:

In studying the reaction of sarsasapogenin with acetic anhydride at 200° we have obtained a product in good yield (after alkaline hydrolysis) of the composition $C_{27}H_{44}O_3$, m. p. 171–173°, which we are tentatively designating as pseudosarsasapogenin. *Anal.* Calcd. for $C_{27}H_{44}O_3$: C, 77.8; H, 10.6. Found: C, 77.8; H, 10.6. Pseudosarsasapogenin upon mild oxidation with chromic anhydride in acetic acid gives a good yield of an unsaturated diketone, m. p. 201–203°. *Anal.* Calcd. for $C_{21}H_{30}O_2$: C, 80.2; H, 9.6. Found: C, 80.1; H, 9.6. This diketone upon reduction with sodium and ethanol gave a product, m. p. 236–239°, which gave no depression with an authentic sample of pregnanediol-3(α),20(α), m. p. 237–239°. *Anal.* Calcd. for $C_{21}H_{36}O_2$: C, 78.8; H, 11.3. Found: C, 78.7; H, 11.3. Acetylation of this reduction product with hot acetic anhydride gave an acetate of m. p. 177–179° which gave no depression with an authentic sample of the diacetate of pregnanediol-3(α),20(α) m. p. 177–179°. *Anal.* Calcd. for $C_{25}H_{40}O_4$: C, 74.2; H, 10.0. Found: C, 74.2; H, 10.0.

The ready availability of sarsasapogenin makes it now one of the most suitable sources of hormones such as progesterone, testosterone and desoxycorticosterone. The details of the work concerning the preparation and reactions of pseudosarsasapogenin, and its conversion to the above hormones will be published in a forthcoming issue of THIS JOURNAL.

We wish to thank Parke, Davis and Company for their generous help and assistance in the various phases of this work.

SCHOOL OF CHEMISTRY AND PHYSICS
THE PENNSYLVANIA STATE COLLEGE
STATE COLLEGE, PENNA. RUSSELL E. MARKER
EWALD ROHRMANN

RECEIVED NOVEMBER 21, 1939

2-(*p*-AMINOBENZENESULFONAMIDO)-THIAZOLE: A NEW CHEMOTHERAPEUTIC AGENT

Sir:

Fosbinder and Walter [THIS JOURNAL, **61**, 2032 (1939)] reported the preparation of 2-(*p*-aminobenzenesulfonamido)-thiazole and stated that it had good activity in experimental streptococcic and pneumococcic infections in mice. Our own studies had already reached the point where promising pharmacologic and chemotherapeutic results (van Dyke, Rake, Greep, McKee, in press) warranted therapeutic trial of this drug and we assembled the following descriptive data for that purpose.

The 2-(*p*-aminobenzenesulfonamido)-thiazole prepared by us had the m. p. 197–197.5° (uncor.), 202.0–202.5° (cor.).

Its solubility in alcohol at 26° was 525 mg. per 100 cc. In water at 26° the solubility was about 60 mg. per 100 cc., giving *p*H 6.03, which is almost twice the solubility of sulfapyridine.

Our 2-(*p*-acetaminobenzenesulfonamido)-thiazole had m. p. 256–257° as reported by Fosbinder and Walter. **2-(*p*-Aminobenzenesulfonamido)-thiazole sodium salt** was prepared by a method essentially that described by Marshall [*Science*, **88**, 597 (1938)] for the sodium salt of sulfapyridine, m. p. 256.0–256.5° (uncor.) or 264.5–265.0° (cor.). *Anal.* Calcd. for $C_9H_8N_3O_2S_2Na$: Na, 8.30. Found: Na, 8.33. It was readily soluble in cold water. A 2% solution had a *p*H of 9.57.

2-(*p*-Aminobenzenesulfonamido)-thiazole hydrochloride was prepared by adding alcoholic hydrogen chloride to an alcoholic solution of the free base and adding ether; m. p. 193–197° (uncor.); solubility in water less than 2% with *p*H 1.28; loses hydrogen chloride on standing.

The potentiometric titration curves for the acidification of 2% solution of the sodium salts of 2(*p*-aminobenzenesulfonamido)-thiazole (Sulfathiazole), and sulfapyridine are submitted in Fig. 1. It will be seen that "Sulfathiazole" is more strongly acidic than sulfapyridine.

In addition to the 2-(*p*-aminobenzenesulfonamido)-4-methylthiazole of m. p. 237–238°, we prepared the next higher homolog, 2-(*p*-aminobenzenesulfonamido)-4-ethylthiazole, and found its melting point surprisingly lower, 149.5–150.5°.

Marshall's colorimetric method [*Science*, **88**, 85 (1938)] for the estimation of sulfapyridine has been found applicable to "Sulfathiazole." By this method, however, one cannot distinguish between sulfapyridine and "Sulfathiazole."

A good test has been found which distinguishes clearly between the two drugs. Thus, when a solution of the sodium salt of "Sulfathiazole" is treated with cupric sulfate solution, a characteristic purple precipitate is formed. With sulfapyridine an apple green precipitate is formed which gradually changes to greenish brown. This test has been used successfully on a few mg. of material. The precipitates have been characterized as follows: sulfapyridine, brown; calcd. for $(C_{11}H_{10}N_3O_2S)_2Cu$: Cu, 11.36. Found: Cu, 11.12. "Sulfathiazole," purple; calcd. for $(C_9H_8N_3O_2S_2)_2Cu$: Cu, 11.12. Found: Cu, 11.09.

Since these precipitates can be ashed and esti-

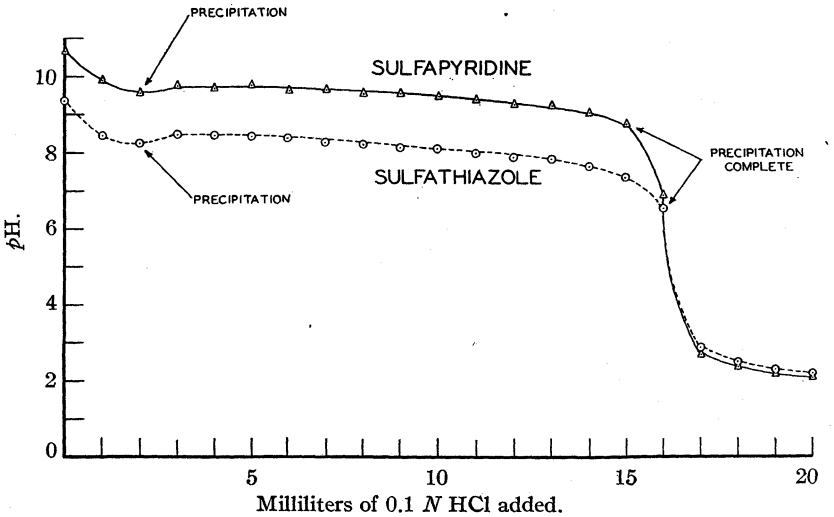


Fig. 1.—Potentiometric titrations of solutions of the sodium salts of sulfapyridine and sulfathiazole: 2% solution of sulfapyridine sodium salt, △; 2% solution of sulfathiazole sodium salt, ⊙.

mated as cupric oxide, we are at present developing quantitative methods for these two drugs as well as sulfanilamide.

MEDICINAL CHEMISTRY LABORATORY W. A. LOTT
THE SQUIBB INSTITUTE FOR MEDICAL RESEARCH
NEW BRUNSWICK, NEW JERSEY FRANK H. BERGEIM

RECEIVED SEPTEMBER 20, 1939

BIOTIN AS A GROWTH FACTOR FOR THE BUTYL ALCOHOL PRODUCING ANAEROBES

Sir:

Recently the "growth factor" requirements of the butyl alcohol-producing clostridia has excited considerable interest.[1,2,3] It has been found that several species of these organisms require a widely distributed organic acid, which cannot be replaced by any known available growth factors.

Using the test conditions of McDaniel, *et al.*,[3] and a culture of *Clostridium butylicum* (Amer. Type Culture Coll. No. 6015), we have shown that biotin[4] is the only accessory substance required by this organism for luxuriant growth even on a synthetic medium.

The results of three tests are given in Table I, the first two on the basal medium of McDaniel, *et al.*,[3] the third using a basal medium exactly the same except that an additional 0.1% asparagin was substituted for the casein hydrolysate. Cultures 2 and 3 were subcultured from the unsupplemented tube of culture 1. Turbidities at the end of the three-day incubation period were measured quantitatively with the thermoelectric turbidimeter described by Williams, *et al.*[5] The galvanometer scale was set to read zero with the uninoculated medium in the cell; a reading of 100 corresponds to complete opacity.

TABLE I

Micrograms supplement per cc. of medium	Turbidities (galvanometer readings) — Subcultures — Culture 1 (1–3 diln.) hydrolyzed casein medium	Culture 2 (1–2 diln.) hydrolyzed casein medium	Culture 3 (undiluted) asparagin medium
Biotin Supplement			
0.000000	15.0	17.0	2.2
.0000133	25.0	19.0	10.2
.0000266	32.0	24.0	29.0
.000053	46.0	34.0	54.0
.00010	60.0	49.0	75.0
.00020	68.0	66.0	88.0
.00066	81.0	67.0	94.0
Liver Concentrate Supplement			
.0133	33.0	28.0	39.0
.0333	52.0	39.0	60.0
.0666	65.0	58.0	79.0
.1332	66.0	66.0	94.0
.2664	67.0	74.0	94.0
.6660	70.0	68.0	96.0

The "liver concentrate" was prepared in accordance with work of McDaniel, *et al.*, and was kindly furnished by Dr. Woolley. Biotin proved to be approximately 500 times as active as this concentrate and it is evidently the only substance required in addition to the ordinary nutrients. Hydrolyzed casein evidently contains small amounts of some substance which is in this case physiologically equivalent to biotin. Whether the response which we have obtained is specific for biotin cannot at present be stated. In any event, these results supply further evidence for the great physiological activity of biotin.

We wish to express our thanks to Professor Kögl, who kindly furnished us with the sample of biotin which made this work possible.

(1) Weizmann, *et al.*, *Biochem. J.*, **31**, 619 (1937).
(2) Brown, Wood and Werkman, *J. Bact.*, **36**, 246 (1938).
(3) McDaniel, Woolley and Peterson, *ibid.*, **37**, 259 (1939).
(4) Kögl and Tonnis, *Z. physiol. Chem.*, **242**, 43 (1936).
(5) Williams, McAlister and Roehm, *J. Biol. Chem.*, **83**, 315 (1929).

DEPARTMENT OF CHEMISTRY ESMOND E. SNELL
THE UNIVERSITY OF TEXAS ROGER J. WILLIAMS
AUSTIN, TEXAS

RECEIVED OCTOBER 13, 1939

ON THE ABSORPTION SPECTRUM OF HYPERICIN

Sir:

The pigments of *Hypericum perforatum* causing photosensitization in animals are spectroscopically closely related to irradiated oxypenicilliopsin from *Penicilliopsis clavariaeformis* [A. E. Oxford, *Chem. and Ind.*, **57**, 975 (1938); C. Dhéré and V. Castelli, *C. R. Soc. Biol.*, **131**, 669 (1939); C. Dhéré, *ibid.*, **131**, 672 (1939)].

Extracted hypericin was found chromatographically to consist of five components, and we have designated the two most abundant as X and Y. Samples were interchanged with Professor Raistrick, and component Y and irradiated oxypenicilliopsin appear very similar but not identical in chemical behavior. We wish at this juncture to supplement spectroscopic observations by Dhéré and Castelli on these pigments. We have checked their absorption maxima in absolute alcohol within 10 Å. and are in fair agreement as to the intensities.

In Table I we show the effect of solvent composition on the absorption maxima. Values are

TABLE I

EFFECT OF SOLVENT ON ABSORPTION MAXIMA

	Solvent	Ia	Ib	Ic	IIa	IIb	IIc	IIIa	IIIb	IV
1	90% aqueous acetone	5955[a]			5510[a]			5140		4770
2	100% acetone	5990	5830		5540	5420		5130		4750
3	33% acetone, 67% ether	5990[b]	5840		5550	5420	[d]	[d]	[d]	4550
4	25% acetone, 75% ether	5990[c]	5830	5690		5420	5290	[d]	[d]	4540
5	100% ether		5815	5690		5410	5300		5060	4550
6	Ether + trace pyridine		5890	5730		5460[a]				Not detd.
7	Ether + *ca.* 20% pyridine	5990[a]			5550			5170		Not detd.
8	Pyridine	6030[a]			5580[a]			5200		4830

[a] Band slightly asymmetric. [b] Ia > Ib in intensity. [c] Ib > Ia in intensity. [d] Band not discernible.

averages of several readings made visually, and are accurate within ± 10 Å. Of particular interest is the co-existence of two distinct spectral types in homogeneous solutions comprised of mixtures of acetone and ether. The case of europium salts [*J. Chem. Physics*, **7**, 824 (1939)] is the only comparable instance of which we are aware.

We have segregated the spectra into three types: A_1, A_2, and B. Hypericin was considered to have four absorption bands in the visible, and this is still true in aqueous acetone, aqueous alcohol and pyridine (type A_1). Unpublished curves for the pigment in 90% aqueous acetone show a slight but definite asymmetry for band Ia and, to an even smaller extent, for band IIa in the regions where Ib and IIb occur as maxima in the anhydrous solvent (type A_2). These curves were obtained spectrophotoelectrically with a high degree of precision and there is no doubt as to the absence of Ib and IIb in the aqueous solvent at room temperature.

The ether spectrum (type B) is essentially different as shown by the fact that Ic (5690 Å.) is absent from anhydrous acetone and alcohol. The pigment is soluble with difficulty in ether. When an ether solution is shaken with water most of the pigment separates at the interface. It has been suggested that a hydrate is formed, as one could not account otherwise for such a decrease in solubility.

Relative intensities, photometrically determined in acetone, are: Ia > Ib, IIa > IIb > IV > IIIa; in ether: Ib > Ic, IIb > IV > IIc > IIIb. In acetone the fluorescence is a vivid red, whereas in ether it is distinctly orange.

The data suggest the existence of a different molecular species in ether, possibly an addition compound because the pigment is hydroxylated. This is capable of co-existence with a second type (A_2) in anhydrous alcohol– or acetone–ether mixtures. In the presence of water or pyridine it disappears, leaving a spectrum of type A_1.

DIVISION OF PHYSIOLOGY, MEDICAL SCHOOL N. PACE
FRUIT PRODUCTS DIVISION, COLLEGE OF AGRICULTURE
UNIVERSITY OF CALIFORNIA, BERKELEY G. MACKINNEY

RECEIVED NOVEMBER 20, 1939

NEW BOOKS

A Text-Book of Quantitative Chemical Analysis. By ALEX. CHARLES CUMMING, O.B.E., D.Sc., F.I.C., and SYDNEY ALEXANDER KAY, D.Sc., formerly Lecturer in Chemistry in the University of Edinburgh. Seventh edition revised by FRANCIS CLINT GUTHRIE, M.A., F.I.C., and JOHN TRENGOVE NANCE, M.A., Lecturer in Chemistry in the University of Liverpool. D. Van Nostrand Company, Inc., 250 Fourth Avenue, New York, N. Y., 1939. xv + 496 pp. 85 figs. 15 × 23 cm. Price, $5.00.

The scope of this book is indicated by the titles of the eight parts into which it is divided, namely: I, General Principles; II, Volumetric Analysis; III, Gravimetric Analysis; IV, Colorimetric Methods; V, Systematic Quantitative Analysis; VI, The Analysis of Simple Ores and Alloys; VII, Gas Analysis; and VIII, Water Analysis. More than the usual number of specific determinations are to be found in each part.

Fundamental principles and theoretical interpretations are only briefly treated. There are simple but adequate directions of procedure. Reasons for a particular step are seldom given. Students might reasonably ask why, on page 216, 2% ammonium nitrate is recommended as a solution for washing precipitated $Fe(OH)_3$, while on page 267, hot water, and on page 397, 2% ammonium acetate are recommended for the same purpose.

The definition of *p*H on page 60 makes use of hydrogen-ion concentration in terms of *grams* per liter rather than in terms of gram-ions per liter.

Useful tables and reference works are included in the Appendix.

CHESTER M. ALTER

Schopenhauer und die Chemie. By A. MITTASCH. Carl Winter's Universitätsbuchhandlung, Lutherstrasse 59, Heidelberg, Germany, 1939. v + 92 pages. 17 × 24.5 cm. Price, RM. 2.50.

Dr. Mittasch, known particularly for his work on catalysis, on its theory and on its practical application in chemical engineering, on its history, and on its background and implications, is to be reckoned among the more philosophical of contemporary writers on the history of chemistry. The present little book supports the conviction, already finding expression in an ever-increasing number of studies and publications, that the history of thought and the history of science is one and the same. Speculation and positive knowledge in the long run are parallel, as the fibers which make up a thread are parallel, more than parallel for they are bound together, intertwined, overlapped.

The book consists of four principal parts, which deal respectively with Schopenhauer's knowledge of the chemistry of his time, with his view of the significance and importance of chemistry, with his philosophy of chemistry, and with the significance for the future of Schopenhauer's philosophy of chemistry. So far as the reviewer can see, Schopenhauer made no greater use of the chemistry of his time than did other contemporaneous alert and intelligent thinkers. Certainly no more than Emerson. No more than Shakespeare in his time. Probably less wisely than Francis Bacon made use of the scientific knowledge of his day. The charge may even be made that Schopenhauer, as several of the philosophants of the present are doing, used the concepts and jargon of science to arrive at conclusions which could have been reached more clearly by less devious methods. His final judgment concerning the order of things is not greatly different from the judgment which Omar Khayyam reached, more than seven centuries earlier, on the basis of scientific evidence only slightly more meager, and refused to accept as final. The book is a reprint from the 26th Yearbook of the Schopenhauer-Gesellschaft, 1939, and will be of interest especially to students of Schopenhauer—for whom, if they happen to be humanists of the old style, Mittasch has done a real, eye-opening service.

TENNEY L. DAVIS

Thermodynamics and Chemistry. By F. H. MACDOUGALL, M.A., Ph.D., Professor of Physical Chemistry, University of Minnesota. Third Edition. John Wiley and Sons, Inc., 440 Fourth Avenue, New York, N. Y., 1939. ix + 491 pp. 52 figs. 15.5 × 23.5 cm. Price, $5.00.

The reviewer liked this book in the previous editions [review of second edition, THIS JOURNAL, 49, 1610 (1927)]. More material is now included, notably on the calculation of thermodynamic functions with the aid of quantum statistical mechanics. The author writes extremely well and clearly. The printing is excellent.

The book seems to be comparatively free from errors. There is considerable revision of the thermodynamic presentation in the direction of the methods of Gibbs and of Lewis and Randall and there are naturally some errors not present in the earlier editions. Some of these follow. Page 44, first line, "if p is constant" invites erroneous interpretation and has no correct one. Page 108, a criterion for stable equilibrium is expressed by a *differential equality* which does not exclude neutral or unstable equilibrium. This is mitigated by the text immediately following. Page 145, the sentence before Eq. (41) and also the one following it imply the popular and unsatisfactory definition of function: y is a function of x if y varies with x. Page 148, the validity of Eq. (60) is not as stated and the conclusion just below Eq. (62) does not really follow. This conclusion implies that we cannot salt-out a dyestuff. Page 211, the expression "in view of equation X-50, it is clear . . ." is optimistic, since in that equation the potentials and mole numbers are for the independent components but in the vanishing term of XII-7 they are for the greater number of "substances." It would seem clearer to begin at once with Eq. (8) as an obvious consequence of the consideration of the free energy as a function (at

constant T and p) of the masses of the "substances" even when they are not independently variable. Page 253, in order to arrive at Eq. (8) one must postulate further that the ratio of the fugacity to the pressure approaches the limit unity as the pressure approaches zero. The substitution of one "zero" for another under the logarithm sign is not legitimate in the circumstances. This too-simple explanation has been given by others, and can here be remedied by a small change in Eq. (6).

The more modern thermodynamic treatment seems to make here a somewhat greater demand on the previous mathematical experience of the instructor than did that of the earlier editions. He should add to the material of the new and useful chapter on Mathematical Apparatus (1) a definition of function, (2) the statement that the mathematicians have proved that Eq. (III-1) applies also when the variables are not independent and (3) a brief discussion of the theory of dimensions, such as that given in the earlier editions, but extended to recognize the mole as a unit of quantity of substance. The addition (2) is the more important as several commentators on chemical thermodynamics have stated or implied the contrary fact about the equation.

L. J. GILLESPIE

Der disperse Bau der festen Systeme. Allgemeine Theorie der Verunreinigung fester Systeme. (The Disperse Structure of Solid Systems. General Theory of Contamination of Solid Systems.) By Professor D. BALAREW, Sofia. Verlag von Theodor Steinkopff, Dresden-Blasewitz, Germany, 1939. 240 pp. 45 figs. Price, RM. 10; bound, RM. 11.50.

This publication covers Volume 50 of the *Kolloid Beihefte* and is published as a separate monograph. During the last few years, Balarew has published his views on the disperse structure of solids in several issues of the *Kolloid Beihefte*. According to Balarew, all solids have a colloidal-disperse structure, regardless of whether they consist of colloidal particles or of more perfect macrocrystals. The latter always are growth agglomerates and have a porous structure. Balarew rejects the view of the physicists (Kossel, Stransky, Volmer) on the growth of crystals and claims that all crystals grow "jumpwise" by addition—not of individual ions—but of elementary building stones. He tries to substantiate his views by referring to many experimental data. His monograph is not easily read, as Balarew repeats himself on almost every page. All authors to whom reference is made (with the exception of Wo. Ostwald) are badly criticized. Such criticism might have a stimulating effect toward further research, were it not for the fact that many references are incomplete and incorrect. To mention one example: the existence of postprecipitation is still denied although it has been established conclusively in a great number of cases.

It is of interest to get acquainted with Balarew's views even if one does not agree with him in many respects. It would have been preferable, however, if the author had published his ideas in a much more concise and exact form. Considering how little is offered, the price of the monograph is very high.

I. M. KOLTHOFF

Anleitung zur organischen qualitativen Analyse. (Introduction to Organic Qualitative Analysis.) By DR. HERMANN STAUDINGER, Professor of Chemistry and Director of the Chemical Laboratory, University of Freiburg i. Br. Third edition, revised with the assistance of Dr. Werner Kern, Frankfurt a. M. Verlag von Julius Springer, Linkstrasse 22–24, Berlin W 9, Germany, 1939. xvi + 157 pp. 14 × 21 cm. Price, RM. 6.90.

Ten years have elapsed since the appearance of the second edition of this little volume. The new edition contains twelve more pages of text than its predecessor and appears to differ from it only in minor clarifications of text, and the inclusion of references to the more outstanding relevant papers of the decade.

As before, the material is divided into a general introductory section (42 pages) and the "special part" (99) which constitutes the real meat of the book. The scheme of identification is based primarily on volatility and solubility. It makes no serious attempt to deal with the characterization of specific compounds but is rather extensively concerned with the behavior of the various classes and groups of organic compounds. For this reason the book is intensely suggestive and continues to be a valuable tool to both teacher and student.

No organic chemist will wish to deprive himself of the services of this stimulating volume. Those who have worn out their old editions will welcome this new one; those who have not yet made its acquaintance cannot afford to delay this privilege any longer.

ERNEST H. HUNTRESS

Justus von Liebig. Die Lebensgeschichte eines Chemikers. (The Life Study of a Chemist.) By RICHARD BLUNCK. Wilhelm Limpert Verlag, Berlin SW 68, Germany, 1938. 320 pp. 14 × 21.5 cm.

This interesting biography of Liebig is addressed to the general reader rather than to the specialist or the chemist. It deals most fully with the years of Liebig's youth and early triumphs, since this period throws most light on his genius and personality.

The biographer is frankly sympathetic and appreciative rather than analytical and critical. He can, however, hardly be blamed for his tolerance; Liebig's brilliance, high ideals, passionate devotion to his subject and commanding personality adequately counterbalance his frequent unreasonableness and indeed perversity. His ardent advocacy of a united Germany at the time when his country was weak and divided also must endear him to the German of today.

One incident in Liebig's career deserves greater emphasis than the biographer gives it. Liebig was once arrested and incarcerated for his participation in a minor political uprising against the government among the students at the University of Bonn. He was pardoned by Duke Ludwig the First, and shortly thereafter, on the recommendation of Liebig's teacher, Professor Kastner, Duke Ludwig granted him funds from his private purse sufficient for a two years' study of chemistry at Paris, the then scientific capital of Europe. It is not every ruler who is wise and fortunate enough to pick a Liebig for his benefactions!

ARTHUR B. LAMB

Iodine and the Incidence of Goiter. By J. F. McCLENDON, Professor of Physiological Chemistry, University of Minnesota. The University of Minnesota Press, Minneapolis, Minn., 1939. vi + 126 pp. Illustrated. 22 × 28.5 cm. $5.00.

In his preface to this book the author points out that the book has been written at the suggestion of and for the benefit of research workers, especially those interested in goiter prophylaxis.

The book does not deal with the anatomy of the thyroid gland, the classification of goiter, or anything directly concerned with medical treatment.

It represents, however, a very complete review of the literature on the incidence of endemic goiter and its correlation to the distribution of iodine. This is the general viewpoint of the book, but it also contains extensive tables of the iodine content of soil, water and atmosphere, and of the various plants and animals, including all foodstuffs. A great material has conscientiously been collected by the author from chemical and medical journals all over the world. The material is condensed in brief chapters in a very successful way, and all figures handy-arranged in tables.

For those studying the problems of the etiology of endemic goiter the book will be very useful. But it is also valuable for all interested in nutrition, as almost all papers concerning the iodine content of foods will be found quoted in the book.

The author hopes that the reader will be convinced of the fact that "iodine is not only a drug, but also an essential food constituent and that lack of it may lead to a deficiency disease just as may the lack of a vitamin. In other words, iodine should have a place not only in an individual but also in preventive medicine, which aims to prevent disease in large populations."

GULBRAND LUNDE

Theoretical and Applied Electrochemistry. By MAURICE DE KAY THOMPSON, Professor of Electrochemistry, Massachusetts Institute of Technology. Third edition. The Macmillan Company, 60 Fifth Avenue, New York, N. Y., 1939. xxi + 535 pp. 234 figs. 15 × 22 cm. Price, $5.00.

"Theoretical and Applied Electrochemistry" consists of three parts; the first is "Theoretical Electrochemistry," with six chapters; the second, "Applied Electrochemistry of Aqueous Solution," with ten chapters; the third "Electric Furnaces and their Products," with five chapters.

The first three chapters deal with Faraday's law, electrolytic dissociation theory and electrical conductance. The fourth chapter entitled "Electrokinetic Phenomena" presents briefly electrophoresis, electroösmosis, the theory for the double layer on a colloidal wall, the ζ-potential of the colloidal particle. The fifth chapter is on electromotive force, and is the longest in the book, 55 pages; it includes seven pages of tables of reference electrodes, standard single potential electrodes, and oxidation–reduction potentials. Chapter six is on electrolysis and polarization, and within it hydrogen overvoltage receives nine pages.

Part II begins with a chapter (VII) on electrochemical analysis; next, chapter VIII, a very important one, on electroplating and galvanoplasty, takes up electroplating equipment, cleaning, pickling, nickel plating, cobalt, cobalt–nickel, zinc, chromium plating and many others. Chapter IX deals with the electrolytic extraction and refining of metals. In electrolytic extraction . . . "the ore is leached with a solvent that dissolves the metal, and the metal is deposited from the purified solution by electrolyzing with an unattackable anode." The solvents for copper ores are dilute sulfuric acid and ferric sulfate, or hot cupric chloride solution.

The definition quoted serves to distinguish electrolytic extraction from electrolytic refining, for in the latter the anodes consist of the impure metal, and the . . . "impure anodes are electrolyzed . . . and deposited on the cathode." The electrolytic extraction of copper, zinc, cadmium, nickel, manganese, silver, and other metals from ores is presented. The electrolytic refining of essentially the same metals is given with the conspicuous exception of Ni. On looking back over the extraction processes, one finds a method for nickel (p. 237, upper half), but to conform with the author's own definition, it should have been classed as a refining process, not as an extraction one. Electrolytic copper refining is fully treated, with many interesting details (pp. 240 to 257).

Chapter X describes electrolytic oxidation and reduction; the products by oxidation include chromic acid, permanganate, ferricyanide, and persulfate. Oddly enough, almost nothing is said regarding the production of hydrogen peroxide by electrolytic methods.

Electrolysis of alkali halides, which forms chapter XI, includes hypochlorite cells, chlorate cells, cells for "the production of chlorine and hydrate" under which latter heading the diaphragm cells are first and well treated, with numerous illustrations (pp. 298–312), and second, the mercury cells (pp. 313–316).

Chapter XII gives the electrolytic production of hydrogen, oxygen and heavy water, and the electrolytic purification of water.

Chapter XIII deals with primary cells, and chapter XIV with the lead storage cell (17 pages), the Edison storage cell (8 pages) and three others. Chapter XV has applications of electrokinetic phenomena (5 pages) and chapter XVI corrosion (2 pages).

Part III, as said before, deals with electric furnaces and their products. Chapter XX in this part deals with "The Fixation of Atmospheric Nitrogen," by the action of electricity on air only, and by nitrifying calcium carbide.

There are problems in nearly all the chapters, and a set of solutions and answers, which will be valuable to readers away from the classroom.

The description of subject matter just given contains at the same time various comments and these will be supplemented by the following remarks:

The preface states that the theoretical part was added to the original applied electrochemistry portion of the first edition at the request of many users of the book; without doubt, such users find it useful to have theoretical considerations at hand. Such a benefit depends in greater part upon a close correlation between the two, really three, parts and it is the reviewer's impression that such correlation might be improved. To give a definite example, let

a casual reader decide that upon coming to the alkali halide cells in Part II, he needs to know the theoretical decomposition voltage for sodium chloride in water solution at a definite temperature. The text for the cells presents no discussion; the index under decomposition voltage refers him to p. 179 where he finds an experimental decomposition voltage defined, but not directions for computation. To find a method for computing the desired voltage will require much searching of the text.

Several passages did not seem quite clear; thus, p. 180, lines 4–12, p. 184, lines 20–25, p. 78, lines 9–12; and the index, it may be remarked, has a startlingly large number of proper names.

The reviewer is anxious to call attention to other features in the book which will be welcomed; several have been indicated previously in the description of the subject matter. The treatment is all-inclusive, or essentially so. Next, the theoretical treatment has been brought into harmony with the latest developments (among others, for example, p. 89). Many items in the "applied" divisions will be novel to a large number of readers. Especially attractive to the reviewer are the sections in Part II dealing with the purification of water by electrolysis (p. 325), the hypochlorite cells (p. 294) and chlorate cells (p. 296), and the formation of sorbitol and mannitol by electrolytic reduction (p. 286).

EMIL RAYMOND RIEGEL

Standard Methods of Chemical Analysis. By WILFRED W. SCOTT, Sc.D., Late Professor of Chemistry, University of Southern California. Fifth Edition, edited by N. HOWELL FURMAN, Ph.D., Professor of Chemistry, Princeton University, in collaboration with eminent specialists. Vol. I, the Elements; Vol. II, Special Subjects. D. Van Nostrand Company, Inc., 250 Fourth Avenue, New York, N. Y., 1939. xxxi + xxi + 2551 + 97 (index) pp. Illustrated. 16 × 24 cm. Price, $17.00.

The last edition of this well-known book was published in 1925. According to the preface of the present edition "an extensive revision ... was in progress during the years 1930–2 and approximately half of the first volume was in galley proof when the work was interrupted by the death of Professor W. W. Scott. A further revision and extension of the book was undertaken in 1936 by the present editor in coöperation with the majority of the former collaborators, or their associates, and a number of new contributors."

As in the previous edition Volume I is devoted to the elements, qualitative tests, and various useful tables, and Volume II is given over to special subjects. Only a page by page comparison of the new edition with the previous one could make clear the extent of the changes and improvements effected by the revision. About one-third of the chapters have been entirely rewritten, and advantage has been taken of a complete resetting of type to revise thoroughly most of the other chapters. Besides these changes eight new chapters have been introduced: Rhenium; Ferrous Alloys based on the methods of the American Society for Testing Materials; Electrometric *p*H Measurement; Colorimetric *p*H Measurement; Conductometric Titrations; Chemical Microscopy; Quantitative Microanalysis; Analysis of Rubber Compounding Ingredients; Quantitative Spectrographic Analysis.

The reviewer's only regret is that the editors did not take the opportunity of a new edition to bring the whole book up to a more nearly uniform level of modernization. For instance, there is an excellent 87-page chapter on Quantitative Microchemical Analysis replete with references through 1937, but there is also a 21-page chapter on Methods for the Determination of Solubility which is reprinted from the 1919 edition of Seidell's "Solubilities." This, of course, is an extreme example and the criticism holds for only one or two of the less important topics.

The value of this book is greatly enhanced by the new edition. The collection of concise and clear procedures for so many diverse analyses will make it practically indispensable in the analytical laboratory; the wide range of topics and the wealth of information will make it a useful acquisition for every chemical library.

ARTHUR F. SCOTT

Essentials of Physiological Chemistry. By ARTHUR K. ANDERSON. Second edition. John Wiley and Sons, Inc., 440 Fourth Avenue, New York, N. Y., 1939. 323 pp. Price, $2.75.

In the second edition, this book has been brought up to date, and contains revised sections on lipids, oxidation and reduction enzymes, respiration, carbohydrate metabolism, vitamins and hormones, etc. There is also added a new chapter on the "Composition of Tissues" which is very helpful in correlating the chemistry of the animal body with its physiology.

Since the book is designed for students of human nutrition it contains many points of interest for the general reader, aside from its value to the student in biochemistry. The writer finds that the material is well organized and generally accurate. He would question, however, the statement that "Colostrum is rich in antibodies and is, therefore, an important factor in rendering infants immune to contagious diseases" (p. 129). How are these proteins taken into the body? He also regrets a diagrammatic formula for oxyhemoglobin which he does not feel represents the present state of knowledge of the substance (p. 222).

WILLIAM F. ROSS

Protein Metabolism in the Plant. By ALBERT CHARLES CHIBNALL, Professor of Biochemistry, Imperial College of Science and Technology, University of London. Yale University Press, New Haven, Conn., 1939. xv + 306 pp. Illustrated. 16 × 24 cm. Price, $4.00.

The appearance of a specialized monograph in plant biochemistry is a rare event. The field of animal biochemistry has attracted so many workers that monographs on various aspects of the field are taken as a matter of course. Even textbooks rarely deal adequately with plant chemistry, and are usually restricted almost entirely to the biochemistry of mammals and of man. Yet, as is well known, most of the important syntheses on which human life depends, such as the production of proteins, carbohydrates, alkaloids and vitamins are carried out by plants. It is to

be hoped that the next decade or so will witness a deeper appreciation of the importance of this fact and a considerable increase in the amount of work carried out on problems of plant physiology and biochemistry.

In this volume of Silliman Lectures, delivered last year at Yale University, Professor Chibnall has covered all aspects of nitrogen metabolism in plants, with the exception of those parts of the field dealing with alkaloids, purines and other non-protein constituents. The limitation on the amount of work done has a certain advantage here, in that it has been possible to include a variety of investigations ranging from the pure chemistry of proteins to the physiology of buds, without sacrificing any of the detail which is essential to critical evaluation of the material.

The book consists really of three parts. In the first five chapters are traced the gradual development of the concept of asparagine and glutamine as intermediates in the breakdown and resynthesis of proteins in seedlings, from the discovery of asparagine in 1806, through the extensive experiments of E. Schulze, lasting over 33 years, to the modern position. It might be suggested that the historical treatment in the opening 3 chapters is unnecessarily extensive. Professor Chibnall's attempt to reduce some of Schulze's experiments to "balance sheets" is certainly not very happy, perhaps because in the "balance sheets" no clear separation is made between the substances lost and those gained. His extensive recalculation of the original data (which must have involved a great deal of labor) has, however, greatly contributed to the clarity of the presentation. Two chapters then discuss the preparation and properties of leaf proteins, a field to which Professor Chibnall and his associates have made major contributions. In the last four chapters nitrogen transformations in isolated leaves are considered. This field, of course, remains in an unsatisfactory state because of the quite unexplained proteolysis which occurs when leaves are detached. Three appendices, one by J. W. H. Lugg, deal with analytical procedures.

The spirit of these lectures is that of the experimentalist thoroughly familiar with the pitfalls of the field, and a number of unpublished experiments from the author's laboratory are included throughout the book. This close contact with the laboratory gives life to all the discussion. In his critical synthesis of miscellaneous facts, garnered from a scattered literature, into a presentation of the subject as a closely interwoven whole, Professor Chibnall has done a great service not only to those in the field but to physiologists and biological chemists in general.

KENNETH V. THIMANN

Spectrochimica Acta. Ein Forschungsarchiv. (Spectrochemistry.) Band I, Heft 1. Verlag von Julius Springer, Linkstrasse 22–24, Berlin W 9, Germany, 1939. 92 pp. 56 figs. 17.5 × 26 cm. Price, RM. 8.60.

A rather inauspicious moment has been chosen for the entrance of this new journal into a field which badly needs a unifying influence. The present literature of spectrochemical analysis is so widely scattered in journals of chemistry, physics, biology, medicine, geology, and metallurgy that it is almost impossible to keep abreast of developments with ordinary library facilities. A journal devoted solely to spectrochemical analysis should be of great assistance in this respect, and it is to be hoped that it can survive the war.

In the first paper, Kaiser reports some experimental results on the effects of various factors on the relative intensities of lines emitted from a spark. From these results he is able to draw conclusions and set up certain rules which should be of great assistance in developing a technique for spark analysis.

Rollwagen has carried out a similar task for the d. c. arc, and emphasizes particularly the essential differences between the cathode layer and the positive column of the arc.

Scheibe and Martin describe a very interesting new technique for local microanalysis, in which a spark strikes to a moving sample, and the spectrum falls on a plate which moves synchronously with the sample. In this way they are able to trace differences of composition of individual grains within a metal, and detect concentrations of impurities at grain boundaries.

Gatterer and Junkes describe the quantitative determination of traces of europium in samarium, and McClelland and Whalley describe a technique which they have found useful in the analysis of various non-ferrous alloys.

The journal also includes a series of abstracts of recent books and papers dealing with spectrochemical analysis.

K. B. THOMSON

BOOKS RECEIVED

October 10, 1939–November 10, 1939

EARLE RADCLIFFE CALEY. "The Composition of Ancient Greek Bronze Coins." The American Philosophical Society, Independence Square, Philadelphia, Penna. 203 pp. $2.50.

FRITZ FEIGL. "Qualitative Analysis by Spot Tests." Second English edition from the third German edition. Nordemann Publishing Co., 215 Fourth Avenue, New York, N. Y. 462 pp. $7.00.

ROBERT J. HARTMAN. "Colloid Chemistry." Houghton Mifflin Co., Cambridge, Mass. 556 pp. $4.75.

WILHELM JOST. "Explosions- und Verbrennungsvorgänge in Gasen." Verlag von Julius Springer, Linkstrasse 22–24, Berlin W9, Germany. 608 pp. RM. 46.50; bound, RM. 49.50.

T. M. LOWRY AND A. C. CAVELL. "Intermediate Chemistry." The Macmillan Co., 60 Fifth Avenue, New York, N. Y. 876 pp. $3.25.

HAROLD C. WEBER. "Thermodynamics for Chemical Engineers." John Wiley and Sons, Inc., 440 Fourth Avenue, New York, N. Y. 258 pp. $3.25.

"Abridged Scientific Publications from the Kodak Research Laboratories." Vol. XX. Eastman Kodak Co., Rochester, New York. 273 pp.

"The Merck Index." Fifth edition. Merck and Co., Inc., Rahway, New Jersey. 1060 pp. $3.00.

Additions and Corrections

NOTICE TO READERS.—For the convenience of those who wish to cut out the corrections and attach them to the margins of the articles corrected, they have been printed upon one side of the page only.

1933, VOL. 55

Victor K. La Mer and W. George Parks. The Partial and Integral Heats of Dilution of Cadmium Sulfate Solutions from Electromotive Force Measurements.

Page 4349. In Table V, the 20° values in the last four columns should read: 0.0207 instead of 0.0144; 0.323 instead of 0.358; 5,236 instead of 5,789; and 3,579 instead of 3,858.—VICTOR K. LA MER.

1937, VOL. 59

C. S. Fuller and C. L. Erickson. An X-Ray Study of Some Linear Polyesters.

Page 347. In Fig. 1(e) and (f) "the fiber axis directions on the X-ray fiber patterns of trimethylene sebacate and diethylene sebacate polyesters were inadvertently rotated through 90 degrees."

Page 348. As a result of the error on Page 347, these corrections are needed in Table II: "The correct lengths corresponding to the chemical repeating units are 15.4 ± 0.1 Å. and 17.8 ± 0.1 Å. for trimethylene and diethylene sebacate, respectively. The fiber periods or lengths of the X-ray repeating units along the fiber axis are probably multiples of these values. The designation of the various reflections in Table II is also erroneous. The general conclusions reached previously in regard to the chain configurations in the solid state of the two esters in question are not altered essentially by these corrections. As in the case of the results previously reported, the above values of the lengths of the chemical repeating units necessitate a considerable shortening of the planar zigzag chain configuration. Present evidence, however, favors a uniform "tub" form of chain instead of one in which the shortening occurs entirely in the glycol portion of the ester as was previously suggested."—C. S. FULLER.

K. A. Krieger and Martin Kilpatrick. The Conductance of Mixtures of Strong Electrolytes.

Page 1879. Column 1, line 18 for "in 1 kg. of water" read "in 1 kg. of solution." The effect of this error is to make the cell constant and the quantities dependent upon it slightly too large. The following changes should therefore be made to convert our conductances to the Jones and Bradshaw standard:

Page 1880. The values in Table I in the columns headed Λ_K(obsd.) and Λ_K(calcd.) and the left member of equation (2) should be reduced by 0.068%.

Page 1881. Column I, following line 18. The column marked Λ(obsd.) should be reduced by 0.068%.

Page 1882. Table III. The values in the column headed 1000 $C_{sp.}$(obsd.) should be reduced by 0.068%. In Table II, Λ_1° becomes 38.59 and ω_{12} and ω_{21} change correspondingly. This change in cell constant enters into the mixture effect in a rather complicated way, the values in Table III, under the heading $\Delta C_{sp.}$ (%) obsd., becoming, reading downward: +0.01, −0.04, −0.09, −0.01, −0.13, −0.04, −0.11, −0.04, −0.08, −0.04, −0.04, −0.07, −0.10, −0.06, −0.09, −0.09, −0.09, −0.10, and −0.12.

It will be observed that the corrected values are in better agreement with the theoretical values than those previously reported. With the exception of three points, the agreement is probably within the experimental error, although the observed values seem to fall consistently below the calculated ones (numerically) at the higher concentrations.—K. A. KRIEGER.

1938, VOL. 60

F. F. Blicke and R. A. Patelski. Hydroxy- and Methoxyphenylanthrones. I.

Page 2640. In column 2, line 2 from end, for "Ethyl 2-(2′-Methoxybenzoyl)-benzoate" read "Ethyl 2-(2′-Methoxybenzyl)-benzoate."

In column 2, line 1 from end, for "2-(2′-methoxybenzoyl)-benzoic acid" read "2-(2′-methoxybenzyl)-benzoic acid."

Page 2641. In column 1, line 16, for "ethyl 2-(2′-methoxybenzoyl)-benzoate" read "2-(2′-methoxybenzyl)-benzoate."—F. F. BLICKE.

Philip G. Stevens, W. Edward Higbee and Robert T. Armstrong. The Influence of Branched Chains on Optical Activity. The Configuration of Propyl-*t*-butylcarbinol, with a Note on the Relation between Rotatory Power and Chemical Character.

Page 2659. In Table III, 5th line, 3rd column, read −0.72 instead of +0.72.—PHILIP G. STEVENS.

E. Bergmann. The Dimerization of 3-Phenylindene.

Page 2816. The formula shown here should have a double bond between the second and third carbon in the left-hand indene ring.

Roger Adams, T. A. Geissman and R. C. Morris. Structure of Gossypol. XVII. Nitration Products of Gossypol Hexamethyl Ether, Gossypolone Tetramethyl Ether and Gossypolonic Acid Tetramethyl Ether.

Page 2971. In column 2, under heading "Oxidation of Compound IV to, etc." line 8, for "Compound V" read "Compound IV" and line 11, for "Compound V" read "Compound VI."—ROGER ADAMS.

Walter A. Hynes, Leo K. Yanowski and Morris Schiller. A Modified Method for the Preparation of Monochloropentamminocobaltic Chloride (Purpureocobaltic Chloride).

Page 3053. "The method described here duplicates almost exactly one proposed by Willard and Hall in their paper, 'The Separation of Cobalt by means of Phenylthiohydantoic Acid,' THIS JOURNAL, **44**, 2219 (1922). Since the method of Dr. Willard was mentioned as a mere incidental to the balance of the work reported and was not indicated in the published title of his article, we had not included his article in our list of literature references."—W. A. HYNES.

George Scatchard, W. J. Hamer and S. E. Wood. Isotonic Solutions. I. The Chemical Potential of Water in Aqueous Solutions of Sodium Chloride, Potassium Chloride, Sulfuric Acid, Sucrose, Urea and Glycerol at 25°.

Page 3066. The points at concentrations above 1 *M* representing the measurements of Frazer and Norris in Fig. 1 and those of Lovelace, Frazer and Sease in Fig. 2, should be lowered about 0.004.

Page 3068. In column 1, line 5 from bottom, for "0.65 cal./mole" read "43 cal./mole."—GEORGE SCATCHARD.

1939, VOL. 61

Dorothy Nightingale and Lee Irvin Smith. The Action of Aluminum Chloride on Aromatic Hydrocarbons. I. The 1,3-Dimethyl-4-butylbenzenes.

Page 102. In column 1, the diagram should read:

1,3-dimethyl-4-*n*-butylbenzene ⟶ 1,3-dimethyl-5-*s*-butylbenzene

1,3-dimethyl-4-*s*-butylbenzene ⟶ 1,3-dimethyl-5-*t*-butylbenzene

1,3-dimethyl-4-*t*-butylbenzene ⟶ 1,3-dimethyl-5-*t*-butylbenzene

—DOROTHY NIGHTINGALE and LEE IRVIN SMITH.

G. P. Baxter (Chairman), M. Guichard, O. Hönigschmid and R. Whytlaw-Gray. Ninth Report of the Committee on Atomic Weights of the International Union of Chemistry.

Page 225. In the ninth report of the Committee on Atomic Weights of the International Union of Chemistry through an unfortunate error the uncertainty in the composition of purpureo ruthenium chloride estimated by Gleu and Rehm (*Z. anorg. allgem. Chem.*, **235**, 352 (1937)) is given as 0.1–0.2 per cent. instead of 0.01–0.02 per cent., and the uncertainty in the atomic weight of ruthenium as 0.3 unit instead of 0.03 unit. In spite of this optimistic estimate by Gleu and Rehm, the Committee feel that further experimental evidence is necessary before making any change in the atomic weight of ruthenium in the Table.—G. P. BAXTER.

Joseph R. Spies and Thomas H. Harris, Jr. Some Salts of 2-Oxy-6,8-diaminopurine.

Page 352. In column 1, line 1 (after table), for "ninety-three milligrams" read "nine hundred and thirty milligrams."—JOSEPH R. SPIES.

Harold Hibbert. Studies on Lignin and Related Compounds. XXXVII. The Structure of Lignin and the Nature of Plant Synthesis.

Page 729. In column 2, line 9, for "IV" read "VI."—HAROLD HIBBERT.

Edward S. Amis and Victor K. La Mer. The Entropies and Energies of Activation of Ionic Reactions. The Kinetics of the Alkaline Fading of Brom Phenol Blue in Isodielectric Media.

Page 910. "In Table IV, columns $k_{k=0}$ and Log $k_{k=0}$ for 31.5% EtOH should read 0.971 and −0.013, respectively; for 42.8% MeOH, the corresponding values are 0.935 and −0.029."—VICTOR K. LA MER.

Roger Adams and Madison Hunt. Structure of Gossypol. XIX. Synthesis of 1,2-Dihydroxy-3-isopropyl-6-benzoic Acid.

Page 1132. Column 1, line 2, for "apogossypolic acid (II)" read "apogossypolic acid (V)."—ROGER ADAMS.

Roger Adams and B. R. Baker. Structure of Gossypol. XXI. Synthesis of 1,2-Dimethoxy-3-isopropyl-4-benzoic Acid and of Apogossypolic Acid.

Page 1139. In column 2, line 10 from bottom, read "b. p. 157–158°" for "b. p. 157–168°."

Page 1140. In column 1, line 13 from top, read "added 5 g. of magnesium" for "added 1 g. of magnesium."

Page 1141. In column 1, last line, read "α-bromoacetate" for "α-bromopropionate."—ROGER ADAMS.

F. F. Blicke and H. C. Parke. Alkylaminoalkyl Esters of Aminonaphthoic Acids as Local Anesthetics.

Page 1202. In Table II, the melting point of compound 6 should read "203–204°" instead of "114–115°."—F. F. BLICKE.

Manfred Kiese and A. Baird Hastings. The Dissociation Constant of Hypobromous Acid.

Page 1291. Line 4. "The statement regarding the absence of data on the dissociation constant of hypobromous acid is in error. Shilov and Gladtchikova, THIS JOURNAL, **60**, 490 (1938), R. M. Chapin, *ibid.*, **56**, 2211 (1934), and A. Skrabal and R. Skrabal, *Monatsh.*, **71** 273 (1938), have found values for the constant."—MANFRED KIESE and A. BAIRD HASTINGS.

Herbert I. Bernstein and Frank C. Whitmore. The Common Basis of Intramolecular Rearrangements. V. Inversion of Configuration in Semipinacolic Deamination. The Configurational Relationship between (+)-Alanine and (+)-Methylphenylacetic Acid.

Page 1324. Column 1. "The first carbon in the second formula is left electronically deficient by the removal of the amino group with complete octet. This should be indicated by six dots and an asterisk."—F. C. WHITMORE.

Herbert S. Harned and Calvin Calmon. The Properties of Electrolytes in Mixtures of Water and Organic Solvents. I. Hydrochloric Acid in Ethanol- and Isopropanol-Water Mixtures of High Dielectric Constant.

Page 1492. The sign on the right of equation (4) should be changed to +, that on the right of equation (5) to −. This error affects the results in columns headed E_c^0 and E_N^0 in the last two columns of Table III (page 1493).—HERBERT S. HARNED.

Frank T. Gucker, Jr., and Charles E. Moser. The Coefficient of Expansibility of Aqueous Solutions of Urea at 27.5° Calculated from the Densities at 25 and 30°.

Page 1558. Column 2. In equation 6 the last term should read:

$$\frac{1}{d_1}\left[\frac{\partial A_2}{\partial T} - 2A_3\alpha_1 + \frac{A_2}{d_1}\left(\frac{\partial A_1}{\partial T}\right)\right]c^3 + \ldots \qquad (6)$$

—FRANK T. GUCKER, JR.

M. S. Kharasch, Cheves Walling and Frank R. Mayo. The Addition of Hydrogen Halides to *cis*- and *trans*-2-Pentene.

Page 1562. In Table II the various temperatures marked 75, 78 and 80 indicate the temperature of an acetone–solid carbon dioxide bath and should be prefixed by a minus sign.—CHEVES WALLING.

Louis F. Fieser and William S. Johnson. Syntheses in the 1,2-Benzanthracene and Chrysene Series.

Page 1652. Column 1, line 5, for "5-Methyl-8-keto-3,4,5,6,7,8-hexahydrophenanthrene (IX)" read "5-Methyl-8-keto-3,4,5,6,7,8-hexahydro-1,2-benzanthracene (IX)."—L. F. FIESER.

Cheves Walling, M. S. Kharasch and F. R. Mayo. The Peroxide Effect in the Addition of Reagents to Unsaturated Compounds. XX. The Addition of Hydrogen Bromide to 2-Butyne and 2-Bromo-2-butene.

Page 1711. In footnote (4) for "see ref. 7" read "see ref. 9."—CHEVES WALLING.

Philip G. Stevens. The Rearrangement of α-Hydroxy Carbonyl Compounds.

Page 1714. Column 1, line 13, for "Fischer's discovery" read "the discovery by Fischer, Taube and Baer." Column 1, footnote (3), for "Fischer, *ibid.*" read "Fischer, Taube and Baer, *ibid.*"—PHILIP G. STEVENS.

James J. Lingane. Thermodynamic Significance of Polarographic Half-Wave Potentials of Simple Metal Ions at the Dropping Mercury Electrode.

Page 2102. "Due to an error in respect to concentration units the calculated average value of k, 0.005 mole fraction per microamp., given in the concluding paragraph is incorrect. The correct average value of k is 5×10^{-6} mole fraction per microamp., or 0.3 millimole per liter of amalgam per microamp. As a consequence the statements in the concluding paragraph are incorrect. The rate of diffusion of the deposited metal atoms in the mercury drops is about equal to that of the reducible metal ions in the solution, and not much slower, as was previously concluded."—JAMES J. LINGANE.

M. L. Wolfrom, D. R. Myers and E. N. Lassettre. The Molecular Size of Starch by the Mercaptalation Method.

Page 2175. Column 2, line 1, in the formula for "%S +" read "%S ×."—M. L. WOLFROM.

James J. Pyle, Leo Brickman and Harold Hibbert. Studies on Lignin and Related Compounds. XLIV. The Ethanolysis of Maple Wood; Separation and Identification of the Water-Soluble Aldehyde Constituents.

Page 2201. In column 1, after the formulas, insert: **"Possible Role of Vanilloyl- and Syringoylacetaldehydes in the Synthesis of Plant Pigments.**—It was shown some years ago by Bülow and Sicherer[9] that benzoylacetaldehyde, in the presence of acids, readily undergoes condensation with a variety of phenols (resorcinol, phloroglucinol, etc.)."

(9) Bülow and Sicherer, *Ber.*, **34**, 3889 (1901).

—HAROLD HIBBERT.

Kinney Hancock and H. L. Lochte. Acidic Constituents of a California Straight-run Gasoline Distillate.

Page 2451. Column 2, first table, first column head should read "*d*-Camphonanic."—H. L. LOCHTE.

Louis F. Fieser. Synthesis of 2-Methyl-3-phytyl-1,4-naphthoquinone.

Page 2560. Column 1. "The last figure of the caption to Fig. 1 should read 3.42 in place of 2.42."—L. F. FIESER.

Daniel B. Clapp. The Reaction of a Thiophene Derivative with Maleic Anhydride.

Page 2735. In line 18, column 2, read "stilbene" for "maleic anhydride."—DANIEL B. CLAPP.

Roger Adams and E. F. Rogers. The Structure of Monocrotaline, the Alkaloid in *Crotalaria Spectabilis* and *Crotalaria Retusa*. I.

Page 2817. To Table II add:

	Alkaloid	Alkanol-amines	Acid
Senecio integerrimus[13]	Integerrimine, $C_{18}H_{25}O_5N$	Retronecine	Integerrinecic acid, $C_{10}H_{16}O_5$
spartioides[13]	Senecionine Seneciphylline Spartioidine, $C_{18}H_{23}O_6N$		
longilobus[13]	Longilobine, $C_{18}H_{23}O_6N$	Retronecine	Longinecic acid, $C_{10}H_{14}O_5$
ridellii	Ridelliine, $C_{18}H_{23}O_6N$		
Erechtites hieracifolia[14]	Hieracifoline, $C_{18}H_{25}O_5N$	Retronecine	Hiercinecic acid $C_{10}H_{16}O_5$

—ROGER ADAMS.

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